

INFANT VACCINE SCHEDULES: MAY VACCINE IMMUNOLOGY SHOW US THE WAY FORWARD?

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Infant vaccine schedules have been derived largely empirically, based on tradition, logistical issues and a very limited number of vaccine studies including protective efficacy as readouts. Consequently, the current heterogeneity of EU vaccine schedules is not based on scientific evidence. Meanwhile, the development of vaccine immunology and the understanding of the progressive immune maturation that takes place in early life has led to a better understanding of what is required for protection, and of the limitations that infant vaccines have to overcome. In addition, the large number of vaccine studies required from the manufacturers of new vaccines have allowed multiple comparisons of the impact of infant vaccine schedule on immune responses. The conclusions from all this has been the demonstration that early priming may generally be achieved with 2 vaccine doses, although a 3rd one may confer benefit against the weaker immunogens, and that a single booster dose after the age of 12 months allows recalling infant-triggered memory cells into sustained antibody responses. Combining early protection with as few vaccine injections / medical visits as possible is therefore now possible using a "2+1" vaccine schedule. Whether science will show us the way forward is thus a matter of choice...

A good test for our society ?

BUILDING UP AN EVIDENCE BASE FOR SUPPORTING HARMONISATION OF IMMUNISATION SCHEDULES IN EUROPE

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Vaccination programmes in European countries have a long and successful history. On the other hand, they are the result of long tradition more than structured evidence-based decision. As a result, immunisation schedules show a wide variation in intervals, number of doses, targeted diseases. European legislation does not support any kind of harmonisation in the field of human vaccination. Conversely, centralised authorization procedures lead to the market vaccine products that granted a unique authorisation at the level of European Medicines Agency but are used in many different ways (in terms of timing and dosing) in each EU country. This could be not a problem *per se*, but it causes several issues when it comes to evaluate effectiveness, safety, impact of vaccination. Not to say that it can lead to confusion among the public and can be used as an argument by anti-vaccine lobbies. Being no legislative support to harmonisation of vaccination programmes, the only way to move forward is to build up a common evidence base for supporting the decision making process in every single EU member state. Decision taken on common basis should automatically lead to a harmonisation process. The European Centre for Disease Prevention and Control is working since its establishment in such direction, trying to stimulate the debate and support any effort at national and Community level.

IMMUNIZATION IN SPECIAL CIRCUMSTANCES: FROM GUIDELINES TO PATIENT CARE, THE INFOVAC EXPERT NETWORK MODEL

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Have you ever wondered whether an unexpected event had been triggered - or not - by an immunization? Have you ever been confronted to patients whose conditions represent a challenge for further immunizations, after an allergic reaction, because of an autoimmune condition or an immunosuppressive regimen? Have you realized, at this time, how the most beautiful official guidelines may not exactly apply to the condition of your patient and felt desperately alone?

If you are confronted to practical immunization issues such as vaccines and allergy, vaccines and immunosuppression, vaccines and autoimmune diseases, vaccines in children with cancer or with neurological disorders, vaccines for children born prematurely or even yet in utero, vaccines for children who had a strong reaction to a previous dose or when you know nothing of their past history... this interactive symposium is for you! Come and test your skills through an anonymous voting system, and learn how to improve clinical vaccinology expertise in your practice, your hospital, your area or your country.

Special warning : you may not leave this symposium without an urgent wish to create an Infovac expert network in your own country ! This is what happened in Switzerland (www.infovac.ch), in France (www.infovac.fr) and in Hungary (www.infovac.hu).

INVASIVE PNEUMOCOCCAL DISEASE IN CHILDREN: A PRIMARY IMMUNODEFICIENCY ?**C. Picard^{1,2}**

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Streptococcus pneumoniae is an encapsulated Gram-positive commensal bacterium which is innocuous in most children. In rare cases, however, this bacterium causes invasive pneumococcal disease (IPD) (meningitis and septicaemia), a life-threatening illness. A number of acquired and inherited host factors have been identified. The best known acquired factors, which also determine susceptibility to recurrent IPD, are coinfection with human immunodeficiency virus and splenectomy. Other acquired factors include certain cancers and traumatic cerebrospinal fluid fistulas. In addition, host genetic factors have long been known to confer predisposition to severe pneumococcal disease, as is attested to by the severity and frequency of such infections in children with sickle-cell disease or certain primary immunodeficiency diseases, which affect one of the steps in the phagocytosis of opsonized circulating pneumococci by splenic macrophages. These primary immunodeficiencies are overrepresented among children with recurrent IPD, and include congenital isolated asplenia, most B-cell deficiencies and more recently described disorders of the Toll-interleukin-1 receptor (TIR)-NF- κ B signaling pathway (IRAK-4, MyD88, IKBA and NEMO deficiencies). However, most cases of IPD are unexplained, as only minority of affected children display any of the known risk factors. We hypothesize that sporadic invasive pneumococcal disease (IPD) may be favored by other undetected, underlying immunodeficiencies, in at least some children. We have undertaken a prospective survey of 125 children with IPD diagnosed in clinical pediatrics departments and by the French Group for Pediatric Infectious Diseases to identify the molecular genetic basis of susceptibility to IPD.

DIAGNOSIS & MANAGEMENT OF INFECTIONS IN CHILDREN WITH IMMUNE DEFICIENCIES

A. Cant

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Chemotherapy, transplantation, primary immune deficiency and HIV compromise different parts of immunity. T lymphocyte deficiency with viral infections, CMV, EBV; protozoa such as *Cryptosporidium* and fungi. B lymphocyte deficiency with bacterial infection, enteroviruses, some protozoa. Phagocyte deficiency with *Staphylococci* and *Pseudomonas*, fungi, particularly *Aspergillus*. Following bone marrow transplantation (BMT), there is a clear sequence of infection risk.

Main sites are respiratory tract, gut, soft tissues and indwelling devices; disseminated infection is a risk. The respiratory tract is vulnerable to *Pneumocystis carinii*, Cytomegalovirus and *Aspergillus*, Influenza A and B, RSV, Parainfluenzae, Adenovirus and Enteroviruses. Pneumonitis and bronchiolitis are common features. Diagnosis is by immunofluorescence, culture and PCR. Anti-virals Foscarnet, Oseltamivir and Cidofovir given early have greatly improved survival. After BMT, infection and inflammation together cause pneumonitis.

Enteroviruses, Adenoviruses, *Cryptosporidium* and *Giardia* are important gut pathogens. *Cryptosporidium* can cause ascending cholangitis and liver disease. Fungal infection is a particular risk in neutropenia on prolonged steroids or Graft versus Host Disease; with persistent fever, skin nodules, chest pain and radiological evidence of infection crossing tissue planes. Cross sectional imaging and biopsy are best diagnostic procedures.

Pre-emptive, early treatment with Amphotericin, Azoles and Caspofungin is needed. CMV, EBV, HHV6 and adenoviral PCR testing allows early pre-emptive antiviral therapy, vital in disseminated disease. EBV B lymphoproliferative disease is treated with anti-B cell monoclonal antibody Rituximab, with a reduction of immunosuppression. Treatments with EBV Cytotoxic T lymphocytes show promise. When treating immunocompromised patients 'think early, look carefully and treat NOW'.

INFECTIONS IN PATIENTS ON THE NEW BIOLOGICAL IMMUNOSUPPRESSIVE AGENTS

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Treatment with biologically derived products ('biologics') - the new class of drugs including monoclonal antibodies, receptor analogues and small molecules binding to or mimicking their molecular targets - has led to remissions and cures of previously untreatable or intractable illnesses. Although generally well tolerated, use of these agents has been associated with increased risk of infection. It is often difficult to differentiate the infectious risk due to the severity of the inflammatory disease, low functional capacity, and co-morbid conditions from the risk associated with immunosuppressive therapy and new 'biologics', often used concomitantly. Nevertheless, serious and sometimes fatal infections due to bacterial, mycobacterial, and invasive fungal, viral, or other opportunistic pathogens have been reported.

In one of the major UK paediatric rheumatology referral centres, 10-15% of ~500 children followed over 10 years had treatment with 'biologics': etanercept (~50), infliximab, adalimumab, anakinra, rituximab, tocilizumab and alemtuzumab (< 10 for each). The main diagnoses were juvenile idiopathic arthritis (JIA) (~400), systemic lupus erythematosus, juvenile dermatomyositis and/or systemic vasculitides (~20 each) and autoinflammatory (periodic fever) syndromes (~10). Serious and life-threatening infections seen were: joint mycobacterium tuberculosis infection (1), recurrent varicella (2), death (2) due to central venous line (CVL)-related bacterial sepsis (alpha-haemolytic streptococcus; staphylococcus epidermidis), and further 2 children died during haematopoietic stem cell transplantation for JIA, from adenovirus reactivation and presumed CVL-related bacterial sepsis (alpha-haemolytic streptococcus).

Physicians treating children with combined immunosuppressive and/or anti-inflammatory treatment and new 'biologics' should be aware of and maintain a high index of suspicion for serious infections.

NEW AND OLD ANTIBIOTICS TO TREAT RESISTANT BACTERIA: LINEZOLID**C. Pulcini***Service d'Infectiologie, CHU de Nice, Hôpital l'Archet 1, Nice Cedex, France*

Linezolid is the first marketed antibiotic of the oxazolidinone class with demonstrated activity against antibiotic-susceptible and antibiotic-resistant aerobic Gram-positive cocci, including methicillin-resistant *Staphylococcus aureus* (MRSA). However, it is mostly used in adults and experience with linezolid in children is limited. Linezolid is available in both intravenous and oral formulations, with near 100% bioavailability of the latter. Linezolid has been approved in many countries for use in the management of community-acquired and nosocomial pneumonia, complicated and uncomplicated skin and soft-tissue infections, and infections caused by MRSA and vancomycin-resistant enterococci, including cases with concurrent bacteremia. Furthermore, studies have demonstrated potential use in febrile cancer patients with neutropenia. Case reports have documented some efficacy in the management of infective endocarditis, tuberculosis, nocardiosis, and in anaerobic infections. In adults, the use of linezolid, particularly when prolonged, may be associated with various clinical and laboratory adverse events, including neuropathy (peripheral or optical), hematological abnormalities (particularly thrombocytopenia or anemia), and hyperlactatemia.

CHILDREN WITH FEVER: CHALLENGES FOR PAEDIATRICIANS AND METHODOLOGISTS**R. Oostenbrink***Outpatient Department General Pediatrics, Erasmus MC - Sophia, Rotterdam, The Netherlands*

Children frequently present with fever at the emergency department. They pose a diagnostic challenge, since fever may be a symptom of either life-threatening diseases like septicemia, meningitis or other serious bacterial infections, but more often it is a symptom of self-limiting viral diseases. To deal with increasing number of patients visiting the emergency department in out-office hours, we need discriminators for absence and presence of serious conditions, to triage patients at presentation.

A recent review on alarming presenting clinical features to identify serious infections in febrile children showed a wide variability in the inclusion criteria of patients and in definition of clinical features, hampering to estimate summary values. Several prediction rules for children with fever have been developed, but validation studies showed limited results hampering their actual implementation in routine practice of emergency medicine. Finally, neither one clinical feature nor a single prediction rule was able to rule out with certainty serious infectious outcomes.

To successfully proceed in diagnostic research of children suspected of serious infections, several issues need to be addressed. What is the most important outcome to focus diagnostic research in children with fever on? How to improve generalisability of research observations to broader settings? Can we decide on acceptable thresholds of risk in febrile children at which clinicians should be expected to take further action? What should be the content of safety-netting to avoid missed diagnoses? In the presentation these questions will be discussed in the perspective of current literature.

DIAGNOSTIC VALUE OF SYMPTOMS AND SIGNS IN ASSESSING THE RISK FOR SERIOUS BACTERIAL INFECTIONS IN CHILDREN WITH FEVER WITHOUT SOURCE

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Background and aims: Differentiating children with minor infections from those who have serious infections is a core function of acute paediatric care, as misdiagnosis is associated with increased morbidity and mortality. Initial assessment of children using symptoms and vital signs may have diagnostic value in ambulatory or primary care settings. We report the findings of 2 research studies of the diagnostic value of symptoms and vital signs in children with acute infections presenting to paediatric settings in England.

Methods:

1) Cross-sectional study of presenting symptoms in 924 children presenting to primary care compared with existing data on symptoms of meningococcal disease in 345 children.

2) Cohort study of 700 children presenting to paediatric assessment unit.

Results: In the primary care study, symptoms of leg pain (LR+ 7.6), cold extremities (LR+ 2.3), photophobia (LR+ 6.5), neck pain/stiffness (LR+ 5.3), confusion (LR+ 24.2), and rash (LR+ 5.5) were all highly specific for meningococcal disease. In the paediatric assessment unit children with serious or intermediate infections (n=313) were significantly more likely than those with minor/no infection (n=387) to have temperature $\geq 39^{\circ}\text{C}$, tachycardia, saturations $\leq 94\%$, or CRT $>2\text{sec}$. One or more of temperature $\geq 39^{\circ}\text{C}$, saturations $\leq 94\%$, tachycardia, and tachypnoea was 80% sensitive and 39% specific for serious or intermediate infection.

Conclusions: Presenting symptoms and vital signs have some diagnostic value in differentiating children with possible serious infection from those with minor infections. Key symptoms and vital signs should be considered as diagnostic "red flags" for clinicians in acute paediatric settings.

INTERPRETATION OF A SINGLE LABORATORY TEST TO DISCRIMINATE BETWEEN VIRAL AND BACTERIAL INFECTIONS IN CHILDREN WITH FEVER OF WITHOUT SOURCE?

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Fever is a common cause of childhood visits to emergency departments and pediatric offices. In the majority of children, the source of a benign infection is diagnosed after a complete history and a careful examination are conducted. In rare instances no primary site of infection is identified despite thorough clinical examination. Although most of these children also have benign and self-limited illness, a few are at risk of developing a severe bacterial infection (SBI) such as bacteremia, meningitis, or pyelonephritis. Because signs and symptoms of SBI are often non-specific, especially in infants, the use of laboratory blood markers of infection is recommended.

There is no ultimate test to discriminate between viral and bacterial infection and often combinations of clinical and laboratory criteria are required. Regardless of which marker is used, the results should modify the *a priori* attitude in the case being managed. Therefore, understanding the kinetics of the marker, its sensitivity and specificity to a specific disease and the prevalence of the disease in the population are of primary importance. The likelihood ratio (LR), which combines the sensitivity and the specificity of a test, is a factor that improves the estimated risk of having a particular disease. The greater the LR is from 1, the more likely the odds of having the disease are increased. If the LR is below 1, the odds are decreased. Examples will be given with two markers, procalcitonin and C-reactive protein, in infants with fever without source.

DEVELOPMENT AND VALIDATION OF CLINICAL PREDICTION RULES IN CHILDREN WITH FEVER WITHOUT SOURCE

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Used alone, no single clinical or biological criterion offers high sensitivity with high specificity for distinguishing between bacterial and viral infections in children with fever without source. Therefore, various teams have proposed combinations of clinical and laboratory criteria; such combinations are called "clinical prediction rules".

The derivation and validation of clinical prediction rules should be performed following the methodological standards proposed by the Evidence Based Medicine Working Group. Classical key issues for predictive tools in the field of "children with fever without source" are: i) the selection of the population to derive the rule; ii) the definition of the outcome, i.e. bacterial infection; (iii) the independence between the predicted variable (the outcome) and the predictors used; (iv) the reproducibility of the clinical predictive variables; (v) mathematical techniques used to derive the rule; (vi) the validation of the rule across various epidemiological contexts (e.g.: age subgroups within the pediatric group, causative bacteria which depends notably on vaccination coverage).

The (elusive?) search for a highly specific and 100% sensitive rule is the main unresolved key issue. What is a clinically acceptable lack of sensitivity given the potential consequences of a diagnosis delay for a child with a severe bacterial infection? Comparison with the performance of routine care can offer a first answer to this question. However, clinicians and methodologists should keep in mind that no rule will be able to detect a bacterial suprainfection that has not already start during a viral infection.

THE IMPACT OF INFLUENZA IN CHILDREN IN THE H1N1 PANDEMICS OF 1918 AND 2009/10**J. Oxford***Virology, St. Bart's and the Royal London Hospital, London, UK*

Our entire world is in the grip of a Darwinian virus, Swine influenza A (H1N1), as it exerts its dominance as the most super-fit virus, pushing aside epidemic influenza and possibly even other respiratory viruses. The distant relative 1918 influenza A (H1N1) is the 'Mother Of All Influenza Viruses' and caused untold devastation in 1918 around the world. Too little emphasised was its attack rate in children. I will refer to this knowledge gap in more detail because the mortality in the under fives in 1918 reached an astonishing 10 per 1000 in that age group, equalling the very well known figure in 25-30 year olds. As in the current pandemic, the incidence rate in five year olds in 1918 was actually the highest in the community, reaching 380 per 1000 in this age. This warning from a resurgent pathogen is timely. Children have been at

the epicentre of this current influenza pandemic wave: they are simultaneously at the core of our families and a target for viruses and bacteria. This is the heart of our symposium. Meningitis C and influenza can interact synergistically in the child and this latter microbe must also be viewed with deep focus, worry and action. But TBE is resurgent as well, spreading beyond its textbook confines of Eastern Europe and Russia. Our warming earth will undoubtedly surprise us nastily in the coming years for alongside TBE we are experiencing the mosquito borne African Chikungunya whilst our domestic herds have the Bluetongue virus for the first time. Darwin would be simultaneously delighted and shocked to view the speed of microbial evolution happening in months rather than over the millennia in humans. But our own lesson must surely be never to give up and never to lower our guard against influenza in particular which will surely search out and slip into unprotected gaps in our young population as the virus did in 1918, 2009 and, likely to repeat the tactic in the oncoming winters of 2010 and 2011 as it mutates to become even fitter.

THE DEVELOPMENT OF VERO CELL DERIVED PANDEMIC- AND SEASONAL INFLUENZA VACCINES

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The Vero cell line is the most widely accepted continuous cell line by regulatory authorities and has been used since decades for the production of, e.g. polio-, rabies- and rotavirus vaccines. Here we report on the clinical characterization of Vero cell derived inactivated pandemic- and seasonal influenza vaccines.

A whole virus H5N1 vaccine based on (Vietnam/1203/2004/H5N1, clade 1) was demonstrated to be safe and had an excellent tolerability profile. A dose of 7.5 µg of a non-adjuvanted vaccine formulation was highly immunogenic and induced antibodies neutralizing homologous strains as well as viruses from other H5N1 clades. A booster dose of a heterologous (clade 2) H5N1 vaccine 12-17 months later resulted in enhanced antibody responses against both the original (clade 1) and the booster (clade 2) strain, indicative of cross-protective memory.

A vaccine against the current pandemic H1N1 strain is being studied in adults and children. In adults, two doses of 7.5µg antigen induced seroprotective HA antibody titers in 89% - 91% of subjects. An ongoing pediatric study demonstrated that after the second dose 100% seroprotection (HI assay) was attained in the 3-8 and 9-17 year old cohorts.

Vero cell derived trivalent seasonal influenza vaccines (split virion), using wildtype virus seed stocks were developed and extensively tested in human studies. Their immunogenicity met all licensure criteria, clinical efficacy was demonstrated and safety profile was comparable to egg derived vaccines¹⁾.

These data indicate that flexible and versatile Vero cell platform can successfully be in the production of pandemic and seasonal influenza vaccines.

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TICK-BORNE ENCEPHALITIS - DISEASE AND VACCINATION IN CHILDHOOD

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Tick-borne encephalitis (TBE) is a preventable disease, which has rapidly become a growing public health problem in Europe and other parts of the world. Until recently TBE was believed to be a rather limited problem in a few well-defined endemic areas; however, this notion has now been revised. In addition, the increasing mobility of people exacerbates the risk of infection. In Europe TBE is considered as the most prevalent tick-transmitted disease after Lyme disease.

TBE is inflammatory disease involving the central nervous system (meningitis, encephalitis, meningoencephalitis) which is caused by TBE virus, belonging to flaviviruses. TBE is spread via the bite of an infected ticks, found in woodland habitats. It can also be transmitted via unpasturised milk from infected goats or cows. Ticks bite humans when they walk through undergrowth or grasses where contact is made. Peak biting times are during the warmer months of August, or following a warm humid summer in September and October. After an incubation period of 2-28 days, symptoms begin with a fever and can progress at varying degrees.

The severity of the disease as well as the long-term sequelae are still not very much known in public. The symptoms of those affected can lead to meningitis, encephalitis or radiculomyelitis which may result in death or long-term neurological sequelae including permanent paralysis in 35-58% of all patients. Also children can be affected in a severe way. The encephalitic cases present with signs of involvement of the brain as ataxia, cognitive dysfunctions, dysphasia, altered consciousness, confusion, irritability, tremor and more rarely seizures and cranial nerve paralysis.

These data demonstrate that the course of TBE in children and adolescents can be associated with an unfavorable outcome and permanent neurological damage.

Due to the risk of a severe course of the disease and no causal treatment availability, immunization against TBE is recommended for infants and children living in or travelling to highly endemic areas. TBE vaccination has been shown to be highly immunogenic in clinical studies and effective in the field.

RECENT STUDIES ON ALTERNATIVE SCHEDULES FOR MENC-CONJUGATE VACCINES**R. Borrow***Vaccine Evaluation Unit, Manchester Royal Infirmary, Manchester, UK*

In 1999, the UK introduced the meningococcal serogroup C conjugate (MCC) vaccine into the childhood immunisation schedule together with a catch-up to 18 years of age. In September 2006, a booster dose of (MCC) and *Haemophilus influenzae* type b (Hib) conjugate vaccine was introduced in the second year of life in England and Wales in the form of a combined vaccine, Menitorix. No data were available on whether Menitorix could be given concomitantly with MMR and Prevenar (PCV7) or on antibody persistence following the booster. In this study children either received Menitorix at 12 to 14 months of age followed by Prevenar and MMR one month later or all three vaccines at the same visit. Antibody persistence to MCC and Hib was followed at 1, 2, 12 and 24 months post-booster. No adverse consequences for either immunogenicity or reactogenicity when Menitorix was administered either separately or together with Prevenar and MMR. For MCC, depending on primary MCC vaccine used 95 to 100% of children were protected 1 month following the Menitorix booster with the greatest magnitude of response seen for those primed with NeisVac-C (MCC-TT). MCC antibody persistence following the booster dose showed the same kinetics as following the primary MCC series. For MCC, 2 years post-booster 27% to 46%, depending on primary MCC, of children remained protected. Studies are now underway examining the possibility of a single primary dose of MCC at 3 months of age with a booster in the second year of life. Meningococcal serogroup C disease is still declining in the UK with only 10 cases confirmed for 2009.

INTRODUCTION: VACCINES IMPROVE WELLBEING OF CHILDREN, THEIR FAMILIES AND SOCIETY

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Vaccines are a deliberate attempt to protect humans against disease and among the most important public health measures of the twentieth century, effectively reducing or eliminating over 26 vaccine-preventable diseases (VPDs). In addition to the significant reduction in mortality rates, dramatic declines in morbidity have been observed following widespread vaccination implementation.^{1,2}

Through vaccination, endemic transmission of polio, measles and rubella viruses has been virtually eliminated in numerous areas of the world and smallpox has been eradicated globally.² However, several VPDs still represent a substantial public health burden. Indeed, VPDs, besides causing mortality and morbidity, are a substantial societal and economic burden which might be prevented by successful immunisation programmes.

In addition to increased efficacy, modern vaccines display an unprecedented good tolerability. Adverse effects of the successful smallpox vaccine included encephalomyelitis at a frequency of 3/10,000 with lasting brain damage, which would make this vaccine unacceptable today. Pertussis vaccine was used widely in most developed countries only after introduction of the acellular vaccine with minimal adverse events. Presently used vaccines show mild local and systemic effects in a small percentage of cases and, with the introduction of the injectable poliomyelitis vaccine, lasting damage following vaccination is almost excluded. Severe anaphylaxis at a frequency of < 1 per 800,000 remains the only life-threatening risk.

This improved risk-benefit ratio has led to an altered view of vaccines. Current opinion regarding the importance of vaccination is widening from immunity against life-threatening diseases to include improvement of clinical outcomes associated with VPDs. Thus, frequent, but not necessarily mortal, diseases have become a target for prevention by vaccination. Examples are gastroenteritis due to rotavirus, the single most common cause of severe, dehydrating diarrhoea in infants and children, and otitis media due to bacterial pathogens such as pneumococci and non-typeable *Haemophilus influenzae*, one of the most common childhood illnesses for which medical advice is sought.^{3,4} Successful vaccination programmes could significantly reduce the burden of these diseases on the community. Other childhood illnesses for which a vaccine might be an important improvement are streptococcal tonsillitis, RSV bronchiolitis, parainfluenzal croup, urinary tract infection due to *Escherichia coli*, and noroviral diarrhoea. Continued efforts to raise disease awareness, emphasising the potential of vaccines in all age groups, is a major step in the progress of public health.

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PREVENTION OF ACUTE OTITIS MEDIA - THE PUBLIC HEALTH PERSPECTIVE

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Acute otitis media (AOM) is a substantial public health burden, being one of the most commonly occurring childhood infections. *Streptococcus pneumoniae* and non-typeable *Haemophilus influenzae* are the pathogens responsible for approximately 80% of cases.¹ By 1 year of age 60-70 % of children will have been diagnosed with at least one episode of AOM, and in approximately one in five children AOM will be recurrent. AOM has a considerable negative impact on the child's quality of life, and is the most common cause for antibiotic prescriptions, thereby contributing to increasing antibiotic resistance.²

Today a number of controversies and issues surround AOM clinical management. These range from over-diagnosis and the impact of various preventive strategies to whether the benefit of immediate antimicrobial treatment outweighs the risk of adverse events and increased antimicrobial pressure. Prevention of AOM through vaccination would circumvent many current issues. Its public health impact results from prevention of morbidity which indirectly reduces antimicrobial pressure and resistance as well as health care and societal costs.

This presentation will discuss current AOM controversies and issues, and outline management and prevention strategies in relation to current consensus recommendations.

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ROTAVIRUS GASTROENTERITIS: BURDEN ON CHILDREN AND SOCIETY

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Globally, diarrhoea is the second most common cause of death in children under 5 years old, resulting in more deaths than AIDS, measles and malaria combined.¹ Rotavirus (RV) is the main cause of severe acute dehydrating diarrhoea (RV gastroenteritis or RVGE) in infants and children in developed and developing countries and is a major worldwide public health care concern.^{2,3} Annually, RVGE has a high mortality with approximately 600,000 deaths worldwide among children of < 5 years⁴; the majority (>85%) of which occur in Africa and Asia.²

In addition, in worldwide surveillance studies (2001 and 2008) RVGE accounted for 40% of all hospitalisations due to diarrhoea among < 5 year-olds.² RV is also the leading cause of paediatric nosocomial diarrhoea.⁵

Recent hospital-based surveillance shows RVGE to place high demands on European health care systems, accounting for 56% of hospitalisations and 33% of ER visits due to community-acquired acute GE (AGE) in children < 5 years.⁶ In addition to requiring hospital care, European children with RVGE are also likely to be treated in primary care settings and it has been shown that about 30% of cases of AGE seen by primary care physicians are rotavirus-positive.⁶ Also primary care-based surveillance has shown that 69.1% of PCR+ RVGE occurred in children < 2 years, 30.1% in those aged < 1 year and 6.9% in infants < 6 months old, which supports the need for early protection.⁷

In Europe, prevalent types (G1–G4 and G9) are responsible for >90% of RVGE cases,⁸ although emerging types such as G8 and G12 are becoming more common.⁹ Both currently licensed rotavirus vaccines have been shown to be highly efficacious against severe RVGE during the first 2-3 years of life.

Although product licences have been granted by the EM(E)A, their inclusion in national immunisation schedules are the responsibility of the health ministries in each country. Unfortunately, in Europe by 2009, few countries had recommended universal rotavirus vaccination and funded the vaccination costs, even if experiences of co-payment and implementation at private market level reached unexpectedly high coverage.

The 2009 recommendation by the WHO's Strategic Advisory Group of Experts (SAGE), the guidelines from ESPID/ESPGHAN, and a longer-term knowledge about the effectiveness, efficacy and safety profiles of the two oral rotavirus vaccines provide strong support to encourage European countries to introduce rotavirus vaccination.

RVGE is a significant global health care and economic burden and intervention is greatly sought.¹⁰ Integration of routine vaccination into national immunisation programmes will have impact on public health⁵ in Europe in terms of reducing disease burden and providing broad protection (as demonstrated in integrated analysis with the human rotavirus vaccine)¹¹ against prevalent strains/types.

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ROTAVIRUS GASTROENTERITIS: THE IMPACT AND BENEFITS OF VACCINATION

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Rotavirus infection is the leading cause of severe acute gastroenteritis among young children worldwide. Virtually all children will have been infected by the age of 5 years and an estimated 600,000 rotavirus-related deaths occur each year, with >85% of these deaths occurring in low-income countries of Africa and Asia.^{1,2}

To reduce the burden of rotavirus disease, safe and effective vaccines were developed and licensed for use in infants. *Rotarix*[™] is an oral G1P[8], live-attenuated human rotavirus vaccine. *Rotarix*[™] is approved in >100 countries based on supportive data from clinical trials and has been incorporated into national vaccination programmes across the world.^{3,4}

The vaccine has demonstrated an acceptable safety profile, with no increased risk of intussusception and is generally well tolerated. It has provided in Latin American and European trials, respectively, 85-96% efficacy against severe rotavirus gastroenteritis (RVGE), 85-100% reductions in hospitalisations associated with RVGE and 42-75% reduction in hospitalisations of all-cause gastroenteritis.⁵⁻⁷ Furthermore, in a trial done in Malawi and South Africa, where the diversity of rotavirus strains is substantial, *Rotarix*[™] reduced significantly the incidence of severe RVGE among African infants during the first year of life.⁸ Of paramount importance were the recent findings from a study in Mexico, showing that after the implementation of *Rotarix*[™] an encouraging reduction in the number of diarrhoea-related deaths was demonstrated.⁹

The *Rotarix*[™] two-dose schedule offers early protection regardless of circulating RV strains and can be completed as early as 10 weeks of age. Although RVGE causes relatively few deaths in Europe compared with developing countries, prevention through vaccination could offer great public health, economic and societal benefits.

Rotarix is a trademark of the GlaxoSmithKline group of companies.

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ROLE OF SYNFLORIX™ IN PNEUMOCOCCAL DISEASE WORLDWIDE

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Pneumococcal disease is still a leading cause of mortality and morbidity worldwide, with a broad spectrum of invasive and non-invasive diseases caused by *Streptococcus pneumoniae*.

Synflorix™ is a new generation of pneumococcal conjugate vaccine that includes 10 globally circulating *S. pneumoniae* serotypes, of which eight are linked to a novel carrier, protein D, derived from *H. influenzae*.¹ Since December 2008 *Synflorix*™ has been licensed in over 50 countries globally for active immunisation against invasive pneumococcal disease (IPD) and acute otitis media caused by the vaccine serotypes.²

The need for vaccines with broader coverage than that offered by PCV-7 has been further emphasised in recent years (and since the introduction of PCV-7) as data show that the bacteriology of IPD has altered.³ Indeed, the prevalence of PCV-7 vaccine-contained types has decreased whilst non-vaccine-contained types have increased.³ New vaccines also need to show improved impact on non-invasive diseases.

Clinical data show *Synflorix*™ elicits an immune response against all vaccine-contained serotypes in a range of ethnic populations and suggests an immune cross-reactivity against some non-vaccine contained serotypes. Furthermore, *Synflorix*™ has a comparable safety and tolerability profile to PCV-7.² *Synflorix*™ can also be administered in a variety of vaccination schedules based on official recommendations and can be given concomitantly with other paediatric vaccines.¹ A previous 11-valent formulation, also composed of protein D conjugated polysaccharides, has been shown to prevent acute otitis media, including that caused by non-typeable *H. influenzae*.² Preliminary data suggest *Synflorix*™ reduces pneumococcal nasopharyngeal carriage.⁴

The unique design of *Synflorix*™ is of utmost relevance considering the current epidemiology of IPD and bacterial respiratory diseases such as otitis media. *Synflorix*™ offers a substantial opportunity to prevent morbidity and mortality due to IPD and otitis media.

Synflorix is a trademark of the GlaxoSmithKline group of companies.

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PERTUSSIS: PROTECTING THE UNPROTECTED

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Pertussis (whooping cough), a vaccine-preventable disease, continues to be a public health concern even in countries with high vaccination coverage. Pertussis is highly contagious in its early catarrhal stage with most clinically recognisable cases occurring in children aged less than 5 years and 90% of all hospitalisations reported in infants aged less than 1 year.^{1,2} However, the real burden of pertussis may not be accurately reflected by epidemiological surveillance due to lack of disease awareness, unrecognised cases in adolescents and adults with mild symptoms who were previously vaccinated, and under-diagnosis due to limited laboratory access or inappropriate diagnostic methods.^{3,4}

Immunity following pertussis vaccination is estimated to wane after 4-12 years.⁵ Indeed, an increasing incidence of pertussis has been observed in schoolchildren previously vaccinated and in adolescents and adults in many European countries, as well as Australia, Canada, Japan and the United States.¹ Pertussis constitutes an important respiratory disease burden in adolescents and adults who also can infect and cause severe disease in young infants, especially in unprotected newborns too young to be vaccinated.⁴ Infants with pertussis typically develop complications, which may lead to hospitalisation and death, but fatal cases and severe complications are rarely observed in adults.^{6,7}

National recommendations vary considerably across the globe. Many countries include a childhood booster dose in their national immunisation schedules and some include adolescent and adult booster doses.^{1,8,9}

Different strategies exist to improve protection against pertussis across all age groups, including those aiming to protect the most vulnerable, e.g. by immunising households of newborns and young infants, and of health-care workers. Recently, it has been recommended in Europe to include a pertussis booster vaccination at adolescence, a strategy that has been shown likely to be cost-effective in modelling studies.^{10,11} A worldwide adolescent and adult booster strategy should be considered to improve immunisation coverage significantly beyond childhood and reduce circulation of infection in the community.

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EXPERIENCE OF VACCINATION AGAINST CERVICAL CANCER: FROM CLINICAL TRIAL DATA TO IMPLEMENTATION

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Cervical cancer is the second most common cancer in women globally and represents a major disease burden. Approximately 500,000 invasive cervical cancer (ICC) cases are diagnosed annually, resulting in over 270,000 deaths.¹

Human papillomavirus (HPV) infection is the necessary cause of cervical cancer. The predominant HPV types observed in ICC are types 16 and 18, which together account for over 70% of ICC cases,² while types 16, 18, 31, 33 and 45 account for 82%.³ Sexually active women are at risk of HPV infection regardless of age, stressing the need for vaccines that provide long-term protection against the most prevalent HPV types found in ICC.⁴ As vaccination is often recommended during early adolescence as well as young adulthood, paediatricians, along with gynaecologists and general practitioners, play an essential role in increasing awareness of the cause of cervical cancer as well as vaccine administration.

In clinical trials, *Cervarix*[®] has been shown to induce high and sustained antibody levels against HPV-16 and HPV-18 which are maintained over the long-term, and efficacy against HPV infection and cervical cancer development remain high.⁵ *Cervarix*[®] can also be co-administered with other paediatric/adolescent vaccines including DTPa-IPV and combined hepatitis A/B.^{6,7}

In the real-world setting, over 10 million doses of *Cervarix*[®] have been distributed, and surveillance data support the safety profile observed in clinical trials.^{7,8} Moreover, following the widespread use of *Cervarix*[®] many valuable lessons regarding implementation and uptake have been learned. The greatest reduction in the burden of cervical cancer may be achieved if vaccination coverage is high and vaccination targets not only young girls but also adolescents and young adult women. Furthermore, in order to achieve high vaccination coverage it is pivotal to develop effective communication to improve patient awareness.⁹

Cervical cancer vaccination offers a substantial opportunity to reduce the burden of cervical cancer and prevent avoidable suffering and death. Health care authorities should consider refining their vaccination strategies to optimise impact.¹⁰

Cervarix (Human Papillomavirus vaccine [Types 16, 18]) is a registered trademark of the GlaxoSmithKline group of companies. Cervarix is approved in the EU for women aged 10-25 years.

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MONOVALENT TO QUADRIVALENT VACCINES: BROADENING PROTECTION AGAINST MENINGOCOCCAL DISEASE

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In many countries, large catch-up campaigns using meningococcal serogroup C conjugate (MenC) vaccines have led to a dramatic decrease in serogroup C disease. It is also believed that a herd immunity effect has contributed to the effectiveness of these vaccines. However, while vaccine effectiveness is high, waning of the protective titer in the youngest population has been of concern. Alternative vaccination schedules and vaccination strategies that offer sustained protection have been considered, eg, a booster dose in adolescents (recently recommended in Austria, Canada, and Switzerland). The rationale for this booster is to ensure that adolescents are adequately protected as they enter a period of increased risk, primarily due to changing behaviors and increased exposure to risk factors, such as close-quarters living, and secondly, to maintain the potential herd effect, by reducing carriage.

Meningococcal ACWY (MenACWY) conjugate vaccines have been developed that offer the possibility of broadening protection. An investigational MenACWY vaccine with CRM₁₉₇ carrier protein (MenACWY-CRM) has been shown to be highly immunogenic in adolescents and adults. In short-term immunogenicity and safety head-to-head trials, more individuals achieved a protective immune response with MenACWY-CRM than licensed comparators, such as MenACWY-D and polysaccharide vaccines. Although these MenACWY vaccines contribute to protection against four of the five disease-causing serogroups, development of a serogroup B vaccine using the same technology has not been possible. An investigational recombinant serogroup B vaccine, containing multiple antigens, is now in Phase III development following reverse vaccinology findings. Results from clinical studies have demonstrated that the vaccine is immunogenic with acceptable tolerability in infants and adults.

MEET THE EXPERTS *HELICOBACTER PYLORI* INFECTION WHICH CHILDREN SHOULD BE TREATED?

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Who should be treated?

- In the presence of *H. pylori*-positive peptic ulcer disease, eradication of the organism is recommended.
- When *H. pylori* infection is detected by histopathology in the absence of peptic ulcer disease, *H. pylori* treatment can be considered.
- A 'test and treat' strategy is not recommended in children.
- In children who are infected with *H. pylori* and who have a first degree relative with gastric cancer, treatment (eradication therapy) can be offered.

What are the appropriate eradication strategies?

- Surveillance of antibiotic resistance rates of *H. pylori* strains in children and adolescents is recommended in the different countries and geographic areas.
- Antibiotic resistance to clarithromycin (CLA) is highly predictive of treatment failure when CLA is part of triple therapy.
- First line eradication regimen are
 - o PPI + Amoxicillin + Imidazole* (*Imidazole = Metronidazole or Tinidazole)or
 - o PPI + Amoxicillin + Clarithromycin or
 - o Bismuth salts + Amoxicillin + Imidazole* or
 - o Sequential Therapy.
- A reliable non-invasive test (¹³C-UBT) for eradication is recommended at least 4-8 weeks following completion of therapy.
- If the treatment has failed there are 3 options recommended
 - o FISH on previous paraffin embedded biopsies if Clarithromycin susceptibility testing has not been performed before to guide therapy,
 - o EGD, culture and susceptibility testing including alternate antibiotics if not performed before to guide therapy,
 - o Modify therapy by adding an antibiotic, using different antibiotics, bismuth and/or increasing dose and/or duration of therapy

VISCERAL LEISHMANIASIS AMONG PEDIATRIC POPULATIONS

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Visceral leishmaniasis (VL), a vector-borne disease caused by obligate intra-cellular protozoa of the genus *Leishmania*, manifests as the most severe and potentially fatal form of leishmaniasis among children. The prevalence rate of VL remains markedly elevated in areas of the Mediterranean Basin where animal reservoirs, particularly canines, are present. In such areas VL is mainly attributed to infection by *L. infantum*, transmitted by phlebotomine sandflies, and is observed to have the highest incidence rate among children aged 1 to 4 years. The disease usually presents with intermittent fever, weight loss, hepatosplenomegaly, pancytopenia, and hypergammaglobulinemia among children. Definite diagnosis among this population group relies on the determination of *Leishmania* presence in tissue specimens or cultures. Direct determination of parasitic infection may be demonstrated from peripheral blood, bone marrow, or splenic aspirates. Serological assays (including enzyme-linked immunosorbent assay and indirect immunofluorescence), as well as PCR, have also been shown to be sensitive for the diagnosis of VL among children.

To date, standard anti-leishmanial treatment of VL among children in the Mediterranean Basin has included the administration of pentavalent antimonial compounds (meglumine antimonite and sodium stibogluconate) at doses of 20mg/kg daily for 30 days. Initial response rates are observed to exceed 90-95%, as most children become afebrile within the first week of treatment and relapse rates are low. However, disadvantages of such management for VL include lengthy hospitalization stay, the need for intra-muscular administration, and transient, albeit non-negligible, side-effects. During the past decade, lipid formulations of amphotericin B (liposomal amphotericin B), at doses of 2mg/kg on an alternate-day regimen for a total of 10 days, has been shown to be highly effective for the treatment of VL, with low levels of toxicity.

In a retrospective cohort study conducted at the Second Pediatrics Department of Pediatrics, "P. & A. Kyriakou" Children's Hospital, University of Athens School of Medicine, Greece between 1/1/2002-1/1/2010, the effectiveness of liposomal amphotericin B among pediatric patients with leishmaniasis was evaluated. During the study period 22 patients (age range 16 months-13 years) with leishmaniasis were admitted to the hospital. All patients presented with fever and splenomegaly, and two thirds of patients presented with hepatomegaly. Additional presenting symptoms included pallor (20.8%), anorexia (20.8%), cough and/or rhinitis (16.7%), vomiting (16.7%), skin rash (12.5%), diarrhea (4.3%), and abdominal pain (4.2%), while half of the patients did not present with any symptoms other than fever. The laboratory assessment of patients indicated that 87.5% had anemia (Hb < 9.0 mg/dl) and/or thrombopenia (PLT < 150000/ μ L), and half of the patients had WBC counts < 4000/mL. In addition, all patients presented with elevated CRP levels (CRP > 10 mg/L) and 62.5% with elevated SGOT (SGOT > 55 U/L) and/or SGPT (SGPT > 45 U/L) levels, respectively.

All patients initially received liposomal amphotericin B at 10 mg/Kg/day for two days. One child was admitted to the ICU and received an additional 5 mg/Kg/day for an additional 2 days. In addition, due to the manifestation of acute kidney failure on the second hospitalization day, one patient continued to receive liposomal amphotericin B at the dosage of 3 mg/Kg/day during the 5th, 6th, and 7th days of hospitalization.

Of the initial study population, 2 (9.1%) patients presented with disease remission. One infant aged 18 months presented with leishmaniasis relapse 3 months later and received 10mg/Kg/day for 2 days. The second infant aged 17 months initially presented with visceral leishmaniasis and who received 10mg/Kg/day liposomal amphotericin B for 2 days also received an additional dose (10mg/Kg/day) on the 5th hospitalization day due to the persistence of clinical symptoms. The patient presented with the first remission at 19 months age and received (10mg/Kg/day liposomal amphotericin B for 2 days). A second remission of the disease occurred at 2 years of age which was treated with a total dose of 30mg/Kg/day over the course of a 10 day period. To date, both aforementioned patients (current ages 5 years and 4.5 years, respectively) have not presented with leishmaniasis relapse.

Our findings indicate that the management of leishmaniasis among pediatric populations with liposomal amphotericin B at 10 mg/Kg/day for two days may allow for both the effective treatment and shorter hospitalization stay of pediatric patients.

TREATMENT OF VISCERAL LEISHMANIASIS IN CHILDREN: GETTING IN RIGHT?D.A. Kafetzis¹, H. Haas²

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Visceral leishmaniasis (VL) is a severe disease associated with infection of the reticuloendothelial system by *Leishmania* species. The infection is acquired through sandfly bites. Recent large scale epidemics of VL in east Africa and India and the emergence of a HIV epidemic make VL a priority for the World Health Organization. Children are at greater risk than adults in endemic areas. Children usually present with intermittent fever, paleness, anorexia, weight loss, and abdominal distension. Splenomegaly, hepatomegaly, lymph node enlargement, thrombocytopaenia, anaemia, leukopaenia and hypergammaglobulinemia are the most common findings in paediatric leishmaniasis. The diagnosis is based on the demonstration of the infecting parasite in various tissues. Molecular methods should be accurate non-invasive tools. For many years the mainstay for treatment of infected children was pentavalent antimony: meglumine antimoniate or sodium stibogluconate. However, these drugs are poorly tolerated and resistance similar to that observed in the treatment of Indian visceral *Leishmania donovani* leishmaniasis has been reported. Currently liposomal amphotericin B is being used instead of antimony. Lipid formulations of amphotericin B were assessed as short duration treatment and were proved to be effective. The optimal duration of treatment remains to be determined. However, their cost precludes their wide use in developing countries. Miltefosine has been demonstrated as the first effective and safe oral treatment of visceral leishmaniasis in India, but has not been evaluated for the Mediterranean disease. Use of combination antileishmanial drug regimens should be promoted to prevent the development of resistance to existing drugs.

PROTEIN-POLYSACCHARIDE CONJUGATE VACCINE FAILURE

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The introduction of protein-polysaccharide conjugate vaccines to protect young children against invasive disease caused by *Haemophilus influenzae* type b (Hib), serogroup C *Neisseria meningitidis*, and *Streptococcus pneumoniae* has led to substantial improvements in child morbidity and mortality for those countries where the vaccines have been introduced. In addition to the direct protection for the individual afforded by these vaccines, population exposure to these colonising organisms has been substantially reduced leading to herd immunity. Vaccine failure is defined as invasive disease in an immunised individual and is a rare event in immunised populations. Vaccine failure could result directly from: storage problems with the vaccine affecting the integrity of the conjugate; incorrect administration, interaction with coadministered vaccines; or inadequate (genetically determined) host responses. Other factors which may affect the strength of the vaccine response include the type of conjugate (e.g. different carrier proteins) and the age of the individual, as immunity wanes rapidly in early childhood. Another component of vaccine failure may be the loss of natural boosting of immunity through reduced colonisation.

Booster doses of conjugates can provide protection for those who made poor initial responses and to maintain protection amongst those whose immunity has waned. Schedules for boosting should therefore be designed to protect through the period of greatest disease risk. Maintaining protection against vaccine-preventable invasive bacterial disease to avoid vaccine failure will be a challenge for child health programmes in the decades to come.

SINGLE NUCLEOTIDE POLYMORPHISMS IN *MAL/TIRAP* AND *INTERLEUKIN-10* GENES ARE ASSOCIATED WITH INVASIVE *HAEMOPHILUS INFLUENZAE B* (HIB) INFECTION IN IMMUNISED CHILDREN

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Background & aims: The development of invasive *Haemophilus influenzae* serotype b (Hib) disease after prior immunisation (i.e. Hib vaccine failure) is extremely rare, suggesting that such children may have an underlying genetic susceptibility in their immune response. This study aimed to investigate single nucleotide polymorphisms (SNPs) known to affect function in biologically plausible genes in relation to the risk of invasive Hib disease and its clinical manifestations.

Methods: Families of UK children with Hib vaccine failure diagnosed between 1992-2005 were identified through national surveillance. Wellcome Trust Case Control Consortium (WTCCC) datasets were used as controls. Nineteen functional SNPs in fourteen immune response genes were investigated.

Results: Of 323 families approached, 260 (80.5%) returned a completed questionnaire. The final cohort for this study comprised 172 children who provided a sample and whose parents self-reported as ethnically Caucasian. The recessive homozygous genotype for a SNP in the *TIRAP* (also known as *MAL*) gene (rs1893352), that is in strong linkage disequilibrium ($r^2=0.93$) with the known functional Ser180Leu polymorphism in Caucasians, was strongly associated with non-meningitis cases of Hib vaccine failure (OR=5.6; 95% CI=2.7-11.5; $P=1.2 \times 10^{-7}$). In addition, the recessive homozygous genotype for another SNP (rs1554286), in strong linkage disequilibrium with both the C-819T ($r^2=0.87$) and C-592A ($r^2=0.75$) promoter polymorphisms in the *interleukin-10* (*IL10*) gene, was associated with epiglottitis only (OR=5.8; 95% CI=2.4-14.2; $P=1.1 \times 10^{-5}$).

Conclusions: Our findings strongly suggest that the development of invasive Hib disease after prior immunisation is in part genetically determined and may direct the immune response to specific clinical manifestations.

RHINOSCLEROMA: A FRENCH NATIONAL RETROSPECTIVE STUDY OF EPIDEMIOLOGICAL AND CLINICAL FEATURES

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Background: Rhinoscleroma (RS) is a rare chronic granulomatous disease of the upper respiratory tract, associated with infection with *Klebsiella rhinoscleromatis*. It is more frequent in certain geographic regions than in others, but other risk factors and the pathogenesis of RS remain unclear.

Methods: We sent a standardized questionnaire to all pathologists and ENT specialists in French University Hospitals, asking whether they had seen patients with RS in the last 16 years (1990-2005). We then retrospectively reviewed the files of all patients identified.

Results: We collected 11 cases of RS with a median age at diagnosis of 35.7 years (range: 5-72). The three patients with a familial history presented early-onset forms of RS. Two unrelated consanguineous families were identified, one of which included two affected siblings. Biopsies had been performed for all patients, and showed granulomas containing Mikulicz's cells. Cultures of biopsy tissue were positive for *K. rhinoscleromatis* in five of the 11 cases. Prolonged antibiotic treatment was administered in all cases, based on ciprofloxacin (7/11), third-generation cephalosporins (2/11), tetracycline (2/11) and clofazimine (2/11). Eight of the eleven patients remained relapse-free during extended periods of follow-up (1.3 to 12 years).

Conclusion: The occurrence of early-onset RS in multiplex and/or consanguineous families suggests that genetic control of the host response to *K. rhinoscleromatis* may be involved in the pathogenesis of RS in endemic areas.

RECOGNITION OF NUCLEIC ACIDS FROM STREPTOCOCCI BY MACROPHAGES REQUIRES LYSOSOMAL MATURATION AND NITRIC OXIDE

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Background and aims: The initiation of an inflammatory response program in tissue macrophages upon contact with invading bacteria is critical for the successful and timely resolution of infection. However, the molecular events underlying the recognition of bacterial particles by macrophages are incompletely resolved. Here, we introduce the essential role of two novel interdigitating signaling loops in transcriptional activation of cytokine genes (e.g. TNF) by streptococci.

Methods: Primary macrophages from mice with targeted genetic modifications and cell lines derived from these mice were stimulated with group B streptococci (GBS) and analyzed by confocal microscopy, quantitative PCR, ELISA and reporter assays.

Results: Lysosomal acidification, modification of endosomal RNA from GBS, and the formation of TNF were substantially reduced in macrophages from iNOS-, and therefore nitric oxide (NO)-deficient macrophages. Moreover, exogenous NO-donors recovered macrophage activation. Furthermore, the NO-dependent lysosomal maturation was linked to translocation of RNA from GBS to the macrophage cytosol. Cytosolic ssRNA from GBS essentially mediated the cytokine response, since RNaseA treatment of GBS and genetic deletion of the cytosolic receptor component IPS-1 reduced the cytokine response. Furthermore, transfection of GBS to the cytosol induced TNF formation.

Conclusions: Macrophages recognize internalized streptococci via two interdigitating loops. First, maturation of bacteria-containing lysosomes is NO-dependent. This process is causally linked to the second loop, which involves the translocation of bacterial RNA to the cytosol and the cytosolic recognition of bacterial ssRNA.

HOSPITALIZATION OF CHILDREN WITH H1N1 2009 INFLUENZA VIRUS IN ISRAEL DURING THE 2009 OUTBREAK - A MULTI-CENTER SURVEY

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Aim of the study: To describe the clinical characteristics of children who were hospitalized with 2009 H1N1 Influenza Virus infection (swine flu) in Israel.

Patients and methods: We collected data for children hospitalized in 7 Medical Centers from July 12 until December 24, 2009, who had swine flu infection confirmed by RT-PCR.

Results: 478 Children were enrolled. Mean age was 6.06 yr. Mean hospitalization stay was 3.86 days. 8.8% of patients were admitted to the ICU, and 3 patients died.

The most frequent clinical presentations were as follows: pneumonia -33.5%, ILI - 29.5%, exacerbation of underlying illness - 9.4% and convulsions in 8.57% of admissions. 51.2% of the children did not have any recognized risk factors for H1N1 influenza infection. Risk factors included respiratory illness in 25.9% of patients, neurologic illness (8.6%), and cardiovascular illnesses (6.3%).

Children with preexisting metabolic and neurological disorders were at the highest risk for severe complications following 2009 H1N1 infection (RR: 6.5 and 2.87 respectively). Hospitalization rate for children younger than 18 years was 0.72/1000.

Mortality rate in Israeli children was 1.6/1,000,000.

Conclusions: Hospitalization rate for children with swine flu in Israel was estimated as 0.72/1000. Even though children with underlying medical conditions and especially patients with neurological and metabolic illnesses are more prone to influenza associated complications, otherwise healthy children are also at significant risk and more than half of the hospitalized children did not have any known risk factors for severe swine flu infection.

AN OPEN-LABEL, RANDOMIZED, PARALLEL-GROUP, MULTI-CENTRE STUDY EVALUATING TWO H1N1 INFLUENZA VACCINES IN CHILDREN AGED 6 MONTHS TO 12 YEARS

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Aims: Children have disproportionately high rates of influenza A (H1N1) disease and frequently transmit the virus. We undertook an open-label, randomized, parallel-group, multi-centre study to evaluate reactogenicity and immunogenicity of two vaccines used in the UK: a non-adjuvanted cell culture-derived whole-virion vaccine and a split-virion egg culture-derived adjuvanted vaccine, in children aged 6 months to 12 years.

Methods: Children at 5 UK sites were randomised 1:1 to a two-dose regimen of 7.5µg monovalent whole-virion (Baxter) or 1.875µg split-virion ASO3-adjuvanted vaccine (GlaxoSmithKline) both influenza A/California/2009(H1N1). Local reactions and systemic symptoms within seven days of vaccination were solicited. Immunogenicity was determined by serum microneutralisation titres obtained at enrolment and 14-21 days post 2nd dose.

Results: 942 children were randomised and 936 were vaccinated (464 adjuvanted, 472 non-adjuvanted). Interim analysis from 727 doses of adjuvanted and 756 non-adjuvanted vaccine showed more frequent local reactions with the adjuvanted than non-adjuvanted vaccine (redness >25mm in 47/727 vs. 3/756 respectively, swelling >25mm in (46/727 vs 6/756). Fever >38°C was noted in 31/727 in the adjuvanted group and 18/756 of those receiving the non-adjuvanted vaccine. Seroconversion (x4 rise in microneutralisation titre) was higher with the adjuvanted than non-adjuvanted vaccine (232/242 paired samples (96% CI 93-98%) vs 223/245 (91% CI 87-94%) respectively.

Conclusion: This is the first direct comparison of an adjuvanted vs. non-adjuvanted H1N1 vaccine. Notably, both vaccines, despite being either whole virion or adjuvanted, had low reactogenicity rates. The adjuvanted vaccine was more immunogenic overall and, importantly, achieved high seroconversion rates in children < 3 years.

POSSIBLE HARMS OF OSELTAMIVIR-INTERPRETING SAFETY IN CONTEXT OF THE H1N1 09 PANDEMIC

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Background and aims: According to a recent meta-analysis in children, vomiting is commonly reported with oseltamivir. Here we present clinical observations of 104 children with proven influenza who were treated with oseltamivir.

Methods: During the 2009 Southern hemisphere winter season (June-September) we studied 220 consecutive hospital admissions aged < 15 years with laboratory confirmed influenza (86% H1N1 09) at the Children's Hospital at Westmead, Sydney, as part of a collaboration between the National Centre for Immunisation Research and Surveillance and the Australian Paediatric Surveillance Unit.

Results: Thirty nine percent (85/220) of these children had vomiting as a presenting symptom; 47% (104/220) were treated with oseltamivir. The proportion with vomiting on presentation who were later treated with oseltamivir was similar (39%[40/104]) to that in children who were not treated with oseltamivir (39%[45/116]). Of 64 children without vomiting at presentation who were subsequently treated with oseltamivir, only one developed vomiting in hospital; this settled within hours and the 5 day course was completed. Chart review showed that no child had an exacerbation of vomiting on oseltamivir treatment and none required anti-emetics or intravenous rehydration. All were discharged from hospital well (median stay 3 days).

Conclusions: The H1N1 2009 influenza A pandemic strain has important clinical differences to seasonal influenza, including much higher rates of vomiting. Our observations indicate clinical benefit and a lower rate of treatment-induced vomiting from oseltamivir than suggested by clinical trials (despite the greater propensity to vomiting with H1N1 09 infection), and support the use of oseltamivir in children.

CHARACTERISTICS OF H1N1 INFECTION IN CHILDREN ADMITTED TO ST MARY'S HOSPITAL, LONDON

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Background: Most children with H1N1 infection have self-limiting disease, but severe morbidity and mortality is associated with pre-existing conditions. This study describes the clinical and laboratory characteristics of children presenting to a major paediatric centre in London.

Methods: Data was analysed retrospectively for all patients aged < 16 years who presented between June and December 2009 with a positive PCR assay for H1N1 on nasopharyngeal aspirate.

Results: H1N1 was detected in 83 children of whom 43 were admitted. In those admitted, 20/43 (47%) had a primarily respiratory presentation. 22/43 (51%) had a risk factor for severe disease: neurodevelopmental delay (11, 23%), immunosuppression, chronic lung disease or sickle cell disease (5 each, 10%). Eleven patients were admitted to the intensive care unit: 3 were previously healthy children with the remainder having at least 1 risk factor. 5/11 children admitted to PICU died, of whom two were previously healthy. Clinical presentations in fatal cases were: ARDS/respiratory failure (3), refractory shock (1), and sepsis/multi-organ failure (1). Initial median CRP in admitted patients was 10 ng/ml, and median lymphocyte count was $1.9 \times 10^9/L$. 34/48 (71%) children presented with a total lymphocyte count below the 10th centile for age. Bacterial superinfection was documented in 6/46 children and suspected in a further 11.

Conclusions: The spectrum of clinical presentation and severity was broad, with a high case fatality rate in those admitted to intensive care (5/11). Lymphopenia was a prominent feature at initial presentation. Bacterial superinfection was found or suspected in over a third of cases.

ASSESSMENT OF POTENTIAL BENEFITS OF POINT OF CARE TESTING FOR PANDEMIC H1N1 INFLUENZA IN THE PAEDIATRIC POPULATION

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Background & aims: In 2009 healthcare worldwide experienced increased demands on resources as a consequence of pandemic H1N1 influenza. Our primary aim was to assess potential impact of near patient testing on clinical practice and cost. We also reviewed presenting symptomatology, and assessed frequency of supplemental investigations, and concurrent or alternate microbiological diagnoses.

Methods: Retrospective review of microbiological and medical records of patients tested for H1N1 influenza on admission to hospital over the period September to December 2009.

Results: Of 191 patients identified, 35 (18.3%) tested positive for H1N1 influenza. 24 (68.6%) of these received oseltamivir, 11(31.4%) did not. Of those who tested negative for H1N1 influenza, 67(42.9%) were treated with oseltamivir. A total of 505 microbiological investigations were performed, and pathogens isolated in 78(40.8%) patients. H1N1 was the most common pathogen, the next being RSV in 27 (14.1%) patients. Of those positive for H1N1, it was sole pathogen in 31 (88.6%) cases. No clinical features reliably predicted a diagnosis of H1N1 influenza.

Conclusions: The majority of patients tested for H1N1 influenza were negative. Point of care testing for H1N1 influenza would allow better utilisation of resources. Confirmation of H1N1 would ensure appropriate commencement of antiviral medication, and avoid further investigations. Early knowledge of negative results would avert unnecessary antiviral therapy, avoiding potential side effects, and provide a per patient drug cost saving of £16.36 (€18.25) in most patients. Further benefits would include less use of personal protective equipment, and less pressure on limited inpatient paediatric isolation facilities.

NEW TRENDS IN DIAGNOSIS AND TREATMENT OF CONGENITAL CMV INFECTIONS

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Cytomegalovirus Disease remains a major cause of morbidity and mortality in European children. The spectrum of disease includes congenital infection, postnatal infection in premature infants and disease in the immunocompromised child. This includes post solid organ of Stem Cell transplantation or less commonly now, in children with HIV. This talk will focus on current and future antiviral therapy for CMV.

The first paediatric studies of the guanosine analog Ganciclovir (GCV) were now over 20 years ago, and yet the optimal dose and duration for many children still remain unclear. There are virtually no studies in premature infants and older teenage children. The oral pro-drug valyl ester Valganciclovir (VGCV) is now licensed in a syrup formulation by the EMA, but only for those over 18 years of age.

There is limited PK data of VGCV in term infants and older children undergoing transplantation, but no other populations. There have been no direct comparison studies between intravenous GCV and oral VGCV. This is related to the difficulty of recruitment into clinical trials and the lack of surrogate markers for successful antiviral therapy. There is a need to improve long term surveillance of children treated with both these agents. Increasing numbers of children are being treated with VGCV in Europe for a range of indications, dosing and duration.

The duration of treatment is also unclear. A US trial from the Collaborative Antiviral Study Group is now actively recruiting into a randomised trial comparing 6 weeks versus 6 months of oral VGCV in children with symptomatic congenital CMV.

A further study is planned on the use of VGCV in children up to 18 months of age. There are only small studies on Cidofovir and Foscarnet in children. With the recent failure of Maribavir in its key phase III clinical study in adults, there remain almost no new antiviral agents specifically for CMV in the pipeline.

This talk will review the current evidence base for treatment and highlight the key areas where more data is required.

“CIPROFLOXACIN USE IN NEONATES: A SYSTEMATIC REVIEW”

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Objectives: Ciprofloxacin has no marketing authorization for use in neonates worldwide but it is prescribed for the treatment of neonatal life-threatening infections, mainly in developing countries and in Europe. Given the concerns about its toxicity in this population and the necessity for its use in specific clinical situations, we conducted a systematic review of the use of ciprofloxacin in neonates.

Methods: We performed a systematic search of PubMed, Embase and the Cochrane Database of Systematic Reviews and bibliographies of relevant articles. We included all studies, regardless of design, that reported efficacy, safety and pharmacokinetics of ciprofloxacin for the treatment of any neonatal infectious condition. We excluded letters, editorials, preliminary reports and abstracts.

Results: Observational cohort studies, case reports and descriptions of patient series account for all literature reviewed. Ciprofloxacin was administrated in neonates as a salvage therapy for sepsis due to multi-drug resistant strains or with signs of clinical deterioration under first-line antibiotic treatment. Initial administration was always intravenous with variable dosing schedule. Overall, treatment efficacy was estimated to be approximately 76.6%. No serious adverse events, particularly joint toxicity, were observed, although evaluation was predominantly clinical and follow-up limited to few months after the end of treatment.

Conclusions: The current literature is insufficient to support use of ciprofloxacin in neonates. Additional high quality studies should be undertaken to provide reliable data on pharmacokinetics, efficacy and long-term safety. As ciprofloxacin was included in the EMEA priority list, the TINN project is currently undertaken to provide currently missing information.

CATHETER RELATED BLOODSTREAM INFECTIONS (BSI) IN NEONATES: RESULTS FROM A FRENCH SURVEILLANCE NETWORK IN 2008

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Background and aims: Critically neonates (NN) often require central venous catheters (CVC). Bloodstream infections (BSI) may complicate these invasive devices.

Methods: In 2006 a catheter related BSI (CR-BSI) surveillance network was implemented in North-Western France in voluntary neonatal intensive care units. Umbilical catheters (UC) and other CVC were analysed separately. The 2008 results are presented.

Results: Eighteen units participated. A total of 1795 NN (accounting for 1606 UC and 1107 CVC) were included. The median birth weight (BW) and gestational age were 1550 g and 32 weeks. The median duration of catheter exposure was 5 days for UC and 14 days for CVC. The incidence of UC related BSI was 3.2/1000 UC days, ranging from 9.7 to 2.7/1000 UC days for NN with BW ≤ 750 g and those weighing more than 2500 g. A total of 155 CVC related BSI were recorded (9.6 BSI/1000 CVC days), with also an higher representativeness for NN with BW ≤ 750 g than NN with BW > 2500 g (18.0 vs. 5.3/1000 CVC days). Coagulase negative staphylococci were the most common microorganisms isolated from blood cultures in UC (50%) and CVC (89%) related BSI, respectively. Risk factor for catheter related BSI could be computed for CVC-related BSI only. In multivariate analysis, BW, duration of hospital stay, duration of catheter exposure, catheter insertion site and mechanical ventilation were independently associated with CR-BSI risk.

Conclusion: This network provides a useful benchmark for neonatal units in France and should be continued.

THE CONTRIBUTION OF INFECTIONS TO NEONATAL DEATHS IN ENGLAND AND WALES

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Background and aims: The contribution of infections to deaths in the neonatal period in developed countries is not well-established. This study aimed to use anonymised extracts of death registrations to determine the contribution of specific infections to neonatal deaths in England and Wales.

Methods: Details of infections associated with deaths in infants aged < 28 days in England and Wales between 2003 and 2005 inclusive were identified from routine anonymised death certificate data provided by the Office for National Statistics to the Health Protection Agency.

Results: There were 768 neonatal deaths over the 3-year period with an infection mentioned on the death certificate, accounting for 11% of all neonatal deaths. Of these, 280 (36%) occurred in term, 129 (17%) in preterm (28-36 weeks) and 359 (47%) in extremely preterm (< 28 weeks) neonates. Half of the term neonates who died (138/280 cases, 49%) had co-morbidities mentioned. A pathogen was recorded on 339 neonatal death certificates (44%), of which 273 (81%) were bacterial, 37 (11%) fungal and 29 (9%) viral. Group B streptococcus was recorded in a third (87/273 cases, 32%) of bacterial infection-related deaths and 11% (87/768 cases) of all infection-related deaths. In contrast, Gram-negative bacteria and fungi were more commonly recorded on the death certificates of preterm neonates.

Conclusions: This study provides a minimum estimate of the contribution of specific infections to neonatal deaths in England and Wales and forms a baseline against which interventions to reduce infection-related neonatal mortality can be monitored.

CHARACTERISTICS OF INVASIVE *STAPHYLOCOCCUS AUREUS* INFECTIONS IN ENGLISH NEONATAL UNITS

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Background and aims: In England *S.aureus* is the most common pathogen causing late-onset (LO) sepsis after CoNS and nearly half of all paediatric MRSA bacteremias occur on neonatal units. However the clinical correlates of disease are poorly described.

Methods: Culture proven *S.aureus* episodes were identified prospectively from 9 English neonatal units participating in the neonatal infection surveillance network (NeonIn). Demographic, risk factors and outcome data were collected.

Results: Between 2004 and 2008 there were 88 episodes of *S.aureus* sepsis (8 MRSA) in 86 infants (44 female). Median gestational age (GA) and birth-weight (BW) were 28 weeks (92% < 37 weeks, 78% < 32 weeks) and 902g (range 510-3650; 92% < 2500) respectively with no significant difference between MSSA and MRSA cases. Overall incidence was 0.6 per 1000 live-births and 5.4 per 1000 NNU admissions. Most episodes (94%) occurred > 48 hours of life (median 13 days (0-138)). Five infants (median GA 40 weeks, BW 2000g) had early-onset sepsis (< 48h) (all MSSA, no deaths). At the time of culture, 69% of infants were receiving respiratory support and 43% had a central line in-situ. 21% had focal infections (cellulitis or skin abscesses). There were 17 deaths, 3 directly due to MSSA sepsis (case fatality 3.4%).

Conclusions: *S.aureus* is a common cause of late onset neonatal sepsis. Premature infants in intensive care settings are most vulnerable and clinical signs are not distinctive. These data support current national guidelines which recommend flucloxacillin as part of the empiric therapy for LO infections.

HOT TOPICS IN PERTUSSIS

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Pertussis, caused by the bacteria, *Bordetella pertussis* or *Bordetella parapertussis*, is a highly contagious respiratory disease that affects all age groups. Infection and complications of the infection may lead to severe illness, hospitalisations and even deaths, particularly in susceptible infants. Furthermore, immunity is not life-long.

Vaccination of toddlers with efficacious pertussis whole-cell (Pw) vaccines led to the control of the disease in children. However, Pw vaccinations did not result in life-long immunity; indeed, the circulation of the bacterium was not controlled in the adult population and circulating isolates are still virulent. Adolescents and adults are now important sources of infection for infants too young to be (fully) vaccinated but also sources of nosocomial infections or infections in collectivities of elderly.

Booster vaccinations are essential to protect susceptible individuals. This is now possible with the development of pertussis acellular (Pa) vaccines, which target, and are thus likely to control, the virulence of this bacterium.

Recommendations for adolescents and adult vaccination have already been established in North American and some European countries. These countries must monitor the disease and circulation of the causative agents to determine whether the increase in herd immunity, resulting from high Pa vaccine coverage, will be sufficient to control the circulation of the bacteria. Analysis of pertussis epidemiology remains important from the perspective of both public health and vaccinology. However, differences in the case definition and biological diagnoses used lead to different awareness of the disease. It is of high importance to harmonize surveillance systems around the world.

SEROPREVALENCE OF PERTUSSIS IN THE NETHERLANDS: INCREASED CIRCULATION OF PERTUSSIS AMONG ADULTS

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Background and aims: Despite a high vaccination coverage (~96%), an increase of reported pertussis cases has been observed in The Netherlands in the last decades. In a cross-sectional population-based serosurveillance study in 2006-2007 we estimated the age-specific seroprevalence of pertussis infection.

Methods: IgG levels against pertussis toxine (PT) were measured in a multiplex bead-based fluorescent immunoassay and divided into four categories: 0-20, 20 to < 62.5, ≥62.5 (suggestive of infection in the preceding 12 months) and ≥125 EU/ml (suggestive of infection in the last 6 months). Weighted seroprevalence rates were calculated adjusted for age, sex, urbanization degree and ethnicity. To exclude high levels of IgG-PT induced by vaccination with acellular pertussis vaccine, only individuals who were not eligible for acellular vaccination (born before 1998) were included.

Results: Overall, 9.3% had a titer above 62.5 EU/ml, and 3.4% above 125 EU/ml. The highest prevalence of presumptive pertussis infection in the past year was seen in 75-79 year-olds (14.4%), followed by 40-44 year-olds (13.4%). Compared to a serosurvey in 1995-1996 the proportion with presumptive pertussis infection increased with a factor 5.5 (4.1-7.4).

Conclusions: The greater proportion of persons with IgG-PT levels >125 EU/ml suggests that circulation of *Bordetella pertussis* increased in recent years. The increase in presumptive pertussis infections is of the same magnitude as the increase in the reported incidence, indicating that the latter is not due to improved reporting rate but to a real increase in the circulation of pertussis. The high circulation poses an increased risk of transmission to very vulnerable infants.

MARKED DECLINE IN PERTUSSIS AMONG 5-14 YEAR-OLD JERUSALEM CHILDREN FOLLOWING THE INTRODUCTION OF A 5TH AND 6TH PERTUSSIS VACCINE DOSE

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Objective: Pertussis remains a cause of considerable morbidity in children worldwide. The routine pertussis vaccination program in Israel was updated twice recently - a 5th dose introduced at age 7 years (2005) and a 6th dose at 13 years (2008).

Methods: Population-based epidemiologic study of pertussis in Jerusalem.

Results: 1660 pertussis cases were reported from 1990 to September-30th-2009. The incidence rates increased sharply from 2.6/100000 in 1990, to 10.1/100000 in 2000, peaking at 28.8/100000 in 2006, then declining to 22/100000 in 2008 and to 15 in 2009 ($p < 0.01$). Most cases (74.9%, 1092/1459 during 2000-2009) were under 20 years. Infants under one year had the highest incidence rate (83.4/100000; 12.5% of cases); specifically those under 6 months (85% of cases under one year). The case distribution among 1-4, 5-9, 10-14, and 15-19 year-olds was: 11.2%, 18.1%, 24.3%, and 8.8%. The vaccination status (age-appropriate) was: unvaccinated (23.6%), partially vaccinated (10%), and fully vaccinated (66.4%). Hospitalization rates were 4.9% overall, infants - 30.8%. Household transmission occurred in 16.9% of cases. The only two age groups showing significant decline ($p < 0.05$) between 2006 and 2009 were children aged 5-9 (68.1% reduction) and 10-14 years (72.9% reduction); there is as yet no significant decline in other age groups (notably infants).

Conclusions: In light of the re-emergence of pertussis, two vaccine doses were added to the routine Israeli schedule. The decline in incidence in the 5-14 year-olds is encouraging. Young infants still present a high disease burden and the incidence in infants should be followed closely.

VIRAL INVOLVEMENT IN PULMONARY EXACERBATIONS IN CYSTIC FIBROSIS

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Background: In CF care, colonizing bacterial pathogens are also thought to be responsible for acute pulmonary exacerbations. Viral involvement is poorly evaluated, possibly due to the lack of sensitive detection methods.

Aims: To evaluate the involvement of viruses in CF pulmonary exacerbations and to identify the main viral pathogens.

Methods: At the onset of any acute pulmonary exacerbation we prospectively collected respiratory secretions obtained by nasal wash, to detect respiratory viruses using multiplex-PCR and viral culture. Blood for viral serology was also collected if possible. Whenever flexible fibroscopy with broncho-alveolar lavage (BAL) was indicated, BAL-fluid was also collected for detection of viral pathogens by multiplex-PCR and culture.

Results: For 199 acute pulmonary exacerbations in 86 CF-patients (median age = 11y 4m, sex ratio: F/M = 42/44), a viral pathogen was detected in 64/199 (32.2%) episodes and in 3/64 episodes 2 viruses were found. The 3 main viral pathogens found were influenza A virus, respiratory syncytial virus and human metapneumovirus, respectively in 15, 15 and 8 episodes.

In 56/64 (87.5%) episodes the viral pathogen was detected on respiratory secretions, in 52/56 (92.8%) cases on nasal washes and in 4/7 (57.1%) cases on BAL-fluid. Viral serology was only positive in 9/30 (30%) episodes.

Conclusions: Common respiratory viruses seem to play a role in an unexpected high proportion (32%) of pulmonary exacerbations in CF-patients of all age groups.

PCR on respiratory secretions obtained by nasal wash is a rapid, sensitive and non-invasive method for viral detection compared to serology.

DOES SEROTYPE-SPECIFIC SERUM IGG (SSS-IGG) ACCURATELY REFLECT PROTECTION AGAINST PNEUMOCOCCAL NASOPHARYNGEAL ACQUISITION (PNPA)?

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Background and aims: SSS-IgG concentration is believed to best reflect protection against PNPA. Since a second year booster increases SSS-IgG, we tested whether this would further reduce PNPA.

Methods: 356 infants received PCV7 at 2, 4, 6 m; 178 (50%) were randomized to receive a booster (Regimen-A) vs. no booster (Regimen-B) at 12m. SSS-IgG against serotypes 6B, 6A, 19F and 23F was measured at 7 and 13m; PNPA was assessed at 13, 18, 19, 24 and 30m.

Results: SSS-IgG concentrations were similar in Regimen-A and Regimen-B at 7m, but significantly higher for Regimen-A (receiving booster) at 13m. However, PNPA was similar (Dagan *et al*, ICAAC 2009). We further assessed relationship between PNPA and SSS-IgG concentrations (**Table**). In Regimen-A, post-booster SSS-IgG geometric mean concentrations (GMCs) correlated with PNPA. However, a strong interdependency was found between post-primary and post-booster responses. For Regimen-B, GMCs were low at 13m and did not predict PNPA. Using cut-offs >1.0 or >5.0 µg/ml did not improve prediction.

Conclusions:

- 1) In subjects receiving 3-dose primary PCV7, booster at 12m did not further reduce PNPA;
- 2) In regimen-B (no booster), SSS-IgG concentrations at 13m could not discriminate between those with or without PNPA, in contrast to Regimen-A. This suggests that PCV7 elicits additional protective mechanisms not fully reflected by SSS-IgG.

Table: SSS-IgG GMC (µg/ml) at 7 m and 13 m in relationship to PNPA at ages 13-30 m

Category	GMC at age 7 months				GMC at age 13 months			
	Regimen-A	P-value	Regimen-B	P-value	Regimen-A	P-value	Regimen-B	P-value
Anti-6B IgG (6A+6B acquisition)								
Acquired	1.13 (39 events)	.001	0.95 (50 events)	.004	4.89 (44 events)	< .001	0.74 (53 events)	.693
Not-acquired	2.61		2.00		13.12		0.82	
Anti-19F IgG (19F acquisition)								
Acquired	1.63 (36 events)	.722	1.79 (32 events)	.276	2.17 (35 events)	< .001	0.59 (29 events)	.722
Not-acquired	1.78		2.30		5.07		0.45	
Anti-23F IgG (23F acquisition)								
Acquired	0.43 (13 events)	.001	1.10 (27 events)	.213	2.60 (15 events)	< .002	0.37 (25 events)	.773
Not-acquired	1.37		0.77		6.42		0.40	

[Table]

BACTERIOLOGICAL CHARACTERISTICS AND PNEUMOCOCCAL SEROTYPES IN CHILDREN WITH ACUTE OTITIS MEDIA (AOM) WITH OR WITHOUT CONCOMITANT COMMUNITY-ACQUIRED ALVEOLAR PNEUMONIA (CAAP)

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Background: *S. pneumoniae* (Pnc) and non-typable *H. influenzae* (NTHi) are the most common AOM pathogens. AOM bacteriology is well-characterized, but bacteriology of CAAP is largely unknown, although an important role of Pnc is assumed. We attempted to determine whether the bacteriology of AOM in children with concomitant CAAP (\leq 48h from AOM tympanocentesis) differs from that of children with AOM without CAAP.

Patients and methods: Children $<$ 5 years admitted to the Pediatric Emergency Room with radiologically-confirmed CAAP and children with AOM, diagnosed by bacterial culture from middle ear fluid (by tympanocentesis), were enrolled. Multivariate regression-analyses were controlled for: age, ethnicity, antibiotic treatment during the last month and whether the child had \geq 3 previous AOM episodes.

Results: Of 6782 AOM, 159 (2.3%) had concomitant AOM+CAAP. Compared to AOM-only children, AOM+CAAP children had a significantly ($P < 0.05$) higher number of positive cultures (132 [83%] vs. 4266 [67%]) and Pnc+NTHi co-infection (34 [21%] vs. 817 [13%], respectively). In a multivariate regression analysis three bacteriologic characteristics were independently higher in children with culture-positive AOM+CAAP: 1) Culture positivity rate (OR=2.60); 2) Pnc+NTHi co-infection (OR=1.75); and 3) prevalence of serotype 14 (OR=2.56). Among pneumococcal isolates, the prevalence of serotypes 1, 3, 5, 7F and 19A (grouped) was significantly higher in AOM+CAAP, than in AOM-only children

Conclusions: Children presenting with AOM+CAAP compared with those with AOM alone had:

- 1) Higher culture positivity rate;
- 2) higher proportion of Pnc+NTHi co-infection, and serotypes often associated with pneumonia (1, 3, 5, 7F, 14, 19A, grouped).

**PATHOGENS IMPLICATED IN ACUTE OTITIS MEDIA (AOM) FAILURES AFTER
PNEUMOCOCCAL CONJUGATE VACCINE IMPLEMENTATION IN FRANCE: DISTRIBUTION,
SEROTYPES AND RESISTANCE LEVELS**

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Background: Prior to 7 valent pneumococcal conjugate vaccine (PCV7) implementation in France, several studies described the microbiology of AOM treatment failures (ATF). The causative pathogens were *S.pneumoniae* (Sp) followed by *H. influenzae* (Hi). The aim of this study was to determine if these otopathogens have shifted to a predominance of Hi.

Methods: Failure was defined as the persistence or the recurrence of AOM symptoms after children had received at least 48 hours of antibiotic (ATB) or had discontinued therapy within 4 days. Standardized history and physical examination findings were recorded and culture of middle ear fluid (MEF) was obtained.

Results: Between 2007 and 2009, 143 children were enrolled by 8 ENT. Mean age was 16.9 ± 9.9 months (median 13.7), 88.1% had received > 1 dose of PCV7 and 70.6% attended day care.

N (%)	ATB before ATF			
	Total N=143 (including 4 children with Sp+Hi in MEF)	Amoxicillin± Clavulanate N=73 (51.1)	Cefpodoxime proxetil N=53 (37.1)	Ceftriaxone/ cefixime/other N=17 (11.9)
No growth	50 (35)	28 (38.4)	16 (30.2)	6 (35.3)
Sp (84.5% serotype 19A)	45 (31.5)	18 (24.7)	21 (39.6)	6 (35.3)
	Tympanocentesis 32 (71.1)			
	Otorrhea 13 (28.9)			
% Penicillin intermediate	92.9	88.9	94.4	100
<i>H. influenzae</i>	45 (31.5)	29 (39.7)	13 (24.5)	3 (17.6)
	Tympanocentesis 41 (91.1)			
	Otorrhea 4 (8.9)			
βlactamase+	7 (15.5)			
BLNAR	15 (33.3)			
βlactamase+ and BLNAR	5 (11.1)			
Other bacteria	7(4.9)	1 (1.4)	4 (7.6)	2 (11.8)

[echech]

Conclusion: Among children with ATF, Sp and Hi are equally distributed: 19A is the main serotype and the main mechanism of resistance for Hi is BLNAR.

SEROTYPE DISTRIBUTION IN PNEUMOCOCCAL PLEURAL EMPYEMA IN BARCELONA, SPAIN (2007-2009)

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Background and aims: The incidence of Pediatric Parapneumonic Empyema (PPE) has raised in Spain and other countries during the past few years. The most common cause is *S. pneumoniae* but etiology and serotype identification are frequently obscured by antibiotic therapy. Our aim was to study serotypes responsible for pneumococcal PPE using conventional microbiological techniques and molecular identification methods.

Methods: We prospectively enrolled children < 5 years old admitted in two large pediatric hospitals in Barcelona with pneumococcal PPE from 1/07 to 11/09. Pleural fluid was cultured and positive cases were serotyped using the Quellung method. Culture negative cases were detected by real time PCR to the pneumolysin gene and serotyped by real time PCR to capsular genes from 23 different serotypes.

Results: We identified 145 cases. The mean age was 35.1±13 months. 50.3% were males. 57% had received seven-valent pneumococcal conjugated vaccine (PCV7). Serotype identification was accomplished in 112 cases (77%). The serotype distribution was: 1 (n=40), 3 (n=20), 19A (n=15), 7F (n=6), 5 (n=3), 14 (n=2), 24F (n=1) and nontypeable nonvaccine serotypes (n=25). PCV7 serotypes were found in 1.7% of cases, 10-valent serotypes in 45.5% of cases and 13-valent serotypes in 76.7% of cases.

Conclusions: 76.7% of pneumococcal PPE in children younger than 5 years old in Barcelona are caused by serotypes included in the 13-valent vaccine.

CHANGE IN PNEUMOCOCCAL SEROTYPES DETECTED IN EMPYEMA IN UK CHILDREN FROM THE ENHANCED SURVEILLANCE PROGRAMME 2006 - 2009

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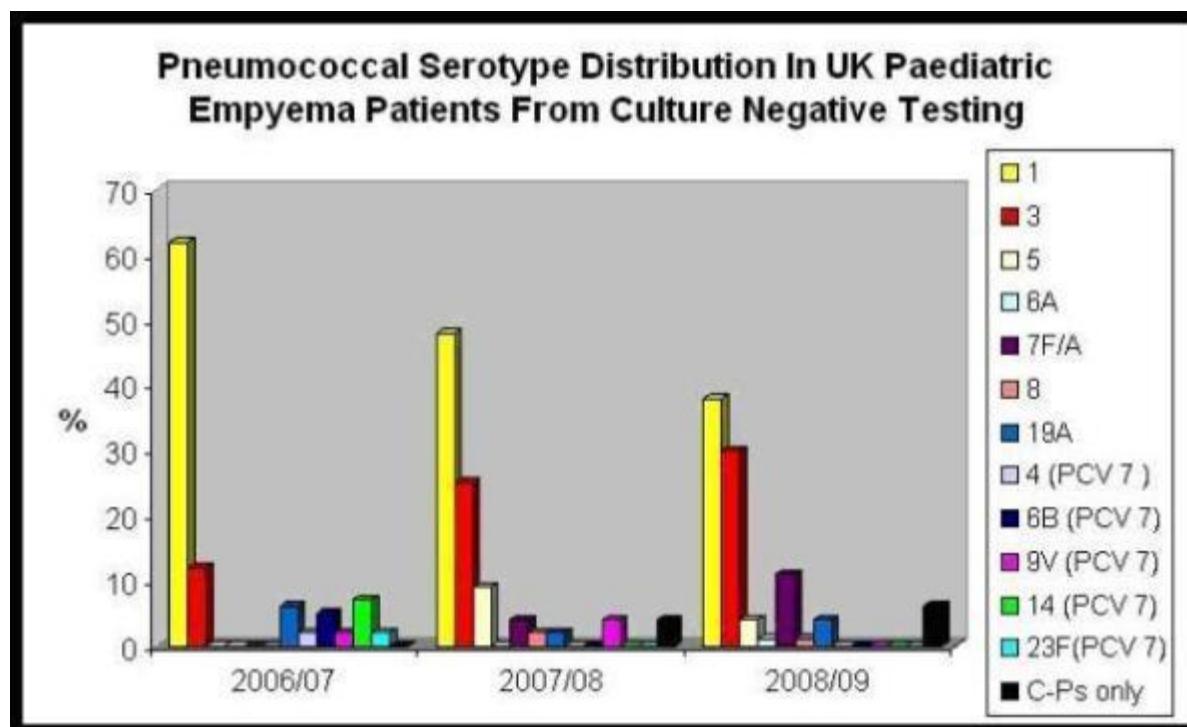
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Background and aims: Following the introduction of seven-valent pneumococcal conjugate vaccine (PCV7), Prevenar[®] in the UK in September 2006 enhanced surveillance of paediatric empyema was established to monitor any consequent changes in serotype distribution. We report the results of non-culture surveillance using an antigen detection assay.

Methods: Culture negative, pneumococcal PCR positive empyema fluid from children (0-16 yrs) is forwarded to the Respiratory & Systemic Infection Laboratory for non-culture serotyping using a Luminex based assay capable of detecting 14 serotypes/groups (1, 3, 4, 5, 6A/C, 6B, 7F/A, 8, 9V, 14, 18, 19A, 19F and 23F) and the common polysaccharide (C-Ps).

Results: Between August 2006 and September 2009, 223 samples were received from 211 patients (64 in 2006-07, 53 in 2007-08 and 94 in 2008-09). 207 serotypes were obtained (93% detection rate).

Conclusions: In 2008-2009 there were no cases due to PCV7 serotypes. Whilst serotype 1 was the most common in each year there was a significant rise in serotype 3 ($P=0.01$)(Fig). Serotype 3 is not included in the 10 valent pneumococcal vaccine but is contained in Prevenar13[®]. Also of note was a decline in overall prevalence of serotype 1, except in under 2 year olds where the numbers of serotype 1 empyemas increased from < 10% to >20% of cases.



[Figure]

RISK FACTORS AND OUTCOME OF *CANDIDA PARAPSILOSIS* BLOODSTREAM INFECTIONS IN CHILDREN

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Background: *Candida parapsilosis* is an important cause of candidemia and its incidence is increasing. The aim of this study was to compare risk factors and outcome of candidemia caused by *C. parapsilosis* (group A) to candidemia caused by all other *Candida* species (group B) in neonatal and pediatric patients.

Methods: Retrospective review and analysis of demographic data, clinical features, therapeutic procedures and outcomes associated with candidemia episodes that occurred at a large children's hospital from 1998 to 2004.

Results: Among 319 candidemia episodes, *Candida albicans* accounted for 125 (39.2%), *C. parapsilosis* for 73 (22.9%) and all other *Candida* species for 121 (37.9%) episodes. Length of hospital stay was 38d for group A vs 33d for group B ($p=0.03$). Time of hospital stay prior to candidemia was 16d for group A vs 12d for group B ($p=0.03$). Patients infected with *C. parapsilosis* were more likely to be mechanically ventilated at the time of candidemia [34/73 (47%) for group A vs 66/246 (27%) for group B ($p=0.002$)]. No significant differences were found between the two groups in patient age, presence of central intravascular or urinary catheters, surgical procedures, previous administration of immunosuppressive or antifungal agents and mortality rates.

Conclusions: In this large study, *C. parapsilosis* is the second most frequent *Candida* isolate. Hospital stay duration prior to *C. parapsilosis* candidemia is longer and likelihood of mechanical ventilation is greater compared to other *Candida* species; however, mortality is not significantly different.

DIAGNOSTIC FEATURES OF INVASIVE ASPERGILLOSIS IN PEDIATRIC PATIENTS

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Background and aims: Non-invasive diagnostic procedures like characteristic radiologic features and biomarkers in blood have shown to be relevant for an early diagnosis of invasive aspergillosis (IA) and improved outcome in adults. The value of these features in children is still unclear.

Methods: All probable and proven episodes of IA in children (0-18 years of age) during a 15-year period (1994 to 2008) in our children's hospital were included. Case record forms were used to collect information on underlying disease, microbiological results, treatment and outcome. We studied reports of plain radiography, CT- and High-Resolution-CT-thorax for specific radiologic findings.

Results: Thirty-five episodes of IA in 33 immunocompromised children were included as either proven (51%) or probable IA (49%). The first diagnostic modalities found to be indicative for IA were a positive galactomannan (GM, 28.6%) or culture (31.4%) or a suspect finding on imaging (31.4%). Testing GM in blood yielded a sensitivity of 70%, in BAL-fluid 81% (combining both: 91%). Performing a (HR)CT yielded new clues for diagnosis in 53.8% in patients with a normal X-thorax. Specific findings (halo sign, air crescent sign) on (HR)CT-scan were less prevalent in children than reported in adults and became more prevalent with time.

Conclusion: (HR)CT-thorax showed much higher sensitivity for diagnosing IA compared to X-thorax. Combining GM-testing in both blood and BAL-fluid increases the sensitivity of this test to 91%. The absence of specific radiological findings of IA urges the need for a standardized study in which every child with suspected IA undergoes a (HR)CT-thorax at subsequent defined timepoints.

RISK FACTORS FOR THE DEVELOPMENT OF INVASIVE CANDIDIASIS WITH *CANDIDA KRUSEI* OR *CANDIDA GLABRATA* AT A US CHILDREN'S HOSPITAL

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Background and aims: *Candida* species are among the most common causes of bloodstream infection and are associated with significant morbidity and mortality. Although common in adults, *C. krusei* and *C. glabrata* occur less frequently in children. Little is known about the risk factors for infection with *C. krusei* and *C. glabrata* in children.

Methods: We conducted a nested case-control study within a cohort of pediatric patients with laboratory confirmed candidemia between January 1999 and December 2004 to evaluate risk factors for development of infection with *C. krusei*/*C. glabrata* compared to other *Candida* species. Demographic/clinical data were collected during the 2 weeks prior to infection. Multivariate logistic regression was performed to determine independent risk factors for infection.

Results: There were 319 cases of candidemia during the study period, 30 with *C. krusei*/*C. glabrata*, and 289 with other *Candida spp.* Independent predictors for infection with *C. krusei*/*C. glabrata* included age between 3 and 17 years (OR 2.78; CI 1.03, 7.55), age greater than 18 years (OR 10.21; CI 3.23, 32.24), and receipt of fluconazole as prophylaxis (OR 4.38; CI 1.77, 10.84). Mortality for subjects with *C. krusei* or *C. glabrata* was 20% compared to 15% for subjects with other *Candida spp.*, which was not statistically significantly different ($p=0.44$).

Conclusions: We found that *C. krusei* /*C. glabrata* were isolated from nearly 10% of all cases of candidemia at our hospital. Older pediatric patients, especially those who have received prophylactic fluconazole, should be considered at risk for infections with *C. krusei* /*C. glabrata*.

INCREASE IN THE PREVALENCE OF ZYGOMYCOSIS IN CHILDREN

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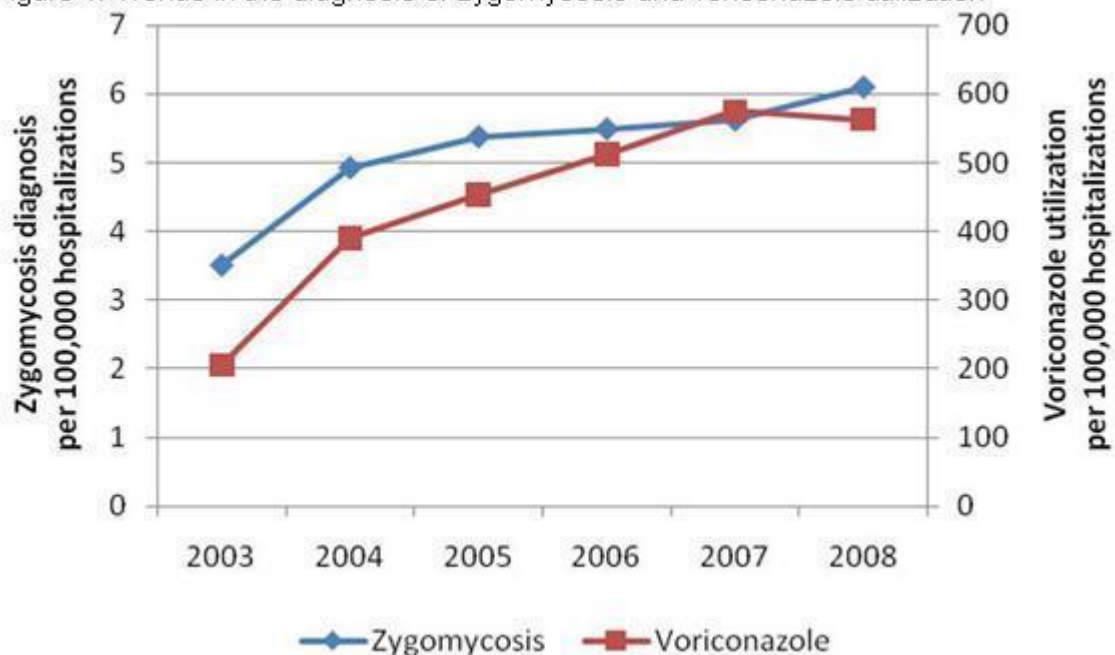
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Background and aims: Zygomycosis is an often fatal fungal infection which has been increasing in prevalence as advancements are made to care for immunocompromised hosts. Previous literature suggests that an association exists between voriconazole use and the emergence of zygomycosis in adults but little is known about trends in children.

Methods: The Pediatric Health Information System (PHIS), an administrative database containing information from 42 US children's hospitals, was used to analyze trends in the prevalence of zygomycosis from January 2003 to December 2008. Disease status was determined using the ICD-9 code for Zygomycosis (117.7). We also gathered information on voriconazole prescription rates.

Results: We identified 151 pediatric hospitalizations with a diagnosis of zygomycosis between 2003 and 2008. The prevalence of zygomycosis statistically significantly increased over the study period ($p = 0.030$), from 3.5 hospitalizations per 100,000 hospitalizations in 2003 to 6.1 hospitalizations per 100,000 hospitalizations in 2008. In addition, voriconazole utilization significantly increased over the study period ($p = 0.035$) from 206 hospitalizations per 100,000 hospitalizations in 2003 to 563 hospitalizations per 100,000 hospitalizations in 2008 receiving voriconazole.

Figure 1: Trends in the diagnosis of zygomycosis and voriconazole utilization



[Figure 1]

Conclusions: The diagnosis of zygomycosis in children has significantly increased over time, as has the prescription of voriconazole. Given that this is a trend analysis that does not control for potential confounding factors, caution should be used in interpreting these results.

INTERNATIONAL PEDIATRIC FUNGAL NETWORK (PFN): A NOVEL MULTICENTER CONSORTIUM FOR INVESTIGATING PEDIATRIC INVASIVE FUNGAL INFECTIONS (IFIS)

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Background: Pediatric and neonatal IFIs are increasing but there has never been a large concerted effort to understand their epidemiology or optimal management. PFN (<http://pfn.pediatrics.duke.edu>) is a novel international consortium of 59 centers, including 34 US and 14 European centers. The mission of PFN is to increase the knowledge of pediatric IFIs and to serve as a vehicle for centers to conduct clinical trials.

Methods: Clinical information is captured through a secure electronic portal. Since Aug 2008, 126 patients have been enrolled in an observational study to examine epidemiology, diagnosis and treatment of IFIs in children and neonates. 87 patients (53 children and 34 neonates) with proven or probable IFIs have completed data through 12-week follow-up.

Results: There were 34 children with candidiasis, 8 with aspergillosis and 11 with other IFIs. Neonatal IFIs largely included candidiasis (n=33). The most common *Candida* species in children were *C. albicans* (n=10) and *C. parapsilosis* (n=10); similarly in neonates the most common species were *C. albicans* (n=9) and *C. parapsilosis* (n=11). Invasive aspergillosis was most frequently treated with voriconazole (64%), while invasive candidiasis with fluconazole (41%) and micafungin (29%). Outcomes in invasive aspergillosis included complete/partial response (n=7) and failure (n=1); whereas, pediatric invasive candidiasis included complete/partial response (n=31) and failure (n=3). Neonatal invasive candidiasis resulted in discharge or cure (n=24) and death or continuation of IFI (n=10).

Conclusion: This large prospective observational study of pediatric and neonatal IFIs focusing on disease epidemiology may be used to design diagnostic and therapeutic clinical trials.

LATENT TUBERCULOSIS INFECTION

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Most people infected with *Mycobacterium tuberculosis* contain the initial infection and develop latent tuberculosis which is characterized by evidence of an immune response against the bacterium but no signs of active infection. Reactivation occurs in about 10% of infected people leading to active and contagious tuberculosis. It has been estimated that about one third of the world's population is infected with the bacillus.

Although diagnosis and treatment of persons with active tuberculosis is the first priority for tuberculosis control, an important second priority in low incidence countries is the identification and treatment of persons with latent tuberculosis infection (LTBI). This treatment aims both to preserve the health of the individual person and to protect the health of the public by reducing the number of potential sources of infection. For many decades, the tuberculin skin test (TST) was the only means of diagnosing LTBI. Interferon gamma release assays (IGRAs) were recently developed and are promising new tools. IGRAs have been introduced into different national guidelines although their role in diagnosis of LTBI and in different groups of patients has not been clearly defined. IGRAs are more specific compared to TST as they are not confounded by previous BCG vaccination. The sensitivity of these tests cannot be accurately assessed in the absence of a gold standard for the diagnosis of latent infection. By using active disease and correlation with the degree of exposure in contact investigations as surrogate markers in different studies it has been shown that these tests have similar or even higher sensitivity to TST. Most studies in children have shown similar findings, however, there is yet insufficient data regarding the performance of IGRAs in young and in immunocompromised children. The kinetics of IFN gamma response as measured by the IGRAs and the prognostic power of a positive IGRA test for the development of active disease also need to be studied further. Current IGRAs are being improved and the role of other cytokines in the diagnosis of TB and LTBI is being investigated.

Regarding treatment for LTBI, isoniazid monotherapy for 6-9 months has been used as the standard regimen. Because compliance has been poor shorter courses of treatment have been proposed such as the isoniazid and rifampin combination for 3 months and other such as isoniazid and rifapentine are under investigation.

PEDIATRIC TB IN EMILIA ROMAGNA REGION (1996 - 2006): INSIGHTS FROM REGIONAL DATABASE ANALYSIS

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Background and aims: Despite Tuberculosis (TB) still represents a major public health concern, surveillance data in the field of childhood TB are limited. This study carried out a retrospective analysis of TB cases in the Emilia Romagna Region (RER, Italy), highlighting data about incident pediatric cases during the time period 1996-2006.

Methods: Since 1996, data for incident TB cases are recorded in the RER database, including both patient's personal details and characteristics of TB at its clinical appearance. Data about incident cases in ≤16 years-old were retrieved, and then analyzed.

Results: Eventually, 180 cases were identified (3.3% of total TB cases; M=52.2%, F=47.8%; IBP=93, NIBP=87). Annual incidence was comprised between 3.1/100,000 (1996) and 4.8 (2006), appearing as significantly increasing at regression analysis ($p=.039$), mainly in subjects 6-16 years-old ($p=.028$). IBP appeared as more frequently contact of cases (RR=1.60 95%CI=1.25-2.05) and more rarely as positive at PPD (RR=.73 95%CI=.56-.95) or a Chest X-Ray (RR=.72 95%CI=.55-.94) at diagnosis. Among cases, at diagnosis 124 had lung involvement (68.9%), whereas 26 showed a peripheral lymph node involvement. Eleven cases had bone TB diagnosis (7 at vertebral column) whereas only 2 TB-meningitis cases were identified. No clinical difference was identified between IBP/NIBP groups.

Conclusions: Pediatric TB represents a particularly difficult challenge, and epidemiological data are scarce. In our study, we presented data about pediatric TB in the RER identifying a significant increase in the diseases incidence and highlighting clinical aspects of pediatric TB.

TUBERCULOSIS IN SOLID ORGAN AND BONE MARROW TRANSPLANT RECIPIENTS IN A TERTIARY SPANISH HOSPITAL

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Aims: To evaluate the incidence, clinical presentation, management and outcome of tuberculosis in pediatric transplant recipients.

Methods: A retrospective review of the medical records of patients who underwent solid organ and bone marrow transplantation between 1985 and 2009.

Results: Tuberculosis developed in 5 of 925 (0.54%) patients undergoing solid organ transplantation (1/49 (2%) intestinal; 3/332 (0.9%) kidney and 1/544 (0.33 %) liver) and in 1 of 331 (0.3%) children after bone marrow transplantation. The median duration from transplantation to diagnosis was 49 months (6-120). Three patients had pulmonary and 3 disseminated disease. Persistent fever and constitutional symptoms were the most common presentations. Diagnosis was achieved with both direct acid-fast stain and culture in 4 patients, and by histopathologic study combined with polymerase chain reaction in 2. An adult source case was identified in 3 patients. Two patients were treated with rifampin-sparing regimens and 4 with the standard 3 or 4-drug regimen, requiring increases of immunosuppressive drug doses. Isoniazid-induced hepatitis was observed in 4 patients and pyrazinamide-induced hyperuricemia in 2, but both effects resolved with dose reduction. Four patients completed the treatment, one is still on treatment and one died while receiving treatment.

Conclusions: The prevalence of tuberculosis in transplant recipients is higher than in the general population. A high index of suspicion is necessary to ensure early diagnosis and prompt initiation of treatment. Standard 3 or 4-combined anti-tuberculosis regimen is effective, but regular monitoring of immunosuppressive drug levels and of renal and liver function is essential to detect drug-induced toxicity.

IDENTIFICATION OF SERUM BIOMARKERS OF PAEDIATRIC TB USING SELDI

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Background and aims: Improved diagnosis of tuberculosis (TB) is essential for reducing the incidence of this disease in sub-Saharan Africa. Currently half of the all cases of infectious TB are undiagnosed. This proportion is higher in children where 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 were collected from children (HIV-negative, < 14 yoa) with active TB (pulmonary TB n=45; extra-pulmonary TB n=45) and controls (Mantoux skin-test negative n=45; Mantoux skin test positive n=45; other infections/ inflammatory conditions n=45). Serum proteomic profiles were obtained by SELDI using cation capture (CM10), anion capture (Q10) and immobilized metal affinity (IMAC30) ProteinChip™ arrays.

Results: Five proteins (4.0 kDa, 4.1 kDa, 9.3 kDa, 14.0 kDa and 17 kDa) were identified that distinguish children with active TB from those with other infections with a sensitivity and specificity of 74% and 94%, respectively.

Conclusions: Identification of protein biomarkers specific to active TB would greatly enhance diagnosis of patients that currently go undetected and continue to spread TB within communities. The biomarkers of active TB identified from our pilot study are currently being investigated in highly characterized cohorts (>1000) of children and adults with TB, latent TB, HIV and in other infections/ inflammatory conditions that mimic TB.

USE OF RAPID DIAGNOSTIC TEST FOR PID

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Prompt identification of infectious agents is essential to plan adequate procedures to limit their spread, initiate specific therapy if required and avoid unnecessary drug prescriptions. Among the different diagnostic methods, serology cannot be used for a prompt diagnosis because it requires two blood samples (the second of which has to be drawn some weeks after the onset of symptoms), cell cultures are complicated and time-consuming, and molecular assays have to be performed in well-equipped laboratories and cannot be used outside hospital. Antigen-based assays are inexpensive, easy to perform, and the result is available in a very short time even in an ambulatory setting or (at least in some cases) at patient's home. For all these reasons, they are widely used in clinical practice especially in children with respiratory tract infections, which are the most common diseases of the pediatric population for which several tests have been recently marketed. The variability in the efficiency of these tests is due to many factors, including the standard used for comparison, the type of test, the circulating pathogen type/subtype, the type of specimen and when it is collected, and the patient's age. However, their overall sensitivity and specificity highlight that they are most reliable when the prevalence of infection is high, which suggests that their routine use should be limited to the peak periods of pathogen circulation. Considering these data, pediatricians should choose the rapid tests that have the highest efficiency and are less expensive, less time-consuming, and easier to perform and interpret.

RAPID MOLECULAR DIAGNOSIS. A NOVEL, ONE-STEP NUCLEIC ACID LATERAL FLOW IMMUNO-ASSAY FOR MALARIA AND ITS EVALUATION IN EDO-STATE NIGERIA

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Background and aim: Malaria is often found in children in malaria endemic countries but is also more and more imported into Europe in children visiting malaria endemic countries. Microscopy is in all cases most frequently used diagnosis, but at low parasitaemia and in areas where microscopy is not routinely performed it becomes less sensitive and time consuming. Molecular tools allow for specific/sensitive diagnosis but current formats, like PCR combined with gel-electrophoresis or in Real Time format, are difficult to implement, especially in resource poor settings.

Methods and results: Development of a simple, fast, sensitive and specific detection system, Nucleic Acid Lateral Flow Immunoassay (NALFIA) for amplified Pan-Plasmodium PCR products is described and the evaluation in a local district hospital in Nigeria is described. Laboratory evaluation showed a lower detection limit of 0.3 - 3 parasites/ μ l, ten-fold more sensitive than gel-electrophoresis analysis. Evaluating over 1200 clinically suspected children with the Pan-Plasmodium assay under field conditions (Edo-State Nigeria), revealed that NALFIA detected more positives than microscopy and that microscopy was poorly performed despite it being routine practice but that there was an excellent agreement between gel-electrophoresis and NALFIA (98.5%; k-value: 0.96) and a perfect agreement between PCR-NALFIA and an alternative Real Time PCR assay.

Conclusion: NALFIA is more sensitive than microscopy and a good alternative to detect PCR products whilst circumventing using electricity or expensive equipment, making NALFIA the first step towards simplified and sensitive molecular field diagnosis.

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PERFORMANCE OF STREPTOCOCCAL RAPID ANTIGEN TEST (SRAT) IN CHILDREN WITH PHARYNGITIS (PH) AND HEALTHY CONTROLS (HC)

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Background: Two drawbacks have been evocated for SRAT: poor sensitivity and inability to distinguish among patients with PH those with truly group A streptococcus (GAS) infection and GAS chronic carriers with acute viral infection. The aim of this study was to assess the performance of SRAT in patients with PH, according to the Mac Isaac Score (MIS), and in HC.

Methods: In this prospective observational study, 17 physicians consecutively included children with PH and HC. They completed an assessment form including signs of MIS and performed pharyngeal double-swab (1 for SRAT and 1 for culture in National Reference Centre).

Results: In 2009, 315 children (mean age 6.1 years) were enrolled. Among 255 PH, 31% were GAS+ (63 heavy and 15 light cultures). Among the HC, 18% were GAS+ (3 heavy and 8 light cultures).

		SRAT performance % [CI 95%]				
(n patients)	Se	Sp	PPV	NPV	LR+	LR-
HC (60)	55 [28;79]	100 [93;100]	100 [61;100]	91 [80;96]	>54 [40;68]	0.5 [0.3;0.6]
PH (255)	78 [68;86]	96 [92;98]	90 [80;95]	91 [86;95]	20 [17;22]	0.2 [0.2;0.3]
MIS						
2 (26)	67 [30;90]	100 [84;100]	100 [51;100]	91 [72;97]	>66 [41;91]	0.3 [0.2;0.5]
3 (74)	61 [41;78]	98 [90;100]	93 [70;99]	85 [74;92]	31 [24;38]	0.4 [0.3;0.5]
4 (99)	87 [70;95]	94 [86;98]	87 [70;95]	94 [86;98]	15 [12;18]	0.1 [0.1;0.2]
5 (53)	90 [69;97]	94 [81;98]	90 [69;97]	94 [81;98]	15 [11;19]	0.1 [0.1;0.2]

[SRAT]

The Se of SRAT varies greatly according to the number of colonies isolated: 90%, CI 95% [81;95] for heavy cultures and 40% CI 95% [23;59] for light culture.

Conclusions: The Se of SRAT is low for HC and low MIS (meaning that a few number of patients would be unnecessary treated by ATB using a STRAT based strategy) but acceptable for higher MIS.

PERFORMANCE EVALUATION OF THE BINAXNOW INFLUENZA A & B KIT FOR DETECTION OF H1N1V PANDEMIC INFLUENZA IN BELGIAN PAEDIATRIC PATIENTS

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Background: Rapid identification of respiratory viruses permits to optimize clinical management and limits viral spread. In April 2009, a new variant of H1N1 (H1N1v) emerged. Many molecular techniques for its specific detection became rapidly available, but even these take often several hours. We evaluated the performance of a rapid (15') antigen detection test (BinaxNOW).

Methods: From week 41 to 45 (peak of first pandemic wave), all respiratory samples from patients with influenza-like syndromes of 3 public hospitals were prospectively examined by the BinaxNOW Influenza A & B assay (immunochromatography), followed by viral culture and/or (in patients at risk) by a specific real-time RT-PCR assay.

Results: Respiratory samples consisted of 48% nasopharyngeal aspirates (NPA), 38% nasopharyngeal (NPS) and 10% throat swabs (TS). The sensitivity and specificity for BinaxNOW was respectively 47 and 98,7% in 1383 samples compared to viral culture and 46,5 and 98,8% in 846 samples compared to PCR-testing.

Significant differences in sensitivity were noticed depending on the type of sampling. NPA gave by far the highest sensitivity for antigen detection with an average of 66,7% (63- 78% depending on sampling experience). The sensitivity in paediatric NPS varied less between the different hospitals (40-42%) and was still much higher than in adult NPS (11,4-20%). TS in children resulted in unsatisfactory results with a sensitivity of 13%, compared to 11% in adults.

Conclusions: BinaxNOW shows excellent specificity and a high positive likelihood ratio, but negative results should be confirmed by additional testing for A/H1N1v. NPA are clearly superior to NPS or TS.

PREDICTION OF HIGH-GRADE VESICO-URETERAL REFLUX AFTER A FIRST UTI IN CHILDREN: CONSTRUCTION AND INTERNAL VALIDATION OF A CLINICAL DECISION RULE

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Background: Urinary tract infection (UTI) leads to a diagnosis of high-grade vesicoureteral reflux (VUR) in ~15% of children. Predicting high-grade VUR (grade ≥ 3) would make it possible to restrict cystography to high-risk children and avoid unnecessary cystographies. We therefore sought to derive a clinical decision rule to predict high-grade VUR in children with a first UTI.

Methods: A secondary analysis of prospective series of children with a first UTI. Logistic-regression modeling and internal cross-validation were performed.

Results: The study included 494 patients (197 boys, high-grade VUR in 11%) from eight centers in seven countries. PCT and ureteral dilation on ultrasonography were significantly associated with high-grade VUR and then combined into a prediction model with an area under the ROC curve of 0.75 (95% CI, 0.69 to 0.81). Given the pre-specified constraint of achieving at least 85% sensitivity, our model led to the following clinical decision rule: cystography should be performed in cases with ureteral dilation and a serum PCT level ≥ 0.17 ng/mL, or without ureteral dilatation when the serum PCT level ≥ 0.63 ng/mL. The rule had a sensitivity of 86% (95% CI, 74 to 93) with a specificity of 47% (95% CI, 42 to 51). Internal cross-validation produced 86% sensitivity (95% CI, 79 to 93) and 43% specificity (95% CI, 39 to 47).

Conclusions: A clinical decision rule was derived to enable a selective approach to cystography in children with UTI; it predicts high-grade VUR with ~85% sensitivity and avoids half of the cystographies that do not find high-grade VUR.

DEVELOPMENT AND QUALIFICATION OF AN IMMUNODIAGNOSTIC ASSAY FOR THE DETECTION OF 13 *S. PNEUMONIAE* SEROTYPE-SPECIFIC POLYSACCHARIDES IN HUMAN URINE

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Background and aims: To improve detection rates of pneumococcal infection we developed a sensitive multiplex assay that can identify 13 serotype-specific *S. pneumococcal* polysaccharides (PnPS: 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F) in human urine.

Methods: Based on Luminex technology, this assay was developed using microspheres coated with PnP specific monoclonal antibodies (mAbs), to detect all 13 types in a single well of a urine sample. Positivity for a specific serotype was based on cutoff values established from a panel of 400 control urine samples which were calculated relative to a standard curve run on each assay plate. Although designed as a qualitative assay, this method is able to quantify the amount of PnPS in a sample and was qualified to address specificity, accuracy and precision.

Results: The assay was specific in that significant signals were detected only when each polysaccharide was paired with its homologous mAb-coated microsphere. The lower limit of linearity ranged from 0.84-10.1 PnPS U/mL. Qualification experiments showed that the assay has acceptable relative accuracy [bias ratio ($\geq 70\%$ -< 143%) and precision (%RSD: 6.8%-< 30%)]. Preliminary assessments of clinical samples obtained from CAP patients demonstrate that this assay is significantly more sensitive than blood culture in identifying *S.Pn.* serotypes.

Conclusions: Results demonstrate that this assay is a noninvasive, sensitive and reproducible method to detect the presence of *S.Pn.* polysaccharides in urine and has the potential to be a useful diagnostic test to support clinical as well as epidemiological evaluation of pneumococcal disease.

ATOPIC DERMATITIS IN INFANTS: AN IMPORTANT ROLE FOR *STAPHYLOCOCCUS AUREUS* NASAL COLONIZATION

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Objective: *Staphylococcus aureus* is an important pathogen associated with atopic dermatitis. Longitudinal data on nasal colonization with *S. aureus* in infancy was recently described. However the risk of developing atopic dermatitis following nasal colonization with *Staphylococcus aureus* in infants is unknown. Therefore, the objective was to study the association between *Staphylococcus aureus* nasal colonization and atopic dermatitis in infancy.

Design: Population-based prospective cohort study of pregnant women and their children.

Setting: This project was embedded in the Generation R Study in Rotterdam, the Netherlands.

Participants: Postnatal, 1,079 Dutch children participated in the Focus Cohort.

Main exposures: Nasal swabs for *Staphylococcus aureus* cultivation were taken at the age of 1.5, 6 and 14 months.

Main outcome: Questionnaires on atopic dermatitis and confounders (parental eczema, birthweight, gestational age and gender) were obtained pre- and postnatal. The outcome was atopic dermatitis in the first and second year of life.

Results: First positive culture of *Staphylococcus aureus* at 6 months was associated with atopic dermatitis prevalence in the first and second year of life (aOR 2.25 95% CI 1.17-4.30 and aOR 2.59 95%CI 1.34-4.91) and also with severity (aOR 3.30 95%CI 1.68-6.47). Moreover, frequent colonization in the first year of life (≥ 2) held a 4.50 (95% CI 1.04-19.43) fold risk to develop moderate/severe atopic dermatitis in the second year of life.

Conclusion: *Staphylococcus aureus* colonization at 6 months as well as frequent colonization in the first year of life is associated with atopic dermatitis and its severity.

DYNAMICS AND DETERMINANTS OF *STAPHYLOCOCCUS AUREUS* NASOPHARYNGEAL CARRIAGE IN HEALTHY KINDERGARTEN CHILDREN

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Objectives: To describe dynamic pattern, molecular characteristics and epidemiological determinants of *S.aureus* carriage among a healthy community of kindergarten children.

Methods: Children (3-6 years) attending 11 kindergartens were sampled over the school year. 7/11 schools were defined as attended by low socioeconomic level population (LSS) and 4/11 by upper one (USS). *S.aureus* was cultured from sequential nasopharyngeal aspirates in autumn, winter and spring. Identification and methicillin resistance were confirmed by PCR. Susceptibility to other antimicrobials was tested by disk diffusion. Genotyping was performed by *spa* sequencing.

Results: 286/830 (34%) samples yielded *S.aureus* from 185/333 (55%) children. Based on genotype analysis, 40/271 (15%) children were persistent carriers and 117 (44%) intermittent carriers. Temporal carriage distribution was similar between LSS and USS but carriage rate was higher among LSS children (39% versus 29% of samples, RR=1.3, CI[1.1-1.6]). *S.aureus* carriage increased over the school year with highest rate after winter season (25%, 35% and 44% respectively, $X^2=18, p< 0.001$). *Spa* typing showed 89 types grouped into 13 *spa* clonal complexes. Genotypic distribution of MSSA was heterogenous with few clusters identified. Among MSSA carriers, resistance to ≥ 1 antibiotic (other than penicillin) was more common in children attending USS than LSS (53% versus 34%, RR=1.6, CI[1.1-2.3]). Fourteen MRSA were recovered from 11 (3%) children in five schools; none of them carried PVL.

Conclusions: *S.aureus* carriage was high and genotypically diversified among kindergarten children but persistent carriage was less frequent than previously reported. Although carriage was more common in children from LSS, resistance in MSSA seemed associated with upper socioeconomic condition.

**PREVALENCE OF VACCINE-PREVENTABLE INFECTIONS AMONG HIV-INFECTED CHILDREN
IN THE UK AND IRELAND OVER 12 YEARS, 1996-2007**

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Aims: To define the current burden of vaccine-preventable disease among HIV-infected children in the UK and Ireland and to consider the implications for vaccination guidelines.

Methods: Analysis of data on hospitalisations of HIV-infected children routinely reported to the Collaborative HIV Paediatric Study (CHIPS) between 1996 and 2007, with additional retrospective data from 1992.

Results: 15 hospital admissions due to invasive pneumococcal disease (septicaemia or pneumonia) were reported to CHIPS, an incidence rate of 1.7/1000 person years (PY). Of 178 children hospitalised due to varicella zoster virus, 105 (59%) had chicken pox and 73 (41%) zoster; an incidence rate of 11.7/1000 and 8.1/1000 PYs respectively. The incidence of hospitalisation for HIV-infected children with pneumococcal disease was 34 fold higher than that of their healthy counterparts; for varicella it was 240 fold and for zoster 800 fold higher than that of healthy children.

Conclusions: The incidence and total duration of hospitalisation for pneumococcal or varicella disease in HIV-infected children suggests a considerable burden of morbidity from potentially vaccine-preventable diseases. These data will be used to update CHIVA vaccination guidelines to include pneumococcal and varicella as routine vaccinations for HIV-infected children. Subsequent evaluation will assess the impact of these guidelines.

LOW LEVELS OF VARICELLA-SPECIFIC ANTIBODIES IN TREATED HIV-INFECTED CHILDREN RESULTS FROM FAILURE TO REACTIVATE ANTI-VZV MEMORY RESPONSES, RATHER THAN LOWER INITIAL RESPONSES OR ACCELERATED ANTIBODY LOSS

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Background and aims: Varicella usually induces lifelong immunity. However, in immunosuppressed patients, severe and/or recurrent disease has been reported. The aim of this study was to compare VZV antibody titers and avidity between HIV+ children, HIV+ adults and healthy children.

Methods: We analyzed yearly blood samples from 97 vertically infected HIV+ children (541 samples) and 78 adults (440 samples) prospectively collected between 1997 and 2008. An age-matched group of 97 healthy children was also tested. VZV IgG antibody titers and avidity were measured with an in-house ELISA, with/without thiocyanate elution. Evolution of VZV antibody across time was examined using mixed linear models.

Results: VZV IgG antibody titers were lower in HIV+ children (767UI/l) than in HIV+ adults (2603UI/l) ($P < 0.001$) or age-matched healthy children (2302UI/l) ($P < 0.001$). Longitudinal analyses showed that lower antibody titers in HIV+ children -compared to adults- did not reflect a faster antibody decline but weaker initial responses to infection. High HIV viral load and absence of HAART were significantly associated with VZV antibody loss. Despite frequent VZV reactivation, the avidity index (AI) remained lower in HIV+ (2.1) than in healthy children (2.5) ($P < 0.001$).

Conclusion: This study confirms that HIV+ children have weaker antibody responses to VZV than HIV+ adults or healthy children. Failure to maintain protective antibody levels results from impaired primary responses rather than accelerated antibody loss.

ONLY ONE QUARTER OF UK PRIMARY SCHOOL CHILDREN REMAIN SEROPROTECTED AGAINST SEROGROUP C MENINGOCOCCAL DISEASE DESPITE IMMUNISATION IN 1999-2000

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Background: Following vaccination with serogroup C meningococcal (MenC) conjugate vaccine, antibody responses and vaccine effectiveness are sustained in adolescents in contrast to rapid waning in young children. We investigated the persistence of serum bactericidal antibody (SBA) titres in primary school-aged children 6 years following immunisation with MenC vaccine. The response to a Hib-MenC booster was also measured.

Methods: A phase IV clinical trial was done in 250 healthy 6 to 12-year-old children. SBA titres were measured before, 1 month and 1 year after Hib-MenC. The correlate of protection was SBA \geq 1:8.

Results: A SBA \geq 1:8 was observed in 61 of 244 (25% (95% CI: 20% to 30%)) participants (mean age 9.1 years, mean interval since MenC 6.75 years). The proportion with SBA \geq 1:8 increased from 12% (95% CI: 4% to 23%) to 48% (95% CI: 29% to 67%) and the SBA geometric mean titre increased from 2.90 (95% CI: 2.11 to 3.99) to 17.20 (95% CI: 6.80 to 43.5) from a mean age of 7.0 to 12.1 years respectively. One month following Hib-MenC booster, all participants had a SBA \geq 1:8 which was sustained in 99.6% at one year.

Conclusions: Persistence of MenC immunity and response to Hib-MenC booster is dependent on age at priming. As a result of waning antibody, the majority of UK children between 6 and 12 years are likely to have inadequate seroprotection against MenC. A booster would be highly effective in this cohort to sustain population immunity against MenC disease. (ISRCTN 72858898).

ARE BOOSTERS NECESSARY FOR TEENAGERS IMMUNIZED AGAINST HEPATITIS B IN INFANCY?

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Background: Duration of protection against hepatitis B afforded by vaccination remains unknown. However, no routine boosters are recommended. According to references, up to 50% of children lose the post-vaccination immune memory during 15 years after immunization. Aim of the study was to determine the immunity against hepatitis B in 10-12-year old children and to establish indications for routine booster doses.

Material and methods: In 130 children aged 10-12 years, immunized against hepatitis B with recombinant vaccine in infancy (10 µg, schedule: 0-1-2-12 months, first dose at birth) humoral immunity (anti-HBs antibodies) and cellular memory (anamnestic response to booster given in children without protective anti-HBs titers) were determined. Titers of anti-HBs ≥10 IU/l were considered protective. Anamnestic response was defined as increase in anti-HBs concentration from < 10 IU/l to ≥10 IU/l 4 weeks after booster dose. Moreover, markers of HBV infection - past (anti-HBc antibodies) and present (HBsAg) were determined.

Results: Protective level of anti-HBs was found in 102/130 (78%) children, 28/130 (22%) did not have humoral immunity, including 9/130 (7%) with undetectable antibodies. Immune memory was determined in 11 children - anamnestic response was revealed in 8/11 (73%). In total, immunity against hepatitis B was revealed in 110/113 (97%) of children. In 6/130 (4,5%) of participants HBV infection was confirmed according to positive anti-HBc, including 2 (1,5% of the study group) with positive HBsAg.

Conclusions: Most children in the studied group had seroprotection and immune memory against hepatitis B 10-12 years after vaccination. No routine booster seems to be necessary.

VIREMIC SPREAD OF VARICELLA ZOSTER VIRUS (VZV) FOLLOWING VACCINATION AND NATURAL INFECTION

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Background and aims: VZV survives in humans, because it is efficiently transmitted and establishes latency in ganglia. Latency allows VZV to reactivate (zoster) after population growth regenerates a susceptible host pool. Suprabasal cells in the epidermis of VZV-infected hosts uniquely secrete infectious virions. Newly enveloped VZV interacts with mannose 6-phosphate receptors (MPRs) that divert it to endosomes; however MPRs, are downregulated as corneosomes mature. Virions are thus shed from the skin and might also infect intra-epidermal projections of neurons to establish latency. Vaccination enables the role of viremia in delivering VZV to ganglia to be tested. In the absence of viremia, latency would be limited to ganglia innervating the vaccination site.

Methods: We used PCR, in situ hybridization, and immunocytochemistry to detect latent VZV in vaccinated and unvaccinated children autopsied after sudden death, and in surgical gut specimens gut.

Results: No VZV was detected in control samples from patients < 1 year of age without a history of varicella, vaccination, or protective antibodies. In contrast, latent VZV was found bilaterally in ganglia at multiple levels in vaccinated children (80% had trigeminal and lumbar involvement) and in those with a varicella history. Latent varicella was also detected in the gut of children after vaccination or varicella. Wild-type VZV was detected in a subset of vaccinated patients.

Conclusions: Viremia occurs after vaccination; viremia may infect ganglia directly or spread VZV to epidermal sites where subclinical infection provides the virions for transport in nerves to ganglia.

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DEATHS ATTRIBUTABLE TO INVASIVE PNEUMOCOCCAL DISEASE IN THE AGE-GROUP TARGETED FOR VACCINATION AFTER INTRODUCTION OF PREVENAR® IN ENGLAND AND WALES

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Background and aims: Enhanced surveillance of invasive pneumococcal disease (IPD) in England and Wales was initiated following introduction of the 7-valent pneumococcal conjugate vaccine (PCV7, Prevenar®) in September 2006. This study describes IPD-attributable deaths in the 3 years after vaccine introduction.

Methods: All IPD cases reported to the Health Protection Agency in the age-group targeted for vaccination were actively followed-up by telephone and postal questionnaires. For children suspected to have died of IPD, detailed information was requested from clinicians, as well as any post-mortem and inquest reports from the Coroner.

Results: Of the 92 deaths, 68 were IPD-attributable, including 14 due to vaccine serotypes (VT) and 49 due to non-vaccine serotypes (NVT). VT-deaths decreased over the 3 years (10, 2 and 2 cases), while NVT-deaths increased (13, 14 and 22 cases). VT serotypes included 14 (n=4), 18C (n=3), 19F (n=2), 6B (n=2), 9V (n=2) and 23F (n=1), while NVT serotypes included 19A (n=6), 3 (n=6), 7F (n=4), 1 (n=3) and 6A (n=3). Among VT-deaths, only one child with immunodeficiency had been appropriately immunised (one dose at 19 months). Other VT deaths occurred in un-immunised children, of whom 3/13 had co-morbidities and 9/13 were aged >4 months. Among NVT-deaths, 20/49 (41%) had co-morbidities - including congenital heart disease (8/20, 40%), prematurity (5/20, 25%) and neuro-developmental abnormalities (4/20, 20%) - and 35/49 (71%) developed IPD >4 months of age.

Conclusion: Deaths due to serotypes included in Prevenar® are now rare, but there appears to be an increase in deaths due to NVT.

THE ROLE OF *STAPHYLOCOCCUS AUREUS* IN ATOPIC DERMATITIS

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Background and aims: The skin of patients with atopic dermatitis (AD) shows a striking susceptibility to colonization and infection with *Staphylococcus aureus* (SA). In this study we evaluated the pathotype of 116 strains of SA from the skin lesion, healthy skin and nares of children with AD, comparing the results with scorad index. We also analyzed the strains isolated from 106 healthy control subjects and from 84 patients' cohabitants.

Methods: The severity of dermatitis was estimated by SCORAD index (severe AD > 40, moderate AD 15-40, mild AD < 15). Nasal and skin (lesional and nonlesional) swabs cultures for SA detection were obtained from patients. Nasal swabs were taken from their partners and from control subjects. We also determined presence of: agr-group, adhesins and toxins (*cna-sdrC-sdrD-sdrE-clfA-eta-etb-eap-sea-seb-sec-sed-tst*), Leukocidin Pantone-Valentine (PVL) genes by multiplex-PCR, antibiotic resistance with MIC. Genotypes were analyzed by PFGE (Pulsed-Field Gel Electrophoresis).

Results: We didn't find significant differences between patients with high and medium / low scorad; all strains showed virulence genes including, among others, a high percentage of adhesins (86%) that indicates a elevated invasiveness, and a notable spread of toxins (72%), considered important factors aggravating the skin lesions. Furthermore, the same genotype was found in several samples taken from the same patient and from related cohabitants.

Conclusions: Our data confirm the pathogenic role of SA in atopic dermatitis, due to its high virulence and easy intrafamiliar spreading, and suggest the use of an appropriate antibiotic therapy in atopic patients and their cohabitants.

NEONATAL HERPES DISEASE IS STILL UNDER RECOGNIZED

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Background and aims: Herpes infection in the neonate is a rare but potentially severe disease. Neonatal HSV infection localized in skin-eye-mouth (SEM disease) has no mortality after antiviral treatment. Disseminated disease can occur, with visceral organ involvement. CNS infection without other visceral lesion is the third clinical presentation, with poor outcome. The delay to diagnosis is crucial to begin acyclovir and then for final prognosis.

Methods: Retrospective cohort of 17 cases over 20 years.

Results:

	SEM disease	CNS disease	Disseminated form
N° of cases	5	3	9
Age at diagnosis (mean / median)	8.4 / 9 days	15.3 / 18 days	11.8 / 13 days
Vesicles present / Day of appearance	4 / D8 (6-11)	2 / D10 (8-13)	4 / D10 (6-14)
Fever present / Day of appearance	1 / D3	1 / D9	7 / D6 (3-11)
Obstructive dyspnoea or changes in the voice	2	2	2
Median delay to start acyclovir	2 days (0-5)	5 days (0-11)	5 days (1-12)
Mean / median duration of acyclovir treatment	18.6 / 21 days	20.7 / 21 days	17.3 / 21 days (in the 3 survivors)
Recovering/Neurologic sequelae/Death	5/0/0	1/2/(1 at 9 months)	3/0/6
HSV1/HSV2/non-typable HSV	3/1/1	0/3/0	6/3/0

[Table

1]

Diagnosis is delayed up to 12 days after the first signs (fever or vesicles). Raucous voice is reported in 6 cases, but physicians are unaware of these signs.

Conclusions: Severity is confirmed in the CNS and disseminated forms, without any improvement in the recent years. Early clinical diagnosis and thus initiation of acyclovir treatment are necessary for a better outcome. Paediatricians have to be aware of some evocative signs, which are uncommon in newborns.

SYSTEMATIC REVIEW OF THE GLOBAL BURDEN OF NEONATAL GROUP B STREPTOCOCCAL (GBS) DISEASE

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Background and aims: Group-B Streptococcus (GBS) has emerged as a leading neonatal pathogen in developed countries since the late 1960s. Disease incidence has been well described in industrialised countries. However there is a general view that the disease burden is lower in the developing world. There are no recent reviews on the global burden of invasive neonatal GBS disease.

Methods: We systematically reviewed global published and unpublished literature on invasive early and late onset GBS disease from 1970-2009.

Results: Overall there were 161 studies from 44 countries with data on 16,963 neonates with GBS. However, there were only 31 studies with population-based incidence data from 15 countries and only two from Africa and Asia (South Africa, South Korea). The overall median incidence was 0.76/1000 live-births [range 0.0-14.7]. The prevalence of early-onset (EO) and late-onset (LO) disease was 0.71 and 0.12/1000 live-births respectively. Serotypes III (44.8%), Ia (23.5%), V (9%) and Ib (7.6%) were the most frequently identified. Overall 1186 deaths were reported (median case fatality ratio 0.09, range 0-0.92).

Conclusion: Neonatal GBS infection appears to be an important cause of morbidity and mortality globally and preventative strategies should be prioritised. Additional high quality incidence data on EO and LO GBS infection are urgently needed from low-income countries.

LYN CONTROLS THE PI 3-KINASE PATHWAY TO NF- κ B ACTIVATION AFTER STIMULATION OF TOLL-LIKE RECEPTOR 2

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Background and aims: Innate immunity involves pathogen recognition by Toll-like receptors (TLRs). In order to recognize Gram-positive bacteria, fungi or mycobacteria, TLR2 heterodimerizes with TLR1 or TLR6 and triggers MyD88-dependent signaling to induce NF- κ B nuclear translocation. TLR2 also activates a Rac1-PI3-kinase dependent pathway which is essential to the transcriptional activity of NF- κ B. Lyn, a src-tyrosine kinase, modulates PI3-kinase activity in B-cells and was recently involved in innate immunity. We tested the hypothesis whether Lyn contributes to the activation of NF- κ B after TLR2 stimulation.

Methods: THP1 monocytes and HEK 293 expressing TLR2 were stimulated by lipopeptides Pam3 or Pam2,

- i) after incubation with PP2, a chemical inhibitor of Lyn,
- ii) after transfection with a Lyn dead-kinase mutant (LynDK),
- iii) or with a specific siRNA.

We studied the effect of Lyn inhibition on TLR2 pathways with reporter gene methods and ELISA, Western-Blot, Immunoprecipitation and video-imaging.

Results: Inhibition of Lyn by PP2, LynDK or siRNA resulted in a dose-dependent decrease in NF- κ B activity after TLR2 stimulation, and reduced significantly IL6 and TNF α release. Inhibition of Lyn did not alter nuclear translocation of NF- κ B but reduced phosphorylation of its p65 subunit. Moreover, inhibition of Lyn abolished upstream activation of PI3-kinase, without affecting Rac1.

Conclusions: Lyn plays a major role in TLR2 signaling. Lyn activates PI 3-kinase to result in transactivation of NF- κ B subunit p65 and production of proinflammatory cytokines. By identifying Lyn as an actor of innate immune response, this study could bring new strategies for immunomodulation therapies in sepsis.

HEMOLYTIC UREMIC SYNDROME ASSOCIATED TO SORBITOL FERMENTING O157:H- SHIGA TOXIN PRODUCING ESCHERICHIA COLI

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Hemolytic uremic syndrome represents the main cause of acute renal failure in children. The major cause of HUS in children is a potentially preventable food borne infection with Shiga toxin-producing *E. coli* (STEC).

From January 1st 1997 to December 31st 2002, 628 patients < 21 years of age were registered in a prospective multicenter study in Austria and Germany. This prospective multicenter study was performed to evaluate the long term clinical course, the correlation between risk factors in the acute phase, long term outcome of HUS and the influence of different STEC serotypes in the course of disease.

Sorbitol fermenting (SF) O157:H STEC were found in 44 patients. This serotype was associated to a severe acute illness. Statistically significant association ($p < 0.05$, χ^2) between SF O157:H and the presence of bloody diarrhea and hypertension was found when compared to O157:H7 serotypes. From 254 patients with detection of O157:H7 two patients died, and from 44 patients with serotype SF O157:H four patients died ($p=0.005$). This reveals that SF O157:H is at least as aggressive as O157:H7. Patients with SF O157:H associated HUS presented sequelae after one year to a larger extent than patients with O157:H7 serotypes.

HUS is a severe disease not only in the acute phase. Disease progression should be noted as critical too, underlining the importance of long-term followup. The detection of STEC should not be limited to the O157:H7 serotypes, since SF O157:H and other non-O157:H7 serotypes are highly virulent and are associated to severe course of disease.

IMPACT OF RAPID PCR DETECTION OF ENTEROVIRUSES IN SPINAL FLUID IN CHILDREN WITH MENINGITIS

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Background and aims: We hypothesised that use of rapid PCR on enteroviruses in spinal fluid significantly reduces duration of hospitalization and use of antibiotics. Cost reduction due to these differences was also expected.

Methods: The study group comprises children admitted to the hospital in 2009 with confirmed enterovirus meningitis. This group was compared to a historical control group consisting of children with confirmed enterovirus meningitis admitted from 2007-2008. In this control group, results for the PCR were available after 3 to 7 days. Starting 2009 we perform this PCR on enteroviruses in spinal fluid in our hospital, making results available within 3 hours. We analyzed both groups for clinical and laboratory parameters, length of hospital stay, use of antibiotics and estimated overall costs.

Results: There were no differences at baseline. The mean duration of hospitalisation was 6.7 days in the control group (range 2.3-41.0) versus 1.8 days in the study group (range 0.8 - 4.6), a significant difference ($p < 0.0001$). Use of antibiotics was significantly reduced ($p < 0.0001$) from 4.5 days (range 1.3 - 12.8) to 0.8 days (range 0.1 - 1.5). Mean costs per patient were 2055 euro (range 694-12285) in the control group compared to 570 euro (range 240-1365) in the 2009 group ($p < 0.0001$), an average reduction of 1485 euro.

Conclusions: Our data show that use of rapid PCR on enteroviruses results in a significant reduction of hospitalisation and of antibiotic treatment. This leads to an important reduction of hospital costs. Rapid enterovirus PCR is an important diagnostic tool in daily management of children with meningitis.

QUANTIFERON-TB GOLD TEST IN TUBE (QTF) IN THE DIAGNOSIS OF LATENT TUBERCULOUS INFECTION (LTBI) AND TUBERCULOSIS DISEASE (TB) IN CHILDREN

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Aims: To compare agreement between QTF and tuberculin skin test (TST) in BCG vaccinated and non-vaccinated children, and in patients with and without risk factors for TB.

Methods: Multicenter prospective study excluding immunocompromised children. TST and QTF were performed on immigrants, TB contacts and TB patients. Agreement between tests was measured using Kappa coefficient. To compare data ANOVA and chi² test were used.

Results: 459 children were included (318 non-infected, 73 LTBI and 68 TB). Mean age was 4,7±3,6 years. 46% had received BCG. All QTF indeterminate results (20/459; 4.3%) were due to low production of interferon-gamma. 98% of TB cases presented QTF positive results and 99% of non-infected cases QTF negative results. Disagreement between TST and QTF was more frequently observed among LTBI cases (52%; 38/73) compare with non-infected or TB cases (0.7%;3/386) ($p < 0,01$). There were more BCG vaccinated children among LTBI cases with negative QTF (76%) than among LTBI cases with positive QTF (40%) ($p=0,003$). LTBI cases with negative QTF presented smaller TST size (12,7±4,7mm) than LTBI cases with positive QTF (17,9±5,7mm) ($p < 0,01$). Agreement in BCG vaccinated children (kappa 0,47) was lower than in non-vaccinated cases (kappa 0,91) ($p < 0,05$). TB exposed patients presented better agreement (kappa 0,76) than non-exposed (kappa 0,44) ($p < 0,05$).

Conclusions: While agreement of TST and QTF is excellent in TB cases, non-vaccinated children and non-infected patients, we have observed an important number of QTF negative results among LTBI cases, especially in BCG vaccinated children. Agreement is better in cases with risk of TB (exposed children).

MULTIRESISTANT-ENTEROBACTER CLOACAE OUTBREAK IN A NEONATAL AND PAEDIATRIC INTENSIVE CARE UNIT ASSOCIATED WITH MULTIDOSE PACKAGING OF ORAL DRUGS, GERMANY 2009

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Enterobacter (E.) cloacae receives increasing attention as a nosocomial pathogen in neonatal/pediatric intensive care units (NICU). In July 2009 an infant died of sepsis due to a multiresistant *E. cloacae* clone in a 95-bed pediatric hospital, also identified to cause bacteraemia in 2 other children and colonize a further 10. Hygiene measures were intensified for infection control, and the Robert Koch-Institute was invited to assist the outbreak investigation.

We conducted a retrospective matched case-control-study. A case was a child in the NICU from 1/5-5/10/09 with laboratory confirmation of the outbreak clone. Controls were patients staying in the NICU (>72 hours before the case's diagnosis) and swab-negative for the outbreak clone. We used standardized questionnaires to collect demographical and medical information. Matched Odds Ratios (mOR) were calculated by bivariate and multivariable conditional logistic regression. Environmental investigations were conducted.

We identified 31 cases (28 colonized, 3 bacteraemic). 29 matched case-control-pairs were included in the study. Multivariable analysis revealed an association between *E. cloacae* diagnosis and the receipt of oral drugs at bed-side from multidose packaging (mOR=1.8/drug administered; 95%CI 1.17-2.85). No specific drug was identified; microbiological investigation of drugs was negative. A different *E. cloacae* clone was isolated from a glove package.

The multiresistant-*E. cloacae* outbreak was most likely caused by contaminated multidose drug packaging and transmitted via hands. No further cases occurred in the 6 weeks after protocols for handling oral drugs were changed (smaller packaging, patient-based storage, limited circulation-time). Special hygiene attention is necessary when using multidose drug packaging.

SUBOPTIMAL CARE IN THE INITIAL MANAGEMENT OF CHILDREN WHO DIED FROM SEVERE BACTERIAL INFECTION: A POPULATION-BASED CONFIDENTIAL ENQUIRY

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Background and aim: Bacterial infections are a major cause of death in children. As the first stage of a procedure intended to improve quality of care, we studied the frequency and types of suboptimal care and medical errors in children who died of severe bacterial infection (SBI).

Method: This retrospective study analyzed all deaths from SBI in pediatric patients at least 3 months old in a geographic zone of France from 2000 through 2006. The medical files were summarized on standardized forms and then evaluated independently by 2 experts who determined whether the initial management before arrival in intensive care was or was not optimal, in comparison with current guidelines.

Results: Of 23 deaths from SBI, 21 could be analyzed; management was considered suboptimal in 76%. The coefficient of agreement between the experts was high, with a weighted kappa of 0.73. The types of errors identified included parental delay in seeking medical care (33%, 95% confidence interval [12-54]), physicians' delay in administering appropriate treatment (antibiotic therapy in the case of purpura, 38% [16-60]), insufficient doses of or failure to repeat fluid resuscitation (24% [9-35]), and overall underestimation of disease severity (38% [16-60]).

Conclusion: This study found a high frequency of suboptimal care in the initial management of children who died of SBI, with four separate types of errors. Other studies are needed to assess the potential avoidability of this type of death.

MANAGEMENT OF CHILDHOOD TOXIC SHOCK SYNDROME IN THE UK

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Background and aims: A UK national study of toxic shock syndrome (TSS) cases in children under 16 years of age was undertaken between November 2008-December 2009. There is little published data about incidence, management and outcomes in children with this condition.

Methods: Paediatrician and burns unit consultants notified the British Paediatric Surveillance Unit of cases. Questionnaires requesting detailed information on case presentation and progression were sent to notifying consultants. TSS cases were identified as staphylococcal or streptococcal if they met the established criteria used by the US Centre for Disease Control and American Academy of Paediatrics (AAP) respectively.

Results: 40 confirmed and probable cases have been identified to date. There were 10 confirmed and 6 probable staphylococcal cases; 14 confirmed and 10 probable streptococcal cases.

75%(n=30) received treatment in paediatric intensive care facilities. 13%(n=5) required haemofiltration, 70%(n=28) invasive ventilatory support and two-thirds (n=27) inotropic support. All patients received antibiotics, with 63%(n=25) receiving clindamycin and one linezolid. 18%(n=7) received immunoglobulin and 38%(n=15) fresh frozen plasma.

7 children died and 8 had residual morbidity.

Conclusions: This study demonstrates streptococcal TSS to be as common as staphylococcal TSS, in contrast to previous literature.

Mortality rate was 17%. It was noted that proven antitoxin therapies which have been shown to reduce TSST 1 and streptococcal exotoxin A production, such as clindamycin and linezolid, appear underused. In contrast, fresh frozen plasma for which there is little evidence base was used in 2/5 of patients.

This study highlights the need for education on management of TSS.

PHENOTYPIC AND GENOTYPIC CHARACTERIZATION OF ESBLs-PRODUCING *KLEBSIELLA PNEUMONIAE* ISOLATES FROM A PORTUGUESE HOSPITAL

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Background and aims: *Klebsiella pneumoniae* is an important cause of nosocomial and community-acquired infections. The aim of this study was to characterize the phenotype and genotype of *K. pneumoniae* isolates from children attending a Portuguese hospital.

Methods: Forty-seven *K. pneumoniae* isolates were recovered from ten children at Santa Maria Hospital, Lisbon, between 2001 and 2009. Antibigrams were determined by disk diffusion method on Müeller-Hinton agar plates. Molecular typing was performed by M13-PCR fingerprinting. *bla*_{CTX-M} and *bla*_{SHV} were amplified by PCR and sequenced. Replicon typing was made to define plasmid incompatibility groups.

Results: Thirty-nine *K. pneumoniae* isolates were obtained from urine culture and eight from other biological products. Most isolates were from Nephrology (n=20), Surgery (n=8) and Emergency (n=7). Four main antibiotypes were found: R1 to R4, according to antibiotic resistance. Among Nephrology isolates, 20% (n=4) were R1, 65% (n=13) were R3 and 10% (n=2) were R4. In Surgery isolates, 37,5% (n=3) were R1, 37,5% (n=3) were R2 and 25% (n=2) were R3. Among Emergency isolates, 85,7% (n=6) were R2 and 14,3% (n=1) were R3. M13-PCR fingerprinting identified two principal clones: M1, which predominated in Surgery and Emergency, and M2, which predominated in Nephrology. Most isolates produced ESBLs, namely CTX-M-15; the SHV-2a and SHV-11 producing isolates showed plasmids with different replication origin, IncA/C and N, respectively.

Conclusions: Multiresistant isolates of *K. pneumoniae* are disseminated in different paediatric units. The presence of the same clones for eight years might indicate an endemic situation at Santa Maria Hospital.

MULTIDRUG RESISTANT PSEUDOMONAS AERUGINOSA INFECTION IN CHILDREN UNDERGOING CHEMOTHERAPY AND HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Background: *Pseudomonas aeruginosa* (PA), an ubiquitous aerobic gram-negative bacterium and opportunistic pathogen, rarely causes disease in healthy persons but is one of the leading gram-negative organisms associated with nosocomial infections. In particular, bacteremia is a serious and life-threatening event in the immunocompromised host. The increasing frequency of multi-drug-resistant PA (MDRPA) strains is concerning as effective antimicrobial options are limited. Since few data are available on MDRPA in children, we started a multicenter survey in the pediatric hematology oncology Italian network AIEOP.

Design and methods: The participating centers were asked to review all cases of PA bacteremia occurring in their patients undergoing chemotherapy or hematopoietic stem cell transplantation (HSCT) between 2000 and 2008. Data on demographics, diagnosis, chemotherapy, as well as details on isolates and antibiotic in vitro sensitivity, treatment and outcome were collected.

Results: 127 patients with PA bacteremia, documented by isolates from blood, were reported from 12 centers; 30% of isolates were MDRPA. Fatal outcome was observed in 19.6% (25/127) but in patients with MDRPA infection was 35.8% (14/39). HSCT was not an independent risk.

Conclusions: This is the largest series of PA bacteremia cases in children treated in pediatric hematology oncology centers. MDRPA accounting for 30% of PA septicemia, was associated with fatal outcome in 35.8% of cases. Monitoring epidemiology of local bacterial isolates is mandatory and will allow altering empiric antibiotic therapy providing a pivotal contribution to reduce fatalities due to PA infection.

ANTIMICROBIAL SUSCEPTIBILITY AND SEROTYPING OF PNEUMOCOCCI IN A TUNISIAN PAEDIATRIC HOSPITAL

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Streptococcus pneumoniae (*Sp*) is a cause of severe infectious diseases. The majority of invasive and non-invasive diseases were associated with a much smaller number of 90 pneumococcal serotypes known.

Objectives: Antibiotic resistance prevalence and serotype distribution of *Sp* isolates in Tunisia.

Methods: 480 *Sp* strains isolated between January 1998 and August 2009, were studied. Isolates were identified as *Sp* by optochin sensitivity and bile solubility tests. Antimicrobial susceptibility was performed by the disk diffusion method using Mueller-Hinton agar supplemented with 5% defibrinated sheep blood as determined by CA-SFM guidelines. Penicillin susceptibility was determined by oxacillin 5mcg disk screening test. MICs of penicillin G, amoxicillin and cefotaxime were determined by E-test (AB BIODISK). *Sp* ATCC 49619 was used as a control strain. Serotyping was performed by rapid latex agglutination and the capsular reaction test (Statens Serum Institute, Copenhagen). Serotyping concerned only 354 isolates : 210 strains (1998-2004) and 54 strains (2007-2009).

Results: Prevalence of penicillin non-susceptible pneumococci (PNSP) isolates was 53.5%. 41% of them had a low level of resistance. Amoxicillin and cefotaxime resistance concerned 30.1% and 14.3% of isolates respectively. Non-invasive isolates were frequently more resistant to penicillin (58.6%) than invasive ones (46.1%). The most prevalent serotypes were 14 (21.5%), 19F (14.1%) and 23F (10.7%). Serotype 14 was the most frequent in invasive (26.4%) and non-invasive strains (17.6%). 25.2% of PNSP strains (210) belong to serogroup 19 and 24.3% to serotype 14.

Conclusion: Prevalence of PNSP is high in *Sp* invasive isolates. The most prevalent serotype is 14.

EXTENDED SPECTRUM BETA LACTAMASE (ESBL) PRODUCING BACTERIA IN A TERTIARY CENTRE

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Background and aims: The spread of ESBL in nosocomial and community-acquired enterobacteria is an important challenge for clinicians as the therapeutic options are limited. The aim was to evaluate diagnosis, risk factors and outcome of children with ESBL infections.

Methods: Retrospective analysis of children with identified ESBL+, in a tertiary centre between 2007 and 2009.

Results: During the study period a total of 1870 *E. coli* and 132 *Klebsiella* spp were assessed for ESBL phenotype and were detected in 29: *E. coli* 5 (0.3%) and *Klebsiella* spp 24 (18%), from 23 children, 14 male, with a median age of 12 months (7days-15years). *Klebsiella* spp was isolated mainly in gastrostomy/wound exudates and respiratory secretions. *E. coli* was found mainly in urine. Three children were previously healthy. The remaining had underlying conditions, namely nephro-urologic malformations (7), biliary atresia (3) and short bowel syndrome (3). Other identified risk factors were: hospitalization (15), use of antibiotics (16), invasive ventilation (12), central line catheter (12) and surgery (9). Of the 29 isolates, 12 were colonisations and 17 infections: urinary tract infections (7), respiratory infections (3), sepsis (3), colangitis (2), peritonitis and wound infection (1 each). The median time between admission and infection was 12 days (1day-5months); 5 were community-acquired. Three children died. The median length of stay was 23 days (4days-10months). There were no outbreaks.

Conclusions: Most children with ESBL infections had risk factors. The main diagnoses were urinary tract and respiratory infections. There was a high mortality and long hospital stay.

CLINICAL CHARACTERISTICS AND OUTCOMES OF PATIENTS WITH ENTEROCOCCI BACTERAEMIA: A FOUR-YEAR RETROSPECTIVE EVALUATION

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Background and aim: Even if enterococci are an important member of normal human microflora, they have an important role in nosocomial infections. In the last decade, enterococcal infections have grown in importance because of the increasing number of cases; and their incremental antibiotic resistance rates. The purpose of this study was to assess the risk factors and outcomes of enterococcal bacteraemia in children.

Methods: A retrospective review of demographic, microbiological and clinical data in children with bacteraemia due to *Enterococcus* spp. at Eskisehir Osmangazi University Hospital from 2004 to 2008 was carried out.

Results: A total of 49 children (27 boys, 22 girls) aged between 0-16 years were included. Univariate analysis showed that intensive care unit stay, mechanical ventilation requirement, urinary catheterization, indwelling catheter, presence of neutropenia and total parenteral nutrition infusion were found to be associated with mortality associated enterococcal bacteriemia. Regarding the high level gentamycin resistance, neutropenia and indwelling catheter were found to be associated with high level gentamycin resistance. When we specially focused on newborn group, previous hospitalization and umbilical catheterization were found to be associated with high level gentamycin resistance. Presence of enterococcal bacteremia is one of the major findings of the newborns which required double-volume exchange transfusion.

Conclusion: *Enterococcus* spp. bacteremia is associated with high mortality and the appearance of high-level gentamicin resistance have been clearly associated with intensive care unit stay and other contributors in intensive care.

MACROLIDE SUSCEPTIBILITY OF *STREPTOCOCCUS PNEUMONIAE* IN GERMANY (1992-2008)**M. Imöhl**¹, R.R. Reinert², M. van der Linden¹¹*Institute of Medical Microbiology & National Reference Center for Streptococci, University Hospital RWTH Aachen, Aachen, Germany,* ²*Wyeth Vaccines Research, Paris La Défense, Paris, France*

Background: The aim of this study was to evaluate the macrolide susceptibility of all *S. pneumoniae* isolates with invasive pneumococcal disease (IPD) that were sent to the German National Reference Center for Streptococci between 1992 and 2008 and to evaluate trends in nonsusceptibility over time. The study was undertaken against the background of an impression of actually declining macrolide resistance rates.

Methods: A population and laboratory based surveillance study was conducted to collect data about macrolide susceptibility of invasive pneumococcal disease. Minimal inhibitory concentrations (MIC) testing was performed using the broth microdilution method as recommended by the CLSI.

Results: Data on macrolide susceptibility were available for 11,808 isolates from IPD. The overall nonsusceptibility rate of all isolates was 16.3% (intermediate (I), 0.3%; resistant (R), 16.0%). Among the most frequent serotypes, highest serotype specific nonsusceptibility resistance rates were observed for the serotypes 14 (69.7%), 6B (33.2%), 19F (26.5%) and 19A (26.1%). Higher resistance rates were observed among children (I, 0.2%; R, 23.8%) than among adults (I, 0.3%; R, 13.4%). Concerning childhood IPD isolates, maximum nonsusceptibility rates during the period under study were observed in 2005 (I, 0.3%; R, 32.3%), while in 2008, 0.0% of isolates were intermediate and 15.2% resistant. Adult IPD isolates maximum nonsusceptibility rates were observed in 2005 also (I, 0.0%; R, 18.6%). Nonsusceptibility rates in 2008 were 0.1% (intermediate) and 12.9% (resistant).

Conclusions: After a continuous increase of macrolide nonsusceptibility in Germany reaching maximum values in 2005, a considerable decrease especially concerning childhood nonsusceptibility was noticed until 2008.

COLONIZATION OF BURN WOUND AND CHANGES OF ANTIBIOTICS RESISTANCE IN PEDIATRIC BURN UNIT

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Background and aims: Bacterial infection remains a major problem in the management of burn victims. Nosocomial infection of *Acinetobacter* species and multi-drug resistant species are major obstacles in treatment of burn. This study is aimed at understanding colonization of burn wound and patterns of antibiotics resistance and choosing the effective antibiotics where MRSA and VRE are increasing in pediatric burn unit.

Methods: Identification of bacteria and antimicrobial susceptibility test were performed in 918 strains(427 children below 15 years old) of positive burn wound culture results. This study was designed retrospectively to investigate the pattern of burn wound colonization and antimicrobial resistance from January 1999 to December 2005 in Hangang Burn Center Korea.

Results: This study revealed that *Pseudomonas aeruginosa*(44.7%) was the most frequently isolated organism. Next were CNS(16%), *Staphylococcus aureus*(14.3%), and *Enterococcus* species(10.4%). *Pseudomonas aeruginosa* was resistant against cephalothin(98.6%), cefepime(69.0%), and ceftazidime(66.2%). The incidence of oxacillin resistance among CNS(89.5%) and *S. aureus*(80.1%) was high. *Staphylococci* was susceptible to vancomycin(99.7%) and teicoplanin(98.2%). For *Enterococcus*, teicoplanin(100%) and vancomycin(97.7%) were the most effective drug. *Acinetobacter* species was resistant to ampicillin-sulbactam(100%), ampicillin(93.9%), gentamicin(85.0%), aztreonam(80.9%) and piperacillin(80.0%).

Conclusions: *Acinetobacter baumannii* was isolated and showed multi-drug resistance but was susceptible to imipenem(33.3%). The spectrum of infective agents varies from time to time. Therefore, we need effective surveillance system for the resistant organisms to control the infection. *Acinetobacter* species rapidly change to multi-drug resistant organism. To prevent infection from various resistant strains, effective antimicrobial treatment is needed with careful surveillance of nosocomial infection.

DETECTION OF E.COLI AND KLEBSIELLA PNEUMONIAE RESISTANT TO CARBAPENEMS AND GENES OF RESISTANCE IN CHILDREN WITH UTI

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Introduction and objectives: Infection by Enterobacteriaceae which are resistant to carbapenems is challenging problem in health care centers. The correct monitoring of patients for treatment by carbapenems was one of the most significant considering in this study.

Methods: The urine samples of patients were gathered during six months. E.coli and Klebsiellae strains were detected. Susceptibility testings such determining of MIC and agar diffusion agar were performed for meropenem and imipenem for these strains and then carbapenemase coding gene detected by PCR method.

Results : 197 strains isolated fro urine samples in which 138 E.coli and 58 Klebsiella pneumoniae were detected . 5 strains of E.coli (3.6 %) and 3 strains of Klebsiella (5.1%) were resistant to Imipenem and Meropenem and then kpc2 and kpc3 genes of their resistance were detected by PCR.

Conclusion: There is no any comprehensive program for screening of resistant strains of bacteria to carbapenems in our country and worldwide but epidemiologic increasing of these strains should be considered.

STUDY OF RESISTANCE PHENOTYPES AND BETA-LACTAMASES GENOTYPES IN ENTEROBACTERIACEAE STRAINS IN CHILDREN WITH ACUTE DIARRHEA SYNDROME

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Background and aims: Strains with decreased sensibility to β -lactams have been selected in the last years in our geographic area. Identification of the *Enterobacteriaceae* resistance phenotypes and β -lactamases genotypes in Dr Victor Babes Hospital, Bucharest (SVB), over Feb 1st-Aug 31, 2009.

Methods: Standard stool cultures for *Enterobacteriaceae* isolation were collected from children 0-4 years with acute diarrheal syndrome hospitalized in SVB. We have used: standard diffusimetric method (CLSI 2009, *E. coli* ATCC 25922) for antibiotic sensitivity testing, double disk diffusion for ESBL screen, PCR detection of *bla* genes, DNA sequencing using ABI Avant 3100 system and the programs BioEdit and BLAST for result's interpretation.

Results: There were isolated 67 bacterial strains from 884 subjects. The etiology was: verotoxic *E. coli*/VTEC/6 strains; enteropathogenic *E. coli* /EPEC/18; *Salmonella* BO/10; *Salmonella* DO/9; *Salmonella* CO/4; *Shigella Flexner*/3; *Shigella sonnei* "S"/ 2; *Klebsiella pneumoniae*/9; others/6.

Resistance pattern was: 3/23 *Salmonella* at ampicillin, 1 ESBL(+) *Shigella flexneri*, 12/24 *E. coli* (EPEC,VTEC) at ampicillin, 1 ESBL(+) EPEC, 5/9 ESBL(+) *Klebsiella pneumoniae*. The resistance genotypes were analyzed in 9 strains (*E. coli*/2, *K. pneumoniae*/7) and the results were: *bla*_{TEM}: 1, *bla*_{SHV}: 1, 11, 14, *bla*_{CTX-M}: 3, 15. In *E. coli* was identified the association of *bla*_{TEM1} and *bla*_{CTX-M15} and in *K. Pneumoniae* we have found: *bla*_{TEM} 1(7), *bla*_{SHV} 1(3), *bla*_{SHV} 11 (3), *bla*_{SHV} 14 (1), *bla*_{CTX-M} 3 (2), *bla*_{CTX-M} 15 (5).

Conclusions: 23/67 strains have a resistance phenotype to one β -lactams and the 9/67 strains have more *bla* genes. The strains carrying *bla*_{CTX-M} are concomitant *bla*_{TEM1} carrier.

INVESTIGATION OF MULTIDRUG , HIGH LEVEL GENTAMICIN RESISTANCE AND AAC (6')-IE-APH (2'')-IA GENOTYPE AMONG ENTEROCOCCAL ISOLATES IN IRAN

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Background: During the last decade, enterococci have become important nosocomial pathogens. This increasing prevalence has been paralleled by the occurrence of multi-drug resistant (MDR) and high level gentamicin resistant (HLGR) strains.

Methods: From September 2005 to 2006, a total of 638 enterococcal isolates were collected from 9 medical centers in Tehran among adults and children. Confirmation of genus, species and detection of gentamicin resistance genes accomplished by PCR method. Antimicrobial susceptibility test was determined with disk diffusion and minimal inhibitory concentration (MIC) of HLGR isolates was assayed by microdilution methods.

Results: The isolates were found to consist of *Enterococcus faecalis* (77.8%) and *Enterococcus faecium* (22.2%). Multi-drug resistance to most prevalent antimicrobials was present in 29% and 72% of the *E. faecalis* and *E. faecium* isolates, respectively. HLGR phenotype was detected in 64% of *E. faecalis* and 92% of *E. faecium* isolates. The *aac* (6')-*le-aph* (2'')-*la* gene were identified in 83% of *E. faecalis* and 100% of *E. faecium* HLGR isolates.

Conclusion: The resistance to several antimicrobials and high level resistance to gentamicin shown by enterococcal strains obtained in this study is of concern because of the decrease in the therapeutic options for treatment of infections caused by enterococci. There was a strong association between high level gentamicin resistance and the *aac* (6')-*le-aph* (2'')-*la* gene. The high prevalence of MDR and HLGR enterococcal strains obtained, revealed the emergence of effective antibiotic therapy for enterococcal infections that should be based on accurate antimicrobial susceptibility tests and species identification.

CO-ADMINISTRATION OF AS04-ADJUVANTED HUMAN PAPILLOMAVIRUS-16/18 VACCINE WITH HEPATITIS B VACCINE IN HEALTHY FEMALE SUBJECTS AGED 9-15 YEARS: MONTH 7 DATA

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Background and aims: This randomised, open, controlled, multicentre study (111507/NCT00652938) evaluated co-administration of GlaxoSmithKline Biologicals' human papillomavirus-16/18 AS04-adjuvanted vaccine (HPV) and hepatitis B vaccine (HepB). Co-primary objectives were to demonstrate non-inferiority of hepatitis B and HPV-16/18 immune responses at Month 7 for co-administered vaccines, compared with vaccines administered alone, in the according-to-protocol cohort.

Methods: Healthy female subjects, age 9-15 years, were randomised to receive HPV (n=247), HepB (n=247) or HPV co-administered with HepB (HPV+HepB; n=247) at Months 0, 1 and 6. Immunogenicity was evaluated at Months 0, 2 and 7. Solicited and unsolicited symptoms were reported for 7 and 30 days after each dose, respectively. Safety was evaluated throughout the study.

Results: At Month 7, the hepatitis B immune response was non-inferior for HPV+HepB compared with HepB alone for anti-HBs seroprotection rates (97.9% versus 100%, respectively). Anti-HBs geometric mean titers (GMTs) [95% CI] were 1280.9 [973.3-1685.7] and 3107.7 [2473.1-3905.1] mIU/mL, respectively. The HPV-16/18 immune response was non-inferior for HPV+HepB compared with HPV alone for seroconversion rates (99.0% and 100% for anti-HPV-16; 99.5% and 100% for anti-HPV-18, respectively) and for GMTs [95% CI] (19819.8 [16856.9-23303.6] and 21712.6 [19460.2-24225.6] ELU/mL for anti-HPV-16; 8835.1 [7636.3-10222.1] and 8838.6 [7948.5-9828.4] ELU/mL for anti-HPV-18, respectively). Incidence and nature of solicited local and general symptoms, and unsolicited symptoms, were similar when vaccines were co-administered or given alone. No vaccine-related SAEs were reported.

Conclusions: Results support co-administration of HPV-16/18 AS04-adjuvanted vaccine with hepatitis B vaccine in females aged 9-15 years.

MACROLIDE RESISTANCE PHENOTYPE AND DETERMINANTS OF HIGH-LEVEL MACROLIDE-RESISTANT *STREPTOCOCCUS PYOGENES* ISOLATED FROM CHINESE CHILDREN AND THE RELATIONSHIP WITH TN6002

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Background: A high prevalence of macrolide resistance *Streptococcus pyogenes* (*S. pyogenes*) in Chinese children have been reported.

Aim: This study investigated the resistance phenotype and determinants and the relationship between Tn6002 on the 191 clinical isolates with MIC of over 512 ug/ml for erythromycin in Chinese children during 2007-2008.

Methods: Resistance genes *ermB*, *ermTR*, *mefA*, *tetM*, *tetO*, *int*, *xis* genes were detected, and two special fragments of Tn6002 were analyzed by sequencing. The emm type and pulsed-field gel electrophoresis were performed to analyze the strains.

Results: Among the isolates, 87.93% of them were resistant to telithromycin; 92.63% were resistant to tetracycline; None of the isolates was resistant to penicillin G, ceftazidime, levofloxacin, and trimethoprim-sulfamethoxazole. All the isolates belonged to the cMLS phenotype. Of the 191 strains, 95.81% (183/191) had the *ermB* gene; 4.19% (8/191) of the isolates contained the *ermTR* gene; but *mefA* was not detected. Among the *ermB* positive strains, 92.35% (169/183) of them carried the *tetM* gene and 93.99% (172/183) was positive for the *int* or *xis* genes. *ErmB*, *tetM*, *int*, and *xis* gene positive profile accounted for 86.91%(166/191) of them, which all carried the special fragments of Tn6002. emm12 and emm1 were the most prevalent types, with the PFGE type of H and A, respectively.

Conclusions: This study indicated that there was a high prevalence of the transposon Tn6002 that carries *ermB* gene among the high-level macrolide-resistant *S. pyogenes* from Chinese children.

RAPID ANTIBIOTIC RESISTANCE DETERMINATION AND GENOTYPING OF *MYCOPLASMA PNEUMONIAE* BY PYROSEQUENCING

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Background and aims: *Mycoplasma pneumoniae* is a common cause of respiratory tract infections in children. The first choice antibiotics for treatment of these infections are macrolides. However, several recent studies have indicated that the prevalence of macrolide-resistance, determined by defined point mutations in the bacterial 23S rRNA, is increasing among *M. pneumoniae* isolates. It is obvious that methods allowing rapid detection of macrolide-resistance can be highly valuable for clinical decision-making. In this study, we set out to determine the utility of pyrosequencing as a technique to assess macrolide-resistance.

Methods: By pyrosequencing, a short DNA sequence is determined in real time, using a PCR fragment as template. We applied this technique on two 23S rRNA gene targets and on a target within the P1 gene of *M. pneumoniae*. While the first two targets are employed to determine macrolide-resistance, the latter is used for subtype classification. The three assays, which can be performed in a single run, were applied on a collection of 120 clinical *M. pneumoniae* isolates.

Results: For each strain, the three targets were readily amplified and sequenced. Two strains were found that harbored a point mutation associated with a macrolide-resistant phenotype. The subtype classification corresponded completely with known sequence information. All pyrosequencing data were obtained within ~15 min after the start of the sequencing run.

Conclusions: Pyrosequencing is a highly valuable technique for both genotyping of *M. pneumoniae* and rapid detection of macrolide-resistance, which is of ultimate importance in controlling *M. pneumoniae* infections.

IMMUNOGENICITY OF PHiD-CV 3-DOSE PRIMARY VACCINATION CO-ADMINISTERED WITH PEDIACEL™ OR INFANRIX HEXA™ IN THE NETHERLANDS

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Background and aims: Pneumococcal non-typeable *Haemophilus influenzae* protein-D conjugate vaccine (PHiD-CV; GlaxoSmithKline Biologicals) has been co-administered with various paediatric vaccines.¹ This study (110142/NCT00652951) evaluated co-administration of PHiD-CV with DTPa-IPV-Hib (*Pediacel*™; Sanofi Pasteur MSD).

Methods: In this single-centre, single-blind study in the Netherlands, infants were randomised (1:1:1) for PHiD-CV and DTPa-HBV-IPV/Hib (*Infanrix hexa*™; GSK Biologicals; Group 1;n=260), PHiD-CV and DTPa-IPV-Hib (Group 2;n=260) or 7vCRM (Pfizer) and DTPa-IPV-Hib (Group 3;n=260) at 2-3-4 months of age. The primary objective was to demonstrate non-inferiority of the immune response 1 month post-dose 3 in Group 2 compared with Group 1 using 22F-inhibition ELISA (pneumococcal serotypes) or anti-protein D ELISA.

Results: Non-inferiority of Group 2 versus Group 1 was demonstrated for protein D and all vaccine pneumococcal serotypes except 18C. For 18C, the upper limit of the 95% CIs for the antibody GMC ratio between groups marginally exceeded the predefined non-inferiority limit of 2. For each vaccine pneumococcal serotype including 18C, percentages of infants reaching ELISA 0.2µg/mL were in the same ranges for both PHiD-CV groups.

Conclusions: Antibody responses elicited by PHiD-CV co-administered with DTPa-HBV-IPV/Hib or DTPa-IPV-Hib were comparable for all vaccine pneumococcal serotypes except 18C. However, as high proportions of infants reached ELISA antibody concentrations ≥0.2µg/mL for all vaccine pneumococcal serotypes, this may be of low clinical relevance.

Reference: 1.Schuerman, Prymula. *Exp Rev Vaccines* 2009;8:1479-500

MACROLIDE RESISTANCE ASSOCIATION WITH GROUP A STREPTOCOCCUS *EMM* TYPES IN LATVIA

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Group A streptococcus (GAS) is a strictly human pathogen that infects individuals of all ages with symptoms ranging from a carrier state to mild or acute pharyngotonsillitis and invasive disease. During the last years treatment of GAS pharyngitis has emerged as a critical issue due to the increased resistance to macrolides. The genetic diversity of GAS isolates correlate with macrolide resistance.

Objective: To identify GAS *emm* types and macrolide resistance rates among pediatric GAS isolates collected from outpatients throat cultures in Children's Clinical University Hospital.

Materials and methods: GAS strains were isolated from pharynx of outpatients having acute pharyngitis symptoms from July 2002 to April 2007. Antimicrobial resistance of the isolates was determined as described in CLSI standarts. Antimicrobial resistance genes (*ermA*, *ermB* and *mefA*) were detected by amplification of streptococcal DNA with specific primers. GAS *emm* types were established by sequencing.

Results: High level of resistance to macrolides was found - 75 isolates out of 96 (78%) were resistant to clindamycin and erythromycin, all strains were sensitive to vancomycin, linezolid, penicillin and ceftriaxone.

Eight *emm* types were identified among first 39 tested GAS isolates, the most common type being 89.0 (29/39; 74%) followed by 77.0 (3/39; 7%). Resistance to macrolides was found in 28 (99%) 89.0 *emm* type strains.

Conclusion: There is extremely high GAS resistance to macrolides - 78% (n=75).

emm type 89.0 accounted to be the most common and for the highest percentage of macrolide resistance.

INTRAMEDULLARY SPINAL CORD ABSCESS. PATHOPHYSIOLOGY AND OUTCOMES**M. al Barbarawi, W. Khraisat***Jordan University of Science and Technology, Irbid, Jordan*

Intramedullary spinal cord abscess in children is extremely a rare infection of the central nervous system; and probably a devastating neurological condition. Clinical awareness of patients at risk is crucial for early diagnosis and intervention as this entity is one of the treatable conditions of paraparesis. Association with congenital neuro-ectodermal abnormality in children is frequent. This pathology high lights the importance of complete neurological checks of infants as a part of their routine physical examination and early management of patients with congenital dermal sinus, prophylactic surgical resection of such a congenital anomaly is recommended by most authors to prevent serious infections of the central nervous system. However, once the abscess is established; immediate surgical drainage along side adequate antibiotics should be instituted. This may guarantee improving neurological outcome.

In this communication the authors present their experience with four cases of intramedullary spinal cord abscess in children treated successfully with surgical drainage, intravenous antibiotics and neuro rehabilitation between 2001 and 2006 and discuss their results. We concluded that early diagnosis and treatment is essential; before a devastating mechanico-vascular insult of the spinal cord is established from rapid formation of the abscess and a swift expansion of the spinal cord within the limited intraspinal space.

INFECTIVE ENDOCARDITIS IN BOY AFTER CIRCUMCISSION

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Background: In Kosova circumcision usually is performed for cultural reasons, rare is performed for reducing the risk of urinary infections, treating of phimosis or balanitis. Complications after circumcision are rare and include bleeding, infection, meatal stenosis, and potentially include sepsis. In children with congenital heart disease exist very high risk for bacterial endocarditis.

Aim of presentation is presenting the boy with bacterial endocarditis after cultural circumcision.

Presentation: 6 years old boy, with mild pulmonary stenosis, 7 days after circumcision with normal local status of circumcision, started to have high fever, night sweats, fatigue, myalgia and arthralgia, headache and dyspnea. By auscultation tachycardia and very quiet heart murmur was noted. After two days heart failure was expressed. In lab erythrocyte sedimentation rate (ERS) and C-reactive protein (CRP) and WBC were increased. From haemoculture three times was isolated *Streptococcus faecalis*. The same bacteria was isolated from region of circumcision. By cross-sectional echocardiography in level of pulmonary valve was identified vegetation of endocarditis and causing severe pulmonary stenosis and insufficiency. Child was treated 6 weeks by two antibiotics according to the antibiogram.

Conclusion: In country where the circumcision is often performed for cultural reasons prophylaxis of bacterial endocarditis is strongly obligated, especially in nondeveloping countries.

LEMIERRE'S SYNDROME CAUSING SEVERE MASTOIDITIS AND EXTENSIVE INTRACRANIAL COMPLICATIONS?

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Introduction: Lemierre's Syndrome can be a life threatening condition and was first described in the 1930s as a rare illness consisting of oropharyngeal infection, thrombophlebitis of the internal jugular vein, and systemic metastatic infection. We discuss an atypical case of this disease and emphasize the need for a high index of suspicion for Lemierre's Syndrome in order to initiate appropriate investigations and treatment.

Case presentation: A highly irritable 4-year-old girl presented to A&E with a severe left otitis media after receiving oral antibiotics. She rapidly deteriorated despite initiation of IV co-amoxiclav and ceftriaxone. CT head scan demonstrated mastoiditis and extensive thrombosis of the cavernous sinuses and internal jugular vein. Antibiotics were changed to meropenem, she underwent corticomastoidectomy and started anticoagulation. MRI head scan additionally revealed skull base osteomyelitis, narrowing of left internal carotid artery (ICA) and cerebral infarcts. She improved on 3 weeks of IV meropenem and clindamycin, and was discharged on oral clindamycin and ciprofloxacin, still continuing anticoagulation. Follow-up MRI demonstrated complete occlusion of the left ICA. All cultures were negative. 16S PCR on mastoid tissue subsequently demonstrated *Fusobacterium Necrophorum*.

Conclusion: This case highlights the challenges in diagnosing and treating Lemierre's Syndrome. It remains unclear and worth discussing whether this life threatening condition with its extended intracranial lesions was exclusively due to *Fusobacterium Necrophorum*, a known opportunistic pathogen, or the consequence of a different microbial entity. We advocate a high index of suspicion for this rare syndrome and early instigation of appropriate treatment and specialist diagnostic tests where required.

COMBINED HAPLOTYPES OF PROTEIN C AND ENDOTHELIAL PROTEIN C RECEPTOR ASSOCIATE WITH PROTEIN C LEVELS IN CHILDREN WITH MENINGOCOCCAEMIA

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Background: Meningococcal disease may present as sepsis, meningitis or a combination of both. Protein C (PC) is activated by binding to the endothelial PC receptor (EPCR). A soluble form of this receptor (sEPRC) inhibits both activated PC activity and PC activation by competing for PC with membrane-associated EPCR. One polymorphism in the EPCR gene (4678G/C) and two polymorphisms in the PC gene promoter (-1654C/T and -1641A/G) have been shown to affect PC levels. In patients with meningococcal sepsis, decreased PC levels have been correlated with severity and poor outcome. This prospective study examined the relationship between protein levels of the coagulation pathway on day 1 and EPCR and PC haplotypes.

Methods and results: 54 previously healthy children with meningococcal infection admitted to St. Mary's Hospital, London, between January 1998 and November 2000, were included in this study. Out of 8 possible combinations, six variants were found. The haplotype combination PC(-1654T - 1641A) with EPCR haplotype A1 (4678G), both of which have been shown to be associated with higher PC levels in controls, was significantly associated with approximately a 50% increase of PC levels when adjusted for age (0.31 vs. 0.20 IU/ml, P = 0.004).

Conclusions: This study provides the first evidence that it is rather an interaction between alleles of protein C and EPCR than single gene haplotypes, which influences levels of protein C in meningococcal sepsis.

THE A1A1 GENOTYPE OF ENDOTHELIAL PROTEIN C RECEPTOR ASSOCIATES WITH BLOOD PRESSURE AND OUTCOME IN CHILDREN WITH MENINGOCOCCAEMIA

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Background: Meningococcal disease may present as sepsis, meningitis or a combination of both. Protein C (PC) is activated by binding to the endothelial PC receptor (EPCR). A soluble form of this receptor (sEPRC) inhibits both activated PC activity and PC activation by competing for PC with membrane-associated EPCR. Three haplotypes of the EPCR gene have been described, the A1 haplotype is tagged by the rare allele of the 4678G/C polymorphism. This haplotype has been shown to affect PC levels and outcome in MI. In patients with meningococcal sepsis, decreased PC levels have been correlated with severity and poor outcome. This prospective, multicentre study examined the relationship between meningococcal disease and EPCR haplotypes.

Methods: Blood samples and clinical information of 419 previously healthy children with meningococcal infection were collected from 107 paediatric hospitals in Germany, Switzerland, Italy, and Austria between 2000 until 2008. The EPCR (4600A/G and 4678G/C) polymorphisms were analysed in all subjects using a TaqMan assay.

Results: Subjects homozygous for the EPCR A1 allele showed higher systolic (SBP) and diastolic (DBP) blood pressure nadirs during their stay in the PICU (86 vs. 77 mmHg SBP, $P = 0.008$ and 46 vs. 40 mmHg DBP, $P = 0.022$) and a markedly reduced fatality rate (0.014 vs. 0.086, $P = 0.026$, OR= 6.9 (95% CI = 1- 51)).

Conclusions: This study provides the first evidence that the same EPCR haplotype associated with higher PC levels and favourable outcome in MI also strengthens cardiovascular response and survival in meningococcal sepsis.

BACTERIAL BLOOD-STREAM INFECTIONS IN NEUTROPENIC CHILDREN WITH HEMATOLOGIC/ONCOLOGIC DISORDERS AT A TERTIARY CARE CENTRE IN SAUDI ARABIA

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Background: The aim of this study is to determine predominant pathogens and their susceptibility patterns among our pediatric neutropenic patients for proper selection of empiric antibiotic therapy.

Methods: Retrospective chart review of pediatric patients with hematologic/oncologic disorders with bacteremia between January 1998 and December 2008. Demographic data, underlying diseases, bacterial isolates, and antibiotic susceptibility were analyzed.

Results: One thousand eight hundred and eighty nine (1889) bacteremia episodes were identified. Gram negative bacteria (GNB) were more frequently isolated causing 954 episodes (51%). Of these, *E. coli* (23%), *P. aeruginosa* (21%), *K. pneumoniae* (18%), *Enterobacter* spp (7.9%), and *S. maltophilia* (7%). Seventy four percent of GNB were susceptible to piperacillin/tazobactam, 66% to ceftazidime, 66% to gentamicin and 41% to piperacillin. Eighty-seven percent of those tested were sensitive to imipenem/meropenem.

Gram positive bacteria (GPC) caused 935 episodes (49%). Of these, coagulase negative staphylococcus was the most frequent (30%), followed by *S. aureus* (24%), *S. pneumoniae* (17%), viridans streptococcus (13%), and *Enterococcus* spp (10%). No VRE was isolated.

Conclusion: Our results concur with observations of other studies that GNB is emerging as major cause for bacteremia in children with cancer. This supports not including vancomycin in the initial empiric therapy for febrile neutropenic patients. Further, there is a potential need for better utilization of conjugate pneumococcal vaccine to decrease the incidence of invasive pneumococcal diseases in our patient population.

BACTERIAL MENINGOENCEPHALITIS WITH DOUBLE AETIOLOGY IN CHILDREN**S.C. Cambrea¹, M.M. Ilie², S. Diaconu², C.N. Rugina³, E. Vasiliu⁴**

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Bacterial meningitis is an important serious illness worldwide. Tuberculous involvement of the central nervous system (CNS) is an important and serious type of extra-pulmonary involvement. It has been estimated that approximately 10% of all patients with TB have CNS involvement. In developing countries CNS tuberculosis is a disease of younger age group, usually childhood. The high morbidity and mortality of tuberculous meningoencephalitis (TBM) warrants an early diagnosis and treatment. On the other hand acute bacterial meningitis in children is a relatively frequent disease. Bacterial meningitis with double aetiology Mycobacterium tuberculosis and other bacteria were disease very rare in clinic.

In Constanta County in the last 3 years (2007-2009) we noticed presence of 6 cases of TBM in children with age between 6 months and 6 years. We present three cases of children aged of 6 months, 3 years and 5 years with meningitis with double bacterial aetiology: tuberculous and other bacteria (*Neisseria meningitidis* - 2 cases and *Streptococcus pneumoniae* - case). Two children were vaccinated BCG and another one wasn't. We analyze aspect of cerebrospinal fluids, electroencephalography (EEG), hemogram and inflammatory tests from blood and cerebral CT/MRI examination.

Diagnosis of TBM was delayed in all cases. Internal hydrocephalus was present in two cases since first days of hospitalization and in third case was noticed later. Ventriculoperitoneal shunt was performed in two cases. In all these cases we registered important neurologic deficits; in one case neurologic deficits recovered, and in other two cases neurologic sequelae were severe and definitive invalidant.

HIB VACCINATION IMPACT ON MORTALITY FROM INVASIVE DISEASES IN UKRAINIAN CHILDREN

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Immunologic prevention of Hib infection was included into Ukrainian Vaccination Calendar at the end of 2006. By the end of 2007 Hib vaccination inclusion in Ukraine was 47%-75% in different regions.

We studied Hib vaccination efficacy in decrease of mortality in children from invasive diseases.

Hib vaccination was performed under scheme 3, 4, 5 months with booster in 18 months. Ministry of Health official statistics was used to make conclusion about index of mortality in 1-year of life children from pneumonia, septicemia, and purulent meningitis per 10 000 alive newborns.

Mortality index in children up to 1 year did not change seriously from 2004 till 2007 and was from 0.9 to 1.3 per 10 000 babies which were born alive. After beginning of Hib vaccination index of mortality from septicemia decreased almost twice (from 1.3 in 2007 to 0.68 in 2008). Index of mortality from pneumonia in children up to 1 year was at the one level from 2004 to 2007 (2.9 - 2.6 per 10 000 of infants born alive) and only after introduction of Hib vaccination decreased to 1.7 (decrease in 1.5 times in 2008). After Hib vaccination started purulent meningitis mortality decreased by 30% in 2008. Making deep analysis we have not found other reasons for decrease of mortality from invasive diseases in 2008.

Hib vaccination made possible to diminish mortality of children younger than 1 year from invasive diseases. This confirms substantial role of Hib infection in etiology of invasive diseases of children in Ukraine.

ACUTE MASTOIDITIS: EXPERIENCE IN A TERTIARY-CARE CENTER IN THE SOUTH OF SPAIN DURING 1999-2008 PERIOD

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Introduction: An increase in both the incidence and severity of acute mastoiditis (AM) has been recently recorded in many different geographical areas. Causes remain unclear.

This study aims to analyze our clinical and epidemiological data to contrast it to these reports.

Material and methods: Retrospective chart review of 145 patients diagnosed of AM from 1999 to 2008 in our tertiary-care center, including clinical, epidemiological, microbiological, treatment and outcome data.

Results: Annual incidence presented a changeable trend throughout the time of the study. Annual mean cases were 14.5 cases per year. Mean age was 4.3 years. 58% were males. 57% received pre-admission oral antibiotics, mainly beta-lactamics (79%). Most frequent presenting clinical findings were fever, protrusion of pinna (74%), otalgia (71%) and postauricular swelling (70%). Microbiological cultures were performed in 59% cases; *S.pneumoniae* was the most isolated. CT scanning was performed in 56% cases. 100% received parenteral antibiotherapy. Median duration of treatment was 5 days. 31% patients underwent some otorhinolaryngology surgical procedure. 12% presented extracranial complications. 8% presented intracranial complications; a significant increase in these complications was observed when comparing the first with the last 5 years of the study.

Conclusions: We report a remarkable changeable trend in the annual incidence of AM throughout the time of study. We cannot confirm the increase reported by others. We underline the increase in the incidence of intracranial complications in the second time period.

COMMUNITY-ACQUIRED *E. COLI* BACTERAEMIA: 1995-2009

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Background and aim: *E. coli* has been the third most frequently isolated bacteria in blood cultures (BC) at our emergency service in the last 15 years. Some authors reported an increase in relative incidence of *E. coli* bacteraemia in recent years. The aim was to analyse trends, clinical, laboratory and microbiological data of *E. coli* bacteraemia.

Methods: Retrospective analysis of cases with positive BC for *E. coli* between 1995-2009. Nosocomial infections were excluded.

Results: *E. coli* was identified in 29 children (16 boys), 12 (41%) cases were diagnosed in the second half of the study. The median age was 1.3 months: 12(41%) were < 28 days and 27(93%) were ≤12 months. Twenty cases (69%) presented in the first 24 hours. Fever was the most common symptom (27, 93%). In the neonatal period the median leukocyte count was $12.5 \times 10^3/\text{mL}$ and median C reactive protein was 11.8mg/dL. The diagnosis were: acute pyelonephritis (APN) (66%), sepsis (21%), meningitis (7%), cholangitis, occult bacteremia and appendicitis (1 each). 7/19 APN were diagnosed in the neonatal period. One child died (sepsis), 1 had a subdural effusion and 2 had brain abscesses. Resistances were: 28% to ampicillin, 15% to amoxicillin/clavulanate, 21% to cefalotin, 0% to cefotaxime and aminoglycosides.

Conclusions: We did not see an increase of *E. coli* bacteraemia over the last 15 years. Infections occurred mainly in the neonatal period and first year of life and the most frequent diagnosis was APN. One third was resistant to ampicillin. Most of the cases had a good outcome.

MYCOPLASMA PNEUMONEA INFECTION IN ADENOID TISSUE

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Objective: Adenoid and tonsils are the main parts of Waldier's ring. Secondary bacterial infections can lead to adenoid enlargement, adenoiditis and sinusitis. Previous studies showed relatively frequent prevalence of Mycoplasma infections in Iranian patients. The use of PCR method for investigation of atypical organisms such as mycoplasma in adenoid tissue can help treatment and reduce unnecessary surgery.

Methods: This is a cross-sectional study from 2006 to 2007 in 53 adenoid samples after adenoidectomy in Raso-e-akram hospital, Tehran, Iran. At first DNA extraction of adenoid tissue were done then mycoplasma DNA detection were performed by PCR method.

Results: Patient's age was between 3 and 14 year (mean = 8 ± 1.98). There were 27 girls (51.9%) and 25 boys (48.1%). The specific DNA of mycoplasma was detected in 12 (27.9%) of 43 patients. Specific DNA of mycoplasma had no significant correlation with sex, age groups and operation season.

Conclusion: PCR is a sensitive and specific method to detect DNA of mycoplasma of patients after adenoidectomy. Mycoplasma infection of upper and lower respiratory infections after age of 3 year can remain as a chronic infection in lymphoid tissues such as adenoid in 30% of children. Antibiotic therapy against mycoplasma can protect from adenoid hypertrophy and decrease the rate of adenoidectomy.

MYCOPLASMA PNEUMONIAE ENCEPHALITIS OF A BASAL GANGLIA

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Introduction: Mycoplasma pneumoniae is usually responsible of lung infections, may also be involved in other extra-pulmonary manifestations such as encephalitic ones.

Encephalitic affection usually results either from a direct invasion of brain parenchyma by bacteria or by an autoimmune phenomenon, or possibly by thromboembolism mechanism.

Comment: Taha is a 5-years-old boy who present at the waning of low acute respiratory infection behavior disorder, agitation, lethargy all associated to fever. Lumbar puncture showed a lymphocytic meningitis. MRI showed involvement of the basal ganglia and white matter, serology showed the presence of IgM in favor of a recent infection with Mycoplasma pneumoniae ; the treatment consisted of antibiotherapy by erythromycin orally for 15 days . The evolution is favourable with a delay of 15 months and a control MRI is normal.

Conclusion: Mycoplasma pneumoniae encephalitis must be considered in case of any severe encephalitis with or without respiratory involvement. Treatment is available. The recovery takes several weeks with the possibility of sequela but the prognosis remains generally favourable.

THE ATHEROSCLEROSIS AND *CHLAMYDIA PNEUMONIAE* IN PATIENTS WITH CARDIOVASCULAR DISEASE (CAD)

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Cardiovascular disease (CAD) is the leading cause of death in developed countries. The cause is multifactorial. A substantial proportion of patients with CAD do not have traditional risk factors. Infectious diseases may play a role in these cases, or they may intensify the effect of the risk factors. The association of CAD and *Chlamydia pneumoniae* infection is firmly established, but causality is yet to be proven. We investigated their presence in carotid atherosclerotic plaques. 102 plaques atherosclerotic in dead patients were available for examination in Tehran, Iran. The highly sensitive polymerase chain reaction method was employed with primers specific for this agent. The presence of *Chlamydia* DNA was detected in 22 (23.3%) out of 102 examined samples. The presence of *Chlamydia* DNA in these patients supports the hypothesis that this agent has an association with atherosclerosis.

ACUTE BACTERIAL MENINGITIS IN CHILDREN: MENINGOCOCCAL OR PNEUMOCOCCAL CAN YOU LOOK AND TELL?

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Introduction: *Neisseria meningitidis* and *Streptococcus pneumoniae* are, nowadays, the leading cause of bacterial meningitis in Portugal. Many experts recommend adding vancomycin and dexametasone to ceftriaxone, in the initial management of pneumococcal meningitis.

The purpose of this study was to determine clinical and laboratorial differences between pneumococcal and meningococcal meningitis when presenting at emergency department and bacteriological results are pending.

Methods: Retrospective analysis of clinical and laboratorial data of 58 children admitted to three portuguese hospitals with the diagnosis of pneumococcal and meningococcal meningitis in a six year period. Univariate analysis was performed, using X²/Fisher's exact test for discrete variables and Student's t-test for continuous variables (significance level 0.05). Age adjustment was performed using binary logistic regression.

Results: A total of 32 cases were attributed to *N. meningitidis* (mean age 2.9±3.2 years) and 26 to *S. pneumoniae* (4.7±4.8 years) (p=0.105). Focal neurologic signs (OR9.8, CI95% 1.1 to 90.9, p=0.036), seizures (OR9.2, CI95% 1.0 to 83.0, p=0.038), lower CSF/serum glucose (0.22±0.23 vs 0.36±0.23, p=0.05) and higher CSF protein (286±181 vs 180±131mg/dL, p=0.026) were more common in pneumococcal meningitis. Hemorrhagic skin lesions (OR0.01, CI95% 0.002 to 0.120, p< 0.001) were more common in meningococcal meningitis. When adjusted for age, the clinical signs reported remained significantly different between groups.

Discussion: The sample is small and the OR values obtained have large confidence intervals. However, the results are in agreement to literature and suggest early treatment as pneumococcal meningitis in a child presenting with focal neurological signs and seizures.

ANTIBIOTIC-LOCK THERAPY (ALT) FOR LONG-TERM INTRAVASCULAR CATHETERS INFECTIONS IN CHILDREN WITH HAEMATOLOGICAL OR ONCOLOGICAL DISEASES

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Background and aims: Infection is a main problem associated with central venous catheters. This study assesses the effectiveness of ALT for treating catheter infections in children.

Methods: Catheter infection was defined as quantitative blood culture counts through a catheter 4-fold greater than concurrent peripheral blood culture. All children hospitalised in the Paediatric Oncology and Haematology Department between January and August 2009 with an episode of catheter infection were included. ALT was started with vancomycin for Gram-positive cocci, amikacin for Gram-negative bacilli, or liposomal anfotericin B for yeasts. Cure was defined as negative cultures and lack of symptoms without catheter removal at 28 days after the therapy.

Results: Twenty-three episodes in 21 children were included. Median age was 4 years (range: 6 months-14 years). The underlying condition was haematological disease (9 patients), oncological diseases (9) and haematopoietic stem cell transplantation (3). The most frequently isolated pathogen was coagulase-negative staphylococcus (19 episodes), *Staphylococcus aureus* (1), *Escherichia coli* (1) and *Candida* sp. (2). Twenty episodes were cured (87%). There were 3 therapeutic failure: reinfection by coagulase-negative staphylococcus (1), withdrawal of the catheter (1 *S. aureus*, 1 *C. parapsilosis*).

Conclusions: ALT seems to be effective for treating long-term catheter infections in this group of patients.

INVASIVE MENINGOCOCCAL DISEASE BEFORE AND AFTER THE INTRODUCTION OF THE SEROGROUP C CONJUGATE VACCINE: EVOLUTION OF *NEISSERIA MENINGITIDIS* SEROGROUPS

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Background and aims: Meningococcal disease is an important public health problem. The serogroup C conjugate vaccine was introduced in Spain in the immunization schedule in October 2000. RT-PCR to *Neisseria meningitidis* has been used as a diagnostic procedure in our hospital since 2003. Our aim was to describe the evolution of invasive meningococcal disease in our hospital in relationship to these factors.

Methods: A retrospective study of all children with microbiologically confirmed meningococcal disease admitted to our hospital between 1997 and 2009 was performed. Children were divided in two groups according to the date of introduction of the serogroup C conjugate vaccine.

Results: 137 patients were studied (56 in the 1997-2000 period [14 cases/year] and 81 in the 2001 - 2009 period [9 cases/year]). Serogroup was identified in 121 cases (88.3%). In the first period, serogroup C represented 38.8% of the isolates (19 cases, 4.8/year) while serogroup B accounted for 61.2% of them (30 cases, 7.5/year); in the second period, 9.7% (7 cases, 0.8/year) of the isolates were serogroup C and 90.3 % (65 cases, 7.2/year) were serogroup B ($p < 0.05$). Nine patients died (6.6%). PCR was positive in 19 patients with negative cultures (28.8%).

Conclusions: A decrease of 74.5% in the proportion of meningococcal disease by serogroup C was observed. Serogroup B incidence of meningococcal disease in our area remained stable; efforts in prevention should focus in this serogroup. PCR is a useful tool in invasive meningococcal disease with negative cultures.

TRENDS IN PAEDIATRIC *STAPHYLOCOCCUS AUREUS* BACTERAEMIA IN A SPANISH TERTIARY-CARE HOSPITAL: A FOURTEEN-YEAR COMPARATIVE STUDY

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Background and aims: Recent reports have suggested that the epidemiological profile of invasive *Staphylococcus aureus* infections is changing. To describe trends in paediatric *Staphylococcus aureus* bacteraemia (SAB) epidemiology, severity and antimicrobial resistance at a tertiary-care hospital from 1995 to 2008.

Methods: The clinical records of children (< 16 years of age) with SAB admitted from January 1995-December 1999, January 2000-December 2002 and January 2006-December 2008 were retrospectively reviewed.

Results: A total of 217 episodes among 206 patients were identified (16, 24 and 22 cases/year in each period respectively). No significant age or gender differences were observed. There were more non-caucasians affected in the latter period ($p < 0,001$). Preexisting comorbidity was frequent (82%, 58% and 69% respectively) ($p=0,011$). Nosocomial SAB predominated in all periods (13, 16 and 15 episodes/year) but an increase in community-acquired cases was observed in the last two periods (2, 8 and 7 episodes/year) ($p < 0,001$). Intravenous catheters were the commonest source of SAB (57%, 43% and 61%). The prevalence of methicillin-resistant SAB increased from 2,5% to 11% to 13,5% ($p=0,03$). Community-acquired methicillin-resistant SAB was only present in the last two periods representing 12,5% and 11% of the total of methicillin-resistant *S. aureus* (MRSA) strains. The mortality rate related to SAB was similar in the three periods (3,8%, 1,4% and 3%).

Conclusions: Community-acquired SAB was more frequent in the last two periods. A five-fold increase in MRSA incidence was observed throughout the years. Community-acquired methicillin-resistant SAB is increasing but it is still uncommon in our area. Overall mortality rates were comparable.

A 3-YEAR STUDY OF *STAPHYLOCOCCUS AUREUS* BACTERAEMIA IN A SPANISH CHILDREN'S HOSPITAL

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Background and aims: *Staphylococcus aureus* is a leading cause of bloodstream infections in childhood, associated with substantial morbidity and mortality. To describe the epidemiology, risk factors, microbiological features and outcome of paediatric *Staphylococcus aureus* bacteraemia (SAB) in a tertiary-care centre over a 3-year period.

Methods: A retrospective medical charts-review of all children (< 16 years of age) admitted to our hospital from January 2006 to December 2008, with blood cultures positive for *S. aureus* was conducted. Relevant information regarding patient demographics, laboratory results and outcome was recorded.

Results: Sixty-six episodes of SAB among 65 patients (63% males, 62% caucasians) were identified. The overall incidence was 3.7 episodes per 1000 hospital admissions. The mean age was 4.5 years (3 days-15 years), 45% younger than 1 year. Forty-five (69%) had preexisting comorbidity. Fifty-four cases (82%) had risk factors associated to SAB. Thirteen episodes were community-acquired, nine were healthcare-associated with a community onset and forty-four were nosocomial. Intravenous catheters were the commonest source of SAB (61%). Four patients had a secondary focus of infection. Only two episodes of endocarditis were identified. Nine cases were due to methicillin-resistant *S. aureus* (MRSA) strains, only one of these was community-acquired. A single patient suffered from recurrent disease. There were five deaths, only two related to SAB (3%).

Conclusions: SAB occurred largely as hospital-acquired infection. The presence of intravascular devices was an important risk factor. Complications such as endocarditis or metastatic infections were infrequent. MRSA bacteraemia was uncommon. The recurrence and mortality rates were low.

PREVALENCE OF ST59-MRSA-IVA COMMUNITY-ACQUIRED METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS IN CHINESE CHILDREN

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Background and aims: Community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA) infections are increasingly noted worldwide. We aimed to investigate the major clone and clinical characteristics of CA-MRSA infections in China.

Methods: One hundred and twenty-eight children with CA-MRSA infections were enrolled in this study. Clinical information was collected and analyzed. Strains from the children were analyzed by multilocus sequence typing (MLST), staphylococcus cassette chromosome mec (SCCmec) typing, and spa typing. The Panton-Valentine leukocidin (PVL) gene was also detected.

Results: ST59-MRSA-IVa with t437 accounted for 45.3% of occurrences, making it the most prevalent clone. We found 10 isolates of ST338-MRSA-IVa clone, which also belongs to CC59. The majority of the 58 strains of ST59-MRSA-IVa with t437 clone were from skin and soft tissue infections (SSTIs) (22; 37.9%), followed by pneumonia (19; 32.8%). The rest was septicemia and vaginitis. In the 22 cases of SSTIs, the majority were impetigo (10; 45.5%) and abscesses (7; 31.8%). The rest was cellulites, infected wounds, omphalitis, paronychia, and folliculitis. Fifteen of the 22 isolates (31.9%) were PVL-positive, and the abscesses infected with PVL-positive strains usually required incision and drainage. In the 19 cases of pneumonia, eight of the strains were PVL-positive, and all the PVL-positive strains with the ST59-MRSA-IVa clone did not cause necrotic cases.

Conclusions: The infections caused by CA-MRSA isolates in Chinese children are largely associated with the ST59-MRSA-IVa clone. The abscesses infected with PVL-positive strains usually required incision and drainage, and PVL-positive strains did not correlate with necrotizing pneumonia. .

BACTERIAL MENINGITIS: CLINICAL AND EPIDEMIOLOGICAL DATA IN PORTUGAL IN A NEW VACCINAL ERA

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Introduction: Meningitis continues to be an important cause of morbidity and mortality in children. Epidemiological changes are occurring since new vaccines reach a major part of the population. This study intended to investigate etiology and antibiotics' susceptibility in an era of high vaccination coverage against *Neisseria meningitidis* (NM), *Haemophilus influenzae* type b (Hib), and *Streptococcus pneumoniae* (PN) (seven serotypes).

Methods: Retrospective analysis of clinical records of children with bacterial meningitis (with bacterial isolate) admitted to three hospitals in Portugal during 2003-2008. Neonates and neurosurgical patients were excluded.

Results: Sixty-three children were included (median age 21,0 months). Bacterial isolates were: NM-32 (50,8%); SP- 26 (41,2%); *Haemophilus influenzae*, *Staphylococcus aureus*- two (3,2%) each and *Streptococcus pyogenes*- one (1,6%). An identifiable risk factor was found in 21 (33,3%). NM serogroups were: B (25), C (one, not vaccinated), Y (one), undefined Y/W135 (three), unclassified (two). SP serotypes were: 19A (three), 23F (two), and 14, 24F, 33F, 34 (one each); 17 strains unclassified. Considering serotypes included in heptavalent vaccine, two had no vaccine and one complete vaccination. We documented one case of Hib vaccine failure. All isolates were sensitive to penicillin and third-generation cephalosporins except one SP 19A resistant to both and one unclassified SP to penicillin.

Conclusions: NM is still the main cause of meningitis in portuguese children, with a high prevalence of serogroup B after universal vaccination against NM-C. SP strains not included in heptavalent vaccine are acquiring a relevant role. Resistance to penicillin is not a major issue in invasive strains.

PREDICTING ACUTE BACTERIAL MENINGITIS IN CHILDREN AT HOSPITAL ADMISSION

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Discrimination between bacterial and viral meningitis at hospital admission may be difficult if there are neither a severe clinical picture nor prompt access to positive bacteriological result. This study aimed to build an easy to perform predictive model for bacterial etiology based on objective laboratorial results readily available on all hospitals.

Retrospective clinical data analysis of children admitted with acute meningitis to three portuguese hospitals in a six year period. Bacterial etiology established by microbiological identification (cerebrospinal fluid (CSF)/blood) and viral etiology whenever negative cultural exam and resolution without antibiotics. Newborns and neurosurgical patients were excluded. We identified variables related to bacterial etiology and selected suitable *cut-offs* using *Receiver-Operating Characteristic* curves.

127 children were included, 63 with bacterial and 64 with viral meningitis. Five variables were found to have major diagnostic value: blood C reactive protein (CRP) (Area Under the Curve (AUC) 0,914), CSF protein (AUC: 0,865), CSF/blood glucose (AUC 0,856), CSF cells (AUC 0,820) and CSF glucose (AUC 0,709). Assigned as *cut-offs* values: CRP >5mg/dL, CSF protein >60mg/dL; CSF/blood glucoses < 0,5; CSF cells >150/ μ l and CSF glucose < 50mg/dl. We tested a model assigning to each variable a rate of 0-2 (first two) or 0-1 and found a classification ≥ 3 to have: 85,2% sensitivity, 83,9% specificity, 86,7% negative predictive value and 82,1% positive predictive value.

This predictive model is simple to use and, after validation in an independent sample, may be useful guiding therapeutic decisions. It should not be considered in newborns, neurosurgical patients, immunodeficiency and clinical severity.

MENINGITIS IN CHILDREN WITH HYDROCEPHALUS IN A SIX YEARS PERIOD**C. Gonçalves¹**, A. Fernandes², C. Calado³, J. Franco⁴, F. Prata¹, J.G. Marques¹

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Background and aims: Children with hydrocephalus and ventriculo-peritoneal shunt (VPS) have a predisposition to meningitis. The aim of our study was to analyze clinical, bacterial and microbiological characteristics of meningitis in this group of children.

Methods: Retrospective collection of data from clinical files of patients admitted with the diagnosis of meningitis and previous hydrocephalus with VPS in one portuguese hospital in six years (2003-2008).

Results: Ten children were selected with a mean age of $25,6 \pm 33,2$ months; 70% were male. Regarding typical clinical signs, 5 presented with vomiting, 3 with neck rigidity and one with headache. None had sepsis. Mean cell count on CSF was $1178,38 \pm 1824,08$ cells, CSF protein $257,48 \pm 203,45$, ratio CSF glucose/Blood Glucose was $0,33 \pm 0,23$, blood leukocyte count was 19597 ± 6538 cells/mm³ and CRP was $9,3 \pm 10,4$ mg/dL. CSF culture was positive in 6 cases: *Staphylococcus aureus* (2), *Pseudomonas aeruginosa* (2), *Streptococcus mittis*(1) and *S. pneumoniae* (1). This children had longer hospitalization (mean:56,6 days; $p=0,007$) when compared with children without hydrocephalus. CNS Imaging showed acute hydrocephalus (1), brain abscess (1) and Extra-Axial Collection (1). None had sequels from the acute episode.

Conclusions: Longer hospital stay is explained by the need for VPS replacement after CSF sterilization. Bacteria causing meningitis are different in children with VPS vs previous normal children. These bacteria may be less invasive, once they arise from contiguity, and not from blood spread, leading to mild clinical course and the achievement of good results with prompt treatment.

LATE ONSET SEPSIS BY STREPTOCOCCUS AGALACTIAE: A SINGLE CENTRE EXPERIENCE WITH ITS CLINICAL AND ANALYTICAL FEATURES

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Introduction: Retrospective review of charts of the patients admitted to a tertiary care children's hospital due to late-onset streptococcal B group sepsis between 1998-2010.

Patients and Methods: Streptococcus agalactiae is one of the main agents that cause sepsis in infants. Late-onset sepsis presents after the seven day of life. In spite of preventive measures, in the last years it seems to have been a slight increase of this entity.

Results: Nineteen cases were reviewed (median age of 48 days-old, male 47%). Only two cases of maternal colonization were found. Thirteen out of nineteen were breastfed. Four of the children had sepsis as first manifestation. Two of them were initially suffering from cellulitis/adenitis, one with onfalitis and another with meningitis. The other cases suffered fever of unknown origin. Three children required PICU. The average stay due to parenteral antibiotherapy was eleven days. The most common regimen was ampicilin plus gentamycin or cefotaxime. The outcome was positive in all cases without neither sequelae nor deaths. The recurrence rate was 1/19%. In this cases also TLR2 pathway was assessed due to lack of inflammatory response.

Conclusions: Late-onset streptococcal B group sepsis typically presents with fever, irritability and loss of hunger. It can also appear like a septic shock or cellulitis/adenitis. In most cases are RNT with adequate weight for its gestacional age, breastfed. Although it is a potential serious infection that must be recognised and treated as soon as possible, a great amount of them gets over without presenting any consequences nor deaths.

EXTENSIVE SPINAL EPIDURAL ABCESS (SEA) IN ADOLESCENTT. El Hayek¹, H. El Fakir¹, H. Haas²*¹Pediatric Surgery, ²Pediatric Emergency, University Hospital of Nice, Nice, France***Objective:** To remind clinicians of a rare diagnosis in children.

Patient: A 13 year-old adolescent presented headache, fever at 39°5C, lumbar pain without neurological deterioration, no cutaneous or other infection causes, and no signs of meningitis. C-Reactive protein and leucocytes were high (168 mg/l; 15500/mm³). A MRI showed a posterior abscess to the spinal cord on the lumbar region. Despite 3 days of triple intravenous antibiotherapy by Ceftazidime, Gentamycine and Fosfomycine, the evolution was bad. A new MRI showed an extensive abscess from C7 to L5. We decided to perform surgery by T5 and L4 laminectomy to evacuate the pus. Susceptible *Staphylococcus aureus* to the choosen antibiotic was cultured from the intraoperative sample. Rapid clinical improvement was observed. Intra-venous antibiotics were continued for 3 weeks, then Oxacilline given orally for a total of 4 weeks. The evolution was good.

Discussion: SEA is a very rare in children. Frequent absence of classic neurologic symptoms is a real difficulty in children resulting in delayed diagnosis and permanent paraplegia in many cases. MRI is indicated in young patients who present fever and back tenderness of unknown cause. There is significant debate in the literature regarding the optimal management. Some have advocated conservative treatment with intravenous antibiotics alone, recent studies have shown that patients treated without early surgery are more likely to have poor outcomes.

Conclusion: An intense back pain in a febrile child leads to think about SEA and justify an early MRI and treatment adding surgery to antibiotics.

EVOLUTION OF PERINATAL EARLY-ONSET SEPSIS AND GROUP B STREPTOCOCCAL INFECTION IN THE PERIOD 2005-2010

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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 - February 2010).

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 5-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.

STAPHYLOCOCCAL ENTEROTOXIN B (SEB) ENHANCER FACTOR IN SEVERITY OF ATOPIC DERMATITIS

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Atopic dermatitis is a chronic, inflammatory skin disease with high prevalence. The skin of patients with AD is usually colonized by *Staphylococcus aureus* its exotoxins especially Staphylococcal Enterotoxin B may enhance the cutaneous inflammation. To determine the prevalence of (SEB)-specific IgE antibodies in AD patients and relationship with severity of disease, forty children with AD were entered the study. All of them fulfilled the criteria of Hanifin and Rajka. Bacterial specimen was isolated from three areas of skin lesions and strain was identified by culture. Serum total IgE and (SEB)-specific IgE antibodies were measured by ImmunoCAP system. The severity of AD was measured by using Scoring Atopic Dermatitis (SCORAD). Forty patients, 13 females and 27 males (ratio=2.07) with median age of 9 months entered the study. Among them 27 patients (67.5%) had positive *S. aureus* cultures that 55.6% showed severe clinical manifestation of AD ($P=0.006$). The mean serum total IgE was 601.5 IU/ml and 40% of patients had high serum IgE levels (≥ 500 IU/ml). There was a positive relationship between SCORAD and serum total IgE level ($r=0.438$, $P=0.005$). Among patients, 17.5% had (SEB)-specific IgE antibodies. There was a significant correlation between the presence of (SEB)-specific IgE antibodies and the disease severity ($P=0.003$). The presence of (SEB)-specific IgE antibodies and culture growth was significant ($P=0.048$).

Due to these results and correlations, it is strongly recommended to educate hygiene to these patients and to perform antibiotic as prophylaxis and treatment strategies against *Staphylococcus aureus* in children with severe atopic dermatitis.

TYPICAL (D- VTEC+) HAEMOLYTIC URAEMIC SYNDROME (HUS) COMPLICATED WITH PANCREATITIS - CASE REPORT

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Background and aims: The typical, non-connected with diarrhea (D- VTEC +) HUS is appeared more rare as a cause of acute renal insufficiency at first childhood than post-diarrheal (D+ VTEC+) HUS.

Methods: 5 years-old boy appears fever - sore throat 2 days long - symptoms for which he is treated with Clarithromycin p.os due to Strep test positive. After one day, abdominal pain, vomits, petechial rash of body and lower limbs appear. The child is pale, dehydrated and suffers from epigastric pain. Laboratory testing: WBC 18.460, N 82%, Ht 21%, Hb 7gr/dl, Reticulocytes 1.6%, PLT 90.000, Coombs(-), ESR 84, CRP 27 (normal ranges 0-0, 5), Ur 155, Cr 1.7, K 3.3, Na 136, SGOT 49, SGPT 16, total bilirubin 1.6, AMS 3.600, lipase 5.402, total protein 6, albumin 3.5, pharyngeal culture :Group A b-hemolytic Streptococcus. Urine sample: Hb ++, albumin ++, RBC 25-27/hpf, granulocytes 13-15/hpf, haemorrhagic cylinders 2-4/hpf, urine AMS 9552, CFR 56ml/min/173m². Urine- stool cultures: normal, abdominal U/S: kidney: with no pathological findings, pancreas:increased dimensions, duodenum:fattening of adjacent wall.

Results: Due to findings of HUS complicated with pancreatitis, the feeding stopped, fluids and electrolytes were regulated, blood transfusion, plasma administration, allopurinol and IV cefotaxime were administrated. Patient's blood pressure was between normal ranges. After 7days of hospitalization he was re-fed and his clinical status and laboratory testing were improved.

Conclusions: The case is presented due to its rarity, especially referring to its cause and its complication.

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EVALUATION OF SERUM COPPER LEVELS IN CHILDREN WITH INFECTIONS

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Background and aims: To evaluate copper serum level alterations, in children with acute infections.

Methods: 80 children were enrolled in this study divided in two groups: Group A: 40 patients with bacterial infections; Group B: 40 patients with viral infections. Samples were collected on the morning of three different periods: a) in the acute phase (admission), b) during the inflammatory process (fourth day of hospitalization), and c) after recovery (about one month after the first sampling) and analyses were performed for: procalcitonin (PCT), serum-amyloid A protein (SAA), CRP, ceruloplasmin and copper.

Results: The results of this study showed that: a) Children with viral infections had significant decreased copper levels in fourth day of hospitalization as compared with admission ($p=0.001$), while a similar trend was detected in bacterial group ($p=0.076$); b) Copper was correlated positive with ceruloplasmin in both patients groups, in all the examined chronic periods and c) In children's viral group we observed significant positive correlations between copper and inflammation markers (CRP, PCT and SAA) ($r=0.43$, $p=0.012$, $r=0.36$, $p=0.042$ and $r=0.49$, $p=0.004$, respectively) at admission, while no such correlation observed in bacterial group.

Conclusions: The alterations in serum copper levels in viral and bacterial infections are mainly due to the increased hepatic synthesis of ceruloplasmin, which mediated by IL-1 and IL-6. In bacterial infections, organism may utilize copper (act as antioxidant) in order to boost the immune system. In contrast in viral infections which characterized from less oxidative stress its increased levels were related with the degree of inflammation.

PREVALENCE OF SHIGA TOXINS(*STX*₁,*STX*₂),*EAE*A AND *HLY* GENES OF *E. COLI* O157:H7 STRAINS AMONG CHILDREN UNDER 5 YEARS OLD IN MARVDASHT (IRAN)

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Background and aims: Enterohemorrhagic *Escherichia coli* (EHEC) strains are the most common enteric pathogens which cause the hemorrhagic colitis, hemolytic-uremic syndrome and especially renal failure in children. The purpose of this study is to survey the prevalence severe diarrhea arising from this bacteria in children under 5 years old in Marvdasht.

Methods: In this study stool samples of children from four original areas in Marvdasht are collected and after enrichment in two culture media ECB, TSB in temperature 37°C, sorbitol fermentation on CT-SMAC evaluated. Then in sorbitol negative bacteria with the use of specific biochemical tests *E. coli* identified. In the next step their β-glucuronidase activity has been tested on specific chromogenic media. Then with the use of specific antisera the isolation of bacteria has been confirmed. Finally with multiplex PCR method presence of virulence genes *stx*₁, *stx*₂, *eaeA* and *hly* has been tested.

Results: Out of 615 children (278 girls, 337 boys), from 7 children *E. coli* O157:H7 isolated (1.14%). A significant difference was seen between isolated bacteria from age groups 18-23 months and other age groups ($P=0.004$) and only 1 case had the *stx*₁ and *eaeA* genes (0.16%) and none of them had *stx*₂ and *hly* genes.

Conclusion: Regarding severity of *E. coli* O157:H7 pathogenesis, low infectious dose and lack of routine assay for detection of this bacteria in clinical laboratory, further and completed studies on diagnosis and genotyping of this *E. coli* O157:H7 strain has been recommended.

Keywords: *Escherichia coli* O157:H7, Acute gastroenteritis, Multiplex PCR

C REACTIVE PROTEIN - DIAGNOSTIC MARKER OF NEONATAL SEPSIS

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Neonatal sepsis is major cause of neonatal mortality worldwide.

Aim: The aim of the study was to assess the diagnostic value of C reactive protein (CRP) in early diagnosis of neonatal sepsis.

Methods: We conducted retrospective analysis of medical records of 337 newborn with suspected infection. Study was done at the neonatal department of Lashvili Children Central Hospital, The following lab data were evaluated: CBC, I:T Ratio, CRP, blood/CFS/urine culture. According to clinical and lab findings we categorized patients into 3 groups : I - proven sepsis with positive blood culture; II - probable sepsis with negative blood culture, but clinical and lab data consisted with sepsis, III - clinical sepsis without any lab change.

Results: 25% of newborns had positive blood culture. The main causative organisms were E. Coli, Staph. Coagulase negative and Staph. Aureus. The low levels of CRP obtained 24 hours apart, 8 to 48 hours after clinical presentation, indicated that bacterial infection was unlikely. CRP more than 6mg/dl had a positive predictive value for early onset sepsis, but high levels of CRP do not always indicate sepsis. So, according our data negative predictive value of CRP was higher.

Conclusion: CRP is valuable test for screening neonatal sepsis and helps in clinical decision making.

RECURRENT NECROTIZING FASCIITIS “3 ATTACKS” IN A CHILD DUE TO STREPTOCOCCUS PYOGENES**C. Kuzdan, A. Soysal, M. Bakır***Pediatric Infectious Diseases, Marmara University, Istanbul, Turkey*

Necrotizing fasciitis (NF) is a rapidly progressive, deep-seated bacterial infection of the subcutaneous soft tissue that may involve any area of the body. Recurrent NF is very rare. Reported here is a rare case of recurrent NF due to *Streptococcus pyogenes*. A 12-year-old female with hereditary sensory and autonomic neuropathy type IV was diagnosed as NF of left knee and limb and tissue culture yielded *S. pyogenes* and she was treated successfully with wide surgical debridement and ampicillin/sulbactam plus clindamycin. Two years after hospital discharge she was readmitted with NF of the right knee and limb. *S. pyogenes* was isolated both from blood and from joint fluid culture. Ampicillin/sulbactam plus clindamycin and intravenous immunoglobulin were given. Although wide surgical debridement, antibiotic treatment and hyperbaric oxygen therapy, progressive tissue necrosis developed and proximal femur amputation was performed. Eight months following second discharge she readmitted with NF of the her left knee and on her left entire leg, *S.pyogenes* was isolated both from blood and from wide surgical debridement culture. Even wide surgical debridement and antibiotic treatment, clinical status of the patient failed to improve and she died. Patients who develop NF are predisposed to severe soft tissue infections due to associated comorbid conditions such as hereditary sensory and autonomic neuropathy type IV. Recurrent soft tissue infection in a patient with previous *S. pyogenes*-related NF should therefore be treated with a high index of suspicion and antibiotic prophylaxis should be discussed.

SURVEILLANCE NETWORK OF BACTERIAL MENINGITIS IN FRENCH CHILDREN: 3376 CASES IN 8 YEARS

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Background: Introduction of vaccines against bacteria involved in bacterial meningitis (BM) in children and recommendations concerning antibiotics prophylaxis have changed BM epidemiology. The GPIP/ACTIV set up an active surveillance network to analyze the clinical and biological features of BM.

Methods: From 2001 to 2008, 252 pediatric wards and 168 microbiology laboratories recorded clinical and biological characteristics of children with BM.

Results: 3376 BM were enrolled. *Neisseria meningitidis* (Nm) meningitis represent 31.7% of cases among children < 24 months and *Streptococcus pneumoniae* (Sp) 29.1%.

Bacteria n= (%)	Case fatality rate %	<1month n=515(15)	≥1<12months n=1215(36)	≥12<24months n=369(11)	≥24 months<5 years n=563(17)	≥5 years n=714(21)
Nm n= 1522 (45)	6.6	16 (3)	437 (36)	213 (58)	371 (66)	485 (68)
Group B n=920		13 (2)	294 (24)	125 (34)	222 (39)	266 (37)
Group C n=426		1 (0.2)	97 (8)	64 (17)	105 (19)	159 (22)
Sp n= 957 (28)	11.5	9 (2)	474 (39)	127 (34)	162 (29)	185 (26)
<i>H. influenzae</i> N=89 (3)	2.3	0	40 (3)	23 (6)	16 (3)	10 (1)
Group B streptococcus N=479 (14)	13.7	304 (59)	175 (15)	0	0	0
<i>E. coli</i> N=192 (6)	10.1	143 (28)	49 (4)	0	0	0
<i>M. tuberculosis</i> N=10 (0.3)	13.7	0	5 (0.4)	1 (0.3)	1 (0.2)	3 (0.4)
Other N=127 (4)	8.7	43 (8.4)	36 (3)	4 (1)	13 (2)	31 (4)

[MEN]

Conclusion: Our survey is among the largest series of BM. In the next years, implementation of new vaccines (PCV13 or meningococcal conjugate vaccine) and/or immunization schedule (reduction of doses number) could impact the epidemiology of BM.

ACUTE B CELL LYMPHOBLASTIC LEUKAEMIA PRESENTING AS NON-TROPICAL PYOMYOSITIS DUE TO *STREPTOCOCCUS G* IN A 6-YEAR-OLD GIRL

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Background: Non-tropical pyomyositis (NTP) in young children is rare. *Staphylococcus aureus* accounts for more than 90% cases. *Streptococcus G* NTP has not been previously reported.

Case report: A previously well 6-year-old girl presented with malaise, high fever with rigors, and painful swelling of the left calf. A Tc99 isotope study revealed increased uptake in the distal left femur and distal left tibia. Ultrasound and CT studies showed extensive oedema of the calf muscles. Blood cultures were positive for *Streptococcus* which gave an initial agglutination result as antigen group C. Further molecular typing revealed *Streptococcus group G, emm type stG6792.0*. Streptococcal G exotoxin, *spgG*, was negative by PCR. There was persistent mild pancytopenia without evidence for DIC, with numerous immature leukocytes including metamyelocytes, band forms, toxic granulations and atypical cells reminiscent of blasts. Treatment with intravenous cefazolin and clindamycin was ineffective and a frank abscess developed requiring drainage. Further investigations showed acute B-cell lymphoblastic leukaemia.

Conclusions: Very few cases of NTP have previously been reported in children of which most were due to *S. aureus*, with an underlying malignancy present. *Streptococcus G* NTP has not been previously reported at any age. The specific *emm* type is rare, only recently reported in Israel. In this case the haematological changes were initially thought to reflect sepsis, since acute leukaemia rarely presents with a broad spectrum of immature cell types. NTP in childhood should prompt consideration of underlying malignancy, as is the case in adults, especially if the aetiologic organism is unusual.

SUPPURATIVE COMPLICATIONS OF ACUTE TONSILLOPHARYNGITIS - ATTITUDE CHANGE

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Background: Acute tonsillopharyngitis is one of most common diseases in childhood. May be associated with suppurative complications, including peritonsillar, retropharyngeal and parapharyngeal abscesses, mostly caused by *Streptococcus pyogenes*, but also by anaerobic microorganisms. These complications can be life-threatening.

Aims: Characterize pediatric patients hospitalized for suppurative complications of acute tonsillopharyngitis. Develop a joint protocol for diagnosis and treatment.

Methods: Retrospective descriptive study based on clinical records review of patients admitted to Pediatrics Department between January2001-May2009.

Results: We had 16patients, median age 10years (minimum: 1year, maximum: 16years); 9female. Presented diagnoses were peritonsillar abscess(14), retropharyngeal abscess(2) and parapharyngeal abscess(1). Most common clinical presentation were fever(16), neck swelling(12), odynophagia(10), bulging of palate(9), feeding difficulty(5), deviation of uvula(3). All had a history of recurrent tonsillitis. Treatment prior to admission was ibuprofen(2), amoxicillin/clavulanate(4), penicillin(4), cefixime(1), without medication record(5). Mean hospital stay (\pm standard deviation): 5 ± 3 days. In 7patients a neck CT scan was performed. Ten patients received incision for drainage and culture, with isolation of *Streptococcus pyogenes* in 1. Blood culture was made in 4patients with no agent isolation. All were treated with IVantibiotics: amoxicillin/clavulanate(7), amoxicillin/clavulanate+clindamycin(5), ceftriaxone+clindamycin(3), penicillin(1) with abscess resolution. Follow-up on Otorhinolaryngology consultation in 11patients, of which 3 underwent tonsillectomy. Recurrence in 3patients(19%) needing re-admission.

Conclusions: These complications that arise from a fairly common infection can be life-threatening, thus it deserves a protocol determining incision for drainage and culture, defined antibiotic therapy and tonsillectomy to decrease its recurrence, as it happens in almost 1/4of patients. This joint protocol has been applied in 2 following hospitalized patients.

MENINGOCOCCAL PURPURA FULMINANS: HYPOCALCEMIA A RISK PROGNOSTIC FACTOR**E. Mallet¹, F. Dumas¹, T. Blanc², A.M. Devaux², P. Ensel²***¹Department of Pediatrics, CIC INSERM 204, ²Pediatric Intensive Care Unit, Rouen University Hospital, Rouen, France*

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

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

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

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

ANTIBIOTIC SUSCEPTIBILITY PATTERNS OF PEDIATRIC *STREPTOCOCCUS PYOGENES* ISOLATES OVER A 34 MONTH PERIOD IN ALEXANDROUPOLIS, THRACE, GREECE

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Purpose: To describe the antibiotic susceptibility patterns (ASP) of *Streptococcus pyogenes* (GAS) isolates derived from children in our area.

Patients and methods: Data were collected over the period 1/1/2007-1/11/2009. *S. pyogenes* identification was carried out by the automated Vitek 2 system. Susceptibility testing against penicillin (P), ampicillin (AM), ceftriaxone (CRO), cefotaxime (CTX), erythromycin (E), clindamycin (CC), tetracycline (TE), chloramphenicol (C), vancomycin (VA), linezolid (LZD), quinopristin/dalfopristin (SYN), moxifloxacin, ofloxacin and levofloxacin was determined by the disk diffusion method according to the 2007 CLSI standards. The results were reported as sensitive (S), intermediate (I), and resistant (R). I and R isolates were grouped together. Not all isolates were tested against every antibiotic.

Results: *S. pyogenes* was isolated in 46 children (25 females) with median age 5 years (range 4.5 months to 11 years). In 10 children, *S. pyogenes* was isolated from otic (8), nasal (1) and vaginal secretions (1). In the remaining 36 children with tonsillopharyngitis, *S. pyogenes* was isolated from the oropharynx. No resistant isolates to P, AM, CRO, CTX, VA, LZD and the three quinolones were identified. (E) resistance, indicative of resistance to other macrolides, was prominent (21/46 or 45.7%). (CC), (C), (SYN), and (TE) resistance was 2.1% (1/46), 3.2% (1/32), 2.2% (1/45) and 14.3% (1/7), respectively.

Conclusions: Macrolides are not a good treatment option for GAS tonsillopharyngitis in our area due to the very high resistance that is likely due to their extensive use and misuse. In b-lactam allergic patients, clindamycin is a better oral therapeutic option.

NEUROBORRELIOSIS IN CHILDREN - CLINICAL MANIFESTATIONS AND THE PROOF OF SPECIFIC DNA

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Background and aim: Neurological involvement, clinical course and outcome were studied in the comparison with the examination of specific DNA in acute phase and convalescence.

Methods: Thirty hospitalized patients younger than 18 years (average 9,8) were enrolled into the prospective study according to the criterions as follows: 1. actually manifested neurological involvement and 2. CSF specific antibody synthesis. Patients were examined before and after antibiotic treatment, after 3 and 6 months. Specific DNA has been examined in all patients in CSF, plasma and urine.

Results: Antibody index CSF/serum was positive in 18 children the rest of them had IgM/G antibodies only in CSF. Before treatment borrelial DNA was found at least one times in 17 children (56,6%), out of them in 11 patients in CSF (36,6%), in 5 in plasma (16,6%) and 12 times in urine (40%). After treatment the PCR positivity was found out in 3 patients (10%). After 3 months two children were positive, and after 6 months all patients remained negative. All tested patients had CSF findings typical for aseptic meningitis, moreover 21 patients had uni or bilateral facial palsy. All children were treated with intravenously given antibiotics. The outcome was really excellent - all patients but one (with myelitis) were free of any neurological sequelae.

Conclusion: The clinical symptoms were uniform, all patients suffered form meningitis accompanied in 21 by facial palsy. Sensitivity of PCR was before treatment 56,6%, after treatment and later was the PCR positivity very rare.

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LONG TERM NEUROLOGICAL OUTCOME OF CHILDREN WITH PNEUMOCOCCAL MENINGITIS

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Background and aims: Acute bacterial meningitis is a life-threatening illness with possible long-term neurocognitive sequelae. The aim of the study was to identify clinical and biological factors associated with death or neurological sequelae in a retrospective cohort of children with pneumococcal meningitis.

Methods: Retrospective cohort study. Inclusion criteria were pneumococcal meningitis beyond 1 month of age; and death or long-term (>10 yrs) follow-up. Clinical and biological data at admission were retrieved from medical charts.

Results: Thirty patients (age at diagnosis 1 month - 5 years) were enrolled between 1990 and 1999. Eight (26.6%) died, two of them suffered from chronic diseases. At diagnosis, the following variables were associated with survival: absence of seizures ($p < 0.01$), absence of respiratory distress ($p < 0.01$), GCS>12 ($p < 0.01$), platelets> 200,000/mm³ ($p < 0.001$), administration of dexamethasone before antibiotics ($p < 0.05$), no need for either ICU or mechanical ventilation ($p < 0.001$). Among children who survived: 11 (50%) did not show any neurocognitive problems; 7 (23.3%) developed hearing loss; 3 (10%) sleep disorders; 2 (6.6%) hemiplegia; 2 (6.6%) epilepsy; 2 (6.6%) mild mental retardation. None developed psychiatric disorders.

Conclusion: Some factors were associated with survival in children with pneumococcal meningitis. The overall prognosis was good in half of the long-term survivors. The main limit of our study is its retrospective nature. However, since the routine use of pneumococcal conjugate vaccines, the incidence of bacterial meningitis has decreased so that prospective studies are difficult to conduct in developed countries.

NINE YEARS OF MENINGOCOCCAL DISEASE - RETROSPECTIVE ANALYSIS IN A REFERENCE HOSPITAL IN SAO PAULO, BRAZIL

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Background and aim: Meningococcal Disease (MD) can be severe disease and a public health problem. The *Neisseria meningitidis* remains the bacteria most often associated with bacterial meningitis in Brazil, despite being vaccine-preventable disease.

The aim of this study was to analyze the outcome of MD at the Institute of Infectious Diseases Emilio Ribas, Sao Paulo, Brazil, referral center for infectious diseases.

Methods: The study was retrospective, with analysis of medical records from January 2000 to December 2008. MD was classified as: Group 1: Meningitis (M), Group 2: Meningococemia (MCC), Group 3: M with MCC. Events analyzed: clinical presentations, the prevalence of serogroups and case fatality ratio, all according to age.

Results: There were 872 hospitalized patients younger than 20 years-old accounting for 87% of total admissions for MD. The highest concentration of patients was below age 5 y (521 cases) and 5 - 14 y (273 cases). The clinical presentation more frequent was Group 3. The case-fatality ratio of MD remained around 8%, significantly higher in Group 2 (58.5%). The proportion of cases from 1 to 14 years and above 15 years was, respectively, in 2000 73% and 27% and in 2008, 50% in each group. Serogroup C predominated in 90.3% of the results in 2008, accounting for more than half of the cases since 2000.

Conclusions: In our study, MD occurred especially below the age of 14 y, although above this age the incidence has been increasing significantly in recent years. Serogroup C *N.meningitidis* predominates currently.

IMPACT OF NONTYPABLE HAEMOPHILUS INFLUENZA INFECTIONS IN THE HOSPITAL CARE SETTING

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Background and aims: Nontypeable *Haemophilus influenzae* (HiNT) is a common pathogen in children although rarely severe and with limited impact in the hospital setting. The aim of this study was to assess its actual role in the hospital care setting (emergency room - ward - critical care), in a tertiary university hospital.

Methods: Observational, retrospective study by record review of all children with an isolation of nontypable *Haemophilus influenzae* during 2008 at any location. For comparison purposes, patients were divided into two groups according to whether admission to hospital was or not required.

Results: HiNT was identified in 90 patients during the study period (Fig).

	OUTPATIENTS / ER	HOSPITALIZED
Nº patients	50 (56%)	40 (44%)
Gender (boys)	28 (56%)	28 (70%)
Mean age (months)	31.9	12.1
Age range (months)	5 -132	1 – 60
Location of isolation	Ear fluid (34%)	Bronchial (70%)
Resistance to amoxicillin	6 (12%)	2 (5%)
Co-infection with other bacteria	21 (42%)	14 (35%)

[Summary of patient characteristics]

In our series the typical hospitalized pediatric patient with a HiNT isolation is an infant, with lower airway respiratory symptoms, co-infected with other bacteria in up to one third of the cases and good outcome. Importantly, the isolation of HiNT explained the admission or conditioned the elected therapy in 25 out of the 40 (60%) hospitalized children where HiNT was isolated. In two cases, HiNT was in blood, with complete recovery after therapy:

- 1) 15-m-o boy diagnosed of HiNT bacteriemia and bronchiolitis; and
- 2) 4 m-o boy diagnosed of HiNT sepsis.

Conclusions: HiNT role in the pediatric hospital setting is probably underexplored and misjudged. Further prospective studies should be warranted.

BORDETELLA PERTUSSIS INFECTION CONFIRMED BY REAL-TIME PCR THE EXPERIENCE OF A PAEDIATRIC HOSPITAL

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Background: In Portugal the Pertussis vaccine is in the National Immunization Program since 1965 . The vaccination coverage is > 90% in the last decade. Three doses of whole cell vaccine are recommended at the age of 2, 4, and 6 months and a fourth dose in the 6th year of life. In 2006 the acellular vaccine were introduced. In spite of that seems that in the last years.the incidence of Pertussis is rising.

Aims: To describe and evaluate the clinical presentation and complications associated with Bordetella pertussis (BP).

Methods: Retrospective study of patients with the diagnosis BP infection by Real-Time PCR in respiratory secretions. The study period was from December 2004 to June 2009.

Results: 38 diagnostics of BP by PCR were performed. Most cases occurred in 2005 (67%). The median age at diagnosis was 60 days (min 20 days, max 3 years). The interval from the onset of symptoms to diagnosis was on average 13 days. The majority had cyanotic paroxysmal cough (81.5%). Apnoeas were found in 29%. Respiratory failure in 10.5%. Seizures in 10.5% and in 8% there was leukemoid reaction. Co-infections in 10.5%. History of contact was reported in 37%, most first-degree relatives (mother 57%).

Conclusions: Most cases concentrated in 2005, a probable outbreak in the community. Despite of not existent deaths, the percentage of cases with serious complications was worrying. With regard to epidemiology, more than one third of children had contact with suspected cases, often more than one in the same family environment.

MORPHOLOGICAL CHARACTERISTICS OF FATAL CASES OF SALMONELLOSIS IN CHILDREN**I. Nezgoda, S. Singh**

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Vinnytsya, Ukraine*

Background and aims: To study the pathomorphological changes in the organs and tissues of children who died from salmonellosis.

Methods: The study of 13 fatal cases of salmonellosis in children who died from gastrointestinal (7 children) and septic (6 children) forms. Fatal cases occurred in children in the first year of life: 10 children up to 3 months and 3 children aged 4,7,8 months respectively. All cases were caused by hospital strain of *S. typhimurium*.

Results: In the gastrointestinal form into intestine there was observed variations of enterocolitis: catarrhal, erosive, pseudomembranous, ulcerative, haemorrhagic, ulcerative-necrotic. The changes in the lungs were manifested in septic as well as in gastrointestinal form. In early stages of the disease - changes similar to the "shock" lung, in late stages - destruction of the lungs in the form of microabscesses and purulent-fibrinous pleurisy. In the liver -fatty degeneration, the disorder of hemodynamics, activation of stellate reticuloendotheliocytes. In the kidneys -tubulointerstitial nephritis with the phenomenon of tubulorrhesis. In the brain -a disorder of hemodynamics, necrotic degenerative processes in the neurocytes.

Conclusions:

1. Morphological changes in salmonellosis depend upon the form of the disease and the duration of the disease.
2. Morphological features of gastrointestinal form is characterized by different histomorphological variants of enterocolitis (catarrhal, erosive, pseudomembranous, ulcerative, haemorrhagic, ulcero-necrotic) and kidney lesion (tubulointerstitial nephritis).
3. The sign of septic form is minimal lesion of intestine (catarrhal enterocolitis), total lesion of liver (serous hepatitis), of lungs (purulent bronchitis, lung abscess), of brain and meninges (meningitis, meningoencephalitis).

RECURRENT PNEUMOCOCCAL MENINGITIS -CASE REPORT-**E. Nicoara, M. Cerbu, A. Crisan***Infectious Diseases, University of Medicine and Pharmacy Timisoara, Timisoara, Romania*

Background and aims: *S. pneumoniae* is one of the most frequent causes of bacterial meningitis in children. *S. pneumoniae* can directly invade the meninges after basilar skull fractures or other trauma that compromises the dura and is the most common cause of recurrent bacterial meningitis in these patients.

The case fatality rate for pneumococcal meningitis is 5-10% and 25-30% of children with pneumococcal meningitis develop permanent neurologic sequelae (eg. hearing deficits, paralysis, hydrocephalus).

Case report: The authors present the case of a 9-year-old boy with recurrent pneumococcal meningitis that evolved well, without sequelae, with complete healing after neurosurgical procedure.

In June 2009 after falling off a bicycle the patient had cranial trauma with depressed right frontal fracture. After 5 weeks he was admitted with fever, headache, vomiting, purpuric rash and stiff neck. Lumbar puncture showed gram positive bacteria with capsule. Agglutination test was positive for *S.pneumoniae*. Pneumococcus was isolated from blood culture and spinal fluid. After treatment evolution was slowly favorable. CT showed a depressed right frontal fracture and a right frontal porencephalic cyst. In December 2008 and April 2009 the child was readmitted with recurrent pneumococcal meningitis that evolved well after treatment with antibiotics. After the last episode the fistula was identified and neurosurgically closed. Afterwards his evolution was good with healing without sequelae.

Conclusions: In cases of recurrent bacterial meningitis, underlying anatomic defects should be carefully evaluated if there are no immunodeficiencies.

PSEUDOMONAS (FLAVIMONAS) ORYZIHABITANS INFECTION IN FOUR HOSPITALIZED CHILDREN

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Background: *Pseudomonas (Flavimonas) oryzihabitans* nosocomial infection is rarely observed, mostly in adults with chronic disease or immunodeficiency, and related to central venous catheter or drain.

Methods: We report four cases of nosocomial infection due to this bacteria in three immunocompetent and one immunocompromised children between September 2006 and January 2009.

Results: Four children aged 9 years, 3 years, 14 and 15 months, have been hospitalized in the same paediatric department for acute dehydration related to hepatitis A infection, aplasia due to chemotherapy for rhabdomyosarcoma, bronchiolitis and gastroenteritis, respectively. All four patients developed acute episode of fever 4, 10, 3 and 4 days, respectively, after the onset of prolonged specific intravenous treatment. In three of them local inflammation was associated with vein thrombosis which was evidenced by ultrasonography. All patients had positive blood culture with *Pseudomonas (Flavimonas) oryzihabitans*. All children were cured with adapted antibiotherapy. Strains were not related according to molecular typing. Environmental water analysis did not find any colonisation with *Pseudomonas (Flavimonas) oryzihabitans*.

Conclusions: These unusual observations illustrate that *Pseudomonas (Flavimonas) oryzihabitans* nosocomial infection may concern (i) children, (ii) immunocompetent, (iii) use of peripheral catheter. This small series suggests that peripheral catheter should be rotated at 3 days if prolonged intravenous treatment is required.

SEVERE PANTON-VALENTINE LEUCOCIDIN *STAPHYLOCOCCUS AUREUS* COMMUNITY ACQUIRED NECROTISING PNEUMONIA IN A 7-WEEK -OLD INFANT

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Background and aims: *Staphylococcus aureus* strains producing the exotoxin Panton-Valentine Leucocidin (PVL) may cause severe invasive infections in children. We describe the youngest infant with PVL-*Staph. aureus* necrotising pneumonia that has ever been reported in the literature. She was the first child to be diagnosed in Malta with PVL-*Staph. aureus* infection.

Methods: A 7-week-old female presented with fever, cough, respiratory distress and signs of a right sided pleural effusion. She had no evidence of septic shock or organ failure. Radiological imaging revealed a right-sided necrotising pneumonia and a large empyema. She had a peripheral leucocytosis ($69 \times 10^9/l$), neutrophilia ($46 \times 10^9/l$), anaemia (8.6g/dl), thrombocytosis ($920 \times 10^9/l$) and a C-reactive protein of 323mg/l. Following drainage of the thick pleural pus she developed a tension pneumothorax, secondary to pneumatocoele rupture, which necessitating the insertion of a second intercostal drain. The abundant Gram-positive cocci seen on examination of the empyema fluid were identified as methicillin sensitive *Staph. aureus*. The infant was initially treated with teicoplanin and ceftriaxone and subsequently switched to cephalexin to receive a total of 6 weeks of antibiotics. Lung healing was complete with no residual pulmonary dysfunction.

Results: Toxin gene profiling of the *Staph. aureus* by a polymerase-chain-reaction assay confirmed the presence of luk-PV which encodes for PVL.

Conclusion: A clinical presentation suggestive of *Staph. aureus* invasive disease in association with a complicated clinical course and an exaggerated inflammatory response suggests the possibility of a PVL producing strain. Appropriate antibiotics, including an agent which inhibits toxin production, should ideally be initiated on clinical suspicion.

THE ROLE OF *STAPHYLOCOCCUS AUREUS* IN ATOPIC DERMATITIS

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Background and aims: The skin of patients with atopic dermatitis (AD) shows a striking susceptibility to colonization and infection with *Staphylococcus aureus* (SA). In this study we evaluated the pathotype of 116 strains of SA from the skin lesion, healthy skin and nares of children with AD, comparing the results with scorad index. We also analyzed the strains isolated from 106 healthy control subjects and from 84 patients' cohabitants.

Methods: The severity of dermatitis was estimated by SCORAD index (severe AD > 40, moderate AD 15-40, mild AD < 15). Nasal and skin (lesional and nonlesional) swabs cultures for SA detection were obtained from patients. Nasal swabs were taken from their partners and from control subjects. We also determined presence of: capsular antigen (*cap5-cap8*), agr-group, adhesins and toxins (*hls-spa-icaA-atl-cna-sdrE-sdrC-fnbA-clfA/B-eta-sea/seq-tstspIB-lukE*), Leukocidin Pantone-Valentine (PVL) genes by multiplex-PCR, antibiotic resistance with MIC. Genotypes was analyzed by PFGE (Pulsed-Field Gel Electrophoresis).

Results: We didn't find significant differences between patients with high and medium / low scorad; all strains showed virulence genes including, among others, a high percentage of adhesins (86%) that indicates a elevated invasiveness, and a notable spread of toxins (65%), considered important factors aggravating the skin lesions. Furthermore, the same genotype was found in several samples taken from the same patient and from related cohabitants.

Conclusions: Our data confirm the pathogenic role of SA in atopic dermatitis due to its high virulence and easy intrafamilial spreading and suggest the use of an appropriate antibiotic therapy in atopic patients and their cohabitants.

THE ROLE OF *STAPHYLOCOCCUS AUREUS* IN ATOPIC DERMATITIS

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Results: We didn't find significant differences between patients with high and medium / low scorad; all strains showed virulence genes including, among others, a high percentage of adhesins (86%) that indicates a elevated invasiveness, and a notable spread of toxins (72%), considered important factors aggravating the skin lesions. Furthermore, the same genotype was found in several samples taken from the same patient and from related cohabitants.

Conclusions: Our data confirm the pathogenic role of SA in atopic dermatitis, due to its high virulence and easy intrafamilial spreading, and suggest the use of an appropriate antibiotic therapy in atopic patients and their cohabitants.

RAPID DIAGNOSIS BY POLYMERASE CHAIN REACTION COMPARED TO CULTURES IN PEDIATRIC EAR INFECTIONS

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Introduction: In spite of the availability of effective antimicrobial therapy otitis media with effusion (OME) remains an important infection for children, leading to serious health problems.

Objectives: To investigate the diagnostic value of polymerase chain reaction (PCR) for the detection of bacterial DNA in OME and to compare the conventional culture methods (gold standard) to the molecular techniques.

Material-methods: A total of 102 middle ear effusions collected from hospitalized and outpatients children were analyzed. Multiplex PCR protocol was applied for the detection of *Haemophilus influenzae*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Streptococcus pneumoniae* and *Streptococcus spp* including *Streptococcus pyogenes* (GAS). Two stepdown multiplex - PCR assays were used for the simultaneous detection of nine main serotypes of *S. pneumoniae* directly in clinical samples.

Results: The frequency of the tested bacteria by the conventional cultures methods was *H. influenzae* 42.1%, *St. aureus* 21.5%, *Gas* 14%, *Ps. aeruginosa* 10.7% and *S. pneumoniae* 8.8%. The sensitivity of PCR assay compared to cultures was 92% for *H. influenzae*, *S. pneumoniae* and GAS while the method indicated 100% total specificity. In comparison to the cultures PCR assay was more sensitive for *S. pneumoniae* (20.5% vs 8.8%) and GAS (23% vs 14%). The most prevalent serotypes of *S. pneumoniae* were 19F, 6, 14, the serotypes 19A, 3 (not included in the 7-valent conjugate vaccine) and a high proportion were not typable.

Conclusions: PCR method could be considered as a rapid, reliable and feasible method for the detection of the most common fastidious bacteria that lead to OME.

EVALUATION OF THE ERADICATION RATE OF HELICOBACTER PYLORI INFECTION IN TUNISIAN CHILDREN USING BREATH TEST

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Aim: Evaluate using breath test (BT) the eradication rate of helicobacter pylori (*H.pylori*) after triple therapy in symptomatic children presenting *H.pylori* gastritis.

Patients and methods: Retrospective study of 100 children presenting chronic *H.pylori* gastritis, having at least one triple therapy and BT control. We studied clinical, histologic and therapeutic data.

Results: 100 children were included. The sex-ratio was 0.6. The median age was 10 years (2.5-15). Symptoms were dominated by abdominal pain (76%) and vomiting (56%). The most frequent endoscopic aspect was nodular gastritis (68%). The chronic gastritis was follicular in 65% and superficial in 35%. The *H.pylori* density was (2+) in 50% , (1+) in 40%. The initial triple therapy (7 to 14 days) consisted in amoxicillin, metronidazole omeprazole(AMO) in 72% and amoxicillin, clarithromycin, omeprazole (ACO)in 23%. One child who had a penicillin-allergy received metronidazole, clarithromycin, omeprazole(MCO). 4% of children received sequential treatment (amoxicillin, omeprazole during 10 days associated to 5 days of metronidazole followed by 5 days of clarithromycin). The BT control was negative in 60%. The non eradicated children (N=40) received a second triple therapy (14 days): AMO in 38% , ACO in 42%, sequential treatment in 18% and MCO in penicillin-allergic child. A second BTcontrol was negative in 28%. The infection persisted after an average of 4 triple therapies in 29 children.

Conclusion: The eradication rate evaluated by BT after one triple therapy was 60%. It increased to 71% after the second treatment. Bacteriologic studies and other therapeutic strategies should be proposed to ameliorate these results.

DETERMINATION OF ASL-O TITRE IN BLOOD DRAWN BY FINGER PRICK

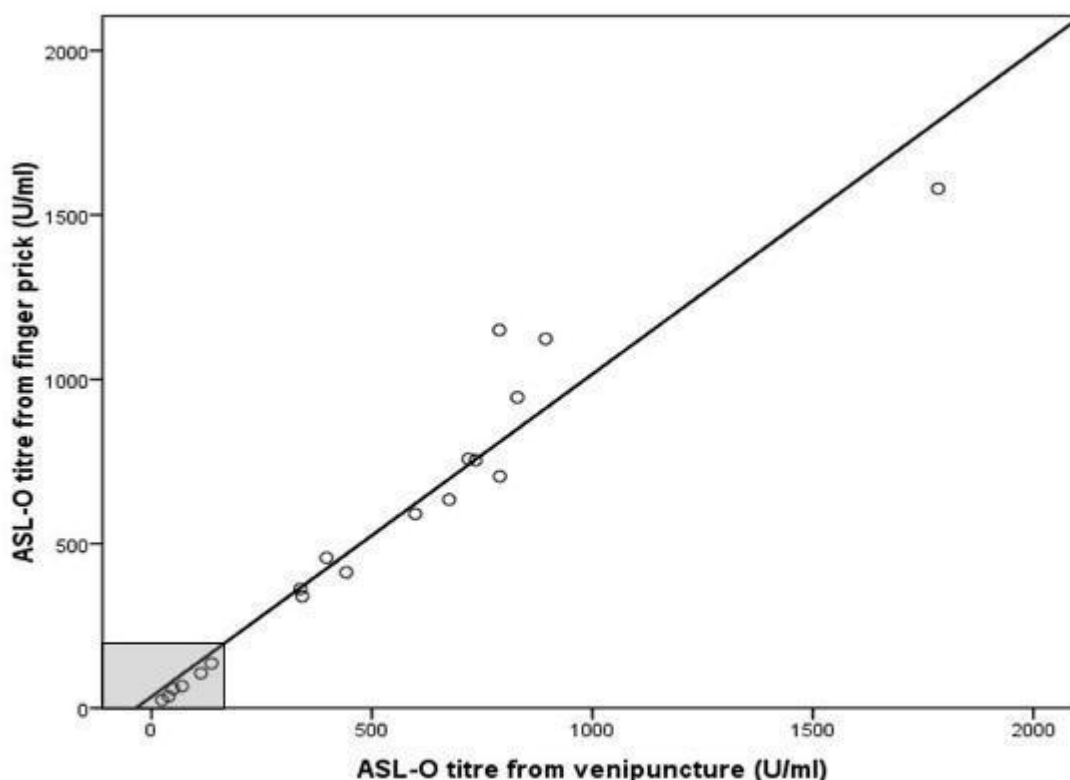
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Background: Repeated episodes of tonsillitis caused by group A streptococci (GAS) may prompt to tonsillectomy. However, clinically signs alone do not allow to distinguish GAS tonsillitis from suppurative tonsillitis of viral aetiology. In addition, up to 20% of healthy school children are asymptomatic GAS carriers. Hence, GAS carriers with viral tonsillitis will be tested positive for GAS. As a consequence, viral tonsillitis will be misdiagnosed as GAS tonsillitis. GAS aetiology can be proven by elevated ASL-O titres 2 to 3 weeks after illness. However, venipuncture to proof GAS aetiology of prior tonsillitis is not desirable in meanwhile healthy children.

Methods: We draw blood by finger prick (0.2ml) and by venipuncture (2ml) in 28 children and adolescents. ASL-O titre was measured by means of a standard immunoturbidimetric test, statistical analysis was performed by means of SPSS for windows (Kolmogorov-Smirnov Test, Pearson's correlation coefficient).

Results: ASL-O titre values from finger prick and from venipuncture show a significant correlation ($r=0.976$, $p<0.001$). At a cut off value of 200 U/ml, results from finger prick have a sensitivity and specificity of 100%, when compared with results from venipuncture. See graph 1.



Graph 1. Correlation of ASL-O titre values from finger prick and from venipuncture. Gray – normal range

[graph 1]

Discussion: Blood drawing by finger prick is a reliable method to determine ASL-O titre. Thus, venipuncture in convalescent or healthy children is not necessary to proof GAS aetiology of previous illness.

PREVALENCE OF NEONATAL CONJUNCTIVITIS DUE TO CHLAMYDIA TRACHOMATIS IN TWO HOSPITALS IN IRAN

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Introduction: One of the most common bacterial infections causing ophthalmia neonatorum is *Chlamydia trachomatis*. Very few studies have been done in Iran to determine the prevalence of *Chlamydia trachomatis* causing ophthalmia neonatorum using cell culture and polymerase chain reaction methods. This study aimed to evaluate the prevalence of neonatal chlamydial conjunctivitis by these methods, in two hospitals, Tehran, Iran.

Material and methods: From March 2008 to May 2009, of the 2253 neonates, 241 (10.7%) with clinical findings of conjunctivitis were included in this study. A total of 241 conjunctival swabs were investigated by cell culture (as the gold standard test), polymerase chain reaction and Giemsa staining. Direct fluorescent-monoclonal antibody test was performed for the last 43 cases in addition to those three diagnostic tests.

Results: Cell cultures were positive for *Chlamydia trachomatis* in 31 (12.9%) neonates. Also *Chlamydia trachomatis* was positive in 40(16.6%) and 18(7.5%) neonates by polymerase chain reaction and Giemsa staining respectively. The sensitivities of polymerase chain reaction and Giemsa staining were 100% and 58.1% respectively. Of the last 43 cases, 4 neonates had neonatal chlamydial conjunctivitis by direct fluorescent-monoclonal antibody test and the sensitivity of direct fluorescent-monoclonal antibody was 50%.

Conclusion: Regarding to high prevalence of neonatal chlamydial conjunctivitis by cell culture, and high sensitivity and specificity (100% and 95.7% respectively) of polymerase chain reaction in the present study, polymerase chain reaction can be considered as a proper diagnostic method for detection of *Chlamydia trachomatis*.

A PROSPECTIVE STUDY OF COMMUNITY-ACQUIRED BACTEREMIA IN JAPAN

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Objective: This prospective study was conducted to clarify clinical and microbiological characteristics of community-acquired bacteremia in Japan.

Object and method: Bacteremic patients were identified in seven out-patient clinics and one ER of a hospital from January 2008 to December 2009. Clinical finding and laboratory data were gathered from each paediatrician. Serum serotypes, drug susceptibilities, the genomic typing (MLST), and the resistant genes of each pathogen were analyzed in Osaka Prefectural Institute of Public Health.

Results: During two years, 56 children of *Streptococcal pneumoniae* and 14 cases of *Haemophilus influenzae* (*Hi*) were included. In cases of *S. pneumoniae*, 54 (96.4%) were occult bacteraemia (OB), and two (3.7%) were bacterial meningitis. 44 (78.6%) isolates were PCV7 serotypes. 12(21.4%) isolates were Genotypic Penicillin-sensitive *S. pneumoniae* (gPSSP). In cases of *Hi*, 13 (92.9%) was *Hib*, and one (7.1%) was *HiNT*. 10 were OB, three were meningitis, and One was epiglottitis and pleural empyema. Three (21.4%) isolates were genotypic low beta-lactamase-negative ampicillin resistant (g-low-BLNAR). 7 (50.0%) were g-BLNAR, and 4 (28.6%) were gene beta-lactamase-positive ampicillin/clavulanic acid-resistant (g-BLPACR), respectively.

Conclusion: The bacteraemia caused by these two bacteria are common as community-acquired bacteremia. The genes mutation is remarkably high prevalence. There is no reason to hesitate to introduce *Hib* vaccine and PCV7 into NIP in Japan.

SUDDEN DEATH CAUSED BY *STAPHYLOCOCCUS AUREUS* CARRYING PANTON-VALENTINE LEUKOCIDIN GENE IN A 2-YEAR-OLD AGE GIRL

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Pneumonia due to PVL positive *S. aureus* is often rapidly fatal. We report on a suddenly died 2-year-old girl whose post-mortem examination revealed a pleuropneumonia due to a PVL-producing *Staphylococcus aureus* strain. For instance, little attention has been paid to the possible genetic predisposition to infection with PVL producing staphylococci. Our patient from consanguineous families is significantly younger than those previously reported. Infection with PVL producing staphylococci can cause diseases ranging from superficial skin infections to deep-seated and systemic conditions such as severe bone and joint infections, septic shock, and necrotizing pneumonia. The immune status of the host could be important. Finally, our case raises the question of the incidence of infection with PVL producing staphylococci in Sudden Infant Death (SIDS). Backwell et al. find that more than 10% of SIDS had *Staphylococcus aureus* in a sterile site. An increased throat carriage of *Staphylococcus aureus*, coliforms, and group B streptococci could be found in a comparison with normal healthy age matched infants. Indeed, staphylococcal toxins have been demonstrated in the tissues of a large proportion of babies deemed to have died of SIDS. However, to our knowledge, Pantone-Valentine leukocidin had never been specifically studied in a cohort of SIDS cases.

EXPRESSION OF SOLUBLE AND CD4⁺ T CELL-BOUND CEACAM1 IN PEDIATRIC SEPSIS

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Introduction: The co-inhibitory molecule CEACAM1 with its self ligand soluble or cell-bound CEACAM1 forms a potent suppressor of T cell responses. In sepsis T cell function is suppressed as displayed by decreased *in vitro* cytokine production and proliferation. We assessed the expression of soluble and CD4⁺ T cell-bound CEACAM1 in pediatric sepsis.

Methods: Circulating soluble CEACAM1 was assessed via Elisa in children with meningococcal sepsis. In addition, the percentage CD4⁺ T cell expressing CEACAM1 was assessed in neonatal late onset sepsis in very low birth weight (VLBW) infants via flow cytometry.

Results: Median (range) serum soluble CEACAM1 levels were higher in children with meningococcal sepsis (n= 20) than in controls (n=26)(53834 pg/mL (39427-268106 pg/mL) versus 9737 pg/mL (5057-34174 pg/mL); P< 0.001). Serum soluble CEACAM1 levels correlated inversely with plasma IL-8 levels (R = -0.618; P=0.043; n=11). Median (range) percentage CEACAM1 Positive CD4⁺ T-cells in late onset sepsis (n=12) were higher than in controls (n=16) (19% (5-76%) versus 7% (2-52%); P=0.019). The maximal CRP level correlated significantly with percentage CEACAM1 positive CD4⁺ T-cells in sepsis patients (R=0.6; P= 0.038).

Conclusion: CEACAM1 expression is increased in pediatric sepsis. Children with meningococcal sepsis had increased serum soluble CEACAM1 during the course of ICU admission. Soluble CEACAM1 was inversely correlated with proinflammatory plasma IL-8 levels. VLBW infants with late onset sepsis had an increased percentage CD4⁺ T-cells expressing CEACAM1.

MENINGOCOCCAL SUSCEPTIBILITY GENES IDENTIFIED USING GENE EXPRESSION PROFILING

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Background and aims: Meningococcal sepsis and meningitis remains one of the most devastating infections affecting young children and adolescents worldwide. Considerable progress has been made in understanding the pathophysiology and immunopathogenesis of the disorder, but mechanisms underlying shock and multi-organ failure still remain poorly understood. We aimed to understand the host response to meningococcal infection using whole-genome RNA expression profiling, both in acute disease and after recovery.

Methods: We used the Illumina Sentrix® BeadChip array to examine patterns of gene expression in peripheral blood from 39 Caucasian paediatric patients with meningococcal meningitis or meningococcal sepsis. We compared gene expression in the acute phase to 21 Caucasian controls, as well as comparing expression levels between different clinical forms and different phases of the disease. Differentially expressed genes were confirmed by real-time PCR. We also determined if polymorphisms in these genes were related to levels of expression in patients with different genotypes.

Results: We identified distinct subsets of genes differentially expressed by >2-fold between cases and controls, acute and convalescence, and meningococcal sepsis and meningococcal meningitis. Multiple biological pathways were found to be activated in the acute samples, including those mainly involved with the inflammatory response and in cell-to-cell signaling and interaction.

Conclusions: RNA expression analysis provides a new way of studying the complex inflammatory and metabolic processes in critically ill children. Our analysis identifies new inflammatory genes and pathways involved in meningococcal sepsis and meningitis, and provides a comprehensive insight into the complexity of the host response to meningococcal infection.

UTILITY OF BLOOD CULTURES IN FEBRILE CHILDREN

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Background and aims: Febrile children under 3 years without identifiable focus are at risk of serious bacterial infection. Empirical treatment with antibiotics pending results of blood culture has been widely followed in clinical practice.

We aimed to examine current practice in the utility of blood cultures in a busy inner-city paediatric A+E department, and ascertain characteristics and outcomes of children who had blood cultures (BC) sent.

Methods: We retrospectively analysed the clinical notes of febrile children in whom BC were sent during a 1-month study period. We studied the incidence of serious bacterial infection, duration of treatment with antibiotics, length of stay in hospital and outcomes.

Results: During the 1-month study period, there were 37 febrile children under 3 years old. 33(89%) were admitted to the hospital. 25 (68%) were started with empirical intravenous antibiotics. The average length of stay was 2.2 days. Serious bacterial infection (SBI) was seen in 4 (11%) children and possible SBI in 14 (38%) children. Viral or other infection was seen in 19 (51%) children. Blood cultures were negative in all the children studied. Other microbiological investigations were diagnostic in 11 children.

Conclusions: The majority of the febrile children under 3 years in our study are admitted to hospital and receive empirical antibiotic treatment. Despite a low yield, blood cultures continue to be frequently utilised and considered an important investigation. Application of alternative diagnostic methods to detect serious bacterial infection may have a role in rationalising management of such children.

SERUM AND CEREBROSPINAL FLUID LEVELS OF COLISTIN IN PAEDIATRIC PATIENTS

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Background and aims: There is a paucity of pharmacokinetic data regarding colistin administration in paediatric patients. Recommended doses of colistimethate sodium (CMS) range between 50,000-75,000 IU/kg/d (4-6 mg/kg/d) in Europe and 83,000-166,000 IU/kg/d (6.6-13.3 mg/kg/d) in USA. Our aim was to determine colistin concentrations in serum and cerebrospinal fluid (CSF) of non cystic-fibrosis infants and children treated intravenously with CMS.

Methods: Blood and CSF sampling was performed from paediatric patients carrying an external ventricular drainage system who were receiving intravenous CMS for Gram-negative bacterial infections. Samples were obtained before and after CMS administration. For determination of colistin concentrations a recently introduced analytical method was employed, using a simple precipitation step followed by Liquid Chromatography tandem Mass Spectrometry.

Results: Five CMS courses in 3 patients were studied. For each course, corresponding CMS doses-patient ages were: 60,000 IU/kg/d-1½ months, 130,000 IU/kg/d-2½ months, 200,000 IU/kg/d-5½ months, 200,000 IU/kg/d-5½ years, 225,000 IU/kg/d-14 years. Mean peak serum colistin concentrations ranged between 0.29-2.64 mg/l and trough concentrations between 0.19-1.83 mg/l. Only in one course (225,000 IU/kg/d-14 years) the peak serum concentration (2.64 mg/l) exceeded the 2 mg/l breakpoint used by CLSI and EUCAST to define susceptibility to colistin for *Pseudomonas aeruginosa* or *Acinetobacter baumannii*. Colistin penetration in CSF was minimal but increased significantly in the presence of meningitis (34-67% of serum levels).

Conclusions: Higher than previously recommended CMS doses may be needed for paediatric patients to treat bloodstream or central nervous system infections caused by Gram-negative bacteria, particularly if these exhibit borderline susceptibility to colistin.

DECREASING ERYTHROMYCIN RESISTANCE OF GROUP A STREPTOCOCCUS ISOLATES FROM A GERMAN PAEDIATRIC TERTIARY CARE CENTRE

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Background and aims: Group A streptococcus (GAS) is still a major pathogen of tonsillopharyngitis in children, with macrolides often being used as a second line treatment. While in the time period between 1990 and 2002 several studies reported on significantly increasing rates of macrolide resistance, a trend towards a decrease in erythromycin resistance over time was found in a study conducted from 1999 to 2003 at our hospital. Only recently there have emerged other reports about declining rates of macrolide resistance in GAS-infections. The aim of this present study was to determine the further development of macrolide resistance at our paediatric centre.

Methods: From 2006 until beginning of 2009 around 350 GAS isolates were collected from children with various infections, the majority of them with tonsillopharyngitis. Resistance rates to erythromycin, clindamycin, azithromycin, penicillin, cefotaxime and tetracycline were determined. All macrolide resistant and intermediate isolates were screened for the presence of genes related to macrolide resistance (*prt1*, *mefA*, *ermB*, *ermTR*).

Results: While in the study from 1999 to 2003 the overall erythromycin resistance was around 13%, erythromycin resistance in our current investigation was now found to be below 5%. Isolates resistant or intermediate to erythromycin or clindamycin were almost always positive for genes promoting macrolide resistance.

Conclusions: A further decline in erythromycin resistance in GAS isolates was noticed in our patient cohort since 2006. It is hypothesized that the increased susceptibility of GAS to erythromycin might be related to a decreased nonreflective use of macrolides.

DETECTION OF GENETIC MUTATIONS ASSOCIATED WITH MACROLIDE RESISTANCE OF *MYCOPLASMA PNEUMONIAE*

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Purpose: The aim of this study was to identify known mutations associated with macrolide resistance in *M. pneumoniae* (MP).

Methods: Nasopharyngeal aspirates (NPAs) were collected from the 62 children diagnosed with MP pneumonia by serologic method or polymerase chain reaction. The 23S rRNA and L4 ribosomal protein genes of MP were amplified and sequenced. To identify mutations in two genes, their nucleotide sequences were compared to those of reference strain M129. Cultivation of MP was carried out for 32 (28 frozen and 5 refrigerated) NPAs and M129 strain using Chanock's glucose broth and agar plate in a 5% CO₂ incubator at 37°C and examined at 2-3 day intervals for 6 weeks.

Results: Among 62 specimens, 17 (28%) had M144V mutations in ribosomal protein L4. The A2064G mutation was observed in 1 (1.6%) among 61 specimens of which 23S rRNA gene was successfully sequenced. Culture for MP was successful from M129 strain and 2 out of 5 NPAs that were kept refrigerated for no longer than 3 days. However, MP did not grow from 28 NPAs that were kept frozen at -80°C since 2003.

Conclusion: We found the M144V mutation of L4 protein was common while that of domain V of 23S rRNA gene was relatively rare among MP. Studies on the prevalence of macrolide resistant MP and the relationship between the mutations of 23S rRNA gene and ribosomal protein L4 will be useful to understand the mechanism of macrolide resistance in MP.

EFFECTS OF LIPOSOMAL TOBRAMYCIN BISMUTH ON *PSEUDOMONAS AERUGINOSA*C. Dorval, M. Alipour, Z.E. Suntres, **A. Omri***Chemistry/Biochemistry, Laurentian University, Sudbury, ON, Canada*

Chronic lung infection caused by *Pseudomonas aeruginosa* is the leading cause of morbidity and mortality in Cystic Fibrosis patients. Once *P. aeruginosa* colonizes the airway mucosa in Cystic Fibrosis patients, a phenotypic mucoid conversion and formation of biofilms become increasingly difficult to clear. A synergistic approach consisting of liposomal tobramycin bismuth alongside alginate lyase is intended to increase susceptibility of *P. aeruginosa* biofilms by reducing alginate and allowing the encapsulated antimicrobial to penetrate the bacteria. The minimum inhibitory concentrations (MICs) and minimum bactericidal concentrations (MBCs) of free and liposomal tobramycin bismuth against two mucoid strains of *P. aeruginosa* were determined by microbroth dilution method while the minimum biofilm eradication concentration (MBEC) was determined in the presence and absence of alginate lyase with the use of Calgary biofilm device plates. The penetration of the antimicrobials was assessed using the immunogold-labeling technique and transmission electron microscopy (TEM). The effects of free and liposomal tobramycin bismuth on alginate reduction were quantified by the carbazole assay. The MICs, MBCs and MBECs were reduced for liposomal tobramycin bismuth when compared to free tobramycin bismuth. The addition of alginate lyase in conjunction with liposomal tobramycin bismuth enhanced biofilm eradication. The TEM study showed that tobramycin penetration is superior when delivered as a liposomal formulation. Alginate was reduced using sub-inhibitory concentrations of liposomal tobramycin bismuth. These findings substantiate the significant role of liposomal tobramycin bismuth in the management of biofilm-associated Cystic Fibrosis lung infection.

PREVALENCE OF NASAL *S. AUREUS* AND MRSA IN HOSPITAL PERSONNEL AND ASSOCIATED RISK FACTORS

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Background and aims: Hospital- and community-acquired *Staphylococcus aureus* infections pose a substantial burden in terms of morbidity, mortality and healthcare costs. The extent of nosocomial *S. aureus* transmission, in particular methicillin-resistant *S. aureus* (MRSA), the prevalence of *S. aureus* colonization, associated risk factors and antibiotic resistance were also analyzed in healthy hospital personnel.

Methods: The samples were obtained by rubbing a sterile cotton swab in both nostrils consecutively and inoculated on 5% sheep blood agar and incubated. Morphologically *S. aureus* was identified by Gram-staining, catalase, and coagulase test by standard methods. Antibiotic susceptibility testing was performed by using disk diffusion method.

Results: The prevalence of *S. aureus* and MRSA nasal carriage was higher in physicians (51.8%, 18.5%), nurses (66.6%, 27.3%) and sanitary workers (59%, 13.6%) as compared to administrative staff (27.6%, 2.1%). There was no difference between carriers and non-carriers with regard to fever or antibiotic usage in the past 30 days, diabetes mellitus, asthma and working duration while smoking exposure was significantly associated ($p=0.006$). The isolates from physician, nurses and sanitary workers were comparatively more resistant to various antibiotics than the isolates from administrative staff.

Conclusions: In conclusion, our study confirms the high *S. aureus* and MRSA nasal colonization in hospital personnel especially in physicians and nurses. As hospital personnel are at high risk of transmitting *S. aureus*. Therefore they should remain vigilant to follow appropriate measures (e.g., use of facemasks) for minimizing transmission.

Keywords: Nasal carriers, hospital personnel, prevalence, risk factors, *Staphylococcus aureus*, MRSA.

MACROLIDE-RESISTANT *STREPTOCOCCUS PYOGENES* FROM CHINESE PEDIATRIC PATIENTS IN ASSOCIATION WITH TN916 TRANSPOSONS FAMILY OVER A 16-YEAR PERIOD

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Background: Resistance of *S. pyogenes* to macrolides has been increasingly detected in several European countries.

Aim: To investigate changes in the antimicrobial susceptibility of *Streptococcus pyogenes* isolates over a 16-year period. 456 Group A streptococci(GAS) isolates were collected from Chinese pediatric patients among 1993-1994 and 2005-2008.

Methods: Susceptibilities to antibiotics were performed using agar dilution methods. The macrolide resistance genes *ermB*, *ermTR*, *mefA* and tetracycline resistant gene *tetM* and the *int* and *xis* genes of Tn916 family were detected by polymerase chain reaction (PCR).

Results: All 456 strains were analyzed by *emm* typing. Selected strains representing each *emm* type were further characterized by pulsed-field gel electrophoresis (PFGE). The resistance rates of erythromycin and clindamycin both significantly increased during the two sample periods (79.7% vs. 94% for erythromycin and 75.4% vs. 96.9% for clindamycin). Telithromycin resistance rate increased from 20.37% to 87.93%. Among the macrolide resistance strains, the rate of strains with the genes *int*, *xis*, *tetM* and *ermB* increased with time (16.05% vs. 86.91%, $P < 0.05$). The *emm1* and *emm12* isolates had high rates of *ermB* gene, which increased after 16 years (65.2% vs. 86.23%, for *emm1* and 7.7% vs. 91.8% for *emm12*).

Conclusions: Significant increases in macrolide resistance may not only be related with the shift in the *emm* types, but also with the change of Tn916 family in the isolates from Chinese children.

THE ARGININE CATABOLIC MOBILE ELEMENT IS ASSOCIATED WITH LOW ANTIBIOTIC RESISTANCE AND LOW PATHOGENICITY IN *STAPHYLOCOCCUS EPIDERMIDIS* FROM NEONATES

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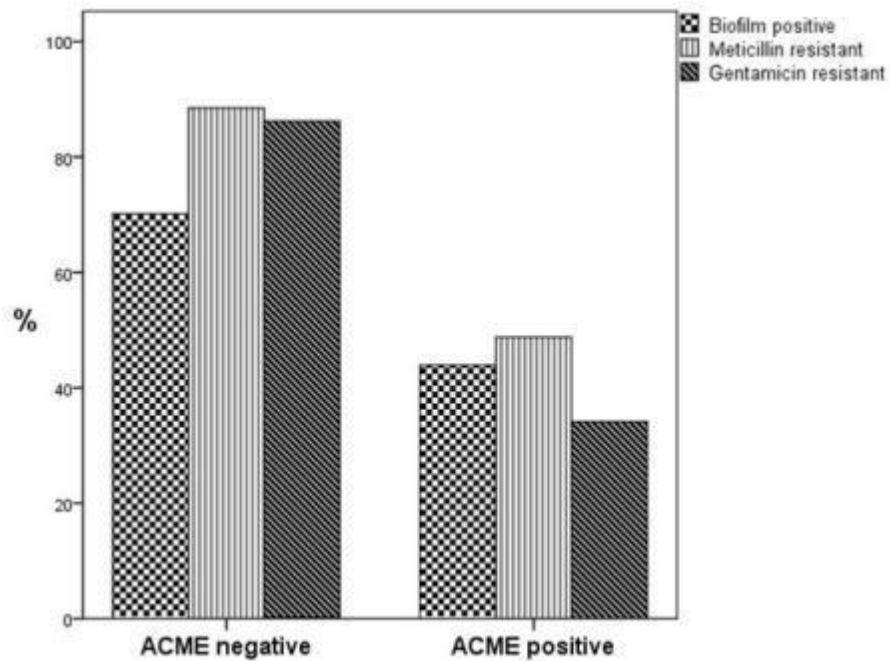
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Background: The arginine catabolic mobile element (ACME) in staphylococci encodes several putative

virulence factors. ACME appears to have been transferred from *Staphylococcus epidermidis* into *Staphylococcus aureus* and is strongly associated with the epidemic and virulent *S. aureus* USA300. *S. epidermidis* is the most prevalent cause of late-onset sepsis in neonates, but there is a paucity of knowledge regarding its virulence factors.

Methods: We analysed the distribution of ACME in 128 *S. epidermidis* blood culture isolates from neonates. We assessed ACME's impact on antibiotic resistance, biofilm production, invasive capacity and host inflammatory response. In a whole blood sepsis model we compared the effect of ACME-positive and -negative isolates leukocyte activation, cytokines and complement activation.

Results: ACME was detected in 15/64 (23%) invasive blood culture isolates and 26/64 (40%) blood culture contaminants ($p=0.02$). ACME-positive isolates displayed less antibiotic resistance ($p < 0.001$) and were collected from more mature neonates ($p = 0.001$). Biofilm production was more prevalent among ACME-negative isolates (61/87) versus ACME-positive (18/41) ($p = 0.004$). Among the 64 neonates considered having an invasive infection, ACME did not influence the maximum C-reactive protein level. There were no differences in the inflammatory response between ACME-positive and -negative isolates.



Biofilm production, meticillin- and gentamicin resistance among ACME-positive and -negative blood culture isolates (n=128) obtained from neonates

[Assosiacion of ACME and known virulensfactors]

Conclusion: ACME in *S. epidermidis* from neonates is associated with less antibiotic resistance and does not appear to be associated with increased pathogenicity.

**DISTRIBUTION OF GENETIC DETERMINANTS CHARACTERISTIC OF THE VIRULENCE
PLASMID pS88 AMONG ESCHERICHIA COLI STRAINS CAUSING BACTEREMIA IN YOUNG
INFANTS**

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A large plasmid, pS88, involved in the virulence of *E. coli* meningitis strain O45:K1:H7 has been sequenced. Its distribution among other extraintestinal pathogenic *E. coli* (ExPEC) than meningitis strains has not yet been investigated. We describe the prevalence of pS88 genes among 120 *E. coli* strains causing bacteremia in young infants (< 3 months).

The bacteremia isolates were obtained between 2001 to 2009 in our paediatric hospital and were secondary to urinary tract infection (UTI, n=73), gut translocation (GT, n=25) or digestive surgery (DS, n=22). Phylogenetic groups and subgroups were determined using a quadriplex PCR (*chuA*, *yjaA*, TSPE4.C2, *svg*). The detection by PCR of the following genetic determinants (*cia*, *colV*, *iss*, *etsC*, *ompTp*, *sitA*, *hlyF*, *iroN*, *iucC*) indicate the presence of a pS88-like plasmid.

pS88-like plasmid was found in 29.1% (n=35) of bacteraemia isolates and in 13.6%, 32.8% and 32% in DS, UTI and GT strains respectively. Among the diverse phylogenetic groups (B2, n=86; B2₁, n=42; D, n=24; A, n=8; B1, n=2) pS88-like plasmid was mainly distributed in the highly virulent subgroup B2₁ (87%) but was also found in non virulent groups A/B1 (11%). Strains harboring pS88-like plasmid comprised several ExPEC associated O serogroups: O45 (40%), O1 (23%), O2 (20%), O18 (3%) but none were O6, O7, or O16.

pS88-like plasmid is not restricted to *E. coli* meningitis strains and might contribute to the virulence of other ExPEC strains. Although it is mainly present in B2 group strains it has diffused in other phylogenetic groups such as B1 or A.

POTENTIAL ROLE OF FIMBRIAL ADHESINS IN PERSISTENCE OF MULTIRESTANT ESBL-PRODUCING *ESCHERICHIA COLI* AND *KLEBSIELLA PNEUMONIAE*

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Background and aims: *Escherichia coli* and *Klebsiella pneumoniae* are common causes of hospital and community-associated infections. Fimbrial adhesins are essential for the initial invasion of the human organism. The aim of this study was to evaluate the importance of fimbrial adhesins in persistence of paediatric infections, from 2006 to 2009, at Santa Maria Hospital.

Methods: *E. coli* isolates were obtained from urinary tract infections (n=12) and *K. pneumoniae* isolates from urinary, blood and respiratory infections (n=22). Patients were from different paediatric units (mostly Nephrology, Emergency and Pneumology). Phylogenetic studies were done by disk diffusion method. Virulence factors were tested through specific PCR reactions for each gene (*fimH* and *ecpA* for *E. coli*; *fimH* and *mrkD* for *K. pneumoniae*) and confirmed by sequencing. Molecular typing was performed by M13 fingerprinting.

Results: Patients were colonized for periods that ranged from two months to two years. One child in particular had alternating infections with both microorganisms. All isolates were multiresistant and produced ESBLs. 33% of *E. coli* isolates had *fimH* and 42% had *ecpA*, while 95% of *K. pneumoniae* isolates had *fimH* and 91% had *mrkD*.

Conclusion: Type 1 fimbriae produced by *K. pneumoniae* are described as functionally and structurally similar to type 1 fimbriae from *E. coli*. We found that *fimH* and *mrkD* seem to have an important role in persistence of ESBL-producing *K. pneumoniae*, but for *E. coli* there may be different mechanisms, other than fimbrial adhesins, that allow permanence for long periods of time.

ANALYSIS OF PHASE VARIATION OF MENINGOCOCCAL OPA GENES

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Background and aims: Opacity-associated (Opa) adhesin proteins are major meningococcal outer membrane proteins involved in infection of the nasopharynx and immune interactions, and are currently being evaluated as a novel serogroup B meningococcal vaccine candidate. Opa proteins undergo phase variation due to the presence of a coding repeat (CR) tract containing the pentameric repeat sequence 5'-CTCTT-3'. Modulation of the number of repeats occurs by slipped-strand mispairing during DNA replication, resulting in regular frameshifting. This is a key mechanism of immune evasion, as Opa proteins are known to induce antibodies following meningococcal infection and after immunisation with outer membrane vesicle vaccines. The dynamics of phase variation of meningococcal Opa proteins is unknown, and has significant implications for bacterial pathogenesis and vaccine development.

Methods: *N. meningitidis* was serially passaged, following which genomic DNA was extracted from single colonies. All 4 *opa* genes were amplified from each DNA sample by polymerase chain reaction and nucleotide sequence analysis undertaken, to include the entire length of each CR tract.

Results: Different *opa* genes possessed different lengths of CR tract at the start, and some *opa* genes maintained a constant number of repeats during serial passage. Other *opa* genes demonstrated phase variation with both increases and decreases in CR tract length observed.

Conclusions: These data provide valuable information for the first time regarding differences in phase variation between different meningococcal *opa* genes, and suggest that differences between Opa variants may exist in terms of their function during infection or potential for inclusion in a meningococcal vaccine.

BIFOCAL SEPTIC OSTEOARTHRITIS DUE TO GROUP A STREPTOCOCCUS: A CASE REPORT**S. Botto Poala, S. Bressan, D. Messina, L. Da Dalt***Paediatrics Department, University of Padua, Padua, Italy*

Multifocal septic osteoarthritis is a rare clinical entity, with only few cases reported to date. We describe a case of osteoarthritis of the right shoulder and knee in a previously healthy 14-month-old boy. He presented with a history of high-grade fever in the previous 72 hours, associated with progressive pain and swelling of the right shoulder and knee. Physical examination findings were consistent with arthritis of the affected joints without other abnormalities. His recent and past medical history were unremarkable. Acute-phase reactants resulted elevated (white blood cell count of 14.530/mm³, neutrophil count of 10.340/mm³, C-Reactive protein of 183 mg/L). The blood culture performed at admission subsequently grew a Group A beta-hemolytic streptococcus (GABHS). Plain radiographs and US of the affected joints revealed soft-tissue edema, mild effusion and widening of the joint capsule. Because of worsening despite appropriate antibiotic therapy with ceftriaxone and oxacillin the child underwent surgical drainage of the knee and arthrotomy of the shoulder. Cultures of the purulent aspirated fluids were negative. An MRI also showed adjacent osteomyelitis of the right humerus. Parenteral antibiotic therapy with ceftriaxone and clindamycin was continued for 6 weeks and the child fully recovered without apparent sequelae after 8 months from infection.

GABHS is an uncommon cause of septic osteoarthritis in childhood, but it may be responsible of severe multifocal joint infections, as shown in our report. Early surgical intervention and prolonged antibiotic therapy remain the key points for a successful outcome.

VARICELLA, IBUPROFEN AND NECROTIZING FASCIITIS

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Background: Chickenpox is usually a benign disease with good prognosis in childhood. It may however be complicated by superinfection and cause severe necrotizing fasciitis.

Case history: A girl of seven years presented in the evolution of chickenpox treated with ibuprofen, a severe septicemia and edematous and necrotic lesions of the left leg and pelvis. The disease was cured surgically by repeated excision of necrotic tissue and also by appropriate antibiotherapy.

Discussion: The clinical presentation of bacterial dermohypodermatitis with necrotizing fasciitis complicating chickenpox remains fairly stereotyped with a worsening of symptoms around the 4th day corresponding to the onset of a septic syndrome, unbearable pain sometimes resulting functional impairment that may precede the appearance of local inflammatory signs.

Additional tests are unnecessary, except perhaps the MRI that highlights the achievement of deep fascia, a specific sign of necrotizing fasciitis, with enhancement by contrast product.

The management should be medico-surgical. The initial antibiotherapy at large spectrum should be adapted according to the type of germ and its microbial sensitivity tests. Surgical intervention should be done early, it confirms necrotic lesions of the aponeurosis and allows its excision; some additional resections are often necessary.

Conclusion: This observation shows the importance of a medico-surgical management of necrotizing fasciitis and is discussing the role of chickenpox, group A streptococcus and non-steroidal anti-inflammatory agents in this disease.

THE STUDY OF CAUSATIVE MICRO-ORGANISMES OF BURN WOUND INFECTION

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Infection remains the leading cause of morbidity and mortality in burn patients. And burn wound infection is the most important type of infection in this patient. The main of this study was to determine prevalence of causative micro-organismes of burn wound infection.

Between 70-90% of pathogens are endogenous, the remainder being acquired by cross infection, principally from the hands of health care workers.

All burn wound infections colonize by organismes in 72 hour after injury. And we must distinguish between true infection from colonization of the wound with micro-organismes.

Gram-positive organismes predominate in burn wounds immediately after the injury. *Staphylococcus aureus* has emerged as the most common gram-positive colonizer of burn wounds.

Gram-negative organismes colonize the eschar and become predominant by the end of the first post-burn week (specially *Pseudomonas aeruginosa*).

The commonest organismes causing invasive burn wound infections are fungi (*Candida* species, *Aspergillus* and *Fusarium* species) late burn wound excision and the peri-operative use of antibiotics are the main reasons for this fungal burn wound infection.

After fungal infection, *Pseudomonas* and *Staphylococcus aureus* are the most common cause of burn wound infection. Also the most common cause of burn wound infection is different in one center from another center.

PERIORBITAL AND ORBITAL CELLULITIS IN CHILDREN: A SINGLE-CENTER EXPERIENCE**E. Farmaki**, I. Tsoutsou, N. Nedelkopoulou, M. Dimitriadou, G. Pardalos, M. Athanassiou-Metaxa*1st Dept of Pediatrics, Aristotle University of Thessaloniki, Hippokration General Hospital, Thessaloniki, Greece***Background:** Periorbital cellulitis (PC) and orbital cellulitis (OC) are two distinct childhood diseases with potentially devastating consequences.**Aim:** To study the predisposing factors, clinical presentation, laboratory and CT findings, management and outcome of these two clinical entities.**Methods:** Children with PC or OC hospitalized in a tertiary care pediatric hospital between 1/2006-6/2009 were retrospectively reviewed.**Results:** Sixteen children (male:11) aged 7m-12yrs (median age:3.5 yrs) were identified. Based on CT/MRI findings, 4 children had OC (diffuse orbital fat infiltration:2, subperiosteal abscess:1, orbital phlegmon:1), all associated with pan-sinusitis. Twelve children had PC related to pan-sinusitis in 3, maxillary and/or frontal sinusitis in 3, insect bites in 3, dental abscess in 1 and conjunctivitis in 1. All patients with OC or post-sinusitis PC were systemically ill and febrile. There were no differences in mean blood cell count, ESR, and CRP between children with OC and post-sinusitis PC. Blood cultures obtained from 7/16 patients were negative. One conjunctivae culture was positive for *S. pneumoniae*. All children were successfully treated with parenteral antibiotics and no surgical intervention was required. Repeat CT scan performed after discharge from the hospital revealed improvement and near complete resolution of the orbital complications and/or sinus congestion.**Conclusion:** Clinical examination and laboratory test are not always helpful to differentiate OC from post-sinusitis PC. CT/MRI scans are necessary both to identify/stage orbital complications and to exclude the presence of sinusitis. In our study, pan-sinusitis was the most common cause, a finding with important clinical implications in terms of choice of treatment.

COMMUNITY-ACQUIRED STAPHYLOCOCCUS AUREUS MUSCULOSKELETAL INFECTIONS IN CHILDREN: ROLE OF PANTON-VALENTINE LEUKOCIDIN AND METHICILLIN RESISTANCE**C. Gouveia**¹, M. Cassiano Neves², M. Ramirez³

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Background and aims: Staphylococcus aureus (SA) is responsible for a multiplicity of infections in humans. In the last years, community-acquired methicillin resistant SA (CA-MRSA) has emerged frequently associated with the presence of the Pantón-Valentine leukocidin (PVL). There is limited data concerning methicillin susceptible (MSSA) or resistant SA musculoskeletal infections in Portugal.

Methods: Retrospective study of children admitted to Hospital Dona Estefânia, from January 2005 through June 2008, with community-acquired SA musculoskeletal infections. Data on demographics, clinical parameters and antibiotic susceptibility were collected. Detection of mecA, LPV, pulsed-field gel electrophoresis profiling (PFGE), and spa typing (only for MRSA) were done.

Results: 21 SA infections were identified: 8 septic arthritis, 6 osteomyelitis and 7 combining both conditions. One isolate (5%) was MRSA (mecA positive) and 2 (10%) were erythromycin resistant (1 iMLS_B phenotype). Most patients were treated with a combination of flucloxacillin and gentamicin and surgical drainage. Cultures remained positive more than 48 hours after adequate therapy in 6 patients and 4 had sequelae.

MRSA (spatype t008) was associated with pyomyositis, but the duration of hospitalization and complications were similar to MSSA. Two isolates (10%) harbored PVL genes, both from the same PFGE clone. Patients infected with PVL positive strains had less frequently bacteremia and were treated with fewer antibiotics.

Conclusions: Methicillin resistance was similar to other European countries. Although PVL-carrying clones have been associated with severe infections our data does not support such association.

MILD STAPHYLOCOCCAL SCALDED SKIN SYNDROME (SSSS): A DISTINCT ENTITY FROM CLASSICAL SSSS?

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Introduction: Staphylococcal scalded skin syndrome (SSSS) is induced by *Staphylococcus aureus* secreting exfoliatine A or B (ETA/B). Typical SSSS associates generalized erythematous exanthema and diffuse skin blisters. We have observed cases of SSSS in which the main clinical sign - the blister - was missing or was scarce resulting in a rash with a desquamation localized in the folds. We consider this clinical form as mild SSSS. The objective of this work is to describe five cases of mild SSSS.

Method: These cases are extracted from a prospective observational cohort on *S. aureus* infections conducted in our 500 bed institution since 1 November 2005.

Results: Five children (7 to 48 months) had fatigue, hyperthermia and exanthema. There were neither blister nor Nikolsky sign but a thin desquamation of perineum and axillaries folds. The children had a favorable outcome. The primary infection focus was a facial impetigo caused by *S. aureus* all having the same characteristic: arg 4, eta, ent M, ent O.

Discussion: We report a mild form of SSSS characterized by the absence of blister and a localized desquamation of the main folds. Mild SSSS must be differentiated from staphylococcal scarlet fever. Five cases have been registered within 4 years suggesting that mild SSSS is more common than typical SSSS. *S. aureus* analysis show that mild SSSS are associated with ETA and that these strains might correspond to the same clone.

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OSTEOMYELITIS AND SEPTIC ARTHRITIS IN CHILDREN AT A UNIVERSITY HOSPITAL, TWO YEAR RESULTS

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Background and aims: Osteomyelitis and septic arthritis in children are serious infection and important because of their potential to cause permanent disability. This study is purposed to analyze the etiology, clinical features, diagnosis, treatment and prognosis of patients experienced in recent two years.

Methods: We reviewed the records of twenty patients, who were diagnosed as osteomyelitis and septic arthritis from March 2008 to June 2009 at Ewha Womans University Mokdong Hospital. Their clinical, microbiological and radiological information were obtained from their medical records.

Results: A total of 20 cases of osteomyelitis and septic arthritis patients were identified. The ages of the patients ranged from 7 months to 18 years and they showed male predominance of 3 times. Fourteen patients with osteomyelitis and 7 with septic arthritis were enrolled, and one had both. Most common affected site of osteomyelitis was tibia (35.7%, 5 of 14) and that of septic arthritis was hip joint (71.4%, 5 of 7). *Staphylococcus aureus* was the most common bacteria responsible for 36.8 % (7 of 19) and 2 cases of these were Methicillin resistant. *Streptococcus pyogenes*, *Streptococcus intermedius* and *Mycobacterium tuberculosis* were also isolated from others. No fatal case was reported. Three children (15 %) had combined diseases, such as Kawasaki disease, hemophagocytic lymphohistiocytosis, and disseminated intravascular coagulopathy.

Conclusions: *S. aureus* was the most common etiologic agents of osteomyelitis and septic arthritis. It is required to monitor these diseases continuously to guide adequate treatment.

CLINICAL AND BIOLOGICAL FEATURES OF *KINGELLA KINGAE* (KK) AND *STAPHYLOCOCCUS AUREUS* (SA) ARTHRITIS IN CHILDREN

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Background: SA and KK are the most frequent pathogens causing septic arthritis in children.

Aim: To compare clinical and biological features of KK and SA arthritis in children

Methods: We retrospectively analysed cases of children hospitalised in Robert-Debré Hospital, from 2000 to 2009, with acute KK and SA arthritis. Only children treated by joint lavage with arthrotomy or arthroscopy and initial probabilistic antibiotic therapy for which the strain was sensitive were included.

Results: 49 cases of KK arthritis and 21 SA arthritis were included for which mean age was 1.6 (range: 0.5-5.6) and 7.5 (1-14) years ($p < 0.0001$). At initial presentation, mean temperature (37.8 vs 37.9°C), median CRP (37 vs 55 mg/l), blood leucocytes (12300 vs 12000/mm³), thrombocytes (412000 vs 302000/mm³) and fibrinogen (5.6 vs 5.4g/l) were similar ($p > 0.05$) between both groups. Rates of CRP < 10mg/l between day 5 to day 7 of treatment were highest in the KK group (81% vs 50%) ($p < 0.05$). Apyrexia was obtained at 0.14 day (range 0-1) for KK group and at 3.45 days (0-27) for SA group ($p < 0.05$). 1/49 (2%) patient need revision surgery with KK arthritis versus 4/21 (19%) with SA arthritis ($p < 0.05$). Mean hospitalisation stay was 7 (3-11) and 13 days (7-39) for KK and SA groups ($p < 0.0001$).

Conclusion: Except age of onset, initial clinical and biological presentations were similar between KK and SA arthritis. In contrast, evolution of KK arthritis was less severe in term of duration of fever, rate of surgical revision and hospital stay.

INCIDENCE AND CHARACTERISTICS OF OSTEOARTICULAR INFECTIONS IN CHILDREN: A ONE YEAR PROSPECTIVE STUDY IN NORTHERN FRANCE

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Background and aims: The incidence of childhood osteoarticular infections is not well known. This study aimed to determine the annual incidence of osteoarticular infections in children and describe the diagnostic methods and treatments for osteoarticular infections.

Methods: A population-based multicenter study was performed between July 1, 2008 and June 30, 2009 in an area of 872 516 children < 16 years of age in Northern France. Children with consensual diagnostic criteria for septic arthritis, acute osteomyelitis and spondylodiscitis were included. A blinded radiologic review was performed. To check out the exhaustiveness of the prospective database, the regional hospital discharge codes were analysed. The corrected incidence of osteoarticular infections was determined using a capture-recapture method.

Results: Fifty two cases of osteoarticular infections were prospectively identified. Six other cases were retrieved in the discharge codes database. Finally, 58 cases were identified: 30 septic arthritis (52%), 24 osteomyelitis (41%) and 4 spondylodiscitis (7%). Our prospective database was 90% exhaustive. The total annual corrected incidence of osteoarticular infections was 7.1/100 000 children (95%CI: 5.3-8.9). The incidence was higher in children under 3 years of age (17/100 000 [95%CI: 11-23]). Bacteria were identified from only 15 patients (26%), with *Staphylococcus aureus* as the most frequent organism.

Conclusion: The annual corrected incidence of osteoarticular infections in Northern France was 7.1/100 000 children under the age of 16 years (95%CI: 5.3-8.9). The use of a *Kingella kingae* PCR would improve the bacteriological diagnosis.

EVALUATION OF PATTERN AND BURDEN OF PERINATAL CLINICAL MALARIA IN NORTH-WEST OF NIGERIA

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Objective: Malaria remains dreadful with high rates of mortality and disease burden. Rarity of its perinatal forms, hence we aimed to evaluate its rate and pattern in Nigerian neonates.

Methods: We prospectively studied infants admitted into the Special Care Baby Unit [SCBU] of Usmanu Danfodiyo University Teaching Hospital, Sokoto, over 1-year period [January 1 - December 31, 2006]. All cases presented as febrile illness. Standard sepsis work-up and Giemsa staining done on blood smear for malaria parasites [MP].

Results: 305 [20%] total deliveries required admission. 190 [62.3%] of these newborns had febrile illnesses. 109 [57.4%], M: F; 1.2:1 were confirmed with Clinical Neonatal Malaria [CNM], with blood containing trophozoites of *Plasmodium Falciparum* parasites. MP density distribution was (1+) in 61/109 [56%]. Table I elucidates the age group and CNM types [Table1]. TABLE 1: AGE GR...Majority [80.7%] cases; Early-Onset [i.e. presentation at < = 14days of age, $p < 0.01$]. Overall incidence was 71.4/1000 live births and 57.6/1000 for the PCNM group.

Preterm newborns had highest frequency; 41/109 [44.7%]. Almost 66% of PCNM were from Primiparous Mothers, $p < 0.0001$ [Table 2]. TABLE 2: Relat.

Pyrexia was the commonest clinical feature; 95.4%. All responded to oral Artemeter-Lumefantrin [Novartis] 10/60mg, 12hourly over 72-hour period, with no demonstrable untoward effects. No mortality occurred.

AGE GROUP, days	n[%]WITH CONGENITAL/PERINATAL CNM	n[%]WITH LATE-ONSET CNM
0 - <= 7	58 [53.2]	-
> 7 - <= 14	30 [27.5]	-
> 14 - 28	-	21 [19.3]
TOTAL [109]	88 [80.7]	21 [19.3]

[TABLE 1: AGE GROUP AND CLINICAL NEONATAL MALARIA]

Parity	Mothers, n [%]	Perinatal/Congenital CNM, [%]
0	58 [53.2]	58 [65.9]
1 to <=4	33 [30.3]	19 [21.6]
>=5	18 [16.5]	11 [12.5]
TOTAL	109 [100]	88 [80.7]

[TABLE 2: Relationship of Maternal Parity to occur]

Conclusion: High rate of Early-Onset Perinatal/Congenital CNM, not previously documented, was

encountered. Response to management was excellent. Routine screening for malaria is strongly recommended.

CONGENITAL CYTOMEGALOVIRUS INFECTION DIAGNOSIS AND TREATMENT. MULTICENTRIC TRIAL

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Introduction: Cytomegalovirus (CMV) congenital infection is very frequent and high neonatal morbimortality. Is very important your diagnostic and treatment s

Objective: To describe the experiential diagnosis and treatment of congenital cytomegalic disease in Colombia.

Material and methods: Descriptive multicentric trial of patients diagnosed with congenital cytomegalic disease showing immunoglobulin G and M ELISA, pp65 antigen or polymer chain reaction (PCR) in 12 new born units in Colombia. Patients were treated with specific hyper immune gamma-globulin and/or ganciclovir. Analysis of variables within the SPSS 15.0 program for calculation of absolute and relative frequencies and verification of statistical significance.

Results: 107 patients with symptoms of the congenital cytomegalovirus infection. 43 (40.2%) received specific hyper immune gamma-globulin, 17(15.9%) ganciclovir, 28(26.2%) received both medications and 19(17.8%) neither one of the treatments. Clinical improvement was evident in 77(87.5%) of treated patients and 1(5.2%) of non-treated patients (value $p < 0.01$). 20(18.7%) newborns died. 11(57.9%) non-treated and 9(10.2%) treated. Results with the different treatments have been analyzed.

Conclusions: A better clinical response and less mortality are found in patients that receive treatment.

Keywords: Congenital cytomegalovirus infection, Ganciclovir, hyper immune gamma-globulin.

VALGANCICLOVIR (VGC) TREATMENT OF CONGENITAL SYMPTOMATIC CYTOMEGALOVIRUS (CMV) INFECTION WITH CENTRAL NERVOUS SYSTEM (CNS) INVOLVEMENT

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Background & aims: CMV is the leading cause of congenital infection and nonhereditary sensorineural hearing loss in children. Treatment with ganciclovir may prevent hearing deterioration in children with CNS involvement. VGC may be an excellent alternative, but experience in children is scarce.

Methods: Retrospective review of infants with congenital CMV infection with CNS involvement treated with oral VGC in our hospital over the last 5 years (2005-2009).

Results: 12 infants (7 males, 3 prematures) were identified: 1 diagnosed during pregnancy, 9 in the neonatal period and 2 retrospectively by PCR in dried blood spots. Clinical findings included petechiae (6), hepatosplenomegaly (6), jaundice (3) anaemia (2) and CNS involvement (12/12): hearing loss (9/12), abnormal CSF (6/12), microcephaly (3/12), neurologic signs (3/12) and abnormal neuroimaging studies (11/12). Ganciclovir was administered initially to 10 infants during a median time of 4.6 weeks. VGC mean treatment duration was 5.3 months (1.5-6 months). No treatment was interrupted, although 5 children had diarrhoea and 4 spat-up or vomited occasionally. No serious adverse events were found. Four patients had grade 3 neutropenia and 2 had elevation of aminotransferases. Before treatment, hearing was normal in 3 patients, 4 had unilateral and 5 bilateral hearing loss. At 6 months (10 cases), 4 patients had improved, 5 remained stable and one worsened. No infant with profound hearing loss at birth improved, in contrast to 4/5 who had mild/moderate hypoacusia.

Conclusions: Valganciclovir is well tolerated and may prevent hearing deterioration in congenital CMV-infected infants with CNS involvement.

PROGRAMS OF CONGENITAL CMV INFECTION'S SURVAILLANCE IN A PREMATURE NURSERY

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Background and aims: Congenital Cytomegalovirus infection is an important cause of neonatal morbidity and mortality and the most prevalent infection-related cause of congenital neurological handicap. Our study aims to evaluate the effectiveness of treatment with glanciclovir on outcomes and side effects in infants with congenital cytomegalovirus infection.

Methods: The diagnosis is based on the CMV-specific antibodies , on detection of the virus in urine and blood by nucleic acid amplification of viral DNA (PCR) and on imaging techniques. Symptomatic newborns, are treated with Gancyclovir i.v. at a dose of 12 mg/Kg/die for 6 weeks. We programmed a follow-up at 3-6-12-24-36 months.

Results: There were four cases (0.86%) of congenital CMV; in all virus was detected in urine samples, only in two of them CMV-DNA was positive in blood. The first case had cerebral ultrasonographic alterations, which disappeared after treatment. The second newborn had a heart disease, chromosome 11's alteration and elevated lever enzymes; he was treated with efficacy. In the third case we decided of not to subject to treatment the newborn, with positive CMV serology, because he had lissencephaly. In the fourth case, during the first quarter of gestation there was CMV infection, but the virus wasn't detected in amniotic fluid; the newborn was asymptomatic and wasn't treated. At the age of 24 months, there aren't sequelae.

Conclusions: An early congenital CMV infection's diagnosis is essential to an efficacious and timely treatment. A final resolution of the problem is the vaccine, still experimental study.

CONGENITAL HERPES SIMPLEX II (HSV-2) WITH LIMB ABNORMALITIES

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Background and aims: The classical presentation of congenital HSV infection is grouped vesicles on an erythematous base and/or widespread skin erosions. Associated limb malformations have been reported only once.

Methods: We present a case of congenital HSV-2 infection in a preterm male infant with extensive skin denudation, vesico-pustules, and limb abnormality.

Results: He was born to non-consanguineous parents at 28 weeks gestation with a hypoplastic left hand without nails, severe skin sloughing over the left side of his body and occasional vesicles. Mother remained asymptomatic throughout pregnancy without any history of illicit drug use or teratogen exposure. He showed hepatosplenomegaly and elevated liver enzymes. Abdominal ultrasound revealed liver and spleen calcifications. Cranial ultrasound scan revealed areas of cerebritis and ischaemia. HSV-2 DNA was detected in skin swabs and blood samples. Cerebrospinal fluid (CSF) was not obtained because of the risk of iatrogenic CNS infection. Maternal blood analysis showed evidence of recent HSV-2 infection. He was treated, following infection screening, with high-dose acyclovir, benzylpenicillin, gentamicin and fluconazole. At day 35, his skin was almost healed with residual cicatrisation, absent HSV-2 DNA on repeat swabs; and resolved viraemia. IV acyclovir was discontinued and oral suppressive therapy was commenced.

Conclusions: This case demonstrates that congenital HSV 2 infection should be considered in newborn infants presenting with limb hypoplasia and skin lesions.



[Hand and Skin Day 1]

EARLY NEONATAL MENINGOCOCCAL INFECTION DU TO A *NEISSERIA MENINGITIDIS* SEROGROUP B

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The early onset neonatal infection with *Neisseria meningitidis* is rare, we reported here a new case.

Case report: T1 was the first twin of bichorial biamniotic pregnancy (the second twin, T2, died of a polymalformatic syndrom on day 7). The vaginal delivery occurred at 35 weeks and 4 days, after 5 hours of amniotic membranes rupture. Birth weight was 2335 g, Apgar score 9-9-10. At H6, he presented a respiratory distress with haemodynamic failure. Antibacterial chemotherapy combining cefotaxime, amoxicillin and gentamicin was started. C reactive protein was 111 mg/L on day 2. Bacterial cultures of lumbar puncture and gastric aspirate were negative, whereas the blood culture was positive with a strain of *N. meningitidis* serogroup B. A *N. meningitidis* serogroup B strain was then also isolated from the vaginal sample of the mother, whereas bacterial cultures of throat swabs of parents were negative for this species. Antibiotherapy was modified at day 2 for cefotaxime alone. Clinical and biological improvement occurred with withdrawal of the antibiotherapy on day 10.

Throat swabs of parents and the anal swab of T2 were positive for the specific detection of *N. meningitidis* by real time PCR using primers *ctrAF* (GCTGCGGTAGGTGGTTCAA) and *ctrAR* (TTGTGCGGATTTGCAACTA) with the probe *ctrAS* (CATTGCCACGTGTCAGCTGCACAT) on a Smart Cycler II® system (Instrumentation Laboratory). The strains isolated from the mother and T1 were compared by pulsed-field gel electrophoresis and were found identical.

Conclusion: We report a new case of *N. meningitidis* serogroup B early onset infection confirmed by molecular study.

EARLY ONSET NEONATAL INFECTIONS - CONSEQUENCE OF PREMATURE RUPTURE OF THE MEMBRANES

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Background: Early onset neonatal infection is the newborn's infection at birth or during the first 3-7 days of life. Infants resulting from deliveries with premature rupture of the membranes (PROM) are highly sensitive to early neonatal infections.

Objectives: To identify the role of the maternal-fetal bacterial infections on the premature birth and establishing risk factors associated with infections that can influence the health of the newborns.

Material and method: 482 newborns resulting from births with spontaneous PROM have been studied, selected from the total number of newborns registered during 3 years in the "Bega" Hospital, Timisoara.

Results: In the study, 186 were premature babies (38.59%). Comparing the newborns of mothers with infectious pathology during pregnancy and the newborns of mothers without pathology, the mortality rate was significantly higher to the first group (10.8% vs. 4.0%). The mortality rate in newborns with early onset infections, resulting from pregnancies with PROM was 4.5%, the main mortality causes being infections with *Staphylococcus aureus*, *Escherichia coli* and *Streptococcus group B*. Premature babies from pregnancies with PROM have a double mortality rate.

Conclusions: The bacterial maternal-fetal infections during pregnancy increases the risk of giving birth to children with low birth-weight and low gestational age. The lower the birth-weight and gestational age of the newborn is, the higher is the probability for the newborn to develop more severe infections.

CONGENITAL MALARIA

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Background: Malaria causes low birth weight, perinatal & infant mortality. Identification of congenital malaria improves perinatal outcome.

Objective: To determine demographic, clinical & hematological

Characteristics of congenital malaria

Study design: Descriptive & cross sectional

Study setting: Study conducted at Pediatric "B" Unit Lady Reading hospital Peshawar & District Headquarter hospital Bannu, 1st January 2008-December 2009.

Methods: 51 neonates & infants (age 0 - 3 months) with clinical suspicion of malaria selected. Patients divided into two groups. In Group 1 upto 28 days of life & Group 2 consisted of patients 29 days-3 months. Information regarding maternal fever, malarial parasite results, birth weight, signs & symptoms recorded on proforma. Blood collected for malarial parasite, peripheral smear, G6PD, TORCH & blood groups. Data analyzed with SPSS version 11. Results presented in frequencies and percentages.

Results: Group I 22 patients (43.1 %) Group II 29 (56.9 %). Male 42 (82.3%), female 9 (17.7%). Weight was between 2Kg - 4.5 Kg. Fever, pallor 100 % Hepatosplenomegaly in 40 cases (78.4%) & poor feeding in 31 (60.8%). Hemoglobin values between 5.5gm/dl-10 gm/dl. Plasmodium vivax was the most common malarial parasite (96.1%) & Plasmodium falciparum isolated in two mothers (3.9%). Three neonates expired (5.9%).

Conclusion: Congenital malaria is mainly caused by plasmodium vivax. Neonates & infants with fever, pallor, hepatosplenomegaly & maternal fever in perinatal period should be screened for malaria.

Keywords: Neonate, infants, congenital malaria, plasmodium vivax, Plasmodium falciparum, Anemia.

LYME BORRELIOSIS DURING PREGNANCY**A. Lakos**¹, N. Solymosi²

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Background and Patients: We have recently published a paper on 95 maternal Lyme borreliosis and the outcome of their pregnancies. Since the closure of the database for that manuscript the number of the pregnant women with *Borrelia* infection observed in our Centre increased to 124, and the statistical analysis strengthened our previous doubtful observations and reached significant results in important aspects by now.

Results: Treatment was administered parenterally to 87 (70%) women and orally to 25 (20.0%). Infection remained untreated in 12 (10%) pregnancies. Adverse outcomes were seen in 7/87 (8%), 9/25 (36%), 8/12 (67%), of the parenterally, orally treated and untreated women, respectively. In comparison to patients treated with antibiotics, untreated women had a significantly higher risk of adverse pregnancy outcomes (OR: 11.62, $p=0.0002$). Mothers treated orally comparing to iv. treatment had an increased chance (OR: 6.28) to have an adverse outcome ($p=0.0014$). The probability of adverse outcome increased by the exposition time (from the first maternal symptom to the treatment or delivery). When the exposition time has reached four months the probability of adverse outcome increased by 33%. We had no chance to examine the bacterial invasion of the foetus. Loss of the pregnancy (N=9), small for gestational age or preterm birth (N=7) were the most prevalent adverse outcomes in our series. The other complications were heterogeneous.

Conclusion: Our results indicate that untreated or orally treated maternal *Borrelia burgdorferi* s.l. infection is associated with adverse outcomes. 'Congenital Lyme disease' similar to the Hutchinson' triad in syphilis is unlikely.

CONGENITAL TOXOPLASMOSIS IN TRENTINO FROM 01/01/2005 TO 30/09/2008: INCIDENCE AND SEROCONVERSION DURING PREGNANCY

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Epidemiology: Congenital *Toxoplasma* infection represents 33% of all vertical infections. Incidence of congenital toxoplasmosis is 3-6/1000 newborns in high risk countries, 1-2/1000 newborns in low risk countries. Fetal disease severity is related to gestational age. **CLINICAL FEATURES IN THE FETUS AND THE NEWBORN.**

Infection during pregnancy can cause a wide spectrum of consequences from none to intrauterine death. Main related problem is corioretinitis (the first cause of blindness around the world).

Materials and methods: A multicentric study run in five neonatal and paediatric units in Trento Province between 01/01/2005 and 30/09/2008. Study objective: to evaluate the incidence rate of newborn disease and of seroconversion rates during pregnancy. During the study period 14,769 babies were born (including twins), and 30 *T. gondii* seroconversions during pregnancy were demonstrated (2.03/1000). Among the babies born from mothers with primary infection during pregnancy, 7 are in the follow-up, 3 were never followed-up, 4 were lost at follow-up, 5 children (0.34/1000) showed post-natal seroconversion (increased IgG titres for *Toxoplasma* after the third month of life). The remaining children do not show any feature of infection to date. The five infected children, all asymptomatic at birth, received a twelve-month course of sulphodiazine and pirymethamine. One child developed seizures during treatment at about 10 months of age.

Conclusion: In our experience disease incidence was lower than expected from the literature. Appropriate follow-up is not correctly executed due to both lack of parental concern for the long term consequences of prenatal infection and lack of appropriate maternal information during pregnancy.

**ANALYSIS OF CASES AT RISK FOR CONGENITAL TOXOPLASMOSIS REFERRED TO
PAEDIATRIC INFECTIOUS DISEASES SERVICE IN MUNICIPALITY OF TAUBATÉ, SP, BRAZIL**

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Aims: To analyze criteria to referral of cases at risk for congenital toxoplasmosis to paediatric infectious diseases service of a university hospital, and what were the main Professional involved in this referral.

Methods: all cases referred as at risk for congenital toxoplasmosis, from 2000 to 2009, were included. Data were collected from hospital charts, concerning referral criteria and professionals involved.

Results: There were 84 cases referred to paediatric infectious diseases service in the period of study. The majority of cases (62,5%) were referred by the neonatologist; only 25% of cases were previously referred by the obstetricianand. Other professionals involved were paediatrician (12,5%). The main reason to referral was positive serology (IgM antibodies) against *Toxoplasma gondii* during pregnancy. Only one pregnant woman was submitted to avidity test and amniocentesis. Congenital toxoplasmosis was confirmed in only 3 cases.

Conclusions: Neonatologists are the professionals most involved in referral of patients at risk for congenital toxoplasmosis to specialist. Although obstetricians diagnostic acute toxoplasmosis during pregnancy, they are not committed to referral of babies at risk to specialist.

CONGENITAL VARICELLA SYNDROME - ASSOCIATED ACHALASIA: THREE-YEARS FOLLOW UP

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Background and aims: Primary varicella-zoster virus (VZV) infection during pregnancy is uncommon. If it occurs between the 8th and 20th week of gestation, congenital varicella syndrome (CVS) results in 1-2% of cases. We report about a CVS - associated achalasia and describe its evolution in a three-years follow up period.

Methods: Retrospective review of a clinical case.

Results: A male infant was exposed to VZV at 15 weeks of gestation and had skin and persistent feeding difficulties at birth, prompting an esophageal biopsy at 18 days. Aciclovir therapy was administered because of a disseminated zoster two days after biopsy. Esophageal tissue demonstrated destruction of neural plexus, with VZV DNA in adjacent epithelial cells. Brain did not show any abnormalities. Radiological studies showed aperistalsis and distension of the esophagus, compatible with achalasia. At first, nasogastric feeding with continuous aspiration of secretions was started, but it was inefficient, with intercurrent aspirative-pneumonia episodes. A percutaneous endoscopic gastrostomy was realized at 2 months of life, with progressive improvement in pulmonary infiltrates and growth. After a 2'5 years period, esophageal peristalsis started a progressive recuperation, allowing a partial oral feeding without pulmonary complications. No metaplasia has been identified within the esophagus.

Conclusions: This case demonstrates that in the fetal age, VZV infection can induce severe destruction of peripheral neural cells. However, clinical improvement can be obtained with surgical therapy and, perhaps, aciclovir. In our knowledge, this is the first case with a significative improvement of esophageal motility without premalignant lesions in a child with CVS.

CMV-DNA DETECTION ON DRIED BLOOD SPOTS AS A SCREENING TOOL FOR THE DIAGNOSIS OF ASYMPTOMATIC CYTOMEGALOVIRUS CONGENITAL INFECTION

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Background: Human cytomegalovirus is the most frequent congenital infection. Ninety percent of congenitally CMV infected infants (cCMV) are asymptomatic at birth. Although, sequelae, such as sensorineural hearing loss (SHL) and psychomotor delay are more prevalent in infants with symptomatic infection, approximately 10-15% of newborns with asymptomatic cCMV may develop SHL.

Aim: To examine the incidence of asymptomatic cCMV infection in Greece.

Methods: Dried blood spots were collected from 1.131 asymptomatic neonates at birth on Guthrie cards. Most mothers were Greek (66.8%), 19% were immigrants from Balkan countries, mainly Albania, 5.6% were Eastern Europeans, 5.8% Asians, while few women were Africans. Prenatal serologic screening indicated that 45% of women were CMV-IgG seropositive. All neonates, but 37 (3.2%) were full-term. Mean birth weight was 3.63 kg. DNA was extracted from dried blood spots and CMV-DNA was detected by polymerase chain reaction technique (PCR).

Results: To date, 760 Guthrie cards have been examined and CMV-DNA was detected in two cards (2.6‰). Both newborns were full-term. Diagnosis was confirmed by PCR on peripheral blood. Head ultrasound was normal at birth and both newborns had normal audiologic testing at birth and six months later.

Conclusions: The prevalence of asymptomatic cCMV infection in Greece is low (0.26%). Guthrie card is a powerful and reliable assay for diagnosing CMV-congenital infection. Prospective follow up of infants with asymptomatic CMV infection and further assessment of the incidence of cCMV infection in Greece will facilitate national decision making on whether screening for cCMV infection should be implemented.

ROLE OF VALGANCICLOVIR IN NEONATAL HEPATITIS WITH CYTOMEGALOVIRUS

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Cytomegalovirus (CMV) is an important cause of neonatal hepatitis and can lead to portal hypertension and chronic liver disease. Role of ganciclovir and its prodrug valganciclovir for treatment of congenital CMV infection is not completely established. There is very little literature on role of valganciclovir in neonatal CMV hepatitis. We report for the first time in India, effectiveness of valganciclovir in 3 infants with neonatal hepatitis and CMV. All 3 infants in age group of 2-4 months with neonatal hepatitis and variable CMV viral load were treated with oral valganciclovir (125-250 mg/m²/day) for 6 weeks and also had clinical improvement and undetectable viral load at the end of therapy. One patient however developed long term sequelae of CMV in form of sensorineural deafness and delayed development.

	Patient 1	Patient 2	Patient 3
Clinical features	2 ½ months - Neonatal cholestasis with clay stools and normal hearing and normal ophthalmology examination. No thrombocytopenia	3 months- Neonatal hepatitis without clay stools with normal hearing and normal ophthalmology. No thrombocytopenia	3 ½ months- Seizures, hearing deficit, visual impairment, neonatal hepatitis with visual impairment and hearing loss. No thrombocytopenia
Bilirubin (mg/dl) total (direct)	11.9 (6.0)	4.8 (2.3)	6.2 (3.1)
SGOT / SGPT (IU/L)	785/ 195	106 /49	128 /135
CMV viral load (copies/ml)	4540	Undetectable	3000
Treatment outcome with valganciclovir	Normal child with normal liver	Normal child with normal liver	Normal Liver functions but hearing impairment and delayed milestone

[Patient

details]

Thus, valganciclovir appears safe and effective in neonatal hepatitis with CMV. However, randomized controlled trials in larger groups are required to determine its efficacy.

PROCALCITONIN USEFULNESS IN NEONATES ADMITTED TO A PEDIATRIC EMERGENCY DEPARTMENT FOR FEVER WITHOUT SOURCE

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Background and aims: Few data exist on laboratory markers accuracy as predictors of severe bacterial infections(SBI) in febrile neonates. Procalcitonin(PCT), thanks to its more rapid kinetics, could be more useful in febrile neonates who, most of the times, are brought to the paediatric emergency department(PED) after only few hours of fever. We aimed to assess the usefulness of PCT determination in neonates with fever without source(FWS), compared to C-reactive protein(CRP), and white blood cell count(WBC).

Methods: Data of neonates (7-28 days) admitted to our PED with FWS from a previous prospective study and those prospectively collected since March 2009 (when routine PCT determination was introduced in our PED) were merged for the purpose of this study. Area under the ROC curves(AUC) as well as positive and negative likelihood ratios(LR) for the traditionally used cut off values were calculated.

Results: Of the 84 neonates finally included,29 had a definite SBI (mostly urinary-tract-infections) and 3 a possible SBI. 87% presented to the PED with fever< 12hours. AUC and LR for each marker are reported in Table 1.

	WBC	CRP	PCT
Definite SBI vs NON SBI (81 patients)	AUC 0.757(0.649-0.845) LR+ 2.8(1.4-5.6) LR- 0.6 (0.4-0.9)	AUC 0.798 (0.695- 0.879) LR+ 16(4-65) LR- 0.4 (0.3-0.6)	AUC 0.844 (0.746- 0.915) LR+ 10(3.3-32) LR- 0.4 (0.3-0.7)
Definite + possible SBI vs NON SBI (84 patients)	AUC 0.736 (0.629- 0.826) LR+ 2.5(1.2-5.2) LR- 0.7 (0.5-1)	AUC 0.813 (0.713- 0.890) LR+ 16(4-65) LR- 0.4 (0.3-0.6)	AUC 0.858 (0.765- 0.925) LR+ 11(3.5-34) LR- 0.4(0.3-0.6)
Definite SBI vs NON SBI in Neonates with negative urinalysis (51 patients)	AUC 0.730 (0.587- 0.844) LR+ 2.3(0.8-7.1) LR- 0.8 (0.4-1.3)	AUC 0.610 (0.464- 0.744) LR+ 8.1(1.6-41) LR-0.7(0.4-1.1)	AUC 0.817 (0.684- 0.911) LR+ 11(2.3-49) LR- 0.5(0.3-1.1)
LR were calculated for the following cut-off values: WBC>15.000/uL, CRP>20 mg/L, PCT>1 ng/mL			

[Table

1]

Conclusions: In neonates with FWS, PCT seems to be a better predictor of SBI. It could be a useful tool in guiding decision on antibiotic therapy pending culture results.

COMPARISON OF QUANTITATIVE PCR AND CONVENTIONAL BLOOD CULTURE FOR THE DIAGNOSIS OF NEONATAL SEPSIS CAUSED BY *ESCHERICHIA COLI*

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Background and aims: *Escherichia coli* (*E. coli*) is the second most frequent pathogen, which causes early onset neonatal sepsis. The objective of this study was to prospectively evaluate the feasibility of quantitative PCR for diagnosis of neonatal *E. coli* sepsis.

Methods: EDTA blood (300 µl) of newborn infants, who underwent a sepsis screen in the first 72 hours of life was analyzed for the amplification of the *uidA* gene by quantitative real time PCR using SYBR Green. Results of the PCR were analyzed on the basis of clinical and laboratory parameters collected during the sepsis work up and were compared to the results of the BACTEC blood culture system.

Results: 72 newborn infants with suspected sepsis were included. 29 of these infants had sepsis confirmed by stringent clinical and laboratory parameters. None of these infants had a blood culture positive for *E. coli*. In contrast, *E. coli* was detected in 3 patients by qPCR. All of these 3 neonates showed clinical and laboratory signs of sepsis. Furthermore, in 2 of the 3 infants with a positive qPCR result, *E. coli* was cultured from ear swabs.

Accordingly, the sensitivity of the qPCR for clinical sepsis altogether was 10,3%. None of the infants, in whom sepsis was eventually excluded, showed a positive PCR result. Time to diagnosis was 3,5 hours.

Conclusion: Quantitative PCR is a potentially useful instrument for the early detection of neonatal sepsis caused by *E. coli*. Larger studies are required to confirm these data.

PRESENTING SIGNS AND SYMPTOMS OF SEPTICAEMIA AND MENINGITIS IN CHILDREN WITH FEVER AT THE EMERGENCY DEPARTMENT IN THE POST-VACCINATION TIME

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Background and aims: Septicaemia and meningitis are rare infections due to new vaccination strategies, but missing these diagnoses has severe consequences. Discriminating children with septicaemia or meningitis, from other infectious diseases (non-SBI) remains an important challenge. Aim of this study is to describe the presenting signs and symptoms of children with septicaemia/meningitis in the diverse population of feverish children at the emergency department (ED).

Methods: Children with fever, aged 1 month - 16 years, attending the ED of the Erasmus MC-Sophia children's hospital, Rotterdam (n=1750, July 2003 -December 2005) and Juliana children's hospital, The Hague (n=967, July -December 2007) were recruited. Presenting signs and symptoms of children with septicaemia/meningitis compared to non-SBI were described with univariate logistic regression analysis.

Results: 22 children were diagnosed with septicaemia/meningitis, median age 1.2 years (IQR 0.5 - 6.7), 68% boys (n=15), median C-reactive protein 176 mg/l (IQR 193). Compared to non-SBI (n=2377), risk factors for septicaemia/meningitis were: age(years): OR 1.13 (95% CI: 1.01-1.26); male sex OR 0.63 (0.26-1.55); duration of fever (days) OR 1.02 (0.75-1.37); tachypnea OR 1.51 (0.55-4.12); tachycardia OR 1.51 (0.59-3.84); body temperature (°C) OR 1.27 (0.75-2.16); ill appearance OR 10.57 (4.11-27.1); prolonged capillary refill (>3 seconds) OR 15.41 (6.30-37.7); chest wall retractions OR 0.59 (0.08-4.37); CRP (mg/l) OR 1.02 (1.01-1.03).

Conclusion: Ill appearance and disturbed peripheral circulation are the most important presenting symptoms to discriminate septicaemia/meningitis from non-SBI in febrile children at an ED. Further research should focus on (multivariate) analysis in a larger group of children with septicaemia/meningitis.

THE VALIDATION OF THE MANCHESTER TRIAGE SYSTEM URGENCY CLASSIFICATION TO DISCRIMINATE SERIOUS BACTERIAL INFECTION IN FEBRILE CHILDREN

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Background and aims: Triage systems are used to assess urgency of care in the emergency department (ED). Aim is to determine predictive value of triage urgency for serious bacterial infections (SBIs) in children with fever at the ED.

Methods: Children with fever, aged 1 month-16 years, attending the ED of the Erasmus MC-Sophia Children's Hospital in 2008 were recruited. Children with chronic co-morbidity were excluded. Triage urgency was determined with the Manchester Triage System (MTS, Urgency (U) level 1-5). The association between triage urgency, age, sex and body temperature (°C) and SBI was assessed using multivariate logistic regression.

Results: 800 children were included: mean age 2.9 years (interquartile range: 0.9-3.8), 62% (n=495) boys and SBI was diagnosed in 11% (n=86, 95% confidence interval (CI): 9-13%, table 1). Discriminative value of MTS (ROC) for SBI was 0.59 (95% CI: 0.53-0.65) and changed to 0.64 (95% CI: 0.58-0.71) with age, sex and temperature added. MTS (urgent vs non-urgent) had a sensitivity 0.43 (95% CI: 0.33-0.54) and specificity 0.69 (0.65-0.72) to detect SBI.

Conclusion: Triage urgency, adjusted for age, sex and temperature, does not predict the presence of SBI in febrile children.

SBI	Urgent (MTS U1-2)	Non-urgent (MTS U3-5)	Total
Pneumonia	20	28	48 (56%)
Urinary tract infection	7	12	19 (22%)
Septicemia/meningitis	3	0	3 (3%)
Other SBI	7	9	16 (19%)
Total	37 (43%)	49 (57%)	86 (100%)

[Table 1. MTS classification of SBI]

PREDICTION OF SERIOUS BACTERIAL INFECTIONS IN FEBRILE CHILDREN AT THE EMERGENCY DEPARTMENT

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Background and aims: To develop and validate a prediction rule to identify children with fever at risk for serious bacterial infections (SBIs).

Methods: Children with fever, aged 1 month-16 years, presenting at the emergency department of the Erasmus MC-Sophia, Rotterdam (n=1750, July 2003-December 2005, derivation population) and the Juliana Children's Hospital, The Hague, The Netherlands (n=967, July-December 2007, validation population) were included. Independent predictors for SBI were identified with multivariate logistic regression. Discriminative ability (ROC) and calibration were determined.

Results: 222 children were diagnosed with SBIs (13%, 95% confidence interval (CI): 11-14%) in the derivation population; 118 (12%, 95% CI: 10-14%) in the validation population. A clinical model included age (odds ratio (OR): 0.3 (95% CI: 0.1-0.8) (1 month-1 year); 1.0 (0.2-6.2) (1-2 years); 1.4 (0.2-9.8) (2-5 years); 1.0 (0.1-7.6) (5-16 years)), duration of fever (OR: 1.2 (1.1-1.3)), tachycardia (OR: 1.3 (0.8-2.1)), temperature (per degree Celsius) (OR: 1.1 (0.9-1.4)), tachypnea (OR: 1.2 (0.7-2.0)), ill appearance (OR: 1.1 (0.8-1.7)), chest wall retractions (OR: 0.4 (0.2-1.1)), prolonged capillary refill (>3 seconds) (OR: 1.1 (0.6-2.2)) and oxygen saturation < 94% (OR: 4.9 (2.2-11.0)). ROC was 0.73 (sd. 0.02). Adding C-reactive protein (10 mg/l, OR: 1.1 (1.1-1.2)) increased ROC to 0.80 (sd. 0.02). In the validation population discriminative value was 0.77 (sd. 0.02). Both clinical and model with CRP calibrated well. A clinical decision tool was developed to discriminate different risk groups for SBI.

Conclusion: A prediction rule with clinical markers, vital signs and CRP is well able to identify SBI in febrile children.

PREDICTION MODEL OF BACTEREMIA IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA

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Background: Infections are serious complications of acute lymphoblastic leukemia (ALL) therapy. The initial assessment of the individualized risk to develop bacterial infections may be effective for prompt diagnosis and treatment.

Aim: To develop a prognostic model, that could estimate the individual risk of bacterial infection at the beginning of FEN.

Material and methods: A total of 122 FEN in children with ALL were retrospectively reviewed. Demographic data, underlying disease, laboratory and blood culture data were recorded. In addition, the mannose binding lectin (MBL) exon 1 polymorphisms were identified. From an initial model containing 6 variables (age, BFM (Berlin-Frankfurt-München) stratification, high fever, CRP, ESR, WBC count and MBL mutation), a final prognostic model was obtained with the following significant variables: CRP>9mg/dl, ESR>70mm/h and MBL mutation presence. A numeric score was given to each variable, based on the relative weight of the independent prognostic significance shown by each single category in the multivariate analysis. The sum of the single scores for each FEN was used to subdivide the study population into three groups: I. low risk (0 points), II. medium risk (1-3), III. high risk (4-5).

Results: Among total FEN number, 45.9% fit in group I, 23.8% in group II and 30.3% in group III. Controlling the sensitivity and specificity of the model, the score proved to be valid in this population (*AUC 88,5% and p= 0.000*).

Conclusions: Prognostic models appear to contribute to the risk classification of immunocompromised children in relation to susceptibility to bacterial infections.

MODIFICATIONS OF THE MANCHESTER TRIAGE SYSTEM IN CHILDREN WITH INFECTIOUS PROBLEMS AT THE EMERGENCY DEPARTMENT

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Background and aims: The presentation of children with fever varies from mild to severe symptoms. A triage system aims to recognize patients who need immediate care and patients who can wait safely. This study aims to improve the Manchester Triage system (MTS) for children with infectious problems.

Methods: We performed a prospective observational study at the emergency departments (ED) of a university and teaching hospital in The Netherlands and included children 0-15 years assigned to MTS flowcharts with possible infectious symptoms such as fever, rash, dyspnea, diarrhea, vomiting, upper respiratory tract and urinary tract problems.

A reference standard based on a combination of vital signs, potentially life-threatening conditions, diagnostic resources, therapeutic interventions and follow-up was used to determine patient's true urgency.

In 2006 8988/13554 children visited the ED with possible infectious diseases. The sensitivity (correct classification of urgency 1 and 2) was 63% and the specificity (correct classification of urgency 3, 4 and 5) 72%. To improve the MTS we developed age and fever dependent modifications and we validated these modifications.

Results: The modified MTS was used in 11,481 patients between May 2007 and April 2008 for respectively 12 and 5 months. 52% (5969/11481) presented with infectious symptoms. The sensitivity and specificity improved to 68% (95% CI 64-72%) and 80% (95% CI 79-80%) respectively. The diagnostic odds ratio increased from 4.4 (95% CI 3.6-5.2) to 8.3 (95% CI 6.8-10.2)

Conclusions: Modifications of the Manchester Triage System resulted in an improved specificity and sensitivity in children presenting with infectious problems.

THE LABORATORY DIAGNOSIS OF BORDETELLA PERTUSSIS INFECTION IN CHILDREN: A COMPARISON OF SEMI-NESTED PCR AND REAL TIME PCR WITH CULTURE

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Background: Worldwide, PCR assays have become a widely accepted laboratory tool for the detection of *Bordetella pertussis* (*Bp*). Little research has compared Conventional semi-nested PCR (CsnPCR) and Real time PCR (RtPCR) for the detection of *Bp*.

Aims: To compare the performance characteristics and diagnostic yield of CsnPCR with RtPCR in the detection of *Bp*.

Methods: CsnPCR and RtPCR were performed on pediatric nasopharyngeal samples from 1/ 2004 until 10/2007 (n=1891) and compared with RtPCR samples from 11/2007-8/09 (n=1693). The detection of *Bp* was based on the amplification of insertion sequence 481 while the gold standard was determined by a positive culture.

Results: The sensitivity, specificity, positive predictive value, and negative predictive value of CsPCR were 100, 81, 20 and 100 percent respectively, versus 100, 85, 26, and 100 percent, respectively, for RtPCR. RtPCR was more specific than CsnPCR, 85% versus 80.7%, respectively (P=0.001). Both CsnPCR and RtPCR assays gave a rise in diagnostic yield of 5 and 3.9 respectively (Mcnemars test P< 0.001). Superiority of CsnPCR was most marked among children ages 0.5-1, 1-6 years and 12-18 years with a diagnostic yield of 15.5, 8.6 and 9 respectively (Mcnemars test P< 0.001).

Conclusions: Both PCR assays were 100% sensitive for detection of *Bp*. A negative PCR virtually excludes the diagnosis of *Bp*. RtPCR is more specific than the CsnPCR method for *Bp* given its lower contamination rate. While PCR assays for *Bp* have 100% sensitivities, cultures should be obtained to enable serotyping and resistance patterns.

DIAGNOSIS OF SUBACUTE SCLEROSING PANENCEPHALITIS WITH MEASLES ANTIBODY INDEX IN THE CSF AND SERUM

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Background and aims: Subacute Sclerosing Panencephalitis (SSPE) is a fatal neurodegenerative disease seen among children and adolescents caused by Measles virus. It can be diagnosed by clinic symptoms, with typical EEG changes and CSF- serum measles IgG antibody index that indicated local measles antibody synthesis. The aim of this study is evaluation of Measles Ig G antibody index in diagnosing SSPE.

Methods: Between February 2006-August 2006, 21 serum and CSF samples of patients with clinical suspect of SSPE that were sent to Ege University Microbiology Laboratory were included in the study. Measles IgG antibodies were detected quantitatively in serum and CSF samples of the patients (CSF: Anti-measles Virus ELISA (Ig G) EUROIMMUN-Germany). Serum and CSF sample dilutions were prepared and quantitative measles IgG were analyzed. Serum/CSF index of 11 patients who have albumin and total immunoglobulin results in simultaneous serum and CSF samples were calculated. The obtained results were evaluated as CSQrel value according to the instructions of manufacturer.

Results: For 21 patients evaluated for SSPE, mean age was calculated as 11. With antibody index, specific diagnosis of SSPE was established in 7 patients out of 11 (64%). Three patients diagnosed as SSPE had the history of measles disease and were unvaccinated. Necessary data for the calculation of the index was not available in 10 patients.

Conclusion: In the 64% of the patients suspected of SSPE by clinical and EEG findings, diagnosis was confirmed with CSQrel value. Serum -CSF Measles antibody index is useful in specific diagnostic of SSPE.

SENSITIVITY AND SPECIFICITY OF THE RAPID INFLUENZA ANTIGEN TEST CLEARVIEW® EXACT INFLUENZA A AND B FOR PANDEMIC INFLUENZA A/H1N1

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Background/aim: Reverse-transcriptase polymerase chain reaction (RT-PCR) is considered the reference test for diagnosis of influenza because of its high sensitivity and specificity. Rapid Influenza Antigen Tests (RIAT) might prove useful because they have a fast turnaround time. Some RIAT have already demonstrated their excellent specificity for diagnosis of pandemic influenza A/H1N1. In these studies the sensitivity is low (30 to 50%) but no study have been performed in a paediatric population which is well-known to have a higher viral loads. We report our study of sensitivity and specificity of the RIAT clearview® influenza A et B.

Methods: In this prospective, observational study, we included 78 patients between 01/09/2009 and 01/12/2009 for whom a RT-PCR have been performed in our paediatric emergency department according to our guidelines. For each patient a RIAT have been performed in the same time.

Results:

	RIAT positive for influenza A	RIAT negative for influenza A	Total
RT-PCR A/H1N1 positive	25	16	41
RT-PCR A/H1N1 negative	1	36	37
Total	26	52	78

[Performance of Rapid Influenza Antigen Test compar]

The overall sensitivity and specificity of the RIAT clearview® influenza A et B were respectively 61% and 97%.

Conclusion: Our results confirm the excellent specificity of the RIAT for the pandemic influenza A/H1N1. The sensitivity seems slightly better than previous study performed in adult population. A positive RIAT allow a rapid and adequate treatment, on the other hand a negative test does not rule out a pandemic A/H1N1 influenza.

ROLE OF PERNASAL IGA TESTING IN DIAGNOSIS OF PERTUSSIS IN AUSTRALIAN COMMUNITY SPECIMENS

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Introduction: Pertussis remains an important and prevalent condition in Australia. Diagnosis of cases may be made difficult because of the effect of vaccination in modifying the clinical signs and symptomatology. Peripheral serology detecting *Bordetella pertussis*-specific IgG or IgA may be helpful in diagnosis but both assays have limitations because of sensitivity and specificity issues. Mucosal *B. pertussis*-specific IgA assays performed on specimens obtained by pernasal aspiration (PNA) has been recognised for 20 years as being very helpful in diagnosing cases of Pertussis.

Methods: We performed a retrospective analysis of *B. pertussis* PCR (in-house protocol) and *B. pertussis*-specific IgA antibody (PanBio, Australia) status in nasopharyngeal specimens obtained from community patients during the last 7 seasons in Western Australia. The Australian national case definition for pertussis was used to identify cases.

Results: 606 definite cases were identified. *B. pertussis* nucleic acid was detectable in 308 cases and mucosal *B. pertussis*-specific IgA in 471. 297 specimens were positive by mucosal IgA assay alone, 135 by PCR alone and 173 by both tests.

Conclusion: We conclude that an assay for mucosal specific IgA is an important adjunct to PCR in diagnosis of acute Pertussis in the community setting. Inclusion of this assay in the PNA testing strategy will result in identification of an increased number of cases of Pertussis when compared to strategies utilising PCR alone.

PERFORMANCE OF NON-CONTACT INFRARED THERMOMETER FOR DETECTING FEBRILE CHILDREN IN HOSPITAL AND AMBULATORY SETTINGS

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Non-contact infrared thermometer (NCIT) is a quick and non-invasive method to measure body temperature, not requiring sterilization or disposables. Thus, it is a candidate for temperature recording in children, particularly in hospital or ambulatory settings. Available data about accuracy of NCIT are conflicting. We aimed to compare a new NCIT with an historical standard method (axillary measurement by mercury-in-glass thermometer) in a large population of children aged >1 month, in hospital or ambulatory settings. Two-hundred-fifty-one children were enrolled in the study. NCIT clinical repeatability was $0.108^{\circ}\text{C}+0.095^{\circ}\text{C}$, similar to the one of the mercury-in-glass thermometer ($0.114^{\circ}\text{C}+0.103^{\circ}\text{C}$; $P=0.517$). Bias was $0.0150^{\circ}\text{C}\pm 0.0881^{\circ}\text{C}$ and the proportion of outliers $> 1^{\circ}\text{C}$ was 4/251 children (1.59%). Significant correlation between temperature values obtained with the two procedures was observed ($r^2=0.837$; $P< 0.0001$). The limits of agreement, by the Bland and Altman method, were -0.62 (95%IC: -0.47 ; -0.67) and 0.76 (95%IC: 0.61 ; 0.91). No significant correlation was noticed between the difference between the body temperature values recorded by the two methods and age ($P=0.226$), room temperature ($P=0.756$) or skin photo type ($P=0.420$). Calculating the ROC curve to determine the best threshold for axillary temperature $>38.0^{\circ}\text{C}$, for a NCIT temperature $=37.98^{\circ}\text{C}$ the sensitivity was 88.7% and the specificity 89.9%. Mean distress score (on a 5-point-scale) was significantly lower using the NCIT than using the mercury-in-glass thermometer (1.92 ± 0.56 and 2.40 ± 0.93 , respectively; $P< 0.0001$). Our data suggest that NCIT is comfortable and accurate in children aged >1 month in hospital or ambulatory settings.

DEVELOPMENT OF A REAL TIME REVERSE-TRANSCRIPTION PCR (RRT-PCR) ASSAY FOR DETECTION OF INFLUENZA A H1N1 2009 FROM CLINICAL RESPIRATORY SPECIMENS

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Background: In March 2009, a pandemic Influenza A virus (2009 H1N1) emerged in North America and spread worldwide, causing more than 9,500 deaths. This 2009 H1N1 strain is a reassortant, containing a swine hemagglutinin (HA) from North America, a neuraminidase (NA) and matrix (MA) from swine European strains and other human and avian origin genes.

Aims: A newly developed H1-09 subtype specific and Internal Positive control (IPC) assay were developed, optimized and utilized in a retrospective clinical study. The results were compared to the CDC rRT-PCR and rapid antigen test.

Methods: A PrimeMix RRT-PCR assay targeting the 2009 H1 hemagglutinin gene was developed from multiple sequence alignments of progenitor strains in GenBank. Additionally, an IPC assay was developed targeting a non-specific RNA in a clinical collection medium (PrimeStore) for monitoring specimens from collection-to-detection. A retrospective clinical study utilized nasal washings collected from two Texas DoD facilities.

Results: The optimized H1-09 PrimeMix assay showed high sensitivity ($10^{-1.0}$ TCID₅₀/mL, equivalent to 1-10 viral copies) and specificity to a reference panel of viruses and bacteria. In the retrospective study, PrimeMix H1-09, FluA and FluB assays identified 79/80 samples compared to CDC Swine rRT-PCR Panel results. FDA-approved Rapid Antigen testing exhibited the lowest sensitivity and specificity among influenza detection methods.

Conclusions: The PrimeMix H1-09 and IPC assays are highly sensitive and specific, exhibiting equivalent results compared to other detection methods. Furthermore, the IPC assay in PrimeStore Collection medium is a novel approach for monitoring specimen integrity from patient collection-to-detection.

**AN AUDIT OF THE IMPACT OF PRE-ADMISSION INTRAMUSCULAR PENICILLIN
ADMINISTRATION ON THE METHOD OF DIAGNOSIS OF INVASIVE MENINGOCOCCAL
DISEASE**

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Background: This retrospective study investigated influence of preadmission IM penicillin (IMp), on the method of diagnosis of invasive meningococcal disease (IMD).

Methods: All cases of IMD treated at two Dublin paediatric teaching hospitals from 2001-2008, were reviewed.

Results: 309 cases identified, 291 (94.1%) serogroup B. Blood culture results were available for 90% (279/309); 35.1% (98/279) were meningococcal culture +. 46.9% (46/98) had a lumbar puncture; 17.3% (8/46) were CSF culture +; 38.9% (14/36) were CSF PCR +; 30% (9/30) were CSF culture negative, PCR +.

64.8% (181/279) were blood culture negative; in 42% (76/181) CSF was taken; 13.2% (10/76) were CSF culture +; 68.8% (42/61) were CSF PCR +. 66% (35/53) who were CSF culture negative were CSF PCR +.

Overall in the study 2/14 (14.2%) were CSF culture + and CSF PCR negative.

Data regarding IMp was available in 287/309; 11.1% (32/287) received IMp. 35.5% (102/287) were blood and/or CSF culture +; 9.4% (3/32) in the IMp group and 38.8% (99/255) in the group who had not received IMp ($\chi^2=10.23$, $p=0.001$).

32 received IMp; 10% (3/30) were blood culture +, 90% (27/30) were blood PCR +, 71.4% (5/7) were CSF PCR +. 0/9 were CSF culture +.

255 did not receive IMp; 38.1% (95/249) were blood culture +, 93.9% (230/245) were blood PCR +, 57.6% (53/92) were CSF PCR + and 15.4% (18/117) were CSF culture +.

Conclusions: Most IMD is diagnosed by PCR alone. Patients who have antecedent IMp are less likely to have positive meningococcal culture ($p=0.001$).

MONOCLONAL ANTIBODY IMMUNOASSAY BASED DETECTION OF DENGUE VIRUS NS1 ANTIGEN

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Background: Every year 100 million dengue virus infections are reported globally. The nonstructural protein 1(NS1) of dengue virus is considered an important target for diagnostics of dengue infection since the protein was abundantly circulating in the blood during acute phase of the disease, in both primary and secondary infection. Moreover, free secreted NS1 levels in plasma correlated with viremia levels, which can be used to diagnose patients at the risk for developing dengue hemorrhagic fever. So detection of non-structural dengue antigens will be of immense benefit for an early and rapid diagnosis of dengue infection due to the long half life in the blood.

Methods: A panel of hybridoma cell lines capable of secreting monoclonal antibody (MAb) that specifically binds with the NS1 protein, was expanded in bioreactor using 5% FBS. The MAbs were purified using Protein-G affinity chromatography. ELISA, SDS-PAGE and Western blot analysis was performed to test the activity, purity and specificity of the purified protein. Subsequently this protein was biotin labelled with Biotin-N-hydroxy succinimide ester (from Sigma). The biotin labelling was confirmed by performing a dot blot on nitrocellulose membrane. The biotin labelled MAb was employed as a detection antibody in sandwich immunoassay to detect the target epitope of the NS1 antigen.

Results: The purified MAbs showed good specificity towards the target antigen in Western blot. A good dot blot was also obtained by using biotin labelled MAb. In both homo and hetero sandwich format the antigen sensitivity was found to be in nanogram levels.

Conclusion: A MAb based immunoassay was developed for detecting Dengue NS1 antigen.

STREPTOCOCCUS PNEUMONIAE SEROTYPING USING AUTOMATED MICROARRAY ASSAYF. Raymond¹, N. Boucher¹, J. Corbeil¹, **A. Gervais**²¹Infectious Disease Research Center, Laval University, Quebec City, QC, Canada, ²Department of Pediatrics, University Hospitals of Geneva, Geneva, Switzerland

Background and aims: The introduction of new vaccines against *Streptococcus pneumoniae* warrants serotypes surveillance, which is costly and labor intensive. Genetic typing of serotypes is warranted, but serotype definition relies on several genes, which makes it complex. A user-friendly assay allowing the identification of *S. pneumoniae* serotypes would be an invaluable tool in the evaluation of new vaccines.

Methods: An automated *S. pneumoniae* serotyping assay using multiplex PCR followed by primer extension and microarray hybridization was evaluated as a proof-of-concept. This assay is implemented in the AutoGenomics INFINITI analyzer, an automated molecular diagnostic system created for clinical laboratories. The assay includes *S. pneumoniae* species detection and serotypes identification. A machine learning approach was used to select a subset of genetic markers for precise serotyping of *S. pneumoniae*.

Results: A panel of 19 previously serotyped clinical specimens covering 13 prevalent serotypes included in vaccines was tested using the assay. All samples were positive for both *S. pneumoniae* species-specific probes. Serotype identification was concordant for 89.5% of samples. Discordant samples were sequenced in order to confirm diagnostic. In all cases, sequencing data was concordant with microarray serotyping, which suggests a higher specificity of the microarray assay compared to traditional serotyping. The microarray assay is robust and could identify serotypes even in cases where results were partial. Six samples could not be associated to a single serotype, but were assigned to subgroups of at most five serotypes.

Conclusions: A single automated assay should simplify the precise identification of all *S. pneumoniae* serotypes.

NEW BREATH TEST FOR DIAGNOSTICS OF *HELICOBACTER PYLORI* INFECTION HAS NO FALSE POSITIVE RESULTS AT OVERGROWTH OF NON-HELICOBACTER UREASE-PRODUCING FLORA

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Urea breath tests are used to detect *H pylori* infection by measuring the urease activity of gastric mucosa. Recently it was shown that overgrowth of non-helicobacter urease-producing bacteria is common for hypochlorhydria and other conditions thus leading to false positive results at standard breath testing.

We analyzed response of the new gas sensors designed by our group [1] to the action of breath gas of 114 adolescents with dyspeptic complaints and 30 healthy coevals. Presence of *H pylori* was estimated basing on level of anti-*Hp* IgG antibodies in blood serum.

Prevalence of *H pylori* infection was 58.8 % in patients and 33.3 % in controls. We found that relaxation time of the sensors was significantly longer in infected patients compared to uncontaminated patients and controls. Further experiments *in vitro* showed that the sensors were irresponsive to the degradation products of urea - carbon dioxide and ammonium vapours.

Thus, the experimental results prove that products of urea decay have a negligibly small impact onto response of the sensors under study. Therefore the new gas sensors may be utilized as a novel nonurease method for detection of *H pylori*. The method does not show false positive results at presence of microbial ureases of non-helicobacter origins, which is a major pitfall of standard urea breath tests.

1. G.V. Kamarchuk *et al.* TCNQ derivatives-based sensors for breath gas analysis. In: "*Breath Analysis for Medical Diagnosis and Therapeutic Monitoring*". A. Amann & D. Smith, eds. World Scientific, Singapore, pp. 85-99 (2005).

ROLE OF PLEURAL ANTIGEN ASSAY IN THE DIAGNOSIS OF PEDIATRIC PNEUMOCOCCAL EMPYEMA

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Background: Conventional microbiological cultures in blood and/or pleural samples (CMC) for pediatric empyema frequently have false-negative results. Newer techniques as real-time polymerase chain reaction (RT-PCR) and rapid pneumococcal antigen detection are reliable tools, but their diagnostic value has not been clearly established for pleural fluid samples.

Methods: Pleural fluid specimens were prospectively collected from all children admitted to our hospital with pneumococcal parapneumonic effusion from Jan-2006 to July-2009. Standard culture, pneumococcal antigen detection by immunochromatographic testing (Binax NOW *Streptococcus pneumoniae*), and real-time PCR were performed on these specimens.

Results: During the study period 55 cases with PPE and a mean (sd) age of 6.5 (6.1) years were enrolled. *St. pneumoniae* was identified in 28 cases (51%): by CMC in 15 cases and by RT-PCR in further 13 cases. Using CMC and/or RT-PCR as the test standard, the latex antigen detection in pleural fluid (LAD-PF) showed a sensitivity of 96% (95% confidence interval: 86-100%), a specificity of 100% (75-100%), a positive predictive value of 100% (98-100%) and a Youden index of 0.96 (0.88-1.04).

Conclusions: LAD-PF by immunochromatographic testing clearly enhances the pneumococcal diagnostic yield of CMC in pediatric empyema patients. LAD-PF doubles CMC sensibility and decreases by half its false negatives rate. This diagnostic capability is only comparable to that of RT-PCR, otherwise not widely available and more expensive and difficult to perform than LAD. LAD in pleural fluid specimens from children provides a rapid, simple, sensitive and reliable method of diagnosis for pneumococcal empyema.

UTILITY OF PCR TESTING FOR INVASIVE MENINGOCOCCAL AND PNEUMOCOCCAL DISEASE IN A PAEDIATRIC EMERGENCY CARE SETTING

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Background and aims: Polymerase chain reaction (PCR) plays an important role in yielding a definitive diagnosis of Invasive Meningococcal disease (IMD). It's utility in an Emergency Department (ED) setting is unclear.

We aimed to identify:

- patients who had PCR testing in our tertiary ED
- correlations between positive PCR and WCC, CRP and blood cultures (BC))
- differences in clinical presentation between patients with positive and negative PCR

Methods: Retrospective analysis of all PCRs between 2002 - 2009. Case notes for patients with positive PCRs were reviewed. Matched controls were selected from the cohort of negative patients.

Results: 1,940 specimens were requested (99 CSF & 1,841 blood samples) in 1,833 patients. 1,772 were sent for meningococcal PCR alone, 34 pneumococcal PCR alone & 134 for both meningococcal and pneumococcal PCR. Male: female ratio was 1.52:1. 1,093 patients were aged < 1 year, with 740 patients > 1 year (age range 2-19 years). 56/1833 (3%) PCRs were positive. 55/56 were meningococcal serogroup B positive, 1 was meningococcal serogroup W135 positive. All pneumococcal PCR was negative. 18/56 (32%) had positive BCs. 26/56 (46%) had a normal WCC. CRP was significantly raised (i.e. >70) in 33/56 (58%) cases and moderately raised in 14/56 (25%) cases.

Tachycardia and prolonged capillary refill time correlated most strongly with positive PCR.

Conclusions: PCR identified more than twice the number of patients with IMD than standard blood culture analysis. We recommend inclusion of PCR testing in the ED investigation of febrile children with suspected IMD.

EVALUATION OF POINT-OF-CARE TESTS IN PEDIATRIC OUTPATIENT CLINIC DURING H1N1 OUTBREAK

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Background and aims: The use of conventional laboratory tests may cause redundant delay in patient flow and unwarranted costs in outpatient clinics. In this study we evaluated, during H1N1 outbreak, the usefulness of point-of-care tests (POCT) including CRP, white blood cell count (WBC) and rapid influenza detection test (RIDT) in pediatric outpatient clinic.

Methods: POCT CRP was performed with Afinion AS100 Analyzer (Axis-Shield) and WBC was analyzed using HemoCue WBC (HemoCue) from finger tip capillary blood samples. Preclinical comparison was done between the POCT devices and routine laboratory methods by using the same blood sample. Comparisons were done with 44 samples for CRP and 77 samples for WBC. The comparison of POCT CRP and WBC with routine laboratory methods demonstrated significant correlation ($r= 0.993$ of CRP and 0.9754 of WBC). The difference between methods in each individual sample was less than 8% for WBC and 20% for CRP. RIDT was performed using Influenza A&B RespiStrip (Coris BioConcept) detection from nasopharyngeal swabs (Copan).

Results and conclusions: 74 patients having clinical symptoms of influenza were analyzed for influenza A using a RIDT and was compared to Influenza A PCR. Of 24 PCR-positive patients, 18 (75%) were positive using RIDT. Of 50 PCR-negative patients, 3 (6%) were positive by RIDT. We found that the usage of POCT CRP, WBC and RIDT is reliable, cost beneficial and of practical value in children with infections. However, negative results obtained by RIDT should be confirmed by PCR. Continuous training and evaluation of proper sampling techniques are reinforced.

VALIDITY OF A RAPID STREPTOCOCCAL TEST (TEST STREP A) IN CHILDREN WITH ACUTE PHARYNGITIS TREATED IN AN OUTPATIENT SETTING

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Background and aims: Beta-hemolytic group A streptococcus is the most common bacterial agent associated with pharyngitis. Rapid antigen detection tests should be used to diagnose pharyngitis in order to make a sure diagnosis and to reduce usage of antibiotics. The aim of the study was to find a validity (specificity, sensitivity, positive and negative predictive value) of a rapid streptococcal test (Test Strep A®, SureScreen, Great Britain) in children with acute pharyngitis treated in an ambulatory care.

Methods: A prospective study was conducted among 188 children (90 girls, 78 boys) aged 2-15 years (mean age 5,5 years, SD 2,6years). Inclusive criteria to the study were: fever > 38°C and sore throat, no cough and sneezing. None of the children received antibiotics prior to testing. In all children rapid streptococcal test and conventional culture (as a “gold standard”) from the pharyngeal swabs were performed. For calculations medical statistical calculator www.medcalc3000 was used.

Results: Number of positive and negative results presents table 1.

	Strep test positive	Strep test negative	Total
Culture positive	46	6	52
Culture negative	17	119	136
Total	63	125	188

[Results of rapid strep test and culture.] Sensitivity of a test was estimated as 88%, specificity as 87%, positive predictive value as 63%, negative predictive value as 97%.

Conclusions: The validity of and examined rapid strep test was high enough and the test should be estimated as useful for clinical practice.

RAPID URINARY ANTIGEN TEST (BINAX NOW) FOR DIAGNOSIS OF S. PNEUMONIA IN CHILDREN WITH UPPER AND LOWER RESPIRATORY TRACT INFECTIONS

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Objective: To compare the prevalence of S.pneumoniae by rapid urinary test and blood culture in children with respiratory tract infection and healthy children (controls).

Materials & methods: This case /control study done in 3 tertiary care centers in Tehran (2006 - 2007). The urinary antigen for S.Pneumoniae tested for 54 CAP; 56 acute rhinosinusitis and 50 healthy children.

Results: Antigenuria detected in 31.5 % of CAP; 31.5 % of rhinosinusitis cases and 6 % (3/50) of controls with significantly differences in CAP and rhinosinusitis cases ($P = 0.01, 0.01$). None cases with non pneumococcal CAP had antigenuria. In compare with blood culture the specificity for Pneumococcal antigenuria test was 94% but sensitivity is undetectable (high negative culture in cases).

Conclusions: Nasopharyngeal carrier states for S.pneumonia in healthy control are very low (6%). Adding the rapid urinary antigen test to conventional cultural methods would be helpful for early diagnosis of pneumococcal respiratory infection.

HIGH-MOBILITY GROUP BOX-1 PROTEIN, LIPOPOLYSACCHARIDE-BINDING PROTEIN, INTERLEUKIN-6 AND C-REACTIVE PROTEIN FOR IDENTIFYING SEPSIS IN CHILDREN: A PROSPECTIVE STUDY

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Background and aims: In children population specific inflammatory markers for identifying sepsis are less studied. The aim of our study was to evaluate the levels of high-mobility group box-1 protein (HMGB1), Lipopolysaccharide-binding protein (LBP), Interleukin-6 (IL-6) and C-reactive protein (CRP) in children with different severity of infections and their abilities for the early diagnosis of sepsis.

Methods: 140 children with suspected or proven infections admitted to the Children's Clinical University Hospital of Latvia during 2008 and 2009 were included in the study. Levels of HMGB1, LBP, IL-6 and CRP were analyzed. Children with suspected or diagnosed infections were categorized into three groups of severity of infection:

- i. infected without SIRS (n=36),
- ii. sepsis (n=91) and,
- iii. severe sepsis (n=13).

For sepsis definition the International Pediatric Sepsis Consensus Conference classification was used.

Results: There was no significant difference in HMGB1 levels among infected patients without SIRS and among sepsis and severe sepsis patients. The levels of LBP, IL-6 and CRP were statistically significantly higher among patients with sepsis compared to those infected but without SIRS ($p < 0.001$). Furthermore, LBP, IL-6 and CRP were significantly higher in children with severe sepsis compared to those ones with less severe sepsis ($p < 0.001$).

Conclusion: In children population significantly elevated levels of LBP, IL-6 and CRP were associated with a more severe level of infection. Whereas LBP, IL-6 and CRP seem to be good markers for identifying children with sepsis, HMGB1 seem to be of minor importance.

A SEMI AUTOMATED REAL-TIME DUPLEX PCR ASSAY FOR RAPID DETECTION OF STREPTOCOCCUS PNEUMONIAE DIRECTLY FROM CLINICAL SAMPLES

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Background: Accurate diagnosis of pneumococcal infections is critical in assessing the effectiveness of pneumococcal-conjugate vaccination on colonization in light of both serotype switching and replacement. Sensitive, rapid, and reliable detection is essential for surveillance of nasopharyngeal carriage. We developed and characterized a semi-automated, real-time duplex PCR assay to detect *S. pneumoniae* (SPn) directly from clinical samples.

Methods: Targeting the *lytA* and *ply* genes simultaneously, we tested 91 SPn serotypes in addition to 26 non-related bacterial strains. Assay sensitivity was established by spiking different concentrations of SPn into naïve human blood. The method was then applied to DNAs extracted by automation from 100 µL of 150 blood (chest X-ray confirmed CAP), 22 pleural fluid (PF), and 147 cerebrospinal fluid (CSF) specimens. In positive DNA, the Prevnar 13 vaccine serotypes were identified by capsule specific real-time PCR.

Results: Detection limits for *lytA* and *ply* genes were reproducibly established at 160 CFU/ml of blood. Only SPn strains were amplified showing an assay specificity of 100%. Of the 150 blood samples, 13% were detected by blood culture while 14% by PCR. Detection rates in PF and CSF were 91% and 12%, respectively.

Conclusion: Our highly sensitive (1.6 CFU per reaction) and specific PCR assay offers rapid detection of SPn in clinical specimens. Substantially increased detection rates observed in PF swabs indicate the usefulness of this assay on samples obtained from sites with higher bacterial burden. Details of the method and a comparison between PCR and blood culture method will be presented at the meeting.

ASSESSMENT RAPID METHODS TO DETECT *STREPTOCOCCUS PYOGENES*. SYSTEMATIC REVIEW AND META-ANALYSIS

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Background and aim: Streptococcal pharyngitis is one of the most frequent reason of consultation in primary and pediatric care. An inadequate treatment could cause adverse effects and bacterial resistance. The rapid antigen tests are an important advance, allowing in a few minutes the diagnosis of infection by *Streptococcus pyogenes*. The aim of this review is to assess the rapid antigen-detection test in the diagnosis of *S. pyogenes* from throat samples.

Methods: Systematic review and meta-analysis (2000-09). Source database: MedLine, Embase, Cochrane Library, Cinahl, CRD, ECRI, Hayes and HTA's agencies. Quality of included studies was measured according to Quadas's criteria. It has been calculated the indexes of diagnostic validity. A meta-analysis was performed in order to synthesize the results of the different evaluated studies.

Results: Twenty four studies were included. The quality was moderate. Sensitivity range was between 65,6% and 96,4%; specificity from 68,7% to 99,3%; the positive predictive value was between 59,4%-97,4%; and the negative predictive value from 87,8% to 98%. The meta-analysis determined a global sensitivity of 0,85 [CI 0,84-0,87], specificity was 0,96 [CI 0,96-0,97], likelihood ratio (+) 22,21 [CI 15,12-32,63], and likelihood ratio (-) 0,15 [CI 0,13-0,18]. The rapid antigen-detection test presented a good diagnostic performance.

Conclusions: Rapid tests offer good accuracy to use them as diagnostic method, however, these devices have to be complemented with the microbiological culture, because there are false positive and negative results.

DEVELOPMENT OF POINT OF CARE ASSAY FOR TUBERCULOSIS**S. Sarkar**¹, L. Tang¹, D. Das¹, T. Lowary², M.R. Suresh¹¹Pharmacy, ²Chemistry, University of Alberta, Edmonton, AB, Canada

Background and aims: Tuberculosis (TB) is one of the major contagious diseases that has infected one third of the global population. The diagnosis of TB in the paediatric population is mainly symptom based. We are hoping to design a simple and low cost immunoswab assay which can visually detect a TB antigen -lipoarabinomannan (LAM) from the patient's body fluids like blood or urine. We are exploiting the advantages of bispecific monoclonal antibody (BsMAb) which can simultaneously target the TB antigen-LAM and the enzyme horseradishperoxidase (HRPO).

Methods: The two cell lines - CS35 and YP4 secreting antibody specific for LAM & HRPO respectively - were first labelled with two different flurophores followed by the fusion in presence of polyethylene glycol (PEG) and finally the fused cells were selected by using fluorescence-activated-cell-sorter (FACS). After successive cloning, the stable clone was expanded and purified. The purified protein was used to design the sandwich ELISA.

Result: The immunoassay was designed on microtitre plate and the antigen detection limit was found to be in the ng/ml range.

Conclusion & future plan: The antibody based immunoassay was developed for detecting the hexasaccharide epitope of LAM antigen of TB bacteria. The assay design using the swabs is under progress.

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PROCALCITONIN AND S-TREM - 1 IN CHILDREN WITH MENINGITIS

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Aims: The discrimination of bacterial from aseptic meningitis, is a difficult decision in the initial care of these children, and represents a diagnostic challenge to the clinician. Several markers such as CRP, s-TREM and procalcitonin have been suggested for this purpose.

The aim of this study was to examine the usefulness of these markers in the evaluation of children with meningitis.

Patients and methods: In this prospective study we evaluated all children (0 up to 16 years of age) presented with meningitis at the ER. We recorded their clinical and routine laboratory data. In addition we tested their sera for CRP, s-TREM and for procalcitonin.

Results: Between May 2007 and Dec 2008, 74 children with meningitis were evaluated. 6 (8.1 %) were diagnosed with bacterial meningitis and 68 (91.8 %) with aseptic meningitis.

Inflammatory parameters in the 2 groups were as follows:

Number No. WBC CRP Procalcitonin s-TREM

Bact. meningitis 6 22,666 (± 1711) 17 (± 3.8) 5.4 (± 9.9) 301 (± 217)

Asep. meningitis 68 12,752 (± 4481) 0.88 (± 0.84) 0.07 (± 0.07) 94 (± 130)

P value NS 0.0001 0.053 0.06

Conclusions: Serum level of CRP, s-TREM, and procalcitonin, were significantly higher in children with bacterial meningitis. Both s-TREM and procalcitonin in addition to CRP may help the clinician in discrimination between bacterial and aseptic meningitis in situations such as partially treated meningitis or in cases that lumbar puncture can not be preformed.

A TUBERCULOSIS CASE DIAGNOSIS BY PROTEIN CHAIN REACTION

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Background: Tuberculosis infection and prevalence has declined in Portugal. The World Health Organization (WHO) estimates that more than $\frac{1}{3}$ of the world's population is infected with *Mycobacterium tuberculosis*. Almost 1.3 million cases and 450,000 deaths occur in children each year.

Methods: Review of a clinical case of a patient admitted at Hospital Central do Funchal.

Results: An 11 years old male, with a history of household contact with tuberculosis and chemoprophylaxis, sent to the Emergency Room with fever, asthenia, malaise and anorexia for one week. Physical examination: good general condition without respiratory distress; diminished breath sounds in 2/3 lower right hemithorax. Chest radiograph showed opacification of the right middle and lower lung fields and pleural effusion. Thoracic CT: "massive pleural effusion in the right hemithorax, conditioning atelectasis of the medial segment [...] no parenchymal condensation". Laboratory analysis: leukocyte 9700/uL, neutrophils 63.4%, LDH 162U/L, PCR 118mg/L, VS 95mm. The pleural fluid contained predominance of mononuclear cells (3560/mm³), proteins 49g/L, LDH 542U/L, ADA 136U/L. Microbiologic study was negative. He began treatment with isoniazid, pyrazinamide, rifampicin and ethambutol. Koch's bacillus was negative in three gastric samples but DNA testing by PCR was positive for *M. tuberculosis*. The child was discharged after 17 days of therapy.

Conclusions: Tuberculosis in children is often diagnosed clinically; laboratory confirmation is unusual. Over 50% have radiographically moderate to severe pulmonary tuberculosis with no physical findings and are discovered by contact history. As it can rapidly disseminate, prompt initiation of therapy is critical even without a laboratory confirmation.

AN IGM FLOW ASSAY AS A RAPID DIAGNOSTIC TEST (RDT) FOR TYPHOID (ENTERIC) FEVER IN CAMBODIAN CHILDREN

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Background: Typhoid (enteric) fever is under-diagnosed in children in the tropics. Traditional diagnostic methods require microbiology facilities, which are lacking in many endemic areas. Cambodian data for disease burden and resistance rates are lacking.

Objectives: To estimate the proportion of febrile children admitted to Angkor Hospital for Children (Siem Reap) that have typhoid (enteric) fever.

Methods: All children (< 16 years) admitted with a history of fever, *and* a documented temperature of $\geq 38^{\circ}\text{C}$ within the first 48 hours of admission, were eligible. Clinical data was recorded. Venous blood was taken for culture and two *Salmonella* Typhi (ST) -specific nucleic acid amplification tests (NAATs). Serum for an ST-specific IgM flow assay was taken at the time of admission, *and* on either Day 10 of fever *or* on discharge.

Results: 134 children were recruited to the study between April and June 2009. Five (3.7%) were confirmed typhoid cases (ST isolated from blood), 18 (13.4%) were suspected cases (positive admission and/or discharge IgM serology or positive NAATs) and eight (6.6%) were possible cases with an appropriate clinical picture but negative on all tests. Only four patients were positive by NAAT. Two of the five (40%) isolates demonstrated decreased susceptibility to ciprofloxacin.

Conclusion: One in six of febrile children admitted to this paediatric hospital in Cambodia had confirmed or suspected typhoid fever. The value of NAATs for the detection of ST in blood appears limited. IgM flow assay positivity exceeded that of blood culture and NAATs. Further evaluation of the assay's specificity is needed.

**PEDIATRIC HOSPITALIZATIONS ASSOCIATED WITH 2009 PANDEMIC INFLUENZA A (H1N1)
PNEUMONIA IN A SECONDARY CARE HOSPITAL**

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Background and aims: In 2009 an outbreak of a respiratory illness later proved to be caused by novel influenza A virus (H1N1) was identified all around the world. Our goal was to evaluate children with pneumonia in whom H1N1 infection was diagnosed by reverse-transcriptase reaction assay, to determine its frequency and to evaluate the clinical presentation, chest x-ray patterns, laboratorial results, treatment, underlying conditions and outcome.

Methods: We conducted a retrospective study involving children who were hospitalized between September and December 2009 at our secondary care Hospital.

Results: Forty children were hospitalized with pneumonia, 13 of them with H1N1 infection (32,5%). The mean age was $3,42 \pm 3,77$ years and 61,5% were male. The main complains at admission was fever and cough (92,3%), rhinorrhea (61,5%), respiratory distress (46,2%) and feeding difficulty (30,8%). Oseltamivir was used in all patients, alone (30,8%) or associated with an antibiotic (69,2%). In 46,2% of patients was initiated in less than 48 hours. The mean length of hospitalization was $5,54 \pm 1,39$ days. There were bilateral infiltrates on chest x-ray in 38,5%. Laboratorial results showed leukocytosis in 15,4% but the majority (53,8%) did not have any analytic change. There was a history of asthma in 15,4% and of immunosuppression plus chronic pulmonary disease in 23,1%. There were no records of morbidity or mortality.

Conclusions: The outcome was favorable in all admitted patients. This study will be continued within the next months to have a more accurate view of the epidemiology and outcome of the H1N1 infection in children with pneumonia.

RICKETTSIAL DISEASES IN CHILDREN IN A UNIVERSITARY HOSPITAL OF CATALONIA

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Background: In recent years, rickettsioses have become one of the most important emerging infectious diseases. One of these new infectious diseases is Tick-borne lymphadenopathy (TIBOLA).

The aim of this study is to describe the epidemiological and clinical aspects of rickettsioses of the spotted fever group in children in Catalonia (North-eastern Spain).

Methods: The study included all patients < 14 years treated in our hospital who were diagnosed of Mediterranean Spotted Fever (MSF) or TIBOLA.

Inclusion period: 1999 - 2008. Serology tests: for *Rickettsia conorii* and *R. slovaca*.

Results: Thirty four patients were diagnosed of TIBOLA and 14 of MSF.

TIBOLA: Mean age: 7.2 years (2-13). 23 were males. 26 cases appeared from October to April. 33 patients were tick bite on the scalp. A necrotic eschar was observed in 27 cases and was surrounded by a perilesional erythematous halo in 21. All patients had painful regional lymphadenopathies. 30 patients received antibiotic treatment. The course of infection was favourable in all cases.

MSF: Mean age: 6.1 years (1-13). 8 were males. 13 cases appeared from June to September. All patients presented fever and exanthema. The tache noire was observed in 13 cases, 7 of them were tick bite on the scalp. All patients received antibiotic treatment. The course of infection was favourable in all cases.

Conclusion: TIBOLA is prevalent in our area, with a clinical and epidemiological aspects completely different from the MSF.

Keywords: Rickettsioses. Mediterranean Spotted Fever, Tick-borne lymphadenopathy.

RED-LOOKING BABIES WITH ABDOMEN ABDOMEN? THINK HUMAN PARECHOVIRUS!

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Background: Human parechovirus is increasingly identified as an important cause of sepsis in young infants.

Aims and methods: We reviewed the clinical profile of infants diagnosed to have HPeV infection admitted between June 2007-June 2008.

Results:

Patient	Age (Days)	Abdominal symptoms	CNS symptoms	Rash	Lymphocyte count on admission (x 10 ⁹ /L)	C reactive protein on admission (mg/L)	Total duration of stay in days (require ICU care)	Site of positive samples	HPeV type
1	25	None	Irritability	Mottling	0.8	<5	7 days	CSF, stool	HPeV3
2	29	Abdomen distention, guarding	Irritability	Mottling	1.5	<5	4 days	CSF	Untyped
3	15	Abdomen distention	Seizure, apnoea, drowsiness	Red looking	1	<5	7 days(ICU)	CSF	Untyped
4	17	Abdomen distention	Seizure, apnoea	Red looking	1.7	<5	12 days(ICU)	Blood, throat, rectal swab	HPeV3
5	32	None	Irritability	Mottling	1.6	<5	1 day	CSF	HPeV3
6	7	Abdomen distention	Seizure, MRI changes	Red Looking	0.6	<5	2 spells >9 days(ICU)	CSF	Untyped
7	50	Abdomen distention	None	Red looking	1	<5	5 days(ICU)	CSF, throat, rectal swab	Untyped
8	27	None	Hypotonia, apnoea	None	0.8	<5	8 days(ICU)	Rectal swab	Untyped

[Clinical profile of infants with HPeV infection]

Five of the eight infants had abdomen distention as a presenting feature. In fact, one infant underwent

a laprotomy, due to suspicion of a surgical cause. In four of these five infants, abdomen distention was accompanied by an erythematous rash, with the infants commented as "red looking" in the medical notes. All but 1 infant had CNS disturbance, from hypotonia(1), irritability(3), aponea(3) to seizures(3). Charecteristic laboratory indices accompanying the septic picture were relative or absolute lymphopenia, and a failure to elevate the CRP.

Conclusions: Whilst a non-specific septic picture with CNS features are common, a characteristically red-looking infant with distended abdomen in the face of lymphopenia and non-elevated CRP should alter the clinician to human parechoviral infection in young infants.

TREND OF CRIMEAN-CONGO HEMORRHAGIC FEVER (CCHF) IN IRANIAN CHILDREN

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Background and aims: Crimean-Congo Hemorrhagic Fever Virus (CCHFV) belongs to Nairovirus genus and Bunyaviridae family and causes a fatal hemorrhagic fever in humans with up to 50% mortality rate. The virus is transmitted to humans by infected tick bite, handling of infected blood or tissues or nosocomially. In this study, probable sera from over the country were analyzed for CCHF through serological and molecular assays.

Methods: Sera of Iranian CCHF probable children, ranging 1 month to 14 years old, were collected from 2000 to 2009 (up to 30 November). They were analyzed by specific ELISA (IgM detection) and by RT-PCR (gel-based and Real-Time) assays.

Results: From June 2000 to 30 November 2009, the serological and molecular findings demonstrated the number of probable, confirmed, and death cases are 150, 33, and 3 respectively. Among confirmed cases, 26 were IgM positive and 7 cases were only RT-PCR positive. Among 33 confirmed cases, 21 (66.7%) were boy and 12 (36.4%) were girl. The results showed that the most infected province with 66.7% of confirmed cases was Sistan-va-Baluchistan.

Conclusions: As Iran is neighbored by two CCHF endemic countries, Afghanistan and Pakistan, Sistan-va-Baluchistan in this area showed the most proportion of CCHF infection among children. Also, in sex distribution, CCHF infection in boys is more prevalent than girls, so, it seems due to boy contribution in high risk professions. Then, with a continuous training program for these children, the incidence of CCHF in these age groups in the endemic regions will be decreased.

ATYPICAL PRESENTATION OF H1N1 INFLUENZA PRESENTING AS DIABETIC KETOACIDOSIS WITHOUT CORYZAL SYMPTOMS

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Background: Swine flu (H1N1 influenza) was first described in the 1918 pandemic, but have made a resurgence in early 2009 (Scalera et al 2009), with young adults and children most affected and the common presentation being coryzal symptoms (Larcombe et al 2009).

Aim: We describe 2 cases of children with confirmed H1N1 influenza who presented with acute diabetic ketoacidosis with no coryzal symptoms.

Clinical presentation: Patient 1 was a 7 year old girl and patient 2 was 12 year old girl. They presented to the Emergency department with symptoms of polydipsia, polyuria and abdominal discomfort. Blood glucose measured 25.0 in patient 1, and in patient 2 blood glucose was 26.0. They were not previously known diabetics. On assessment, they had ketonuria (+++ in both children), glycosuria, with normal pH on the arterial blood samples (compensated acidosis). Nasal swabs sent for PCR of H1N1 returned positive.

Results: Both children were treated with intravenous insulin and fluids as per diabetic ketoacidosis guidelines. Their symptoms rapidly resolved over 24 hours. They were prescribed a 5 day course of oseltamivir for treatment of swine flu. The patients remained normoglycaemic post-recovery, and no medications for blood glucose control were required after discharge from hospital.

Conclusions: Pandemic H1N1 2009 influenza is known to have a wide range of presentation in the paediatric population. A high index of suspicion should be maintained in any child who is unwell in the current pandemic.

SWINE FLU IN INDIAN CHILDREN: CLINICAL PROFILE AND OUTCOME

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Background: During the spring of 2009, a pandemic influenza A (H1N1) virus emerged and spread globally. There is not much data on children with swine flu.

Methods: Using medical charts, we collected data on 80 children seen in our hospital between August and December, who had influenza-like illness and who tested positive for the 2009 H1N1 virus with the use of a real-time RT-PCR.

Results: Of the 80 (45 boys) children we studied, 68.5% were between 5 years to 16 years, and 31.5% were ≤ 5 years age. The mean age of these children was 8 ± 3.5 yr. Contact history was positive only in 21 cases. High grade fever was the most common symptom followed by cough and rhinorrhea. 28.8% of the patients had at least one underlying co-morbid condition. Of the 27 patients who underwent chest radiography during evaluation, 13 children (48%) had findings consistent with lower respiratory tract infection. Antiviral therapy was initiated in 64 patients. Hospitalization was required in 21 (28.8%) children. Mean length of hospitalization was 102.8 ± 54.5 hours, irrespective of underlying disease. Two children developed ARDS and died.

Conclusions: Clinical features and laboratory investigations resembles common viral infections. History of contact was found in $< 30\%$ suggesting that the infection is now wide spread in the community. Recovery was very fast in all the patients irrespective of underlying illness. Though some patients recovered even without antiviral therapy, it was of benefit in majority.

EMERGENCE OF W135 MENINGOCOCCAL DISEASE IN SÃO PAULO CITY, BRAZIL**J.C. de Moraes¹, L. Bricks²***¹Preventive Medicine, Santa Casa de Sao Paulo, ²Vaccines, Sanofi Aventis Sanofi Pasteur, Sao Paulo, Brazil*

Background and aims: From 4 outbreaks of meningococcal diseases (MD) registered in São Paulo city in XX sec, the most relevant was caused by serogroups A and C in 1970's. In 1980's, Men B was the most relevant serogroup, but since 2000, Men C has causing clusters of MD in different areas of the city, and since 2003, Men C became is the most prevalent serogroup in the city. Recently, it was detected a greater number of MD caused by Men W135.

Methods: Descriptive study of MD cases notified in São Paulo city, from 2000 till 2008, based on compulsory registered data of MD obtained with São Paulo state Health Department, by year, age and region. Results will be present in percentage and incidence rates.

Results: In the period of study, there were about 450 MD cases by year (median, 5/ 100,000); from these, 43% with serogroup identification. In 2008, there were 112 cases of MD (1.2/100,000), mostly caused by Men C (77%), followed by W135 (11%) and B (10%). In central region, the most crowded, the incidence rate was higher in comparison with other areas.

Conclusions: The incidence rate of MD caused by W135 was higher then that caused by Men B in 2008. The emergence of this serogroup is cause of concern because of the risk of outbreaks in population with little previous exposure to this serogroup, and the absence of registered vaccines against W135 in Brazil till 2009.

HOSPITAL ADMISSIONS ASSOCIATED WITH PANDEMIC H1N1 INFLUENZA IN MADRID, SPAIN

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Background & aims: To describe the epidemiological and clinical features of pandemic H1N1 influenza in hospitalized children.

Methods: Multicenter retrospective case series including children < 14 years diagnosed with pandemic H1N1 influenza by polymerase chain reaction and admitted to one of fifteen pediatric hospitals in Madrid from May to October 31st 2009.

Results: 282 cases were identified; 174 (62%) were boys. Mean age was 5.4 years, 16% were infants < 1 year. Risk factors for severe influenza were found in 77 (27%) patients (six had more than one risk factor): 23 (8%) immunosuppression, 21 (7%) moderate/severe asthma, 7 (2.5%) other respiratory diseases, 12 (4%) cardiopathy, 14 (5%) neurological/neuromuscular disease. The most frequent reasons for admission were breathing difficulty (34%) and high fever (21%). Ninety-two percent of children had respiratory symptoms and 38% vomiting or diarrhoea. Chest radiograph was done in 86%: 31% were normal, 39 % had peribronchial markings with hyperinflation and 23 % areas of consolidation. Ninety-two patients (33%) had complications, including suspected bacterial pneumonia (16%) and severe bronchospasm (4%). Seventy-five percent of children received oseltamivir, 49% antibiotics, and 46% bronchodilators. Twenty-eight patients (10%) were admitted to intensive care units, 16 of them had risk factors and 7 required mechanical ventilation. Four (1.4%) patients died (2 leukemias, 1 encephalopathy and 1 Edwards syndrome).

Conclusions: Most hospital-admitted children with pandemic H1N1 influenza have respiratory symptoms and radiographic findings of viral pneumonia. Complications are frequent, but severe cases occur mainly in previously ill children and global mortality is low.

RE-EMERGENCE OF FATAL PERTUSSIS CASES IN CHILDREN: RESULTS FROM A LONG-TERM SURVEILLANCE PROGRAMME IN THE CZECH REPUBLIC

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The mortality analysis in the former Czechoslovakia showed a significant reduction in the pertussis death rates after 1953 in children under one year of age due to chloramphenicol therapy. In 1957, before the start of the routine vaccination, the death rate in these children was still 45.0/100,000. After the vaccination was introduced, this rate dramatically decreased.

The incidence data were obtained from the archives of the National Institute of Public Health, archives of the Institute of Health Information and Statistics, Communicable Disease Information System and Communicable Disease Notification System in the Czech Republic (EPIDAT). The mortality data were obtained, apart from the aforementioned sources, also from the literature.

In 1962, the death rate in children under one year of age was 0.14/100,000 only. The overall mortality rate decreased from 6.9 /100,000 in 1949 to 0.02 in 1962. In children above one year of age, no death was reported from 1966 to 1970 when one death from pertussis was confirmed.

After 35 years, three deaths of pertussis were reported in 2005, 2007 and 2009 in the Czech Republic. All three cases occurred in unvaccinated children under one year of age. The epidemiological investigation resulted in laboratory confirmation of the source of infection in the family in two cases. The suspected source of infection in the third case, based on the epidemiological investigation and case history, were family members as well.

Vaccination of adults, especially parents, grandparents and other persons caring of the youngest still unvaccinated children should be considered.

NO EVIDENCE FOR XENOTROPIC MURINE LEUKEMIA VIRUS-RELATED VIRUS (XMRV) SEQUENCES IN SAMPLES FROM JUVENILE IDIOPATHIC DISEASES

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Mammalian retroviruses cause a variety of diseases in their hosts including hematological, neurological, and immunodeficiency disorders that develop through neoplastic, lytic or inflammatory mechanisms. In addition to the human T cell leukemia and the human immunodeficiency viruses (HTLV and HIV, respectively), a novel infectious human retrovirus, the xenotropic murine leukemia virus-related virus (XMRV), has been reported in 2006 as infecting some RNase L-deficient patients who develop a familial form of prostate cancer. Recently, XMRV has also been found in association with chronic fatigue syndrome.

Here, we tested whether XMRV was associated with pediatric idiopathic infectious diseases whose symptoms suggest retroviral infections.

A total of 73 samples were obtained from 44 children who exhibited either of the following hematological, neurological or inflammatory pathologies: autoimmune hemolytic anemia, aregenerative anemia, thrombocytosis, idiopathic thrombocytopenic purpura, neutropenia, idiopathic aplasia, leucosis, encephalitis, Henoch-Schönlein syndrome, dermatomyositis, and juvenile idiopathic arthritis (JIA). Samples were selected and collected within the last two years in Montpellier hospitals. DNA samples were extracted from blood (44 samples) or synovial fluid cells (JIA, 29 samples). Samples were screened for the presence of XMRV using nested PCR with primers spanning the receptor binding domain (RBD) of the SU *env* gene.

Amplification of XMRV RBD sequence was negative for blood and synovial fluid samples in all patients, indicating that XMRV (or other xenotropic-MLV related retrovirus) does not seem to spread in pediatric patients. We will discuss the implications of our results in the context of XMRV prevalence in the general human population.

RHEUMATIC HEART DISEASE - AN OLD DISEASE REVISITED

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Background: Rheumatic fever (RF), once the most common cause of acquired cardiac disease in children, has seen a steady incidence decrease in the last decades in the developed countries.

Aims: Characterize rheumatic heart disease (RHD) in children in our hospital.

Methods: Retrospective study between January 2001 and May 2009. Demographic, clinical, laboratory and imagiologic findings were analysed.

Results: Of the 25 patients the majority were females (60%), with a mean age of 12 years (5 to 17). 90% were non-caucasian and all were from Africa. All were admitted with chronic RHD, (mean evolution 3 years). Seven patients had recurrences of rheumatic fever due to irregular secondary prophylaxis; the major symptoms at presentation were due to congestive heart failure (HF). Complications occurred in 10 patients (40%):atrial fibrillation (3), stroke (2) and severe HF (7). Risk factors for complications were female gender (70%vs53%;p=0.36), irregular profilaxis (60%vs35%;p=0.33), poli-valvular involvement (60%vs33%;p=0.21) and severe mitral regurgitation (70%vs42%;p=0.47) but no significance was found due to sample size. Chronic severe MR was the most common form of RHD (70%) followed by mild aortic regurgitation and mild mitral stenosis. Thirteen had left cavity dilation. Fourteen needed surgical mitral valve correction. All received medical treatment in the majority (n=16) with benzathine penicillin every 4 weeks.

Conclusions: RF is still a major public health problem in developing countries. Due to late diagnosis and incorrect treatment and prophylaxis these patients come to our attention late in the disease progression, already with severe forms of RHD, manageable only with surgical repair.

PAEDIATRIC HOSPITALISATIONS ASSOCIATED WITH 2009 PANDEMIC INFLUENZA A/H1N1 IN SOUTHERN GERMANY

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Background: Data on complications associated with the 2009 pandemic influenza A/H1N1 (PIA) are limited. We therefore investigated PIA hospitalisations and estimated the incidence in a geographically defined region in Germany.

Methods: From July 2009 to February 2010, we analyzed data of all children aged ≤ 18 years with PIA confirmed by polymerase chain reaction (PCR) admitted to two paediatric hospitals in Wuerzburg, Southern Germany. Incidence estimates were calculated using the catchment area of the hospitals (City of Wuerzburg and two adjacent districts), including a study population of 66,300 children ≤ 18 years of age.

Results: A total of 92 children (61% males) were hospitalized with PCR-confirmed PIA. Their median age was 6.9 years (IQR 1.6-11.6) and median (IQR) duration of hospital stay was 3 (2-5) days. Five (5.4%) children, median age 10.0 years (IQR 0.9-11.8) were admitted to ICU for a median duration of 3 days (IQR 2-29.5). One eleven-year-old girl with underlying severe neurological impairment died due to pneumonia and respiratory failure. The incidence of PIA hospitalisations in children ≤ 18 years (0-4 years, 5-18 years) from the Wuerzburg area ($n=69$) was estimated to be 104 (172, 79) /100,000 (95% CI: 82 to 133).

Conclusions: The hospitalisation incidence of PIA was twice as high, when compared with previous incidences for seasonal influenza A in Germany (Weigl et al. 2002), and four times higher for the age group 6-16 years. Complications among hospitalized children were lower compared to children with PIA hospitalisations in Argentina (Libster et al. 2010).

PERTUSSIS IN CHILDREN - A PORTUGUESE HOSPITAL STUDY

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Background and aims: Despite universal immunization against *Bordetella pertussis* infection, outbreaks continue to occur in countries, as Portugal, with excellent vaccine coverage. Without booster vaccinations, adolescents and adults are susceptible to this disease, becoming its major reservoir. Review the cases of bordetella pertussis infection in children from a peripheral hospital in Lisbon.

Methods: Retrospective study of children with a positive polymerase reaction (PCR) for *Bordetella pertussis* in nasopharyngeal swab, between January 2007 and September 2009. Demographic, clinical, laboratory, imagiological, therapeutic data and outcome were analysed.

Results: Total of 15 children: 11 boys, median age 2 months (min 1, max 9). Five had symptoms seven days before admission and eight a familiar symptomatic contact. Ten children weren't vaccinated and only one had two doses of pertussis vaccine. Two children had normal white blood cells count at presentation. All children were treated with macrolide antibiotics. Complications included: respiratory insufficiency (6), apnea (4), bradycardia (3) bacterial pneumonia (2), atelectasis (2) and otitis media (1). Three patients had more than one complication. Intensive care was needed in five patients and four required ventilation. One child died after a nosocomial septicemia. Co-infections occurred in eight patients: adenovirus (2), metapneumovirus (2), influenza (2), parainfluenza (2), respiratory syncytial virus (1) and *Enterobacter aerogenes* (1).

Conclusions: Even if this is a small sample we had a great number of complications and a mortality case. New vaccine strategies are needed, like adolescent booster vaccination, to reduce hospital admissions and complications among the most susceptible group: little infants.

PAEDIATRIC PATIENTS WITH H1N1 INFLUENZA EVALUATED IN A PORTUGUESE HOSPITAL, SEPTEMBER-NOVEMBER 2009

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A new pandemic influenza (H1N1) virus emerged in 2009, causing new medical challenges. Knowledge about this new disease is vital to improve children's care.

An observational analytical study was conducted from September 11th to November 18th. All positive children for H1N1, diagnosed by reverse-transcriptase polymerase-chain-reaction assay (PCR), were included. Criteria for specimens' collection were based on Portuguese Health Ministry Guidelines. Detailed information on exposure, symptoms and clinical course were analysed. Statistical analysis was made using PASW-Statistics.

We found 726 patients positive for H1N1: mean age 7.97 years (SD±4.35). Maximum number of cases occurred 4-6 weeks after the first case. Median time onset of illness-PCR was 1 day (range 0-9 days).

Most frequent symptoms were fever (96,8%) and cough (84,7%). Children younger than 12 months were more irritable ($p < 0,001$). Adolescents had more headache, myalgias and sore throat ($p < 0,001$).

Risk factors were found in 58,9% of patients, most common: asthma (29,6%) and age under 5 years (20,7%).

Hospitalization occurred in 107 cases; 7 needed intensive care and no deaths occurred.

Complications were found in 31% of the admitted patients (5,9% of all cases): respiratory insufficiency (15,9%), lobar pneumonia (12,1%); encephalitis (0,9%).

Oseltamivir was prescribed to 326 (44,4%) patients. The mean time onset of illness-initiation of oseltamivir was 1,51 days (SD±1,43). Children with complications had a later start of treatment (1,00 vs 2,00 days, $p < 0,001$).

Infection by 2009 H1N1 influenza has different presentations according to age group. Risk factors and delayed treatment were associated with a higher complication rate.

CONGENITAL CHAGAS DISEASE AS A RESULT OF ACUTE MATERNAL *T. CRUZI* INFECTION BY ORAL ROUTE**A.Y. Pinto¹, V.C. Valente¹, S. Aldo Valente¹, A. Figueira²***¹Evandro Chagas Institute, Ananindeua, ²Pará State University, Belém, Brazil*

During Dec, 2006, a female, 24 years-old, her parents and husband coming to our laboratory in view to improve the diagnosis of prolonged febrile illness. We conducted serological and parasitological tests and confirmed Chagas disease by positive *T. cruzi* blood culture in two of them besides to clinical and serological findings compatible with acute Chagas disease in all examined person. They received daily doses of benznidazol. The young female did not complete her treatment due to serious drug intolerance and amenorrhea. Pregnancy was confirmed and her treatment was interrupted. Child was born in Apr, 18 2007, female, premature birth, low birth weight and signs of Respiratory Distress Syndrome. At the perinatal period, screening diagnostic tests for congenital infections including Chagas disease, were negative. Chagas disease was made just four months after birth by clinical suspicion: convergent strabismus, microcephaly and delayed psycho motor development. At this time, the assay tests for *T. cruzi* infection shows positive seroconversion. Magnetic resonance shows cystic lesion and intracranial calcifications. Child received treatment with benznidazol as other members of the family. Authors discuss the necessary revision of treatment recommendation in pregnant with Acute Chagas disease.

THE WHOOPING-COUGH IS OF RETURN

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The whooping-cough is a toxic bacterial infection due to *Bordetella pertussis*, it is the infectious leading cause of mortality of the infant of less than two months in France.

Our **objective** is to determine that the prevention is more than ever essential.

Materials and methods: Retrospective study made on files of patients recruited from 4/1/2008 to 7/31/2008.

This study relates to the epidemiologic, clinical, therapeutic data and evolutionary forecast.

Results: Frequency of age < 02 month, the female sex is more touched the majority of the children is not vaccinated and is not contaminated by adults.

Two cases of malignant whooping-cough.

The thrombocytose is present at the majority of the patients.

A death: sudden death.

Conclusion: The whooping-cough was and remains threatening and sometimes mortal from where interest of the prevention.

WHOOPING COUGH IN TUNISIA: THE RESURRECTION

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Background and aims: *Bordetella pertussis* is the agent responsible of pertussis. *B. parapertussis*, *B. bronchiseptica* and *B. holmesii* may also cause a pertussis-like respiratory disease. Despite high vaccination rates for primary immunization in young children, pertussis continues to be a global concern. Adolescents and adults have been identified as a source of transmission of pertussis to very young infants non or partially vaccinated. The study aim was to analyse the epidemiology of pertussis in Tunisia using reference biological diagnoses.

Methods: Between March 2007 and November 2009, 295 clinical samples were received from 284 infants with a diagnosis of whooping cough, pertussoid cough or pertussis-like syndrome. The laboratory diagnostic criteria were culture isolation of *Bordetella* species on Bordet-Gengou medium and real-time PCR targeting the insertion sequences IS481 for *B. pertussis*, *B. bronchiseptica* or *B. holmesii* and IS1001 for *B. parapertussis*.

Results: Among the investigated children suspected of pertussis, the diagnosis was retained positive for 115 (41%), of whom 52% were less than 2 months old and had no dose of vaccine. Real-time PCR showed that 105 DNAs yielded the IS481 and that the IS1001 was detected in only 4 DNAs. Simultaneous positive signals were noted in 11 DNAs thus suggesting a co-infection. In two cases, the mother was shown to be a potential source of the infection.

Conclusions: Pertussis is making a come back globally. Improvements in the surveillance of pertussis among young infants are required to guide the development of new vaccine strategies to protect this vulnerable population.

EPIDEMIOLOGY OF INVASIVE MENINGOCOCCAL DISEASE (IMD) IN CHILDREN IN IRELAND IN THE POST MENINGOCOCCAL C VACCINATION ERA (2000-2008)

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Background: Meningococcal C vaccination was added to the Irish immunisation schedule in October 2000. This study describes the epidemiology of IMD in children in Ireland in the post vaccine era.

Methods: IMD was defined as PCR or culture positivity from a normally sterile site. Cases of IMD from 2001-2008 inclusive treated at Dublin's two tertiary paediatric hospitals were identified from the Irish Meningococcal and Meningitis Reference Laboratory database. Residual morbidity was defined as persisting abnormality at most recent OPD visit. Retrospective review of case notes used a standardised data collection tool. A previous study of 407 cases, 1995-2000, provided comparative data¹.

Results: 309 cases were identified; serogroup (gp)B 291(94%), gpC 10(3%) & others 8; 180/309(58%) male; median age 1.6 yrs (range 0.1-17.7yrs). Symptoms and signs included rash (90%), fever (77%), lethargy (51%) and irritability (42%). 94/309 (30.4%) attended GP prior to presentation and 28/94(29.7%) received IM penicillin. There were 12 deaths: 11/291(3.7%) gpB, 1/1 gpY, 0/10 gpC. Morbidity persisted in 14/291(4.8%) gpB and 2/10(20%) gpC. GpC accounted for 3.2%(10/309) cases vs. 25.5%(104/407) in the prevaccine era. Overall mortality rates remain unchanged [3.8%(12/309) vs. 3.9%(16/407)]. Morbidity persisted in 5.4%(16/297) vs. 11.2%(44/391) in the prevaccine era (p=0.009).

Conclusions: GpC cases have declined with none detected in our institutions from 2003-2008. Mortality rates are unchanged. There has been a decline in the rates of residual IMD morbidity, possibly due to improvement in medical and ICU management, or the reduction in prevalence of serogroup C disease.

1. Healy et al. *Clinical Infectious Diseases* 2002

IMPACT OF VARICELLA ZOSTER VIRUS EXPOSURE ON PERIOD PREVALENCE AND AGE OF ONSET OF HERPES ZOSTER IN FRANCE: MONA STUDY

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Context: Repeated contact with children suffering from varicella might play a significant role in maintaining immunity against varicella zoster virus (VZV) and reduce the risk of herpes zoster (HZ) in adulthood.

Objectives: To evaluate the period prevalence and the age of onset of HZ in a population with little or no exposure to children (monks/nuns) compared to that in populations with different levels of exposure to children: the general population and pediatricians.

Method: A national, observational, multicentre, epidemiological study in an "exposed/non-exposed" design was conducted by means of self-administered questionnaires. Monks and nuns (in 40 isolated monasteries) who regularly came into contact with groups of children under 10 years of age were excluded from the principal analysis population.

Results: The principal analysis population comprised 920 monks/nuns (41.5% nuns), 1,533 individuals (51.9% women) from the general population and 788 pediatricians (47.9% women). The reported period prevalence of HZ was 16.2% in the monks/nuns, 15.1% in the general population and 12.3% in pediatricians (p adjusted for sex and age = 0.59). The mean reported age of onset of HZ was 54.8, 48.6 and 35.1 years, respectively ($p=0.0005$). Women exhibited HZ significantly more often than men in all populations [21% vs 13% (monks/nuns- $p=0.002$); 18% vs 12% (general population- $p=0.002$)] but pediatricians 13% vs 12% ($p=0.44$).

Conclusion: In this study no difference in reported period prevalence of HZ was demonstrated in these three populations with a very different exposure to children. Amazing statistically significant differences in mean reported age of onset of HZ were observed.

MOLECULAR CHARACTERIZATION OF ENTEROVIRUSES DETECTED FROM AN EPIDEMIC OF HAND, FOOT AND MOUTH DISEASE (HFMD) IN INDIA, 2009

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Background and aims: HFMD is a common childhood illness. Outbreaks of HFMD are known to be caused mainly by Coxsackie virus A 16 (CA-16) and Enterovirus-71 (EV-71). Other EV types, CA-1, CA-6, CA-10, echo-4 have also been found associated in sporadic outbreaks. During June-October, 2009, suspected HFMD outbreaks were reported from Kerala, West Bengal and Orissa states of India. A study was carried out to characterize the viral etiological pathogen(s) using molecular approach.

Methods: A total of 50 HFMD cases investigated in the study included, thirty five from Kerala, eight from West Bengal and seven from Orissa. EV detection and molecular typing was carried out in vesicular fluid, stool, serum and throat swab samples by RT-PCR of 5'NCR, VP1 gene, sequencing and phylogenetic analysis.

Results: EV positivity was detected in 57.2% (20/35), 62.5% (5/8) and 71.4% (5/7) of the specimens from Kerala, West Bengal and Orissa states respectively. Typing of VP1 gene sequences indicated presence of CA-16 in West Bengal and Orissa while CA-6, Echo-9 and EV-71 were detected in Kerala. CA-16 strains were closer to Malaysian strains with 91.2-95.6% nucleotide identity while CA-6, Echo-9 and EV-71 showed 94.8-95.7%, 95% and 94.4% nucleotide identity respectively with corresponding Japanese, Australian and French strains.

Conclusion: The study documents association of CA-16, Echo-9 and EV-71 and emergence of CA-6 in causing HFMD in India.

THE EPIDEMIOLOGY OF *HAEMOPHILUS INFLUENZAE* MENINGITIS IN 13 EUROPEAN COUNTRIES WITH ESTABLISHED HIB IMMUNISATION PROGRAMMES BETWEEN 2000 AND 2006

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Background and aims: Routine immunisation against *Haemophilus influenzae* b (Hib) has dramatically reduced the incidence of invasive Hib disease. This study describes the epidemiology of *Haemophilus influenzae* (*Hi*) meningitis in 13 countries with established Hib immunisation programmes.

Methods: An international collaboration was initiated in 1996 to monitor the impact of Hib immunisation on invasive *Hi* disease (www.euibis.org). Participating countries that routinely immunised against Hib by 2000 and serotyped >50% of all clinical isolates were included.

Results: Thirteen countries reported 815 *Hi* meningitis cases between 2000-2006. Of 731 cases with known serotypes, Hib accounted for 524 (72%), non-capsulated *Hi* (*ncHi*) for 155 (21%) and non-b encapsulated *Hi* for 52 (7%) cases, mainly Hif (n=36) and Hie (n=10). Hib was responsible for 75% (479/640) of *Hi* meningitis among < 5 year-olds and 49% (45/91) among 5-14 year-olds, while *ncHi* was responsible for 18% (118/640) and 41% (37/91), respectively. Case fatality ratios were lowest for Hib (21/524, 4.0%), followed by non-b encapsulated *Hi* (3/52, 5.8%) and *ncHi* (9/155, 5.8%), but increased with age for both Hib (3.0%, 3.9% and **8.9%**) and *ncHi* (4.8%, 5.3% and **8.1%**) among < 1, 1-4 and 5-14 year-olds. Case fatality among non-b encapsulated *Hi* only occurred among < 1 year-olds where 2/3 children with Hia and 1/18 with Hif meningitis died.

Conclusions: Hib remains the most important cause of childhood *Hi* meningitis even in countries with established Hib immunisation programmes. Further studies are required to explain the higher case fatality ratios for Hib and *ncHi* in older children.

USE OF INSECT REPELLENTS FOR INFANTS AS PROTECTION MEASURE AGAINST MOSKITO BITES IN REUNION ISLAND DURING CHIKUNGUNYA EPIDEMICS IN 2005-2006

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Population of Reunion island faced a chikungunya virus epidemic in 2005-06. The personal protection for children is based on repellents and impregnated mosquito-net and clothes during day time. There was no clear international consensus on the use of repellents in young children.

Methods: The GPTrop underwent a retrospective randomised survey by questionnaire among parents of children under 30 months during chik epidemic in Reunion to measure frequency of repellent use, to identify the repellent substances used, to estimate their efficacy, to measure frequency of repellent side effects, to measure frequency of mosquito-net use and to estimate prevalence of Chik among protected children versus less protected children.

Results: 382 children under 30 months were included. $\frac{3}{4}$ of children have been protected with repellents during chik epidemic. Main active repellent substance used were IR 3535® (77%) and citriodiol (17%). 86% of parents noticed a repellent efficacy on mosquitoes lasting more than 3 h in 52% of answers. Mild cutaneous side effects (8,6%) and allergic general reaction (1,4%) were reported. 3 children had febrile seizures after repellent application (1,1%) without evidence based imputability. 70% of children were protected by mosquito-net during day time.

Prevalence of chik among children protected by repellent and mosquito-net (8%) was inferior to these of children of same age, less protected during the very epidemic in Mayotte island (17% ± 7 %).

Conclusion: Repellents IR 3535® and citriodiol use on young children is safe and reduce the risk of chikungunya infection in complement of mosquito-net use.

INFLUENZA ACTIVITY AND INCREASED RISK OF INVASIVE MENINGOCOCCAL DISEASE IN CENTRAL ONTARIO, CANADA: A CASE-CROSSOVER ANALYSIS

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Background: In temperate climates, invasive meningococcal disease incidence tends to coincide with or closely follow peak incidence of influenza virus infection; at a seasonal level, increased influenza activity appears to correlate with increased seasonal risk of invasive meningococcal disease. We used a case-crossover design to evaluate the acute effects of weekly influenza activity on invasive meningococcal disease risk.

Methods: We evaluated 240 cases of invasive meningococcal disease reported in Central Ontario, Canada, from 2000 to 2006. Exposure information included data on air pollutants, ultraviolet radiation, weather, and weekly influenza A, influenza B, and respiratory syncytial virus (RSV) activity. A matched-period case-crossover study was performed with random directionality of control selection. Effects were estimated using conditional logistic regression.

Results: Increasing weekly influenza A activity was associated with an acute increase in the risk of invasive meningococcal disease (odds ratio per 100 case increase in influenza: 2.69, 95% CI: 1.42 to 5.10). Adjustment for ambient ultraviolet radiation strengthened this effect (adjusted OR: 3.53, 95% CI: 1.34 to 9.32). No differences in effect were observed in subgroup analyses by serogroup or by flu season vs. non-flu season. No modification of effect was observed by age group. No change in meningococcal disease risk was seen with increasing influenza B or RSV activity.

Conclusions: We have identified a strong, acute effect of changing influenza activity on invasive meningococcal disease risk. Further study is required to provide insight into whether this effect is driven by increased colonization, increased transmission, or increased propensity for invasive disease.

HEARING LOSS AFTER MENINGOCOCCAL SEROGROUP B DISEASE: FINDINGS FROM A NATIONALLY REPRESENTATIVE CASE-CONTROL STUDY

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Aims: There remain over 1000 cases of meningococcal serogroup B (MenB) disease in the UK each year. Vaccines to prevent other causes of meningitis and septicaemia have been successfully introduced into many countries. Estimates of the sequelae of Men B disease in the modern era are needed to inform the development and introduction of future vaccines.

Methods: We present interim results from a nationally representative case-control study. Cases were identified via the Meningococcal Reference Laboratory and controls via case GPs. Consenting subjects underwent a standardised assessment of hearing (pure tone audiometry followed bone conduction assessment if abnormal) together with other assessments. Mild hearing loss (HL) was defined as any hearing loss ≥ 20 dB in either ear, with moderate HL defined as ≥ 40 dB. Analyses were undertaken adjusted for age and sex. The study was funded by the Meningitis Trust.

Results: Interim data were available for 121 cases and 89 controls. 9.9% of cases and 7.9% of controls had some HL ($p=0.8$), with bilateral HL identified in 5.8% of cases compared with 3.4% of controls ($p=0.4$). Moderately severe bilateral HL was identified in 6.6% of cases compared with 2.2% of controls ($p=0.1$). 3 survivors (2%) had cochlear implants compared with no controls.

Conclusions: These interim results suggest MenB disease may be associated with small increases in HL, although differences between survivors and healthy controls were not significant. Hearing outcomes from MenB disease may have been overstated previously. These data will form the basis for cost-effectiveness analyses of new MenB vaccines.

HEPATITIS A SEROPREVALENCE AND EPIDEMIOLOGICAL SHIFT IN CENTRAL ADANA, TURKEY FROM 1999 TO 2009

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Aim: The aim of the study was to determine the epidemiological shift that may have occurred in the last 10 years of Hepatitis A virus (HAV) seroprevalence.

Material and Method: In 1999, we reported the anti-HAV seroprevalence in 711 children aged between 2 and 16 years children with various socioeconomic levels in Adana city center (1). Ten years later we repeated the same study at the same locations in a similar population with the same method.

Results: Anti-HAV seroprevalence among pre-school children 24 to 84 months in 1999 and 2009 were 20 % vs 32,4 % in Socloeconomic Status (SES) Group 1; 25,6 % vs 16,8 % in SES Group 2 and 7,8 % vs 18,8 % in SES Group 3, respectively ($p>0.05$). In 2009 anti-HAV seroprevalence among school-age children 85 to 198 months decreased from 85,7 % to 53,8 % in SES Group 1; 64,4 % to 36 % in SES Group 2 and 43,7 % to 29,3 % in SES Group 3, respectively compared to 1999 ($p< 0,0001$, $p< 0,05$).

Conclusion: Our study showed that anti-HAV seroprevalence, regardless of SES differences, has decreased statistically significantly during the last 10 years in school-aged children. Results showed that, not withstanding SES, anti-HAV seroprevalence has shifted to further ages. Since adolescents and young adults will be at risk of symptomatic HAV infection, routine hepatitis A vaccination of children in our region should be initiated.

Reference: 1) Yapicioglu H, Alhan E, Bozdemir N, Yaman A, Cetiner S. *Ind. Pediatrics*, 2002; 39: 936-41.

EPIDEMIOLOGY OF ROTAVIRUS ACUTE GASTROENTERITIS IN CHILDREN IN A REGION OF QUEBEC, CANADA (2002-2008)

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Background and aims: Available literature on rotavirus acute gastro-enteritis (AGE) surveillance rarely includes data on short term hospitalization and/or outpatient visits amongst the same population. The aim of this study was to assess the burden of rotavirus AGE on the whole health care system.

Methods: A retrospective cohort study of all children < 5 years old with an AGE from 2002-2008 was performed in Estrie, a rural region in south eastern Quebec, Canada (pop.: 298,780). Data on hospital admissions and emergency department (ED) visits came from the only hospital who serves this region, outpatient data came from public insurance system. Since identification for rotavirus was not systematic, we used two methods of indirect estimation.

Results: A total of 558 to 903 rotavirus associated hospitalizations were estimated during a 6-year period. Short-term hospitalizations represented 54% of all hospitalizations. Estimation of ED and ambulatory visits due to rotavirus was respectively 622 to 1508 and 1792 to 4136 for the period. The epidemic curve showed a periodicity with higher incidence in March and April. The annual incidence rate of rotavirus AGE hospitalization was estimated between 52 to 84/10,000 children, emergency department visits ranged from 57 to 139/10,000 and ambulatory visits ranged from 166 to 383/10,000.

Conclusion: Most available retrospective studies, probably underestimated rotavirus hospitalizations, because they did not take into account short term hospitalizations. Furthermore, our data on emergency and outpatient visits give an exhaustive appraisal of the burden of rotavirus, a crucial information to the evaluation of immunization programs.

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 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 to 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 study period. 74% were under 5 years which represents an 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 3.5mon- 8years 11months). Average duration of fever prior to therapy was 7.68 days (median 7 days, range 1-28 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.

MENINGOCOCCAL DISEASE IN BRAZIL: CHALLENGES ASSOCIATED THE WITH EMERGENCE OF SEROGROUPS W135 AND Y

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Background: In Brazil, meningococcal disease (MD) causes substantial morbidity and mortality, with periodic occurrence of outbreaks. In the last decade, serogroups B and C have been the most common serogroups, but the recent emergence of W135 is causing concern.

Methods: Descriptive study of serogroup distribution of MD in Brazil and in 4 selected states (RJ, SP, MG and RS), from 2000-2008. MD is of compulsory notification, and data were collected from official sites and publications identified in PUBMED, SCIELO, WHO and PAHO websites, from January/2000 to December/ 2009.

Results: The number of cases of MD reported decreased from 5,019 in 2000, to 2,555, in 2008, but the CFR was persistently high, varying between 10 and 38%, depending on the age and form of presentation. Although representing one fifth of the country population, SP State reported 46% of MD cases in 2008. Serogroup C became prevalent during the study period, but the emergence of serogroups W135 and Y was recently reported, representing 9% to 18% of the cases in SP, RJ, RS and MG states in determined periods.

Conclusions: Interestingly, the emergence of previously rare serogroups, like W135 and Y, as a cause of MD in Brazil was identified in states where surveillance is well established. Our findings highlight the importance of a better laboratory-based surveillance, with phenotypic and molecular studies on *N. meningitidis*, in order to have more reliable information about the serogroup distribution. This information will contribute to propose new strategies of vaccination to prevent this frightful disease.

INVASIVE BACTERIAL DISEASES IN ITALIAN CHILDREN AFTER THE INTRODUCTION OF THE VACCINES AGAINST H.INFLUENZAE, S.PNEUMONIAE AND N. MENINGITIDIS SEROGROUP C

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Background: In Italy, data on invasive bacterial diseases (IBD) derive from statutory notification and national surveillance system. Vaccines against *Haemophilus influenzae* (Hib), *Streptococcus pneumoniae* (PNC) and *N. meningitidis serogroup C* (MenC) are available since 1995, 2001 and 2002 respectively and recommended by the National Vaccination Plan. From 2001 decision and implementation of vaccination strategy are of the 21 regional Authorities.

The aim of this study is to evaluate the impact of vaccinations on the IBD incidence.

Methods: Data on immunization coverage have been provided by ICONA 2008, a national cluster sampling survey conducted on children belonging to 2006 birth cohort.

Results:

Incidence 0-4 yrs: Meningococcus trend almost stable from 1994 (2.1*100.000) to 2007 (2.0*100.000). In 2008 there is a small decrease (1.6 *100.000). For MenC the incidence is almost stable from 1994 (0.2*100.000) to 2008 (0.3*100.000) with a peak of 1.7 in 2004.

PNC: increasing from 1994 (0.7*100.000) to 2008 (3.2*100.000).

Hib: significantly decreasing from 1994 (2.7*100.000) to 2008 (0.2*100.000).

Vaccination coverage: Hib, PNC and MenC: at national level 96%, 55% and 37% respectively; at regional level coverage ranging between 91% to 100%; 20% to 95%; and 8.4% to 84.3% respectively.

Conclusion: A strong impact of the Italian vaccination policy is evident only for Hib whereas for the other two vaccines, MenC and PNC the coverage is not high enough in all the Italian regions to achieve a significant decrease in diseases incidence.

INFLUENZA VIRUS SURVEILLANCE SEASON, STATE OF SÃO PAULO, BRAZIL, 2008-2009

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Background and aims: Due to the potential pandemic influenza virus of the follow-up of its surveillance is the only tool suitable to detect new strains and to adopt strategies to minimize its dissemination. In April 2009, a new viral subtype pandemic influenza A (H1N1) emerged and spread globally. We describe the surveillance of influenza and the profile of viral circulation in the state of São Paulo (SP), seasonality from 2008 to 2009.

Methods: The surveillance of influenza based on sentinel units, distributed in strategic areas. Virus isolation attempts were performed in cell culture of MDCK, Vero and Hep-2. IIF assay using monoclonal antibodies was performed in order to identify the isolates. Antigenic Characterizations of the identified viruses were realized by HI by using immune sera provided by World Health Organization. Molecular assay was also performed during our epidemiological surveillance tasks (RT-PCR).

Results: From the EW 13, 2009, the percentage of care for cases of flu-like illness presented above that of 2008. In 2008, there was a higher proportion of parainfluenza virus (43.9%), followed by RSV (28.5%). At the beginning of 2009 prevailed RSV (45.6%), with subsequent replacement by influenza A virus (28.2%), predominantly A/H1N1. Viral strains identified in 2008 were: A / Brisbane/59/2007-Like H1N1; B/Florida/04/2006; B/Ohio/01/2005; B/Malaysia/2506/2004.

Conclusions: The strategies of preventable influenza virus vaccine by matching the circulating strains and including those in the vaccine composition epidemiological surveillance of influenza virus is a powerful strategy towards monitoring strain oseltamivir resistance.

INCIDENCE OF DENGUE INFECTION IN PEDIATRIC PATIENTS OF A TERTIARY CARE HOSPITAL

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Background and aims: Dengue is one of the most important mosquito-borne viral infections that may lead to an undifferentiated fever, Dengue Fever (DF) or Dengue Hemorrhagic Fever (DHF). Since, patient's age is an important variable for case fatality (mostly in DHF & DSS cases). Therefore this study was conducted in pediatric patients to investigate incidence of dengue infection along with disease severity, circulating serotypes and genotypes of Dengue virus.

Methods: During July 2007-December 2009, 278 serum samples of clinically suspected pediatric Dengue cases from Lok Nayak Hospital, Delhi were screened by MAC-ELISA for the presence of Anti-dengue IgM. mRT-PCR (Harris et.al.) was performed on 100 early (< 5days) samples of the year 2007 and 2008 for detection and serotyping of virus strains. Genotyping (Domingo et al.) followed by direct sequencing was also performed.

Results: Anti-dengue IgM was detected in 19.78% (55/278) cases. As per WHO criteria, 39 were DHF (including three DSS cases) and 16 of DF cases. Among studied samples, DEN2- 4(50%) was the predominant serotype followed by DEN1-3 (37.5%) and a co-infection incidence (DEN3 and DEN2).

Conclusions: DEN2 genotype II was the predominant circulating strain during 2007 while in 2008 DEN 1 genotype III was the predominant followed by DEN2. The plenty of DHF cases 70.90% (39/55) in pediatric group is due to the rigorous immune response, circulating serotype and change in serotype circulation over the year. Co-circulation of more than one serotype (hyper endemic) in this particular region may have influence to disease severity among pediatric population.

A STUDY ON RISK FACTORS OF RECURRENT OTITIS MEDIA IN TWO CENTERS IN SEOUL, KOREA

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Introduction: There is notably insufficient research on recurrent otitis media(ROM) and it is hardly proven so far whether risk factors of otitis media can be directly applied to ROM. Few studies have been done on the risk factors on ROM. The purpose of this study was to evaluate the risk factors in children with ROM.

Method: This study was conducted from July to October 2009 on infant out-patients less than 60 months old at Hanil General Hospital and Kyunghee University Hospital by questionnaires and interviews. Of the total of 373 children, 173 were excluded, and among the remaining 200 children, 40 had ROM, while 160 were classified as control group.

Result: It is found that use of day-care centers($P=0.000$, $OR=7.50$), allergic rhinitis($P=0.023$, $OR=4.13$), history of bronchiolitis($P=0.003$, $OR=4.16$), poor economic conditions($P=0.000$, $OR=5.68$) have close correlations with ROM. Risk factors such as sex, age, breast-feeding, use of pacifiers, atopy, pneumococcal vaccination, influenza vaccination, smoking of parents, family history of otitis media are found not relevant.

Conclusion: The risk factors of otitis media generally known in the previous studies did not have statistical relevance in this study. It is identified that independent risk factors of ROM include use of day-care center, allergic rhinitis, history of bronchiolitis and low socioeconomic conditions.

THE BURDEN OF PERTUSSIS IN THE ASIA-PACIFIC REGION

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Background and aims: Childhood vaccination has reduced pertussis burden but does not offer lifelong protection. Disease resurgence has been observed in several countries.

Methods: A retrospective review of literature published since 1990 focused on disease incidence, hospitalisation, mortality and case confirmation.

Results: 45 reports were analysed, mostly from Australia and New Zealand. Vaccination is scheduled at 2, 4 and 6mo, 4 and 12-17y in Australia, and 6 weeks, 3 and 5mo, 4 and 11y in New Zealand.

Most hospitalisations occurred in infants < 3 months (5% of all notifications; 50% of all hospitalisations) with a higher risk of ICU admission and mortality. Mortality rates ranged from 0-6%. In hospitals, laboratory confirmation of pertussis cases varied from 65-73%.

The highest pertussis incidence occurred in age groups < 1 and > 20y (83% of cases in 2005 were in >20 y). In Australia the incidence in 10-19 y decreased substantially from 2004, and a pertussis outbreak started at the end of 2008 and continued through 2009.

Notification of pertussis by medical practitioners was low: 4-40% in three studies. 70% of GPs knew about all notifiable diseases and reporting by GPs tended to be of laboratory-confirmed cases. This leads to substantial under-reporting of pertussis.

Country	Study	Year	Incidence (/100,000)	Hospitalisation rate (/100,000)	Mortality (%)	
Australia	Chuk et al.*	1997–2006			3/55 (5.5%)	
	Elliott et al.*	2001		56/100,000 live births	4/140 (3.0%)	
	Torvaldsen et al.*	2001	61 (5–10 y)			
			223 (12–14 y)			
			196 (5–10 y) 160 (12–14 y)			
	Torvaldsen et al.*	1997	76 (5–9 y)			
			65 (10–14 y)			
	Surveillance [#]	2009	122.7			3/8058
			68.0			
			25.4			
			53.1			
54.9					1/11,201	
43.5					2/8749	
23.1						
Wood et al. [#]	1993–2004				18 deaths in this period	
Bangladesh	Bonanni et al.*	1986–1987			10/300 (3.3%) (<1 y)	
Nepal	Surveillance [#]	2002	18			
		2001	20			
		2000	25			
		1999	28			
New Zealand	Somerville et al.*	2004–2005		196/100,000 infants <1 y	1 /110 (1%)	
	Somerville et al.*	2000–2004		1.55	5/1140 (0.5%)	
		1995–1999		1.33	1/1810 (0.1%)	
	Surrige et al.*	1991–2003			4/72 (6%)	
	Blakely et al. [#]	1996–1997	19.8	6.7	0	
Surveillance [#]	2009	28.5				

*Hospital-based. [#]Community-based

[Incidence, hospitalisation and mortality]

Conclusions: The reported incidence of pertussis is increasing in the Asia-Pacific region and under-reporting is substantial and heterogeneous.

**ACTIVE HOSPITAL-BASED SURVEILLANCE OF INVASIVE PNEUMOCOCCAL DISEASE (IPD),
CLINICAL AND CHEST X-RAY POSITIVE PNEUMONIA IN INFANTS/YOUNG CHILDREN IN
HUNGARY**

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Background/aims: *Streptococcus pneumoniae* (SP) is the leading cause of vaccine-preventable disease in children < 5 years of age. We prospectively estimated the incidence of IPD, clinical pneumonia, and chest X-ray positive pneumonia (CXR+Pn) in infants and young children in Budapest and Pest County.

Methods: One-year, prospective, hospital-based surveillance study (2/29/2008 - 2/28/2009), in children from 28d to 60m of age. Eligibility criteria: children residing within the surveillance area with temperature $\geq 39.0^{\circ}\text{C}$ in 24 hours prior to screening and/or clinical suspicion of IPD or pneumonia.

Results: 3032 subjects enrolled, mean age: 22.1 months (S.D. 14.3). SP was detected in 21 isolates from 18 subjects (source: 17 blood, 2 CSF, 2 pleural fluid). Final IPD diagnoses: sepsis 7(38.9%); bacteremia 5(27.8%); bacteremic pneumonia and/or empyema 4(22.2%); meningitis 2(11.1%). Incidence rate of IPD overall and in children from 28d to < 24m was 22.1/100,000 and 28.1/100,000 (highest incidence 12m to < 24m: 42.0/100,000). Overall incidence rate of clinical pneumonia and CXR+Pn was 1066.2/100,000 and 169.7/100,000. Incidence rates of clinical and CXR+Pn in children 28d to < 24m were 1,344.6/100,000 and 168.5/100,000.

Serotype analyses n (%): 14: 4(23.5%); **19F:** 3(17.6%); **6B:** 2(11.8%); **10A:** 2(11.8%); 1(5.9%) each **3, 4, 6A, 7F, 18C, 19A;** isolate not tested 1(N/A). Coverage by the pneumococcal conjugate vaccines PCV7, PCV10, and PCV13 was 64.7%, 70.6%, 88.2%, respectively.

Conclusions: IPD and pneumonia cause considerable burden of vaccine-preventable disease in Budapest and Pest County. Pneumococcal conjugate vaccines with demonstrated effectiveness in reducing the incidence of IPD and pneumonia offer substantial public health benefits.

EPIDEMIOLOGY OF MENINGOCOCCAL INFECTION AND MENINGOCOCCAL MENINGITIS IN SPANISH PAEDIATRIC POPULATION: HOSPITAL ADMISSIONS OVER AN ELEVEN YEAR PERIOD (1997-2007)

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Background and aims: Estimate the burden of hospitalizations due to meningococcal infection (MI) and meningococcal meningitis (MM) in Spanish paediatric population during an eleven-year period (January 1st, 1997 through December 31st, 2007).

Methods: All hospital discharges in Spanish hospitals for meningococcal infections and meningococcal meningitis (9th International Classification of Diseases codes 036 and 036.0, in any listed diagnosis) for children up to 14 years old during an eleven-year period were obtained from the national surveillance system for hospital data maintained by the Ministry of Health and covering more than 98% of Spanish hospitals. The annual incidence of hospital admissions, mortality and fatality rate were calculated by using municipal population data.

Results: A total of 8204 and 3415 hospitalizations for meningococcal infections and meningococcal meningitis in children up to 14 years old were reported with an annual hospitalization rate of 12.4 and 5.2 cases per 100,000 children, respectively, and decreased significantly in children up to 4 years old during the study period. Mortality and case-fatality rate were 0.52 and 0.09 per 100,000 children and 4.2 and 1.8%, for meningococcal infections and meningococcal meningitis respectively.

Hospitalization, mortality and case fatality rates decreased significantly with age reaching their maximum values in < 1 year old children with (48.7 per 100,000 population, 2.7 per 100,000 and 5.5% for MI and 25.4 per 100,000 population, 0.5 per 100,000 and 1.9% for MM, respectively).

Conclusions: Burden of meningococcal infections still poses an important morbidity in paediatric population in Spain especially in the youngest age group.

A RETROSPECTIVE STUDY OF FOODBORNE DISEASES IN MONGOLIA

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Background: Salmonella infections and dysentery cause gastrointestinal and systemic diseases worldwide and are the leading causes of food-borne illnesses in Mongolia. Among intestinal infections shigellosis 14.7%, salmonella 1.6%, and diarrhea 1.3 %. Therefore the current situation and the trends in the incidence of the common intestinal infections and the risk factors for transmission needs to be studied in Mongolia.

Objective: To describe demographic, temporal and geographical distributions, and reported risk factors of the some common intestinal infections reported to a surveillance system in Mongolia.

Methodology: Descriptive analyses were performed on data on salmonellosis cases reported in Mongolia between 1996 and 2008. Long term dynamics of salmonellosis which were registered between 1996 and 2008 were analyzed by regression analysis. Mean of monthly dynamics was analyzed by NCSS program and seasonal variations were determined and future trends for 2009-2017 was projected through Arima model.

Results: The mean annual rates of infections with all *Salmonella* serotypes and with *Salmonella* serotype typhimurium were 0.8 cases and dysentery was 8.3 cases per 10,000 persons. There have observed differences in the incidences of dysentery and salmonellosis according to the regions. Central and Khangai regions had the highest incidences during the warm seasons in Mongolia. The incidence of dysentery has a tendency to be stable or similar to the current trends whereas the incidence of salmonella has a tendency to decrease in the future.

Conclusions: Information on demographic, temporal and geographical distributions and risk factors is critical in planning disease control strategies.

NEISSERIA MENINGITIDIS: A BASELINE DYNAMIC TRANSMISSION MODEL FOR THE CZECH REPUBLIC

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Background and aims: With new multivalent meningococcal conjugate vaccines imminent, a better understanding of *Neisseria meningitidis* transmission is important. Dynamic transmission models are powerful mathematical tools for simulating disease transmission in a population and assessing the subsequent potential impact of vaccination.

Methods: We developed an age-structured realistic dynamic transmission model for *N. meningitidis* for use in Europe. The Czech Republic was chosen as currently it does not routinely vaccinate against meningococcal disease and has representative age- and serogroup-stratified data at the population level for both carriage and invasive meningococcal disease (IMD). Carriage prevalence from a nationwide study in 1996 was used in conjunction with national surveillance data from 1999-2008 for confirmed IMD, for model calibration and validation. The model accounts for serogroups B and C *N. meningitidis* separately, pooling all other serogroups. We use realistic demography and an empirical social contact matrix (POLYMOD) to model the mixing between different age groups.

Results: Our model reproduces well the age- and serogroup-specific carriage prevalence, and also the incidence of IMD. Serogroup-specific estimated correlation between the calibrated model and data is significant (maximum p-value 0.0015). Moreover, the model captures well the invasive disease data for 2007 and 2008, not used for calibration - an additional validation of its predictive value.

Conclusions: We developed a realistic dynamic baseline transmission model for *N. meningitidis*, calibrated and validated against epidemiological country-level data. This model can be used to assess vaccination schedules, thereby serving as a useful tool in decisions to implement vaccination programmes against *N. meningitidis*.

INFECTIOUS DISEASE HOSPITALIZATION DISPARITIES IN THE AMERICAN INDIAN AND ALASKA NATIVE INFANT POPULATION, UNITED STATES, 2005-2007

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Background: American Indian and Alaska Natives (AI/ANs) have experienced a disparate infectious disease (ID) burden. This study updates the burden of ID hospitalizations among AI/AN infants.

Methods: Primary ID hospital discharge data for AI/AN infants during 2001-2007 in the United States were selected from the Indian Health Service direct and contract healthcare service inpatient data by using ICD-9-CM codes for IDs. The hospitalizations for the general US infant population were selected from the Nationwide Inpatient Sample (2001-2007) and the Kids' Inpatient Database (2006). Hospitalization rates for ID and ID groups were examined for both populations.

Results: First-listed ID accounted for half of all AI/AN infant IHS/tribal hospitalizations. The ID hospitalization rate for AI/AN infants in 2005-2007 (8,624 per 100,000 infants) was lower than that for 2001-2003 (11,652). However, the rate remained higher than that for the general US infant population in 2005-2007 (6,247; 95% CI=5721-6774 per 100,000 infants). The highest rates were for AI/AN infants living in the Alaska (15,413) and the Southwest (10,457) regions. Lower respiratory tract infections accounted for three-quarters of the ID hospitalizations for AI/AN infants compared to 57% (SE=0.4%) of those for the 2006 general US infant population.

Conclusions: Although the ID hospitalization rate for AI/AN infants decreased over time, it remains higher than that for the general US infant population. Prevention measures to reduce ID infant morbidity, particularly for lower respiratory tract infections and in high-risk regions, would have a significant impact in closing this disparity gap.

KAWASAKI SYNDROME AND COMPLICATIONS AMONG CHILDREN IN DENMARK

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Background and aims: Kawasaki syndrome (KS), an acute febrile illness of unknown etiology, causes significant morbidity with cardiac (including coronary artery abnormalities [CAA]) and noncardiac complications among children worldwide. We conducted a national study of clinical characteristics and treatment of KS patients in Denmark.

Methods: A retrospective hospital chart review of children < 15 years of age with KS as identified from the Danish National Hospital Register for 1994-2007.

Results: Among 307 patients whose medical records had sufficient information, 264 met the KS (n=259) or atypical KS (n=5) definition. Among these 264 children, 189 (71.6%) were < 5 years of age. Almost two-thirds of the KS patients were male. Only 2 (0.8%) of the 264 patients were readmitted with recurrence of KS. Among the KS patients, 92.7% of the patients (243/262) were treated with intravenous immunoglobulin (IVIG) and 81.7% of these patients (197/241) received IVIG within 10 days of illness onset; of these patients, 4.1% (8/195) received a second treatment. A total of 35 (13.5%) of patients were diagnosed with CAA. The development of CAA was significantly associated with patients who were infants, boys, and children who had not received IVIG treatment < 10 days of symptom onset ($p < 0.01$).

Conclusions: The risk factors for CAA need to be taken into account during hospitalization for KS and further investigated. The findings should be useful in improving the treatment of patients with KS, thereby reducing the number of children suffering from acquired heart disease, a severe complication of KS.

MENINGOCOCCAL DISEASE AND MENINGITIS IN THE 19TH CENTURY: GAPS IN CLINICAL LITERATURE

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Background: Meningococcal disease is a long-standing public health issue. Early attempts at control and prevention may shed light on current understanding..

Methods: Search in Biosys, Medline, Embase and Web of Science using the terms: meningitis nineteenth century. Review authoritative and historical texts as well as Google were conducted.

Results: Five publications in English were indexed, as were 1 in Polish and 1 in Icelandic (abstract in English); 1 discussed meningococcal disease. Yet, an unindexed recent text referenced 37 sources published between 1684 and 1991 and a Google search of “meningococcal disease nineteenth century prevention and control” yielded 86 hits. Authoritative 19th century texts by Hirsch, Condie and Netter reveal that treatment of meningitis of any etiology was viewed as generally futile. Symptomatic treatments including bloodletting, cupping, opium, potassium bromide were described as outmoded, and newer recommendations to reduce fever, such as icing, were described. Much of the texts were devoted to descriptions of the disease and its effects: Netter devotes 6 paragraphs to prevention and treatment in a 150-page text. Attempts at prevention were limited to the observation that meningococcal disease was “transportable” (Hirsch), leading to difficulties in identifying index cases and isolating contagion.

Conclusions: Scientific databases index scant information on meningitis during the nineteenth century regardless of etiology, while authoritative texts and Google reveal that historical texts describing meningococcal disease exists. Prevention of meningococcal disease is a recent development. More peer-reviewed research is needed.

MENINGOCOCCAL VACCINATION: EARLY HISTORY AND HISTORICAL SOURCESL. DeTora¹, M. Kyaw², L. Jacintho da Silva²¹*Scientific Affairs, ²Epidemiology, Novartis Vaccines and Diagnostics, Cambridge, MA, USA*

Background: Historical patterns of vaccination in response to meningococcal disease may inform current efforts to develop broad-coverage vaccines. Although the Goldschneider et al studies in the 1960's led to the first vaccines to be widely used and effective in disease control, vaccination against invasive meningococcal disease began during the early 20th century.

Methods: Literature search performed in Medline (terms: "meningococcal," "vaccines," "meningococcal vaccines," and "history" in all fields or as MeSH terms). Recent authoritative texts and additional historical sources were reviewed against these results.

Results: Nine peer-reviewed sources indexed in Medline discuss the early history of vaccination against meningococcal disease. Recent epidemiology papers were limited in geographic scope and most numerical epidemiology data in authoritative texts was collected before 1998. The history of meningococcal vaccination and serologic evaluations thereof predates Goldschneider. Sophian and Black registered the first inactivated whole-cell vaccine following an epidemic in Texas. Although field studies were completed in Kansas City and Dallas, little data remain. Serology measures of agglutination and complement fixation were used to evaluate efficacy. The American Medical Association indicated that meningococcal vaccines would not be of value in the prevention of disease. Concerns about heightened susceptibility to disease following vaccination were common. Yet, 4 meningococcal vaccines were commercially available in the United States in 1922.

Conclusions: Early doubts about meningococcal vaccine usefulness do not reflect ongoing experience. Further literature review and an update of epidemiology data are needed.

POLIO ERADICATION IN NIGERIA - IMPLICATIONS OF A SEROTYPE 2 CIRCULATING VACCINE-DERIVED POLIOVIRUS FOR GLOBAL ERADICATION PLANNING

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Background: The largest recorded outbreak of a 'circulating' vaccine-derived poliovirus (cVDPV), detected in Nigeria, provides a unique opportunity to analyze the pathogenicity, clinical severity and efficacy of control measures for cVDPVs relative to wild poliovirus (WPV).

Methods: Cases of paralysis due to serotype 2 cVDPV (cVDPV2), serotype 1 WPV (WPV1) and serotype 3 WPV (WPV3) in Nigeria were identified from 1 January 2005 to 30 June 2009. The clinical characteristics of these cases, the clinical attack rates for each virus, the effectiveness of oral polio vaccines (OPV) against paralysis by the cVDPV and WPVs were compared.

Results: No significant differences were found between the clinical severity of the 278, 2323 and 1059 AFP cases with cVDPV2, WPV1 and WPV3 respectively in their stool. The estimated average annual clinical attack rates of WPV1, cVDPV2 and WPV3 were 6.8 (95% credible interval: 5.9-7.6), 2.7 (1.9-3.6) and 4.0 (3.4-4.7) per 100,000 susceptible children respectively. The estimated efficacy of trivalent OPV against paralysis by cVDPV2 was 38% (15-54%) per dose, substantially higher than that against paralysis by WPV1 or WPV3. More frequent use of serotype 1 and 3 monovalent OPVs has resulted in improvements in vaccine-induced population immunity against these serotypes and declines in immunity to cVDPV2.

Conclusions: The attack rate and severity of disease associated with cVDPV can be similar to those of WPV. Strategies for interrupting their circulation should be similar. International planning for the management of post-WPV risks must encompass scenarios under which virulent and pathogenic cVDPVs could emerge.

NEONATAL MORTALITY STRUCTURE IN III LEVEL HEALTH CARE CENTRE

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Neonatal mortality rate still remains as one of the main component in mortality rate of children under 5. Analysis of neonatal mortality rate may provide the possibilities to understand gaps in perinatal services and shows which service must be strengthened.

The aim of the study was to assess neonatal mortality and morbidity structure according birth weight. For this reason we analyzed retrospectively 1053 medical records of newborns admitted to Iashvili Central Children Hospital in current year. The results of the study show, that From 1053 newborns 74% were term and 26% preterm, among preterms 61,9 % were low birth weight, 27,1% very low birth weight and 11% extremely low birth weight. From the term newborns 12 % were SGA. The total mortality rate was 13,2%. Mortality rate in term newborns was 5,6 % while among preterms 35,2 %. The mortality rate was inversely proportional to birth weight. Preterm babies accounted for 26 of admitted newborns, but contributed for 68.5% of neonatal deaths [$p < 0.001$]. The causes of neonatal deaths found were birth asphyxia and HIE (20%), infections (37.1%), RDS (31.4%), congenital malformation (8,6 %), hemolytic anemia (2.9 %). In ELBW infants the main cause of death was RDS while in term infants - infection.

Conclusion: There is need to identify strategies to reduce the incidence of prematurity and low birth weight babies. Comprehensive antenatal coverage and adequate care followed by optimal management of newborns at birth is likely to reduce neonatal mortality rate and improve quality of life among survivors.

EPIDEMIOLOGICAL SHIFT IN HEPATITIS A IN TURKEY**Z. Kurugöl, A. Aslan, G. Koturoglu***Pediatrics, Ege University, Izmir, Turkey*

The epidemiology of hepatitis A virus has shown a shifting pattern with a corresponding increase in the age of exposure from childhood to early adulthood. The study was designed to determine age-specific hepatitis A seroprevalence in the 1- to 65-year-old unvaccinated population in İzmir, Turkey and to assess whether there is the epidemiological shift in hepatitis A. A total of 600 subjects were selected for the study. For each participant, a questionnaire was completed to provide information on socio-demographic characteristics and previous hepatitis A history. Anti HAV-IgG were measured by ELISA method. The results were compared with the data of the study acquired in Izmir at 1998. While the overall prevalence of anti-HAV was 71% in 1998, anti-HAV seroprevalence was 54% in 2008. In 1998, seroprevalence was 21% in 3-4 year olds, subsequently increased to 38% in 5-6 year olds, 66% in 10-14 year olds, 79% in 15-19 year olds and 94% in 20-29 year olds. Exposure to HAV occurs generally in childhood after beginning elementary school. In 2008, anti-HAV seroprevalence were relatively low for age groups 5-6, 7-9 and 10-14 (10, 22 and 23%, respectively). For age groups ≥ 15 years, HAV seroprevalence increased with age, rising to 38% in 15 -19 year olds and to 84% in the 20 to 29 years of age group. Exposure to HAV occurs generally in young adults or those older. In conclusion, there is a shift in the age of exposure with HAV towards older age groups in Izmir, Turkey.

BURDEN OF INVASIVE GROUP B STREPTOCOCCAL DISEASE (GBS) IN EUROPEAN NEONATES

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Background: Invasive GBS is the most damaging neonatal infection worldwide. No vaccine is available to protect this vulnerable population. Epidemiologic data are necessary to guide preventative efforts such as vaccine development and universal or risk-based GBS screening.

Methods: Data on neonatal morbidity, mortality and serotypes associated with GBS derived from a PubMed literature search were analyzed. The terms used for search included “group B streptococcal disease/infection/sepsis”, “group B streptococcus/streptococci”, “newborns/neonates/infants” and “Europe”.

Results: Twenty-three studies from 20 European countries reported relevant data on neonatal GBS disease. Geographical variations in incidence and case-fatality rates were observed multiple studies and countries. The incidence of invasive GBS per 1000 live births was < 1 in 13 studies (9 countries), 1-2 in 6 studies (6 countries) and >2 in 1 study (1 country). The incidence of early-onset GBS was at least 40% higher than late-onset disease. Case fatality rates were 3%-10% from 2000-2008 but higher rates of 13%-23% were observed in Sweden and Denmark before 2000. Data on serotype distribution was available in nine countries. Of the known serotypes I to V, >80% of cases were caused by serotypes Ia, Ib, III and V except 71% in Italy.

Conclusions: Neonatal GBS causes a significant health burden in Europe despite current preventative measures. Given patterns of infection, the vaccination of child bearing women against serotypes Ia, Ib, III and V could theoretically reduce the vast majority of invasive disease in neonates.

PERTUSSIS AMONG ADOLESCENTS AND ADULTS FOLLOWED IN GENERAL PRACTICE IN A REGIONAL FRENCH SAMPLE, IN 2008

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Background and aims: Fifty years after the introduction of pertussis vaccination, adult to infant transmission of pertussis is observed, but the incidence of pertussis among adolescent and adult populations consulting general practitioners (GP) in France is not known.

Methods: This prospective study assessed the frequency of pertussis in patients aged more than 13 years who consulted GP for a persistent cough. GP were located in Ile-de-France (Paris and the surrounding area). "Confirmed cases" were either PCR positive or serologically confirmed, "clinical cases" were clinically diagnosed without laboratory confirmation, and "epidemiological cases" were patients coughing without laboratory confirmation but with a close contact with a confirmed case.

Results: The incidence of pertussis is described below

Coughing patients	N= 230	Cases per year/ 100 000 habitants [IC 95%]
Without biological sample	26 (11%)	
With negative laboratory confirmation	158 (69%)	
Pertussis confirmation	46 (20%)	145 [121 ; 168]
<i>Confirmed</i>	21	66 [46; 76]
<i>Clinical</i>	24	75 [62 ; 98]
<i>Epidemiological</i>	1	3 [0 ; 7]

[Table

1]

Patients were 44 years old, 66% were women, and the median duration of the cough at enrollement was 24 days.

Conclusions: In France, where pertussis vaccination coverage is high, pertussis is still a cause of persistent cough in adults who can transmit the disease to newborns. French vaccine strategy recommending adult vaccination, in order to prevent transmission to newborns, is in accordance with these data.

FRENCH EPIDEMIOLOGIC SURVEY OF ACUTE OTITIS MEDIA (AOM) IN AMBULATORY PRACTICE

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Background: In US, pneumococcal conjugate vaccine (PCV7) reduced the burden of AOM and changed the profile of the disease. Prior to PCV7 implementation in France, AOM represented 8% of pediatrician visits and failure rate was 12%. The aim of this study is to describe features and failures of AOM after PCV7 implementation.

Methods: From 2007 to 2008, 30 pediatricians enrolled patients 3 to 36 months old with AOM. Standardized history and physical examination findings were recorded. Factors related to AOM failures were identified by multivariate logistic regression.

Results: AOM accounted for 5.8% of the 43 433 visits, or 6.2 cases/week/pediatrician. Among 3141 evaluable AOM cases (mean age 16.7 ± 8 mo, peak incidence at 10 mo), 99% had been vaccinated with PCV7 and 42.1% attended day care (DCC). Recurrent AOM comprised 24.5% of cases and 51% of children had received ATB in the last 3 months. At the time of diagnosis, 47.1% had fever $\geq 38.5^{\circ}\text{C}$, 74.5% otalgia and 4.7% otorrhea. Febrile and painful AOM accounted for 29.5% of cases and conjunctivitis-otitis syndrome for 18.2%. ATB was prescribed in 98.7% of cases (cefepodoxime proxetil, 59% and amoxicillin/clavulanate, 37%). The failure rate was 6.4%; among them, children had received cefepodoxime proxetil in 64.7% of cases and amoxicillin/clavulanate in 26.2%. Failure risk was greater in children in DCC (OR=1.50, [1.10;2.05]), < 18 months (OR=1.47, [1.06;2.04]) and with history of recurrent AOM (OR=1.45, [1.02;2.06]).

Conclusion: Despite PCV7 implementation, AOM remains a very frequent and problematic childhood infection and a major reason for ATB prescription.

A EPIDEMIOLOGY OF BLOODY DIARRHOEA AMONG CHILDREN LESS THAN TEN YEARS OF AGE IN BAGHDAD

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Bloody diarrhea in young children is usually a sign of invasive enteric infection that carries a substantial risk of serious morbidity and death. Among important risk factors associated with bloody diarrhoea is poor environmental sanitation. In Iraq diarrhoea is the second common cause of mortalities among children. Sanitary condition in Iraq had been deteriorating during the last decade, particularly following the last war.

Aims: To evaluate the prevalence of bloody diarrhoea among children with diarrhea < than 10 years old, to identify the most commonly causative agents & factors that may be associated.

Material & method: Mother interviewing of 1500 children was done. All clinical examination. Then after general examination and cultured of stool was performed for each child - Result of prevalence of bloody diarrhoea was (28%) patients < 10 years with diarrhea.

Entamoeba Histolytica was the main causative agents (83.58%), with significant higher (97.5%) among age group (1-3 years). Non-typhoid salmonella (4.28%), Shigella (2.14%), those were mainly among age group (4-6 years).

The male to female ratio was 1.42:1, with no significant association. Children significantly higher rate (66.6%) of cases among age group (7-9 years).

Significantly higher prevalence of bloody diarrhoea (41.9%) among those live in rural areas. Significant higher rate (34.1%) among those don't have refrigerators for food storage. and (86.4%) of those above 5 years who use to eat outside home. Regarding their mothers, significant higher prevalence (31.5%) among children belong to illiterate mothers, and (36.5%) among children on exclusive bottle feeding. Bloody diarrhoea was seen in a higher rate among children who use teats & have thumb sucking habit (33.9%), (29.4%) respectively. Significant association of bloody diarrhea and fever, dehydration, convulsion but not with vomiting.

Conclusion: Association of environmental sanitation and bloody diarrhea be considered as a serious public health problem in Iraq.

EPIDEMIOLOGICAL ASPECTS OF MENINGOCOCCAL DISEASES (MD) IN PARANA, BRAZIL, 1998 - 2008

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Background and aims: Despite improved access to health services and the performance of surveillance with the early identification of cases and the early initiation of chemoprophylaxis for contacts, meningococcal disease is still an important cause of morbidity and mortality, particularly in infants and young children. This study presents an analysis of the epidemiological profile of MD, Parana, Brazil, to implement control measures.

Methods: Using descriptive study method, we analyzed data from MD of State of Parana, from 1998 to 2008. The criteria for confirmation of cases are standardized by the Ministry of Health of Brazil (clinical, laboratory, epidemiological). The etiological diagnosis was realized by the LACEN-PR (Central Laboratory of the Parana) the Institute Adolfo Lutz, São Paulo.

Results: 2643 cases of MD were confirmed during the study period, and 2258 (85.4%) aged under 20 years. The group at highest risk is under 1 year (incidence ranged from 20.6 to 49.7 per 100,000 inhabitants). The lethality was above 20% for the population aged 0 to 4 years and less than 15% for the other groups.

Currently the prevalence of serogroup B (50%) is nearly equivalent to the group C. The strains were further identified: B: 4: P1.15 and C: 2b: P1.3. In recent three years were registered 16 cases of meningococcal W135 and a smaller number of cases of Y.

Conclusion: Over 50% of MD is preventable by vaccines. Considering the importance of this disease, health authorities should consider the inclusion of the vaccine in routine immunization.

PERTUSSIS EPIDEMIOLOGY IN PARANA, BRASIL: ARE NEW STRATEGIES FOR CONTROL NECESSARY?

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Background and aims: Despite high immunisation coverage and the inclusion of the second booster dose of the DTPw vaccine, the number of cases of Pertussis has increased. International publications have shown an increase in the number of cases in adults resulting in greater difficulty of diagnosis. In addition, booster dose of adult type acellular pertussis vaccine has been considered. The aim of this study was evaluate the profile of Pertussis in Parana State with a view to their control.

Methods: Retrospective study of all cases confirmed Pertussis infections reported among 1997-2008 in the Department of Health of Parana (SESA-PR).

Results: The number of cases reported was 1206 and 487 (40.38%) were confirmed. The criterion for confirmation most frequently used was the clinical and epidemiological. The number of cases increased from 14 in 2000 to 71 in 2008, occurring more frequently in the warmer months. The great majorities (79.8%) of cases were from children under 1 year and 95% of the hospitalized cases were in this age too. Approximately 50% of total of reported cases were hospitalized. The vaccination coverage rates have been above 80%.

Conclusions: Although Pertussis in Parana is reportable since 1997, fail on its diagnosis contributes for underreporting. There are some evidences for this: a large number of cases are hospitalized; there is difficulty to diagnostic laboratory. To improve the epidemiological surveillance is important to devise new strategies for Pertussis control.

REVIEWING HEPATITIS B EPIDEMIOLOGY IN ETHNIC MINORITY CHILDREN IN ENGLAND

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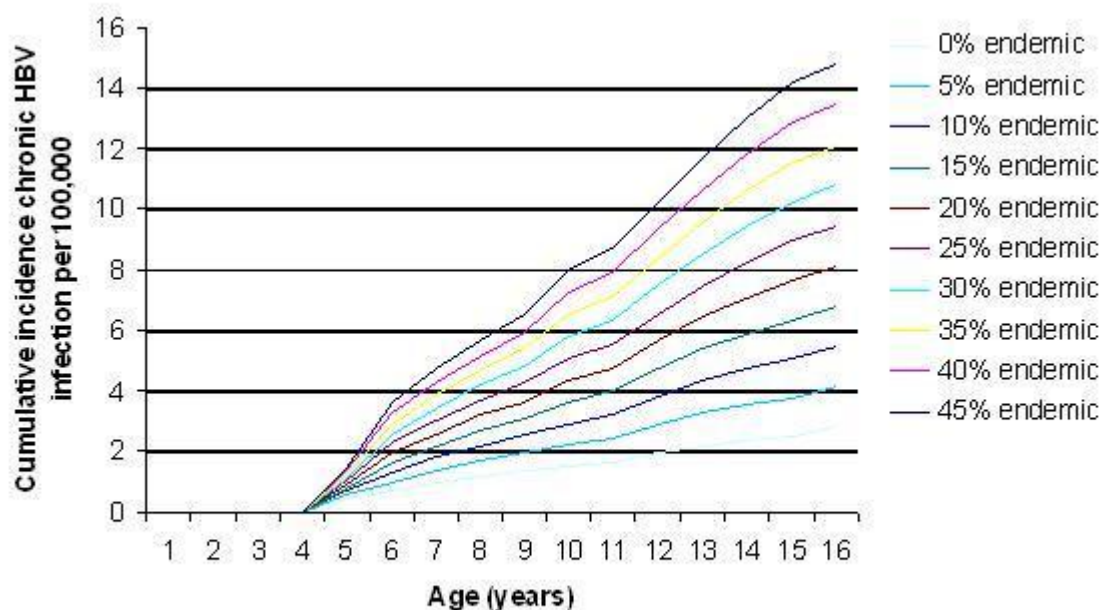
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Background: Universal immunisation against hepatitis B infection (HBV) has not proven cost-effective in England. We review the epidemiology of HBV in ethnic minority children to inform the cost-effectiveness of a geographically selective policy.

Objectives: To estimate HBV incidence in each English Primary Care Trust (PCT) based on the proportion of children born to mothers from endemic countries.

Methods: Cumulative incidence of chronic HBV was estimated from confirmed cases of acute HBV and the proportion of children born to women from endemic areas for each PCT in 2006.

Results: 14.3% women giving birth in England (2006) were born in endemic countries but this varied across PCTs from 1.5% to 58.1%. 15 PCTs (9.9%) reported more than 40% antenatal population born in endemic regions. The cumulative postnatal incidence of chronic HBV for these PCTs is considerably higher than the overall incidence (13.7 per 100 000 compared with 7.0 per 100 000 at 15 years).



[Cumulative incidence of chronic HBV infection]

Conclusion: HBV incidence varies across England, being higher in areas with a high proportion of the population born in high-endemicity countries. The estimated cumulative postnatal incidence of chronic HBV is particularly high for 15 PCTs. These areas would more likely benefit from a universal programme.

HEALTH CARE USE AND SOCIETAL BURDEN DUE TO CHILDHOOD OTITIS MEDIA IN SPAIN**R. Morano, I. Pérez Escolano***HealthEconomics, GlaxoSmithKline, Madrid, Spain*

Background and Aims: The objective of this study is to estimate health care resources consumption and societal impact of otitis media (OM) in children < 5 years old in Spain.

Methods: An internet survey was conducted using a specific questionnaire on the use of direct medical and indirect resources of childhood diseases. Questionnaire was distributed to a representative parent's panel of children < 5 years old in Spain.

Results: Data were captured for 2.216 disease episodes among children < 5 years old in Spain. Among those children, 183 had a confirmed diagnosis of OM and 119 had symptoms consistent with OM. The prevalence was estimated to be 20% on children experiencing at least one episode of OM annually. The incidence was estimated to be 459 new episodes per 1.000 children below 5 years of age.

Parents of sick children sought medical care in 98% of cases and 27% turned to Emergency Room. Antibiotics were prescribed in 82% of the cases, and drugs without prescription were bought by parents in 64% of the episodes.

Approximately 30% of parents had to take days off from their job while they were seeking for medical assistance for their sick child.

The total cost (direct and indirect) of an episode of confirmed OM in Spain was estimated to be 362 €.

Conclusions: The medical and economic burden of OM could be considerable in Spain. Any intervention that would mitigate burden of OM may have a major impact on families' quality of life and societal costs.

FEVER IN CHILDREN AFTER INTERNATIONAL TRAVEL: EPIDEMIOLOGICAL, CLINICAL AND DIAGNOSTIC FEATURES IN A PEDIATRIC TERTIARY CARE CENTER IN FRANCE

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Background: Available data concerning children with fever after international travel, particularly in tropical or subtropical areas, are limited.

Methods: Children attending the emergency department of the Robert Debré Hospital, Paris, France, between July and December 2007, for fever occurring within three months of returning from travel abroad, were included in a retrospective study.

Results: 538 patients were included and returned mainly from North Africa (NA) (n = 214), Sub-Saharan Africa (SSA) (n = 185) and Europe (EU) (n=67). The median age was 2.8 years (IQR: 1.4; 5.8). The proportion of children younger than 2 years old was respectively 40.7%, 28.7% and 47.8% (p< 0.01). The median time between returning and onset of fever was 5 days (IQR: 0; 18). Cosmopolite infections accounted for 86.4% of final diagnoses (98.9% and 66% in NA and SSA groups, respectively). The overall proportion of fever with unknown origin was 19.3%. Malaria was the most frequent tropical disease observed. Excluding malaria, the proportion of digestive infections was higher in children returning from NA (38.5%) than in children returning from SSA (24.5%) (p< 0.0001). The predictive value of clinical findings on admission was poor. Malaria was associated with thrombocytopenia and a stay in an endemic country (> 30 days OR: 3.13, 1.02-9.59).

Conclusion: Cosmopolite infections were the leading cause of fever in French children returning from international travel. However, the frequency of tropical diseases are likely to be underestimated. Prevention strategies should also be particularly targeted to parents of infants and children traveling to NA.

FACTORS IMPACTING SETTING OF CRITERIA FOR A TENDER TO PURCHASE A PNEUMOCOCCAL (PNC) CONJUGATE VACCINE TO NATIONAL VACCINATION PROGRAMME

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Background: Based on favourable cost effectiveness analysis in 2008 with conservative estimate of positive indirect impact, Finland decided to include PCV into its NVP starting from 2010. To aid National Advisory Board of Vaccines (KRAR) in setting criteria for choice of PCV, i.e. price alone or price and quality, the epidemiology of pneumococcal and *Haemophilus* (Hi) diseases were updated.

Methods: Data from national infectious disease registry for IPD and Hi in all ages, antimicrobial resistance (AMR) of Pnc isolates, and published literature on these diseases and immunogenicity of PCV10 and PCV13 and expected VE were reviewed.

Results: In 2008, of total 97 IPD among children < 5years, serotypes covered by PCV13 were observed in 16% more cases than those by PCV10. Of total 834 IPD among ≥5s, difference was 15%. No major changes had occurred in rank order of serotypes. AMR of Pnc had steadily increased. Registry and published Finnish epidemiology and trial data were used to extrapolate Pnc serotypes and Hi causing pneumonia or AOM. Invasive Hi were reported in 45, of which only 5 among < 5s. We compared assumed effectiveness of PCV10 and PCV13 in present Finnish epidemiologic situation. It was not possible to perform formal CEA. Finally, KRAR decided that PCV purchase criteria be mostly based on price, less on quality.

Conclusion: The decision making process, and outcome of tender (finalized 2/2010) will be discussed as a case study on how epidemiological data and cost effectiveness analyses can be utilized and interpreted on country level.

EPIDEMIOLOGY AND CARDIAC COMPLICATIONS OF KAWASAKI DISEASE IN ICELAND**G. Óskarsson**^{1,2}, H. Sif Ólafsdóttir², Á. Haraldsson^{1,2}¹*Children's Hospital Iceland, Landspítali - University Hospital,* ²*Faculty of Medicine, University of Iceland, Reykjavík, Iceland*

Aim: To perform an epidemiological survey of Kawasaki disease (KD) in Iceland during the period of 1996-2005 with mid-term follow up of prognosis and complications.

Methods: The study was a retrospective analysis where all cases of KD during the period between 1996-2005 were identified. Chart records were reviewed, and all children offered follow up with clinical evaluation and echocardiography.

Results: 30 children were diagnosed with KD, and the annual incidence was 10.7/100.000 children below 5 years of age. The boy:girl ratio was 2.3:1. All 30 children were treated with intravenous gammaglobulin, without any major adverse events related to the treatment. The median (range) time from the start of illness to treatment was 6 days (3-31 days). Two children (6.7%) developed coronary aneurysms and 3 (10%) coronary ectasia. There was no mortality. Follow up echocardiography was performed in 23 of 30 children 4 to 13 years after KD. Two of the children still had coronary ectasia, and 6 (26%) had mitral regurgitation.

Conclusions: The incidence of KD in Iceland in 1996-2005 was comparable to an earlier Icelandic study and reported incidence in the Nordic countries. All children received treatment with intravenous immunoglobulin. Coronary involvement during the acute phase was mild, and all coronary aneurysm regressed. Even if serious cardiac complications were not seen, less severe cardiac sequel such as mild mitral regurgitation and coronary ectasia seem common at mid-term follow up.

TRENDS IN PAEDIATRIC INFECTIOUS DISEASES HOSPITALISATIONS OVER THE LAST FOUR DECADES IN A TERTIARY UNIT

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Infectious diseases are still a major cause of paediatric hospital admissions in developed countries, though changes in the spectrum of diseases have been observed over the last decades.

Aims: This study describes the epidemiological features of the hospitalisations in a Portuguese tertiary paediatric infectious diseases unit over the last decade. We compare the results with published data from the previous three decades in the same unit.

Methods: A retrospective study was carried out using discharge records concerning children admitted to our unit during the period from 1999 to 2008. Demographic data and primary discharge diagnosis were analysed and compared with data from 1969 to 1998.

Results: We had 4793 hospitalisations during the studied period, representing 15% of all admissions to the paediatric department. The median age was 2.4 years and 55% were male. The median length of stay was 5 days. The most frequent cause of admission was respiratory tract infections, followed by ENT, central nervous system, gastrointestinal and skin/soft tissue infections. When compared to the previous decades, there was a significant reduction in the number of measles, bacterial and aseptic meningitis, pertussis and septicaemia cases.

Eight patients (0.2%) died during this period and half of them were HIV-positive. The mortality rate suffered a substantial drop compared to the previous decades (6.9% in 1969-1978).

Conclusions: We observed important changes in the infectious diseases entities conditioning hospital admission in our unit. These findings are probably related to changes in the Portuguese immunisation programme, including the introduction of new vaccines.

HOSPITAL-BASED SURVEILLANCE TO CHARACTERIZE MENINGOCOCCAL STRAINS IN SAO PAULO, BRAZIL

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Background and aims: A significant increase in the proportion of serogroup C cases was reported in the last years in Sao Paulo city, where meningococcal disease (MD) was previously associated to serogroup B. To better understand the recent changes in the epidemiology of MD in our region, we determined the distribution of serosubtypes of *N. meningitidis* isolates.

Methods: We performed serogrouping and serotyping of all strains of *N meningitidis*, isolated from blood or CSF, of patients admitted with MD in two large hospitals in Sao Paulo, between 2005 and 2009.

Results: A total of 49 *N. meningitidis* strains were characterized. Serogroup C was prevalent, identified in 36 isolates (72.9%); serogroup B, 6 isolates (12.5%); serogroup W135, 6 isolates (12.5%) and serogroup Y, 1 isolate (2.1%).

All serogroup C isolates belonged to a single phenotype (C:23P1.14-6); serogroup W135 isolates belonged to two phenotypes (W135:2bP1.5,2 and 2aP1.2) and for serogroup B isolates a high diversity of phenotypes was found.

Conclusions: Predominance of serogroup C in the last years is probably related to antigenic replacement of strains from different phenotypes to a single phenotype, C:23P1.14-6, usually associated to ST-103 complex. Emergence of W135 is probably also related to antigenic replacement of circulating strains to phenotypes 2bP1.5,2 and 2aP1.2, usually associated to ST-11 complex. Monitoring the spread and the virulence of emerging phenotypes of *N. meningitidis* is critical to understand the epidemiology of MD and to anticipate the appropriateness of incorporating different meningococcal conjugate vaccines and the candidate genome-based meningococcal B vaccine.

MENINGOCOCCAL DISEASE IN BRAZIL: IS IT TIME FOR UNIVERSAL VACCINATION?**M. Safadi¹, R. Sini J de Almeida¹, G. Oselka²***¹Pediatric Infectious Diseases, FCM da Santa Casa de Sao Paulo, ²University of Sao Paulo, Sao Paulo, Brazil*

Background and aims: Review the current status of meningococcal disease (MD) epidemiology in Brazil to provide information for appropriate policies on the incorporation of different meningococcal vaccination strategies for disease control.

Methods: National Surveillance Data on MD cases, reported from 2000 to 2009, were analyzed.

Results: MD is endemic in Brazil, with periodic occurrence of outbreaks and marked differences from region to region. The overall incidence of MD per year varied from less than 1 case per 100,000 in the Northern region to more than 3 cases per 100,000 in Sao Paulo, the most populated state of the country. The highest age-specific incidence of MD occurred in infants less than 1 year of age and the overall case fatality rates were consistently high, around 20%. During the study period, the incidence of serogroup B disease decreased and serogroup C, associated to the ST-103 complex, became prevalent, with several outbreaks reported. Emergence of serogroup W135, associated to the ST-11 complex, was recently reported in the States of Sao Paulo, Rio de Janeiro and Rio Grande do Sul.

Discussion: MD is associated with a high morbidity and mortality in Brazil, highlighting the importance of incorporating a meningococcal vaccine in our National Immunization Program. The unpredictable and dynamic changing serogroup epidemiology of MD emphasizes the need of ongoing surveillance to provide data for appropriate decisions regarding the urgent incorporation of universal meningococcal conjugate vaccines for disease control in Brazil.

EPIDEMIOLOGY OF KAWASAKI DISEASE IN NORTHERN EUROPEAN COUNTRIES

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Background and aims: To describe the incidence of Kawasaki disease (KD) in Northern European countries.

Methods: Data were obtained from hospital discharge databases (ICD9 code 446B or 446.98 or ICD10 code M30.3) from 1998-2005 in four Northern European countries. Denominator data were obtained from the national bureaus of statistics in the respective countries. Age distributions were compared by chi square.

Results: During the 8 yr. period of this survey, a total of 963 KD pts. were recorded in the registries. Average incidence rates per 100,000 children less than 5 years were as follows: Finland 10.0, Iceland 9.4, Norway 5.2, and Sweden 8.0.

The percentage of patients < 5 yrs. was as follows: Finland 71.7%, Sweden 72.4%, Norway 68.0%, and Iceland 84.2%. During the period 1999-2002, 88.9% of Japanese KD patients were less than 5 years as compared to only 71% of Northern European patients ($p < 0.001$).

Conclusions: The incidence rate of KD in Northern Europe was relatively constant over the study period. The age difference between Northern European and Japanese KD patients was consistent over time. The reason for this age difference remains unknown.

INTUSSUSCEPTION IN THE FIRST YEAR OF LIFE: A UK NATIONAL SURVEILLANCE STUDY

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Background and aims: Rotavirus infection is the commonest cause of severe childhood diarrhoea, which is substantially reduced by vaccination. Initial attempts at rotavirus vaccination seemed to increase the risk of intussusception. Although trials with newer vaccines suggest no increased risk, the earlier finding may adversely affect uptake. A UK study carried out over a decade ago showed an annual incidence of 66 per 100,000 infants. We aimed to estimate the current, national incidence of intussusception among UK and Irish infants prior to vaccine introduction.

Methods: We carried out prospective active surveillance of intussusception from 1 March 2008 to 31 March 2009 via the British Paediatric Surveillance Unit (BPSU). Clinicians were requested to notify cases less than a year old using the established BPSU system.

Results: The completion rate was 95.4% (374 questionnaires received/392 cases notified). 259 cases were confirmed, 105 were duplicates and 13 'probable/possible' cases. Two-thirds of confirmed cases were boys (64.9%) and the median age was 6 months. The annual incidence of intussusception among UK and Irish infants was 30 and 33 cases respectively per 100,000 infants. The highest country incidence was observed in Northern Ireland (46) followed by Scotland (31), England (30) and Wales (19). In England, London showed the highest incidence (54) and West Midlands (11) the lowest.

Conclusions: The incidence of intussusception appears to have declined over the last 20 years. Our study provides current national incidence, which is important to monitor changes in incidence following rotavirus vaccine exposure and to inform vaccine policy.

ACUTE OTITIS MEDIA (AOM) AT THE PAEDIATRIC OUTPATIENT DEPARTMENT OF THE MEDICAL UNIVERSITY GRAZ, AUSTRIA

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Background: Acute otitis media (AOM) is a major cause for paediatric outpatient visits and a common reason for antibiotic prescription. However, most data on incidence and antibiotic prescription rates are based on studies performed in the USA. Data from Central Europe are scarce.

Methods: Our clinic is the only paediatric tertiary care centre in southern Styria and additionally serves as a primary care centre, especially beyond office hour. 140.000 children aged 0-14 years are living in the catchment area.

We screened electronic documents of year 2008 from the paediatric outpatient department for the diagnosis "otitis", "AOM" and the according German denominations and analysed episodes of AOM (age, season, and therapy).

Results: In 15.721 out of 32.044 outpatient visits an electronic document was available. In 589 (3.74%) diagnosis of AOM was found. For seasonal and age distribution see table I.

	age (months)					all age groups
	0 - 12	13- 48	49 - 72	73 - 120	> 120	
January	1.33	6.85	5.93	3.13	1.00	3.66
February	2.50	6.85	6.38	1.83	1.08	3.83
March	3.02	8.03	4.51	2.66	0.00	3.66
April	3.47	5.34	6.50	2.03	0.49	2.95
May	0.68	3.48	5.04	0.78	0.37	1.85
June	2.17	3.43	5.43	3.39	0.65	2.64
July	0.65	3.90	6.98	1.63	1.27	2.74
August	1.86	1.61	1.74	2.89	1.19	1.79
September	1.29	5.51	6.47	0.90	0.29	2.81
October	2.52	6.99	7.09	1.43	0.65	3.96
November	4.40	7.38	3.52	2.03	0.48	3.99
December	3.97	9.57	12.42	4.79	1.47	6.75
Year 2008	2.67	6.48	6.55	2.33	0.72	3.74

Tab I. Patients with AOM, expressed in % of electronically documented outpatient visits

[graph 1]

In AOM patients, prescription rates of antibiotics, nose drops and anti-inflammatory drugs/analgetics were 70.8%, 76.7 and 53.8%, respectively. Prescribed antibiotics were (amino-)penicillins (34.3%), aminopenicillin/BLI (13.2%), cephalosporins (generation 1, 14.6%; 2, 0.7%; 3, 28.5%) and macrolides (8.6%).

Discussion: AOM is an important cause for paediatric outpatient visits and antibiotic prescription, especially in young infants and during winter season.

Establishment of guidelines for diagnosis/treatment of AOM and introduction of free pneumococcal vaccine might reduce diagnosis of AOM and antibiotic consumption in children.

SYMPTOMS THAT KEEP CHILDREN HOME FROM SCHOOL: AUTOMATED TECHNOLOGY FOR EPIDEMIOLOGICAL SURVEILLANCE

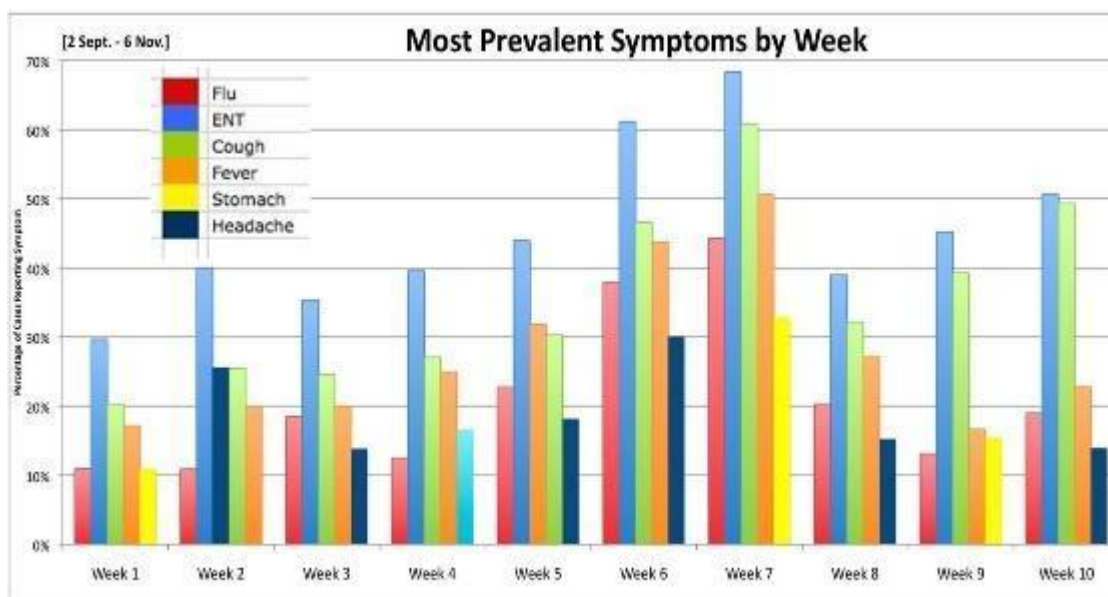
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Background / aims: Children in preschool and school are among the first in community to demonstrate symptoms of emerging diseases. School absenteeism is an early sign of outbreaks, but is currently an imprecise tool. This project tested the feasibility and utility of automatically surveying parents who call their child's school to report absenteeism because of illness.

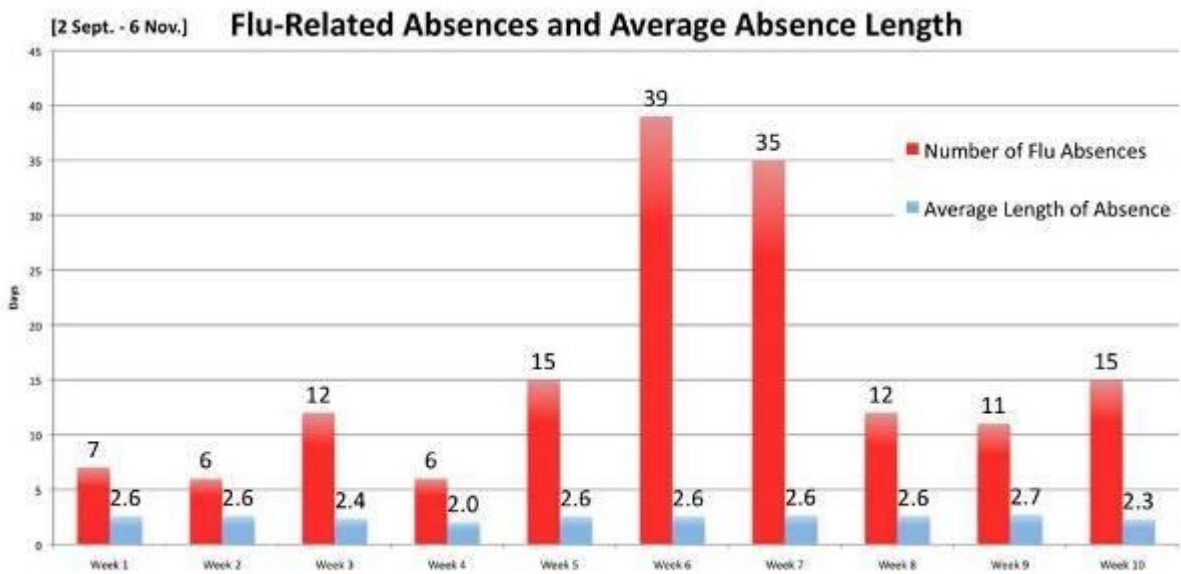
Methods: An interactive, voice-response telephone questionnaire was established in a school system to characterize a child's illness. Parents responded "yes" or "no" to symptoms (e.g., diarrhea, rash, fever). Software analyzed absenteeism data at least daily for trends. Coincidentally, H1N1 affected this school region during the experimental period.

Results: Over 75% of parents utilized the automated questionnaire when calling the school to report an ill child and 83% of them completed the entire questionnaire. During the first several months of testing the surveillance system, there was a H1N1 flu outbreak (flu symptoms on Graph 1).



[Graph 1]

Average duration of absence from school was also collected (Graph 2).



[Graph 2]

Conclusions: Automated monitoring of student symptoms is feasible. Implementing this system in all schools (or a critical sample of schools) can provide useful epidemiological information to public health authorities.

VARIATIONS IN THE EPIDEMIOLOGY OF VARICELLA INFECTION DURING THE PRE-VACCINATION ERA: A RESULT OF THE IMPACT OF CLIMATE CHANGE?

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Background and aims: The transmission rate of air-borne infectious diseases may vary according to climate conditions. The study aims to assess time trends of the epidemiology of varicella infection during the pre-vaccination era during which climate changes were notable.

Methods: A retrospective study among all pediatric and adolescent patients (N=2075) admitted to the "Aghia Sophia" Children's Hospital during the period 1982-2002 with varicella infection was conducted in Athens, Greece. Hospital admission date was determined retrospectively from case records. No exclusion criteria were applied. The Chi-square test for linear trend was applied to assess the study objectives.

Results: During the period 1982-2002 a total of 2075 patients with varicella infection were admitted to the hospital. Overall, the highest prevalence rate of varicella infection was during the spring (n=911; 43.9%) and winter (n=582; 28.0%), while the lowest prevalence rate was during the autumn (n=198; 9.5%). Moreover, the highest prevalence rate was during the months of May (n=372; 17.9%) and April (n=272; 13.1%), while the lowest was in August (n=28; 1.3%). During the years 1982-2002, a significant decrease in the prevalence of varicella infection was observed during autumn (p=0.0010) and winter (0.0228). Furthermore, a significant decrease in varicella infection prevalence occurred in October (p=0.0151), November (p=0.0015), and December (p=0.0005), while an increase was observed during March (p=0.0467).

Conclusions: During the period 1982-2002, the prevalence of varicella infection has increased during the spring and decreased during the fall. This may be attributed to climate changes associated with prolonged both winter and summer seasons, respectively.

EFFECT OF A SINGLE DOSE GROUP C MENINGOCOCCAL VACCINATION PROGRAM ON THE EPIDEMIOLOGY OF INVASIVE MENINGOCOCCAL INFECTIONS IN FLANDERS

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Background and aims: An epidemic increase of meningococcal C infections in Flanders in 2001 made it necessary to implement a vaccination campaign. The campaign was aimed at groups with highest age-specific incidence older than 12 months with single dose vaccination. Additionally vaccination was offered systematically in the vaccination program at the age of one year. The impact of the vaccination campaign and program was evaluated with epidemiological data of invasive meningococcal diseases.

Methods: Data from all notifications of meningococcal infections in Flanders since 1999 were examined, including data from the national meningococcal reference laboratory. For children and adolescents vaccination data were looked for systematically to exclude vaccine failure.

Results: Since the start of the campaign there was a fast decrease in cases in the age groups vaccinated, with no cases of vaccine failure. Herd immunity was seen with a drop in incidence in all age groups including babies. Since the end of the campaign in 2004, only sporadic cases of meningococcal C infections are notified. No cases were younger than 25 years with the exception of two children recently arrived from Africa in 2007.

Conclusions: A vaccination program with systematic single dose vaccination at the age of one year seems to be sufficient to maintain the herd immunity effects for meningococcal C infections after a vaccination campaign. No cases of vaccine failure could be documented.

REFERRAL TYPE IS NOT A GOOD ESTIMATOR FOR SEVERITY OF ILLNESS IN YOUNG CHILDREN WITH FEVER VISITING THE EMERGENCY DEPARTMENT

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Background and aim: Self-referred patients are often thought to mainly present with non-urgent problems and to be the major cause of emergency department (ED) overcrowding. A proposed solution is the gatekeeper function of General Practitioner Cooperatives. The aim of our study is to characterize young febrile children referred or self-referred to the ED, during out-of-hours care, focusing on severity of illness. This insight may contribute to additional management interventions.

Methods: Observational study, including 1624 referred or self-referred children with fever, aged 0-5 years, visiting the ED (January 2006-April 2008). Data on patient characteristics, urgency, diagnostics and treatment were extracted from the computerized Manchester Triage System (MTS) of the ErasmusMC/Sophia Children's Hospital, Rotterdam and Juliana Children's Hospital, The Hague, The Netherlands. Statistical analysis was performed using Pearson's Chi-Square tests.

Results: Sixty-eight percent of patients were self-referred, with 59% boys, median age 1.5 years (inter quartile range (IQR):0.8-2.9) and median body temperature 38.8°C (IQR:38.2-39.6). Referred patients showed similar numbers. Thirty percent of self-referrals were classified as high urgent (MTS U1/U2), 5% needed extensive diagnostic tests and 14% were hospitalized. These figures were substantially higher in the referred patient group (42%, 10% and 31% respectively; all $p < 0.0001$).

Conclusion: Although less frequent than referred patients, a substantial part of self-referred young febrile children was classified as high urgent and still 14% were hospitalized. We conclude that referral type alone is not a good estimator for severity of illness and other characteristics need to be defined to guide interventions against ED overcrowding.

SAFETY NETTING IN LOW URGENT CHILDREN AFTER EMERGENCY CARE CONSULTATION: PREDICTORS FOR ACUTE FOLLOW UP VISITS

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Aim: To assess which factors predict necessary follow visits to improve safety netting, for low urgent children presenting at the emergency department.

Methods: A telephonic questionnaire was performed in low urgent children, who visited the emergency department of a paediatric university or a large teaching hospital, 2-4 days after their ED visit. Parents were asked about acute follow up visits within 48 hours. Follow up visit with interventions were defined as visits in which diagnostics or therapeutic interventions were performed, the patient was subsequently hospitalized or a follow up visit was scheduled.

Results: In 3,975/5,425 (76%) patients a questionnaire could be performed. 112 (2%) patients gave no consent, others could not be reached (1,025, 20%) or could not be contacted because of logistic problems (n=122, 2%). 114 patients (3%) had a scheduled and 184 patients (5%) an unscheduled follow up visit of which respectively 66% and 64% were necessary. Patients under one year (OR 2.6, 95% CI 1.9-3.6) and patients with skin (OR 4.0, 95% CI 2.5-6.5), respiratory problems (OR 2.3, 95% CI 1.6-3.4) and gastrointestinal problems (OR 2.9, 95% CI 2.1-4.2) compared to patients with trauma had more often a follow up visit with intervention. Patients with gastrointestinal problems had the shortest time to a follow up visit (median 31, IQR 16-43 hours) and patients with respiratory problems the longest time (median 45, IQR 27-61) (Log rank, $p < 0.001$).

Conclusion: Safety netting should focus on young children and patients with skin, respiratory or gastrointestinal problems.

COGNITIVE OUTCOMES OF MENINGOCOCCAL SEROGROUP B DISEASE: FINDINGS FROM A NATIONALLY REPRESENTATIVE CASE-CONTROL STUDY

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Aims: Estimates of the sequelae of Men B disease in the modern era are needed to inform the development and introduction of future vaccines.

Methods: We present interim results from a nationally representative case-control study from 5 English regions. Cases were identified via the Meningococcal Reference Laboratory and controls via case GPs. Consenting subjects underwent a 2.5 hour standardised assessment of hearing (audiometry), IQ and other cognitive function and psychological function. Analyses were adjusted for age and sex. The study received ethics approval and was funded by the Meningitis Trust.

Results: Cognitive data were available for 143 cases and 97 controls. MenB survivors had lower verbal IQ (case mean 99, control mean 104; $p=0.02$) and performance IQ (98 versus 102; $p=0.04$) than controls. Findings were similar when repeated in those without significant hearing loss. Working memory was significantly poorer in cases (mean attention/concentration index on Children's Memory Scale = 95.3 in cases, 103.6 in controls; $p=0.008$) however verbal memory was minimally impaired. MenB survivors were also more likely to have any mental health disorder (24% v 11%; $p=0.04$), to receive Disability Living Allowance (9% v. 1%; $p=0.009$) and additional educational support (19% versus 6%; $p=0.01$).

Conclusions: These interim results suggest MenB disease is associated with a significant burden of cognitive, psychological and educational sequelae in survivors. These data will contribute to cost-effectiveness analyses of new MenB vaccines.

A HISTORICAL REVIEW OF MENINGOCOCCAL DISEASE IN EUROPE, 1945-2000

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Background and aims: Currently serogroups B and C cause the majority of meningococcal disease in Europe. A literature review was undertaken to investigate the changing epidemiology of meningococcal disease in the region and historical distribution of serogroups responsible.

Methods: Systematic literature review using Medline and Embase and restricted to epidemiological, surveillance and outbreak studies undertaken in Europe, 1945-2000.

Results: Meningococcal disease in Europe since 1945 has been in a continued state of flux. The prevalence of serogroups shows considerable variation with serogroups A, B and C all having dominated at some time, the current dominance of B and C being relatively recent. Throughout the 20th century serogroup A caused both epidemic and endemic disease. Since the 1970s it has declined in prevalence though continued to cause significant disease in Eastern Europe (particularly Russia and Romania) and to a lesser extent in Greece and Italy during the 1990s. W-135 was prevalent in several countries in the 1970s (6-8% of infections) and outbreaks linked to the Hajj pilgrimage were observed in 2000. Disease due to serogroup Y was rarely observed, except in Sweden where it caused some significant disease (9.2% of infections) 1993-96. W-135 and Y have tended to affect an older population and have higher case-fatality rates (10-18%) compared with more common serogroups (5-10%).

Conclusions: The epidemiology of meningococcal disease in post-war Europe has changed with little predictability. All five major serogroups have been observed to a greater or lesser extent suggesting polyvalent conjugate vaccines should be considered for routine immunisation.

VIRIDANS STREPTOCOCCAL BLOOD STREAM INFECTION IN PEDIATRIC HEMATOLOGY ONCOLOGY

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Introduction: Viridans streptococci (vs) are a heterogenous group of bacteria which have come to assume an increasingly greater importance for all health care workers involved in the management of immunocompromised patients.

Patients with VS infection are at risk of developing a toxic shock-like syndrome (VSSS) characterized by hypotension and ARDS with a mortality rate ranging from 40% up to 100%.

Materials and methods: A retrospective evaluation of the Clinical and Microbiology records of children 0-14 years treated at the Pediatric Hematology Section of the KFSH & KFCCC, for Blood Stream Infection due to viridans Streptococci, between Jan 2003 and Dec 2008.

Results: A total of 70 episodes of Bacteremia with VS were identified during this 6 year period, *S. mitis*: (43%), *S. oralis*: (13%), *S. sanguis*: (7%), *S. savarius*: (4%) and other unidentified Viridans streptococci (32%).

Majority > 75 % present with severe neutropenia (ANC < 500) and fever. No mortality directly related to Viridans Streptococcal Infection in these patients.

Conclusions: Viridans Streptococci are an important cause of infection in our patients. It is often present with respiratory distress, mucositis and hypotension. There is no mortality among our children due to VS sepsis.

CANDIDA BLOOD-STREAM INFECTIONS IN CHILDREN AT A TERTIARY CARE CENTRE IN SAUDI ARABIA

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Background: *Candida* spp are the second most frequent isolates from blood cultures in hospital with large populations of immunocompromised patients.

Objectives: To study the trend of candidemia in pediatric patients (0-14 years) at King Faisal Specialist Hospital & Research Centre (KFSH&RC) and to evaluate demographic data, underlying diseases, candida isolates, the risk factors and the outcome of candidemia.

Method: Retrospective chart review utilizing the microbiology & Infection Control Data-Bases of pediatric patients with candidemia between January 1996 and December 2007.

Results: Total of 575 Candidemia episodes were identified in adult and pediatric patients at our center. Of these 310 episodes were in children. One hundred six (106) were in pediatric patients with haematology oncology disorders (34%), 61 were in children with cardiovascular diseases and 53 were in neonates. *Candida albicans* were the most frequently isolated (50%) followed by *C. parapsilosis* (20%). The predominant isolates vary by the underlying diseases and location e.g. *Candida albicans* is the common candida spp isolated, followed by *C. tropicalis* in pediatric patients with hematology oncology disorders. *C. krusei* were more frequently isolated in adults patients compare to children (15% vs 1%).

Conclusion: *Candida* is not uncommon blood stream isolates in our patient population and *Candida albicans* is the common candida spp isolated, followed by *C. parapsilosis* and *C. tropicalis*. Presence of CVL and prolonged use of broad spectrum antibiotics are major risk factor for candidemia. *Candida* blood-stream infection remains a significant cause of morbidity and mortality among pediatric patients not restricted to those with hematology oncology disorders.

TIGECYCLINE TREATMENT OF MULTI-DRUG RESISTANT CORYNEBACTERIUM JEIKEIUM INFECTION IN A CHILD WITH RELAPSING AND REFRACTORY ACUTE LYMPHOBLASTIC LEUKEMIA

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Corynebacterium jeikeium infection occurred primarily in neutropenic patients who have central venous catheters. A 6 years old girl has been followed for three years with three times relapsed acute lymphoblastic leukemia. During the intensive chemotherapy protocols, she had febrile neutropenia episode which is unresponsive to conventional antibiotic treatments. Her recurrent blood cultures and central venous catheter cultures revealed C. jeikeium which was resistant to all antibiotics except tigecycline. She has been treated with tigecycline at 1 mg/kg dose every 12 hours. After tigecycline treatment, fever has been resolved and repeated blood cultures revealed any microorganism after 14 days of treatment. Tigecycline appears to hold promise as a novel expanded spectrum antibiotic in adults however routine use in pediatric patients is not recommended yet. In vitro studies showed tigecycline is a good alternative for the non-diphtheria corynebacteria as well as other multi-drug resistant microorganism infections. Here in we present a child with relapsed acute lymphoblastic leukemia who was successfully treated with tigecycline due to multi-drug resistant-tigecycline susceptible C. jeikeium sepsis without removal of her central venous catheter. To the best of literature knowledge, our patient is the second reported case who treated with tigecycline during childhood, also first reported case who received tigecycline due to C jeikieum infection in children as well as adults. Our case also provides clinical guidance in the use of tigecycline in children where there are no better alternatives although further studies about the efficacy and safety of tigecycline needed.

ACUTE DISSEMINATED AND FATAL TOXOPLASMOSIS AFTER HAPLO-IDENTICAL BONE MARROW TRANSPLANTATION DESPITE ATOVAQUONE PROPHYLAXIS

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Reactivation of toxoplasmosis after bone marrow transplant (BMT) is a rare event but severe event with high mortality rates up to 80% mostly due to delayed and frequent post-mortem- diagnosis. Toxoplasmosis reactivation is usually prevented with trimethoprim-sulfamethoxazole (TMP-SHX) prophylaxis in immunosuppressed patients. However, atovaquone can be considered as an alternative agent according to Centers for Disease Control and Prevention when TMP-SHX has to be stopped in intolerant patients. Nevertheless there is limited experience in the use of atovaquone in *Toxoplasma gondii* infections.

We describe a 19 year old young man with acute disseminated toxoplasmosis reactivation five months after haplo-identical hematopoietic stem cell transplantation from his mother for acute lymphoblastic leukaemia despite atovaquone prophylaxis. Identification of free forms (tachyzoites) and pseudocysts in multiple organs during necropsy was diagnostic of disseminated toxoplasmosis, with further post-mortem confirmation by PCR in plasma. Our case report illustrates that BMT patients treated with atovaquone for toxoplasmosis prophylaxis should be considered at risk for *T. gondii* disease and could benefit of protozoal replication monitoring by RT-PCR. While the best strategy to treat reactivation/infection with *Toxoplasma* is not standardized, switching to another agent, or adding a second drug to atovaquone should be considered.

CENTRAL VENOUS ACCESS DEVICES AND BLOODSTREAM INFECTIONS IN PAEDIATRIC HAEMATOLOGY-ONCOLOGY PATIENTS IN A TROPICAL REGIONAL REFERRAL MEDICAL CENTRE

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Background: With recent advances in combination chemotherapy for childhood cancer, central venous access devices (CVAD) are widely used in the region. We reviewed our experience in our paediatric haematology-oncology unit which is a regional referral centre to determine the infection rates associated with CVAD.

Methods: The records of all patients managed in our centre in the last four years were studied. All patients with a CVAD were entered into the study. Complications associated with catheter use and all positive blood cultures were recorded. NNIS criteria were used for the definitions of primary bloodstream infections (BSI).

Results: A total of 70 children had CVADs, 40 Hickman catheters(HC) and 30 Port-a-Caths (PAC). 23 catheter associated BSIs were detected, 9 caused by *Pseudomonas aeruginosa* and 4 by coagulase negative staphylococci. HC had 2.41 BSIs per 1,000 catheter days compared with 0.85 per 1,000 catheter days for implanted ports (PAC). The relative risk of BSI for HC was 2.13, 95% CI 0.95-4.74($p=0.047$). This was especially marked for gram-negative BSI; (RR 3.00, 95% CI 0.93-9.70, $p=0.043$).

Conclusion: HC are associated with a higher infection rate especially gram-negative BSI than PAC in our centre. This may be related to increased skin colonisation in our tropical climate which leads to BSI through the extra-luminal route of CVAD contamination. Efforts should be directed at novel strategies to prevent CVAD infection such as antiseptic impregnated dressings which may have particular applications in the tropics.

ETIOLOGY AND DIAGNOSIS OF INVASIVE FUNGAL INFECTIONS (IFIS) IN NEONATES AND CHILDREN: RESPONSES TO A QUESTIONNAIRE

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Background and aim: IFIs are a serious cause of morbidity and mortality in premature neonates and immunocompromised children. ESPID IFI Study Group is a novel group with the mission to support antifungal collaborations. The aim of this survey was to investigate epidemiology and diagnosis of invasive *Candida* and *Aspergillus* infections in neonates and children in Europe.

Methods: An e-questionnaire was formed and circulated to ESPID members during summer of 2009.

Results: Only 18 questionnaires completed were returned by PID specialists, neonatologists and pediatricians in Ped HemOnc, Ped Transp departments of 9 European countries, Israel and Malaysia. All of them cared for patients with *Candida* infections and 97% of them cared for patients with *Aspergillus* infections during the last 3 years. The number of cases of invasive *Candida* and *Aspergillus* infections treated per year during 2006-2008 ranged from 1-50 and 0-30 respectively. The most common *Candida* spp. was *C. albicans* followed by *C. parapsilosis*, *C. tropicalis* and *C. glabrata*. *A. fumigatus* was the most commonly encountered *Aspergillus* species with *A. flavus*, *A. terreus* and *A. nidulans* more rare causes of infection. Identification of *Candida* and *Aspergillus* spp. was available at local laboratory in 83% and 77%, respectively, by cultures (100%), galactomannan assay (66%), PCR (33%) and glucan assay (17%). The most common types of invasive *Candida* and *Aspergillus* infections were fungemia (95%) and pneumonia (89%) respectively.

Conclusion: The incidence of IFIs varies from center to center. These data can serve as the basis for collaborative efforts to combat IFIs.

MANAGEMENT OF INVASIVE FUNGAL INFECTIONS (IFIS) IN NEONATES AND CHILDREN: RESPONSES TO A QUESTIONNAIRE TO ESPID MEMBERS

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Background and aim: IFIs cause significant morbidity and mortality in high-risk neonates (HRN) and hematological patients (HP). ESPID IFI Study Group is a novel antifungal interest group. The aim of this survey was to investigate the management of these patients in Europe.

Methods: An e-questionnaire was formed and circulated to ESPID members during summer of 2009 for completion.

Results: 18 questionnaires completed by PID specialists, neonatologists and pediatricians in Ped HemOnc departments in 11 countries were returned. 72% and 89% of the participants give antifungal prophylaxis in HRN and high-risk HP, respectively [fluconazole (85%) for neonates; both fluconazole (39%) and itraconazole (37.5%) for HP]. Empirical treatment is applied by 95% respondents in HRN [fluconazole (47%), amphotericin B (AMB) deoxycolate (23.5%), lipid AMB (29.5%) and caspofungin (5.8%)], while by 83.3% in HP [lipid AMB (73.3%), fluconazole (13.3%), AMB deoxycolate (13.3%) and caspofungin (6.6%)]. Decision for treatment depends on *Candida* or *Aspergillus* species isolated (95%) and less on MIC values (61%). In HP 72% would start therapy against *Aspergillus* with any pulmonary infiltrate while 38.8% with only ≥ 1 positive galactomannan results. 95% of them would initiate immediate treatment with one positive blood culture for *C. albicans* and 55% with one positive sputum culture for *A. fumigatus*. Removal of catheter and antifungal therapy for candidemia is the treatment of choice for 95% of respondents.

Conclusion: A relatively small percentage of ESPID membership returned the questionnaires completed. The great majority of respondents use both prophylactic and empirical antifungal strategies.

POSACONAZOLE IN THE TREATMENT RHINO-ORBITO-CEREBRAL MUCORMYCOSIS: A CASE REPORT

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Rhino-orbito-cerebral mucormycosis (ROCM) is a rare, fulminant opportunistic fungal infection that is mostly seen in immunocompromised patients. We present here a 13-year-old girl who was previously diagnosed as cirrhosis due to autoimmune hepatitis admitted to our hospital with complaints of swelling, pain and chemosis on her left eye. Her paranasal sinus CT examination at admission revealed pansinusitis. She underwent endoscopic sinus drainage and histopathologic examination of specimen showed fungal hyphal elements staining with periodic acid-Schiff. She was assumed as fungal sinusitis and voriconazole therapy was initiated. During the her follow-up her kranial MRI revealed that abscesses formation in cavernous sinus on the 13th day of treatment. Then, amphotericin B was added to treatment, unfortunately, we could not perform surgical drainage to abscess within cavernous sinus. Diagnosis of ROCM was done after re-evaluation of sinus histopathologic specimen by mycolog. Patient therapy was re-organized as hyperbaric oxygen therapy with amphotericin B plus voriconazole. However, lesions progressed with this treatment. Then posaconazole was added in to treatment instead of voriconazole. We got regression on kranial and orbital lesions on 23th day of this treatment. Near-complete regression was achieved with this treatment by the 9th month of treatment. The prognosis of ROCM is poor especially patients with brain, cavernous sinus or carotid involvement. Here we showed that long-term oral therapy with posaconazole has been associated with good clinical response. Antifungal treatment plus hyperbaric oxygen therapy may decrease morbidity and mortality in the patients who could not undergo surgical debridement.

LECTINS (CARBOHYDRATE-BINDING PROTEINS) OF HUMAN PROBIOTIC BACTERIA: TYPES AND FACTORS OF ANTIFUNGAL ACTION

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Background: We isolated and standardized acidic and basic lectins of bifidobacteria and lactobacilli (aLB, bLB, aLL, bLL) of human origin.

The **aim** was to study L antifungal action against pathogenic fungi of human origin.

Methods: Standard procedures and conditions were used for isolation and growth of fungi on agar in dishes. For antifungal study, discs contained subagglutinating doses of L (peripheral agar) or standard dose of antibiotic (centre).

Results:

1. L revealed antifungal activities (growth inhibition, biofilm lysis, prevention of coupled mycoparasitism) against nistatin-resistant *Candida albicans* clinical strains. The character of activities depended on clinical strains and L type.
2. *C.albicans* growth inhibition was within dish sector around L discs: in central direction (LL>LB; aLL[1 inhibition zone]>bLL[3 zones]; residual colonies in zones) and in peripheral direction (LB>LL; aLB>>aLL; absence of colonies in zones).
3. Heat denatured aLL and aLB revealed decreasing of fungal growth inhibition in central or peripheral zones, respectively. *C.albicans* films formed were degraded in these zones later (programme event) due to L antifungal activity reactivation by fungal metabolites.
4. The forming of *Aspergillus niger* coisolate (from the same patient) films was initiated by *Candida* films. L inhibition zones for *A.niger* were the same as for *C.albicans* (prevention of coupled mycoparasitism).
5. Probiotic bacteria high molecular mass polysaccharides or lipids decreased antifungal activity of bLB or aLL, respectively. 6. Antifungal synergism between L types was observed.

Conclusions: It seems, L system of probiotic bacteria can decrease the risk of antibiotic-resistant infections in human and can allow decreasing of effective doses of antibiotics needed for therapy.

BK VIRUS ASSOCIATED HEMORRHAGIC CYSTITIS IN CHILDREN FOLLOWING HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Background: Hemorrhagic cystitis (HC) due to BK virus is a serious complication in children undergoing hematopoietic stem cell transplantation (HSCT). Currently there are only limited data on the epidemiology, clinical characteristics, optimal treatment and outcome of these infections.

Aims: To describe the epidemiology and clinical course of children with HC following HSCT.

Methods: The medical records of all children aged 0- 20 years who underwent HSCT in Schneider Children's Medical Center between 2000 and 2008 and were diagnosed with HC by positive urine PCR for BK virus were reviewed for demographic, clinical and microbiological data.

Results: Of 318 children who underwent HSCT during the study period, 17 children (5.3%) developed BK associated HC. Seven recovered with only supportive treatment. Eight patients were treated with cidofovir, seven with oxybutynin, two with bicarbonate and two with phenazopyridine. Estrogen and prostaglandin were given each to one patient. Hyperbaric oxygen therapy was initiated in six patients between three to 37 days after the onset of bleeding. Six patients were treated with more than one drug. None of the patients had relapse of HC and one patient died. Compared to patients who did not develop HC, acute myeloid leukemia, use of cyclophosphamide in the conditioning regimen, unrelated donor and older age were all significantly associated with the development of HC.

Conclusions: BK associated HC is relatively uncommon in children undergoing HSCT. Outcome of HC is generally good. Further prospective studies are required to define the optimal therapy.

FUNGAL INFECTIONS IN HIV INFECTED PATIENTS

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Background and aims: HIV as we all know remains to be a global pandemic. HIV infection causes gradual loss of immune system particularly the cell-mediated immunity and hence predisposing a person to several opportunistic infections including fungal infections. Fungal infections vary in their course depending on geographical regions. Lack of information on patterns of fungal infections initiated us, to conduct this study.

Materials and methods: Fifty-five HIV sero-positive patients admitted in Civil Hospital, India, during January 2007 to January 2009 were included in this study. The study group comprised of 32 (58.18%) males and 23 (41.81%) females. Relevant clinical samples were processed for detection of fungal pathogen using standard mycological technique.

Results: Fungal infections were suspected in 43 (78.18%) of the patients. Candida species topped the list being present in 27 (62.79%) of the patients, mostly in the form of oropharyngeal Candidiasis. Two patients presented with systemic candidiasis. Cryptococcal meningitis and Dermatophytosis was documented in equal proportions being in 6 (13.95%) each. Geotrichosis candidum in 4 (9.30%) patients were other fungal infection encountered. Pneumocystis carinii (Pneumocystis jiroveci) in spite of being suspected clinically in 11 (20%) patients could not be confirmed microbiologically.

Conclusion: Fungal infections remain to be a major threat in Immunocompromised patients. Great care should be taken and treatment instituted as soon as possible. Keeping in mind above stated patterns of possible fungal infections, periodical checkup charts should be implemented.

ANTIFUNGAL SUSCEPTIBILITY OF CANDIDA SPECIES ISOLATED FROM CASES OF VULVOVAGINITIS IN GIRLS

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Background and aims: Vulvovaginal candidiasis affects approximately 20% of adult women each year, however, few studies show the frequency of VVC in girls. This study aims to evaluate the prevalence of yeast vaginitis in girls and sensitivity of yeasts to antifungal drugs commonly used in medical practice.

Methods: Collected from 20 patients, fifteen were culture positive for yeast.

Results: The mean age was 14.41 years (SD 2.998737). *Candida albicans* was the species most frequently isolated (86%), followed by *C. glabrata* (7%) and *Trichosporon* sp (7%). The highest minimum inhibitory concentration was found to ketoconazole (3.589). And two samples of *C. albicans* were susceptible dose dependent to fluconazole. All samples were very sensitive to voriconazole (MIC 0.01675), amphotericin B (0.164125) and itraconazole (0.0435).

Conclusions: These data suggest that before 17 years of age, the yeasts of this site has a lower sensitivity to antifungal drugs, which can lead to an increased problem with the beginning of adulthood.

YEASTS FREQUENCY ISOLATED FROM BLOOD AND CATHETER FROM A CHILDREN HOSPITAL IN SAO PAULO, BRAZIL

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Nosocomial yeast infections have been attracting more attention over the last decades due to their increased frequency and their high mortality rates, mainly in patients already weakened by other diseases. Catheters often contribute to the disease's pathogenicity by serving as the substrate for the formation of biofilms that protect embedded yeast cells from the effective penetration of antifungal drugs. The present study was aimed at identifying and evaluating the frequency of yeasts in samples, in São Paulo, Brazil. A total of 333 samples of yeasts were identified in the period from 1993 to July 2009, all obtained from the blood or from catheters, the breakdown being 228 samples (68.5%) from the blood and 105 samples (31.5%) from catheters. From the blood, 33.3% were identified as *Candida albicans*, 16.6% *Candida tropicalis*, 12.7% *Candida sp*, 12.3% *Candida parapsilosis*, 7.9% *Candida glabrata*, 7.5% *Candida guilliermondii*, 7% *Candida krusei*, 0.9% *Candida lusitanae*, 0.9% *Pichia anomala*, and 0.9% *Trichosporon asahii*. From catheters, were identified as 47.6% *Candida albicans*, 14.3% *Candida sp*, 10.5% *Candida parapsilosis*, 8.6% *Candida tropicalis*, 6.6% *Candida guilliermondii*, 4.8% *Candida krusei*, 3.8% *Candida glabrata*, 2% *Pichia anomala*, 0,9% *Rhodotorula rubra*, and 0,9% *Trichosporon asahii*. The results of this study suggest that *Candida* is the yeast genus most frequently involved in nosocomial infections, since in both groups it was found in 95% of the identifications, the most frequent species being *Candida albicans*.

RETROSPECTIVE AVALIATION OF CANDIDIASE IN CHILDREN PUBLIC HOSPITAL OF SÃO PAULO BRAZIL, IN PERIOD OF 2003 AND 2006

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Background and aims: The purpose of this study was to evaluating the incidence and distribution of *Candida* species responsible for nosocomial candidiasis in a Public Children Hospital. We have strains of *Candida* spp during 2003-2006.

Methods: This strains were isolated from blood, urine and other biological specimens (39,09%; 46,91% and 14,01%, respective).

Results: From strains 45,60% were identified as *C. albicans* and 54,40% as non- albicans species. The distribution of this strains was: in 2003, 40,22% and 59,78%; in 2004, 39,68% and 60,32%; in 2005 56,86% and 43,14%, in 2006 40,00% and 60,00% of this the albicans and non—albicans species, respectively. A higher incidence of this *C. albicans* strains was observed in candiduria cases (58,33%) and in 69,17% of the candidemia cases we isolated non-albicans species ($p < 0,05$). We observed that occurred a significative increased of candiduria and the frequency of *C. albicans* (10,32% to 16,92%) - $p < 0,05$, but a decrease occurred in 2006.

Conclusions: In our children's hospital , over the tree year period, a trend of increased of non-albicans isolated from blood and the *C. albicans* strains from urine was noted. Rapid identification of species is a crucial information for the clinician because we assist to the emergence of this non-albicans species wish can be resistant to the antifungal.

OPPORTUNISTIC INFECTION IN IMMUNOCOMPETENT PATIENTS

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Objective: We report two cases of *Pneumocystis jiroveci* pneumonia in children with normal immunological status. Mycotic infections depend on acquired and innate immunity and also on environmental conditions.

Case report: Two Vietnamese infants, living in an orphanage, present a pneumonia with severe hypoxemia. They were respectively three and five months old. Microscopic analysis of bronchoalveolar lavage reveal the presence of *Pneumocystis jiroveci*. Total recovery occurs with cotrimoxazole treatment. Human Immunodeficiency Virus (HIV) serology was negative and immunologic repeated investigations were normal.

Conclusion: Most of *Pneumocystis jiroveci* pneumonia cases admitted to intensive care occur in immunocompromised children (HIV, Hereditary immunodeficiency, neoplasia, bone marrow transplantation). These two cases show, the importance of environmental condition: Asiatic origin, child care center despite the normal immunological status and a favourable outcome without relapse under treatment.

PERSISTANT *CANDIDA ALBICANS* CEREBROSPINAL FLUID (CSF) SHUNT INFECTION DUE TO INCREASED MIC TO AMPHOTERICIN B DURING THE TREATMENT

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Use of CSF shunt devices is a common practice in neurosurgery, and infection of the shunt is the most frequent complication. Herein, we presented a case with persistent *C. albicans* CSF shunt infection.

Case: A three-month-old boy who was previously underwent CSF shunt operation because of hydrocephalus presented with one month history of fever to private hospital. CSF culture yielded *C. albicans* and initially fluconazole plus caspofungin were started. Despite treatment with those antifungals *C. albicans* growth in CSF culture persisted. Based on MIC value (Amph B < 1 mcg/mL) amphotericin B was started but *C. albicans* was not eliminated from CSF culture and amphotericin B replaced by flucytosine plus caspofungin. Then patient was referred to our hospital because of persistent *C. albicans* growth in CSF culture despite 28 day antifungal treatment. In our hospital *C. albicans* were also isolated from CSF cultures. Fluconazole and amphotericin B MIC level were determined 1 mcg/mL and 2 mcg/ml, respectively. Then, voriconazole plus flucytosine treatment were initiated. With this treatment *C. albicans* growth in CSF culture ceased, new VP shunt was inserted and patient was discharged from the hospital. Resistance to amphotericin B in *C. albicans* is rare. In patients with persistent growth of candida antifungal susceptibility tests should be repeated whether there is an increase in the MIC levels as it occurred in our case. This may help for reorganisation of treatment.

PHARMACOKINETICS OF PROPHYLACTIC MICAFUNGIN IN VERY LOW BIRTH WEIGHT INFANTS

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The incidence of Candidal infection is increasing due to greater survival of preterm infants. In Japan, the only antifungal drug licensed for intravenous injections in children is micafungin.

Micafungin was first administered, to 25 very low birth weight infants, 12 to 24 hours after birth at a dose of 1mg/kg/day. Medication was administered once per day for 6 weeks or until endotracheal intubations and a central vein route became unnecessary. Blood samples were collected 2, 8, 12, and 24 hours after the start of micafungin infusion and 24 hours after the final administration. The pharmacokinetic parameters of micafungin in all neonates were estimated from the concentration-time data using first order kinetics with a one compartment model. The clinical efficacy and safety of micafungin was evaluated by subject's prognosis, the existence of Candida infections, and adverse drug reactions.

The micafungin pharmacokinetic parameters were as follows: the apparent distribution volume was 0.76 ± 0.28 L/kg, the elimination rate constant was 0.12 ± 0.041 L/hr, the elimination half-life was 6.7 ± 2.2 hr, and the total clearance serum was 0.089 ± 0.047 L/kg/hr. The mean serum concentration of micafungin at 2 and 24 hours after first medication was 1.3 and 0.20 mg/L, respectively. The mean concentration of micafungin 24 hours after the final medication was a significant 0.1 mg/L higher than after the first medication. In all cases, micafungin was well tolerated and there were no adverse events leading to study discontinuation. There were no cases of fungal infection or mortality.

ASSESSMENT OF HELICOBACTER PYLORI CAG A & VAC A VIRULENCE GENES IN RECURRENT ABDOMINAL PAIN AND ASYMPTOMATIC EGYPTIAN CHILDREN

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Background: H.pylori infection is one of the commonest causes of recurrent abdominal pain (RAP). Its colonization induces chronic gastritis in all hosts but not all people get symptomatic. Differences in virulence factors influence the clinical outcome. Patients with high antibody levels against VacA and CagA proteins showed severe gastric pathologies and have a greater risk for developing adenocarcinoma.

Aim: To differentiate between H pylori strains present in RAP and asymptomatic children through assessment of Cag A and VacA virulence genes.

Subjects and methods: This study included 26 children with RAP aged 5-12 years. The mean duration of RAP was 2.11±1.07 years. 18 asymptomatic children of the same age and sex were recruited as controls. All children were subjected to assessment of H.pylori IgG antibodies in sera using ELISA technique. Positive antibody cases & controls were subjected to H.pylori antigen detection in saliva by immunoassay and identification of Cag A & Vac A virulent genes in saliva by PCR.

Results: H.pylori IgG antibodies were high and showed no significant differences in both cases & controls (73.1% & 72.2%). H.pylori antigen in saliva was present in 57.9% of IgG +ve cases & in 46.2% of IgG +ve controls with no significant differences between both groups. Cag A gene was detected in 10.5% of cases & in 7.7% of controls with no significant differences between them. None of our tested children had Vac A.

Conclusion: CagA & VacA genes couldn't help in differentiation between H pylori strains present in RAP and asymptomatic children.

PEDIATRIC INFECTIONS WITH CAMPYLOBACTER

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Aims: Evaluate the epidemiology and clinical features of Campylobacter in infants.

Methods: Clinical data is recorded and evaluated for 43 children, with positive campylobacter stool cultures admitted to the Montpellier University Hospital (France) between January 2008 and June 2009. The results are compared with two studies performed in the same hospital between 2000-2006 and in 2007.

Results: The patient population included more girls than boys (1,26/1), the mean age is 54 months, 40% have less than 2 years. 90% of children required hospitalization with a mean stay of 75hours. 81% are hospitalized for acute gastro-enteritis. No serious illness (septicemia, Hemolytic-uremic syndrome) is recorded. The clinical features are fever in 74%, bloody stool in 60% (isolated in 4,6% of cases), diarrhea in 84% and abdominal cramps in 53% of the population. The distribution of disease-causing agents is: *C. jejuni* 93%, *C. coli* 4,7 % and *C. arcobacter* 2,3 %. The rates of resistance are high, 40% for Cephalosporins third generation, 51,2% for Trimethoprim, 46,5% for Amoxicilline, and less than expected for Erythromycine 4,7%.

In our study, Campylobacter is found to be significantly higher in infants older than 6 months. The number of antibiotic treatments increased. Abdominal sonography necessary in 90% of cases was abnormal in 67% with pancolitis in 20% of the cases.

Conclusions: Campylobacter infection is increasingly noted in cases of childhood invasive diarrhea, inducing an increased morbidity. Slow culture development renders clinical to bacteriological correlation difficult, but the presence of bloody stools is a strong diagnostic element.

ANTIBIOTIC-ASSOCIATED DIARRHEA IN CHILDREN

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Background and aims: Antibiotics are the most frequently prescribed drugs aiming to resolve infectious diseases. Antibiotic-associated diarrhea (AAD) is a common adverse event in children. The aim was the evaluation of incidence of AAD in children admitted to our hospital and determination of risk factors for AAD.

Methods: Our study took place at Children Hospital from January 2008 to June 2009. Medical records and microbiology data of children with AAD were study. AAD was defined as three or more stools a day of liquid consistency for at least two days from the start of antibiotic administration. Exclusions criteria: acute/chronic diarrhea, immunodeficiencies and no history of antibiotics before diarrhea started.

Results: Out of 97 stool samples from 81 children with diarrhea, 37 (45.67%) had AAD caused by *Candida albicans* (59.45%) and *Pseudomonas aeruginosa* (40.54%). 32.43% of patients were infants, 40.54% toddlers and the rest were between 3 and 18 years old. Antibiotics were prescribed for chest infection (35.135%), pharyngotonsillitis (27.02%) and acute otitis media (16.12%). The antibiotics associated with AAD were Cephalosporins (45.94%, 50-100mg/kg/day bid), Amoxicillin/Clavulanate (20%, 30-50mg/kg/day bid) and Clarithromycin (13.51%, 15mg/kg/day bid). AAD began 6.8 ± 3.1 days after start of antibiotic with duration of 4.8 ± 2.3 days. 18.19% of children needed antipseudomonal antibiotics despite withdrawal of offending antibiotics. The relative risk of onset of AAD in a child receiving Cephalosporins was 2.1 and 1.83 when the child was aged less than 2 years.

Conclusions: Diaper-wearing group and the use of Cephalosporins are major risk factors for AAD.

BURDEN OF ROTAVIRUS HOSPITALISATION IN VERY PRETERM INFANTS: A REGIONAL OBSERVATIONAL SURVEY

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Aims: The purpose of the study was to determine the hospitalisation rate for rotavirus disease in 0-24 months old very preterm infants before Rotavirus vaccines introduction into immunization program in France.

Methods: Four hundred sixty eight infants born before 33 Gestational Weeks between 01/01/2000 to 31/12/2002 were included in this regional prospective observational study. On inclusion, the parents were informed about annual follow up program until the age of eight and written permission was obtained. The data were prospectively recorded through a standard medical support according to a procedure approved by CNIL for data processing. Medical records were obtained in the case of hospitalisation.

Results: Follow up was completed for 443/468 infants(94.7%). Median initial hospitalisation stay before discharge was 60 days[19-396]. Forty-five percent of children(200/443) were hospitalised at least once (Mean: 2 events per infant, 78.5% for medical and 21.5% for surgical events). Acute gastroenteritis (AGE) represented the second etiology(20,9%:50/239) after bronchiolitis(59.8%:143/239) among infectious diseases readmissions. The median age for AGE rehospitalisation was 9 months[3-22]. Laboratory screening was available for 62% (31/50) and Rotavirus identified in 48.4%(15/31). **The hospitalisation rate for documented Rotavirus infection was 3.2%(14/443).**

Conclusion: Data from this study support the important impact of AGE in 0-24 months old very preterm infant rehospitalisations. Rotavirus represented half of the laboratory diagnosis and the hospitalisation rate observed was higher than in young children < 5 years old. Rotavirus vaccination could be helpful to reduce readmission in this vulnerable population. Initial stay before hospital discharge could be use to begin immunisation.

**BURDEN OF ROTAVIRUS (RV) ACUTE GASTROENTERITIS (AG) IN PORTUGAL -
MULTICENTER PROSPECTIVE STUDY: 2008-2009**

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Background: RV is an important cause of AG in children. Data on the burden of disease in Portugal was limited.

Methods: A prospective, multicenter, observational study was conducted in children < 5Y with AG, from October08 to March09, in 11 paediatric Emergency Services, all over the country.

Results: A total of 1096 children were included. The mean age was 14 months: 20% were < 6 months and 87% were < 36 months. 15% were admitted to the ward and the mean duration of stay was 2.7 days (1-14). 1102 (31.7%; 28.9%-34.5% CI 95%) were found to be RV positive, with the highest proportion in March (50.3%). Incidence of RVAG was higher among children 13-24months (P=0.019) with 30% of all RVAG cases occurring in this age group. Children with RVAG were more likely to have fever (57.7% vs 48%; P=0.003), vomiting (91.6% vs 63.2%; P< 0.001) and dehydration (41.8% vs 21.4%; P< 0.001), and, therefore more severe disease than children with RV negative AG. The proportion of hospitalisations was significantly higher among children with RVAG than for those who were RV negative (24% vs 11%; P< 0.001). The most frequent genotypes were G1P[8] (41.8%) and G4P[8] (35.3%), with variations between different regions of the country.

Conclusions: RV accounts for a significant proportion of AG cases in children < 5Y of age in Portugal. RVAG is more severe and results in more hospitalizations. G1 and G4 types were found in ~80% of the cases. Routine vaccination could significantly reduce the burden of RVAG.

ROTAVIRUS VACCINATION IN NORTHEAST BRAZIL: A LAUDABLE INTERVENTION, BUT IS IT COST-BENEFICIAL?

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Introduction: Rotavirus vaccines have been internationally recommended to reduce diarrhoea morbidity and mortality and its associated costs. In March 2006 a rotavirus vaccine (Rotarix®) was introduced in the Brazilian immunization program.

Objectives: To assess the impact of rotavirus immunization on ambulatory consultations and hospitalizations and all-cause diarrhoea health costs in children < 2 years.

Methods: The study took place in Sergipe State and Aracaju city in northeast Brazil. Diarrhoea morbidity data and health system's costs were obtained from the State's community health care system (SIAB) and the national public health database (DATASUS). The families' "out-of-pocket" costs were assessed by interviewing care-givers. Ambulatory consultation and hospitalisation incidence trends and associated costs were calculated for 25 months (February 2004- 2006) before and 25 months after (March 2006- 2008) vaccine introduction.

Results: All-cause diarrhoea morbidity in children < 2 decreased during the entire study period (February 2004- March 2008). However, the decreasing trends in ambulatory consultations and hospitalisations were not significant before, and became statistically significant after, vaccine introduction. The vaccine introduction may have contributed to reduce the number of ambulatory consultations, hospitalization expenses and parents' out-of-pocket expenses. These savings, however, did not offset the additional expenses incurred by the costs of the rotavirus immunization.

Conclusions: The reduction in diarrhoea incidence is likely to be multi-factorial, with rotavirus vaccination having an additive effect. Despite a reduced incidence, the vaccine did not result in significant cost savings for the health system. A longer period of follow-up is needed to corroborate these findings.

GENETIC CHARACTERIZATION OF ROTAVIRUS IN CHILDREN WITH ACUTE GASTROENTERITIS, KOREA

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Background and aims: Most common found genotypes of group A rotavirus are G1, G2, G3, G4, and G9. Recently, the detection of unusual genotypes and combination is increasing. The purpose of this study was to investigate the genetic characterization of group A rotavirus during 2007-2009.

Methods: A total of 143 rotavirus positive stool samples were included in the study for genetic characterization. To determine the G and P types, multiplex heminested PCRs were performed. For G-typing, primers for G1, G2, G3, G4, G8, G9, G10 strains were included. PCR for the VP7 gene were performed using Beg9 and End9 primers. PCR for the VP4 gene were done using Con3 and Con2 primers.

Results: The distribution of group A rotavirus genotypes was as follows; G9P[8] (32.1%), G1P[8] (20.7%), G3P[8] (11.7%), G12P[8] (0.7%), and untyped (1.9%). G9 genotypes were predominant during 2007-2008. G1 was predominant and G3 was emerging during 2008-2009. Unusual combination of G and P types were detected and mixed infection were in 15.7%. Phylogenetic analysis of G1 rotavirus revealed that most of strains from 2007 to 2009 clustered in Ic lineage and some in Ia, II, and IV. The G2 strains clustered in IV and V, G3 in IIIId, and G9 in Id, respectively. Most of the P[8] strains clustered in IIIa, and P[4] strains in V.

Conclusions: Continuous surveillance for the detection of various genetic strains and a new genetic recombinant is needed to delineate the clinical correlation and significance of this genetic diversity in future studies.

CAMPYLOBACTER IS THE LEADING CAUSE OF BACTERIAL DYSENTERY AMONG HOSPITALIZED CHILDREN IN THE WESTERN GALILEE REGION IN ISRAEL

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Background and aim: *Campylobacter* is the leading cause of bacterial gastroenteritis in the developed world, especially in children > 5 years old, but has a relatively small importance in dysentery. The aim of the study was to evaluate the bacterial etiology of dysentery in hospitalized children in the Western Galilee Region in Israel.

Methods: A retrospective chart review. The charts of all children hospitalized in the Western Galilee Hospital with gastroenteritis of bacterial origin between 9/07- 8/09 were reviewed.

Results: 99 children were included with 101 pathogens: *Campylobacter* in 61, *Shigella* in 24, and *Salmonella* in 16. The age range was: 8 days-13 years; median: 1.2 years. Dysentery was evident in 63 children (64%) of which 69% were infected with *Campylobacter* and 19% with *Shigella*. Seventy seven percent of children < 1 year of age had dysentery (34/44); *Campylobacter* was the infecting cause in 94%. All children with *Campylobacter* dysentery were < 3.5 years of age. Antimicrobial susceptibilities in *Campylobacter* and *Shigella* for azithromycin were: 98% vs. 46% susceptible, ampicillin: 56% vs. 13%, and ceftriaxone: 63% vs. 96% respectively. There were no statistically significant relationships between pathogens/dysentery and temperature, WBC, electrolytes and season.

Conclusions: *Campylobacter* was the leading cause of gastroenteritis and dysentery among hospitalized children in the Western Galilee Region. *Campylobacter* was more common in children < 1 year of age; these children are more likely to have dysentery. Appropriate empiric antimicrobial therapy for dysenteric children is problematic due to widespread resistance in the causative bacterial pathogens.

BURDEN OF VIRAL GASTROENTERITIS IN HOSPITALIZED CHILDREN IN SPAIN

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Aims: The aim of this study was to obtain epidemiological data regarding the burden of viral acute gastroenteritis in children less than 2 years of age in Spanish hospitals.

Methods: All children aged 1 to 23 months admitted to 3 hospitals during a six-month period (October 2006-March 2007) were followed for the presence of acute gastroenteritis (AGE) from the time of hospital admission until 72 hours after hospital discharge. AGE was defined as the occurrence of at least 1 liquid or 2 semiliquid stools in a 24 hr. period. A stool sample of children with AGE was tested for calicivirus (norovirus and sapovirus), rotavirus, adenovirus and astrovirus by RT-PCR.

Results: Of the 1,576 hospitalized children, 1300 (82.5%) were fully monitored (i.e. our study cohort). A total of 242 children had AGE (18.6% of the cohort) and stool samples from 217 children were obtained (89.7%). Results are shown in table 1 and 2.

Table 1 Frequency of detected viruses	Total		
	Frec.	%	95% CI
Rotavirus	91	42%	35.14-48.73
Norovirus	72	33.2%	26.68-39.68
Astrovirus	7	3.2%	0.64-5.81
Adenovirus	2	0.92%	0.11-3.29
Rotavirus+Astrovirus	6	2.7%	0.35-5.18
Rotavirus+Norovirus	3	1.4%	0.29-3.99
Astrovirus+Norovirus	2	0.92%	0.11-3.29
Rotav.+Astrov.+Norov.	2	0.92%	0.11-3.29
Virus Negative	32	14.7%	9.80-19.70
Total	217	100.0%	

[Frequency of detected viruses]

Table 2 Direct economic costs	Frec. of community cases	Median of hospital days	p25	p75	Spanish cost/day	cost/ case
Rotavirus	56	5	4	6	477.8€	2389€
Adenovirus	1	3	-	-	477.8€	1433.4€
Astrovirus	7	5	5	8	477.8€	2389€
Norovirus	48	6	4	7.5	477.8€	2866.8€

[Direct economic cost]

Conclusions: Between October of 2006 and March of 2007, viruses were detected in 85% of the acute gastroenteritis in hospitalized children 1-23 months old of age; rotavirus was the most frequent, followed by norovirus.

A SINGLE BLIND STUDY ON CLINICAL EFFICACY OF SACCHAROMYCES BOULARDII OR METRONIDAZOLE IN SYMPTOMATIC CHILDREN WITH BLASTOCYSTIS HOMINIS INFECTION

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Introduction: Although many Blastocystis infections remain asymptomatic, recent data suggest it is also a frequent cause of symptoms. Therapy should be limited to patients with persistent symptoms. Our goal was to compare the natural evolution (no treatment) and S.boulardii or metronidazole.

Material and method: Children presenting with gastrointestinal symptoms (abdominal pain, diarrhea, nausea-vomiting, flatulence) since more than 2 weeks and confirmed B. hominis were eligible for inclusion. Randomization was performed by alternating inclusion: group A S. boulardii (250mg twice a day, Reflor[®]) during 10 days; Group B metronidazole (30 mg/kg twice daily) for 10 days; Group C no treatment. At day 15 and 30 after inclusion, patients were re-evaluated and stool samples were examined microscopically. In Group C, children that were still symptomatic and/or were still B. hominis infected on day 15, were treated with metronidazole for 10 days.

Results: There was no statistically significant difference between study groups for age, gender and the presence of diarrhea and abdominal pain. Clinical cure was observed in 77.7% in S. boulardii, 66.6% in metronidazole group, both treatment choices have a better cure rate than without treatment group (40%) on Day15 (p Group A-C =0.031). Disappearance of the cysts from the stools was 80% in Group B, 72.2% Group A and 26.6 % in Group C (p= 0.011 Group B-C;p= 0.013 Group A-C). Cure rate at Day 30 was similar between S. boulardii and metronidazole group.

Conclusion: Metronidazole or S. boulardii have potential beneficial effects in B. hominis infection (symptoms, presence of parasites).

FIRST ROTAVIRUS GENOTYPING DATA IN LITHUANIA

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Background and aims: Lithuania is a member of the first European rotavirus surveillance network, EuroRotaNet, comprising 16 different European countries. In three consecutive RV seasons Lithuania will provide data of 1410 genotyped rotavirus samples. This is the first data of rotavirus genotypes circulating in Lithuania during 2005-2009 seasons.

Methods: Faecal samples, positive for group A rotavirus antigen, were collected at Vilnius University Children's hospital and genotyped according to EuroRotaNet genotyping protocol.

Results: A total of 357 rotavirus positive samples were characterised during three consecutive rotavirus seasons. Samples were collected from different areas of Lithuania, but the majority of it 90.7% were from Vilnius district. A total of 88.8% samples were collected from urban population.

Most common were human rotavirus genotypes G1P[8], G2P[4], G3P[8], G4P[8], and G9P[8], their incidence varied from 84.1 to 96.5% among seasons. Reassortant of human RV strains (G2P[4] and G4P[4]) were detected only in 2005/2006 RV season and occurred in 5.5% of cases. Potential zoonotic strains (G6P[9], G9P[9] and G12P[4]) were found in all seasons and occurred in 2% of cases.

Conclusions:

1. Most common rotavirus genotypes in Lithuania are G1P[8], G2P[4], G3P[8], G4P[8] and G9P[8].
2. Incidence of the genotypes differs among seasons.
3. This preliminary data needs to be confirmed by completing of ongoing study.

ETIOLOGY OF GASTROENTERITIS IN CHILDREN HOSPITALIZED IN THE DEPARTMENT OF PEDIATRICS AT WARSAW BIELANY HOSPITAL; 2008-2009⁽¹⁾

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Background: Rotavirus preventive vaccine, better accessibility of diagnostic methods and hospitalization conditions improvement can affect epidemiological trend of gastroenteritis in children.

Aim: Defining the etiology in community acquired and nosocomial gastroenteric infection in hospitalized children; 2008-2009. Assessment of the correlation with respect to age, sex, hospitalization conditions and epidemiology role.

Materials and methods: We reviewed 654 case histories of patients with colitis and/or gastritis symptoms (17% of all admissions in the period of question). In those cases stool was examined for rota-and adenovirus and additionally for norovirus antigen from march 2009. Stool culture was also analized.

Results: We were able to determine the etiology of gastroenteritis in 48% of the admitted cases. Majority of these were children age 6-24 months old-43%. Colitis was noticed a bit more often in boys-55%. The most often cause of the incidences was viral infection-83%, mostly rotaviral-63%. Norovirus was responsible for 11% and adenovirus for 8% of gastroenteritis. Bacterial etiology was: *Salmonella. Enteritidis* (11%), *Yersinia enterocolitica* (3%), *EPEC* (2%), *Campylobacter jejuni* (1%). We noted a decrease in rotaviral infections- from 79% to 39%. Norvirus accouned for 30% of all gastroenteritis cause in 10 months (from March to December 2009). In the period in question we did not observe a decrease of nosocomial infection incidents (1.5% versus 1.4%).

Conclusions: Results indicate a decrease of rotavirus infections. Norovirus is a significant cause of gastroenteritis in children including ward infections. Unfortunatly there is no decrease of nosocomial infections instead of better hospitalization conditions and respected epidemiology rules.

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ROTAVIRUS GASTROENTEROCOLITIS IN HOSPITALIZED BULGARIAN CHILDREN

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Background and aims: Rotavirus (RV) infection is a major cause of infectious gastroenterocolitis (GE) in children worldwide. The aim of the study was to evaluate the epidemiological and clinical characteristics of RVGE in hospitalized children as well as to determine the G and P types among detected rotavirus strains.

Methods: The study involved children with RVGE admitted to University Hospital, Sofia for the period January-December 2008. Stool samples were tested for RVs by enzyme immunoassay (EIA). Genetic characterization of detected RV strains were performed using reverse transcription-polymerase chain reaction (RT-PCR). All samples were also culture to exclude the presence of enteropathogenic bacteria, i.e. *Shigella* spp., *Salmonella* spp. and *E. coli*.

Results: A total of 117 children with laboratory confirmed RVGE were evaluated. The mean age was 18 months. Nosocomial RVGE accounted for 14 cases (11,9%). Family contact was reported in 5 (4,3%). The peak number of RVGE was in August and September with 18 cases (15,5 %) and 24 cases (20,5%), respectively. Diarrhea, vomiting and fever were the presenting symptoms, commonly in combination. Severe signs of dehydration were found in 76,9% children, requiring intravenous fluid replacement therapy. The dominant RV genotype was G4P[8] (54/116, 46,5%), followed by G1P[8] (29/116, 25,0%).

Conclusions: RVGE is a common cause for severe dehydration in hospitalized children. The disease is not uncommon in summer months. Molecular-epidemiological studies provide important information about rotavirus burden and rotavirus strains in circulation in each country in pre- and postvaccine era.

PROSPECTIVE EVALUATION OF INDIRECT COSTS CAUSED BY ACUTE ROTAVIRUS GASTROENTERITIS: THE ROTACOST PROJECT

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Background and aims: Impact of rotavirus in developed countries is mainly economic. Our aim was to assess the indirect costs induced by rotavirus acute gastroenteritis (RAGE) in Spain.

Methods: A prospective observational study was conducted from Oct-2008 through Jun-2009 including 682 children up to 5 years-old with AGE attended in primary care (n=18), and emergency room and hospital settings (n=10), covering Galicia and Asturias (North-West Spain). All non-medical expenses incurred were recorded in detail using personal interviews and telephone contacts.

Results: Of 682 enrolled children, 207(30.4%) were rotavirus positive and 152(22%) had received at least one dose of rotavirus vaccine. The mean (standard deviation) indirect cost caused by an episode of AGE was estimated at 135.17(182.70)euros. Costs were 1.7-fold-higher when acute gastroenteritis was caused by rotavirus as compared to other etiologies: 192.7(219.8)euros vs.111.6(163.5)euros(p< .001). The costs for absenteeism were the most substantial with an average of 91.41(134.76)euros per family, resulting from the loss of 2.45(3.17) days of work. In RAGE group the cost was 120.4(154)euros compared to 75.8(123) of the other etiologies(p=.002), due to the loss of 3.5(3.6) vs 1.9(2.9)days of work(p< .001). Meals costs were 2-fold-higher in RAGE:48.5(55)vs24.3(46)euros[p< .001]. Travel costs were 2.6-fold-higher in RAGE:32(92)vs12.5(21.1)euros [p=.005]. There were no differences between groups regarding hiring of caregivers or purchase of material costs. Patients with RAGE were admitted to hospital more frequently (47.8% vs 14%)[p< .001].

Conclusions: Rotavirus generates a significant indirect economic burden. These data should be considered in the decision-making process of inclusion of rotavirus vaccine in the national immunization schedule.

THE ROLE OF BREAST MILK IN PREVENTION OF H. PYLORI INFECTION IN EARLY INFANCY**M.A. Moslehi¹, N. Pishva², Z. Alian¹***¹Pediatrics, Shiraz University of Medical Sciences, ²Neonatology Center, Nemazee Hospital, SUMS, Shiraz, Iran*

Background and aims: Breast milk contains different antibacterial and antiviral antibodies in the form of secretory IgA that prevents the adhesion of microorganisms to the gastrointestinal mucosa. Moriera, et al. (2005) suggested that H. pylori infection is associated with surrogate markers of fecal exposure, thus oral route is relevant in the transmission. There are few data available from developed countries to elucidate this association. This study was undertaken to compare the incidence of H.pylori infection between exclusively breast fed and exclusively formula fed infants in similar conditions.

Methods: From March 2005 to September 2006, ninety healthy infants between 2 to 6 months old were studied. Forty-three of the infants were formula fed and 42 were exclusively breast fed. None of the infants were receiving baby food. Fresh stool samples were collected from the healthy mothers and their infants who were referred to Mottahari Well Baby Clinic.

Results: From 90 fresh stool samples studied for H .pylori antigen, 41(46.5%) were found positive. The rate of H.pylori infection in breast fed infants was 32% and in formula fed infants was 60%. The rate of H. pylori antibody in mothers of both groups (breast milk and formula fed) was similar and 70%. The rate of the infection in formula fed infants whose mothers were antibody positive was 60% and in infants whose mothers were sero-negative was 61.5%.

Conclusions: The incidence of H.pylori infection is significantly lower in the infants who are exclusively breast fed (P= 0.006).

IS ROTA VIRUS GASTROENTERITIS A MORE SEVERE ILLNESS IN PATIENTS OF NON IRISH ANCESTRY?

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Introduction: Rotavirus is a leading cause of severe diarrhoea among young children. No clear racial predilection has been demonstrated. In Ireland rota viral infection classically causes a self limiting illness lasting 2-3 days in the local population. We have noticed significant numbers of non-Irish patients attending our paediatric services inflicted with rotavirus tend to become more ill than anticipated.

Aims: The aim of our study was to determine if paediatric patients in Ireland of non-Irish ancestry suffer a more protracted illness with rotavirus gastroenteritis than their Irish counterparts.

Methods: Patients who attended a paediatric hospital between 01/01/2007 and 31/12/2008 with a diagnosis of rotavirus gastroenteritis their case notes were reviewed and the following information recorded: necessity of hospital admission, length of stay, level of dehydration, electrolyte abnormalities and other complications.

Patients were segregated into 2 groups according to information obtained from their social history (Irish vs. non-Irish ancestry).

Results: During the 24 month study period 286 patients met the inclusion criteria of whom 252(88%) were of Irish and 34(12%) of non-Irish ancestry. Hospitalisation was required in 85% (242) of cases 88% of the non-Irish and 84% of the Irish group. Moderate dehydration was seen in 44%(15) of the non-Irish and in 35%(89) of Irish group.

Average length of stay in hospital for Irish patients and non Irish patients was 2.3 and 3.08 days respectively.

Conclusion: Children of both Irish and non-Irish ancestry exhibit significant morbidity when infected with rotavirus with the latter group suffering a more severe illness hence extra caution is required in their management.

NOROVIRUSES IN SEASONAL ACUTE GASTROENTERITIS IN CHILDREN ADMITTED TO HOSPITAL

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Background and aims: Noroviruses (NoVs) are important causative agents of acute gastroenteritis (AGE) in children. The role of NoVs will be emphasized after reduction of rotaviruses (RVs) following vaccinations. NoV genotype GII.4 has recently emerged as a predominant NoV type. We investigated the incidence and circulating genotypes of NoVs in children hospitalized or seen as outpatients.

Methods: A prospective study of AGE was conducted from August 2006 to August 2008. Stool samples were collected from children aged < 15 years seen in the outpatient clinic or hospitalized for AGE. NoVs and RVs were analyzed by RT-PCR and sequenced.

Results: A total of 809 stool samples were studied. NoV was found in 218 (27%) cases: in 118 (35%) of 341 stools obtained in the 1st and in 100 (21%) of 468 stools in the 2nd season. Genotype GII.4 predominated with 113 (96%) cases in the 1st season and 74 (74%) cases in the 2nd season. Other NoV genotypes seen in order of frequency were GII.7, GIIB, GI.3, GII.1, GI.4, GI.6, GII.2 and GIIC. There were no cases with more than one type of NoV present. RVs were found in 128 (38%) and 293 (63%) cases in these two seasons, respectively. Mixed infections with both NoV and RV were found in 12 and 25 cases, respectively.

Conclusions: In a "low" RV season NoVs were equally common as RVs as causative agents of acute GE in children admitted to hospital. NoV genotype GII.4 predominated over the other NoV types.

CLINICAL AND RADIOLOGICAL FEATURES OF ROTAVIRUS CEREBELLITIS

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Background and aims: The purpose of this retrospective study was to identify and report the clinical and radiological features of rotavirus cerebellitis.

Methods: Patients with rotavirus gastroenteritis exhibiting cerebellar lesions on MRI were collected from multiple centers in Japan. Their clinical, laboratory, and radiologic data were reviewed retrospectively.

Results: Thirteen patients were identified. A diagnosis of acute cerebellitis was made for 11 of the 13 patients; injury due to hypovolemic shock for the other two patients. All 11 patients with acute cerebellitis had disorders of consciousness with onset on days 2 to 4, followed by mutism in 10. Other cerebellar symptoms included slow speech or dysarthria following the mutism, hypotonia, ataxia, and dysmetria. MRI lesions in the vermis or cerebellar cortex were seen at some point (day 5 to 1 month) in nine. A reversible splenial lesion (three isolated and three with concurrent cerebellar lesions) was found in six patients scanned between days 4 and 6. Transient lesions in the cerebellar white matter/nuclei were seen in six patients during days 5 and 7. The final MRI performed after 1 month showed cerebellar atrophy in eight patients.

Conclusions: The 11 patients with rotavirus cerebellitis exhibited nearly identical clinical and MRI features. Involvement of the cerebellar white matter/nuclei may be associated with the mutism characteristic of rotavirus cerebellitis. An isolated splenial lesion with homogeneously reduced diffusion is not always a benign sign indicative of complete clinical and radiological recovery in patients with rotavirus gastroenteritis.

EFFECT OF HERPES VIRAL INFECTIONS ON CLINICAL COURSE CHRONIC VIRUS HEPATITIS C IN CHILDREN

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Aim: To study the effect of herpes virus infections on children clinical course of chronic virus hepatitis C.

Methods: We observed 25 children (12.1 years \pm 1.1 years) with HCV. The diagnosis was confirmed by detection RNA in blood serum by PCR and histological markets of chronic hepatitis. All children were subjected to serologic blood examination by immune-enzyme analysis method (IEA) showing the presence of IgM and IgG to cytomegalovirus (CMV), IgM and IgG to viruses of simple herpes 1-2 types (HSV 1-2), IgM and IgG to Varicella-zoster virus (VZV), presence of Epstein-Barr virus markers (EBV): IgM-VCA-EBV, IgG-EA-EBV, IgG-NA1-EBV, and also defining DNA of CMV, EBV, HSV 1-2, human herpes virus 6 type (HHV6) in blood cells with PCR method.

Results: Active herpes virus infection was found in 24 of 25 children (96%). In this group EBV infection have 6 children (24%), HSV1-2 was revealed in 12 cases (48%), HHV6 was found in 8 children (30%). CMV we diagnosed only in 1 case. 83% of then have combinatory herpes viruses and 4 children have mono herpes form (16.7%)/ HCV with HSV1-2 and HHV6 infections have higher level of cytolysis (ALT 110 ± 14.3 opposite 66.1 ± 5.7 Ед/ml). Cholestatic hepatitis with high level of GGT and AP we found in children with HCV and HSV1-2 infections: (GGT 56.7 ± 5.4 opposite 20.1 ± 1.6 Еl/ml, $p < 0.001$).

Conclusion: Combinatory herpes viruses (especially HSV1-2 and HHV6) and HCV infections have unfavorable course with high citolysis and cholestasis.

ASSOCIATION BETWEEN INFANTILE COLIC AND INTESTINAL LACTOBACILLUS MICROFLORA

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Background and aims: Infantile colic is a common problem for family and health professionals. The cause of it has not been definitely identified. The aim of this study is to determinate the association between infantile colic and intestinal microflora.

Methods: This case-control study employed in two groups of breastfeeding term infants, aged between 16-60 days, 35 colicky (Case) and 35 non-colicky (Control) infants.

Colic defined by the Wessels criteria (Rule of Three). Stool samples were cultured on selective media. Subspecies of lactobacilli in two groups were defined by specific tests.

Results: The mean ages of colicky and non-colicky infants were 39.2 ± 11.6 and 41 ± 5.9 days respectively. Different colonization pattern of lactobacilli were found among colicky and non-colicky infants. *Lactobacillus acidophilus* was found only in non-colicky infants (7 versus 0) and *Lactobacillus Plantarum* and *Holotolerans* only in colicky ones. (2 versus 0).

Conclusions: Different intestinal lactobacillus flora in colicky and non-colicky infants may contribute to the cause of colic and further studies recommended.

CHILDREN´ INFECTIVE ENDOCARDITIS FROM 1992 TO 2008 IN ROUEN HOSPITAL**M. Caseris**, I. Durand, E. Mallet, D. Pinquier*Rouen University Hospital, Rouen, France*

Background: Infective endocarditis in children is rare. The purpose of our study was to assess the characteristics of children with endocarditis in our hospital, their diagnostic and their treatment.

Methods and results: We conducted a 17-year retrospective review of children treated for endocarditis in Rouen hospital from 1992 to 2008. 15 children were included, median age was 9 years. 87% had congenital heart disease with mainly ventricular septal defect. None of them were neonates, neither on central catheter. None of them were classified as « rejected endocarditis » according to the Duke criteria. In 47% of cases *S. aureus* was found, always meticilline sensitive. 87% of children had echocardiographic signs of endocarditis. 84,7% were treated by synergic double antibiotherapy adapted to the bacteria. 67% had complications and 13% needed cardiac surgery in emergency. There's no death in our cohort, but one relapse. Antibiotics were administred before the realisation of hemocultures in 47% cases, and a bad dental hygiene was found in 20% children at risk of endocarditis, showing the need to enhance the education of parents, general practitioners and dentists of children at risk.

Conclusion: Infective endocarditis is rare with a classic children at risk profil in our cohort. Diagnostic and therapeutic are well done in our hospital, but complications are still high. Enhancing education appears usefull.

IMMUNE RECONSTITUTION OF PERIPHERAL LYMPHOCYTE SUBSETS IN BRAZILIAN CHILDREN WITH VISCERAL LEISHMANIASIS TREATED FOR 30 DAYS WITH MEGLUMINE ANTIMONATE

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Background and aims: In Northeastern Brazil, visceral leishmaniasis (VL) is an endemic disease caused by *Leishmania donovani chagasi*. We have assessed the immune reconstitution of peripheral lymphocytes in children and adolescents with VL treated with meglumine antimonite for 30 days.

Methods: 24 patients (F/M: 14/10) with symptomatic VL with median age of 3.5y (Q1-Q3: 2.1-5.5) diagnosed by microscopic identification of the parasite in bone marrow aspirate were assessed before (T1), immediately after (T2) and 3-6 months (T3) after treatment. A 4-mL peripheral blood sample was collected at the 3 time points. Immunophenotyping of lymphocytes was performed by flow cytometry and compared with 104 age-matched healthy controls from Sao Paulo, a non-endemic city in the Southeastern region of Brazil.

Results: Hemoglobin levels, leukocytes and platelets increased in concomitance with clinical improvement. Total lymphocytes, CD3+ T cells, CD4+ T cells, CD8+ T cells and NK cells reached normal levels for age at T2. B cell numbers increased at T2, but expected values for age were only attained at T3. An expansion of peripheral memory and terminally differentiated CD4+ T cells was observed at T2 and T3, with a return to CD25 expression at T2. CD8+ T cells had an increase of the terminally differentiated subset, but activation as assessed by CD38 expression and cytotoxic activity indirectly evaluated through CD56 expression were maintained at T3.

Conclusions: Despite an increase in peripheral lymphocyte numbers, after 3 months of treatment of VL, patients still present with activation markers in cells from peripheral blood.

IMMUNOLOGICAL AND VIROLOGICAL RESPONSES IN HAART ERA IN THE MADRID COHORT OF HIV-INFECTED CHILDREN

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Background and aims: To describe the immunological and virological responses in naïve HIV-1 infected children who started HAART at 6,12 and 24 months and to compare it in two periods of time in the HAART era.

Methods: 108 naïve perinatally HIV-1 infected children started HAART since 1997 in the Madrid cohort until December 2008. 93 patients were selected out fulfilling the criteria of HAART initiation with 2 NRTI plus either 1 NNRT or 1 PI. The follow-up time was 24 months. Those patients who switched antiretroviral therapy were considered virological failures. Two periods were compared: A (1997-2003) and B (2004-2008).

Results: 65 children started HAART in period A and 28 in period B. Median age at HAART initiation was 4.5 years. 52% were female, 25% were from immigrant origin (10% Hispanic, 15% Sub-Saharan Africa). A PI-based regimen was given in 75% (nelfinavir 48%, lopinavir/ritonavir 25%, others 27%) and a NNRTI-containing regimen in 25% (EFV 73%, NVP 27%). By intent to treat analysis, an undetectable viral load (< 400 copies/ml) was maintained at 24 months in 55% children. In period A, 40% of children achieved undetectable viral load compared to 78% in period B ($p < 0.01$). Baseline and follow up data are represented in Table 1

Median	CD 4 percentage	CD4 count	Plasma HIV-RNA Viral (copies/ml)
Baseline	18	378	103400
6 month	24,7	519	<400
12 month	32	686	<400
24 month	30	775	<400

[Table

1]

Conclusions: With the advent of HAART, most naïve patients maintained an undetectable plasma viral load with an increasing rise in CD4 over time. Virological responders increased over time.

TUBERCULOSIS AND RISK OF DEATH WITHIN ONE YEAR OF ANTIRETROVIRAL THERAPY INITIATION IN CHILDREN

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Background and aims: Tuberculosis (TB) is common in HIV infected children with immune deficiency. We investigated factors associated with risk of death after initiation of antiretroviral therapy (ART) in HIV co-infected children.

Methods: Data prospectively collected between December 1999 and December 2007 in the PHPT Observational Cohort of Children on ART were used. The role of baseline factors; i.e. age, sex, type of caregiver and household income, HIV stage, CD4%, HIV RNA load, and first line regimen, in the risk of death of ART naïve children during the first year of ART initiation, was studied using Cox regression models.

The TB group included all children treated for active TB less than 9 months before or within one year of initiation of ART.

Results: There were 55 and 507 children in the TB and the non-TB groups with, respectively, baseline median age 8 and 7 years ($P=0.20$), CD4 3% and 7% ($P=0.01$), HIV RNA load 5.34 and 5.09 \log_{10} copies/ml ($P=0.004$). 22 and 8 deaths were recorded (97% related to infection), respectively. The cumulative risks of death at one year was 15.0% in the TB group versus 4.5% in the non-TB group ($P=0.001$). However, in a multivariate analysis, only baseline HIV RNA load ($P=0.02$) and CD4% ($P=0.04$), and not TB ($P=0.20$) remained significantly associated with the risk of death.

Conclusions: Children affected by TB were at higher risk of death but this risk was mainly explained by the intensity of HIV replication and the level of immunodeficiency.

VACCINATING HIV-POSITIVE CHILDREN IN THE WEST MIDLANDS**L. Teoh***Heartlands Hospital, Birmingham, UK***Objectives:**

- 1) To design a vaccination proforma tailored for our population of children with HIV.
- 2) To test the feasibility of obtaining all their vaccination records
- 3) To find out how many are fully immunised according to standard UK vaccination schedules, and how many are subsequently protected against those diseases.00

Method: The proforma is based on the latest guidance from CHIVA and the Department of Health. It includes age of diagnosis, previous immunisations, CD4 status, serology results, foreign travel and previous contacts with illness. An appropriate vaccination schedule is then recommended.

Results: Vaccination records were obtained for 85% of children, although 20% of these had to be contacted by phone. The vaccinations requested in the notes had only been given in 39% of cases.

Very few children were fully protected against any of the diseases. The most striking lack of protection was against Hep B, followed by Pneumococcus and Meningitis C. Only two children had been given the varicella vaccine, but most children had natural immunity.

Conclusions: Vaccinations in our population of HIV children are currently haphazard. This is partly due to the large number of factors to consider for each child, and the lack of clear national guidelines. Other causes are poor compliance, a mobile patient group, and imperfect communication between general practitioners and paediatricians.

Having piloted a vaccination proforma, and obtained vaccination records for the majority of children, we hope to improve our immunisation coverage in this vulnerable population.

CLINICAL PRESENTATION OF PAEDIATRIC HIV INFECTION IN THE PREVENTION ERA

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Background: This study reviews the diagnosis of HIV infected children in the era of successful antenatal intervention programmes in order to facilitate earlier diagnosis and inform screening programmes.

Methods: Retrospective chart analysis of HIV infected children presenting for the first time to our unit from 2004-2008. A missed opportunity for earlier diagnosis was defined as any hospitalisation in Ireland prior to diagnosis. CDC disease classification was used.

Results: 24 infected children, 19 newly diagnosed at presentation, were identified. 22/24(92%) were born to African mothers, 17/22(77%) in Africa. Of African-born children, 4 were diagnosed prior to arrival in Ireland, 2/4 had received ART there.

21/24(87.5%) were vertically infected. Maternal seroconversion in pregnancy was documented in 3/5 Irish born children. Diagnosis followed a parental diagnosis in 13/24 (54%) and 11(46%) were the index case in the family (2/11 diagnosed as part of the asylum screening process, 9/11 with symptomatic diseases).

Excluding those diagnosed before arrival in Ireland (5) and infants monitored from birth (2), the median age at diagnosis of 17 late presenters was 11 yrs (range 0.3 - 16.1). 7/17(41%) late presenters had a missed opportunity for earlier diagnosis with median time lapse 1.8yrs (range 0.1 - 4.4), 5/7 had CDC stage C disease at diagnosis.

Conclusion: Some children acquire infection despite antenatal prevention programmes, mostly due to maternal seroconversion. Repeat testing in pregnancy could impact this.

The missed late presentation and missed opportunities for earlier diagnosis highlights the need for a more proactive approach to HIV testing of children.

NON-TOBACCO SUBSTANCE & SEXUAL ABUSES INFLUENCING HIV TRANSMISSION AMONG STREET CHILDREN IN KOLKATA CITY

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Background & aims: Globally, an estimated number of 300 million street children are struggling for basic needs to survive. Kolkata, one of the four major metropolitan cities of India, has an estimated number of 10,714 street children. Deprived of basic needs, a large number of street children in Kolkata are known to be the victims of sexual exploitation and addiction to different substances. Substance and sexual abuses have been documented as two important socio-behavioral problems associated with blood borne infections like HIV & STIs among them. This study was conducted to understand the problem of non-tobacco substance & sexual abuse among street children that might facilitate HIV/STI transmission.

Methods: It was a community-based cross-sectional study. A total of 554 street children (out of 600) were selected using conventional cluster sampling technique for 'Hard-to-Reach Population'. Informed consent was obtained. A pre-tested questionnaire was introduced for studying risk behaviors. Following interview, 3 - 4 ml blood sample was collected for testing HIV & STIs. Data was analyzed using 'Epi Info'. Ethical clearance was obtained from Institutional Ethical Committee of National Institute of Cholera & Enteric Diseases, Kolkata.

Results: The study revealed the prevalence of non-tobacco substance & sexual abuse of 30% and 9% respectively. Sero-prevalence of HIV was 1% and VDRL was 4%. The study also highlighted a number of factors associated with said abuses.

Conclusions: This 1% HIV sero-prevalence in street children is a matter of concern. An urgent community-based intervention is required to prevent further spreading of HIV in them.

EVALUATION OF HIV-1 GENETIC DIVERSITY IN INFECTED MOTHERS FROM TWO REGIONS OF PORTUGAL ENROLLED IN A STUDY OF MOTHER-TO-CHILD TRANSMISSION

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Background and aims: A significant decrease in HIV mother-to-child transmission (MTCT) has been observed in Portugal. Nevertheless, new cases of MTCT still occur every year in our country.

It has also been suggested that geographical differences in the prevalence and rates of MTCT may be affected by the diversity of HIV-1 genetic forms.

We evaluated the molecular diversity of circulating viral subtypes and their potential impact on HIV-1 MTCT by analysing HIV-1 infected mothers from two major cities in Portugal.

Methods: Assignment of a viral subtype was achieved by sequencing *env* C2V3C3 region and *nef* gene from 68 HIV-1-infected mothers living in Oporto (n=15) and Lisbon (n=53) area. Conservation/disruption of functional domains in target regions was also investigated.

Results: Combined molecular data analysis revealed that, globally, subtypes B, G and the recombinant forms BG and AG accounted for 100% and 64% of all viruses identified in mothers living in Oporto and in Lisbon area, respectively. The genetic forms classified as A, D, F, AJ, DG, AU, CU, AGEG were exclusively identified in Lisbon group.

The high prevalence of non-B variants found in both regions was predominantly associated with the African origin of mothers ($p=0.017$). No significant differences were found between transmitter and non-transmitter mothers and a specific genetic form. Despite the occurrence of signatures, which were associated to viral diversity, the analysis of Env and Nef motifs revealed a high degree of conservation.

Conclusions: Continuous surveillance is required to be aware of the HIV diversity impact in antiretroviral drugs susceptibility.

HRQOL IN HIV-INFECTED CHILDREN USING PEDSQL™ 4.0 AND COMPARISON WITH NON-INFECTED CHILDREN

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Background and aims: To assess the reliability and validity of Pediatric Quality of Life Inventory 4.0 (PedsQL™ 4.0). Also to determine the association of HIV infection, treatment regimens and type of care received on QoL in paediatric patients.

Methods: Study was conducted from January to December 2008 at Dr. Ram Manohar Lohia Hospital, New Delhi, India at HIV paediatric OPD. PedsQL™ 4.0 was administered to 100 HIV-infected and 200 uninfected children aged 8-12 years and their primary caregivers.

Results: Internal consistency reliability exceeded 0.70 for both proxy-reported and self-reported scales. Intraclass correlation coefficient demonstrated mainly larger values for parent proxy-report (interval of 0.926 to 0.952 with 95% confidence) than for child self-report (interval of 0.891 to 0.928 with 95% confidence). Factor analysis showed that 5 factors were optimal and were extracted from PedsQL. HIV infection was associated with a negative impact on QoL among children with lower scores for physical, school, and emotional functioning and health symptoms. In contrast, uninfected children had lower social functioning scores. Our results showed antiretroviral treatment to be associated with improved QoL among HIV-infected children. We even identified infected children living at home to be at a higher distress of psychosocial functioning and health symptoms when compared with children living in care homes.

Conclusions: PedsQL™ is a reliable and valid measure of QOL for children living with HIV/AIDS and uninfected group. Application of this data will be helpful for programme managers to device care and support programme for both infected and uninfected children.

IMPACT OF HAART ON SURVIVAL, WEIGHT GAIN AND RESTING ENERGY EXPENDITURE IN HIV-1-INFECTED CHILDREN IN INDIA

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Background and aims: In resource-limited countries, use of HAART in HIV-infected children is still poorly documented in terms of impact on survival, immune system and growth. This study evaluates the effect of HAART on survival and immune response in HIV-infected children and investigates response to nutritional support.

Methods: In December, 2002 a cohort study was carried out on vertically transmitted children and was observed longitudinally for CD4⁺ T-cell count, antiretroviral treatment and weight until last follow-up on 31 December 2007. Z-scores were calculated for CD4⁺ T-cell count to account for age-related differences. Nutritional supplementation was given to these children and resting energy expenditure (REE) was calculated.

Results: Total of 180 children were assessed, 100 (56%) of whom were on HAART. Baseline BMI differed in the two groups ($p < 0.05$). Median duration of survival from diagnosis date was 15.1 years. Survival was significantly longer for those on HAART. During HAART, a CD4 Z-score increase of 1 SD was associated with a 0.35 increase in weight Z-score ($p < 0.001$). The increase in the daily energy intake due to nutritional supplementation was associated with the gain in weight Z-score while REE was independently associated with change in body weight Z score both in HAART and no-HAART groups ($p < 0.001$).

Conclusions: Survival rates of children improved which correlated with an increase in CD4⁺ T-cell count concurrent with the expanded use of HAART. HAART had a positive effect on growth in HIV-1-infected children. Nutrition supplementation improved the health of children in no-HAART and HAART groups.

10 YEARS OF EXPERIENCE IN PROPHYLAXIS OF MATERNO-FETAL TRANSMISSION OF HIV INFECTION IN CONSTANTA COUNTY

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Introduction: Constanta is one of the most affected county by HIV from Romania. In the last years we noticed an increasing number of children exposed to HIV through mother-to-child transmission.

Objective: To assess mother-to-child transmission (MTCT) rate of HIV infection over a period of 10 years (January 2000 - December 2009).

Material and method: Relevant parameters in children: birth weight, duration and type of antiretroviral treatment (ARVT), ELISA-HIV and viral load (VL). Relevant parameters in mothers: type of delivery, ARVT received previously/during delivery, VL and CD4 count. Statistical analysis was performed using student test (t-test).

Results: MTCT rate decreased gradually from 40% in year 2000 to 0% in years 2006, 2007, and 2008 ($p = 0.003$). 92 children and 76 HIV+ mothers have been monitored. Out of the 92 children, 10 were HIV+, and 82 were HIV- ($p = 0.0038$). All 28 children who were under 18 months of age present VL < 50 copies/ml, except two infants. Out of the 92 children studied, only 2 deceased. 81 children received ARVT after birth: 5/10 of HIV+ and 76/82 HIV-. Only 9 infants were breast feed (5/10 of HIV+ and 4/82 HIV-). From all deliveries 16 were vaginal (5/10 of HIV+, 11/82 HIV-). Out of all 76 HIV+ mothers, 60 received ARVT during pregnancy/delivery. At delivery, mothers' CD4 median value was 430.7/mm³. In 44 mother-child pairs with complete ART prophylaxis, MTCT rate was 0%.

Conclusions: After January 2000, the MTCT rate continuous decreased. The MTCT rate was 10.86% in Constanta County.

THE PREVALENCE OF VITAMIN D DEFICIENCY IN A COHORT OF HIV INFECTED CHILDREN IN THE SOUTH-WEST OF THE UK

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Background and Aims: The prevalence of vitamin D deficiency in HIV+ individuals is variable and the role played by the virus is uncertain. Furthermore, the introduction of HAART treatment, in particular with NNRTIs, has been associated with symptomatic deficiency. It is recognised that vitamin D plays a role, not only in bone health, but also in the function of the immune system. Vitamin D deficiency is also associated with an increase in the risk of cardiovascular disease. Despite this, the prevalence of vitamin D deficiency in HIV+ children in the UK is unknown. Vitamin D levels in children under the care of a paediatric hospital in the South-West of the UK are described.

Methods: The serum 25-hydroxy-vitamin D levels were measured in 27 HIV+ children (3-18 years). The relationship between vitamin D levels, anti-retroviral treatment and CD4 counts was assessed.

Results: 58% of children were deficient (< 50nmol/L) or severely deficient (< 25nmol/L) in vitamin D. In 23% this was associated with a raised PTH level. Only 27% were found to have adequate (>75nmol/L) levels. The HAART treatment the children were receiving did not influence this, nor was there any association with CD4 counts/percentages.

Conclusions: There is a high prevalence of vitamin D deficiency in HIV+ children. This has implications for bone health but may also compromise immune function. Minimising risks of cardiovascular disease is also central to maximising life expectancy as vertically infected children enter adulthood. The development of evidence-based treatment strategies in this area is urgently needed.

REDUCED CD4+ T CELL COUNTS AND HIGH B CELL APOPTOSIS IN VERTICALLY HIV-EXPOSED NON-INFECTED CHILDREN AND ADOLESCENTS

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Background and aims: The HAART has decreased the vertical transmission of HIV-1 infection permitting the birth of many HIV-exposed non-infected (ENI) children. Nowadays, the concern is whether HIV and/or antiretroviral exposure could cause long-term consequences to those children and adolescents. The aim of this study was to evaluate lymphocyte subsets, their activation markers and spontaneous apoptosis in ENI children and adolescents who were or not exposed to antiretroviral drugs during pregnancy and early infancy.

Methods: We assessed 20 vertically HIV-exposed non-infected children and adolescents who were or not exposed to antiretroviral (ARV) drugs during pregnancy and early infancy. ENI children and adolescents were aged 6-18 years and they were compared to 25 age-matched healthy non HIV-exposed children and adolescents (Control). Immunophenotyping of lymphocytes was performed, including immune activation and apoptosis evaluation.

Results: ENI individuals had lower CD4+T cells/mm³ (Control: 1120.3 vs. ENI: 876.3; t test, p=0.030) and higher B cell apoptosis levels than Control group (Control: 36.6% vs. ENI: 75.4%; t test, p< 0.001). When ENI children and adolescents were separated according to antiretroviral exposure during pregnancy and early infancy, both ENI individuals who were exposed and not exposed to ARV had higher B cell apoptosis than Control group (Control: 36.6%, ARV exposed: 82.3%, ARV non-exposed: 68.5%; Kruskal-Wallis, p< 0.05), but no statistical difference was noticed between those exposed and not exposed to ARV.

Conclusions: Subtle long-term immune alterations that might persist among ENI individuals, but the clinical consequences if any are unknown, and these children require continued monitoring.

STARTING HAART IMMEDIATELY AFTER BIRTH LED TO A LACK OF EVIDENCE OF VIRAL REPLICATION AND HIV-1-SPECIFIC IMMUNE RESPONSES

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Background: The success of HAART has changed the natural course of HIV-1 infection. However, individuals with a long period of undetectable HIV-RNA still have viral replication since latently infected resting memory CD4+ T cells persist.

Methods: A child who was born from an HIV-infected mother was examined. The baby was started on HAART immediately after birth and maintained undetectable viremia during the following 22 months. HIV antibody tests, plasma viral load, proviral load and HIV-specific immune responses were assessed in order to establish or discharge definitive HIV infection in the baby.

Results: At birth, the baby had HIV-positive antibodies, as expected. Plasma HIV-RNA was 10,000 copies/mL. Moreover, HIV-DNA was positive in PBMC in several longitudinal exams conducted within the following 3 months of life. After 22 months on stable HAART, HIV antibodies were negative by EIA and Western Blot. Proviral-DNA was repeatedly negative, as well as HIV sequences examining distinct regions of the pol and env genes. Then, specific cellular immune responses against gag and env proteins were negative. On the basis of these results, HAART was interrupted. On day 22 after stopping HAART, plasma HIV-RNA rebounded to >500,000 copies/mL and CD4+ T-cells dropped to 13%. HAART was immediately resumed and HIV antibodies became detectable at this time.

Conclusions: Very early HAART use in newborns from HIV-infected mothers may be associated with long-term control of viral replication, lack of HIV antibody production and good clinical and immunological outcomes.

MOTHER TO CHILD TRANSMISSION OF HIV INFECTED PREGNANT WOMEN FROM 2000 TO 2007 IN CATALONIA (SPAIN): THE NENEXP PROJECT

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Background and aims: Despite the availability of highly effective preventive measures, HIV mother to child transmission (MTCT) is still a matter of concern in developed countries.

Aim: To assess the rate of HIV MTCT and its risk factors in an 8-year cohort study in Catalonia.

Methods: Mother-infant pairs were included if maternal HIV infection had been diagnosed before or during pregnancy, or within 72 hours post-delivery. Means and percentages were calculated with 95% confidence intervals for quantitative and categorical variables, respectively. Odds ratios (ORs) were calculated to assess transmission rates determinants on the basis of the comparison of HIV-infected and uninfected babies.

Results: Overall 579 pregnant women, 647 pregnancies and 663 infants were enrolled in the NENEXP project during 2000-2007. Nine out of 663 infants were diagnosed with HIV infection, transmission rate of 1.36 % (95% CI: 0.62%-2.56%).

From univariate analysis, late diagnosis of maternal HIV infection (at or after delivery, 2% of HIV-infected mothers) and vaginal instrumented delivery were risk factors for MTCT.

In the multivariate analysis receiving ART during pregnancy, low (< 1000 copies) maternal viral load and male gender of the infant decreased the risk of MTCT.

Late identification of maternal HIV infection was confirmed as a risk factor for HIV MTCT.

Conclusions: Unknown HIV maternal status at delivery was observed in 2% of HIV-infected pregnant women, being the main risk factor for MTCT in our study.

An effort to both early identification of HIV-infected women and fully implement effective HIV MTCT preventive measures is needed.

AN ANIMAL ASSISTED THERAPY (AAT) PROGRAMME FOR CHILDREN WITH HIV

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Aims: The aims of this programme were: 1. to experiment Animal Assisted Therapy (AAT) for children with HIV infection, 2. to evaluate if “taking care of the dog” could help in opening channels of communication about the illness and assist in the elaboration and transformation of anger and depression issues.

Methods: For a period of six months, eleven children from 5 to 14 years of age, divided in two groups: group 1 with knowledge of diagnosis and group 2 not yet informed of diagnosis, were involved in bimonthly AAT sessions. The setting was a adequately large room of the hospital and the actors were children, 2 dog-handler teams, the psychologist, a special needs teacher and the head nurse.

Results: Encounters with the dog allowed the children to verbalise very intense personal experiences: fear, anger, suffering, death fantasies, need of affection and nurturing. The small group size, with peers of the same health condition, allowed them to experience mirroring and alleviate feelings of loneliness and diversity. In the sessions with the psychologist of the hospital, significant changes were observed: all the children spontaneously spoke of encounters with the dog, externalising emotions that they had not discussed for a long while.

Conclusions: Overall, in this experience, the relationship with the dog proved a powerful vehicle and activator of deep set emotions and AAT proved a valuable tool that enhanced the ability and intervention of the health professionals in the difficult task of supporting children with HIV infection.

IMPROVEMENT IN ADHERENCE AND QUALITY OF LIFE IN HIV ADOLESCENTS USING ONCE-A-DAY COMBINED TABLET OF EFAVIRENZ+EMTRICITABINE+TENOFOVIR (ATRIPLA®)

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Background: Adolescence is a complicated life period in which HIV patient commonly have low levels of adherence. One of the ways to improve adherence may be to reduce the usually high number of pills by using combined products with more than one drug.

Methods: Retrospective study of three patients currently on a single daily dose of Atripla® tablet (EFV + FTC + TDF), in the beginning and after at least six months of treatment.

Results: Main results are exposed in table. Patient 1 has been on combined EFV + FTC + TDF for 8 months, patient 2, 12 months and patient 3, 6 months. None of them have had nor previous failure or experience with 3TC and the only case with past contact with NNRTI was patient 2 (NVP during 5 months). Patient 3 was interrupted unilaterally by the parents. All three patients reported an important improvement in quality of life since the beginning of this therapy.

Conclusions: Combined EFV + FTC + TDF is a good safe option in selected HIV-infected adolescents, showing maintained viral suppression and an improvement in quality of life.

	Gender	Age (years)	Viral load before/after Atripla® (copies/ml)	CD4 before/after Atripla® (cells/ μ L(%))	Total cholesterol before/after Atripla® (mg/dl)	Triglycerides before/after Atripla® (mg/ml)	Adherence before/after Atripla® (%)	Previous treatment to Atripla®
1	M	15	<37/<37	1950(37)/1575(33)	146/137	123/44	85-95/>95	FTC+DDI+ FOS/rtv
2	F	17	<37/<37	1260(37)/1874(38)	151/167	89/64	65-75/>95	FTC+DDI+ EFV
3	F	12	23600/<37	357(15)/456(15)	117/144	69/107	- />95	Interrupted during 5 years (see text)

[Table 1]

OUTCOME OF *PNEUMOCYSTIS JIROVECI* PNEUMONIA IN HIV-INFECTED CHILDREN AT A UK INTENSIVE CARE UNIT IN THE HAART ERA, 1999-2008

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Background: *Pneumocystis jirovecii* pneumonia (PCP) is the commonest presenting opportunistic infection in undiagnosed HIV-infected infants. It continues to have high mortality. We present a retrospective case series spanning ten years, of children aged under two years admitted with PCP to St Mary's Hospital London, a tertiary hospital serving a large paediatric HIV population.

Results: Nineteen HIV-undiagnosed children presented with PCP. Median age at admission was 4 months. All received cotrimoxazole and corticosteroid therapy. Median length of PICU stay was 13.5 days (range 1 - 64). All required mechanical ventilation (median 6 days, range 1-64). Mortality was 7/19 (37%). Non-survivors spent longer in PICU than survivors (28.5 vs 9 days, $p=0.037$), and survival was not significantly different with stratification by sex, age, CD4 count, viral load or initial alveolar-arterial oxygen gradient.

CMV co-infection or colonisation was identified in 11/19 (58%) of infants; of these nine received ganciclovir. There was a non-significant trend towards increased mortality in CMV-positive (5/11, 45%) versus CMV-negative patients (2/8; 25%).

Conclusion: Whilst the number of HIV-infected infants born in the UK has dramatically reduced due to antenatal screening and MTCT interventions, undiagnosed cases presenting with PCP remain at high risk of severe disease and death. The survival data presented here are comparable to those from a decade ago, in stark contrast to improvements in other areas of HIV care. Whilst delayed suspicion of HIV and possibly CMV infection might contribute, management of PCP is hindered by our poor understanding of PCP immunopathology and its optimal treatment.

EVOLUTION OF THE STRUCTURED TREATMENT INTERRUPTION IN HIV INFECTED ADOLESCENTS

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Structured interruption for HIV pediatric antiretroviral treatment is controversial, and questionable for cases of "intolerance, obvious non-observance or patient's choice" (Yeni, 2008). But adolescents with chronic illness are often non- or poorly observant, repeatedly asking to stop treatment. For HIV infection, both non-observance for anti-retroviral treatments and viral resistance to molecules impact on life expectancy.

Background and aims: Faced with poor observance in adolescents, doctors often doubt. Structured treatment interruption modifies the doctor/adolescent relationship and allows for addressing their illness differently, which is important for these adolescents who most often have been asymptomatic for a long time.

Methods: In the pediatric consultation for infection at Montpellier University Hospital, under optimal conditions (high nadir and $CD4 \geq 20\%$ ($350/mm^3$)), and after failed personalized assistance, the treatment was interrupted with a strict follow-up care jointly with a psychologist. Treatment resumed at the rate of $CD4 < 350/mm^3$.

Results: Treatment interruption was proposed to 5 out of 29 children, actually all 14 years old girls. Two returned to treatment after 23 months and are now observant, 1 has disappeared from protocol, 2 are still in interruption after 4 and 29 months. None has shown clinical difficulty, significant viral load rebound or rapid decrease in CD4.

Conclusion: There is no consensus in pediatrics when it comes to treatment interruption. Studies using adults do not support it. However, with non observant adolescents, wouldn't it be preferable in certain cases to back up treatment interruption rather than ignore poor observance?

TWO STRATEGIES TO PREVENT MALARIA IN HIV-INFECTED CHILDREN IN BURKINA FASO, A FIELD EXPERIENCE

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Background and aims: HIV and Malaria are among the most important childhood killers in sub-Saharan Africa, they are even worse when striking together. We used the intermittent malaria prophylaxis with Sulphadoxine/Pyrimethamine (S/P) in a cohort of HIV+ children and compared the incidence of fever with HIV+ children on routine Cotrimoxazole (T/S) prophylaxis.

Methods: During the peak malaria seasons 2007 - 2009 all HIV+ children followed at the Centre Médical St Camille at Ouagadougou not needing T/S prophylaxis according to WHO guidelines, received monthly S/P during their regular follow up visits. In 2007 and 2008 febrile episodes were collected monthly by standard anamnesis while in 2009 families were followed in addition prospectively by weekly phone calls. Clinical malaria episodes were defined as fever with or without chills, gastrointestinal disorders and general weakness.

Results: In total 110 children completed three 5 months follow-up periods. Among children on S/P the percentage having had at least one episode of clinical malaria at the end of each 5-month-peak-malaria period was 8,3%, 4,4% and 11,8% respectively, while the percentage for those on T/S were 10,5%, 7,0% and 10,7%.

Given a baseline incidence of Malaria among children in Burkina of at least 40%/year (WHO), both regimen showed good and almost equivalent protection against clinical malaria.

Conclusion: While the two groups were different in age and immunological status, this field-experience-data show that for HIV+ children not needing T/S prophylaxis, intermittent therapy with monthly S/P may be equally effective in preventing malaria in Burkina Faso.

THE TREATMENT OF ADOLESCENT WITH HIV- INFECTION

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Many HIV infected children on HAART are becoming adolescents in Poland.

Aim: To evaluate ARV therapy in adolescents.

Materials and methods: Currently our Department takes care of 82 HIV infected children. 10 were transferred to the adult care. 27 (33%) are adolescents (15 males, 12 females), at age: 13-18 years (mean 14,7). Length and effectiveness of ART was analysed.

Results: The duration of treatment: 1 month - 15 years (mean: 10 years). The patients are on 1 - 9 ART regimens (mean - 4). Seven had started with ZDV monotherapy. Viral failure was the most often reason for changing therapy before HAART (1997). After 1997 usually more than one of following reasons resulted in ART switch: 71 % AE (68% - lipodystrophy, 3% - neutropenia, anemia, hypersensitivity), 30% viral failure, 16% contamination of NFV. All of adolescents receive drugs once or twice daily. 22/27 (81%) patients regularly receive drugs. In 21 treatment is successful, in one we observe persistence of low level viremia. None of 21 treated patients developed triple class resistance. 5/27 interrupt their treatment, 2/5 stopped therapy. All of them are viremic. Sex maturity rating of Tunner Scale: 1 child - preadolescent, 13 (48%) - III/IV, 13 (48%) - V stage. 19 (70%) adolescents know their HIV status. 8 of them prepare and take drugs by themselves. In 8 cases HIV status is undisclosed with no influence on adherence.

Conclusions: Treatment in adolescents must be acceptable by themselves. Regimens should be simple and possible to use in childbearing age. Although difficult, ART is successful in most cases.

PCR PATTERN OF HIV-EXPOSED INFANTS IN A TERTIARY HOSPITAL**B. Onankpa**¹, P. Ibitoye¹, T. Yusuf¹, D. Idowu²¹*Paediatrics, ²Haematology, Usmanu Danfodiyo University Teaching Hospital, Sokoto, Nigeria*

Background: Prevention of mother- to- child transmission of HIV still poses a serious challenge in a resource-limited setting.

Aims: To determine PCR pattern of HIV- exposed infants.

Methodology: Aa 16-month prospective study of HIV-exposed infants at Usmanu Danfodio University Teaching Hospital (UDUTH), Sokoto, Nigeria. All pregnant women that presented to our ANC (ante natal clinic) between January, 2008 to May, 2009 were screened for HIV; confirmation for seropositivity was from a positive ELISA and then a Western Blot assay. PCR was done for all the HIV-exposed babies at 6-8 weeks of age.

Results: There was a total of 2,256 deliveries during the 16-month study period. Fifty two (2.3%) mothers were positive for HIV. Sixteen (30.8%) of these mothers were on HAART before pregnancy, 22(42.3%) commenced HAART during pregnancy while, 14(26.9%) mothers never received HAART during pregnancy. Eleven (21.2%) of the HIV-exposed babies had a positive PCR i.e. one(1) baby for mothers that were on HAART before pregnancy, three(3) babies for mothers commenced on HAART during pregnancy while, 7 babies were for mothers who never had HAART during pregnancy. Twenty one babies (40.4%) including the 11 positive ones for HIV (positive PCR) were breast fed.

Conclusions: Mother-to-child transmission of HIV is still of serous concern in the study area (21.2%), this probably, represent the pattern in other poor resource settings. There is the need therefore, to intensify and sustain the current effort by all stake holders in the prevention of mother-to-child transmission of HIV.

Keywords: PCR pattern, HIV-exposed, Tertiary Hospital. Presenter: Dr. Ben Onankpa Presentation: Power point.

LATE PRESENTATION OF VERTICAL HIV INFECTION IN AN ADOLESCENT: A BURKITT LYMPHOMA MIMICKING EBV DISEASE

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Burkitt's lymphoma (BL) is a common comorbidity of infection with the human immunodeficiency virus in adult age particularly in developing countries, but rarely represents the initial clinical manifestation of vertical HIV infection in adolescent in western Europe. We report the case of a 17 year-old boy firstly misdiagnosed as EBV infection, subsequently diagnosed as Burkitt's lymphoma and vertical HIV infection. Familiar history showed mother's death for lymphoma and remote history a single episode of bronchopneumonia at the age of 4 years. Initial clinical examination revealed good general health condition except for the enlargement of the right side cervical lymph nodes over 3 cm of diameter, hepatosplenomegaly and tonsillopharyngitis. Biological tests showed mild elevation of sedimentation rate and CRP, hypergammaglobulinemia and positive blood PCR for EBV. Due to the persistence of tonsillopharyngitis over two weeks we performed lymphonode biopsy which showed a typical pattern of Burkitt lymphoma. Meanwhile, T cell immunophenotyping revealed marked immunosuppression (CD4 count 114/mm³ 35%). Thus, HIV serology was performed, resulting positive. On the basis of these findings a diagnosis of HIV-related Burkitt lymphoma was established both in the patient and subsequently confirmed in his mother by further clinical investigations. The boy received four courses of chemotherapy in association with four antiretroviral drugs (lopinavir/ritonavir + abacavir/lamivudina) leading to complete remission (CR) of the tumor. After three years of follow-up the patient is still under antiretroviral therapy with complete viral suppression, good immunoreconstitution (CD4+ count 790/mm³ or 23,4%) and complete remission of the lymphoma.

EFFECTIVENESS AND SAFETY OF ATAZANAVIR/RITONAVIR IN PREGNANCY: REPORT OF 22 PATIENTS

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Background: Ritonavir-boosted atazanavir (ATV/r) is one of the recommended protease inhibitors in initial combination regimen for antiretroviral treatment. However there are concerns about its use during pregnancy.

Methods: Prospective multicentre cohort study of HIV-pregnant women receiving ATV/r- containing regimen during pregnancy and delivery in the Madrid cohort of mother-infants pairs.

Results: Among 803 mother-infant pairs followed 22 HIV patients received ATV/r. (7 of them treated before pregnancy). Median age was 31.5 years (29-38), most of them were Caucasian and main HIV route of transmission was heterosexual. Four mothers were coinfecting with HVC. Median exposure in utero to ATV/r was 4 months. Table 1 shows median CD4 and viral load during pregnancy and delivery.

The safety and tolerance of ATZ/r-containing regimens were good. No significant increase in aminotransferases, although a mild and non-clinically significant elevation in bilirubin was observed in the third trimester (Table 2).

Median gestational age at delivery was 38 weeks (range: 36-39) and median birth weight was 2785 g (range: 2380-3130). Four newborns required phototherapy (maximal bilirubin range:16 mg/dL) and no children was infected after at least 18 months monitoring.

Conclusions: ATV/r was well tolerated, with good immunological and viral responses in pregnant women. ATV/r containing regimen were effective on reducing the risk of HIV mother-to-child transmission. Neonatal jaundice may occur in newborns exposed to ATR in utero. Its incidence could be increased. Further and larger studies are needed to evaluate possible side effects in newborns.

	1st trimester	3rd trimester	Delivery
CD4 (%)	22,5 (13,5-32,5)	24 (18-33)	21 (17-33)
CD4 (/mm ³)	452 (198-702)	423 (203,5-693,5)	456 (336-728)
Viral load (copies/ml)	59 (50-5079)	50 (<20-500)	<20 (<20-195)

[Table

1]

	1st trimester	3rd trimester
AST (UI/mL)	19 (16-26)	20 (14-27)
ALT (UI/mL)	17,5 (12-22,5)	15 (10-22)
GGT (UI/mL)	11 (9-30)	20 (13-29)
Cholesterol (mg/dL)	177,5 (149-197)	202 (179-271)
Triglycerides (mg/dL)	116,5 (99,5-129,5)	199,5 (142-392)
Bilirubin (mg/dL)	0,45 (0,3-2,5)	1,2 (0,36-2,3)

On behalf of the Madrid Cohort of Mother-infants Pairs: O Nieto, P Rojo, D Blazquez, LI González-Granado, A Navas, E Iglesias, S Guillen, ML Navarro, J Saavedra, P Miralles, J Berenguer, MD Gurbindo, MA Muñoz, P Segovia, MI de José, JM Peñas, S salas, I Bates, MJ Santos, N Martinez Guardia, C Calvo, MA Roa, C Garaulet, J Regidor, J Beceiro, S Oñate

CAN GLOMERULAR HYPERFILTRATION MEASUREMENT PREDICT LATER DEVELOPMENT OF HIV-ASSOCIATED NEPHROPATHY?

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Background and aims: Kidney disease has been reported in 30 a 55% of the HIV-infected children, but the accurate assessment of kidney function is not well defined in this population. The objective of this study was to prospectively identify the alterations in kidney function in a cohort of HIV-infected children and adolescents through estimated glomerular filtration rate (GFR).

Methods: A cohort of 100 HIV-infected children and adolescents regularly followed in a Reference University Pediatric HIV Center in Sao Paulo- Brazil was evaluated. All the patients had at least two evaluations of BUN and serum creatinine, Glomerular filtration rate (GFR) estimated using serum creatinine (SCr), proteinuria, leucocyturia, hematuria and microalbuminuria. Clinical data, anthropometric measurements and ARV therapy received were registered.

Results: The patients age varied from 3 to 23 years and 54/100 were male. Clinical and immunological categories were defined according to the 1994 CDC classification: N=7, A= 17, B= 44, C= 32; only 11 patients had no immunodeficiency. 16% of the patients had leucocyturia or hematuria or proteinuria and 22% had microalbuminuria. Glomerular hyperfiltration was found in 89%. Leucocyturia, hematuria and proteinuria was found only in symptomatic and immunodeficient children (clinical class A, B, C; immunological class 2 and 3), but glomerular hyperfiltration was found even in asymptomatic and non immunosuppressed patients (class N and 1)

Conclusions: Glomerular hyperfiltration could be an useful predictor of later development of nephropathy in HIV-infected children and adolescents.

LIPODYSTROPHY SYNDROME IN PEDIATRIC HIV/AIDS

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Background: Highly active antiretroviral therapy improves survival of HIV-infected children. A long-term side effect is lipodystrophy syndrome (dyslipidemia with abnormal fat distribution).

Objectives: To determine the prevalence of dyslipidemia in HIV-infected children; the association between antiretroviral regimens and dyslipidemia; the changes in waist circumference for age (Wa/A), hip circumference for age (Hi/A) and waist-to-hip ratio (WHR), and their association with dyslipidemia.

Method: A cross-sectional study was conducted at Queen Sirikit National Institute of Child Health, from April 1, 2006 - October 31, 2007. Fasting lipid levels, waist circumference, and hip circumference were obtained from HIV-infected children.

Results: Two hundred twenty HIV-infected children were enrolled. The prevalence of abnormal total cholesterol (TC), LDL-cholesterol (LDL), HDL-cholesterol (HDL), and triglycerides (TG) were 26.4, 22.7, 5, and 24.5 percent, respectively. Hypercholesterolemia (TC or LDL) was 28.2 percent. Children receiving one boosted protease inhibitor (bPI) plus non-nucleoside reverse transcriptase inhibitor (NNRTI) plus nucleoside reverse transcriptase inhibitor (NRTI) regimen had the highest mean TC and LDL, followed by those receiving 2 bPI ± NRTI. TC and LDL were significantly higher in these 2 groups. There was no difference in HDL among regimens. Wa/A, Hi/A and WHR were not significantly different from general population. Significant associations were found among abnormal WHR and high TC ($p=0.042$), abnormal WHR and low HDL ($p=0.013$), and abnormal Wa/A and high TG ($p=0.003$).

Conclusions: The prevalence of hypercholesterolemia was 28.2 percent. TC and LDL were highest in children receiving regimens containing bPI. Abnormal WHR and Wa/A were associated with dyslipidemia in HIV-infected children.

ASSOCIATION OF SERUM CYTOKINES & ALBUMIN IN VISCERAL LEISHMANIASISA. Sanaei Dashti¹, A. Alborzi², M. Rasooli²*¹Shahid Beheshti University of Medical Sciences, Tehran, ²Shiraz University of Medical Sciences, Shiraz, Iran*

Background and aims: It is assumed that synthesis of albumin, is decreased in response to three cytokines; interleukin- 1(IL-1), IL-6 and tissue necrosis factor (TNF). Investigating the cause of hypoalbuminemia in visceral leishmaniasis (kala azar), this study was designed to measure the levels of these cytokines in these patients and to assess any correlation between their levels with serum albumin.

Methods: From March 2007 to May 2008, thirty kala azar patients, were enrolled in the study. We measured the serum levels of albumin, IL-1 , IL-6, and TNF in the patients at the pre-treatment state and also in 15 patients one week after treatment and in 38 healthy children. Cyokines were measured via Sandwich- ELISA and P value under 0.05 was considered significant.

Results: Albumin was decreased and IL-6 and TNF were increased significantly in the pre-treatment state. IL-1 was decreased in the pre- treatment state, but not statistically significant. Using Pearson correlation coefficient, there was a negative association between serum albumin and IL-6 levels in both the pre- and post-treatment states ($r = -0.43$ and $r = -0.35$ respectively). In the post-treatment state serum albumin increased and IL-6 levels decreased. This increment wasn't statistically significant, that could be explained by the low number of patients.

Conclusion: Serum IL-6 and TNF are increased significantly in the active phase of kaka azar. Also, there is a negative association between serum levels of IL-6 and albumin in the active and convalescent states of the visceral leishmaniasis.

THE ROLE OF TLR4 POLYMORPHISMS IN THE PATHOGENESIS OF RSV INFECTION IN GREEK INFANTS AND YOUNG CHILDREN

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The aim of this study was to identify the role of polymorphisms -299A/G and -399C/T of TLR4 in the pathogenesis of RSV infection in Greek infants and young children.

Methods: Our study included two groups of Greek infants and young children (A and B) ≤2 years old. Group A consisted of 50 infants with bronchiolitis and group B of 99 previously healthy children (control group) without a history of bronchiolitis. RSV was identified by PCR of genetic material that was extracted from nasopharyngeal samples, collected from all patients. TLR4 genotyping was performed by PCR-RFLP in all infants.

The results of genotype and allele frequency analysis are shown in the Table 1.

SNPs	Genotypes	Genotypes		Allele	Allele
-299 A/G	Group A n (%)	Group B n (%)		Group A n (%)	Group B n (%)
AA	45 (90)	93 (93.9)	Allele 1(A)	92 (92)	187 (94.45)
AG	2 (4)	1 (1)	Allele 2(G)	8 (8)	11 (5.55)
GG	3 (6)	5 (5.1)			
-399 C/T	Group A n (%)	Group B n (%)		Group A n (%)	Group B n (%)
CC	31 (62)	51 (51.5)	Allele 1 (C)	74 (74)	137 (69.2)
CT	12 (24)	35 (35.4)	Allele 2 (T)	26 (26)	61 (30.8)
TT	7 (14)	13 (13.1)			

[Table

1]

Conclusions: TLR4 polymorphisms (-299A/G, -399C/T) do not seem to be associated with RSV bronchiolitis in Greek infants and young children. The frequencies of the two polymorphisms between children with RSV and non RSV bronchiolitis and between the RSV serotypes A and B had also no statistically significant differences.

FUNCTIONAL EPSTEIN-BARR VIRUS RESERVOIR IN ACUTE INFECTIOUS MONONUCLEOSIS

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Background and aims: During acute infectious mononucleosis (AIM), EBV-latently-infected memory-B cells (EBV- limBcs) represent a large fraction of memory-B cells.

Methods: We explored the EBV-functional-reservoir in six AIM infants by enumerating BZLF1- or gp350-secreting-cells (SCs).

Results: Following in vitro B-cell polyclonal activation, BZLF1-SCs and gp350-SCs represented 8000-24000 and 1000-3000/10⁶ B cells, respectively. Furthermore, spontaneous-gp350-SCs, that reflect ongoing viral replication, were rare (10-30/10⁶ B cells) contrasting with high levels of circulating plasma cells (6.1-49.2% of CD27+ B cells).

Conclusions: In AIM, intense in vivo terminal-B-cell replication is polyclonal and probably mediated by a bystander effect, it could unmask EBV-limBcs to specific cytotoxic T-cell response and consequently the EBV-limBcs generating EBV lytic were destroyed. Then these facts contribute to the rapid decay of EBV-limBcs and to reach EBV-limBcs levels from chronic infected patients.

SEROPREVALENCE OF IMMUNOGLOBULIN M/A/G ANTIBODIES AGAINST BORDATELLA PERTUSSIS AND BORDATELLA PARAPERTUSSIS AMONG ASYMPTOMATIC CHILDREN AT 6-8 OF AGE IN TURKEY

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Objective: *B. pertussis* and *B. parapertussis* are closely related species that cause whooping cough, an acute, immunizing disease. Pertussis infection is a vaccine preventable disease, but immunity following the vaccination or natural disease is not life-long. Although the mechanisms of protective immunity and serology of pertussis have been well studied, those of parapertussis have not. Children in Turkey are not given a preschool booster so we determined serology of pertussis after several years from the last dose of pertussis vaccine. We also obtained parapertussis seroprevalence which may induce pertussis serology.

Material and methods: We examined IgM, IgA and IgG antibodies against *B. pertussis* and *B. parapertussis* among 100 asymptomatic children aged from 6 to 8 years who got regular vaccination. The antibody titers were measured by indirect immunofluorescence test (IFA).

Results: Ten of them had IgA titers of $> \text{ or } = 100 \text{ EU/ml}$, 33 had IgM titers of $> \text{ or } = 320 \text{ EU/ml}$ who could be considered as acute or recent pertussis infection and IgG-antibody rate of pertussis was 89%. *B. parapertussis* antibody levels of IgG, IgA and IgM were detected in 33%, 17%, and 11% respectively.

Conclusion: We suggest 2 explanations for the acquisition of pertussis and parapertussis antibodies in our children:

(1) asymptomatic pertussis and parapertussis infections are common;

(2) Although higher values of IgG observed, acute infection markers still persisted, one problem in this regard may be waning immunity against pertussis.

Of the strategies considered, the addition of a preschool booster is therefore a priority in Turkey.

BURKHOLDERIA CEPACIA- AN OLD BUT RARE PATHOGEN IN CHRONIC GRANULOMATOUS DISEASE (CGD) IN EUROPE

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Chronic granulomatous disease (CGD) is a rare primary immunodeficiency (PID, incidence 1:250000) characterized by an abnormal neutrophil respiratory burst due to defects of the NADPH oxidase resulting in impaired intracellular killing of pathogens, typically being *S. aureus*, *Nocardia* and *Aspergillus* species.

We present the case of a previous healthy 20-month old boy, born to non-consanguineous parents with no previous family history of PID, who was referred to us with a 4-week history of pneumonia and persistent temperature. A CT of the chest showed right-sided focal consolidation and bilateral enlarged lymphadenopathy. A FBC was normal (neutrophils $6.9 \times 10^9/l$) whilst inflammatory markers were raised (CRP 147mg/l, ESR 115mm/h). Tuberculosis and HIV were excluded. A bronchoscopy was unremarkable and a bronchial lavage negative for bacteria, fungi, viruses and *Pneumocystis jiroveci*. Immunology studies revealed an impaired neutrophil respiratory burst. Empiric therapy was initiated with imipenem and septrin with excellent clinical response being afebrile within 24-hours and subsequent normalising of inflammatory markers. Subcultures of pulmonary FNA grew *Burkholderia cepacia* at 15 days. Treatment was continued for 3 weeks and he was discharged in excellent clinical state with septrin and itraconazole prophylaxis. Phenotypic and genotypic studies are currently pending. He likely suffers from a mutation in the gene for the phagocyte oxidase *p47phox* (autosomal recessive inherited) as his mother's neutrophil function tests were normal. In Europe (excluding U.K) presentation of CGD with *Burkholderia cepacia* is rare. This case highlights the importance to suspect a PID and to initiate appropriate investigations to allow prompt and optimum management.

CORRELATION BETWEEN WHITE BLOOD COUNT AND SERUM NEOPTERIN CONCENTRATION IN HEALTHY AND INFECTED CHILDREN

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Background and aims: Neopterin (NT) belongs to the group of chemical compounds called pteridines. In the human body, NT is synthesized in monocytes/macrophages as the result of stimulation by INF-gamma which is secreted by Th1 lymphocytes. Increased serum neopterin concentration is observed in many pathologies where cellular immunity is involved such as viral and intracellular bacterial infections, autoimmune and malignant diseases.

The aim of the study was to determine correlation between the serum neopterin concentration and white blood count in healthy and infected children.

Patients and methods: The group of 381 children were investigated. The age ranged from 0.08 to 17.99 years.

Patients were divided into three groups: acute illness such as diarrhea or urinary tract infection (127 children), chronic diseases like inflammatory bowel disease and juvenile idiopathic arthritis (149 children), and healthy children (105).

The concentration of a serum neopterin was evaluated using the immunoabsorbent assay method (ELISA) with coated plates technique.

Results: The analysis showed poor but statistically significant positive correlation between serum neopterin concentration and white blood count (N=381, $R_s=0.19$; $p < 0.001$).

Statistically significant correlation between serum neopterin concentration and lymphocytes count wasn't observed (N=381, $R_s=0.12$; $p=0.052$). Poor, but statistically significant positive correlation between serum neopterin concentration and monocytes count was observed (N=381, $R_s=0.24$; $p < 0.001$),

Conclusions: Serum neopterin concentration positively correlates with the white blood count and monocytes count. The correlation between serum neopterin concentration and lymphocytes count was not observed.

THE INFLUENCE OF *MYCOBACTERIUM BOVIS* BACILLE CALMETTE-GUÉRIN VACCINE STRAIN ON THE IMMUNE RESPONSE AND PROTECTION AGAINST TUBERCULOSIS

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More than 100 million doses of Bacille-Calmette-Guérin (BCG) vaccine are given each year to protect children against tuberculosis (TB). Subsequent to its first use in 1921, BCG was distributed worldwide. Culture under dissimilar conditions led to the evolution of genetically different BCG vaccine strains. Animal and human studies suggest that the BCG vaccine strain influences the immune response and protection against TB. However, there is currently insufficient data to favour or recommend one BCG vaccine strain. This study investigated the influence of BCG vaccine strain on the immune response in infants.

Newborns were randomly allocated to be immunised with one of three BCG vaccine strains (BCG-Denmark, BCG-Japan or BCG-Russia). Ten weeks later the mycobacterial-specific cellular immune response was measured with intracellular cytokine assays and analysis of cytokines and chemokines in supernatants.

Data from 167 BCG-immunised infants was included. BCG-Denmark and BCG-Japan induced significantly higher proportions of multifunctional CD4 T cells than BCG-Russia. Similarly, BCG-Japan induced significantly higher concentrations of Th1 cytokines in supernatants than BCG-Denmark or BCG-Russia.

Multifunctional CD4 T cells have recently been found to correlate with protection against TB in animals. Immunisation with BCG-Denmark or BCG-Japan may therefore be associated with better protection against TB than immunisation with BCG-Russia. However, until correlates of protection against TB are determined in humans, cautious interpretation of these findings is warranted. The use of a BCG vaccine strain with even a moderately higher protective efficacy would have a large effect on TB morbidity and mortality in infants on a global scale.

KAWASAKI'S DISEASE - AN UNUSUAL PRESENTATION

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Atypical presentations of Kawasaki disease have been described in form of intestinal pseudo obstruction, tonsillitis, hemorrhagic serous effusions, thrombocytopenia and non-fulfillment of all criteria for diagnosis of Kawasaki disease. However presentation of Kawasaki disease with shock and need for inotropic support have not been described earlier.

Case report: A 4 years old girl presented with intermittent fever for 4 days, generalized edema with oliguria for 2 days, erythematous rash for 1 day and vomiting - 2 episodes. On examination, she was febrile with tachycardia with signs of shock (hypotension, poor peripheral perfusion). She had anasarca with petechial rash over trunk, hands and legs. She had significant cervical lymphadenopathy and oral cheilosis. There was no strawberry tongue or conjunctival congestion. On systemic examination, she had tender hepatomegaly with splenomegaly. Her investigations initially showed anemia, normal WBC count and platelets = 4,30,000 cells/cumm and ESR of 4 mm at end of 1 hour. Her blood culture was negative. Her liver enzymes were deranged. She was treated with IV Ceftriaxone and Dopamine. Her repeat hemogram after 5 days showed platelet count of 4,77,000/cumm and ESR of 135 mm at end of 1 hour. A 2D Echo was done which showed mild pericardial effusion and dilated coronary arteries. She was treated with intravenous immunoglobulin on the suspicion of Kawasaki's disease to which the patient responded. ESR decreased to 40 mm on Day 9 of admission and 20 mm on Day 15. She was started on Aspirin and advised regular follow-up.

HUMORAL AND CELLULAR IMMUNE RESPONSES TO MEASLES AND TETANUS: IMPORTANCE OF TIME ELAPSED SINCE LAST EXPOSURE AND NATURE OF ANTIGEN

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Background: As vaccination becomes the most common way individuals acquire immunity to pathogens, the study of immunologic memory to vaccine antigens is increasingly necessary.

Methods: Healthy adults with previous exposure to measles (wild virus or vaccine) and different time intervals since last tetanus vaccine were assessed for cellular and humoral immune response pre- and post-vaccine rechallenge. Humoral immunity was tested by ELISA and cellular immunity was tested by intracellular IFN-gamma cell detection after *in vitro* stimulation with specific antigens.

Results: While cellular immunity was comparable among vaccinated individuals and those who had measles, higher antibody levels were found among those who had the disease in the past (natural measles: 3.31 IU/mL; vaccine: 1.17 IU/mL; $p=0.003$). CD4⁺ T cell tetanus immune responses depended on time elapsed since last immunization (up to 10 years: 2.03%; delayed vaccination: 0.84%; $=0.004$). Individuals with up-to-date vaccination against tetanus showed higher antibody levels than individuals without vaccination over the last ten years (up-to-date vaccination: 2.21 IU/mL; delayed vaccination: 0.12 IU/mL; $p< 0.001$). Upon a vaccine rechallenge, both tetanus and measles antigens showed an increase in specific cellular immunity and antibody levels. Measles humoral response was much more intense among individuals previously exposed to wild virus. Individuals who were previously vaccinated for measles were immune and responded to an antigen rechallenge efficiently but less intensely than those who had the disease.

Conclusions: In an era when natural boosters are less frequent, an immune surveillance might be necessary to investigate waning immunity as it occurs for tetanus.

NASOPHARYNGEAL BACTERIAL COLONIZATION AND GENE POLYMORPHISMS OF MANNOSE-BINDING LECTIN AND TOLL-LIKE RECEPTORS IN INFANTS

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Background and aims: Nasopharynx contains various bacteria species among which *Streptococcus pneumoniae*, *Moraxella catarrhalis*, *Haemophilus influenzae* and *Staphylococcus aureus* are common ones. Single nucleotide polymorphisms (SNPs) in genes encoding mannose-binding lectin (MBL), toll-like receptor (TLR) 2 and TLR4 have been reported. The aim of this study is to investigate whether there is an association between nasopharyngeal bacterial colonization and genetic variation of these proteins in infants.

Methods: From August 2008 to July 2009, 319 nasopharyngeal swabs and 165 blood samples were taken from 3-month-old infants in a prospective cohort study. The semi-quantitative culture was used for identification of different bacterial species and the pyrosequencing-based method was used for detection of SNPs in MBL, TLR2 and TLR4.

Results: A number of 191 (60%) swabs were positive for at least one of the four bacterial species: 45 (14%) for *S. pneumoniae*, 73 (23%) for *M. catarrhalis*, 83 (26%) for *S. aureus* and 3 (1%) for *H. influenzae*. Sixteen (5%) swabs were culture negative. Of 165 infants with blood samples, 30% had SNPs in MBL, 5% in TLR2 (R753Q) and 16% in TLR4 (D299G). Colonization rate of *S. pneumoniae*, *M. catarrhalis* and *S. aureus* was significantly higher in infants with allele variants of MBL than those without ($P=0.002$). However, there was no difference in the bacterial colonization between infants with and without mutations in TLR2 ($P=0.266$) or TLR4 ($P=0.081$).

Conclusions: *S. pneumoniae*, *M. catarrhalis* and *S. aureus* seem to colonize more often nasopharynx of infants with allele variants of MBL.

COMPARASION SEASONAL AND SWINE FLU IN BOSNIAN CHILDREN DURING AUTUMN 2009**A. Bajraktarevic***Pediatrics Department, Public Health Insitution of Health Center Sarajevo, Sarajevo, Bosnia-Herzegovina*

Background: Seasonal flu and swine H1N1 are both influenza viruses that can cause mild to severe illness. Pandemic H1N1 influenza virus is similar in a number of ways to seasonal influenza, but at the same time, there are some key differences between the two. Recommended duration of antiviral treatment is five days.

Methods: Real-time reverse transcriptase polymerase chain reaction diagnostic method for the detection of pandemic H1N1 2009 viruses and other seasonal viruses in complicated cases . Until 25th November 2009 we confirmed 124 cases swine H1N1 in kids from total number 401 cases, but authors evaluated 66 cases swine flu and 73 seasonal flu kids cases.

Results: Diarrhea is not normally a symptom of seasonal influenza, although it had been seen in some Bosnain children cases of the H1N1 swine flu and can be a symptom in ours investigation (37%). The symptoms for both seasonal flu and H1N1 are the same in the most children cases in Bosnia and Herzegovina. It could be difficult to distinguish between the swine and seasonal influenza in the early stages of these infections, but a flu could be identified by a high fever with a sudden onset and extreme fatigue.

Conclusion: During community outbreaks of influenza, the highest attack rates occured among school-aged and preschool aged Bosnian children in day nurseries. Secondary spread to adults and other children within a family is common. The vaccination program was plagued by delays and public relations problems.

Keywords: Children, Influenza, Comparasion, Swine flu, Seasonal flu.

REDUCTION OF THE BURDEN OF INFECTIONS AMONG PRESCHOOL CHILDREN BY IMPROVED HYGIENE ROUTINES IN GOTHENBURG'S DAY-CARE CENTERS

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Background and aim: Children attending day-care centers receive more infections than home-cared children. The city of Gothenburg, with 0.6 million inhabitants, have more than 350 day-care-centers.

A project was started 2006 with the aim to reduce the increased burden of infections by improving hygiene routines in day-care-centers.

Method: A special skilled nurse visits all centres three times for inspection, education and

follow-up. All day-care units get individual counselling. Before the visit a questionnaire is sent to the day-care centers with questions of physical conditions of the institution and the daily hygienic routines. Focus is on hand-hygiene, diapering, food-hygiene, cleaning and disinfection of environmental surfaces etc.

Guidelines have been developed for hygiene routines and for how to handle infections in day-care centers. Parents can take part of the guidelines at the projects web-site.

Absence for the children is registered in four different categories such as upper airway tract infection, gastroenteritis, infection of other causes and no infective cause.

Result and conclusion: Preliminary results indicate that improved hygiene routines can reduce absence caused by infections diseases in day-care centers. It also shows that education of staff improves the management of outbreaks, and gives possibilities to minimize outbreaks.

CONTACT TRACING OF PAEDIATRIC PERTUSSIS CASES AT A TERTIARY HOSPITAL IN BARCELONA

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Background and aim: Pertussis is a notifiable disease not fully controlled despite current vaccination strategies. The aim of this study is to determine the prevalence of pertussis among contacts of confirmed paediatric cases at a tertiary hospital in Barcelona.

Methods: A cross-Sectional study design was used. Epidemiological and microbiological investigation was performed on close contacts of children under sixteen years old with microbiologically confirmed pertussis attended at Vall d'Hebron Hospital from 2005 to 2008. Pertussis prevalence among contacts was analysed according to the cases' age. Contacts' age, history of pertussis vaccination and clinical characteristics were collected, as well as relationship with corresponding case and setting of contact.

Results: Three hundred and seventeen contacts of sixty-nine cases were reviewed. Pertussis prevalence among contacts was 30.6% (n=85), 45.9% were laboratory-confirmed cases and 65.9% met the criteria for primary cases. 96% of the primary cases were frequent contacts, 67.9% were co-inhabitants, and 33.9% were parents. A probable source of infection was identified for 53.6% (n=37) of the total cases and for 66.7% (n=32) of those under six months old (OR: 6.4, IC95%: 2.0-20.6).

Conclusions: Pertussis prevalence among contacts is similar to comparable studies. Contact tracing of patients with pertussis allows identification of a large number of additional cases and improves control measures and epidemiological data. Because it is more likely to find the source of infection through the contacts of children under six months and because this age group is the most vulnerable, preventive strategies must be targeted primarily to this group.

RAPID ROOT CAUSE ANALYSIS TO INVESTIGATE THE SOURCES OF CASES OF HOSPITAL-ACQUIRED ROTAVIRUS (HARV)

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Background & aims: Although the disease burden of HARV may be considerable there is little understanding of how RV is acquired in hospital. We undertook a prospective investigation of all hospitalised rotavirus cases during the 2008-09 RV season (November 2008-March 2009) to try to identify sources of infection and opportunities to interrupt nosocomial transmission.

Methods: All faeces samples received in the Microbiology Department are tested for RV by enzyme immunoassay. All cases with symptom onset >48 hours after hospital admission were considered hospital-acquired. A rapid bedside root cause analysis on each of these was undertaken.

Results: 13/55 (26.7%) rotavirus cases in hospitalised patients were hospital-acquired. HARV cases had been hospitalised for 4-164 (mean 47; median 17) days before symptom onset. All had significant underlying medical conditions. Only one patient was aged over 2 years. 5 cases were considered to have arisen from patient-to-patient transmission of RV, including 3 cases epidemiologically linked to a single community-acquired case on the same ward. No failures of compliance with infection control measures were documented in any of these cases. 3 further cases were attributed to symptomatic siblings, who in two cases had visited the hospital immediately before they became unwell. In 5 cases no possible source of infection could be identified.

Conclusions: A significant proportion of hospitalised cases of RV infection were nosocomially acquired. These were in longer-stay patients with significant underlying pathologies, and occurred despite apparent compliance with infection control precautions. RV vaccination might therefore offer the best chance of controlling RV infections in hospitals.

CENTRAL VENOUS CATHETER-RELATED BLOODSTREAM INFECTIONS - A PROSPECTIVE ONE YEAR STUDY AT THE UNIVERSITY CHILDREN'S HOSPITAL BASEL, SWITZERLAND

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Background: Central venous catheters (CVC) carry the risk of acquisition of bloodstream infections (BSI).

Methods: We prospectively assessed incidence and risk factors of CVC related BSI in all patients under care in our institution with indwelling CVC on April 1, 2008 or inserted thereafter until March 31, 2009.

Results: There were 219 CVC for a total of 14782 CVC days in 162 patients (92 males, 57%) including neonates and patients with haemato-oncological, surgical, and other diseases. Mean age at CVC insertion was 1.8 months (IQR 0-51 months). Twenty BSI occurred in 17 CVC in 14 patients (9 male). Overall BSI incidence (per 1000 CVC days) was 1.35 (9.7 for silastic catheters in neonates; 9.5 for conventional CVC; 3.5 for Broviac; 0.4 for Port-a-cath). CVC remained ≤ 14 days in 119 (54%) patients, 15-90 days in 45 (21%) patients, and >90 days in 55 (25%) patients. Respective BSI incidences in these 3 categories were 3.2, 4.4, and 0.9, reflecting the comparatively low rate of BSI in Port-a-cath CVC which usually remain inserted for prolonged periods. Predominating organisms cultured were coagulase-negative staphylococci (N=8) and *S. aureus* (N=3). Analyses on risk factors for CVC related BSI are in progress.

Conclusions: CVC related BSI incidence varies by type of catheter and patients with highest risk in neonates (short term silastic catheters) and by far lowest risk for Port-a-cath in chronically ill patients. Prophylactic measurements to reduce CVC related BSI should be tailored to individual types of catheters and patient characteristics.

OUTBREAK OF BLOODSTREAM INFECTIONS CAUSED BY *SERRATIA MARCESCENS* IN A PEDIATRIC DEPARTMENT

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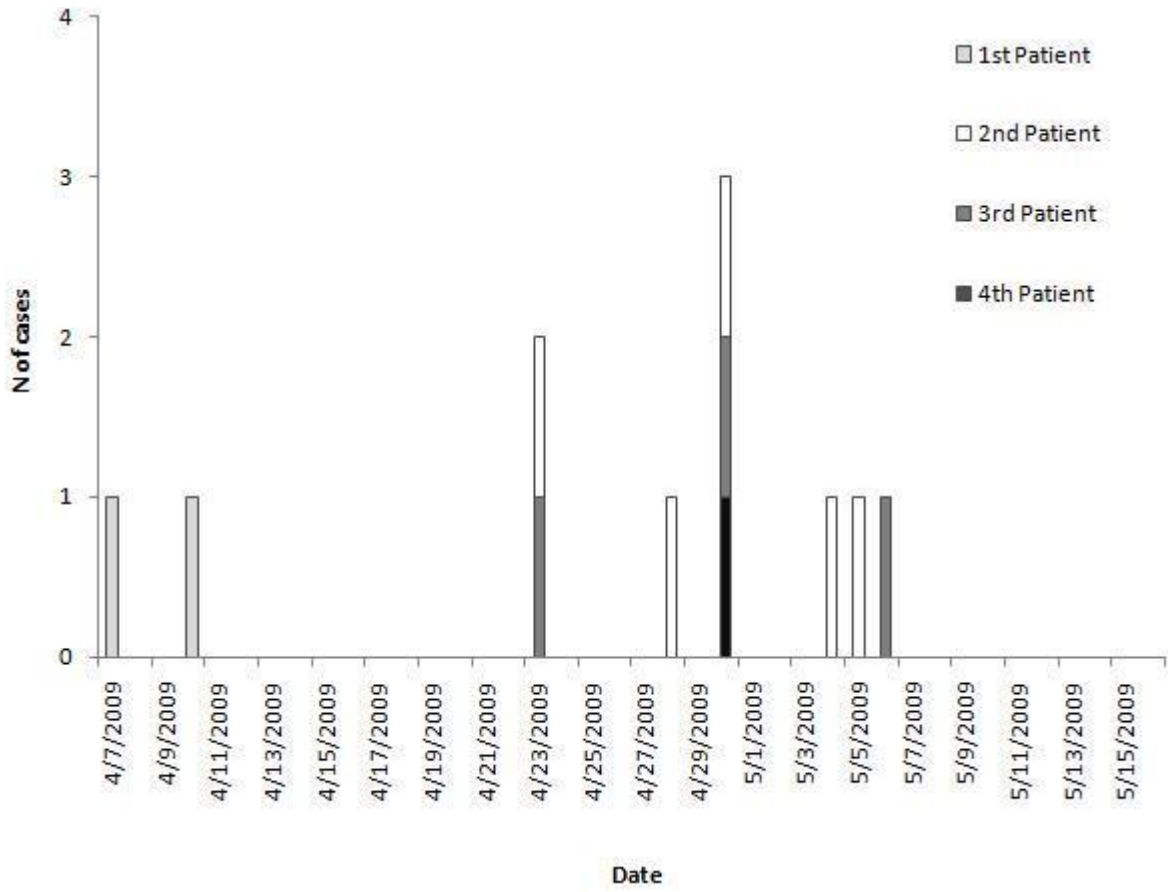
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Background and aims: *Serratia marcescens* can cause healthcare-associated infections. We herewith report the investigation and control of an outbreak of *S. marcescens* bloodstream infections (BSI) in a pediatric department.

Methods: From April to May 2009, temporally related cases of *S. marcescens* BSI were found in a 40-bed general pediatric department of a tertiary care hospital. An outbreak investigation and a case-control study were conducted including case identification, review of medical records, environmental cultures, patients' surveillance cultures and personnel hand cultures. Controls were patients without *S. marcescens* BSI but hospitalized at the department during the outbreak. Enhanced infection control measures were immediately implemented by the Infection Control Committee.

Results: During the study period, four patients had 11 episodes of *S. marcescens* BSI (figure), demonstrating the same antimicrobial susceptibility pattern. Patients' surveillance cultures and personnel hand cultures were negative. In 1 case-patient, *S. marcescens* grew from cultures of intravenous infusion systems. In the case-control study, there was no difference in demographics, kind of intravenous therapy, place or length of stay. Case-patients had vascular access changes significantly more frequently than controls. There was no other *S. marcescens* infection since the last (11th) BSI episode up to 6 months later.

Conclusion: Prompt recognition and adherence to infection control policies were important factors for combating this outbreak of *S. marcescens* BSI.



[Figure]

RATES OF INVASIVE PROCEDURES AND TREATMENTS IN NEWBORNS WITH SEPSIS

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Aims: The incidence of infection in Neonatal Intensive Care Units has been reported as between 39.8% to 51.8%. Prematures are more prone to be infected because of that invasive procedures and immune system deficiencies. Mechanic ventilation, surfactant implementation, invasive procedures such as umbilical catheter usage during follow-up increase the risk of sepsis.

Methods: We evaluated 21 patients that diagnosed with sepsis in our neonatal intensive care unit retrospectively. The patients diagnosed with sepsis using töllner sepsis scoring were researched for gestational age at onset of sepsis, C-reactive protein level, microorganisms grew up in the blood culture, antibiotic sensitivity, invasive procedures and mortality rates.

Results: We found that 58 (24.3%) of 238 patients followed up in neonatal intensive care unit were preterm, 180 of them (% 75.7) were term. 8.7% of them (n:21) were diagnosed with sepsis. 57.1% of patients with sepsis was preterm. Sepsis rate in preterms was 20.6% and 0.04% in terms. 30.4% of newborns with sepsis were umbilical catheter inserted. 56,5% of them were intubated or with nasal CPAP, 9.5% given ibuprofen, because of the PDA, 50% surfactant-applied. 30.4% of the newborns with sepsis had at least one apnea and bradycardia period and only 17.3% of them took aminofilin treatment.

Conclusions: Increase in the frequency of premature infants by assisted reproductive techniques and use of new treatment modalities lead to a rise in the number of patients in the NICUs. So that early and late complications of premature infants started to be seen more often than before.

umbilical catheter	30.4%
respiratory support (nCPAP-entubated)	56.5%
surfactant	50%
aminophylline	17.3%
erithrocyte suspension	19%
neupogen	4%
platelet suspension	14.2%
fresh frozen plasma	19%

[rates]

SEROPREVALENCE IN A POPULATION OF PEDIATRIC PATIENTS WITH BREAKTHROUGH VARICELLA OCCURRENCE

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Purpose: There are different principles regarding varicella vaccination depending on social requirement. This study was performed to show the case of breakthrough outbreak of chickenpox among group of people in the healthcare center and evaluate the seroprevalence of patients who have been managed with chronic neurologic diseases in the center.

Methods: We defined patients with varicella occurred in April 2009 as index case and investigated past history for chickenpox and the varicella specific IgG in 62 patients (children) and 156 healthcare workers with the possibility of exposure to the index cases.

Results: The varicella vaccination rate in children was 90.3%. 61.3% of all patients were seropositive where 63.6% of patients were aged between 12 months and 23 months and 87.5% between 24 and 35 months. Seropositive rate has decreased for patients aged between 36 months and 59 months while the seropositive prevalence has increased for patients over 5 years old. 32.1% of patients with history of vaccination showed seronegative (Among patients vaccinated, 32.1% showed seronegative result). Among 14 patients developing chickenpox during the study, 2 patients were evaluated for varicella specific IgG just before occurrence and they showed IgG positive. Healthcare workers(adults) working showed the positive seroprevalence rate of 96.2%.

Conclusion: The breakthrough varicella can play in healthcare centers with affiliated group housing. We need to investigate status of vaccination and immunogenicity according to ages and reflect appropriately on vaccination policy taking into consideration of social and medical requirement in local area.

COST ANALYSIS OF REDUCING DAY-CARE ASSOCIATED INFECTIONS IN GOTHENBURG, SWEDEN

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Background: Children attending day-care centres are more prone to become infected than children in family home-care. This increased morbidity is estimated to 30 %. The infections are mostly uncomplicated but may require medical interventions. Day-care associated illness may lead to economical consequences in the society. For example loss of income for the parents, costs for medicines and health care as well as loss of production. In 2006, a program was started in the City of Gothenburg (a municipal with 600 000 inhabitants and more than 350 day-care centres), that focused on improving hygiene standards at all registered day-cares in the city. An especially skilled and dedicated nurse visited all pre-school day-care units inspecting and teaching basic hygiene routines. Absence due to illness was continuously measured.

Aim: The main goal of this analysis is to identify, quantify and evaluate costs for day-care associated illness. The analysis also describes how the costs are allocated among different actors and how every separate actor is affected.

Method: A cost-of-illness-analysis that considers both direct and indirect costs. The analysis has a societal viewpoint and a human capital approach.

Results and conclusion: The preliminary analyses show that the project can be regarded as very cost-efficient. There is, however, an imbalance in the sense that the actors carrying the costs are not those that primarily get the benefits. If the project continues successfully and cuts the infection rates with 25% among pre-school children in Gothenburg, The economic savings would be approximately 400 0000 €.

OSELTAMIVIR FOR PROPHYLAXIS OF NOVEL INFLUENZA IN CHILDREN

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Background and aims: Because H1N1 influenza isolates show universal resistance to M2 inhibitors neuraminidase inhibitors are the treatment of choice. While oseltamivir has been approved for children older than 1 year of age, zanamivir is only approved for use in children older than 6 years of age. The purpose of this study is to introduce the use of oseltamivir for post-exposure prophylaxis during pandemic outbreaks in Japanese children.

Methods: All patients presenting with influenza-like illness and receiving oseltamivir after a pandemic (H1N1) 2009 infection was first detected in Japan were studied. We targeted only close contacts of treated index cases who could be identified and prophylaxed within 24 hours of case identification.

Results: A total of 992 children (1-15 years) and 1221 adults (20-89 years) were treated with oseltamivir. Of them, prophylactic prescription account for 14(1.4%) and 205(17%) in children and adults, respectively. 55% of subjects receiving oseltamivir prophylactically have been contact closely with children of family members with influenza-like illness. Symptom onset was found in 2(1%) of 205 adults receiving oseltamivir prophylactically, whereas there was no child who developed influenza-like illness. Adverse effects including neuropsychiatric events and gastrointestinal symptoms were not reported either adults or children during a prophylactic treatment.

Conclusions: An important feature of influenza virus is its potential for transmission by infectious individuals who are truly asymptomatic and undiagnosed. Although the impact of post-exposure prophylaxis depends critically on the transmissibility of resistant strains, our results suggest the clinical effectiveness and safety of prophylactic oseltamivir treatment in children.

THE ONSET OF PANDEMIC INFLUENZA A (H1N1)V VIRUS INFECTION IN A PEDIATRIC HOSPITAL IN PORTUGAL

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Background and aims: The first pediatric case of influenza A (H1N1)v infection in Portugal was diagnosed on June 14. In order to organize the health care, a containment of the disease was made for three months. In October, the influenza activity entered in pandemic phase. We characterized initial cases of (H1N1)v infection in children.

Methods: Descriptive study between June and October. Demographic, epidemiological, clinical and therapy data were analyzed.

Results: In 619 cases, 514 were evaluated; the mean age was 8.5 years (min-30days; max-17y). There was an increase of cases over the months with a peak in August (31.7%) and October (45.3%). There were 23.3% imported cases, 26.8% secondary transmission (9.5% in the context of outbreaks) and then started an increase of tertiary cases. The disease was mild in 94.1% of cases. Complications occurred in 28 (5.4%) children: pneumonia (13) respiratory distress (9), myocarditis (1) and others (5); 46.6% of them were in risk groups: asthma (10.7%), children < 1 year (14.2%) and postpartum period (3.6%).

Risk factors for complications were age < 2 years (12.1%vs4.4%;p=0.024;OR 2.985; 1.204-7.404) and chronic disease (14%vs4.4%;p=0.007;OR 3.567; 1.492-8.527). 5.2% were hospitalized (1.6% for social reasons). 12% were treated with oseltamivir, based on clinical severity and chronic illness. One child with hypertrophic cardiomyopathy died with myocarditis.

Conclusions: The initial cases were imported or secondary transmission. Most cases have mild illness. Complications, hospitalization and therapy need were more common in risk groups. Complications were not higher than expected, despite the low rate of treatment.

2009 H1N1 INFLUENZA-ASSOCIATED PNEUMONIA IN CHILDREN

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Background and aims: The understanding of 2009 H1N1 infection is still evolving. The aim was to review 2009 H1N1 Influenza-associated pneumonia.

Methods: Retrospective review of all H1N1 confirmed cases that had a chest X-ray (CXR), between July and December 2009. H1N1 RT-PCR was performed based on clinical findings, presence of underlying medical conditions and in all cases of confirmed pneumonia. CXRs were reviewed by a single radiologist.

Results: 75 (28%) of 266 H1N1+ cases had a CXR: 18 (24%) had bilateral interstitial infiltrate (BII), 14 (19%) lobar consolidation (LC; 7 with pleural effusion), 6 bronchopneumonia. The median values for children with BII were: age-3 years, duration of disease at presentation-1.5 days(0-5), leukocyte count 7.700/ μ L(1.100-15.300) and C-reactive protein (CrP)-1.8mg/dL(0.6-3.4); 7 had underlying medical conditions; 7 were admitted with a median length of stay of 3 days (2-20). For those with LC the median values were: age-6.7 years, duration of disease at presentation-3 days(0-8), leukocyte count-11.200/ μ L(3.300-39.500) and CrP-11.6mg/dL(2.6-36.8); 6 had underlying medical conditions, 11 were admitted with a median length of stay of 7 days(3-27). Four children were admitted to ICU: 2 with BII; 3 ventilated; 1 previously healthy. Children with BII were younger ($P=0.01$), presented earlier ($P=0.03$) and were discharged earlier ($P=0.06$). Blood cultures were negative. The outcome was good in all.

Conclusion: Of the H1N1+ cases, 38(14%) had CXR-confirmed pneumonia of whom half needed hospitalisation, 4(10%) in ICU. 37% had underlying medical conditions. Children with BII were younger and presented earlier than children with LC. There were no deaths.

THE 2009 INFLUENZA A(H1N1) PANDEMIC IN THE PEDIATRIC POPULATION IN ISRAEL**D. Engelhard¹**, D. Averbuch¹, A. Tenenbaum¹, E. Shmueli¹, T. Shoat², E. Anis², D. Wolf¹, I. Grotto²*¹Hadassah University Medical Center, ²Ministry of Health, Jerusalem, Israel*

Background & aims: The 2009 Influenza A(H1N1) pandemic affected Israel since April 2009. Our goal was to describe the national epidemiology of H1N1 and to analyze the characteristics of the children with moderate-severe disease who needed admission to our two hospitals, of 25 throughout Israel, during 2009.

Methods: Monitoring system, including clinical surveillance and a network of sentinel clinics throughout the country; Severe morbidity and mortality reported daily to the Ministry of Health; Retrospective analysis of the data collected from the computerized patients' files.

Results: Influenza like illness occurred more in children than in adults. However, severe morbidity and mortality occurred much more in adults. 72 children with documented A(H1N1) infection were hospitalized in our two hospitals. Their age was 17 days to 16 years (median 5 years and 9 months), 41 were males, 31 non-Jews. The main reasons for hospitalization were moderate-severe respiratory symptoms in 37 (51%), gastrointestinal symptoms in 10 (14%). 25 children had pneumonia. 3 children were admitted to PICU, 2 were ventilated. 27 children (38%) were without any risk factor. Those with risk factors included mainly 29 (40%) with underlying lung disease including asthma and 10 (14%) with neurological disorders. The main clinical symptoms were fever 96%, and cough 76%. 20 (28%) were hypoxic. WBC < 5,000 was found in 20 (28%), platelet counts < 100,000/mm³ in 10 (14%). Oseltamivir was well tolerated.

Conclusion: Despite the summer season in Israel, A/H1N1 caused significant morbidity&mortality in Israel, although children usually did not have severe and fatal disease.

EVALUATION OF INFLUENZA-RELATED MORBIDITY IN CHILDREN ADMITTED TO THE HOSPITAL

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Background and aims: Impact of seasonal influenza in children admitted to the hospital is not precisely defined. However, this information is essential to understand whether influenza vaccination has to be universally administered in pediatrics. This study was planned to increase our knowledge on influenza-related morbidity in childhood.

Methods: All the children < 14 yrs admitted to five Italian Children's Hospital for influenza-like illness (ILI) during the seasons 2007-2008 and 2008-2009 were enrolled. Clinical data regarding ILI and a nasopharyngeal swab were systematically collected at admission. On respiratory secretions, RT-PCR for detection of influenza viruses was performed. All the children were followed-up during hospital stay until discharge.

Results: A total of 955 patients were influenza positive (20.5%: virus A, 716 cases; virus B, 226). In influenza-positive children < 5 yrs, the incidence of community-acquired pneumonia was significantly more common than in the influenza-negative of all the age groups (63.3% vs 46.5%; $p < 0.05$). Use of antibiotics and antipyretics were significantly more relevant in influenza-positive children of all the age groups than in those influenza-negative ($p < 0.05$). Households of children with influenza experienced a significantly higher number of ILI ($p < 0.001$), received a significantly higher number of antibiotics ($p < 0.001$), lost a significantly higher number of school ($p < 0.001$) or work days ($p < 0.001$) than those of children without.

Conclusions: Seasonal influenza has a significant impact in children admitted to the hospital and their families, highlighting its medical and socioeconomic morbidity and suggesting the benefits of systematic influenza vaccination in the first years of life.

EARLY CORTICOSTEROIDS TREATMENT FOR SEVERE PNEUMONIA IN CHILDREN WITH NOVEL SWINE-ORIGIN INFLUENZA A (H1N1) VIRUS INFECTION

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Background: Some experimental and clinical studies for influenza viruses suggest that the pathogenesis of lung injury in these infections is associated with cell-mediated immune reaction of the host.

Methods: A total of 126 children with S-OIV infections diagnosed by real-time reverse transcriptase-polymerase chain reaction were analyzed. We compared the clinical features and laboratory findings of 51 patients with pneumonia and 75 patients without, and compared a subgroup with severe pneumonia (25 patients) and a subgroup with mild pneumonia (26 patients). Mini-pulse methylprednisolone (10 mg/kg) was infused into the pneumonia patients with severe pneumonia (9 patients) and those who showed rapidly progressive pneumonia during oseltamivir treatment (2 patients).

Results: Compared with the patients without pneumonia, those with pneumonia included more males ($P=0.001$), had higher hemoglobin levels, leukocytes counts and C-reactive protein (CRP) levels and lower lymphocyte differentials ($P < 0.001$). The patients with segmental/lobar pneumonia had higher leukocyte counts, CRP values and lower lymphocyte differentials ($P=0.002$) than those of patients with bronchial/interstitial infiltrations. Among pneumonia patients, the patients who were treated with corticosteroid showed the lowest lymphocyte differential ($6.9\pm 5.2\%$). The clinical symptoms of all patients treated with corticosteroids improved and their pneumonic infiltration ceased immediately without adverse reactions

Conclusion: In S-OIV infections, the severity of pulmonary lesions was associated with the lymphocyte differential at presentation and male patients seemed to be more vulnerable to the progressive pneumonia. Rapid corticosteroid treatment halted clinical and radiographic exacerbation. Early antiviral agents and the proper use of immune-modulators may reduce morbidity and prevent progressive fatal pneumonia.

PANDEMIC INFLUENZA (H1N1/09) IN A TERTIARY PAEDIATRIC EMERGENCY DEPARTMENT**S. Mc Ardle**¹, C. O'Maoldomhnaigh¹, D. Mills¹, B. Conway¹, N. O'Sullivan², S. Walsh¹, R. O'Sullivan¹¹*Emergency Medicine, Our Lady's Children's Hospital, ²Microbiology, Our Lady's Children's Hospital, Crumlin, Dublin, Ireland*

Background and aims: Rates of influenza A virus (subtype H1N1) infection are higher in children with specific subgroups deemed high risk. National clinical pathways to co-ordinate the response to pandemic H1N1 were adopted by our tertiary centre. We aimed to quantify the burden of Emergency Department (ED) and hospital care resulting from pandemic H1N1.

Methods: Prospective collection and extraction of data from the *Symphony* ED information system.

Results: ED attendances increased 30% during the pandemic period (July 18 to December 31 2009). Influenza-like illness (ILI) increased dramatically at week 12 (mid-October). Total number of ILI cases seen in ED was 2,079. 499 patients with ILI were admitted to hospital during the pandemic. 91/499 (18.2%) tested positive for H1N1. 414/499 patients (19.9% of ED attendances with ILI) were admitted via the ED. 215 patients (51.9%) were < 2yrs, 62 patients (15%) were between 2 and 5yrs and 137 patients (33.1%) were >5yrs. 708 cases (49.9%) were commenced on antiviral therapy. 80 patients (3.8%) were already on antiviral therapy at the time of ED attendance. Rates of confirmed H1N1 in patients admitted rose over the study period in direct correlation with increased rates of ED attendance.

Conclusions: Pandemic H1N1 led to significant increases in ED attendances at our hospital. Half of all attendances required antiviral therapy. 1 in 5 patients, the majority < 2yrs, were admitted. This figure appears higher than originally predicted, perhaps reflecting the tertiary nature of our patient population. 1 in 5 of admitted patients tested positive for H1N1.

EPIDEMIOLOGY OF THE FIRST WAVE OF SWINE FLU PANDEMIC AS IT PRESENTED TO GPs IN ENGLAND

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Background: The first wave of the swine flu pandemic in England occurred in midsummer 2009. We compared clinical incidence data for respiratory infections with those reported in recent seasonal influenza epidemics.

Methods: Weekly age specific incidence (0-4, 5-14 yrs) of ILI and selected respiratory conditions reported in the RCGP sentinel practice network were examined from 2001 to 2009. Epidemic periods were defined as the 11 weeks centred on the all age ILI peak incidence week. Excess incidence (observed over expected) was calculated for the first pandemic wave (weeks 24-34, 2009) and compared with equivalent excesses in four recent epidemic periods (H1 virus dominant in years 2007-08, B in 2005-06, H3 in 2003-04 and H3/H1 in 2001-02). Expected incidence was based on the average incidence in the matching winter weeks in 2001 to 2009 excluding epidemic weeks.

Results: The excess incidence of ILI in the swine flu period was 948 per 100,000 in age 0-4 and 807 per 100,000 in age 5-14, which respectively compare with excesses ranging between 64-757 and 50-378 in the four comparison epidemics. There were almost no excesses of otitis media, acute bronchitis, URTI or asthma during the pandemic whereas in the seasonal epidemic periods there were substantial excesses of all the other respiratory diagnoses examined.

Conclusions: The excess incidence of ILI in children during the first pandemic wave was higher than recent seasonal epidemics suggesting ready transmission. The excesses in other respiratory infections were lower, suggesting the pandemic was a mild illness with few complications.

PRESCRIBING IN A PANDEMIC: USE OF OSELTAMIVIR IN PAEDIATRIC INTENSIVE CARE**A. Seale**^{1,2}, F. Toussaint¹, A. Finn^{1,2}, J. Fraser¹¹*University Hospitals Bristol NHS Foundation*, ²*Bristol Children's Vaccine Centre, University of Bristol, Bristol, UK*

Background and aims: The first UK paediatric intensive care unit - (PICU) admissions with H1N1-Swine Origin Influenza Virus (H1N1) were reported as having high levels of co-morbidity and unusual presentations for influenza, including shock. As treatment with oseltamivir is most effective within 48 hours of symptom onset, UK national guidelines - (published October 2009) indicated that in this pandemic, presumptive treatment for H1N1 should be started in all children with fever and critical illness admitted to PICU.

This study was set up to monitor practice in a regional UK PICU for testing and presumptive treatment of H1N1; both prior to the publication of national guidelines and consultant discussion (first period) and following this (second period).

Methods: Data were collected on all admissions to PICU with an infectious illness in the two periods; analysed with Stata version 9.

Results: 36 children were included; 72% were tested for H1N1 on admission (first period), increasing to 88% (second period). Presumptive prescribing increased from 11% (first period) to 50% (second period). Of those that were H1N1 positive, 6 of 8 had co-morbidities and all except one presented with respiratory or neurological symptoms.

Conclusions: Testing for H1N1 was high in both periods. Presumptive prescribing of oseltamivir increased following publication of national guidelines and their discussion within the consultant team but only to 50%. Presentations to PICU with confirmed H1N1 infection were similar to those in early UK reports. This study highlights the need for ongoing audit in a pandemic situation to ensure new national guidelines are rapidly and appropriately implemented.

SAFETY DATA FROM CLINICAL TRIALS AND PHARMACOVIGILANCE OF MASS VACCINATION WITH MF59®-ADJUVANTED H1N1 INFLUENZA VACCINES

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Background: The safety and immunogenicity of MF59®-adjuvanted (+MF59) influenza vaccines have been established for seasonal vaccines. This analysis evaluated the safety of MF59-H1N1 influenza pandemic vaccines.

Methods: Clinical safety data were pooled from trials involving children aged 6 months to 17 years given MF59-adjuvanted cell culture-derived (Celtura® CCIV, N=320) or egg-derived (Focetria® TIV, N=320), or non-adjuvanted (-MF59, N=80) A/H1N1 vaccines. Pharmacovigilance data from an estimated 12 million doses in both children and adults were analysed.

Results: Clinical data showed increased local but not systemic reactogenicity for +MF59 versus -MF59 vaccines. Solicited AEs were mild/moderate and did not increase with the second dose, no deaths were reported. With CCIV, 42 SAEs occurred in 29 subjects; 4 considered possibly vaccine-related (vasculitic rash in preexisting disease, uveitis, facial paresis, convulsion). With TIV 16 SAEs occurred in 10 subjects, none considered vaccine-related. Unsolicited AEs had similar frequency in +MF59 and -MF59 subjects. Post-licensure events of special interest, i.e., neuritis, convulsions, SMQ anaphylaxis, encephalitis GBS/demyelination, Bell's palsy, or vasculitis ranged from 0.003 to 0.113/100,000 person-months for TIV; none were reported for CCIV. Seventeen fatalities among 12 million TIV doses; an incidence of 7.4/100,000 person-years against an expected background rate of 760/100,000 person years. No known fatalities occurred among 2.6 million doses of CCIV distributed. No signals of causal relationships are evident for SAEs or fatalities, even assuming a huge underreporting.

Conclusion: This analysis supports the good safety profile of MF59-adjuvanted H1N1 **pandemic influenza vaccines**.

References: Pellegrini M. *et al. Vaccine* 2009; 27:6959-5965.

BACKGROUND RATES OF CONDITIONS THAT MAY PRESENT AS POTENTIAL ADVERSE EVENTS FOLLOWING H1N1 VACCINATION IN AUSTRALIA

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Background and aims: Rapid population interventions with new vaccines create uncertainty for health care providers and the community, especially regarding potential uncommon or rare adverse events following immunisation (AEFI). Victorian state-held databases, covering nearly 5 million adults and children, were used to determine expected rates of admissions and emergency visits for specific acute neurological and allergic events that would have presented even the the absence of any vaccination.

Methods: The Victorian Admitted Episodes Dataset (VAED) and Victorian Emergency Minimum Datasets (VAED) were analysed for the 5 year period 1/07/2004 to 30/06/2009 prior to H1N1 vaccination. Non-duplicate admissions and emergency visits for ICD-10AM codes including Guillain-Barre syndrome (GBS), multiple sclerosis, transverse myelitis, seizures, syncope, anaphylaxis and urticaria were extracted, with recurrent episodes excluded from analysis unless more than 28 days since last discharge. Incidence rates were calculated as the number of events during the year period divided by the time at risk in the population based on population numbers in 2006.

Results: Combined databases showed 727 first events and 1017 episodes of GBS, and 100,683 first events and 113,537 episodes of syncope. For every 100,000 vaccinees per annum, assuming no relationship with vaccination, 0.47 episodes of GBS, and 5.72 episodes of multiple sclerosis are expected in the 6 weeks following vaccination. For anaphylaxis, 0.29 and 2.00 episodes are expected within 1 day and 1 week respectively.

Conclusions: State held health datasets can inform post-licensure safety surveillance in mass immunisation interventions regarding expected rates of conditions that may be perceived as AEFI.

RAPID-TEST SENSIVITY AND ESPECIFITY FOR NOVEL SWINE-ORIGIN INFLUENZA A (H1N1) VIRUS IN CHILDREN

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Backgrounds and aims: Since the start of a pandemic caused by new influenza A H1N1 is seeking tools that enable rapid diagnosis of infection by providing preventive measures and early treatment of patients who require it. The aim of this study is knowing the accuracy of rapid influenza diagnostic test BD Directigen (RIDT) in children.

Methods: A descriptive, analytical and retrospective which were included those patients under 18 years with clinically compatible or contact with a confirmed case of influenza A to which both underwent RIDT such as RT - PCR for the new influenza virus A (H1N1). The samples were collected by nasopharyngeal aspirate or swab.

Results: We included 170 patients younger than 18 years, 54.7% male, with a median of 6.29 years and 24.7% (n = 42) of children under 2 years. 42% of the samples were collected by nasopharyngeal aspirate, 57% by swab and 1% unknown; being positive 41.8% of RIDT and 59.4% of the RT-PCR. The rapid test has an overall sensitivity of 70.29% (CI: 60,8-78,3), a specificity of 100%, NPV of 69.7% (CI: 60.7-77.9) and a PPV of 100% (CI : 94.8-100). The RIDT sensitivity increases in children under 2 years up to 90% (CI: 69.9 to 97.2%). Samples obtained by aspirate have higher sensitivity than obtained by swab (77.4% versus 68.1%).

Conclusions: RIDTs for influenza A (H1N1) pandemic in children showed good sensitivity and specificity, with similar results to those obtained in seasonal influenza A.

SOCIETAL IMPACT OF INFLUENZA IN CHILDREN: ANALYSIS OF FOUR RANDOMIZED CONTROLLED STUDIES

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Background and aims: Influenza in children results in significant healthcare utilization and decreased productivity from missed school and parental missed work. Two 2-year placebo-controlled studies in children 6-83 months and two 1-year trivalent inactivated vaccine (TIV)-controlled studies in children 6 months to 17 years collected data on healthcare utilization and absenteeism. In these studies, there were 86-93% and 32-52% fewer cases of culture-confirmed influenza with live attenuated influenza vaccine (LAIV) compared with placebo and TIV, respectively. LAIV is not approved outside of the United States, South Korea, Israel, and Hong Kong.

Methods: Unscheduled healthcare provider visits, lost days of parent/guardian paid work, and lost days of daycare/school were calculated by study and treatment group among subjects with culture-confirmed influenza.

Results:

Table 1. Demographics of Study Participants

Study	Age	Region ¹	Year	Dominant Strain(s)
Belshe Y1	15-71 m	US	1996-97	H3N2; B
Belshe Y2	27-83 m	US	1997-98	H3N2
Vesikari Y1	6-35 m	EU	2000-01	H1N1
Vesikari Y2	18-47 m	EU	2001-02	H3N2
Ashkenazi	6-71 m	EU	2002-03	H1N1; B
Fleming	6-17 y	EU	2002-03	H1N1; B

¹LAIV is not approved outside of the United States, South Korea, Israel, and Hong Kong.

Table 2. Healthcare Provider Visits and Absenteeism Among Subjects With Culture-Confirmed Influenza Illness

Study	Unscheduled Visits						Missed Days Daycare/ Pre-School/School						Parent/Guardian Missed Days Work					
	LAIV			Placebo			LAIV			Placebo			LAIV			Placebo		
	N	n	%	N	n	%	N	n	n/N	N	n	n/N	N	n	n/N	N	n	n/N
Belshe Y1	14	6	43	94	28	30	14	4	0.3	94	53	0.6	14	2	0.1	94	20	0.2
Belshe Y2	15	7	47	56	28	50	15	1	0.1	56	28	0.5	15	2	0.1	56	14	0.3
Belshe Pooled	29	13	45	147	54	37	29	5	0.17	150	81	0.54	29	4	0.14	150	34	0.23
Vesikari Y1	18	11	61	88	57	64	18	44	2.4	89	209	2.3	18	17	0.9	89	109	2.3
Vesikari Y2	28	5	18	139	38	27	28	52	1.9	139	320	2.3	28	16	0.6	139	117	0.8
Vesikari Pooled	46	16	35	221	93	42	46	96	2.1*	228	529	2.3*	46	33	0.72	228	226	0.99*
Study	Unscheduled Visits						Missed Days Daycare/ Pre-School/School						Parent/Guardian Missed Days Work					
	LAIV			TIV			LAIV			TIV			Not collected					
	N	n	%	N	n	%	N	n	n/N	N	n	n/N						
Ashkenazi	29	5	17	60	9	15	29	44	1.5*	60	185	3.1	Not collected					
Fleming	50	8	16	73	12	16	50	146	2.9	73	237	3.2	Not collected					

*Statistically significant vs Belshe Pooled at $P < 0.01$.

†Statistically significant vs TIV at $P < 0.05$.

[Tables 1 and 2]

Conclusions: Among children with influenza illness, the proportion who required a healthcare provider visit and the number of days of daycare/school absenteeism or parental missed work were similar across treatment groups. In the EU studies versus the US study, there was a higher rate of child missed school/daycare (1.5-3.2 vs. 0.1-0.6 days per child with influenza) and parent/guardian missed work (0.6-1.5 versus 0.1-0.3 days). More research should be conducted to better understand the societal impact of pediatric influenza in the EU, as data regarding influenza-associated absenteeism from the US might underestimate the true burden in the EU.

Sponsored by MedImmune.

THE IMPACT OF 2009 PANDEMIC INFLUENZA A (H1N1) ON THE EPIDEMIOLOGY OF PATHOGENS CAUSING ACUTE RESPIRATORY TRACT INFECTIONS IN CHILDREN

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Background and aims: In Germany, the novel pandemic 2009 influenza A (H1N1) virus (A(H1N1)2009) caused a wave of high activity around November. The aim of this study was to investigate the prevalence of 19 respiratory viruses in children hospitalized for lower respiratory tract infections during winter season 2009/2010 and to observe a possible impact of H1N1 influenza virus on the epidemiology of the other epidemic viruses.

Methods: Specimens were nasopharyngeal aspirates from children admitted to study hospitals in the area of Mainz, Wiesbaden and Kiel, Germany, with acute community acquired lower respiratory tract infections. Specimens were subjected to a previously described multiplex reverse transcription polymerase chain reaction to detect the following microorganisms: enterovirus, influenza virus type A and type B, respiratory syncytial virus (RSV), parainfluenzavirus type 1-4, adenovirus, *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, rhinovirus, human metapneumovirus (hMPV), coronavirus OC43 and 229E, A(H1N1)2009, *Bordetella pertussis*, *B. parapertussis*, and *Legionella pneumophila*.

Results: A total of 1435 clinical specimens were collected from Jul-2009 to Feb-2010. A total of 190 specimens were positive for influenza A(H1N1)2009. An epidemic of seasonal influenza (A or B) was until now not observed. The RSV and hMPV epidemics appeared several weeks later than expected from our data collected in the PID-ARI-Network within the past 10 years.

Conclusions: Due to the new influenza A virus H1N1 the epidemiology of other epidemic viruses like RSV and hMPV may have been delayed. By the time, no epidemic of seasonal influenza has yet been observed.

PANDEMIC INFLUENZA INFECTION IN ADMITTED PATIENTS IN A TERTIARY PAEDIATRIC HOSPITAL: 119 CASES

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Objective: To describe 2009 H1N1 infection in admitted patients in a tertiary paediatric hospital.

Methods: Patients admitted with confirmed 2009 H1N1 infection (by RT Real-Time PCR in respiratory fluids) were prospectively included from July to November of 2009.

Results: 119 patients (69 males). Median age was 5.6 years (SD: 5). 12% were less than 3 months-old. 28%, 3 months to 2 years-old. 15%, 2 to 5 years-old. 45%, more than 5 years-old. 57 % were previously healthy patients. 85% fulfilled the diagnostic criteria of the WHO. The other patients had respiratory symptoms without fever mainly (12). At diagnosis: 67% were hypoxemic, 63% had respiratory distress and 57% had altered auscultation (mainly wheezing). Chest-X-ray was performed in 68% (44% had interstitial pneumonia, 40%, lobar consolidation and 7% pleural effusion). Main reason for admission was respiratory distress with hypoxemia. Mean time from onset of fever to admission was 2.7 days and median time of admission was 4 days. Bacterial coinfection was present in 15 (12%) (*S pneumoniae* pneumonia, mainly).

3 patients had arrhythmias, 2, encephalitis, 2, shock (1, miopericarditis) and 1, hepatorenal syndrome.

24 patients were admitted in ICU. Three patients died (see detailed data in complementary abstract (*Jordan et al*)).

Conclusions: Not all the patients fulfilled WHO criteria. School-aged children were the most affected group. Most of the patients were previously healthy. Respiratory distress with hypoxemia was the main cause of admission. Mortality is not absent and many patients required ICU admission.

AVIAN INFLUENZA INFECTIONS: DIFFERENCES BETWEEN CLINICAL PRESENTATION AND CASE FATALITY RATES IN CHILDREN AND ADULTS

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Background and Aims: Human H5N1 influenza infections continue to cause infections with high mortality. Understanding paediatric/adult presentation differences may expedite diagnosis.

Methods: Multi-country observational study of laboratory-supported H5N1 infection. Data sources were primarily clinical records, published case series and governmental reports.

Results: 320 patients from 12 countries were available for analysis: 51% were < 18 years. Children presented significantly more frequently with raised ALT/AST, rhinorrhoea and unexplained respiratory illness with cough, shortness of breath or difficulty breathing. Case fatality rate (CFR) increased with age: children < 5 having the lowest CFR (22%), versus overall 55% CFR. Presenting symptoms significantly associated with higher adult CFR were: unexplained respiratory illness; fever; myalgia; fatigue/malaise approached significance. There were no significant differences in adult/paediatric CFR for abnormal ALT, AST, and LDH on presentation. There were no significant differences in adult/paediatric CFRs prognosticated by leucopenia, lymphopaenia, or thrombocytopenia emerging during treatment.

Sign, symptom or finding on presentation	Present in patients < 18 years (%)	Present in patients ≥ 18 years (%)	p-value
Abnormal ALT	21/46 (46)	8/46 (17)	<0.01
Rhinorrhoea/nasal discharge	30/78 (39)	7/48 (15)	<0.01
Unexplained respiratory illness with cough, shortness of breath or difficulty breathing	98/109 (90)	75/103 (73)	<0.01

[Differential paediatric and adult presentations]

Sign or Symptom on Presentation	CFR Patients < 18 years N=164	CFR Patients ≥ 18 years N=156	p-value
Fever	56/121 (46%)	73/104 (70%)	<0.01
Myalgia	2/9 (22%)	14/22 (64%)	0.05
Unexplained respiratory illness	58/98 (59%)	57/75 (76%)	0.02

[Differential paediatric/adult CFR by presentation]

Conclusions: There are differences in adult and paediatric H5N1 presentation. Certain signs and symptoms may differentially prognosticate adult/paediatric clinical course in H5N1 infection.

NOVEL INFLUENZA A(H1N1)V 2009 INFECTION IN INFANTS UNDER 6 MONTH-OLD IN THE SOUTH-WEST OF FRANCE

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Background: French Authorities recommended influenza vaccination for family of children under 6 month-old.

Methods : we identified clinical and microbiological data for all infants < 6 months of age with laboratory proven A(H1N1)v influenza infection in Aquitaine, during a 4 months period (6/09/09-6/01/10). We compared those < 3 month-old (group A) with the older group (B).

Results: 72 cases were analysed. Median age was 3 months (mean 3,15). One child was 16 days-old and 25 were 1-3 month-old. Hospitalisation rate was much higher (92%) in group A than in group B (50%), but length of stay (LOS) was similar (median 3 days). Among the 47 hospitalised children, 20 (43%) had a ≤ 2 days LOS. Five required oxygen therapy and 1 went in PICU, as nine infants had respiratory risk factors.

In group B 16 babies had digestive symptoms and 2 febrile seizures. High level fever $\geq 39,5^{\circ}\text{C}$ was noticed in only 1 baby in group A and 9 in group B. 25 of all the cases had at least one dose of antibiotics, mainly ceftriaxone. No bacteraemia was registered, one bacterial pneumonia was diagnosed. Conjunctivitis was noticed in 5 cases. According to French rules oseltamivir was given to 72% of the cases in each group.

Conclusion: morbidity and mortality in infants < 6 month-old with novel influenza 2009 infection seem to be low in our cohort. Even if infants < 3 month-old are more likely to be hospitalised, LOS is short and outcome generally good.

INCIDENCE OF NEUROPSYCHIATRIC ADVERSE EVENTS IN NOVEL INFLUENZA PATIENTS TREATED WITH OSELTAMIVIR IN JAPANESE CHILDREN AND ADOLESCENTS

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Background and aims: Oseltamivir is approved for the treatment of seasonal influenza in adults and children aged 1 year or older. However, several reports from Japan provide some evidence for neuropsychiatric adverse effects. The objective of the current study was to evaluate the incidence of neuropsychiatric adverse events in influenza patients receiving oseltamivir in Japanese teenagers.

Methods: All patients presenting with influenza-like illness after a pandemic (H1N1) 2009 infection was first detected in Japan who were treated with neuraminidase inhibitors were examined. They were asked to provide specimens for a rapid EIA assay in detecting novel influenza A (H1N1) virus via nasal swabs.

Results: A total of 1954 children (1-19 years) and 1374 adults (20-89 years) are treated with neuraminidase inhibitors. Oseltamivir was prescribed to 50% of children and 87% of adults. 302 (24%) of 1235 teenagers and 804 (82%) of 982 children aged less than 10 years old (younger children) were treated with oseltamivir. Neuropsychiatric adverse events were found in two cases (0.16%) of 1235 teenagers receiving oseltamivir and in 4 cases of 982 younger children. Time from the beginning of oseltamivir treatment to neuropsychiatric adverse events was 48 hours later in teenagers, whereas it was within 48 hours in 4 of 5 younger children.

Conclusions: Although Japanese authorities strongly urge physicians not to prescribe oseltamivir to adolescents, the incidence of these adverse events was less in teenagers than reported. Younger children rather than teenagers should be closely monitored for signs of abnormal behavior throughout the treatment period.

EXPERIENCE WITH PROPHYLACTIC LACTOBACILLUS ACIDOPHILUS FOR THE PREVENTION OF INTRAHOSPITAL INFECTION IN A NEW BORN UNIT IN COLOMBIA

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Objective: To determine the efficacy of prophylactic Lactobacillus Acidophilus (LBA) administration to newborn admitted to the NICU for the prevention of Intrahospital Infection (IHI)

Methods: An analytical study of historical cohorts was designed having two different groups of patients. The first group did not receive LBA. The second group received oral prophylactic dose of 10.000.000 live LBA daily, from their time of admission into the New Born Unit and for the complete duration of their stay. The frequency of associated neonatal infection was calculated during hospitalization in both groups of patients and the results were analyzed in search of statistical associations. The first group corresponds with babies who were admitted into the New Born Unit between May 2005 and March 2006 for total (n) of 1402 patients and the second group babies from April 2006 to December 2008 for a total (n) of 5599. Both groups (n: 7001) had an instrument for data collection that contained demographic and socio-economic variables as well as other risk factors for neonatal infection. Microsoft Excel 2003 and the program SPSS 15.0 were used as tools to process data and calculate Relative Risk (RR), statistical significance with 'p' values lower than 0.05.

*p value < 0.001	Without LBA n= 1402	With LA n = 5599	RR (95% CI)
Culture + IHI n (%)	85 (6.0)	168 (3.0)	0.50 (0.39, 0.65)*
Gram (+) sepsis n (%)	43 (3.0)	92 (1.6)	0.54 (0.37, 0.77)*
Gram (-) sepsis n (%)	37(2.6)	52 (0.9)	0.35 (0.23, 0.53)*
Fungus n (%)	5 (0.3)	24 (0.4)	1.20 (0.46, 3.14)

[Results]

Conclusions: The results from this study show a significant statistical association between the administration of live prophylactic Lactobacillus Acidophilus and the decrease in the frequency of intrahospital infection. Administering live prophylactic Lactobacillus Acidophilus to neonates who are admitted into New Born units may be a strategy to decrease the frequency of intrahospital infection.

EARLY DIAGNOSIS OF LATE NEONATAL SEPSIS BY USING SERUM INTERLEUKIN 10**H. Boskabadi**, G.A. Maamouri, J. Tavakkol Afshari*Mashhad University of Medical Sciences, Mashhad, Iran*

Background: Late-onset sepsis is responsible for high rates of morbidity and mortality in neonates particularly in developing country. We have investigated whether serum interleukin 10 (IL-10) levels may predict late-onset sepsis in neonates prior to positive blood cultures.

Material and methods: Eighty eight neonates, with a gestational age of 28 to 40 weeks, and suspected of infection 72 hours post-partum, were originally investigated. Complete data were available from 77 neonates. They were categorized on the basis of their clinical presentation, laboratory parameters and blood culture results into:

1) cases [definitive infection (with positive blood or/and cerebrospinal fluid (CSF) cultures) or clinical sepsis (clinical and laboratory evidence of infection, but without positive blood or CSF cultures)]

2) controls (physiologic hyperbilirubinemia or routine feeding). For each neonate, samples were taken for serum IL-10, C - reactive protein (CRP), blood culture and other laboratory tests. Receiver-operating characteristic (ROC) curves were used to determine the serum IL-10 thresholds for the sepsis group versus healthy neonate group

Results: Serum IL-10 and CRP were significantly higher in the order of definitive infection > clinical sepsis > controls respectively ($P < 0.001$). Using the cut-off value for IL-10 of $>14\text{pg/ml}$, sensitivity, specificity, positive predictive values (PPV) and negative predictive values (NPV) were %77.7, %87.8, %73.6, and %90 respectively. Serum levels IL-10 in non-surviving neonates (138.6pg/ml) were higher than in survivors (34.62pg/ml) ($P < 0.001$).

Conclusions: IL-10 may be an early predictive marker of neonatal infection, and may be associated with infection severity.

REDUCING NEONATAL NOSOCOMIAL BLOODSTREAM INFECTIONS THROUGH PARTICIPATION IN A NATIONAL SURVEILLANCE SYSTEM: EFFECT OF TWO INTERVENTIONS

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Background and aims: Our NICU participates since 2000 in a German nosocomial surveillance system for neonatal intensive care patients with a very low birthweight (NEO-KISS). Nosocomial bloodstream infection (BSI) rates should decrease significantly during the first years of participation.

Methods: Standardized infection rates (SIR) of a single hospital are calculated by dividing the number of the hospital's infections by the number of infections expected based on the birth weight distribution among the patients in the NEO-KISS reference data base. Ongoing data analysis led to two interventions in our unit: swab collection of PVC-puncture sites in 2006 and introduction of closed infusion systems for infants less than 1000 g in 2007.

Results: Most PVC-associated BSI were caused by *S. aureus*. After both interventions the sepsis-SIRs for PVC- and CVC-related BSIs were reduced to a sepsis-SIR now of **1.15** (SIR sepsis and pneumonia combined **1.01**). (Between before and after both interventions) the crude incidence rate ratio (IRR) for sepsis and pneumonia combined was IRR = 0.51 with 95% confidence interval 0.28-0.91).

Conclusions: Instead of many incidence densities of BSIs for different birth weight groups SIRs indicate a relative risk of getting a specific nosocomial infection for single institutions. By SIR it is easy to show the results of specific interventions. Both interventions resulted in a significant drop of (device-associated) neonatal nosocomial BSIs.

RISK FACTORS FOR CHAGAS DISEASE IN A COHORT OF BOLIVIAN PREGNANT WOMEN

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Background and aims: Risk factors of Chagas disease have not been extensively evaluated, especially in non-endemic areas. With new migratory flows among endemic and non-endemic countries assessment of Latin-American people coming from endemic areas should be implemented.

Methods: A cohort of Bolivian pregnant women was evaluated until December 31, 2009 since June 1st, 2006. Epidemiological risk factors were evaluated within that period of time: having lived in mud house, the presence of the vector in the surroundings, relatives affected or died due to the disease or living in a rural area. We determined the prevalence of Chagas Disease in this cohort, the rate of vertical transmission and the risk factors to assess which subjects should be at high risk of infection.

Results: The prevalence of Chagas Disease in the Bolivian cohort was 14% (71/510). The rate of vertical transmission was 2,8% (2/71). The two children vertically infected were diagnosed by polymerase chain reaction and were cured after treatment with benznidazole. In a univariate analysis the factors associated with higher risk of infection ($p < 0,05$) were blood transfusion and having lived in mud house. In the multivariate analysis these two variables were statistically significant with $p < 0,05$.

Conclusions: Blood transfusion and having lived in mud house are independent risk factors of Chagas Disease in a cohort of Bolivian pregnant women living in a non-endemic area. The prevalence in this cohort is high enough to promote systematic screening in Bolivian pregnant women. At least women having received transfusion and having lived in mud house should be screened.

THE ROLE OF INSULIN IN GROUP B STREPTOCOCCAL SEPSIS

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Background: Group B streptococcus (*Streptococcus agalactiae*, GBS) is the most frequent cause of neonatal sepsis and meningitis. Besides newborns, patients with type II diabetes are at particular risk of invasive GBS infections. Newborn, in particular preterm, infants and patients with type II diabetics exhibit insulin resistance, and mice with diabetes have a more severe course of GBS sepsis. Previously, we have found that Toll-like receptor signaling is essential for immunity against GBS. Here we addressed, whether insulin modulates the TLR-dependent response to GBS in phagocytes.

Material and methods: Human and mouse polymorphonuclear granulocytes and mouse macrophages were pretreated with insulin and stimulated with GBS or synthetic analogs of GBS substructures. Moreover, signaling intermediates (MyD88, IRAK, TRAF6 or TAB1/TAK1), were overexpressed to analyze the regulatory role of insulin in ligand independent TLR signaling. Subsequently, cells were analyzed for cytokine formation (ELISA), intracellular protein activation (western blot), *il-8* gene activation (luciferase assay, PCR), and antibacterial properties (migration, phagocytosis, killing).

Results: We found that insulin significantly reduces inflammatory cytokine induction in both mouse and human PMNs through interaction with the insulin receptor. Notably, insulin- and TLR- signaling pathways are interdigitated downstream of TAB1/TAK1. In contrast to strictly TLR depending functions, antimicrobial properties such as migration, phagocytosis and intracellular killing were not modulated by insulin.

Conclusion: Ligation of the insulin receptor specifically interferes with inflammatory TLR pathways in PMNs stimulated with GBS. In contrast, directly antibacterial PMN properties are maintained. It is conceivable that insulin treatment modulates GBS-induced inflammation *in vivo*.

PREDICTED AND MEASURED PAGIBAXIMAB SERUM LEVELS IN VERY LOW BIRTH WEIGHT (VLBW) INFANTS

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Background: Pagibaximab, an anti-staphylococcal monoclonal antibody evaluated for prevention of staphylococcal sepsis in VLBW infants, reported no staphylococcal sepsis at serum levels ≥ 500 ug/ml.

Aim: Develop a dosing scheme to attain pagibaximab serum levels ≥ 500 ug/ml in VLBW infants.

Methods: Serum pagibaximab levels from 100 VLBW infants infused with pagibaximab or placebo for one to three doses were used to develop a pharmacokinetic model and dosing regimen. This regimen was prospectively evaluated in planned and scavenged samples obtained for 35 days from VLBW infants infused with pagibaximab and serum pagibaximab levels were compared.

Results: The concentration time course of pagibaximab was best described with a two compartment model with linear elimination from the central compartment. Pharmacokinetic parameters from this model were (mean \pm SE): CL (ml/h) 0.446, V₁ 75, V₂ 138, C_{0int} 12.3, K_e 0.000836, t_{1/2} 15.4 days. Using this model a dosing scheme of 100mg/kg daily for 3 days, then weekly for 3 weeks was developed to achieve target levels for ≥ 35 days. The observed pharmacokinetic estimates from infants who received this regimen from both scavenged and planned samples were similar and as predicted by the model. However, inclusion of scavenged samples caused some model instability due to lack of accurate sampling times. In either set of samples, all serum levels were ≥ 500 ug/ml.

Conclusion: We developed a computer model-based dosing regimen for pagibaximab in VLBW infants to maintain serum levels ≥ 500 ug/ml and prospectively confirmed this regimen. Phase 3 studies can proceed with confidence that pagibaximab target levels can be achieved and maintained.

REAL TIME PCR FOR THE DETECTION OF GROUP B STREPTOCOCCUS (GBS) IN NEONATES UNDERGOING SCREENING FOR SEPSIS

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Aims: To prospectively evaluate PCR for the detection of GBS in neonatal blood and ear swab specimens.

Methods: Subjects were recruited from two UK level 3 neonatal units. All babies undergoing a septic screen in the first 72 hours of life were eligible for inclusion. Septic screening involved the routine collection of blood for culture. A deep ear swab was stored in serum tryptone glucose glycerol broth at -20C for PCR analysis. An additional aliquot of blood was stored in an EDTA eppendorph prior to DNA extraction and analysis. DNA extraction was performed using the Roche MagNA Pure DNA III kit and amplification using lightcycler assays. The primers used target the *cylB* gene which encodes a haemolysin specific to group B streptococcus.

Results: 243 babies were recruited. 7 blood samples were GBS PCR positive; only 4 of these babies were blood culture positive. Four babies were blood culture positive but blood PCR negative. PCR analyses of these culture isolates were positive, confirming the presence of the *cylB* gene. 37 ear swabs were PCR positive only 1 swab was PCR negative but culture positive.

Conclusions: PCR can detect GBS from neonatal blood samples and ear swabs. PCR may also be positive in samples from symptomatic infants where conventional culture is negative. It therefore may be useful as an adjunctive method for the diagnosis of GBS colonisation and infection. Further refinement will be needed to minimise false negative results.

DIFFERENTIAL ROLE OF THE LECTIN-PATHWAY OF COMPLEMENT ACTIVATION IN SUSCEPTIBILITY TO NEONATAL SEPSIS

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Objective: The incidence of bacterial sepsis is highest during the neonatal period. Mannan-binding lectin (MBL), M-, L- and H-ficolin recognize microorganisms and activate the complement system via MBL-associated serine proteases (MASPs). We investigated lectin pathway cord blood concentrations in infants with neonatal sepsis.

Study design: Case-control study including 47 infants with culture-proven neonatal sepsis and 94 matched controls. MBL, M-, L-, H-ficolin, MASP-2 and MASP-3 were measured in cord blood using EIA/TRIFMA. Multivariate logistic regression was performed.

Results: Infants with gram-positive sepsis had significantly lower H-ficolin cord blood concentrations compared to controls ($p=0.005$), while infants with gram-negative sepsis had lower MBL ($p=0.084$). When excluding patients with postoperative sepsis, multivariate analysis confirmed that low H-ficolin $< 12000\text{ng/ml}$ was associated with a significant risk of gram-positive sepsis (OR 3.71, 95%-CI 1.26-10.92, $p=0.017$). Low MBL $< 300\text{ng/ml}$ was associated with a significant risk of gram-negative sepsis (OR 4.39, 95%-CI 1.10-17.45, $p=0.036$). M-ficolin cord blood concentrations correlated with the number of circulating phagocytes, and high M-ficolin $>1000\text{ng/ml}$ was predictive of early-onset sepsis (OR 10.92, 95%-CI 2.21-54.02, $p=0.003$). All lectin pathway proteins increased with gestational age ($p<0.001$).

Conclusions: This is the first study assessing the complete lectin pathway of complement activation in invasive infections. Low MBL concentrations appear to be an important susceptibility factor for gram-negative sepsis, and low H-ficolin for gram-positive sepsis. In contrast, M-ficolin reflects phagocytic activity and was elevated in early-onset sepsis. The decreased expression of lectin pathway proteins in neonates may contribute to neonatal immunodeficiency.

BACTERIAL PROFILE OF NEONATAL SEPSIS AMONG NEONATES WITH VLBW IN NICU OF IMAM KHOMEINI HOSPITAL AHVAZ- IRAN

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Introduction: Premature neonates are prone to severe infections due to immature defense mechanism and invasive conservative procedures. The aim of this study was the assessment of frequency of bacterial agents, type and mortality rate of sepsis among neonates with very low birth weight (VLBW).

Materials and methods: All VLBW neonates with clinical features of sepsis and positive blood culture were included. Bacterial agents were described. On the basis of time of onset of sepsis cases were divided in two groups, early (first 3 days after birth) and late onset sepsis (4 days till 28 days after birth).

Results: Of total 142 positive blood cultures during 4 years, 52(36.6%) blood cultures were belong to neonates with less than 1500 gram birth weight. *Klebsiella* spp (30 cases, 57.6%) were the most common organism, *Enterobacter* spp in 10 cases (19%) and *Acinetobacter* spp in 5 cases (9.6%) were other common agents which isolated. Fourteen (26.9%) neonates had early onset sepsis and 38 (73%) neonates had late onset sepsis, 32(61.5%) neonates were male, and 28 (53%) neonates died.

Conclusion: In our study sepsis among neonates with VLBW are mostly due to gram negative organisms rather than gram positive organisms, and *Klebsiella* spp were the most common agents. Our results suggest that empirical antibiotic therapy for this group of neonates might be revised.

Keywords: VLBW, *Klebsiella*, neonate, sepsis

IMPACT OF INTRA-ABDOMINAL PATHOLOGY IN LATE ONSET BLOOD STREAM INFECTIONS IN NEONATAL INTENSIVE CARE PATIENTS

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Background: Late onset (> 7 days of life) blood stream infections (LO-BSI) are a common complication in neonatal intensive care units (NICU). Intra-abdominal (IA) pathology is common in neonates, often requiring surgery. We postulate that IA pathology, objectively identified by need for IA-surgery (IA-Sx), is a risk factor for LO-BSI in NICU patients.

Methods: Charts of NICU patients with LO-BSI from 7/1/05-6/30/09 were reviewed, data on demographics, IA pathology, IA-Sx, microbiology and outcomes were collected. Total number of admissions and IA-Sx were obtained from medical records. Risk of mortality for LO-BSI patients, LO-BSI after IA-Sx, and microbiology of LO-BSI in IA-Sx patients were evaluated.

Results: During this period there were 3274 NICU patients; 164 of them had 213 LO-BSI events; 508 patients had IA-Sx, 68 of them also had BSI. There were a total of 134 deaths, 22 among LO-BSI subjects. Patients with LO-BSI had higher mortality (13.4% vs 3.4%; OR 4.15 CI 2.55-6.75; $p < 0.001$). BSI was more frequent among IA-Sx patients (13.4% vs 3.5% OR 4.30 CI 3.1-5.96; $p < 0.001$). LO-BSIs among IA-Sx patients were more likely to be polymicrobial (32.3% vs 12.3% OR 3.48 CI 1.73-7.0; $p < 0.001$). Mortality among LO-BSI subjects was not impacted by IA-Sx (14.7% vs 12.5%)

Conclusions: Mortality is higher among NICU patients with LO-BSI; IA pathology as measured by IA-Sx is a risk factor for LO-BSI, polymicrobial LO-BSIs are more common among IA-Sx patients. Infection control practices and antibiotic treatment options need to be developed to address these differences.

GROUP B STREPTOCOCCUS (GBS) SEPSIS OF LATE-ONSET: THE PATHOGENESIS

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Unlike the early-onset GBS infection, in the late-onset infection, the vertical transmission assumes a less important role and the dominant mode of GBS transmission is not so well understood.

Infant male, born at 33 weeks of gestation by emergency caesarean section for intestinal obstruction and sepsis of the mother (with foul ascitic fluid). After birth he was treated with ampicillin and gentamicin for signs of sepsis with a good response and was discharged at 18th day of age. Blood and urine cultures of the newborn were negative as well as the antigen detection of GBS in blood and urine. The ascitic fluid culture of the mother was also negative.

He appealed to the emergency department at 50th day of age by fever, irritability, grunting and poor feeding. The diagnostic tests performed were consistent with bacterial infection without a focus so that broad-spectrum antibiotics and supportive measures were initiated. Blood culture revealed a GBS sensitive to ampicillin. Good clinical outcome. After discharge, the state of colonization of the mother for GBS was investigated and was positive.

The vertical transmission in this case is unlikely for the following reasons:

- (1) birth by caesarian section (with lack of passage through the birth canal or rupture of the fetal membranes),
- (2) initial negative microbiological studies and
- (3) the antibiotic therapy made after birth, to which the GBS isolated in the second admission was sensitive.

We conclude that the infection was acquired horizontally from mother or from human milk.

SHOULD COMPLETE BLOOD COUNT BE PART OF THE EVALUATION OF FEBRILE INFANTS AGED ≤ 2 MONTHS? - A PROSPECTIVE STUDY

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Objective: To determine the utility and importance of total white blood cell count (WBC) and absolute neutrophil count (ANC) as markers of serious bacterial infection (SBI) in hospitalized febrile infants aged ≤ 2 months.

Patients and methods: Data on WBC and ANC were collected prospectively for all infants aged ≤ 2 months who were hospitalized for fever at our center from 2005 to 2009. The patients were divided into two groups by the presence or absence of SBI.

Results: A total of 1257 infants met the inclusion criteria, of whom 134 (10.7%) had a SBI. Mean WBC, ANC, and %ANC were significantly higher in the infants who had SBI than in those who did not (14 ± 6.4 vs. 10.9 ± 4.5 K/micl, $p < 0.001$, 7.5 ± 4.6 vs. 4.5 ± 2.8 K/micl, $p < 0.001$, 51.3 ± 14.7 vs. 40.7 ± 14.7 , $p < 0.001$, respectively). The area under the ROC curve was 0.73 (95% CI: 0.67-0.78) for ANC, 0.70 (95% CI: 0.65-0.76) for %ANC, and 0.69 (95% CI: 0.61-0.73) for WBC. The independent contribution of these three tests in reducing the number of missed cases of SBI was significant.

Conclusion: Although WBC, ANC and %ANC are only modest predictors of SBI in febrile infants aged ≤ 2 months, complete blood cell count should remain as part of the routine laboratory assessment in this age group since it is reducing the number of missing infants with SBI. Of the three parameters, ANC and %ANC serve as better diagnostic markers of SBI than total WBC.

NEONATAL UREAPLASMA PARVUM (UP) MENINGITISY. Aujard¹, V. Biran², O. Baud³, E. Bingen⁴, H. Boutignon⁵

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Background: *Ureaplasma* species as pathogens in neonatal meningitis remains contentious because 1-9 % of CSF in newborn are positive with *Ureaplasma*, more commonly without clinical symptoms. *U. parvum* is the predominant species isolated in CSF. First case of *Ureaplasma* meningitis was described in 1986 (K Waites et al). We report the case of *U. parvum* meningitis with CNS lesions.

Case report: Full term newborn with birthweight 3560 g. On day 10, fever (38.6 C) revealing an aseptic meningitis : CSF : 289 cells/mm³ - PMN, 3 %. Bacterial cultures are sterile, enterovirus and *Herpes simplex* PCR negative. Cefotaxime and acyclovir are stopped on day 16. On day 17, clinical intra cranial hypertension and seizures occur with quadriventricular dilatation on brain scan. CSF control before ventricular derivation : 1610 cells/mm³ - 86% PMN; protein, 5.2 g/l and glucose, 0.1 mmol/l. ARN 16 S PCR is positive in CSF and trachea for *Ureaplasma*; identified as *U. parvum* (CNR Mycoplasma Bordeaux). Treatment combines ciprofloxacin (40 days) + chloramphenicol (21 days). Outcome is favourable at 8 months.

Conclusion: Seventy two cases of neonatal *Ureaplasma* meningitis are reported from 1989 to 2009. Prematurity rate is 86 %. Onset of meningitis occurs in the first 2 weeks of life in 90 %. *Ureaplasma parvum* is in cause in 72 % of cases. *Ureaplasma* isolation needs specific growth media and ; for PCR, with specific primers. For treatment, erythromycin is ineffective and chloramphenicol and ciprofloxacin or doxycycline are recommended for 3 weeks.

NEONATAL COMPLICATIONS OF PROLONG RUPTURE OF MEMBRANES

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Background: Prolong premature rupture of membranes (PROM) is a common and significant cause of preterm birth and perinatal morbidity and mortality. This study was compacted to detect the prevalence of PROM, maternal risk factors and mother use antibiotic on neonatal complication.

Methods: This cross-sectional study was performed at Ghaem hospital Mashhad, Iran, between March 2008 to April 2009, to evaluate neonatal outcome of babies born to mother prolong premature rupture of membranes (PROM > 18 hours). 150 newborns were included in this study. Mother risk factors, history of mother use antibiotic and neonatal complication registered. Eligible infants were categorized into group I (symptomatic infants), II (mother chorioamnionitis) and III (asymptomatic infants).

Finding: 150 infants were recruited in to the present study, 12(7.7%) infants had definitive infection (meningitis, sepsis, pneumonia), 101(67%) premature delivery and 88(58.6%) had history of antibiotic intake. Maternal risk was including : previous PROM (10%), addiction (8%) , high urinary tract infection (5/3), diabetes (5/3), Placenta abruption (4.66%) , preeclampsia (3/3) and cerclage (2%). The most neonatal complication was including prematurity (67.3%), Respiratory Distress Syndrom (RDS , 22.6%), Asphyxia (8.6%), sepsis (4%), meningitis (5.2%), pneumonia (1.3%) and death (4.6%). History of antibiotic intake in mother was negative in 4 case sepsis and 1 case meningitis.

Conclusion: The most complication of PROM was Prematurity and its problem, but Infection is one important modifiable risk factor. Antibiotic treatment of women with history of PROM improves neonatal outcome by decrease neonatal sepsis and RDS, but increase number of meningitis and pneumonia.

NEONATAL STAPHYLOCOCCAL EPIDURITIS

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Background and aims: Epiduritis is an exceptional disease in neonates. Clinical signs are unspecific and diagnosis is often delayed.

Methods: Analysis of 4 cases of neonatal epidural abscess observed in 18 years.

Results:

Case 1: A 5 day-old male needs an exchange transfusion through an umbilical catheter (*S. aureus* positive culture). At 1 month pleuro-pneumopathy and T5 spondylitis are diagnosed. At 2 months cerebral ventricular dilatation reveals cord compression by a para vertebral abscess and destruction of 2 vertebrae. Long term evolution is bad with spastic paraplegy.

Case 2: A 2 month-old female is admitted after malaises. Lumbar mass is noted and X-ray shows vertebral osteolysis of T12-L1. MRI finds a voluminous psoas abscess and epiduritis. Abscess puncture confirms *S. aureus* infection. Kyphosis requires later vertebral osteosynthesis.

Case 3: A 16 day-old girl is admitted for fever. Lumbar puncture shows albumino-cytologic dissociation. Spinal X-rays and medullar US are normal as blood culture is positive for *S. aureus*. MRI reveals retro-pharyngeal abscess and cervical epiduritis. Trans-pharyngeal puncture and antibiotic treatment lead to clinical recovering with cervical vertebral fusion of C1-C2.

Case 4: A 2 month-old very premature boy develops a *S. aureus* septicaemia complicated by thoracic spondylitis with para vertebral abscess and cord compression. Complete destruction of T6-T7 is responsible of severe kyphosis.

Conclusions: Epidural abscess is uncommon after neonatal *S. aureus* bacteriemia, but vertebral or CSF anomalies must lead to spinal MRI. Surgical treatment in the acute phase is controversial.

TWO YEAR SURVEY ON THE FREQUENCY AND ANTIFUNGAL SUSCEPTIBILITY OF *CANDIDA* SPP. IN A CHILDREN'S HOSPITAL IN ATHENS, GREECE

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Background: In the last 5 years reduction in the relative *Candida albicans* infection rates and a shift towards the non-*C. albicans* is reported. Hitherto, records on the occurrence and susceptibility of yeast pathogens from children's hospitals are extremely rare in Greece. Our aim was to determine the frequency and susceptibility profiles of yeast isolates from hospitalized children for the years 2008-2009.

Methods: Bloodstream and CSF shunt yeast isolates were recovered from 41 (22 male and 19 female) neonates (n=34) and children (n=7), with serious underlying disease. All isolates were identified by the API Aux 20C system and tested for susceptibility to amphotericin B, fluconazole, voriconazole, posaconazole and caspofungin by the gradient MIC method.

Results: Of the 41 clinical isolates 22 (53.7%) were *C. albicans*, 13 (31.7%) *C. parapsilosis* and 2 (4.9%) *C. glabrata*. Rare yeast species were isolated from 4 bloodstream infections in neonates (*C. famata* and *Cryptococcus terreus*) and children (*C. rugosa* and *C. guilliermondii*), while only *C. albicans* and *C. parapsilosis* were isolated from CSF shunts. Fluconazole, itraconazole and voriconazole resistance (CLSI M27-A3, 2008) was only recorded for *C. glabrata* and *C. guilliermondii*, while high posaconazole and caspofungin MICs of > 32 mg/L were respectively recorded for *C. guilliermondii* and *C. terreus*.

Conclusions: In our neonatal and child population cohort, that comprised epidemiologically distinct cases, *C. albicans* was the main pathogen followed by *C. parapsilosis*. No significant antifungal resistance was recorded. Yet, hospital-specific epidemiological records on yeast species distribution and their susceptibility can support therapeutic decisions.

COMPARISON CLINICAL DIFFERENCE BETWEEN THE NEW AND OLD DIAGNOSTIC CRITERIA OF NEONATAL SYSTEMIC INFLAMMATORY RESPONSE SYNDROME IN NEONATAL SEPTIC SHOCK

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Background and aims: To explore the clinical difference between the new (2005) and old (1996) diagnostic criteria of neonatal systemic inflammatory response syndrome (nSIRS).

Methods: A total of 117 cases with neonatal septic shock including 90 male and 27 female were analyzed according to the neonatal shock score, old and new diagnostic criteria of nSIRS and diagnostic criteria of neonatal organic function failure.

Results: In 117 cases there were 20, 83 and 14 cases with mild, moderate and severe shock, respectively. Most of them got ill within 3 days afterbirth and died within 3 days of hospitalization. The most primary disease was sepsis. Most babies combined with 2-3 organic function failure, respiratory failure was the most common. There were 53 cases (45.3%) and 49 cases (41.9%) which conformed with old or new diagnostic criteria, respectively. The most conforming item was the change of body temperature (49 and 40 cases, respectively), but the change of heart rate was rare (16 and 20 cases, respectively). In above cases the number of cases and mortality rate which coincided the 2-4 items of diagnostic criteria and mortality rate which coincided the number of same organic failure were no significant difference ($p>0.05$) between old and new diagnostic criteria.

Conclusions: The coincidence rate is not high neither old and new diagnostic criteria of nSIRS in neonatal septic shock. The new standard is not better than old one. Therefore we should improve the diagnostic criteria of nSIRS in the future.

ACHROMOBACTER XYLOSIDANS NEONATAL SEPTICEMIA- A CASE REPORT

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Background and aims: *Achromobacter xylosoxidans* (AX) is an aerobic, gram-negative bacillus. Most clinical reports published involved nosocomial infections in immunocompromised patients. Cases of sepsis in neonates have been rarely reported. The outcome of such infections is often fatal.

Methods: We report a case of neonatal septicemia by AX in a preterm infant.

Results: A 1700gr male infant was born by cesarean delivery after a 33weeks', triple gestation, following in vitro fertilization. A few minutes after birth, the baby appeared breathing difficulty and grunting, but had very low oxygen requirements. He was transferred to our Department a few hours after birth. 48 hours later, the baby's condition worsened suddenly and he presented pallor, episodes of bradycardia and decreased activity. Hematologic tests showed: WBC count: 700/mm³ (Neutrophils: 55%, Mononuclears: 15%), Hb:16,9 gr/dL, Ht:50,4%, Platelet count: 173000 /mm³, CRP: 3,9 mg/dL. Coagulation studies revealed prolonged prothrombin time and partial thromboplastin time. Antibiotic treatment was then started with cefotaxime, ampicillin and meropenem. Mechanical ventilation and support of the circulation were initiated; however, the neonate presented gradually worsening multi-organ deficiency and died within 36 hours. Cultures taken from blood and cerebrospinal fluid were both positive for AX. The antimicrobial susceptibility test showed susceptibility to Meropenem only. The two other preterm babies born with the same gestation were not affected.

Conclusions: *Achromobacter xylosoxidans* is a pathogen of clinical significance, that can lead to fatal complications in preterm neonates.

NEONATAL PARECHOVIRUS ENCEPHALITIS WITH WHITE MATTER INJURY

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Objective: Human parechovirus has been described as a cause of neonatal sepsis. We report a case of twin sisters who presented during their first month of life with parechovirus encephalitis with white matter injury.

Case: Twin1 presented at day 23 of life with fever and decreased feeding. She had a full septic screen and intravenous antibiotics were commenced. The pregnancy was IVF conception to non-consanguineous parents. Maternal antenatal history was unremarkable. The twins were born at 38weeks GA by elective caesarean section for breech presentation.

Twin1 developed seizures on day 2 of admission, treated with phenobarbitone infusion. MRI brain showed extensive areas of restricted diffusion involving primarily the subcortical white matter of both frontal lobes, and to a lesser extent the parietal and temporal lobes. By day 4 she was clinically well with a normal examination and normal electroencephalogram.

Cultures and PCR analysis for neurotrophic and respiratory viruses in both serum and CSF were all negative. Serum was positive for parechovirus.

In view of her sister's illness twin2 was admitted for observation. She developed a temperature on day 2 of admission and seizures the following day. MRI brain revealed small focal areas of restricted diffusion in both cerebral hemispheres. She was also positive for parechovirus on serum PCR analysis.

Conclusion: Parechovirus should be considered when investigating neonatal sepsis, especially in the presence of seizures and white matter changes on imaging. Changes may only be apparent on diffusion weighted imaging, particularly if done early in the course of the illness.

SEPSIS IN A NEONATAL INTENSIVE CARE UNIT - 3 YEARS OF EXPERIENCE**I. Giannakopoulos, A. Karatza, E. Ziazios, K. Kritikos, S. Mantagos, A. Varvarigou***Neonatal Intensive Care Unit, University of Patras, Patras, Greece*

Background and aims: To evaluate the incidence of neonatal sepsis, from 2006 to 2008 in the neonatal intensive care unit (NICU), of the University of Patras Medical School.

Methods: Retrospective analysis of all neonates diagnosed with neonatal sepsis from 1/1/06 to 31/12/08 was performed. Neonatal sepsis was considered in the presence of relevant clinical signs and symptoms and laboratory verification of blood stream infection with positive culture and isolation of the responsible microorganisms.

Results: During the study period 993 neonates were admitted in NICU, and 152(15.3%) cases of sepsis were identified, 92(60.5%) of which occurred in males. Median gestational age and birth weight were 33weeks and 2093gr, respectively. Prematurity was present in 79.6%, low birth weight in 65.7% and very low birth weight (VLBW) in 36.1%. One hundred and six(69.7%), neonates were ventilated and 98(64.5%), had central catheters. Sixty five(42.7%) had early onset sepsis, (S.epidermidis:42, Klebsiella:6, Candida spp:4, Acinetobacter:3, Enterobacter:3, B. streptococcus:2, Pseudomonas:2, E. coli:1 and S.aureus:1). Eighty seven(63%) had late onset sepsis all of which occurred in VLBW infants. Blood cultures isolated S.epidermidis:58; Akinetobacter:7, Candida spp:5, Enterococcus:5, S.aureus:3, Pseudomonas:2, Klebsiella:1 and E. coli:1. The clinical signs most often noted were cardiopulmonary instability, respiratory distress and feeding intolerance. One hundred thirty seven (90.2%) had increased C-reactive protein, 22.9% had thrombocytopenia and 31.9% had leukocytosis overall. Mortality was 20.4%.

Conclusions: The incidence of neonatal sepsis was 15.3%. Late sepsis was more frequent in VLBW infants and late premature infants and the more commonly isolated microorganism was Staphilococcus epidermidis.

MRSA ON A NEONATAL UNIT (NNU): ADMISSION SCREENING OR SURVEILLANCE CULTURES?

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Background & aims: Neonates are at greater risk of invasive MRSA infections than older children. In the UK MRSA screening of NNU admissions, and of obstetric cases where NNU admission is expected, is now required. Our aim was to use historical data to investigate whether such screening might help control MRSA in an NNU.

Methods: All NNU babies had admission swabs; regular surveillance swabs collected from babies receiving respiratory support. The likely source of new MRSA cases was assessed, and infection control precautions instigated. The notes of 22/24 MRSA-positive babies from January 2004 to June 2009 were reviewed.

Results: 19/22 babies had negative admission screens, but only 2 cases were definitely or probably NNU-acquired. The median age at MRSA detection was 4 days (range 0-152 days), and was unaffected by mode of birth (Caesarean section 4 days; vaginal delivery 5 days). 16/22 babies were found to be MRSA-positive on surveillance samples; 5 had superficial infections (skin, umbilicus, eyes); 1 had fever. None had bacteraemia. 5/5 mothers tested were MRSA-positive. 6 babies had healthcare workers as parents. Only 4 babies received topical decolonisation treatment: successful in 3. Overall, 10/22 babies had at least one set of negative swabs.

Conclusions: MRSA was uncommon, not associated with serious morbidity, and colonisation was often short-lived. Most cases were detected only after admission, although vertical transmission was probably the main means of acquisition. Ongoing surveillance is important to promptly identify colonised babies. Maternal screening also has a potential role in identifying babies at risk.

DEVELOPMENT OF INTESTINAL FLORA IN NEWBORNS HOSPITALISED AT A NEONATAL INTENSIVE CARE UNIT (NICU)

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Background and aims: Whereas human gut is sterile at delivery, bacterial colonisation occurs within the first days/weeks thereafter. We describe development and spectrum of intestinal flora after delivery in NICU patients.

Methods: We included term and preterm newborns hospitalised at the NICU Graz from June 2006 to May 2009. Stool samples were routinely taken at the NICU twice a week. All children received prophylaxis to prevent necrotising enterocolitis (NEC) with *Lactobacillus rhamnosus*, Nystatin and either Gentamicin or Colistin. We retrospectively analysed intestinal aerobic bacterial flora and included the 20 most commonly detected species in further analysis (SPSS for Windows, Mann-Whitney U test).

Results: Out of 26.274 isolates in 1413 newborns, we identified 4363 primary isolates of 76 different species. The median age at first detection of intestinal colonisation with respective species is 9 (1-372) days. For more details of the 20 most commonly detected species see table I.

species	number	age (days) at colonisation		
	n=1413	median	range	
Gram-positives	Coagulase negative Staphylococcus*	1159	7	1-372
	Group D Streptococci*	1156	8	1-277
	Streptococcus faecium	220	8	1-86
	Streptococcus faecalis	83	13	1-121
	Lactobacillus	77	5	1-28
	Staphylococcus haemolyticus	61	6	2-30
	Staphylococcus aureus	57	13	1-72
	Viridans Streptococci*	33	16	3-284
Gram-negatives	Escherichia coli	301	11	1-202
	Klebsiella oxytoca	277	15	1-202
	Enterobacter cloacae	243	16	1-112
	Pseudomonas aeruginosa	221	5	1-372
	Klebsiella pneumoniae	203	13	1-121
	Morganella morganii	74	14	1-58
	Citrobacter freundii	53	18	1-202
	Serratia marcescens	47	14	2-91
	Klebsiella pneumoniae ESBL pos.	34	27	3-64
	Proteus mirabilis	24	11	2-26
	Enterobacter sp.*	23	24	6-79
	Stenotrophomonas maltophilia	15	6	6-44

table 1: The 20 most commonly detected species; number and age at first colonisation, * not specified

[table I]

Colonisation with Gram-positive bacteria occurs significantly earlier than with Gram-negative bacteria: 1 to 372 (median 8) vs. 1 to 366 (median 13) days, $p < 0.001$.

Conclusions: Development of intestinal flora of NICU patients begins within the first days of life and has to be kept in mind as a possible source of late onset sepsis. Colonisation with Gram-positive bacteria is observed earlier than colonisation with Gram-negative bacteria.

EMERGING ROTAVIRUS GENOTYPE STRAIN G9[P6] IN A NOSOCOMIAL OUTBREAK ON A NEONATAL MEDIUM CARE UNIT

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Background and aim: Although Rotavirus (RV) is a common cause of gastroenteritis in children under the age of five and is associated with substantial morbidity and mortality, neonatal RV infections have rarely been surveyed. Two consecutive episodes of an outbreak of Rotavirus on a neonatal medium care unit were observed in May 2009. We investigated the genotype of the RV, the prevalence among neonates and how the outbreak can be confined.

Methods: Stool samples of symptomatic neonates, and during the second episode stool samples of all neonates, were tested for RV antigens by using immunochromatography. Reverse transcriptase polymerase chain reaction (RT-PCR) was performed on 10 samples positive for RV, followed by genotyping. Staff members and samples of the environment were also tested for RV by RT-PCR. An infection control advisor attended shifts on the ward to observe the routines of the nurses and medical staff.

Results: Eighteen of 44 neonates were tested positive for RV antigen and RNA. Genotyping of the samples revealed the G9[P6] strain. Two RV positive neonates were asymptomatic. One male premature neonate developed a serious neurologic complication. None of staff members were positive for RV.

Conclusions: The RV strain G9[P6] can present as a hard to eradicate nosocomial pathogen. The severity of clinical symptoms and the prolonged persistence of the virus on the ward may at least partially be ascribed to lack of maternal antibodies against this rare serotype. Atypical RV strains can cause severe illness among neonates, therefore genotyping during an outbreak is recommended.

E.COLI AS A LEADING CAUSE OF NEONATAL SEPSIS: A 12 YEARS EXPERIENCE IN A NEONATAL INTENSIVE CARE UNIT

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Background and aims: After the implementation of a risk- based approach in 2003, the incidence of early-onset (EOS) group B *Streptococcus* (GBS) sepsis in our centre decreased. However, there are concerns that this approach may raise the incidence of non-GBS antimicrobial-resistant microorganisms such as *Eschericia Coli* (EC). Our objective was to evaluate trends and clinical data of newborns with EC sepsis.

Methods: Clinical data analysis of all newborns with positive EC blood cultures admitted to our unit between 1998 and 2009.

Results: 19 proven EC sepsis (overall incidence rate of 0.49/1000 live births) were identified (0.31/1000 before 2003; 0.82/1000 thereafter).

Median gestational age was 30 weeks; median birth weight 1780 grams and median length of hospitalization 8 days. 16 (84%) were preterm and 15 (79%) were low-birth weight. Antibiotic prophylaxis with ampicilin was administered to the mother in 10 cases. The main diagnoses were sepsis (19), which in 4 cases was associated with meningitis, 3 with necrotizing enterocolitis and 2 with pneumonia and pyelonephritis. Eight cases were EOS while 11 were late-onset (LOS). Ampicilin plus gentamicin/netilmicin was the first line treatment in 11 cases while other combinations were used in the remaining. EC was resistant to ampicilin in 17 (89,5%) cases but resistant to gentamicin only in 2. There were 8 (42%) deaths (4 with EOS; 4 with LOS).

Conclusions: EC is becoming a leading cause of neonatal sepsis. Despite our small series the incidence of EC sepsis in our unit is lower from that found in the literature.

FECAL CALPROTECTIN LEVELS AS PREDICTIVE MARKER FOR NEC IN VLBW - INTERIM RESULTS FROM A PROSPECTIVE MULTICENTRIC TRIAL

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Background: Necrotising enterocolitis (NEC) is the most common gastrointestinal emergency in neonates with high mortality and morbidity especially in very low birth weight infants (VLBW).

Methods: In order to assess the suitability of fecal calprotectin levels as predictive marker for NEC in VLBW we started a prospective multi-centre study in May 2008. Up to September 2009, 227 patients were included with complete data available in 168 cases. The mean gestational age was 29.1 weeks (23.0-34.1) and mean birth weight 1048g (354-1490g). 11 patients suffered from NEC defined as NEC-stage \geq II (6.6%). 6 of those presented with classical and 5 with fulminant NEC defined as progression to NEC-stage III within 6 hours after onset of disease. The mean meconium calprotectin level in healthy VLBW was 158.5 μ g/kg (5.8-310.8) and was significantly higher compared to preterms who eventually developed NEC (36.6 μ g/kg; 18.4-78.3; $p=0.018$).

In all cases calprotectin levels increased above 450 μ g/kg. 5 out of 6 patients (83%) with classical presentation showed elevated calprotectin levels $>250\mu$ g/g 24h before clinical suspicion of NEC. In contrast, calprotectin levels in patients with fulminant NEC did not increase before laparotomy.

Discussion: Fecal calprotectin seem to be a sensitive marker for classical NEC. However, patients with a fulminant NEC do not show an increase in calprotectin levels early in the disease which might indicate to an impaired immunological response in such patients. Finally, VLBW who eventually developed NEC had significantly lower meconium calprotectin levels which might be suitable for early risk assessment of future NEC development.

ROTAVIRUS INFECTION AS COMMON CAUSE OF NEONATAL FEVER**C.-R. Kim**¹, S.H. Yoon¹, S.M. Lee¹, J.W. Oh¹, M.K. Yum¹, J.O. Kang²¹*Pediatrics, ²Laboratory Medicine, Hanyang University Guri Hospital, Guri-si, Republic of Korea*

Purpose: Although neonatal fever can be related to serious bacterial infection, most common symptom of neonatal rotavirus (RV) infection was also fever in previous our study. We studied to see the proportion of RV infection as the cause of neonatal fever.

Methods: We reviewed electronic medical records of 48 newborns \leq 28 days of life who were admitted to Special Care Nursery of Hanyang University Guri Hospital for fever \geq 38°C from 2005 to 2009. All the newborns were tested with CBC, urinalysis, CRP, cultures of blood, urine and cerebral spinal fluid as well as stool RV ELISA. We also had additional tests which were respiratory virus PCR for respiratory symptoms and stool culture and occult blood for diarrhea.

Results: They were all term infants. Age on admission was 13 \pm 8 days of life. Peak body temperature was 38.4 \pm 0.4°C. Nineteen patients (40%) had unknown cause of fever. Causes of fever were found in 29 patients. There were 21 viral infection (44%) and 8 bacterial infection (17%). The viral infections included 12 RV (25%), 6 enterovirus, 2 respiratory syncytial virus, and 1 rhinovirus. Genotype of RV was all G4P[6]. Only 3 of 12 RV-infected patients had diarrhea. The bacterial infections included 6 urinary tract infection (4 *Escherichia coli*, 1 *Klebsiella pneumoniae* and 1 *Enterococcus faecalis*), and 2 sepsis and meningitis (all *Streptococcus agalactiae*).

Conclusions: RV was the most common cause of neonatal fever. We should include sepsis workup as well as stool RV test for neonatal fever, irrespective of diarrheal symptom.

RAHNELLA AQUATILIS SEPSIS IN A PREMATURE NEWBORN

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Rahnella aquatilis, an infrequently isolated gram-negative rod, is the only species of the genus *Rahnella* within the *Enterobacteriaceae* family. The organism's natural habitat is water, from which most isolates have been recovered. The organism is rarely isolated in clinical specimens and infection in immunocompetent person is unusual. The infections ascribed to this organism are bacteremia, sepsis, respiratory infection, urinary tract infection, and wound infection in immunocompromised patients and infective endocarditis in patients with congenital heart disease. Here we present a one-month-old boy who was born prematurely at 27th week of gestation by cesarean section with a birth weight of 730 g. During the his treatment for ventilator associated pneumonia due to *Stenotrophomonas maltophilia* with ciprofloxacin, he developed nosocomial bacteremia caused by *Rahnella aquatilis* which was resistant to piperacillin, cephalosporins, and susceptible to carbapenems and aminoglycosides. The patient was successfully treated with a combination of amikacin plus meropenem. Although *R. aquatilis* is a one of the saprophytic organisms it may cause life-threatening infection in newborn.

THE INFLUENCE OF *UREAPLASMA UREALYTICUM* COLONIZATION AT BIRTH TO NEONATAL OUTCOMES IN PRETERM INFANTS

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Purpose: *Ureaplasma urealyticum* (*U. urealyticum*) colonization is shown to be associated with perinatal mortality and morbidity including pneumonia, sepsis, and bronchopulmonary dysplasia (BPD) in preterm infants. This study investigated whether *U. urealyticum* from the tracheal aspirate immediately after birth is associated with the development of BPD and early onset neonatal sepsis.

Methods: Polymerase chain reaction (PCR) was performed from tracheal aspirates collected within 24 hour of birth from 176 preterm infants who were born < 35 weeks and admitted to the Neonatal Intensive Care Unit in Bundang CHA Hospital.

Results: *U. urealyticum* was detected in 37 of 176 preterm infants (21.0%). Gestational age ($29^{+5}\pm 2^{+5}$ wk vs. $30^{+6}\pm 2^{+5}$ wk, $P=0.013$) and birth weight (1.39 ± 0.44 kg vs. 1.59 ± 0.55 kg, $P=0.037$) were lower in the *U. urealyticum* positive group compared to the control group. The incidence of early onset neonatal sepsis (16.2% vs. 6.5%, $P=0.045$) and BPD (45.9% vs. 29.5%, $P=0.047$) was higher in the *U. urealyticum* positive group compared to the control group, but the severity of BPD was not different between the groups. However, Multiple logistic regressions analysis revealed that the presence of *U. urealyticum* was not independently related to the development of early onset neonatal sepsis and BPD.

Conclusions: The results suggest that the colonization of the lower respiratory tract by *U. urealyticum* might not be related to the development of neonatal sepsis and BPD directly in preterm infants.

THE EUROPEAN CONGENITAL CMV INITIATIVE (ECCI) REGISTRY: “FIRST DO NO HARM”?**S. Luck¹, P. Griffiths¹, M. Sharland²***¹Centre for Virology, Royal Free Campus, University College London Medical School, ²Paediatric Infectious Diseases, St George's University of London, London, UK*

Background and aims: Treatment with IV Ganciclovir has been reported to improve outcome in selected babies with congenital cytomegalovirus (cCMV). The availability of valganciclovir makes treatment of less severely affected babies more feasible, but without any evidence for benefit. There is currently no ongoing EU wide surveillance of babies treated with these antiviral agents, which have potential carcinogenicity.

Methods: A web-based registry was developed into which any baby treated for cCMV in the UK from 2002-2017 can be enrolled. Informed consent for data entry is obtained from parents thus requiring local research approval at each centre. Detailed information relating to treatment received, side effects, therapeutic drug monitoring, viral load and outcome is entered by clinicians.

Results: Local approval for the first site was gained in April 2007. 15 UK sites have now enrolled 26 babies. 14/26 babies were born 2008-2009 and 10/26 were < 38 weeks gestation. 24 babies had CNS symptoms and 10 received oral valganciclovir at some stage during their treatment. We know of a further 21 babies treated for cCMV in the UK over the same period, but 16 have not yet been enrolled due to delays in obtaining local approvals.

Conclusions: Many babies are being treated with valganciclovir in the UK. This European initiative ultimately aims to monitor long-term trends in treatment and toxicity throughout Europe and provide a platform for further studies. The first few years of this ESPID-funded registry have identified some of the challenges of multicentre cohort studies within current regulatory constraints.

HALF OF THE PRESCRIPTIONS FOR ANTIMICROBIALS IN HOSPITALISED NEONATES ARE UNLICENSED

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Background and aims: Off-label drugs including antimicrobials are more often prescribed to neonates than other paediatric ages. We aimed to describe the characteristics of antibiotic use in patients aged 0-28 days in both Estonian third level paediatric hospitals and to determine the rates of off-label prescribing.

Methods: All prescriptions including antibiotics to neonates were prospectively recorded during 6 months in Tartu University Clinics (01.02. to 31.07.2008) and Tallinn Children Hospital (01.02. to 31.07.2008). Drug-licensing status was determined according to the Summaries of Product Characteristics (SPCs) in the Estonian drug register. The days of drug use to 100 NICU days was used to characterise antimicrobial consumption (AC).

Results: Of the 490 neonates admitted 210 (64%) received 552 prescriptions for 19 different antibacterial, antiviral and antifungal products (1-8 antimicrobial products per child). Of premature babies (birth weight < 1500g) 78% were treated with antimicrobials. The most commonly consumed agents were gentamicin, ampicillin and penicillin (313, 161, 91, respectively). The use of unlicensed agents was high; altogether only 12/19 (63%) drugs and 310/552 (55%) prescriptions were licensed for use in neonates but none except amikacin had specific information in SPC for premature babies. The agents without licensing information were gentamicin (AC=313), meropenem (AC=62), piperacillin-tazobactam (AC=56), cefepime (AC=3), cephazoline (AC=3), nystatin (AC=3), ceftazidime (AC=0.6) and linezolid (AC=0.3).

Conclusion: In neonates the pharmacokinetic studies and SPC updates are urgently needed for several antimicrobial agents especially with regards to premature babies.

NEONATAL MASTITIS

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Background and aim: To evaluate clinical features, treatment and microbiological findings in young infants with mastitis.

Methods: Retrospective review of medical records of infants with breast inflammation during the first 2 months of life, observed in a tertiary hospital, between 2000 and 2009.

Results: 21 children were included, all full-term infants, 14 (67%) girls, median age 22 days (5-39). The median number of cases/year was 2 (1-7). The first sign was swelling in 12 children and erythema in 7. It was unilateral in 19. Fever was present in 4 and in general, there was a lack of systemic manifestations. None had evidence of skin infection at another site.

Overall there were 11 (52%) cases of breast abscess (BA). Ten required incision and drainage and in one case there was spontaneous drainage. The median age at presentation of cases with BA was 24 days compared to 19,4 days for children who did not develop BA ($p=0,27$). Gram stain showed gram-positive cocci in all cases with positive culture. Methicillin susceptible *Staphylococcus aureus* (MSSA) were isolated in 6 cases and methicillin-resistant *Staphylococcus aureus* (MRSA) in 3 children with no risk factors identified. There was one relapse due to MSSA and no other complications. Maternal skin or soft-tissue infections were not found.

Conclusions: Abscess formation occurred in half of the cases. In cases with available Gram stain a pathogenic organism was identified. No gram-negative bacteria were found. *S. aureus* was the isolated bacteria in all cases but 1/3 were MRSA.

A COMPARATIVE STUDY OF BLOOD CULTURE SAMPLING FROM UMBILICAL CATHETER LINE VERSUS PERIPHERAL SITE

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Background: Neonatal sepsis is an important cause of death and morbidity in newborns and is diagnosed by isolation of organism in blood culture.

The objective of the present study was to determine, whether an indwelling umbilical catheter, could be an alternative site for blood culture.

Methods: In a prospective study over 6 months during 2006, 141 paired blood cultures from 134 infants, were done simultaneously from peripheral site and umbilical catheter (mostly U.V.C), during the first four days of life. Majority of these infants were preterm and admitted to NICU for special care. These infants had indwelling umbilical line and had indication of sepsis workup.

Results: In our study in 16 infants blood culture pairs were positive for one organism in both peripheral vein and umbilical site. 71.6% of total cultures (n=11) pairs were negative in both sites. A total of 22 pairs were positive in one site only, with 5 positive from peripheral vein only and the other 17 from umbilical site. Two pairs were positive in both sites with two different organisms. In over all 16 infants (11%) of blood were considered to be contaminated. Contamination rates were 2.4% and 9.2% for peripheral and umbilical catheter sites. Contamination rate increased after 48 hours of age in umbilical catheter.

Conclusion: The result showed that after 2 days contamination rate for blood culture taken from catheter line increased and specificity decreased. We recommended that blood culture via umbilical catheter in first 2 days in sick neonates with indwelling catheter can be an alternate site of blood culture sampling.

DIAGNOSIS OF EARLY ONSET SEPSIS IN PREMATURE NEWBORNS BY MEASUREMENT OF CORD C - REACTIVE PROTEIN AND INTERLEUKIN-6

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Background: The purpose of this study was to determine the relationship between early onset sepsis and increased levels of C-reactive protein (CRP) and interleukin-6 (IL-6) in cord plasma.

Methods: A prospective study was conducted in 141 premature infants delivered with gestational ages of 26-35 weeks. IL-6 and CPR were measured by enzyme-linked immunoassay in the cord plasma of the neonates. According to clinical, laboratory

Findings and blood culture results, newborn infants were allocated into four groups (A-D): documented early onset infection, clinical sepsis, possible infection, and control groups respectively.

Results: Mean IL-6 levels in group A-D was 264, 212, 160, and 33.3 pg/ml respectively. Difference between groups was statistically significant ($p=.002$). With cut off point of 18

Pg/ml, the sensitivity and specificity of IL-6 for diagnosis of early onset sepsis was 72% and 55% respectively. There was not significant difference between mean levels of CRP among

groups ($p=0.28$).

Conclusion: Having considered the relatively good sensitivity and moderate specificity of cord IL-6, using this test can be recommended as a useful detector of early onset sepsis and

non-infected sick neonates.

Keywords: Premature newborn, sepsis, CRP, interleukin-6

NEONATAL SYSTEMIC CANDIDIASIS IN INTENSIVE CARE UNIT - 3 YEARS IN REVIEW

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Background: Candida infections are frequent and major causes of septicemia in neonatal intensive care units (NICU's), and they are associated with high morbidity and mortality rates. The most frequently fungal infections are caused by *C.albicans* or *C.parapsilopsis*.

Methods: Retrospective analysis of all NICU's patients with systemic candidiasis from 1/1/2006 to 31/12/2008 at Patras Hospital. Demographic data, etiological agent, clinical presentation, treatment, morbidity and mortality.

Results: Twenty two patients were reviewed, 14male/8female, the median gestational age at birth was 31 weeks(24-40weeks), median birth weight was 1783g(710-4150g), 20preterm, 8 with extreme low weight(< 1000g) at birth. Admission motives: prematurity=18, necrotizing enterocolitis=2, others=2. Candida infection represented 22/152(14.4%) of nosocomial sepsis and affected 22/993(2.2%) of all NICU admitted patients. Candida was isolated in 98 blood cultures and 2 in peritoneal fluids. Four Candida species were identified: *C.albicans*=16, *C.parapsilopsis*=4, *C.tropicalis*=1 and *C.Torulopsis*=1. Seven patients were treated with amphotericin B. Subsequently, fluconazole was added in 11 patients and caspofungin (1mg/kg/day for 2 days and 2mg/kg/day for the next days) was added in 9 patients. The risk factors identified were: prolonged antibiotics course=23, central venous catheters=20, mechanical ventilation=22, parenteral nutrition=23, abdominal surgery=3 and necrotizing enterocolitis=3. Severity parameters considered were: anemia, leucopenia, thrombocytopenia, transfusional support, and higher mechanical ventilation parameters. Nine deaths occurred.

Conclusions: This study emphasizes the frequency of Candida infections and the high morbidity and mortality associated. The introduction of new antifungal drugs could be useful in cases of preterm infants with systemic candidiasis. The authors enhance the need of scrupulous hygienic and infection control measures

SEVERE DESHYDRATATION AND THROMBOCYTOPENIA IN A NEONATE WITH HUMAN HERPES VIRUS 6 INFECTION

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Introduction: Symptomatic neonatal infections with Human Herpesvirus 6 (HHV6) are rarely reported. We report here a neonatal case of HHV6 infection confirmed by PCR, with an original clinical presentation, revealed by vomiting and thrombocytopenia.

Case report: A girl was born after an uneventful 41 weeks pregnancy and delivery, weighing 2920g. At 25-day-old she was brought to our hospital for vomiting with severe deshydration. Clinical examination revealed tachycardia without haemodynamic failure.

Laboratory findings show hypernatremia, C-reactive protein 47 mg/L, white blood cell count 8200G/L, platelet count 64000G/L that rapidly dropped to 12000G/L 2 days later.

Antibacterial chemotherapy was started until bacterial cultures (blood, urine, lumbar puncture) returned negative. Symptomatic treatment and platelet transfusion was performed.

She was seronegative for Parvovirus B19, and Herpes simplex virus. Rotavirus, astrovirus and adenovirus research in stools were negative.

HHV6 Polymerase Chain Reaction was positive in blood but negative in bone marrow. From retrospective examination of sera, HHV6 seroconversion took place 2 weeks after the beginning of the disease. The infant did well and was discharged to home after 15 days. At 2 years old clinical examination was normal.

Conclusion: Previously reported cases of neonatal HHV6 infection were hepatitis, seizures, fever with exanthem subitum. Though thrombocytopenia may alert, such a rapid drop, associated with marked deshydration, is uncommon.

PREVENTION OF GROUP B STREPTOCOCCAL DISEASE: STATISTICAL REVIEW OF SANTO ANDRÉ HOSPITAL'S PEDIATRIC DEPARTMENT DURING 2009

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Backgrounds and aims: Group B Streptococcus (GBS) remains one of the most common causes of neonatal infection. A maternal screening and risk factor-based protocol was implemented in our department in January 2009, consisting on maternal intrapartum chemoprophylaxis using ampicillin.

The goal of this study was to determine the incidence of streptococcal infection during 2009, evaluate the effectiveness of our approach and compare it with previous years' rate of disease.

Material and methods: A population-based study was prospectively conducted in our department during 2009, based on the review of medical records of both newborns and mothers.

Results: Among 2229 live births, there was no case of early-onset GBS disease.

Antenatal screening was documented in 78% of mothers. GBS colonization was found in 14%. There were 416 infants exposed to intrapartum antibiotics. Chemoprophylaxis was administered in 88% of women with positive cultures and in 18% with unknown colonization status. When chemoprophylaxis was administered, at least 1 dose was given (≥ 2 hours prior to delivery) in 85% of cases.

Risk factors were identified in 11% cases: intrapartum fever occurred in 1,3%, urinary tract GBS infection during pregnancy in 1,7%, previous infant with GBS disease in 0,1%, gestational age < 37 weeks in 7,1% and prolonged rupture of membranes (>18 hours) in 1,6%. Women with identified risk factors, not GBS colonized, received chemoprophylaxis in 49% of the cases.

Conclusions: Our approach has shown great effectiveness, as there was not any case of early-onset disease, compared to previous years.

RISK FACTORS FOR ENTEROCOCCAL COLONIZATION IN A NEONATAL INTENSIVE CARE UNIT

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Background and aims: Enterococci colonization and infection with resistant or multiresistant strains are emerging in Neonatal Intensive Care Units (NICUS). The aim of the study was to characterize risk factors associated with Enterococci species colonization in a NICU.

Methods: Between January 2005 and April 2006 a cohort of 163 newborns, hospitalised more than 48h at the NICU of Fernando Fonseca' Hospital, were followed prospectively for enterococci colonization by weekly rectal swabs until discharge. Colonization rate, demographic and clinical parameters of mother and newborn were analysed.

Results: The newborns studied had a mean birth-weight of 2441g, mean gestational age of 35 weeks and 49% were female. Mean colonization rate was 82% at 30 days of admission; with a mean time of 10 days, being shorter for resistant than multiresistant strains (6vs12days; $p < 0.05$). The time to colonization by any enterococci was associated with mothers age (RR between 0.93-1.00), number of days at the Intermediate Care Unit (RR1.01;CI 95% 1.00-1.03) and addition of lipids to parenteral nutrition (RR=1.84;CI 95% 1.22-2.88). The factors involved in colonization by multiresistant or resistant strains were antibiotic uptake (OR=11.71;CI 95% 2.05-66) and number of days at the Intensive Care Unit (OR=1.01;CI 95% 1.01-1.06). Newborn weight and gestational age (OR=0.99;CI 95% 0.98-0.99) were indirectly related with colonization by a gentamicin resistant strain (OR= 0.81 and 0.99 respectively).

Conclusion: In our study antibiotic use and length of stay are risk factors for enterococci colonization in newborn.

Caution should apply to avoid the increase the enterococci colonization in NICUS.

MOTHER TO CHILD TRANSMISSION OF CHLAMYDIA TRACHOMATIS IN WOMEN ATTENDING ANTENATAL CLINICS IN NIGERIA

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This study sought to trace the transmission of Chlamydia trachomatis from mother to child. 1456 endocervical swabs and blood were collected from pregnant women and their spouses and neonates and umbilical cord fluids. 1456 pregnant women 674 umbilical cord fluids were collected during birth. Blood samples and umbilical cord fluids were tested using the compliment fixation test. Umbilical cord fluids were also tested for Chlamydia trachomatis by culturing into the yolk sac of embryonated eggs. Of the 1465 blood samples from pregnant women, 1155 tested positive to Chlamydia complement fixing antibodies with 87.4% having diagnostic titre of 1:16 while 850 endocervical swabs were positive to Chlamydia trachomatis. From the neonates, were 211 positive to Chlamydia complement fixing antibody of which 60% had diagnostic titre of 1:16. Of the 1456 males, 1102 were positive to Chlamydia complement fixing antibodies with 71% having diagnostic titre. And 413 umbilical cord fluids were positive to Chlamydia complement fixing antibodies while 312 umbilical cord fluids were positive to Chlamydia trachomatis by culture methods. All the positive neonates had their mothers positive to CCFA as well as culture. Of the 211 neonates were 63 with their umbilical cord fluids, their mothers as well as their fathers testing positive to CCFA and their mothers to Chlamydia trachomatis. 36 umbilical cord fluids were positive to Chlamydia trachomatis along with the women. Statistical analysis using Fischer test indicates that all the result were significant ($F=2.342$: $CI=99$). This is a strong evidence of transmission from mother to child.

Subjects tested	Number tested	Number positive (%)
Endocervical swab	1456	850 (58.4)
Blood (females)	1456	1155 (79.3)
Blood (Males)	1456	1102 (75.7)
Umbilical cord	674	413 (61.3)
Neonates	674	211 (31.3) 211 (31.3) 211 (31.3)
Total	5716	3731 (65.3)

[Table 1: Monitoring transmission of Chlamydia trac]

NOSOCOMIAL INFECTION AGENTS AND ANTIBIOTIC RESISTANCE PROFILES IN A NEONATAL INTENSIVE CARE UNIT: AN EXPERIENCE OF ONE YEAR

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Nosocomial infections are responsible for significant mortality and morbidity in hospitalized newborns. Especially very low birth weight infants are under high risk. Therefore it's important to know pathogenic agents and their antimicrobial resistance profiles in a neonatal intensive care unit when choosing an empiric antibiotic treatment. Between January 2008 and January 2009 we performed a prospective study to determine hospital-acquired infections in our unit, to assess pathogenic culture results and to evaluate antibiotic susceptibility patterns by using patient-based active surveillance system. During the study period we hospitalized 372 newborn babies in our unit and we ascertained 30 nosocomial infection attacks in 16 (4.3%) infants. Our overall hospital infection rate was 8.07%. Premature infants had an infection rate of 75%. Most nosocomial infections were bloodstream infections (43%). Most common causitive pathogens were *P.aeruginosa* (20%), *K.pneumonia* (20%) and *Candida* species (20%). Gram negative agents were responsible for 48%, gram positive agents were responsible for 32% and *candida* species were responsible for 20% of nosocomial infections. Ampicilline and aminoglycoside resistance ratios were 100% in gram negative agents. Expanded spectrum beta-lactamase positivity was detected as 100% in gram negative enteric bacilli. Methycilline resistance ratios in coagulase-negative staphylococci was 80%. There was no apparent resistance against glycopeptides among gram positive agents. The overall mortality rate was 1.8%. In conclusion hand hygiene standing first on the list, all nursery personnel should strictly obey preventive principles against nosocomial infections. Active surveillance and rational antibiotic usage may be helpful in decreasing the frequency of resistant nosocomial infections.

FEVER AMONG INFANTS YOUNGER THAN 3 MONTHS OF AGE: CASE SERIES OF EIGHT YEARS

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Background: Management of fever in young infants is a common dilemma for clinicians. We aimed to elucidate the epidemiology and etiology of fever in infants < 3 months of age, admitted to our Paediatric Department over an 8 year period.

Methods: Review of the medical records of febrile infants < 3 months of age, from 1 January 2000 to 31 December 2007. Statistical analysis was performed using SPSS 17.0 for Windows. $P < 0.05$ was considered statistically significant.

Results: Of 117 hospital admissions (115 patients), 20 (17.0%) were neonates and 97 (82.9%) were infants aged between 1-3 months. Fever without focus occurred in 69.2%. Serious bacterial illness (SBI) was diagnosed in 35.0%: pyelonephritis - 56.1%, bacteremia - 21.9%, pneumonia - 17.0%, meningitis - 7.2%, meningococemia - 2.4% and omphalitis - 2.4%. Blood, urine and CSF cultures were positive in 10.6%, 27.0% and 18.7%, respectively. The most common isolated pathogens were: *Streptococcus agalactiae* (blood and CSF), *Neisseria meningitidis* (blood and CSF) and *Escherichia coli* (urine and blood). Indeterminate febrile illness and bronchiolitis were the most frequent non-bacterial infections diagnosed. Magnitude of fever ($p=0.599$), bad peripheral perfusion ($p=0.844$) and fever without focus ($p=0.872$) were not predictors of SBI. A significant difference between leukocytosis $\geq 15.000/\text{mm}^3$ ($p=0.006$), CRP $\geq 5\text{mg/dl}$ ($p=0.001$) and type of infection was found. Mortality rate was 0.85%.

Conclusions: Our study has a higher prevalence of SBI compared to literature. As our trial included only admitted patients, this high prevalence may reflect good admission criteria for febrile infants. All other results were similar to literature.

GROUP B STREPTOCOCCAL INFECTION - A CASE REPORT OF LATE-ONSET DISEASE**E.P.M.N. Pereira, J.P.S.A.B. Agro***Hospital de Santo André EPE, Leiria, Portugal*

Background: Group B *Streptococci* are a major cause of infections in infants from birth until 3 months of age. Early-onset disease occurs after vertical transmission because of colonization of mother's genitourinary tract. The origin of late-onset disease remains less clear.

Case report: A female baby was born at 30 weeks gestation from caesarian section with a birth weight of 1140g. It was a triplet pregnancy, complicated by intra-uterine growth restriction and fetal suffering. She was the second twin, with Apgar scores 5/8. Ventilation was required between 24 hours and 3 days of life. She developed a clinical picture of sepsis at 7 days of life and was started on ceftazidime and vancomycin. A *Staphylococcus epidermidis* was isolated from blood cultures. At 53 days, she was again noted pale, lethargic with apneas and a new course of antibiotics was commenced with ampicillin, ceftazidime and vancomycin. A Group B *Streptococcus* was isolated, so vancomycin and ceftazidime were stopped. The infection was successfully resolved and the baby girl was discharged at 72 days of life. Maternal genital swabs were taken about 2 months after delivery and proved to be negative.

Conclusions: Late-onset disease is believed to reflect delayed infection after early colonization, due to either vertical or horizontal transmission. In our case report, early colonization within the mother's genital tract is less likely as there appeared to be no maternal carriage. Person-to-person transmission can occur and, although uncommon, our case report probably illustrates a nosocomial infection caused by Group B *Streptococci*.

MENINGITIS IN A PORTUGUESE NEONATAL INTENSIVE CARE UNIT**D. Pereira Moreira, M. Cordeiro, A. João***Centro Hospitalar Vila Nova de Gaia/Espinho - EPE, Porto, Portugal*

Background and aims: Bacterial meningitis is more common in the first month of life. Despite advances in infant intensive care, neonatal meningitis remains a devastating disease. Our aims were to evaluate the incidence, etiology, risk factors and outcomes of neonatal meningitis.

Methods: Retrospective study of newborn admitted in our neonatal intensive care unit with meningitis between 2000-2009 (10 yaers). Demographic and clinical data, from newborns and respective mothers were analyzed.

Results: Of 7565 inpatients newborns, 17(0,22%) cases of meningitis were diagnosed. Majority of newborns were male (64,7%). Mean gestacional age was 37 (27-41) weeks, with 7(41,2%) premature and 6(35,3%) premature rupture of membranes. Mean birth weight was 2970(880-4080) grams, with 6(35,2%) very low birth weight. Mean age at diagnosis was 9(0-29) days old, 6 (35%) cases of early onset. The most commonly clinical presentation was irritability (94,1%), poor feeding (88,2%), respiratory distress (64,7%), fever (58,8%), poor tone (47,1%), hypotension (35,3%) and seizures (29,4%).

Mean white blood cell count and C reactive protein, respectively was: 10558/uL (2320-21170) and 7,90(0-25,62) mg/dL. Meningitis was confirmed by culture in 13 (76,4%) cases: *Group B Streptococcus* (GBS) (7), *Escherichia coli* (3) and others (3). Eleven cases had a concomitant-positive blood culture. There were complications in 8 (47%) cases.

The mortality rate was 5,9%. Of the 16 survivors, there were sequelae in 7(43,8%) newborns (3 premature): development delay(6), neurological(4), hearing loss(4) and decreased visual acuity(1).

Conclusions: The most commonly isolated pathogen was GBS. One high rate of newborns were left with sequelae, however mortality was low.

DOES CEFTRIAZONE INCREASE NEONATAL HYPERBILIRUBINAEMIA?**B. Rutterman**¹, M. Duijsenberg², C. Obihara¹¹*Pediatric, ²Pharmacology, St. Elisabeth Hospital, Tilburg, The Netherlands*

Background: Ceftriaxone is a broad-spectrum antibiotic which covers most of the pathogens involved in neonatal serious bacterial infections. In most hospitals, it is no longer a first choice antibiotic, since in-vitro studies have shown that Ceftriaxone may competitively displace bilirubin from its binding with albumin, thereby increasing the chance of hyperbilirubinaemia. Up to date, no such relationship has been found in-vivo. The relationship between Ceftriaxone and neonatal hyperbilirubinaemia has never been studied as a primary research question. Our study aims to address the question whether Ceftriaxone is related to increased risk of neonatal hyperbilirubinaemia.

Methods: This analyses is based on data retrieved from the National Neonatal Registration, LNR (a registration database for perinatal data of Dutch children). We analysed all neonates seen by a paediatrician in 2007.

Results: Of the 957 neonates who were seen by a paediatrician, 76 (7.9%) received phototherapy for hyperbilirubinaemia. Ceftriaxone had been significantly more prescribed to neonates who developed hyperbilirubinaemia, than to those who did not (39.5% vs 13.2%, OR 4.26, 95% CI 2.58-7.02). Covariate analysis amongst Ceftriaxone-treated neonates identified one significant confounder, prematurity (gestational age < 37 weeks), which explained 93% of the risk model. No other significant cofounders were found.

Conclusions: The increased risk of Ceftriaxone on neonatal hyperbilirubinaemia is explained for 93% by the confounder prematurity. Based on this retrospective analysis, the conclusion cannot be made on the relationship between Ceftriaxone and the risk of neonatal hyperbilirubinaemia in Dutch children. This relation needs to be studied further in a randomised controlled trial.

SEASONAL VARIABILITY OF RESPIRATORY SYNCYTIAL VIRUS INFECTIONS IN AUSTRIA: A 16 YEARS ANALYSIS

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Background and aim: To analyze year-to-year variability of respiratory syncytial virus (RSV) seasons in a middle European country (Austria).

Methods: Data from a local database (1994- 2002) and a nationwide electronic epidemiological monitoring system called RSV-Hotline (2002- 2009) were analyzed regarding year-to-year variations of onset, duration, peak and end of RSV seasons. Peak season was defined between November and April and divided into an early (November to January) and a late peaking season (February to April).

Results: Over the last 16 years in total 1579 infants, 1144 nationwide and 435 regionally, were hospitalized in Austria due to RSV- infection. During the study period median month of peak was March, median onset of season mid- October and median end of season May. Median duration of season was 8 months, ranging from 5 to 12 months. In 23% of the time (40/180 months) RSV-infection occurred in the non peaking season (March- September). There were 4 early peaking and 12 late peaking seasons without a strict order of appearance. Six seasons showed a biphasic cycle and three seasons a continuing RSV activity throughout the year. Analysis also revealed cycling activity of RSV with severe seasons being followed by mild ones and vice versa.

Conclusions: During the study period overall seasonal activity of RSV peaked in March. Three of 16 seasons showed continuous activity throughout the year. Nearly a quarter of RSV activity occurred outside the peak seasons from November to April. Data are helpful for clinicians in guiding palivizumab prophylaxis.

VANCOMYCIN-RESISTANT *ENTEROCOCCUS FAECIUM* MENINGITIS IN PREMATURE INFANTS SUCCESSFULLY TREATED WITH LINEZOLID: REPORT OF 3 CASES

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During the last decade enterococci has become one of the leading cause of nosocomial infections. They causes mostly surgical site infections, urinary tract infections and bacteremia in hospitalised patients but enterococcal meningitis are quite rare , accounting for only 0.3% to 4% of cases of bacterial meningitis which is associated with a high mortality rate. Enterococcal meningitis has been described most frequently in patients with neurosurgical conditios such as head trauma, shunt devices, or cerebrospinal fluid leakage. Treatment of enterococcal infections is problematic especially those happened by vancomycine resistant strains. Here we present 3 cases of nasocomial meningitis in infants caused by vancomycin-resistant *Enterococcus faecium* (VRE) which was genetically identical in a neonatal intensive care unit at the same time period. All 3 patients were treated with linezolid, 2 of them discharged without any sequale but 1 dead because of candidemia. Among 3 patients 2 had previous gastrointestinal colonization with VRE but one did not have documented VRE colonization. Control of the VRE infections and colonization in NICU was achieved by enhanced contact isolation precautions, cohorting of patients and staff, and improved environmental decontamination. The patients with meningitis were treated successfully with linezolid.

DO WE NEED SURVEILLANCE SYSTEMS ON NOSOCOMIAL INFECTIONS IN THE NICU?**W. Stelzl**¹, G. Hartmann², W. Dietz¹, B. Simma¹¹*Department of Pediatrics, ²Department of Microbiology, University Teaching Hospital, Landeskrankenhaus Feldkirch, Feldkirch, Austria*

Objectives: Nosocomial infection rates are high in the premature infant population. In order to keep these rates as low as possible we decided to participate in the national Neo-KISS (Krankenhaus/Hospital-Infektions-Surveillance-System). As a member of VON (Vermont Oxford Network) we tried to answer the following question: Do we additionally need Neo-KISS?

Methods: We compared the results of Neo-KISS (n=96) and VON (n=98) on nosocomial infection rates over a three-year-period from 2007 - 2009 in the group of VLBW infants (< 1500g) and looked at stratified subgroups (i.e. birthweight, device-association).

Results: VON infection rate 2007 - 2009 was significantly elevated: 26.5%, reference 18.5%. Neo-KISS standardized infection rate for all VLBW was in normal range: 0.85, reference median 0.91. For 2008 Neo-KISS showed an elevated incidence density of central venous catheter associated bloodstream infections: 20.13, 95% CI 4.15 - 58.84, reference median 7.89. Change of antibiotic therapy, improved hygienic management and ward rounds by microbiologists helped to decrease the incidence density again in 2009: 6.71, 95% CI 0.17 - 37.39, reference median 7.89.

Conclusions: In addition to VON we gain important information by Neo-KISS, which allows us to take effective measures.

Keywords: Neo-KISS, Vermont Oxford Network, surveillance, nosocomial, infection, premature, VLBW, ELBW

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

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

Methods: To compare the sensitivity of *cyiB* PCR and conventional culture-based methods for GBS detection, 216 clinical specimens were analysed (EDTA blood and ear swabs from 72 neonates undergoing sepsis screens and vaginal-rectal swabs from the mothers of these babies).

Results: GBS was detected in 6 of 72 neonatal bloods samples analysed; 4 were GBS-positive by PCR and culture, one by culture alone and another by PCR alone. All ear swabs from the 6 GBS blood-positive neonates were GBS-positive, as were corresponding maternal vaginal/rectal swabs. PCR detected GBS in 12 swabs which were GBS culture-negative; conversely, one swab was GBS-negative when analysed by PCR, but GBS-positive by culture.

Conclusions: PCR amplification of *cyiB* was of comparable sensitivity to culture for GBS detection from bloods and of significantly higher sensitivity for detection from swabs. Used alongside culture, this molecular detection tool could greatly improve GBS detection, and given its rapidity, may be of considerable value in the neonatal intensive care setting.

GROUP B STREPTOCOCCUS INDUCES ANTI-APOPTOTIC SIGNALS THROUGH A TOLL-LIKE RECEPTOR-INDEPENDENT PATHWAY**J. Wennekamp, P. Henneke***Centre of Chronic Immunodeficiency/ Department of Paediatrics and Adolescent Medicine, University Medical Centre Freiburg, Freiburg, Germany*

Background and aims: Group B streptococcus (GBS) is a leading cause of sepsis and meningitis in newborn infants. Previous studies have shown that recognition of GBS cell wall by macrophages depends on the Toll-like receptor (TLR) adapter Myeloid Differentiation factor (MyD)88, whereas single TLRs are dispensable. GBS has been reported to induce macrophage apoptosis. We previously found that GBS cell wall rather induces an anti-apoptotic signaling program. GBS-induced anti-apoptosis is independent of TLR2. However, in striking contrast to the inflammatory program, the anti-apoptotic response was preserved under conditions known to abrogate Nuclear factor (NF)- κ B activation. Here we aimed to further dissect the role of TLR signaling in GBS-induced anti-apoptosis.

Methods: Primary and/or immortalized bone marrow-derived macrophages from WT and MyD88^{-/-} mice and macrophages deficient for both essential TLR adapters MyD88 and TRIF were co-incubated with various apoptosis-inducing agents (Actinomycin D, Staurosporine) and ethanol-/heat-fixed whole GBS organisms for 24h. Apoptosis was assessed by FACS analysis of Propidium Iodide-stained cells, active-caspase-3 staining or TUNEL.

Results: In accordance with our previous results, we found that GBS-induced anti-apoptosis is not directly linked to the strictly MyD88-dependent inflammatory NF- κ B activation: The anti-apoptotic program is preserved in MyD88^{-/-} macrophages. Intriguingly, GBS-induced anti-apoptosis occurs independently of TLR-signaling altogether, since MyD88/TRIF^{-/-} macrophages do not differ from wild type cells in this respect.

Conclusions: In macrophages, GBS cell wall induces anti-apoptotic signals through a MyD88/TRIF-independent program that is clearly distinct from the inflammatory response.

**KNOWLEDGE, ATTITUDE AND PERCEPTION ABOUT MALARIA AMONG MARRIED WOMEN:
IMPLICATIONS FOR INFANT MORTALITY IN LAGOS STATE****O. Adeyemi, A. Oyenuga***Sociology, Lagos State University, Lagos, Nigeria*

In Nigeria today, Infant and mortality rates are exceedingly high, and the country ranks 15th highest in one million children dying annually from preventable disease. Malaria is by far the most important cause of morbidity and mortality among Nigerian infants and young children. It exacerbates poverty, by diminishing productivity and household income, with further negative consequences for health and well-being of people in the country. The study therefore examines the knowledge of married women about malaria and its implications on infant mortality. A multi-stage random sampling procedure was employed in administration of 1500 questionnaires to married women. For qualitative data, Focus Group Discussion (FGD) was also used to collect information from the respondents. The data collected from this survey was subjected to three levels of analysis, univariate, bivariate and multivariate analysis. Logistic regression was employed to determine the relationship between dependent variable. The prevalence of malaria is very high in the area. Two of every four children of women interviewed had malaria in the last two weeks preceding the survey. Also 60% women interviewed had malaria during pregnancy. Only three out of every ten respondents have bed net and sleep under it. Findings revealed that majority of the mosquito bites normally occurred at night. Income, place of residence and education are significant factors influencing fever in the area. Urban poor are more vulnerable to the public health problems stemming from poor sanitation and water-related diseases. It is therefore necessary to reach the urban poor with education and outreach services

TREATMENT OF TOXOPLASMIC LYMPHADENITIS WITH CO-TRIMOXAZOLE: DOUBLE BLIND, RANDOMIZED CLINICAL TRIAL

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Background and objectives: Lymphadenitis is one of the presenting signs of toxoplasmosis. This study was performed to determine the therapeutic effects of co-trimoxazole (CTM) on toxoplasmic lymphadenitis (TL) in Ahvaz from 2005 to 2007.

Methods: Forty six patients with TL were enrolled in this randomized, double blind, placebo controlled trial study. Diagnosis was based on clinical examination, serological tests (chemiluminiscent) and histopathological examinations. Palpable lymph node, IgM>8 IU and follicular hyperplasia were defined as positive findings. Patients were randomly assigned to the comparison groups (23 patients in each group). CTM group were treated by CTM (48 mg/kg/day divided in 2 doses) for 1 month. Placebo group were treated by placebo for 1 month. The patients were followed up by physical and serological examination in month 1, 3 and 6. No palpable lymph node and IgM< 6 IU were defined as clinical and serological response. Results were analyzed in SPSS software using chi-square test.

Results: Clinical response was observed in 15(65.2%) in CTM group and 5 (21.7%) in placebo group. Serological response in CTM and placebo group was 65.2% and 13.1% respectively. Cure rate in CTM and placebo group was 65.2%, 95% CI 42.7-83.6 and 13.1%, 95%CI 2.7-33.5 respectively (P< 0.05). There was significant difference in therapeutic effect between 2 groups (P< 0.05). There was no difference in the site of infection between 2 groups (P>0.05).

Conclusion: CTM has a good therapeutic effect on TL and may be used in selected patient who treatment is required.

Keywords: Toxoplasmosis, Lymphadenitis, Co-trimoxazole.

**COMPARISON OF IN VITRO ACTIVITY OF ERTAPENEM WITH OTHER CARBAPENEMS
AGAINST EXTENDED-SPECTRUM BETA-LACTAMASE PRODUCING ESCHERICHIA COLI AND
KLEIBSELLA SPECIES**

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Objective: To evaluate ETP susceptibility of ESBL-producing Enterobacteriaceae clinical isolates in tertiary pediatric care center in Turkey

Design/ methods: All isolates of ESBL-producing Enterobacteriaceae isolates were collected from clinical specimens from children and susceptibility tests were performed via Vitek 2 compact system

Results: 99,0 % of the ESBL-producing E.coli isolates were found to be sensitive to Ertapenem, 99,5 % to Imipenem and 100 % were sensitive to Meropenem . Among the kleibsella species, 91,5 % of the isolates were sensitive to ertapenem, 99,3 % to Imipenem and 100% to Meropenem

Conclusion: The results of our data including isolates from children showed that ETP had high in vitro activity againsts majority of the ESBL producing E. coli and Kleibsella species like as published studies before. However more clinical studies were required for clinical activity of Ertapenem and clinical importance of the resistant isolates.

MYCOPLASMA PNEUMONIAE INFECTION COMPLICATED BY SEVERE ISOLATED MUCOSITIS IN A YOUNG GIRL: A CASE REPORT

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Stevens-Johnson syndrome is a well recognized extrapulmonary manifestation of *Mycoplasma Pneumoniae* (MP) infection. Few cases of isolated mucositis associated with (MPAM), without skin lesions, have been described, mainly in young male patients.

We report the case of a previously healthy 9-year-old girl who was hospitalized because of one-week fever, cough and malaise and subsequent development of stomatitis and bilateral conjunctivitis. She had been receiving azithromycin for 3 days and ceftriaxone since the day before admission, because of a right lower lobe infiltrate on her chest radiograph. Physical examination showed a pale skin with no rash or lesions, bilateral injected conjunctiva, swollen, erythematous lips, diffuse aphthous lesions of the oral mucosa and crackling rales at the right base on auscultation.

Laboratory evaluation revealed only a slightly increased C-reactive protein (15 mg/L) and erythrocyte sedimentation rate (53 mm/h). An echocardiography excluded coronary arteries abnormalities. Despite treatment with clarithromycin, ceftriaxone, acyclovir, and supportive therapy her mucosal lesions progressively worsened requiring parenteral nutrition. Ulcerations also developed on the genital mucosa causing dysuria and periungueal erythematous swollen round lesions appeared, with no other skin involvement. Microbiologic tests for viruses (including Herpes) resulted negative while MP serum antibodies were positive in a titer of 1:5120. A 4-day course of intravenous immunoglobulins was then administered with good clinical response.

Children with a respiratory illness and severe isolated mucositis should be promptly tested for MP. Intravenous immunoglobulins can be considered a valuable treatment for severe MPAM with no improvement after appropriate antibiotic therapy and supportive care.

GUT ECOSYSTEM CHANGES IN CHILDREN WITH ATOPIC ECZEMA

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Background and aims: Changes in intestinal flora can potentially increase risk of numerous diseases. The role of different microorganisms needs to be determined during allergy.

Aim of study was to investigate intestinal microbial flora in different age of children with atopic eczema.

Methods: Retrospective study of children with atopic eczema was done during period 2007 -2009. Totally, 154 faecal samples were examined. Children were divided into: Group I - 113 children aged 1-3 year-old; group II - 41 children aged 3-5 year-old. Stools were collected into sterile tube. 1 g of stool was diluted 1:10 with saline solution up to 10¹¹ dilution. Sample from each diluted tube was cultured on selective medium. Colonies were obtained after several (according to bacterial type) days of incubation at 37°C.

Results: In a first group counts of Escherichia coli with low enzymatic activity was higher - 89 cases (78.8%) compared to second group - 28 cases (68.3%). Proportion of Bifidobacteria and Lactobacteria was lower in all children with atopic eczema. Children who developed allergy were more often colonized with Haemolytic Escherichia Coli 34 (22.1%), Staphylococcus aureus 24 (15.6%), Candida albicans 16 (10.4%) and Proteus 15 (9.7%) at age of 1-5 years. These children had higher count of combination of above-mentioned microbial flora - 58 (37.7%) cases at the age of 1-3 years compared to 14 (9.1%) of 3-5 year-old children.

Conclusions: Children with atopic eczema reveal:

1. diminished Bifido- and Lactobacteria colonization.
2. Disproportion of intestinal flora prevails at 1-3 years of age.

ANGIOSTRONGYLUS EOSINOPHILIC MENINGITIS IN MAYOTTE ISLAND. REPORT OF 7 NEW PEDIATRIC CASES

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Background: *Angiostrongylus Cantonensis* is the principal cause of eosinophilic meningitis after eating intermediate hosts, or contaminated vegetables. Adults develop benign meningitis whereas severe disease may occur in children.

We describe consecutive pediatric cases newly diagnosed in Mayotte, Comoros Islands.

Patients-methods: We reported a serie of 7 consecutive pediatric cases with eosinophilic meningitis in Mayotte from November 2006 to May 2009. Diagnosis was established on clinical, or serological (immunofluorescence testing for antibodies against *A. cantonensis*) criteria. We used a clinical definition of eosinophilic meningitidis that included hypotonia or nuchal rigidity, eosinophilia in peripheral blood or in cerebral spinal fluid (CSF), and eating history.

Results: The median age was 9 months. All cases occurred during the rainy season.

The exposure history was reported in only two cases : one child ate a slug, one played with a snail.

All cases presented fever and hypotonia, four developed encephalitis, four had unspecified abdominal symptoms.

Eosinophilia was present in peripheral blood of all patients and in initial CSF of six of them.

The outcome was bad : only two patients completely recovered ; one died ; three had neurological consequences (2 psychomotor retardation, 1 epilepsy).

Only three children had a positive serology.

Conclusions: Diagnosis of *Angiostrongyliasis* must be considered for meningitis with eosinophilia occurring in children living in Mayotte.

Young pediatric cases are severe or fatal.

Since the efficiency of antiparasitic treatment is nowadays not yet proven, educating the susceptible population is essential for prevention and

control of the disease.

INFLUENZA RAPID ANTIGEN TESTS (IRAT) TO IMPROVE THE MANAGEMENT OF INFLUENZA IN CHILDREN IN PRIMARY CARE

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Background: Diagnosis of influenza based only on symptoms lacks of accuracy in children. The aim of this study is to evaluate the impact of IRAT in the management of influenza like illnesses in children in primary care.

Methods: Patients with clinical symptoms suggesting influenza were included after national influenza activity first increased above baseline levels according to the French influenza surveillance network (GROG). Clearview influenza A&B tests® were used for detection of influenza A and B virus antigen from nasal swabs.

Results: In 2008-2009 during 26 weeks period [46-19], 774 pediatricians and general practitioners included 20.034 children (mean age 4.5 ± 3.5 years, median 3.4). For 75.1% of patients, onset of symptoms was < 48h (34.3% < 24h, 13.2% < 12h). IRAT+ accounted for 54.3% of cases: A+, 45.4%, B+, 7.6% and A+B+, 1.3%. High risk children were 5.4%, among them, 21.6% were influenza vaccinated in 2007 and 28.7% in 2008. IRAT was positive in 37.6% of vaccinated children (in 2007 and in 2008) vs 54.5% in non vaccinated children ($p < 0.001$).

(%)	Prescription % CI 95%	
	Antiviral	Antibiotic
Overall population n=20034	20.5 [20;21]	17.9 [17;19]
IRAT+ (54.3)	35.2 [34;36]	13.6 [13;14]
IRAT- (45.7)	1.1 [0.9;1.3]	22.9 [22;24]
High risk children n=1059	27 [24;30]	27.4 [25;30]
IRAT+ (57.8)	46.5 [42;51]	20.4 [17;24]
IRAT- (42.2)	0.5 [0.1;2]	35.1 [31;40]
Acute otitis media and/or pneumonia n=2578	14.7 [13;1]	87.8 [86;89]
IRAT+ (48)	27.7 [25;31]	84.8 [83;87]
IRAT- (52)	0.5 [0.2;1.2]	90.6 [89;92]

[VIL]

Conclusion: More targeted influenza management with antivirals and antibiotics occurs when IRAT

results are available in overall children population and high risk children. Influenza vaccination among high risk children needs to be improved.

INFLUENZA RAPID ANTIGEN TESTS (IRAT) TO IMPROVE THE MANAGEMENT OF INFLUENZA IN PEDIATRIC EMERGENCY CARE UNIT

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Background: Diagnosis of influenza based only on signs and symptoms lacks of accuracy in children. The aim of this study is to evaluate the impact of IRAT in the management of influenza like illnesses in pediatric emergency care unit.

Methods: Patients with clinical symptoms suggesting influenza were included after national influenza activity first increased above baseline levels according to the French influenza surveillance network (GROG). Clearview influenza A&B tests® were used for detection of influenza A and B virus antigen from nasal swabs.

Results: In 2008-2009 during 20 weeks period [50-17], 33 emergency care units included 4480 children (mean age 3.9 ± 3.4 years, median 2.9). For 66% of patients, onset of symptoms was < 48h (28.3% < 24h, 14.6% < 12h). IRAT+ accounted for 51.9% of cases: A+, 44.4%, B+, 6.2% and A+B+, 1.3%. High risk children were 5.1%, among those, 16.9% were influenza vaccinated in 2007 and 18.7% in 2008. IRAT was positive in 41.7% of vaccinated children (in 2007 and in 2008) vs 52.1% in non vaccinated children.

(%)	Prescription % CI 95%	
	Antiviral	Antibiotic
Overall population n=4480	11 [10;12]	13.6 [13;15]
IRAT+ (51.9)	20.1 [18;22]	11.9 [11;13]
IRAT- (48.1)	0.4 [0.2;0.8]	15.7 [14;17]
High risk children n=223	17.9 [13;24]	40.5 [34;47]
IRAT+ (51.1)	32.7 [25;42]	31 [23;41]
IRAT- (48.9)	1.1 [0.2;5.8]	50.5 [41;60]
Acute otitis media and/or pneumonia n=395	17.2 [14;22]	77.2 [73;81]
IRAT+ (57.5)	28.7 [23;35]	69.9 [64;76]
IRAT- (42.5)	0	87.5 [81;92]

[hop]

Conclusion: More targeted influenza management with antivirals and antibiotics occurs when IRAT results are available. Influenza vaccination among high risk children needs to be improved.

PEDIATRIC USE OF CARBAPENEMS**X. Durrmeyer¹, R. Cohen²***¹Neonatal Intensive Care Unit, ²CLIN, Centre Hospitalier Intercommunal de Creteil, Créteil, France*

Increasing incidence of infections due to multi-drug resistant Gram negative bacilli (GNB) is currently observed in the adult and pediatric population. Therapeutic options are unfortunately limited to treat such infections. It is the clinician's responsibility to use wide-spectrum antibiotics when appropriate, but also to limit the use of these drugs to the sole situations where such a potent treatment is required. Carbapenems are the most efficient beta-lactams, especially against GNB, and the most preserved from resistance so far. This communication summarizes microbiological, pharmacokinetic and pharmacodynamic characteristics of currently available carbapenems. Their clinical use in different pediatric settings is then discussed, based on available published evidence. In order to maintain their microbiological efficiency and to limit the emergence of carbapenem-resistant strains, carbapenems should be exclusively used for infections due to GNB resistant to other beta-lactams. According to superior pharmacokinetic-pharmacodynamic properties, better tolerance and easier use in the pediatric population, meropenem should logically be preferred to imipenem in most pediatric indications in the next years.

AVIAN INFLUENZA INFECTIONS IN CHILDREN: SYMPTOMS & TREATMENT**O.A. Faik***Yuzuncu Yil University, Van, Turkey*

Background: Human infections with influenza A H5N1 continue to cause infection: presentation and effective treatments for children ages 18 and younger are of obvious interest.

Methods: This is a registry-based observational study of cases with laboratory support confirming H5N1 infection. Data were obtained primarily from clinical records, published case series and reports from governmental agencies.

Results: 166 patients ages ≤ 18 years from 12 countries were available for analysis. Fever was the most common presenting complaint, followed by unexplained respiratory symptoms, sore throat, headache, and tachypnea. Rhinorrhea was twice as common in children ≤ 5 yrs (~60%) compared to ages 6-12 yrs (30%, $p=0.01$). Also common at presentation among children ages ≤ 5 yrs were abnormal breath sounds (57%), tachypnea (56%), fatigue or malaise (50%), and diarrhea (39%).

Case fatality rates (CFRs) increased with age from 43% to 86% among those with no documentation of receiving any anti-influenza antiviral. Oseltamivir was the most commonly used anti-influenza antiviral reported (84/92; 91%). The CFR among cases aged 1-5 treated with oseltamivir (12%) is significantly lower than the CFRs for all older age groups (range 45-68%, $p < .001$ for all groups).

Seven patients received greater than the standard dose of oseltamivir; CFR=28.6% compared to CFR=71.4% in adults. Eleven patients ≤ 18 received oseltamivir for more than 5 days; 9 survived and two died.

Conclusions:

1. Oseltamivir is effective in children, imparting a survival benefit at all ages
2. Avian influenza has non-specific symptoms, with rhinorrhea being especially common in children under 5.

THE UPIIP'S WEB: AN OPEN DOOR FOR THE KNOWLEDGE OF INFECTIOUS DISEASES IN PAEDIATRICS WORLDWIDE (WWW.UPIIP.COM)

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Background and aims: The importance of expertise in paediatric infectious diseases (PID) is increasing in the recent years since the number of immunocompromised patients, the differences with adult patients and the emergence of new drugs are also raising. In addition, the use of new technologies should allow spreading and sharing knowledge among the different groups dedicated to PID.

Methods: In May 2009 the Pediatric Infectious Diseases and Immunodeficiencies Unit's (UPIIP) web was created with 3 different aims: to present the program "I am not alone", pretending to provide comprehensive, holistic care to HIV-infected children and adolescents; to release our Master in PID-pioneer in Europe -; and finally to share our experience with a larger number of paediatricians.

Results: Since it was put up on the net until December 2009, the web has been visited more than 25.000 times (3.500 visits per month on average) coming both from Spain and abroad, mainly Portugal and South America. Several private and public entities have chosen the web to exhibit their support to our speciality. The page rank (Google®) is of 5. Our master in PID is already in its second year with much approval. Both the web and the master have been considered of interest by the Sociedad Española de Infectología Pediátrica (SEIP).

Conclusions: The use of new technologies is an efficacious method to spread scientific knowledge. The future of paediatric infectious diseases lies on a high degree of specialization, reachable with masters as the one presented herein.

SEASONAL INFLUENZA: WHAT ARE THE BENEFITS OF EARLY NEURAMINIDASE INHIBITOR THERAPY IN YOUNG CHILDREN?**T. Heikkinen***Turku University Hospital, Turku, Finland*

Seasonal influenza affects all age groups, but the attack rates are clearly highest in children. Secondary illnesses, such as acute otitis media, pneumonia and sinusitis, are also particularly common, especially in young children < 6 years. Oseltamivir is an orally administered antiviral for the treatment and prophylaxis of seasonal influenza A and B infections in children ≥ 1 year and pandemic infections even in infants < 1 year. When started within 48 hours of symptom onset, oseltamivir significantly reduces the severity and duration of influenza in children 1-12 years by 29% and 1.5 days, respectively. Moreover, the rate of complications requiring antibiotic treatment may be reduced by up to 40% and that of acute otitis media by up to 44%. A study in adults has demonstrated that treatment within 12 hours of symptom onset shortens the duration of illness significantly more than treatment at 48 hours. In our recent placebo-controlled study among children 1-3 years, initiation within 24 hours of symptom onset shortened the time to resolution of illness by 3.5 days in those infected with influenza A viruses. A marked reduction in the rate of acute otitis media was also observed when treatment was initiated within 12 hours of symptom onset. This finding is in agreement with those of other recent studies which demonstrate that influenza-infected children who receive oseltamivir are less likely to develop secondary illnesses and to be hospitalised than those without antiviral treatment. Oseltamivir is well tolerated by children, with an almost similar overall adverse event profile to placebo.

CHARACTERIZATION OF THE PATTERN OF ANTIMICROBIAL UTILIZATION IN A PEDIATRIC INTENSIVE CARE UNIT (PICU) USING DAYS OF THERAPY (DOT)

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Background and aim: Monitoring of antimicrobial use is basic in guiding antimicrobial stewardship programs. The aim of this study was to characterize the pattern of antimicrobial use in a PICU.

Methodology: A prospective analysis of monthly antimicrobial use at a patient-level was conducted in an 8-bed polyvalent PICU of a tertiary-level hospital from January to November 2009. Antimicrobial use was calculated as DOT of each antimicrobial agent/category divided by 100 bed-days (DOT/100BD).

Results: During study period there was a median monthly rate (MMR) of 12 admissions and 144 bed-days in the PICU. Aminoglycosides constituted the most common used antimicrobial category (MMR 84 DOT/100BD) with amikacin being the most prevalent agent (MMR 69 DOT/100BD). Glycopeptides (vancomycin and teicoplanin) were the second most used antimicrobial category with MMR 36 DOT/100BD. Both piperacillin/tazobactam (the only used beta-lactam/beta-lactamase inhibitor combination) and carbapenems (meropenem and imipenem/cilastatin) had MMR 22 DOT/100BD. Colistin was the fifth most common used antimicrobial agent (MMR of 21.5 DOT/100BD). Clindamycin, 3rd and 2nd generation cephalosporins were also frequently used with MMR's of 19, 18 and 16 DOT/100BD, respectively. Use of other common antimicrobial agents included metronidazole, cotrimoxazole and clarithromycin, with MMR's of 12, 10 and 9 DOT/100BD, respectively. Utilizations of linezolid and ciprofloxacin (the only used fluoroquinolone) were infrequent.

Conclusion: High prevalence of use of antibiotics and especially of aminoglycosides and glycopeptides was found in this study. Relatively high rates of colistin utilization are of concern. Judicious use of all antibiotics cannot be overemphasized.

RESISTANCE: EXPERIENCE WITH THE NEURAMINIDASE INHIBITORS IN PANDEMIC (H1N1) 2009 AND SEASONAL INFLUENZA**L. Jennings***Canterbury Health Laboratories, Christchurch, New Zealand*

Influenza surveillance data show that the prevalence of oseltamivir-resistant seasonal H1N1 viruses is now very low, and that pandemic (H1N1) 2009 is the dominant H1N1 strain. Reports to date of resistance to oseltamivir in the pandemic (H1N1) 2009 virus are in most cases sporadic and geographically dispersed, according to worldwide surveillance up to early February 2010. New cases are being reported each week, but there is no evidence that resistant viruses are circulating within communities: the great majority (>99%) of over 20,000 clinical specimens or isolates of the pandemic (H1N1) 2009 virus tested across the six international WHO regions were sensitive to oseltamivir. A worldwide total of 225 oseltamivir-resistant pandemic (H1N1) 2009 isolates had been reported to the WHO by 3 February 2010. All have the H275Y mutation, which confers resistance to oseltamivir, but not zanamivir. With the exception of patients with immunosuppression, which is the largest single grouping affected, the disease course in those infected with oseltamivir-resistant pandemic (H1N1) 2009 has been uncomplicated and similar to seasonal influenza in the majority of cases. The antiviral resistance in pandemic (H1N1) 2009 is drug-induced, in contrast to the naturally-acquired resistance (not related to drug use) in seasonal H1N1 viruses that emerged in the 2007-08 northern hemisphere season. Large-scale clinical trials of oseltamivir treatment of seasonal influenza virus have suggested a low incidence of drug-induced resistance in immunocompetent adults (0.32%) and children (4.1%). The current reported frequency of drug-induced resistance in pandemic (H1N1) 2009 virus infections appears consistent with this observation.

MANAGEMENT OF PERI-ORBITAL / ORBITAL CELLULITIS IN CHILDREN**A. Kage***University of Leicester NHS Trust, Leicester, UK***Aim:**

1. To find out if there was uniformity in choice of antibiotics.
2. Are blood cultures, swabs and other blood tests helpful in management.
3. Look at involvement of other specialities in terms of follow-up and management.

Methodology: Retrospective analysis of case notes with a diagnosis of preseptal / orbital cellulitis in 2006-2007 across 2 DGH. 15 such cases were recruited.

Results: There was no uniformity in the antibiotics used. (5 different combinations were used). Blood cultures were negative in 13 cases. 6 out of 15 had CRP < 15. Eye swab was positive in 3 cases. Allied specialities were involved in 9 cases. Only 1 out of the total 15 cases developed an abscess and incidentally did not have anti-staphylococcal cover.

Recommendations: Education programme to raise awareness of complications of pre-septal/ orbital cellulitis.

- Involve ophthalmology and otolaryngology at the earliest.
- Twice daily assessment of colour vision, eye movements and pupil reflexes, for early identification of complications.
- Ensure adequate analgesia.
- Re-audit , preferably with the use of one antibiotic combination, also looking at indications for changing from IV to oral along with total duration.

ASEPTIC MENINGITIS IN CHILDREN

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Aim: Aseptic meningitis is an inflammation of the meninges caused mainly by nonbacterial pathogens, certain unique agents, or disease processes. Our objective was to determine the aetiological, clinical and laboratory features as well as the outcome of children with aseptic meningitis.

Methods: We studied all patients with aseptic meningitis admitted during the period August 2006 to September 2009. This period, a total of 54 children, 34 male (63%), was hospitalized with the above diagnosis (study group). Every patient underwent lumbar puncture on days 1, 3 and 7, PCR of the CSF for VZV, CMV and HSV and antibody testing for HSV, CMV, EBV, VZV, Adenovirus, Coxsackie and Echo virus, in CSF and serum on the same days.

Results: Patients' mean age was 7 years (2,5 months to 13 years). Mean hospitalization stay was 5,8 days. Most of the patients had fever (41/54) and headache (49/54). Additional symptoms were present in 12 patients (4 drowsiness, 2dizziness, 3seizures, 2photophobia and 1 hypotonia). No patient received intravenous antibiotics. The laboratory testing (PCR, antibodies in CSF and serum) failed to identify any aetiological agent of the disease. An interesting observation was that CSF leucocytes delayed to normalize after 2-3 days of disease, despite patient's improvement. All patients recovered fully without sequelae.

Comments: Identification of some aetiological pathogen of aseptic meningitis seems difficult. The disease is mild and self-limited. It is important to differentiate it from encephalitis, tuberculous meningitis or inadequately treated bacterial meningitis, as these conditions may result in severe complications if untreated.

ACUTE HEMORRHAGIC LEUKOENCEPHALITIS

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Background: Acute hemorrhagic leukoencephalitis (AHLE) is a rare demyelinating disease characterized by an acute rapidly progressive fulminant inflammation of the white matter. It is a more severe form of acute disseminated encephalitis (ADEM) characterized by a fulminant clinical course.

It is usually preceded by an infectious illness, such as measles, mumps, rubella and respiratory infectious. Nevertheless, no virus or other infectious agent has been isolated from the CSF or brain in case of ADEM.

Patient report: We are reporting a previously healthy 13-year-old girl, admitted to an American military hospital in Harat (north of Afghanistan) because of fever and alteration of consciousness. The mother reports her right side face was swelled at the evening and then at the mid night she got non responsive to the verbally calling.

After four days she was referred to our PICU in Mashhad- Iran. On admission, She had right side parotiditis. Her initial MR imaging revealed mainly involving the white matter containing multifocal hemorrhages without edema.

We found leukocytosis with predominant polymorphonuclear cells in the peripheral blood. Cerebrospinal fluid showed white blood cell count of 3-4 cells/mm³, increased protein level (69mg/dl). The result of immunologic and microbiologic studies were negative.

Second MRI (20 days later) showed multiple hemorrhagic lesions in the pons and both thalamuses .

Patient was treated with Methylprednisolon, IVIG, Acyclovir and plasmaphoresis. She was extubated and attained a remarkable healing.

Keywords: Acute hemorrhagic leukoencephalitis, Acute disseminated encephalomyelitis

ETIOLOGY AND OUTCOME OF NONTRAUMATIC COMA IN CHILDREN ADMITTED TO PEDIATRIC INTENSIVE CARE UNIT

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Objective: Nontraumatic coma is a relatively common condition in children. The purpose of this study was to determine clinical presentation, etiology and outcome of nontraumatic coma in children.

Methods: In a retrospective cross sectional study over a period of 5 years, files of 150 children aged between 1 month and 14 years admitted with nontraumatic coma to pediatric intensive care unit of Rasool Akram hospital were reviewed. Historical, presenting symptoms, clinical and laboratory data were collected. Etiology of coma was determined on the basis of clinical history and relevant investigations. The outcome was recorded as died or neurological condition at discharge as normal, mild or sever disability. Chi-square test was used to test the differences in categorical variables.

Findings: There were 63 (42%) boys and 87 (58%) girls. The mean±SD age of patients was 2.7±2.35 years. Etiology of coma in 49 patients (32.7%) was infectious (meningitis, encephalitis, respiratory and systemic). Other causes were status epilepticus 44 (29.4%), metabolic (diabetic ketoacidosis, inborn errors of metabolism) 11 (7.3%), intoxications 10 (6.7%), accidental (drowning, electrical shock, suffocation) 9 (6%), shunt dysfunction (secondary to congenital brain malformations) 7 (4.6%), others (acute disseminated encephalomyelitis, vasculitis, hypertensive encephalopathy) 11 (7.3%), unknown 9 (6%). Infection occurred significantly ($P=0.002$) in children under 2 years of age, whereas accidents and intoxications were more prominent ($P=0.004$) in those between 2 and 6 years.

Conclusion: Our results showed that infection was the most common cause of nontraumatic coma in childhood. Accidents and infection had higher mortality than other causes.

ACUTE MASTOIDITIS (AM) IN CHILDREN - A 10 YEAR RETROSPECTIVE STUDY

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Background and aims: A growing incidence of AM has been reported. Our aim was to review our experience in the last decade.

Methods: Retrospective analysis of the medical records of children with AM from January 1999 to June 2009. Inclusion criteria was the presence of at least one physical sign of mastoiditis, with concomitant or recent (≤ 4 weeks) acute otitis media (AOM).

Results: There were 128 episodes, with a median of 11 episodes/year (8-20), with half of the cases occurring in the first 5 years. The median age at diagnosis was 19 months (4 months - 15 years); 54% were < 2 years; 57% were male. 18% of the cases had recurrent AOM. AM was the first evidence of AOM in 62 (48%) children; 45% were on antibiotics for AOM mainly amoxicillin or amoxiclav. The most frequent signs were: retroauricular swelling (80%) and redness (87%), protrusion of the auricle (60%), fever (73%), earache (59%), otorrhoea (33%). CT scan was performed in 30%. 83% received intravenous antibiotics with good outcome; the remaining required surgery. Complications were registered in 13%: periosteal abscess (13), osteitis (5), lateral sinus vein thrombosis (2). Bacteria were isolated in a small number of cases, of which *S. pneumoniae* was the most frequent.

Conclusions: We did not find an increasing incidence of AM in recent years. Half of the children had not seen a doctor for AOM and AM was the first evidence of AOM. Most children made an uncomplicated recovery. Microbiological investigation needs to be improved.

OCCULT BACTEREMIA - A PORTUGUESE HOSPITAL STUDY**T. Marques, M. Ferreira, M.J. Brito***Pediatrics, Hospital Prof. Doutor Fernando Fonseca, EPE, Lisbon, Portugal*

Background and aims: Occult bacteremia (OB) is defined by pathogenic bacteria in blood of febrile children less than 36 months, without ill appearance or focus of infection. Serious bacterial infections may occur in few cases.

Evaluate the characteristics, diagnosis and outcome of OB and identify eventual risk factors for severe invasive disease.

Methods: Retrospective study (4 years) of children 1-36 months admitted with OB. Two groups were identified: Group A (with OB) and B (without OB). Demographic, clinical, laboratory, therapeutic data and outcome were analysed.

Results: Of 131 cases, 48(36,6%) did not present criteria for OB. Of the remainder 83, 23 had: pyelonephritis (12), adenovirus infection (5), respiratory infection (3), pneumonia (1), meningitis (1), mastoiditis (1) - Group A. OB was diagnosed in 60 cases, the mean age being 11,3±6,37 months. Eighteen (30%) and 38 (63%) had pneumococcal and meningococcal vaccine, respectively. Most children (80%) had fever $\geq 39^{\circ}\text{C}$ for a mean of 44 hours ($\pm 41,92$) with a mean leukocyte, neutrophil and serum C-reactive protein count of 23,346/mm³ ($\pm 6,500$), 15,445/mm³ ($\pm 5,914$) and 9,23mg/dl ($\pm 6,8$), respectively. Nine (15%) had positive blood cultures: *Streptococcus pneumoniae*(7); *Streptococcus* group B(2). Pyrexia time was earlier in OB after initial antibiotic therapy (29,78vs48,04H; $p=0,004$). No statistic differences were found between age, fever, temperature and laboratory findings in either group.

Conclusions: A high number of children with initial diagnose of BO had other diseases. No predictive factors were found for OB, but earlier pyrexia after antibiotics suggest bacteriemia, and if it does not happen we must think of other pathology.

THE RISK OF FALSE CLAIMS OF ASSOCIATION OF mtDNA SNPS AND MENINGOCOCCAL DISEASE DUE TO POPULATION STRATIFICATION

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Background and aims: It has been recently suggested that mitochondrial DNA (mtDNA) variants are predisposition risk factors to several complex, multi-factorial, diseases (Alzheimer, Parkinson, cancer, etc), and also to various infectious diseases. There are reasons to believe that most (if not all) the positive findings of association observed in these studies are spurious, because most of them are not supported on a replication sample, do not take into account multiple testing in their statistical analysis, and none of them consider the potential confounding effect of population stratification.

Methods: We have recently investigated the mtDNA haplogroup background in a cohort of Spanish meningococcal disease (MD) patients (N=307) using 25 different SNPs (Single Nucleotide Polymorphisms). This prospective study was performed through a national research-network on MD (ESIGEM network-www.esigem.org) that includes 39 hospitals (Salas et al. 2009). Cases were compared with two different samples of healthy ethnicity-matched Spanish controls. Moreover, 34 ancestry informative markers were genotyped in order to monitor potential hidden population stratification.

Results: Association analysis suggested an overrepresentation of the synonym mtSNP G11719A in cases respect to one of the control groups, but not to the other. Analysis of spatial patterns of variation in different Spanish sub-populations indicates significant levels of stratification for the G11719A variant.

Conclusions: We have demonstrated that inadequate geographically unmatched samples, even in small geographic locations, can lead to spurious findings of association due to the high level of population stratification that characterizes mtDNA variation in human populations. In our opinion, all published mtDNA association studies should be quarantined.

PAEDIATRIC USE OF ANTIVIRALS IN SPAIN: ADMINISTRATIVE, LEGAL STATUS AND RECOMMENDATIONS OF USE

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Background: Pharmacokinetic, efficacy or safety data are unavailable for paediatric drugs currently prescribed in Spain; major differences exist in their administrative status and authorized use. TEDDY network (Task-force in Europe for Drugs Development for the Young: LSHB-CT-2005-005216, 7thFP-EU) promotes the availability of safe and effective medicines for children in Europe integrating existing expertise and good practices, stimulating further developments.

Aims: To study the paediatric use of antivirals available in Spain.

Methods: We find all antivirals' summaries of product characteristics (SPC) by consulting Spanish and European Medicines Agencies (AEMPS, EMEA) and identify their administrative, legal status and recommendations of use in Spain. We classified every drug in one or more of the groups:

- 1) Availability of SPC;
- 2) National labeled drugs with paediatric indications (NLD);
- 3) Off-label drugs (OL);
- 4) Unlicensed drugs and magistral formulae (UL-MF);
- 5) Drugs prescribed by "Compassionate Use" (CU).

Results: There are 47 antivirals available in Spain; 39 of them (83%) have SPC in AEMPS or EMEA webpages. Only 11 (23%) are NLD. Up to 62% (29) can be used as OL drugs in some paediatric groups; 49% may need MF to obtain an appropriate dosage; 31 (66%) need CU to be use in most paediatric ages.

Conclusions:

- 1) Only 23% of antivirals available in Spain are NLD with paediatric indications.
- 2) Because most antivirals are now improperly labeled or prescribed outside normal regulatory channels, the official regulatory status for prescribing these drugs should be urgently addressed by new European Paediatric Regulation, with active involvement of TEDDY.

BLOOD LOSS RELATED TO PARTICIPATION IN PK STUDY IN VLBW NEONATES: REVIEW OF PRESENT PRACTICE AND A COHORT STUDY

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Background and aim: To generate overview of existing guidelines regulating research-related blood loss in infants and to provide scientific evidence on the safe amount of blood drawn from VLBW neonates for study purposes.

Methods: Members of international paediatric research networks were asked about institutional/national guidelines on the volume of blood samples allowed in paediatric clinical trials. A post-hoc analysis of a PK study of penicillin in 18 neonates with birth-weight < 1200g, gestational age < 28 weeks was performed. Haemoglobin, haematocrit, hemodynamic parameters, fluid intake and number of blood component transfusions were recorded. The results were compared to a gestational age, birth-weight and postnatal age matched control group of 35 neonates.

Results: Recommendations on acceptable research-related blood loss varied tenfold. In the PK study a median of 2.3 ml/kg of blood (2.4% of calculated circulating blood volume (CCBV)) was collected from each neonate. There were no differences in haemoglobin or haematocrit values between the two groups during a 7 day follow-up period. Median number of blood component transfusions (n = 2 in both groups), median volume of transfused red blood cells (22 vs 24 ml/kg in the study vs control group) and total daily fluid requirement were similar in both groups.

Conclusions: Scientific data on the safety of neonatal PK studies are urgently needed. Up to 2.3 ml/kg of blood (corresponding to 2.4% of CCBV) can be drawn from a preterm neonate for scientific purposes without increasing the need for red blood cell transfusions or compromising haemoglobin or haematocrit values.

ATTITUDE TOWARDS VACCINATION IN THE NETHERLANDS

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Background and aims: Anti-vaccination movements require increased knowledge on vaccination attitudes. We therefore studied determinants associated with participation in the national immunization program (NIP) and intention to accept future vaccinations.

Methods: Questionnaire data of a cross-sectional population-based serosurveillance study (2006/7) were used. Multiple logistic regression (N = 5911) and multivariate multiple logistic regression (N = 2283), using hierarchical models, were used to study determinants of NIP participation and intention to accept future vaccinations, respectively.

Results: Age 30-44 years, low education and income, non-Western ethnicity, orthodox reformed individuals (ORIs), living in low urbanization areas and having anthroposophic, homeopathic or religious ideas on vaccination were associated with higher risk of non-participation in the NIP. For ORIs and the general population disagreeing that vaccinations protect their child, agreeing that vaccination of healthy children is unnecessary and doubts regarding vaccine safety were associated with less acceptance of future vaccinations. For anthroposophists disagreeing that vaccinations protect their child and agreeing that vaccination is no good for development of their children's immune system were significantly associated with less acceptance of future vaccinations.

Conclusions: Our results confirm that religious groups and anthroposophists refuse (some) vaccinations. Furthermore we found lower NIP participation for individuals with non-Western ethnicity and those with lower social economic status. The association with uncertainty to accept future NIP vaccination was the result of specific opinions on vaccination among various groups of individuals. The study results will be used in the design of more in depth studies on NIP acceptance and for health promotion communication.

INTRACRANIAL COMPLICATIONS OF SINUSITIS. A CASE REPORTJ. Lopez¹, M. Giner¹, R. Ballester¹, L. Fernandez¹, M. Otero¹, **S. Negre**²*¹Departamento de Enfermedades Infecciosas, ²Hospital Infantil La Fe, Valencia, Spain*

Introduction: Sinusitis is a prevalent infection, which usually responds well to oral empirical antibiotics. However, patients may develop occasionally severe complications, which require prompt diagnosis and a more aggressive approach.

Case report: We report the case of a 12-year-old boy who presented with pansinusitis. Due to the severity of his symptoms, we treated him with intravenous ceftriaxone with good response. After 7 days we switched to oral amoxicillin-clavulanate. 3 days later, the patient worsened and developed severe headache and stiff neck. Lumbar puncture showed polymorphonuclear pleocytosis, hypoglycorrhachia and high protein. Cavernous sinus and left ophthalmic vein thrombosis, and persistent pansinusitis were found on magnetic resonance imaging (MRI). An endoscopic sinus surgery was performed and intravenous antibiotics were started again, this time with intravenous (iv) ceftriaxone combined with linezolid. The culture from surgical specimen showed *Streptococcus B* haemolytic group C and gram negative bacillus at the direct examination. The treatment was switch to iv meropenem. The patient improved over the following days. Low molecular weight heparin was started 7 days after surgery. A control MRI demonstrated resolution of the ophthalmic vein thrombosis and a partial improvement of the cavernous sinus thrombosis. At discharge the patient continued treatment with levofloxacin.

Comments: Empirical therapy of sinusitis must cover gram positive bacteria but we must not forget anaerobic. It requires a close monitoring in order to prevent complications. In severe cases surgery could be necessary. Intracranial thrombosis is a very severe complication of sinusitis. Strong headache or neurological abnormalities should always alert us.

INNOVATING ON RESEARCH IN PAEDIATRIC INFECTIOUS DISEASES IN SPAIN. TEDDY NETWORK OF EXCELLENCE

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Introduction: TEDDY (Task-force in Europe for Drugs Development for the Young) is a European Network of Excellence founded by the 7th Frame Program of the EU, Project number LSHB-CT-2005-005216.

Implementation and development of TEDDY network on infectious diseases:

1.- PHARMACOEPIDEMIOLOGY: Setting up the new structure data base on off-label and off-patent anti-infective drugs in Spain and collaborating into TEDDY network on priority list on anti-infective drugs for the EMEA in which are urgent to develop a Paediatric Investigation Plan (PIP) in order to adequate the use on the Industry technical data.

2.- CLINICAL TRIALS AND PRACTICAL APPLICATION: There have been analyzed the "new PIP's impact" and the repercussion on determined clinical trials on paediatric infectious diseases. Set up the analysis of the situation of antibiotic resistance in children in Europe.

3.- SET UP OF THE SPANISH PAEDIATRIC BIO-BANKS: Setting up the development of the rational for the new "Bio-banks" of the paediatric samples in Europe, with high grade of exigencies on bioethical and samples preservation for the future research.

Conclusions: Important resources increasing on research and development from the EU it have set up in Spain since last five years looking for the optimization on paediatric drugs. Nevertheless our Country is far away from the European media. Spanish participation on European networks of excellence as TEDDY is principal. to continuous the input to the paediatric research, TEDDY is a wonderful example to continue increasing the researching and developing on Spain specially on paediatric Infectious diseases areas.

STRATEGIES FOR THE DEVELOPMENT OF NEW VACCINES

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The reputation of vaccination rests on a two hundred year old history of success against major infectious diseases. In general, two achievements have been crucial to the success of vaccines: the induction of long-lasting immunological memory in individuals and the stimulation of a herd immunity that enhances control of infectious diseases in populations. However, when one reviews the vaccines now available it is apparent that most successes have been obtained when the microbe has a bacteremic or viremic phase during which it is susceptible to the action of neutralizing antibodies, and before replication in the particular organ to which it is tropic.

Success has also been achieved against some agents replicating on respiratory or gastrointestinal mucosae, against which it has been possible to induce immune responses acting locally as well as systemically. Control of intracellular pathogens has not been achieved, except partly with the BCG vaccine against tuberculosis, and modern efforts are directed towards pathogens against which cellular immune responses are critical.

Newer approaches in vaccine production such as reassortment, recombination, virus-like particles, nucleic acid immunization, vectors, reverse genetics and additional routes of administration may circumvent prior difficulties. The target of vaccination will shift towards adolescents, adults, patients in hospital and those with chronic diseases and possibly will extend to therapy as well as prevention. The major scientific problems to be solved are maintenance of immune memory, immaturity and post-maturity of the immune system, and adjuvants capable of stimulating selective cell types

NEW TRENDS IN ANTIFUNGAL THERAPY IN CHILDREN

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Invasive fungal infections constitute an important cause of increased morbidity and mortality in immunocompromised children, premature neonates and patients with various risk factors. During the last decade a number of antifungals has been studied mainly in adult patients. Such agents are newer triazoles, voriconazole and posaconazole, and echinocandins (caspofungin, micafungin and anidulafungin). Most of these antifungals have not been studied in neonates and some of them not even in older children. None of the triazoles and only micafungin has been studied in neonates. Among infants and older children, voriconazole has been pharmacokinetically studied and used for mould coverage (mainly aspergillosis). Pharmacokinetic data on echinocandins have been recently published and allowed use of agents from this category to treat invasive candidiasis causing less toxicity to hematological and ICU patients. Questionnaire-based studies of antifungal use conducted in US Children's Hospitals and among ESPID members revealed that use of deoxycholate amphotericin B has been reduced dramatically in the last years, whereas use of lipid amphotericin B and voriconazole has been increased correspondingly. Echinocandins appeared in the antifungal armamentarium during the last years. After several control studies of prophylactic fluconazole administration to very low birth-weight neonates conducted during the last decade, there is a trend of increased use of this strategy in NICU's with high incidence of *Candida* infections in the very low birth-weight neonates. Preemptive therapy with use of several laboratory markers such as beta-glucan, galactomannan, PCR or others will improve diagnosis and management of invasive fungal infections in neonates and children.

SYDENHAM'S HEMICHOREA - NOT GONE NOR FORGOTTEN

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Background: Sydenham's chorea (SC) is one of the major clinical manifestations of acute rheumatic fever, reported in 20% of cases of this disease, and is the most common form of acquired chorea in childhood. SC is a movement disorder caused by group A streptococcal infection and characterized by chorea, emotional lability and hypotonia. Females are affected more frequently than males (2:1) and some cases show a familial predisposition. Only 20-30% of the patients have hemichorea.

Case report: A 6-year-old boy, previously healthy, with a family history of Huntington's disease, born from a non-tested and asymptomatic mother, presented with complaints of migratory arthralgia with 3 weeks of evolution, asthenia, depressive mood, and rapid, irregular and non intentional movements of the right arm and leg. On physical examination he had a grade III/VI systolic murmur and choreiform movements of both right limbs. Laboratory examination revealed elevated ESR (63mm/h) and C-reactive protein (25mg/L); anti estreptolisina title was 1824U/mL and anti-neuronal antibodies were negative. Cardiac evaluation showed mild aortic and mitral regurgitation and a prolonged PR interval. Brain MRI was normal. He was treated with penicillin, haloperidol, captopril and furosemide. One month later his mood had improved and the choreiform movements and hypotonia had practically disappeared.

Conclusion: Although the incidence of SC has diminished, being rare in developed countries, isolated cases still persist. The occurrence of SC in families with Huntington's disease highlights the relevance of differential diagnosis of those forms of chorea.

MONOVALENT TO QUADRIVALENT VACCINES: BROADENING PROTECTION AGAINST MENINGOCOCCAL DISEASE

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In many countries, large catch-up campaigns using meningococcal serogroup C conjugate (MenC) vaccines have led to a dramatic decrease in serogroup C disease. It is also believed that a herd immunity effect has contributed to the effectiveness of these vaccines. However, while vaccine effectiveness is high, waning of the protective titer in the youngest population has been of concern. Alternative vaccination schedules and vaccination strategies that offer sustained protection have been considered, eg, a booster dose in adolescents (recently recommended in Austria, Canada, and Switzerland). The rationale for this booster is to ensure that adolescents are adequately protected as they enter a period of increased risk, primarily due to changing behaviors and increased exposure to risk factors, such as close-quarters living, and secondly, to maintain the potential herd effect, by reducing carriage.

Meningococcal ACWY (MenACWY) conjugate vaccines have been developed that offer the possibility of broadening protection. An investigational MenACWY vaccine with CRM₁₉₇ carrier protein (MenACWY-CRM) has been shown to be highly immunogenic in adolescents and adults. In short-term immunogenicity and safety head-to-head trials, more individuals achieved a protective immune response with MenACWY-CRM than licensed comparators, such as MenACWY-D and polysaccharide vaccines. Although these MenACWY vaccines contribute to protection against four of the five disease-causing serogroups, development of a serogroup B vaccine using the same technology has not been possible. An investigational recombinant serogroup B vaccine, containing multiple antigens, is now in Phase III development following reverse vaccinology findings. Results from clinical studies have demonstrated that the vaccine is immunogenic with acceptable tolerability in infants and adults.

CASE REPORT: FOURNIER'S GANGRENE IN AN 11-YEAR-OLD GIRL**M. Tsinti**¹, T. Tsekoura¹, E. Blevrakis², I. Vlachakis², A. Tsimiligaki-Christaki¹¹*Department of Pediatrics, Venizelion General Hospital,* ²*Department of Pediatric Surgery, University of Crete, Heraklion, Greece*

Background and aims: Fournier's gangrene is a necrotizing fasciitis of the perineum and the genital area, a rare disease in children, usually following infection or trauma of the genitourinary tract, the colon or the perineal soft tissue. Multiple bacteria of the regional flora are usually isolated.

Methods: We report a case of Fournier's gangrene in an otherwise healthy 11-year-old girl.

Results: The child presented ill-appearing with fever for 5 days (40°C). Physical examination revealed erythema, swelling and necrotizing lesions with purulent exudate in the vulva, with severe pain. The inflammatory markers were elevated and the urinalysis was abnormal. Ultrasound-imaging of the perineum revealed fluid collection, air-bubbles and edema in the subcutaneous tissue and enlarged inguinal lymph nodes. After puss and blood cultures were taken antibiotic-treatment, with vancomycin, meropenem and clindamycin was initiated and the patient was admitted to the pediatric-surgical department. The patient was afebrile after 48hrs of treatment. The necrotic lesions were confined to the subcutaneous tissue and the fascia and did not expand to the muscles or the abdomen. Enterococcus faecium and Staphylococcus aureus were isolated from the lesions and the blood. Four surgical procedures were undertaken to remove the necrotizing lesions and to put suprapubic catheter and colostomy. The wounds healed after 45 days of treatment. Autoimmune, malignant and infectious diseases were excluded.

Conclusions: Early diagnosis of Fournier's gangrene according to the clinical picture, imaging and laboratory findings and initiation of aggressive antibiotic and surgical treatment lead to the optimal outcome.

A SEROLOGICAL STUDY ON TOXOPLASMA GONDII INFECTION IN A CHILDREN HOSPITAL IN GREECE

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Objective: The aim of this study is to determine the seroprevalence of Toxoplasmosis in children over a period of five years (2004-2009) with generalized or cervical lymphadenopathy.

Material and methods: Analysis of the serological response to *Toxoplasma gondii* of 992 patients aged from 1 to 14 diagnosed with generalized or cervical lymphadenopathy was carried out. All patients were tested for the TORCH series. A pair of blood samples was collected from each patient. Blood samples were tested for specific IgG and IgM antibodies with Microparticle Enzyme Immunoassay. The existence of both IgG and IgM antibodies or the quadruple title of the IgG antibodies confirmed the diagnosis.

Results: Out of 992 children examined, 62 (6,5 %) were found positive for IgG antibodies against *Toxoplasma gondii* and 18 (1,8 %) were positive for IgM antibodies while 15 (1,5 %) were positive for both IgG and IgM. After a period of two weeks all positive sera were tested again and there was a significant increase of IgG titers. The three (3) children with only IgG antibodies showed IgM positive antibodies as well. The seroprevalence tended to increase with age. The peak prevalence was seen in the 8-14 age groups. No significant differences of seropositive rates between sexes were detected.

Conclusion: The frequency of Toxoplasmosis in Greece, though relatively low, is not rare. The habit of eating well-cooked meat and the good socioeconomic status of most of the children may contribute to the low prevalence. The above results suggest that *Toxoplasma gondii* infection should be considered in any child with lymphadenopathy.

PANDEMIC (H1N1) 2009 IN CHILDREN: IMPACT AND PRACTICAL EXPERIENCES OF THE NEURAMINIDASE INHIBITORS

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Over 212 countries and overseas territories worldwide have now reported confirmed cases of pandemic (H1N1) 2009 influenza. Children and adolescents are highly susceptible to infection and have been disproportionately affected: >50% of the cases reported in Europe by 7 August 2009 involved individuals ≤ 19 years old and around one in three children < 15 years were infected in areas of England with high incidence rates. In most cases, symptoms have been mild and typical of influenza, although fever may be absent in infants and diarrhoea may be more common in young children. Severe or complicated disease has been reported in a minority of cases, and is characterised by signs of lower respiratory tract disease, central nervous system involvement, complications of low blood pressure, myocarditis or rhabdomyolysis, or invasive secondary bacterial infection. Deaths are uncommon (~ 1 per 100,000 children), but may occur with a higher frequency than that reported for seasonal influenza (~ 0.1 per 100,000 children). Risk factors are age < 5 years and the presence of underlying illnesses, particularly neurodevelopment conditions; bacterial co-infection may also increase the risk of death. WHO recommends early treatment with the oral neuraminidase inhibitor (NI) oseltamivir for children of all ages with severe or progressive pandemic (H1N1) 2009 influenza, and oseltamivir or the inhaled NI zanamivir (children ≥ 5 years only) for those at high risk for severe or complicated disease. Recent studies consistently demonstrate the benefits of early antiviral treatment, including faster viral clearance, shorter hospital stay, lower risk of progression to severe illness and improved survival.

SEROTYPES CAUSING INVASIVE PNEUMOCOCCAL DISEASE IN CHILDREN AND SEASONAL INFLUENZA EPIDEMIC THRESHOLD IN MADRID (PERIOD 2008-2009)

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Background and aims: The invasive pneumococcal disease (IPD) shows an important flu-like seasonality. The aim of this study was to relate the distribution of *Streptococcus pneumoniae* serotypes causing IPD in children to the seasonal influenza epidemic period (SIEP) in the Madrid Autonomous Region (MAR) during 2008-2009.

Methods: Cases of IPD in children less than 16 years old were identified by the Surveillance System of IPD of the MAR. Strains were serogrouped using a latex agglutination test (Pneumotest-Latex) and serotyped by the Quellung reaction. Data of influenza were obtained from the SENTRY Medical Network of the MAR. The SIEP was defined as the period when the seasonal influenza epidemic threshold (SIET) was surpassed. The SIET was calculated as the mean weekly incidence in the 5 preceding seasons.

Results: During the 22 weeks of the study 92 strains of *Streptococcus pneumoniae* were serotyped. Four serotypes represented 78.3% of the isolates: serotype 19A (29.3%), 1 (28.3%), 5 (10.9%) and 7F (9.8). The SIEP lasted from week 50 of 2008 to week 7 of 2009. Most of the strains of serotypes 19A (70.4%), 1 (69.2%) and 5 (70.0%) were isolated outside the SIEP. Most of the strains of serotype 7F (55.6%) were isolated during the SIEP. Most (55.0%) of the strains of other serotypes less frequent were isolated during the SIEP.

Conclusions: The relationship between influenza virus and IPD in children could be dependent on serotype. The most frequent serotypes isolated in children during this study predominate outside the SIEP.

ANTIBIOTIC SUSCEPTIBILITY AND SEROTYPES OF NASOPHARYNGEAL STREPTOCOCCUS PNEUMONIAE IN SOUTH AUCKLAND CHILDREN

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Streptococcus pneumoniae (S.pn) is a major cause of childhood morbidity and mortality; nasopharyngeal colonisation precedes invasive disease. Reduced S.pn nasopharyngeal carriage of vaccine and antibiotic resistant serotypes is well described internationally following conjugate S.pn vaccine (7vCV). Disproportionately high rates of invasive pneumococcal disease (IPD) among Auckland infants have been reported. This study aims to characterise S.pn serotypes and antibiotic susceptibility in this population prior to 7vCV New Zealand introduction.

Methods: Children ≤ 2 years admitted to Kidz First Children's Hospital, South Auckland with acute respiratory infection between August 2007 and August 2008 were included. Nasopharyngeal aspirates (NPA) were cultured for S.pn and antibiotic susceptibility performed via standard methods. Clinical and Laboratory Standards Institute MIC criteria for oral penicillin and ceftriaxone (meningitis) were used. The National Reference laboratory serotyped isolates.

Results: Of 732 NPA, 218 (30%) were positive for S.pn. Of 209 viable isolates 45% were penicillin non-susceptible with 27% resistant. 36% were ceftriaxone non-susceptible with 5% resistant. Amongst penicillin-resistant isolates, 34% were resistant to ≥ 3 additional antibiotics. Of the 137 isolates serotyped, most frequent were 19F (20%), nontypable (15%), 23F (10%), 6B (11%), 19A (7%).

Conclusions: Significantly higher rates of penicillin resistance (pen R) and ceftriaxone non-susceptibility (ceft NS) were observed compared with national IPD surveillance over the same ages and period (pen R: 27% vs. 6%. ceft NS: 36% vs 13%). 7vCV covers 53% of serotypes found in nasopharyngeal isolates. This highlights the value of future monitoring of invasive and non-invasive S.pn following 7vCV introduction for therapy decisions and future vaccine development

PNEUMOCOCCAL BLOOD STREAM INFECTIONS IN PEDIATRIC HEMATOLOGY ONCOLOGY**I. Bin-Hussain¹, I. Barron², A. Al Belgaumi³**

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Materials and methods: A retrospective evaluation of the clinical and microbiology records of children with hematological oncological disorders treated at KFSH & KFCCC with Blood Stream Infection due to *S. pneumoniae* (SP) between Jan 1998 and Dec 2008.

Results: A total of 164 episodes of Bacteremia with *Strep pneumoniae* were identified during this 11 yr period. Infections occur mainly in children > 3year of age. Fever present in 82% and 31% presented with pneumonia in addition to positive blood culture. Sixty percent of the isolate are resistant to penicillin.

Conclusions: *S pneumoniae* remains the significant cause of morbidity and mortality among our patients not restricted to those with severe neutropenia. This is a potentially preventable disease especially with the availability of conjugate pneumococcal vaccine which is included on our recently established immunization program for these high risk patients.

INVASIVE PNEUMOCOCCAL DISEASE IN CHILDREN: AN ISLAND'S REALITY

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Background: Invasive Pneumococcal Disease (IPD) in children is the major cause of morbimortality worldwide and the major vaccine preventable infectious disease. The heptavalent pneumococcal conjugated vaccine (PCV7) was licenced in Portugal in 2001 and there is an estimated vaccination rate in Madeira Island of 77,9%.

Method: Descriptive observational prospective study, conducted in Hospital Central do Funchal (Madeira Island) between July 2006 and June 2009, in children younger than 15 years old (population of 45.000) with positive culture for *Streptococcus pneumoniae* in normally sterile body fluids.

Results: 26 cases of IPD were analyzed. There was a male preponderance (65,4%) and 53,8% of children attended a daycare center/school. Clinical presentation: pneumonia (n=15), meningitis (n=5), occult bacteremia (n=4) and pneumonia with effusion (n=2). Age range: 1-169m, median 64m, with 34,6% under 24m (n=9). Complications occurred in 26,9% (n=7). Less common serotypes were identified in patients with risk factors (n=8). None of the serotypes included in PCV7 were isolated in the vaccinated subset (n=14), while 2 included in PCV7 were isolated in the non-vaccinated subset (n=12). New serotypes not included in PCV7 were identified (n=24): serotype 1 (n=10) associated with pneumonia (60% of cases) and children >60m (n=8); serotype 19A (n=5) associated with occult bacteremia (50% of cases) and children < 24m (n=4). There were no fatalities.

Conclusions: There was a higher incidence of IPD in children older than 60m presenting as pneumonia. Herd immunity might have been accomplished due to the high rate of vaccination. Continuous clinical and epidemiological surveillance is extremely important.

LONG-TERM EFFECTS OF PCV7 IMPLEMENTATION IN ITALY ON NON- AND INVASIVE PNEUMOCOCCAL SEROTYPES

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Background and aims: Long-term epidemiological changes after PCV7 implementation in terms of pneumococcal serotypes distribution is fundamental to define the effectiveness of vaccination, but European data is limited because relatively recent vaccine introduction and difficulty to rapidly reach high vaccine coverage. 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.

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 coverage in the five regional districts ranging between 36.5 and 60%, between 74 and 90.2% and between 84.9 and 92.9% in 2003, 2004 and 2005, respectively. In the last years the coverage is >80% in every districts. During surveillance period, 166 strains were collected and characterized: an increase of non-PCV7 serotype illness has been observed, reaching 93.7%, 86.7%, 58.3% and 81.8% in 0-5 and 6-17 year children and 18-64 and >64 year adults, respectively. PCV13 would offer a significant added benefit covering 37.5%, 60%, 66.7% and 63.6% of pneumococcal illness in the above mentioned age groups.

INVASIVE PNEUMOCOCCAL DISEASE (IPD) AMONG CHILDREN IN MENDOZA ARGENTINAH. Abate¹, **A. Falaschi**¹, L. Balbi², B. Garcia², A.M. Rosaenz¹¹*Pediatrics Infectious Diseases Service, ²Microbiology Department, Hospital Dr H J Notti, Mendoza, Argentina***Background and aims:** IPD in children is the major cause of morbimortality in the world.

To describe epidemiological characteristics of IPD, in children who received medical care at a children's hospital in Mendoza, Argentina from 01-Jan-1993 to 31-Dec-2009.

Methods: Descriptive study that included subjects with *Spn* isolation in blood and/or CSF or any other normally sterile fluids in which clinical charts were assessed for demographical, clinical and microbiological data - Resistance to penicillin and ceftriaxone were considered according to the cut-off points by the CSLI 2009 - Serotypes distribution was determined.**Results:** 461 Cases of IPD were analyzed: Meningitis 140(30.36%), pneumonia with pleural effusion 120(26.03%), pneumonia 105 (22.78%) and bacteremia 61(13.23%) Age Range: 1-180 m., median 20 m. Relationship male/female: 1.29 (257/195). 76.2% (349/458) were < 5 years old and 53.27% (244/458) < 2 year old. 209 strains were typed (45.33%) the most frequent types: 14 (25%) and 5 (16%) representing 30% and 13% respectively in isolations from < 2 year old, serotype 1 (14%) representing 37% in > 60 m. Meningitis cases were 81.61% (111/136) sensitive to penicillin and non-meningitis 99.7%% (311/312) were sensitive . 1 meningeal strain with intermediate resistance to C3- Overall Mortality: 5.85% (27/461) for meningitis: 12.14% (17/140).**Conclusions:** The majority of IPD were pneumonias in boys < 5 years old. Most frequent serotypes 14, in < 2 year old and serotypes 1, in > 5 years old. All cases were sensitive to penicillin in non-meningeal processes. The highest mortality was for meningitis.

NASOPHARYNGEAL (NP) COLONIZATION WITH *STREPTOCOCCUS PNEUMONIAE* (SP) IN CHILDREN IN BRASOV, ROMANIA: ANTIBIOTIC RESISTANCE, SEROTYPE DISTRIBUTION AND CONJUGATE VACCINES COVERAGE

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Background: information on SP-NP colonization in Romnia is limited.

Objectives: To study SP colonization rates, serotype distribution, conjugate vaccines (PCV) coverage and antimicrobial susceptibility from healthy children < 5 years of age.

Patients and methods: SP-NP cultures were obtained in a day-care center (DCC), immunization clinics, hospital's emergency room and children hospitalized for elective surgery during April 2008-January 2009. Antimicrobial susceptibility was determined by MIC (penicillin and ceftriaxone) and disk diffusion (TMP/SMX, erythromycin, clindamycin and chloramphenicol).

Results: 100 children were enrolled at each center (total=400). Highest (77%) colonization rates were recorded at DCC. Colonization rates among children < 12, 13-24 and 25-36 months of age were 59%, 73% and 43%, respectively. Most frequent serotypes were 23F, 6B, 19F, 14, 6A and 19A (25%, 15%, 13%, 10%, 8% and 5%, respectively). PCV7, PCV10, PCV13 serotypes represented 66%, 66% and 80%, respectively. 83% and 18% of all isolates were penicillin and ceftriaxone-nonsusceptible, respectively. Overall TMP/SMX, erythromycin, clindamycin and chloramphenicol resistance were 66%, 62%, 57% and 4%, respectively. 138/205 (67%) isolates were multidrug-resistant (MDR). Penicillin resistance (MIC $\geq 2\mu\text{g/mL}$) was common in serotypes 6B, 14, 19F and 23f (58%, 45%, 62% and 67% of all isolates, respectively). 93% of MDR isolates were covered by PCV13. Serotype and resistance distribution were similar between centers.

Conclusions:

- 1) High NP colonization and high rate of MDR-SP rates were observed;
- 2) PCV7 and PCV10 coverages were moderate;
- 3) >90% MDR isolates were covered by PCV13.

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INVASIVE PNEUMOCOCCAL DISEASE (IPD) IN BARCELONA, SPAIN

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Background and aims: During the last years we have observed a significant increase in the rate of IPD caused by virulent non-PCV7 serotypes in Barcelona, Spain. The aim of this study is to analyse the clinical presentation and serotype distribution of IPD.

Methods: Prospective study comprising all children < 5 years with IPD who were admitted to Sant Joan de Deu Hospital and Vall d'Hebron Hospital (two tertiary-care pediatric hospitals), between January 2007 and October 2009. IPD was defined as the presence of clinical findings of infection together with isolation or detection of DNA of *S. pneumoniae* in a sterile fluid sample.

Results: We included 263 patients (52.5% male), mean age was 30 months (SD 15.6); 141(53.8%) had received at least 1 dose of PCV7. The diagnosis was made by positive culture in 78(30.2%) patients; in the remaining patients the diagnosis was made only by Real-Time PCR. We could identify the serotype in 207 cases; 186(89.9%) of them were non-PCV7 serotypes, 118(57%) non-PCV10 serotypes and 58(22.1%) non-PCV13 serotypes. The most frequent identified serotypes were 1 (50; 24.1%), 19A (30; 14.5%) and 3 (27; 13.0%). Clinical presentation was pneumonia in 206 cases (78.3%; 134(65%) empyema), meningitis in 25(9.5%) and bacteraemia in 21(8%). Pneumonia was mainly related with serotype 1 (24.3% of cases) and bacteraemia with serotype 19A (28.6% of cases). Meningitis had not a predominant serotype related.

Conclusions: The non-PCV7 serotypes were responsible for 89,9% of the IPD cases; 1, 19A and 3 were the most frequent serotypes. Pneumonia was the main clinical IPD presentation. New conjugate vaccines cover the majority of IPD serotypes.

PNEUMOCOCCAL CARRIAGE DURING A PCV7-VACCINATION PROGRAM IN CHILDREN AT INCREASED RISK FOR PNEUMOCOCCAL INVASIVE DISEASE

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Background and aims: The use of a vaccine to prevent nasopharyngeal (NP) carriage represents a option to reduce the incidence of pneumococcal disease. We determine pneumococcal carriage and serotype distribution in children at high risk for invasive disease during a vaccination program with the PCV-7 vaccine.

Methods: 110 children aged 2-59 months with chronic heart disease (n=26), sickle cell anemia (n=25), HIV infection (n=18), chronic renal failure (n=12) and others (n=29) were enrolled in this study. Children received the PCV7 according to a pre-establish schedule. NP samples were obtained before each vaccine dose and 2 months after finishing the schedule. Pneumococcal isolates were serotyped.

Results: Out 268 specimens, 64 yielded pneumococcus. Pneumococcal carriage was found in 24 (20%) of the patients prior to the first dose and in 18 (20%) out of 88 who completed the vaccination schedule. The table shows the distribution of the serotypes pre- and post-vaccination

Serotypes	Pre- Vaccination N (%)	Post Vaccination N (%)
PCV7	14 (12,7)	4 (4,5)
PCV13 (additional serotypes)	5 (4,5)	5 (5,7)
Non vaccine types (NVT)	5 (4,5)	9 (10,2)
Negative	86 (78,2)	70 (79,5)
Total	110	88

[Serotypes before and after vaccination]

Conclusion: The introduction of PCV7 vaccine doesn't lower the carriage rate (20%) but is associated with a shift to non-vaccine serotypes. The introduction of the conjugate vaccine PCV13 may offer a better coverage for invasive serotypes in this population.

PNEUMOCOCCAL PNEUMONIA HIGHLY PROBABLE IN IMMUNIZED CHILDREN CARED IN GROUP SETTINGS

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Reduction of invasive pneumococcal diseases was obtained after introduction of pneumococcal conjugate vaccine (PCV) but infections, specially otitis, due to non vaccine serotypes persist. However, the rate of pneumococcal pneumonia in children previously immunized with PCV is widely unknown. Pneumococcal origin of community-acquired pneumonia remains difficult to affirm because blood culture is usually negative in children, but high procalcitonin (PCT) and C-reactive protein (CRP) blood levels are excellent predictors of pneumococci. Duration of fever 48h or less after initial antibiotic treatment is usual in pneumococcal pneumonia without pleural effusion. We consider that rapid decrease of fever and high PCT and CRP give pneumococcal origin highly probable.

Among 259 patients < 7 years hospitalized from 2003 to 2008 for community-acquired pneumonia without pleural effusion, 47 had PCT > 4 and CRP > 120, blood culture being positive for *S pneumoniae* in three. In these 47 patients fever disappeared in 48h or less after initiation of antibiotics. This group, with highly probable or certain pneumococcal pneumonia, includes 20 patients hospitalized before 2006 (date of generalization of PCV) and 27 in 2006-2008. Out of these 27 hospitalized in 2006-2008, 21 had previously received pneumococcal-conjugate vaccine and 19 of these 21 were attendees of nursery school or day-care centers, and only 2/20 in 2003-2005 were in day-care centers, both received PCV.

These data show that pneumococcal pneumonias are possible in immunized young children cared in group settings. These data have to be considered for emergency antibiotic treatment.

TRENDS OF SEROTYPE DISTRIBUTION AND ANTIBIOTIC RESISTANCE OF *S.PNEUMONIAE* STRAINS CAUSING ACUTE OTITIS MEDIA IN YEARS 1999, 2006 AND 2009

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Background and aims: To assess the trends of distribution of serotype and antibiotics resistance among strains *S. pneumoniae* causing acute otitis media among children < 5 year old after inclusion PCV7 vaccination into routine use in year 2008.

Methods: The otitis media study followed children < 5 years of age in years 1999, 2006 and 2009. Myringotomy was performed to verify of diagnosis of AOM and middle ear fluid was aspirated for culture of bacterial pathogens. Clinical specimens cultured in laboratory following standard procedures, susceptibility testing according CLSI guidelines. Pneumococci were serotyped using the Quellung method using specific antisera (SSI, Denmark).

Results: In years 1999, 2006 and 2009 in 143, vs.133, vs.118 of patients, tympanocentesis and aspiration of middle ear fluid were done. Prevalence of bacterial pathogens caused AOM and trend of *S. pneumoniae* antimicrobial resistance was observed.

The overall coverage of serotypes contained in PCV-7 causing AOM in children < 5 years of age was followed 1999-65.8%, 2006-88.5% and 2009-70.7%. In year 2009 has increased frequency of serotype 3(8%) and 19A (10,7%).

Conclusion: In era PCV-7 vaccination was serotype 23F most common among AOM isolates and was recorded increased number of serotype 3 and 19A isolates after PCV-7 routine use from year 2008. Prospective surveillance for AOM among children, vaccination, consumption of antibiotics and resistance is going on.

	1999	2006	2009
<i>S. pneumoniae</i>	50,3%	45,9%	63,6%
<i>H. influenzae</i>	20,9%	24,1%	20,3%
<i>M. catarrhalis</i>	1,4%	1,5%	0,9%

[Percentage of AOM caused by *S. pneumoniae*, *H. infl*]

	1999 (n=72)	2006 (n=61)	2009 (n=75)
Penicillin sensitive	64,1%	49,2%	62,0%
Penicillin intermediate	14,6%	37,7%	28,2%
Penicillin resistant	21,3%	13,1%	9,9%
Amoxicillin	25,0%	11,0%	7,0%
Erythromycin	64,1%	47,5%	40,9%

Trimethoprim/cotrimoxazole	85,9%	75,4%	73,2%
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[Trend of antimicrobial resistance of S. pneumoniae]

NEW PNEUMOCOCCAL VACCINES AGAINST ACUTE OTITIS MEDIA: POTENTIAL HEALTH AND ECONOMIC IMPACT IN CANADA

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Background and aims: Acute otitis media (AOM) is a very common early infancy and childhood disease. We estimate the potential impact of an infant vaccination with the new 10-valent pneumococcal non-typeable *haemophilus influenzae* protein-D conjugate vaccine (PHiD-CV) compared with the routinely used 7-valent (PCV-7) and the candidate 13-valent (PCV-13) vaccine on the burden of AOM in children < 10 years in Canada.

Methods: We used a recently published static, deterministic, age-compartmental, population model which simulates a one year cross-sectional benefit of a universal infant vaccination program at a vaccine steady-state. Canadian epidemiologic and demographic data were used in the model. Results were presented from both payer and societal perspectives, assuming vaccine price parity, 100% vaccination coverage, no herd protection and a 4 dose vaccination schedule. One-way sensitivity analysis was performed.

Results: Compared with PCV-7, vaccination with PHiD-CV could prevent an additional 171,162 ambulatory visits for AOM, 144,632 antibiotic prescriptions for AOM, and 9,827 hospitalizations for myringotomy per year. Compared with PCV-13, PHiD-CV could prevent 123,385 ambulatory visits for AOM, 104,269 antibiotic prescriptions for AOM, and 7,084 hospitalizations for myringotomy per year. The direct AOM cost savings of a PHiD-CV program is projected at \$17.1M and \$12.3M compared to PCV-7 and PCV-13 respectively; the indirect cost savings is estimated at \$25M and \$18M respectively, compared to PCV-7 and PCV-13.

Conclusions: PHiD-CV may offer substantial benefits in terms of reduced ambulatory visits, antibiotic prescriptions and hospitalizations for AOM compared to PCV-7 and PCV-13; translating into substantial cost-savings to the Canadian healthcare system.

INVASIVE PNEUMOCOCCAL INFECTIONS IN HELSINKI CHILDREN BEFORE USE OF PNEUMOCOCCAL CONJUGATE VACCINE

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Background and aims: During the last decade vaccination with pneumococcal conjugate vaccines (PCV) has been started in many highly developed Western countries resulting in a marked decrease in the incidence of invasive pneumococcal disease (IPD). Finland has not yet incorporated PCV in the national immunization program. We describe the patients treated for IPD in Children's Hospital, University of Helsinki before the use of PCV.

Methods: Patients treated for IPD in Children's Hospital from 2002 to 2008 were sought using the hospital discharge register and laboratory data. The hospital records of the patients were reviewed. The data concerning hospital stay, treatment and outcome, pneumococcal serotype and antibiotic susceptibility were recorded.

Results: In total 130 IPD were diagnosed in 125 children between January 2002 and June 2008. The yearly number of IPD increased from 10 cases in 2002 to 26 cases in 2007. There were five deaths, all in patients with meningitis (5/21, 25%), total mortality 5/125, 4%. Eighty-five (78%) of the 109 pneumococcal isolates with serotype available are included in PCV7. Ninety-seven of 119 (81,5%) pneumococci were fully susceptible to penicillin, 14/119 (12,6%) had reduced susceptibility and 7/119 (5,9%) were resistant to penicillin. The proportion of erythromycin resistant infections was 31,9%.

Conclusions: An increase in the yearly number of pneumococcal infections treated in Children's Hospital was seen between 2002 and 2008. There was a high level of macrolide resistance among the pneumococcal isolates. Considering the serotype distribution a marked benefit is expected from including PCV in the vaccination program.

PRE AND POSTVACCINATION INCIDENCE OF PARAPNEUMONIC PLEURAL EFFUSION IN LIMOUSIN REGION

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Background and aims: The aim of our study was to compare the incidence of parapneumonic pleural effusion in the Limousin region based on a comparison of a pre- and post-vaccinate period.

Methods: Data of children aged 0 to 18 years old hospitalized for parapneumonic pleural effusion were collected in the Limousin hospitals between two periods namely period A from January 2000 to December 2005 and period B from January 2006 to March 2009. In this region, vaccination is recommended since 2006. The medical records were selected with the inclusion criteria of radiological parapneumonic pleural effusion and a clinical and biological context of *Streptococcus pneumoniae*. The main endpoint was the number of parapneumonic pleural effusion cases over each period in order to calculate the incidence within each period.

Results: A total of 35 children were included: 7 during period A and 28 during period B. The incidence was 0.796 per 100,000 children for period A and 4.66 per 100,000 for period B ($p < 0,04$). Twenty-two per cent of children were vaccinated over period B. Bacteriological tests allowed to identify 15 *S. Pneumonia* over the two periods (40%). All serotypes were non-vaccine serotypes (1, 3 and 19A).

Conclusion: This study confirms a significant increase of parapneumonic pleural effusion in Limousin. It confirms the emergence of non-vaccinate serotypes.

EMERGENCE OF NEW PNEUMOCOCCAL SEROTYPES FOLLOWING THE INTRODUCTION OF THE PNEUMOCOCCAL CONJUGATE VACCINE-7: KUWAIT EXPERIENCE

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Background and aims: The pneumococcal conjugate vaccine-7(PCV-7) was introduced in Kuwait in August 2006. This study evaluated the impact of PCV-7 on vaccine and non-vaccine serotypes from invasive isolates. The coverage rate for the invasive isolates in children up to 5 years by the PCV-7, PCV-10 and PCV-13 was estimated.

Methods: All isolates from invasive pneumococcal disease IPD in children and adults were serotyped from November 2006 to December 2009 and data were compared to the data prior to the introduction of the 7-valent vaccine.

Results: A total of 87 IPD isolates(82 from blood and 5 from CSF) were analyzed. Out of those, 29(33%) were from children up to 5 years. The commonest serotypes were 19F, 9V, 19A, 6A, 15C, 5, 15B, 18C and 3, compared to 23F, 14, 19A and 6A before the introduction of the PCV-7. The estimated serotype coverage by the PCV-7, PCV-10 and PCV-13 were 44%, 50% and 69%, respectively in children less than 2 years old and 54%, 62% and 84%, respectively in children 2-5 years. Before the introduction of the PCV-7 in Kuwait the estimated serotype coverage of the PCV-7 for IPD in children less than 2 years and children 2-5 years was 55% and 62%, respectively.

Conclusion: With the emergence of new pneumococcal serotypes, broader vaccine coverage is needed for the prevention of IPD in children.

CLINICAL AND BIOLOGICAL PROGNOSTIC FACTORS IN PNEUMOCOCCAL MENINGITIS

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Introduction: Pneumococcal meningitis (PM) results in a high rates of morbidity and mortality in children. **Aim:** to evaluate clinical and microbiological prognostic factors of PM outcome.

Methods: Prospective clinical study, of PM cases admitted to PICU at Sant Joan de Déu Hospital, from January 2000 to November 2009.

Results: A total of 63 patients were included, 66.6% males. The median age was 39.8months (range 1m-16years) and the median PICU length of stay was 3.8 days (range: 1-30 days). The median fever duration before admission was 96.5 hours (range 1h-14days) and 18 patients received antibiotics previously. Two patients had a CSF fistula as a risk factor, and 9 cases (14%) had a medium otitis. Eight patients (12.6%) were vaccinated with pneumococcal heptavalent conjugate vaccine (PCV7). There were 15 PCV7-serotypes, 27 non PCV7-serotypes, and the other 21 were unknown. Outcome: six patients (9.5%) died and 23 (36.5%) had neurological handicaps. A higher PRISM and SOFA scores, lower Glasgow Coma Scale, lowest age, lower cerebrospinal liquid leukocytes count, needs of mechanical ventilation and inotropic support, were associated with higher mortality or sequelae, with significant statistical differences ($p < 0.05$). There were collected 6 cases with cefotaxime resistance, all they until 2006 year. No differences were found between isolated serotypes (vacunal or not), neither to antibiotic sensibility, regarding outcome.

Conclusions: The prognostic factors are similar to those described in the literature, although they haven't been reported all together. The most prevalent serotypes were non PCV7-serotypes.

EMERGENCE OF MULTIDRUG-RESISTANT, OPTOCHIN-RESISTANT AND BILE-SOLUBLE PNEUMOCOCCUS-LIKE STREPTOCOCCI IS NOT ASSOCIATED WITH 7-VALENT PNEUMOCOCCAL CONJUGATE VACCINATION IN INFANTS IN BANGLADESH

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Recently the association between emergence of MDR, optochin-resistant and bile-soluble pneumococcus-like streptococci and 7-valent pneumococcal conjugate vaccine (7-PCV) vaccination in infants has been raised. We studied phenotypic and genotypic characteristics of optochin-resistant and bile-soluble pneumococcus-like streptococci isolates from nasopharyngeal swabs of pregnant mothers vaccinated with 23-valent pneumococcal polysaccharide vaccines (23-PPV) or influenza vaccine (control) and their infants vaccinated either with 7-PCV or *Haemophilus influenzae* type b vaccine (controls, Hib) at 6, 10 and 14 weeks of ages. Half of the infants of mothers vaccinated with 23-PPV got either PCV7 or Hib. Similarly, half of the infants of mothers vaccinated with influenza vaccine got either PCV7 or Hib vaccines. A total of 1507 (32%) optochin-susceptible *S. pneumoniae* was obtained from 4721 swabs. Thirty-seven (0.8%) optochin-resistant and bile-soluble pneumococcus-like streptococci were isolated, and characterization by antibiotic susceptibility, serology, *lytA* gene PCR and MLST identified 34 isolates as *S. mitis*-like strains, two as *S. pneumoniae* and one *S. pseudomoniae*. Of 34 *S. mitis*-like strains, 2 were isolated from mothers vaccinated with 23-PPV and three from control mothers. In infants of mothers (No = 157) vaccinated with 23-PPV, 8 pneumococcus-like streptococci were isolated from infants vaccinated with 7-PCV compared to 10 from controls (Hib group). Similarly, 8 pneumococcus-like streptococci were isolated from infants receiving 7-PCV compared to 6 from controls whose mothers were controls (influenza group, No = 159). Isolation of pneumococcus-like streptococci from control infants and 7-PCV vaccinated infants suggested no association between 7-PCV and emergence of pneumococcus-like streptococci in children in Bangladesh.

FURTHER INCIDENCE TRENDS OF INVASIVE PNEUMOCOCCAL DISEASE MORE THAN 2 YEARS AFTER INTRODUCTION OF 7-VALENT PNEUMOCOCCAL CONJUGATE VACCINATION IN GERMANY

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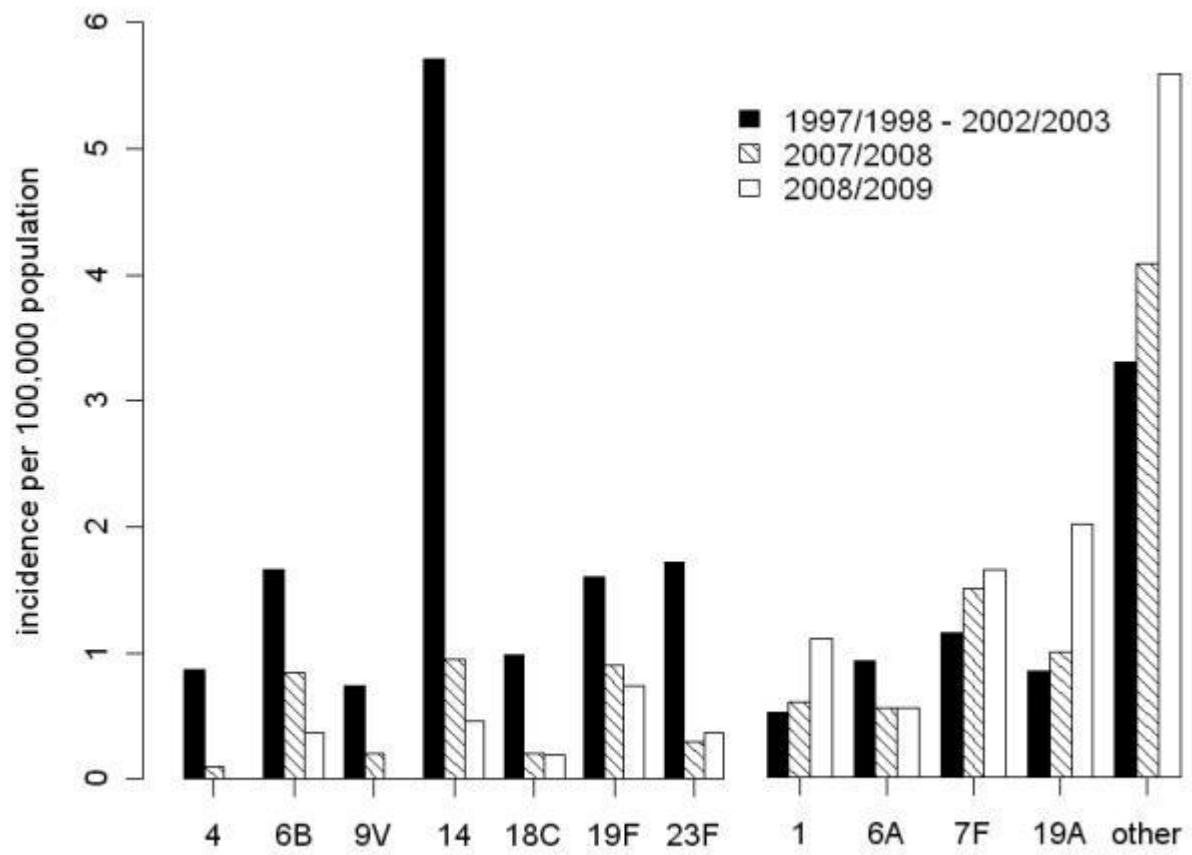
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Background and aims: One year after general introduction of 7-valent pneumococcal conjugate vaccine a 50% reduction in incidence of invasive pneumococcal disease (IPD) has been observed among children younger than 2 years in Germany. We aim to assess further changes in incidence of IPD.

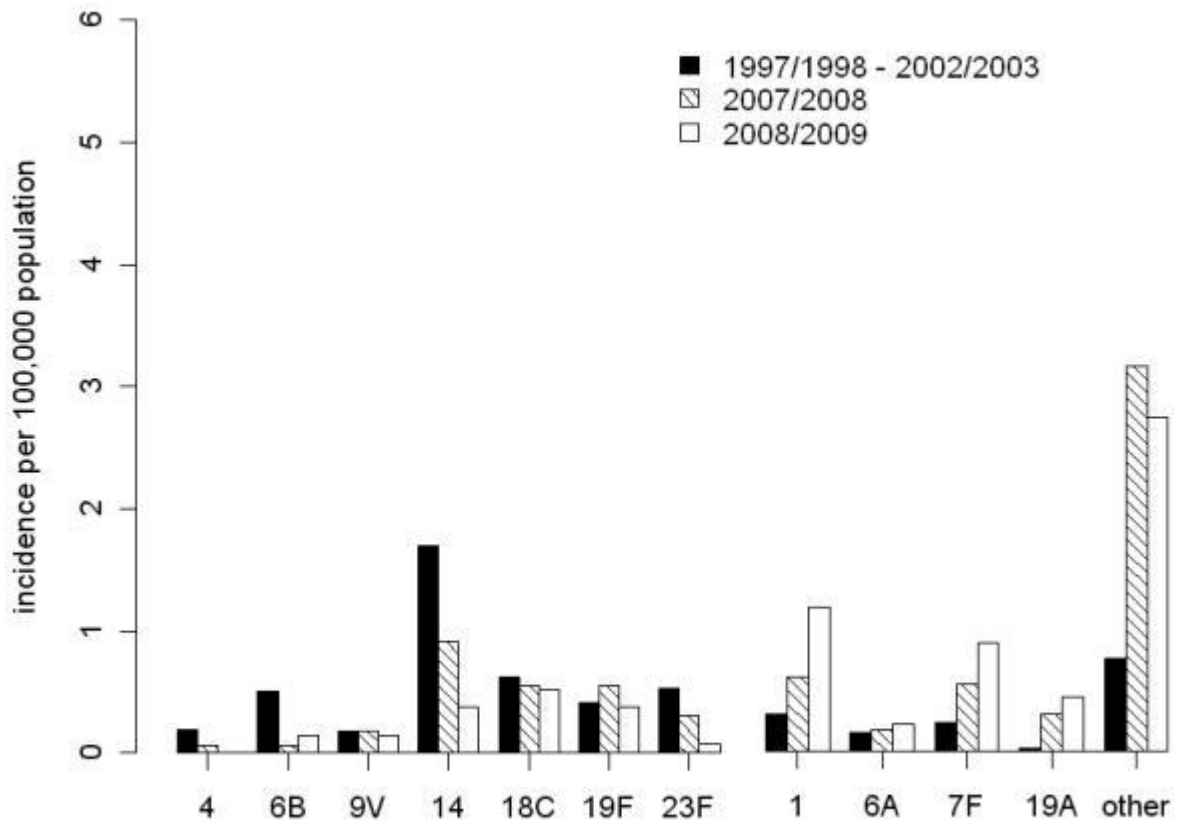
Methods: Incidence estimates of IPD are based on capture recapture estimates combining reports of IPD among children aged younger than 16 years from pediatric hospitals and microbiological laboratories in Germany. Serotyping is performed in the National Reference Center for Streptococci.

Results: There was no further decrease in incidence among children younger than 2 years with 13.0 (11.1 - 15.0) per 100,000 in pneumococcal season 2008/2009 compared to 11.2 (10.1 - 12.3) per 100,000 in 2007/2008. The incidence among children aged 2-4 years and 5-15 years also remained stable. Overall, the incidence of non-vaccine serotypes in children increased while the incidence of vaccine serotypes showed only minor further decreases comparing 2008/2009 with 2007/2008, and remained still relevant.

Conclusions: Better vaccination rates and higher-valent vaccines have the potential to reduce the burden of IPD in Germany considerably in the future.



[Incidence of IPD among children aged 0-1 year.]



[Incidence of IPD among children aged 2-4 years.]

DISTRIBUTION OF SEROTYPES ASSOCIATED WITH PNEUMOCOCCAL PNEUMONIA AMONG CHILDREN < 5 YEARS IN SAO PAULO, DURING THE PRE-VACCINE ERA

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Background and aims: Pneumococcal disease is a leading cause of morbidity and mortality in Brazil. The aim of this study was to describe the distribution and antimicrobial susceptibility of serotypes associated with pneumococcal pneumonia (PP) among children younger than 5 years of age in Sao Paulo, before the introduction of the 10V-pneumococcal conjugate vaccine in our National Immunization Program in 2010.

Methods: We performed a 10-year (1999 - 2008) hospital-based surveillance in Sao Paulo, including all children < 5 years admitted due to pneumonia, with isolation of *S. pneumoniae* from blood or pleural fluid. Isolates were serotyped and tested for antimicrobial susceptibility.

Results: During the study period 104 children aged < 5 years were admitted with PP and serotype identification was available for 89 (85,6%).

The prevalent serotypes were: 14 (52.3 %), 6B (16.2 %), 1 (6.9%), 5 (5.8%), 9V (4.6 %) and 18C (4, 6%). Only three of the isolates had reduced susceptibility to penicillin (two strains of serotype 14 and one of 6B), all associated with intermediate resistance (MIC = 4). Four children died (case fatality rate of 4%).

Conclusions: Penicillin should remain as the empiric treatment of choice for children with community acquired pneumonia. Based in our data, the heptavalent pneumococcal conjugate vaccine would potentially prevent 78.6% of the PP cases and the recently licensed 10-V and 13-V vaccines would potentially prevent, respectively, 92.1% and 96.6% of the PP cases.

INCIDENCE SURVEILLANCE OF INVASIVE PNEUMOCOCCAL DISEASE IN CHILDREN UNDER FIVE YEARS OF AGE IN LOMBARDY (NORTHERN ITALY): AN INTERIM ANALYSIS

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Background and aims: Invasive Pneumococcal Disease (IPD) incidence is relevant in infants and younger children, but data on incidence in Italy are lacking. The aim of this study is to estimate the incidence of invasive pneumococcal disease (IPD) in the Lombardy region, Northern Italy, and to identify the circulating *S. pneumoniae* serotypes.

Methods: An observational, prospective, multicentric, population-based ongoing active surveillance system of IPD and pneumococcal serotyping that recruits all children < 5 years with suspected invasive pneumococcal disease at emergency room visit in 10 hospital centers, representatively distributed in the monitored area, started on September 1, 2008. Blood sampling for culture and sensitivity and serotyping was performed.

Results: A total of 135 children with suspected IPD were recruited till up August 31, 2009 (46.7% aged < 24 months; 56.2% boys). Seventeen children (12.6%) (median age 24 months) had *S. pneumoniae* isolated. Overall incidence (number cases per 100,000 per year) of IPD was estimated around 60 (95% CI 30-90). Pneumonia was found in 9 cases (52.9%), sepsis in 6 (35.3%), meningitis in 2 (11.8%). Strains included in the 7-valent vaccine accounted for 4 cases (never previously vaccinated) of 13 cases available for serotype determination. Serotypes not included in the 7-valent vaccine accounted for 9 (69.2%) cases (19A, three cases; 7F, two cases; 1, two cases; 12B, one case; 15C, one case).

Conclusions: These results confirm the burden of IPD in younger children and suggest that vaccination possibly by the 13-valent vaccine option might notably decrease the incidence of IPD.

TRANS-TYMPANIC MEMBRANE DELIVERY OF MOXIFLOXACIN INTO CHINCHILLA MIDDLE EAR: A MODEL FOR THE TREATMENT OF OTITIS MEDIA

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Background and aims: The chinchilla is an established model for the treatment of acute otitis media. This study was conducted to:

- i. develop a gel-based formulation that provides sustained release of moxifloxacin to facilitate penetration across the tympanic membrane in order to maintain unbound drug concentrations above 10 µg/ml for a minimum of 24 to 48 hours.
- ii. characterize the extent of moxifloxacin delivery in the chinchilla via the intact tympanic membrane using microdialysis.

Methods: Poloxamer-based thermosetting formulations loaded with 1% or 3% moxifloxacin were tested in normal, uninfected chinchillas with pre-treatment of a penetration enhancer. A small volume (0.25 to 0.65 ml) of gel formulation was instilled as a liquid adjacent to the tympanic membrane via the external ear. Unbound moxifloxacin concentrations in middle ear fluid (MEF) were continuously monitored using online microdialysis for up to 100 hr post-dose. Animals were freely moving, with access to food and water.

Results: 1% moxigel dosing provided mean maximum moxifloxacin concentrations in MEF fluid of 57.8 µg/ml; MEF levels remained above 10 µg/ml for approximately 29 hr. 3% moxigel dosing yielded mean maximum MEF concentrations of 130.4 µg/ml; MEF levels remained above 10 µg/ml for approximately 47 hr.

Conclusion: Values of the areas-under-the-curve (AUC) for 24 hr divided by the MIC in MEF following a single dose of both 1% and 3% moxigel, as well as the associated C_{max}/MIC values, were in a range reported to result in rapid, concentration-dependent killing of bacteria that are prevalent causative agents in otitis media.

PNEUMOCOCCAL NASAL COLONIZATION AMONG INFANTS OF WOMEN WHO RECEIVED PNEUMOCOCCAL PS23 VACCINE IN BANGLADESH

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Background: Invasive pneumococcal disease caused by *Streptococcus pneumoniae* (Spn) is a leading cause of illness and mortality among children in developing countries. We have assessed the effect of pneumococcal polysaccharide vaccine (PPS) given to pregnant women on colonization of their infants by vaccine serotypes in Bangladesh from data collected in 2004-2005.

Methods: 340 women were randomized to receive either 23-valent PPS or inactivated flu vaccine. Their infants were then randomized to receive either Haemophilus influenzae type b or pneumococcal conjugate vaccine. Nasal swabs and serum samples were collected on all infants at 6, 10 and 14 weeks. From preliminary data we have estimated the pneumococcal colonization among infants by vaccine serotype.

Preliminary results: We have performed a preliminary analysis on initial serotype data from the earliest Spn positive nasal swabs for 71 infants: 51 of maternal PPS group, 20 of control group. In the PPS group 23 infants (45%) were infected with vaccine type pneumococcal isolates compared with 15 infants (75%) in the control group ($p=0.0231$). We are completing the serotyping of the early Spn nasal isolates and analysis of maternal passive serotype-specific antibody Geometric Mean Titer in infants.

Conclusions: These preliminary results suggest that maternal immunization with PPS reduces early vaccine-type pneumococcal acquisition and colonization in their infants.

PNEUMOCOCCAL SEROTYPES AFTER THE INTRODUCTION OF THE HEPTAVALENT CONJUGATE VACCINE IN GREECE

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Background and aims: The objectives of the present study were to determine the serotype distribution and antimicrobial resistance of *S. pneumoniae* causing invasive pneumococcal disease (IPD) or acute otitis media (AOM) in children ≤ 11 y.o. after the introduction of the 7-valent vaccine (PCV-7) in the Greek National Immunization Schedule (January 2006).

Methods: This prospective study was conducted between September 2008 - December 2009 in 8 tertiary care hospitals across Greece. Serotyping was performed by latex agglutination and quellung reaction using anti-sera (Statens Seruminstitut, Copenhagen, Denmark) and susceptibility testing by E-test. Isolates were considered susceptible, intermediate or resistant to penicillin if MICs were ≤ 0.06 $\mu\text{g/mL}$, 0.12-1 $\mu\text{g/mL}$, or ≥ 2 $\mu\text{g/mL}$ respectively.

Results: Amongst 119 cases reported (57 boys, 62 girls, 81.5% ≤ 5 y.o., IPD: 54, AOM: 65), the commonest serotypes for IPD were 19A (22.2%), 7F (22.2%), and 3 (9.3%) and for AOM 19A (33.8%), 19F (23.1%), and 6A (10.8%). 57.4% (IPD) and 43.1% (AOM) of children had received at least one dose of PCV-7. In children ≤ 5 y.o., 11.9% (IPD) and 30.9% (AOM) infections were caused by vaccine serotypes. Intermediate resistance to penicillin exhibited 10/53 (18.9%) IPD isolates and 11/65 (16.9%) AOM isolates. One IPD isolate and ten AOM isolates had high level resistance to penicillin. Resistance was commonest among serotypes 19A and 19F.

Conclusions: In children ≤ 5 y.o., the majority of IPD and AOM infections were caused by non-vaccine serotypes. The commonest serotypes were 19A, 7F, 19F, 3, and 6A. Penicillin resistance was commonest for 19A and 19F.

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

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Background and aims: In 2006, a general recommendation for pneumococcal conjugate vaccination was issued in Germany. In this study we evaluate the bacteriology and *S.pneumoniae* serotype distribution of nasopharyngeal carriage of children suffering from severe AOM with efflux, from Oct. 2008 to Oct. 2009.

Methods: Swabs were taken from the nasopharynx of children with spontaneous draining AOM (regardless of immunization state) and analysed for bacteriological content. *S.pneumoniae* were serotyped with Quellung reaction. *S.pyogenes* were *emm*-typed. *H.influenzae* was typed using type-specific antisera.

Results: Among 459 patients with AOM, nasopharyngeal swabs were obtained from 375 individuals. 311 swabs were positive for either *S.pneumonia*, *S.pyogenes*, *H.influenzae* or *M.catarrhalis*. 181 swabs contained one, 101 had two and 29 had three isolates. The highest carriage rate was found for *S.pneumonia* (63.3%), followed by *H.influenzae* (42.8%), *M.catarrhalis* (37.0%) and *S.pyogenes* (5.8%). For all cases with *S.pneumonia* the serotype of the nasopharyngeal isolate was the same as for the isolate from middle-ear fluid (mef). The same was found for the *S.pyogenes* isolates which showed the same *emm*-type. Almost all *H.influenzae* isolates were non-typable (NT), which was also found for the corresponding mef-isolates. The most prevalent *S.pneumonia* serotypes were serotype 3 (25.0%), 19A (10.3%), 11A (9.3%) and 19F (6.9%). Coverage of PCV7 was 12.7%, PCV10: 16.7%, PCV13: 55.9%.

Conclusions: Nasopharyngeal swabs were obtained from two-thirds of patients suffering from AOM. The most commonly carried bacterium was *S.pneumonia*. Carried *S.pneumonia* were the same serotype as the isolates from middle-ear fluid. Most prevalent serotypes were serotypes 3 and 19A.

ETIOLOGY OF MIDDLE EAR FLUID OF INFANTS WITH ACUTE OTITIS MEDIA (AOM) IN GERMANY

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Background and aims: In 2006, a general recommendation for pneumococcal conjugate vaccination was issued in Germany. In this study we evaluate the bacteriology and *S.pneumoniae* serotype distribution of middle ear fluid from children suffering from severe AOM with efflux, from Oct. 2008 to Oct 2009.

Methods: Swabs were taken from middle ear fluid of children with spontaneous draining AOM (regardless of their immunization state) and analysed for bacteriological content. Serotyping of *S.pneumoniae* isolates was performed using the Neufeld Quellung reaction. *S.pyogenes* were *emm*-typed by sequencing of the *emm*-gene. *H.influenzae* was typed using an agglutination test with type-specific antisera.

Results: Among 459 patients analyzed, 71.9% were vaccinated with pneumococcal conjugate vaccine. For 223 isolates only physiological ear-flora or other bacteria not related to AOM could be isolated. 64 isolates showed no growth at all. The remaining 177 isolates were *S.pyogenes* (53, 29.9%), *S.pneumoniae* (47, 26.6%), *S.aureus* (40, 22.6%), *H.influenzae* (30, 16.9%) and *M.catarrhalis* (7, 4.0%). The most prevalent *S.pneumoniae* serotypes were serotype 3 (38.6%), 19A (22.7%), 19F (9.1%), 21 (6.8%), 1 and 23A (4.5% each). Coverage of PCV7 was 9.1%, PCV10 13.6% and PCV13 75.0%.

Conclusions: From almost half of the specimens no bacteriological agent could be isolated, implicating a possible viral origin of infection and showing the difficulty of proper diagnosis of AOM in small children. Among cases with a bacterial etiology *S.pyogenes* and *S.pneumoniae* were most prevalent. Only 4 cases with PCV7 serotypes were found. Coverage of PCV13 is high mainly because of serotypes 3 and 19A.

HAEMOPHILUS INFLUENZA NASOPHARYNGEAL CARRIAGE BEFORE AND AFTER PNEUMOCOCCAL CONJUGATE VACCINE IMPLEMENTATION

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Background: Several studies have investigated the impact of 7 valent pneumococcal conjugate vaccine (PCV7) on pneumococcal and staphylococcal (Sa) nasopharyngeal (NP) carriage. None in our knowledge has investigated this impact on Haemophilus influenzae (Hi) carriage. The aim of this study was to compare Hi NP carriage before and after PCV7 implementation.

Methods: Prior to PCV7 implementation (1993 to 2000), we used data from 4 successive randomised trials who compared several antibiotic regimens for the treatment of acute otitis media (AOM). After PCV7 (2006 to 2009), we used data from an ongoing surveillance study. Standardized history and physical examination findings were recorded, NP swabs were collected (same methodology of sampling and cultures) from young children suffering from AOM or healthy. Diagnostic criteria for AOM included the Paradise algorithm associated with fever and/or otalgia and /or irritability/ and/or conjunctivitis.

Results: 5228 children were enrolled: 4322 with AOM, 1807 before PCV7 implementation, 2515 after and 906 healthy controls.

	AOM before PCV7 n=1807	AOM after PCV7 n=2515	Healthy controls after PCV7 n=906
Age (months)			
mean±SD	14.6±7.6	13.8±5.1	13.1±5.4
median	12.8	13.1	12.3
PCV7 vaccinated	0	2469 (98.2)	888 (98.0)
Conjunctivitis	436 (24.1)	626 (24.9)	/
Carriage n (%)			
All Hi isolates	849 (47.0)	1221 (48.5)	128 (14.1)
βlactamase +	328 (38.6)*	209 (17.1)*	18 (13.9)
Hi alone	201 (11.1)	279 (11.1)	26 (2.9)
Hi+Sp	200 (11.1)	237 (9.4)	26 (2.9)
Hi+ <i>B. catarrhalis</i> (Bc)	154 (8.5)**	259 (10.3)**	26 (2.9)
Hi+Sa	8 (0.5)	18 (0.7)	5 (0.6)
Hi+Sp+Bc	275 (15.2)	391 (15.5)	41 (4.5)
Hi+Sp+Sa	1 (0.06)	15 (0.6)	0
Hi+Bc+Sa	7 (0.4)	7 (0.3)	3 (0.3)
Hi+Sp+Sa+Bc	3 (0.2)	15 (0.6)	1 (0.1)
All Sp isolates	1047 (57.9)	1465 (58.3)	271 (29.8)

*p<0.001 **p=0.05

[HI]

Conclusion: After PCV7 implementation, no significant change in the Hi overall carriage rate was observed. Hi strains producing βlactamase had greatly decreased.

SEROTYPE DISTRIBUTION AND SUSCEPTIBILITY OF SPANISH *STREPTOCOCCUS PNEUMONIAE* ISOLATES FROM MIDDLE EAR FLUID IN 2000'S

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Background and aims: Trends of serotype (St) prevalence among children middle ear isolates were analysed.

Methods: Databases of the Pneumococcal Reference Laboratory were analysed. Time trends were explored by linear regression analysis.

Results: 1997-2000 data: 481 isolates (70.7% 7-PCV St; 6.7% St-19A; 7.7% St-3; 4.4% St-6A; 16.6% Other-St; 69.0% PEN-NS; 7.1% AMX-NS; 55.3% ERY-NS).

	2001	2002	2003	2004	2005	2006	2007	2008	2009
Total no.	210	171	159	180	166	176	173	220	141
7-PCV-St(%)	62.9	63.7	48.4	35.6	24.1	18.8	13.3	10.0	10.6
St-19A(%)	9.5	12.3	17.0	21.1	31.9	31.3	38.7	46.8	35.5
St-3(%)	8.1	7.6	12.6	12.2	13.3	11.9	8.7	12.7	14.2
St-6A(%)	5.7	6.4	5.7	2.8	6.0	2.8	3.5	1.8	4.3
Other-St(%)	13.8	9.9	16.3	28.3	24.7	35.2	35.8	38.6	35.5
PEN-NS(%)	58.1	58.5	42.8	36.7	45.8	41.5	47.4	53.2	51.1
AMX-NS(%)	8.1	8.8	8.2	6.7	6.0	10.8	10.1	25.0	24.1
ERY-NS(%)	51.0	51.5	45.3	42.8	48.8	49.4	48.6	52.7	44.7

[01-09 isolates; %St and %non-susceptibility]

There was a significant decreasing trend for 7-PCV-St ($R^2=0.944$; $p<0.001$), with significant increasing trends for St-19A ($R^2=0.901$; $p<0.001$), St-3 ($R^2=0.463$; $p=0.030$), and other non-7-PCV-St ($R^2=0.877$; $p<0.001$), but not for St-6A ($R^2=0.311$; $p=0.094$). No significant trends in NS were found for PEN and ERY, with a significant increasing trend for AMX ($R^2=0.528$; $p=0.017$), due to the continuous increase in AMX-NS among PEN-NS St-19A isolates from 9.1% (2005) to 45.2% (2009).

Conclusion: The significant decrease in 7-PCV-St began prior to vaccine introduction (2001), with the highest decrease from 2002 on, accompanied by increases in non-7-PCV-St, mainly 19A.

BACTERIAL-HOST INTERPLAY IN ACUTE OTITIS MEDIA: EFFECT OF STREPTOCOCCUS PNEUMONIAE ON MORAXELLA CATARRHALIS ADHESION TO RESPIRATORY EPITHELIAL CELLS

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Background and aims: Acute otitis media affects up to 80% of children by the age of one year, and is commonly caused by both *Streptococcus pneumoniae* (Sp) and *Moraxella catarrhalis* (Mx). The interplay between these species within the respiratory tract may have a role in the progression from a state of carriage to symptomatic disease. We therefore aimed to study if Sp influenced Mx adhesion.

Methods: Ethanol-killed Sp preparations with wild-type pneumolysin (Ply⁺), a pneumolysin mutant lacking cytotoxicity (PdT), or lacking pneumolysin (Ply⁻) were incubated overnight with Detroit (nasopharyngeal) or A549 (lung) cells. Subsequent adhesion of Mx to these cells was assessed using viable colony counting and immunofluorescence.

Results: Colony counting revealed that Mx binding to Detroit cells increased by 35% ($p=0.02$) and 39% ($p=0.01$) when cells were pre-incubated with the Ply⁺ and Ply⁻ phenotypes respectively. Such increases were even more pronounced with A549 cells, where Mx binding increased by 72% ($p=0.0002$) and 67% ($p=0.00004$) respectively, compared to controls. In contrast, the pneumolysoid-expressing Sp did not significantly increase Mx binding to either cell line. These effects were confirmed by immunofluorescence microscopy.

Conclusions: Exposure of epithelial cells to Sp results in a significant increase in subsequent adherence of Mx. Initial observations point to a Ply-independent mechanism as the increase is observed both in the presence and absence of Ply. However, the paradoxical effect of the PdT phenotype suggests some role for Ply. The molecular basis of the interplay between these two organisms is currently under investigation.

IMPACT OF PCV-7 ON PNEUMOCOCCAL NASOPHARYNGEAL CARRIAGE IN CHILDREN AND THEIR PARENTS IN THE NETHERLANDS

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Background: In April 2006, heptavalent CRM-197-conjugated pneumococcal vaccine (PCV-7) was implemented in the Dutch NIP for infants at 2, 3, 4 and 11 months of age. We studied the effect of implementation of PCV-7 on nasopharyngeal pneumococcal carriage in children and parents between February and July 2009.

Methods: We performed a cross-sectional study, collecting nasopharyngeal samples from healthy vaccinated children before the booster dose at 11 months (n=329) and at 24 months of age (n=330). In addition, in the latter group we obtained nasopharyngeal samples from one of the parents (n=324). Nasopharyngeal samples were cultured for pneumococci and serotyped by Quellung reaction. Data were compared with unvaccinated controls and their parents (n=319, n=321 and n=296, respectively) from study (NCT00189020) before introduction of PCV-7 in the NIP.

Results: Vaccine serotype carriage decreased from 38% to 8% ($p < 0.001$) in 11-months old children and from 36% to 4% ($p < 0.001$) in 24-months old children. We observed a similar decrease in carriage for all vaccine serotypes. Non-vaccine serotypes increased from 29% to 39% ($p = 0.005$) at 11 months of age and from 30% to 45% ($p < 0.001$) at 24 months of age. Serotypes 19A, 6A and 11A were the most frequently carried serotypes. In parents, vaccine serotype carriage had decreased from 8.4% to 0.6% ($p < 0.001$) and non-vaccine serotypes had increased from 8% to 15% ($p = 0.02$).

Conclusions: Compared to the pre-vaccination era, marked reduction in vaccine serotype carriage was observed in infants and parents 3 years after implementation of PCV-7 in the Netherlands.

INCREASE OF NASOPHARYNGEAL CARRIAGE WITH SEROTYPE 19A PNEUMOCOCCI AFTER PNEUMOCOCCAL CONJUGATE VACCINATION

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Background: In several countries, an increase of pneumococcal disease caused by multiresistant serotype 19A pneumococci was observed after the implementation of 7-valent pneumococcal conjugate vaccination (PCV-7). Since fluctuations in time and selective antibiotic pressure may have contributed, we evaluated the effect of PCV-7 on nasopharyngeal acquisition of serotype 19A and its clonal composition in a randomized controlled trial in a setting with low antibiotic resistance.

Methods: Before implementation of PCV-7 in the Dutch national immunization program, 1003 healthy infants were randomly assigned to receive 2-doses of PCV-7 at 2 and 4 months; 2+1-doses at 2, 4 and 11 months or none (controls) and followed up to 24 months of age. Nasopharyngeal swabs were obtained with 6-months intervals. Pneumococcal serotyping was done by Quellung reaction and 19A-isolates were genotyped by MLST.

Results: Among all children, 19A was the second most frequently carried non-vaccine serotype after 6A. Of 158 19A-isolates, identified in 135 children, 128 isolates were new acquisitions in children 6 months of age and above. The risk of 19A-acquisition was higher in vaccinees in particular after the booster compared to controls (overall aOR 1.77, 95% CI 1.14 - 2.77; p=0.01). Acquisition of clonal complex (CC) 199 was most frequent and significantly higher after receiving a 2+1-schedule (p=0.04), but other clonal complexes also increased after vaccination. Antibiotic resistance rates were low ($\leq 3\%$).

Conclusions: PCV-7 induces a dose-dependent increase in serotype 19A-acquisition compared to unvaccinated controls, primarily due to expansion of predominating CC199 but also a diffuse increase in other CCs.

EFFECT OF 7-VALENT PNEUMOCOCCAL CONJUGATE VACCINE ON *S. AUREUS* CARRIAGE AND OTHER RESPIRATORY PATHOGENS: A LONGITUDINAL RANDOMIZED CONTROLLED TRIAL

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Background: Heptavalent pneumococcal vaccine (PCV-7) was shown to reduce pneumococcal vaccine serotype nasopharyngeal carriage and (respiratory) disease. However for otitis, replacement by nonvaccine serotype pneumococci but also other nasopharyngeal commensals (nontypeable *H. influenzae*) reduced net-vaccine benefits. We investigated the effect of PCV-7 on nasopharyngeal colonization with common non-pneumococcal bacteria frequently involved in respiratory tract infections in infants before large-scale implementation of PCV-7.

Methods: The present study was part of a randomized controlled trial in which 1003 healthy newborns were randomly assigned to receive 2 primary doses of PCV-7 at 2 and 4 months of age with or without a booster dose at 11 months or no PCV-7 (controls). Nasopharyngeal carriage with *S. aureus*, *H. influenzae* and *M. catarrhalis* was studied over a 2-year follow-up period with 6-months interval.

Results: No substantial differences in carriage with these pathogens were observed in the first 2 years of life, except for a doubling of *S. aureus* carriage at 12 months of age 1 month after the booster in infants following a 2+1-dose PCV-7 schedule compared to unvaccinated controls (10.1% versus 5.0%; $p=0.01$). Although point estimates for *S. aureus* carriage remained higher, the difference was no longer significant at the age of 18 and 24 months.

Conclusions: The 2+1-dose PCV-7 schedule did not induce substantial changes in nasopharyngeal colonization with several potential pathogens, except for a temporary dose-dependent increase in *S. aureus* shortly after the booster dose. This may especially be relevant after implementing more doses or broader coverage vaccines and warrants future monitoring.

A HIGH-THROUGHPUT QUANTIFYING ANTIBODIES AGAINST 16 MAJOR STREPTOCOCCUS PNEUMONIAE SEROTYPES IN INTRAVENOUS IMMUNOGLOBULIN CONCENTRATES (IVIG)

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Background and aims: Evaluating the efficacy of antibodies against individual pneumococcal serotypes in clinical trials requires a validated and accurate method for quantifying their concentrations in plasma.

Because of the large number of pneumococcal serotypes defined by differences in the capsule antigen immunochemistry and given the large number of samples collected, an automated high-throughput quantifying pneumococcal serotype-specific antibodies (HTQ) was developed, combining a robotic device, ELISA methodology, and data processing. The HTQ process was validated and compared with routinely used manual ELISAs dedicated to 16 serotypes.

Methods: Existing manual in-house ELISAs were adapted to the HTQ process and validated according to ICH-Q2(R1). A liquid handling automate device (Tecan Genesis) was used for coating, sample dilution, and performing the different ELISA steps. Calibration was done with 89-SF (FDA). Test specificity was enhanced by pre-incubating the samples with cell-wall polysaccharide (CWP) and a rare capsular serotype, 22F.

Results: The HTQ approach improved quantification of anti-pneumococcal antibodies, allowing up to 1,400 tests/day. No effect of 22F was observed for the major serotypes 19A and 14. These data confirm previous results showing a high reproducibility of pneumococcal-serotype-specific antibodies in 9 plasma pools and 7 IVIG batches (Multigam[®]) produced over 2002-2004 period. The most abundant specific antibodies were those against serotypes 14, 19A, and 6B.

Conclusion: By measuring specific anti-pneumococcal antibodies in plasma pools it was possible to determine the mean level of each serotype in the Belgian healthy donor population. IVIG contain specific anti-pneumococcal antibodies at levels that could be sufficient to protect patients.

SEROTYPE DISTRIBUTION AND CLONAL ANALYSIS OF THE INVASIVE STREPTOCOCCUS PNEUMONIAE ISOLATES IN TURKISH CHILDREN

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Background: Heptavalent pneumococcal conjugate vaccine (PCV7) has been implemented into the routine immunization schedule recently in Turkey. We aimed to see the serotype distribution and clonal distribution of pneumococcal strains causing invasive diseases in children prior to and in the early period of the routine vaccination.

Methods: Pneumococcal isolates obtained from cerebrospinal fluid and blood cultures of pediatric cases (≤ 18 yrs) were collected from fifteen different health centers, serving about 55% of country population. All samples were serotyped with Quellung reaction. APAI and SMAI restriction enzymes were used for genotyping by PFGE using Apal and Smal restriction enzymes.

Results: In total 202 invasive *S. pneumoniae* isolates were analyzed. Most common serotypes were 19F, 6B, and 14. Serotype coverage of 7, 10 and 13 valent PCVs were 69.4%, 75.7%, and 85.2%, respectively in the 0-2 year age group. These vaccines had coverage rates of 47.5%, 53.9% and 66.3% for invasive isolates obtained from all children up to 18 years of age, respectively. Most frequent non-PCV7 serotypes were 19A and 3. There was no clonal distribution in PFGE analysis even in the same serotypes.

Conclusion: For children < 2 yrs in Turkey, PCV7 appears to cover about 70% of invasive pneumococcal infections; PCV10 and PCV13 seem to increase this coverage rate by 9% and 22.7%, respectively. Surveillance of pneumococcal diseases is essential to monitor the disease dynamics after routine use of PCV7 and evaluate the need for candidate pneumococcal conjugated vaccines.

STREPTOCOCCUS PNEUMONIAE AND PANDEMIC INFLUENZA COINFECTION IN ADMITTED PATIENTS

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Objectives: To describe pandemic influenza and *Streptococcus pneumoniae* coinfection in admitted patients in a tertiary paediatric hospital.

Methods: We include prospectively patients admitted from July to November and 2009 H1N1 infection confirmed by RT Real-Time PCR in respiratory fluids. Invasive *S pneumoniae* infection was considered when it was microbiologically confirmed by PCR or culture in sterile fluids.

Results: Of 119 patients with 2009 H1N1 infection, 12 (7 males) have demonstrated *S pneumoniae* infection (two diagnosed by blood culture and the rest by PCR in blood or pleural effusion). Median age was 4.1 years (interquartile range (IQR): 1.5-8.5). One had a previously known disease (sickle-cell disease).

All had fever and respiratory symptoms. Median time from onset of fever to admission was 4.5 days (IQR, 2.5-6). Seven had respiratory distress. Median C-reactive protein value was 243 mg/L (IQR, 129-289). Chest-X-ray shows lobar-consolidation in 11 (3 of them with pleural effusion) and non-consolidated pneumonia in 1. Main reasons for admission were respiratory distress and hypoxemia (8) and pleural effusion (3). Oseltamivir and antibiotics were given to all at admission. Two patients were severely ill and needed non-invasive ventilation (both previously healthy). Median time of admission was 5 days (IQR, 3.5-9.5).

Main Serotypes found were 1, 3, 5 and 14. *S pneumoniae* coinfecting patients had higher percentages of band neutrophils and higher levels of C-reactive protein than non-coinfecting patients.

Conclusions: Pneumococcal coinfection in pandemic influenza admitted patients is frequent. In coinfecting patients, hypoxemia was the main complication followed of pleural effusion.

DRAMATIC INCREASE OF PARAPNEUMONIC EMPYEMA INCIDENCE IN A FRENCH PEDIATRIC TERTIARY CARE CENTER DURING THE PANDEMIC INFLUENZA A (H1N1)

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Background and aims: Secondary bacterial respiratory infections are known to be associated with influenza. We observed during the influenza A (H1N1)v pandemic an increase of parapneumonic empyema.

Methods: Data were retrospectively collected from children hospitalized for empyema from January 1st 2006 to December 14th of 2009 in the general pediatric unit of Robert Debré Hospital, Paris, France.

Results: During the study period 37 children were admitted for a parapneumonic empyema. Eighteen of them were admitted in 2009. The incidence of parapneumonic empyema was respectively 2.3, 3.37, 3.6 and 9.4 for 1000 patients admitted in 2006, 2007, 2008 and 2009 (up to December 14th, 2009). The epidemic of influenza A (H1N1)v in France began week 37 with a peak at week 44. Eleven children were admitted from the end of September (week 39) to December 14th, 2009 (week 49) (incidence: 22/1000 admissions, median age 2 years 8 months). None of them had underlying medical condition. *Streptococcus pneumoniae* was the single found bacterial pathogen in 7/11 cases through cultures or pneumococcal antigen detection in pleural fluid or through blood cultures. No bacterial pathogen was detected in 4 cases. Naso-pharyngeal H1N1v PCR was performed in only 3/11 children and was positive in one patient.

Conclusion: The dramatic increase of admission for parapneumonic empyema in children is likely related to the influenza A (H1N1)v pandemic. Paediatricians should particularly consider the high incidence of such complications during Influenza A (H1N1)v pandemic even in children without underlying medical condition.

SEROLOGY (IGA & IGG) MAY IMPROVE ETIOLOGIC DIAGNOSIS OF CHILDHOOD PNEUMOCOCCAL PNEUMONIA: FIRST RESULTS FROM THE PEDIATRIC PNEUMOCOCCAL PNEUMONIA TRIAL

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Background and aims: There are few comprehensive studies of etiology of childhood community-acquired pneumonia (C-CAP) and blood culture (BC) is only positive in $\pm 10\%$ of cases. Addition of serotype specific IgG & IgA serology (IgG&IGA-SSS) could improve this diagnostic rate.

Methods: In a multicenter trial aiming to study the etiology of C-CAP, blood samples for BC, and for acute and convalescent serology were taken in children < 15y with X-ray confirmed C-CAP. We present the results of the IgG&IgA-SSS against the pooled serotypes of the 23v-polysaccharide vaccine and against serotype 1, 5, 6B, 7, 9N+V, 14, 19A, 19F, 23F, in 19 BC-positive children. 11/19 children received ≥ 1 dose of Prevenar®. All isolated *S. pneumoniae* strains were serotyped at the reference laboratory. Seroconversion definition: a > 3-fold rise in the Ab-concentrations for IgG and/or a ≥ 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: The pooled 23-valent test didn't show seroconversion. IgG-SSS matched BC-results in 15/19 cases. In 2 cases, serology couldn't identify the serotype. In 2 other cases, serotyping and serology revealed discrepant results. IgG-SSS and IgA-SSS results were always concordant. The interpretation of IgG&IgA-SSS wasn't hindered by previous vaccination.

Conclusions: These results suggest that IgG&IGA-SSS could help in identifying the bacterial etiology in C-CAP and provide important epidemiological information. Serological testing of supplementary blood samples from children with negative BC will now be performed.

IS THERE A ROLE FOR POINT OF CARE TESTING IN MANAGING INFANTS WITH BRONCHIOLITIS?

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Background and aims: RSV causes a predictable burden on paediatric services every winter. Recent experience with the novel H1N1 pandemic has highlighted the need to optimise provision of resources such as cubicles to improve management of future pandemics.

Methods: Our audit evaluated the impact of a rapid RSV immunoassay on managing infants with bronchiolitis. The POC test was performed in the emergency department and was only requested on children meeting clinical criteria for admission. Data on disease severity, investigations, management and place of admission were collected prospectively. Children offered POC testing were compared to a cohort of children investigated with routine PCR testing available within 24 hours.

Results: The incidence of RSV positivity was over 90% and disease severity was comparable in both groups. Over 60% of children testing positive to the POC test were cohorted on admission, compared to only 8% in the control group. There was a 50% reduction in blood tests performed on the children diagnosed with the POC test. Antibiotic use was 9% in the POC group, compared to 23% in the control group.

Conclusions: This study shows that the introduction of a rapid POC test for RSV had a considerable impact on the management of infants admitted with bronchiolitis. Perhaps more significantly, it offers a simple way of cohorting children in a time effective manner. This not only has implications during the RSV season, but may have a more far-reaching effect by aiding in the efficient allocation of invaluable resources during a future influenza pandemic.

DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF COMMUNITY-ACQUIRED PNEUMONIA (CAP) IN CHILDREN < 5 YEARS IN SOUTHERN ISRAEL

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Background and aims: Lower respiratory tract infections are major causes of morbidity and mortality in children < 5 years. Two populations reside in southern Israel: The Jewish population, resembling a western socioeconomic middle-class and the Bedouin population, living in lower socioeconomic conditions and overcrowding. Our goal was to compare selected epidemiologic and clinical characteristics of Bedouin and Jewish children with CAP.

Methods: All chest radiographs of children < 5 years obtained at the pediatric emergency room (PER) or pediatrics wards between 2001 and 2007, were evaluated for pneumonia according to WHO's criteria. Demographic and clinical data were collected to determine morbidity, hospitalization and mortality rates. Multivariate Regression models were used to control for patient's age in clinical data analysis.

Results: 38,045 chest radiographs were evaluated and CAP was diagnosed in 5,965 (15.6%) of them; 5,394 (90.4%) were alveolar pneumonia (WHO Working Group Criteria). The cumulative risk of presenting to the PER with CAP before 5 years of age was 8.3% and 5.4% in Bedouin and Jewish children, respectively ($P < 0.01$), while the respective cumulative risk for hospitalization was 5.8% and 2.2%, respectively ($P < 0.01$). The following findings were significantly more prevalent in Bedouin than in Jewish children: tachypnea, 71.9% vs. 61%; hypoxemia, 31.7% vs. 18.6%; mortality rates, 3% vs. 0.3%, respectively.

Conclusions: CAP burden is high in children < 5 years in southern Israel. Bedouin children presented with a more severe course of disease and had higher hospitalization and mortality rates than Jewish children.

ANTIBIOTIC EXPOSURE IN CHILDREN AND ADOLESCENTS WITH LOWER RESPIRATORY TRACT INFECTIONS

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Background and aims: The rate of reported antibiotic (AB) use in children with lower respiratory tract infections (LRTI) of presumably viral origin is high. The aim of this study was to evaluate the antibiotic (AB) exposure of children and adolescents with lower respiratory tract infections (LRTI) in our institution.

Methods: Previously healthy patients admitted for LRTI treatment to the University Children's Hospital Basel, Switzerland (01/2005-12/2008) were identified by ICD-10 codes and text search of electronic medical records. Data were extracted into a structured database and cases were classified as LRTI or community acquired pneumonia (CAP) according to stringent case definitions.

Results: Included were 204 patients; 116 male (57%); mean age 4 yrs (range 0.1-18); mean duration of hospitalisation 4 days (range 1-33). Classified as CAP, bronchitis, or bronchiolitis were 111 (45%), 83 (41%), 10 (5%) respectively. Of these 101 (91%), 63 (76%), and 2 (20%) received AB, respectively. Among 166 receiving AB 61% had pneumonia. 32 (100%) of patients with a CRP ≥ 120 and 79 (72%) with a CRP < 40 g/l received AB. An organism was identified in 88 (25 *M. pneumoniae*, 2 *S. pneumoniae*, 1 *H. influenza*, 2 *B. pertussis*, and 58 viral pathogens). Mean duration of AB was 11 days (range 1-44), including a mean of 2 days (range 1-15) iv treatment .

Conclusions: Antibiotic use in patients with LRTI other than pneumonia and low CRP was higher than expected. Reliable diagnostic tests or clinical rule sets guiding confident restriction of antibiotic use are needed.

**SEROPREVALENCE AND AGE VARIATION OF *CHLAMYDIA PNEUMONIAE* AND
MYCOPLASMA PNEUMONIAE INFECTION IN CHILDREN**

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Objective: *Chlamydia pneumoniae* (CP) and *Mycoplasma pneumoniae* (MP) cause respiratory tract infections including community-acquired pneumonia in children. We performed a laboratory-based multicenter surveillance in Germany to determine the prevalence of antibodies against CP and MP, and age-dependent differences in seroprevalence.

Materials and methods: All serum samples submitted to three laboratories located in North and South Germany for CP and MP serology between June 2008 and May 2009 were included. Results of IgM, IgA, and IgG antibodies against CP and MP (ELISA medac, Wedel, Germany) were evaluated in 5002 children and adolescent < 1 up to 20 years.

Results: The total seroprevalence indicating infection with CP and MP was 34% and 26%, respectively. The prevalence of infections increased with the age of patients up to 60% caused by CP and 47% by MP. Serological evidence of acute CP and MP infection was found in 2-8% and 0-7% of patients, respectively, depending on the age group of patients. Highest rates of acute infections were determined in the age group of 16-20 years with CP and in the age group of 6-15 years with MP.

Conclusion: According to our serological data, seroprevalence by CP and MP is already high in the young population. Serological indication of CP or MP infection increases with age but acute infections with CP reach their peak in older adolescent than acute infections with MP.

REDUCTION IN WHEEZING DURING THE THIRD YEAR OF LIFE AMONG CHILDREN BORN AT 32-35 WGA WHO RECEIVED PALIVIZUMAB PROPHYLAXIS

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Background: Respiratory syncytial virus (RSV) lower respiratory tract infections in infancy have been associated with recurrent wheezing in early childhood. In the Palivizumab Long-Term Respiratory Outcomes Study, palivizumab prophylaxis during the first year of life resulted in significantly lower incidence of recurrent wheezing in preterm infants during 24 months of follow-up, compared with no prophylaxis. However, data on early childhood wheezing with emphasis on clinically-significant events are limited, particularly in late preterm infants.

Methods: Clinically-significant wheezing during the third year of life was assessed in children enrolled in the above mentioned study who were born 32-35 wGA, using a new endpoint, serious early childhood wheezing (SECW), that captures both frequency and severity (≥ 3 episodes of physician-diagnosed wheezing; use of asthma control medication for ≥ 3 consecutive or ≥ 5 cumulative months; or systemic corticosteroid use).

Results: 53 children born 32-35 wGA received palivizumab prophylaxis, and 114 did not. Demographic differences were observed between the palivizumab-treated and untreated cohorts in: mean gestational age, mean birth weight and mean number of siblings in household. In the third year of life, serious wheezing occurred in 5.7% (3/53) of palivizumab-treated infants versus 21.9% (25/114) of untreated infants (Relative reduction of 74%; $P = 0.008$).

Conclusion: Although the original study was not powered to demonstrate a difference for this new endpoint, in this cohort of children born 32-35 wGA, palivizumab use during the first year of life was associated with a statistically significant reduction in SECW in the third year of life, compared with no prophylaxis.

GENETIC SUSCEPTIBILITY TO RESPIRATORY SYNCYTIAL VIRUS IN PREVIOUS HEALTHY CHILDREN: A REPLICATION-COHORT STUDY

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Background: Respiratory syncytial virus (RSV) is the most common cause of severe lower respiratory tract infection in children aged less than 1 year. Our previous study showed that susceptibility to severe RSV bronchiolitis is predominantly associated with single-nucleotide polymorphisms (SNPs) in innate immune genes.

Aim: Replication of previous studied associations of genetic polymorphisms and severe RSV bronchiolitis, in a new cohort.

Methods: 162 Dutch children without pre-existent pathology, hospitalized for RSV bronchiolitis, were included in a new cohort. 7 SNPs in 7 genes were analyzed in DNA of these children and 1008 controls. VDR, NOS2A, IFNA13, IFNA5 and JUN play a role in innate immunity, IL10 in adaptive immunity and FCER1A in allergic asthma.

Results: SNPs in VDR, NOS2A and IFNA13 genes showed a trend to increased susceptibility to severe RSV infection, while the SNP in IFNA5 and the heterozygous version of the IL10 gene reduces susceptibility. Other SNPs could not be replicated. Analysis of the complete cohort, including the cases of the first cohort, significantly confirmed the previously found associations.

Conclusions: Replication of genetic association studies is crucial for a correct interpretation. In this new cohort, no statistical significant associations were found between the studied SNPs and the susceptibility to severe RSV bronchiolitis, although there was a trend in the same direction for five SNPs as was seen in our previous cohort. Future research should focus on replication of the findings of this study as well as the functional significance of the informative SNPs.

RESPIRATORY VIRUS INFECTIONS, AN OVERWHELMING PROBLEM IN A LIMITED-RESOURCE COMMUNITY LIMA PERU

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Aims: Describe the impact the respiratory virus have in the hospitalization rate of less than 2 years old children old in an important zone of Lima Perú.

Methods: Review of Pediatrics database of the main district hospital since July 2003- to July 2004. Results of laboratory tests (DFA) are included. The demographic, clinical and discharge diagnosis data were collected.

Results: There was an important prevalence of virus in less than 2 years old children admitted with Acute-severe Lower respiratory infections(ALRI), the percentages were between 32 to 61%. More than 80% did not required antibiotics, but almost all arrived with severe pneumonia; the mean length of hospitalization (LOH) was 5.6(+/-4.5 days), readmission during the next month of discharge was about 2%. The survey included 262 children. DFA was positive against the main respiratory virus RSV, influenza, parinfluenza, adenovirus being positive in 50-70%. Coinfections were described. Almost half of patients with antibiotics had an underlying problem, like Congenital Diseases, undernutrition.

Conclusions: Acute respiratory virus must be the main cause of disease in under 2 years children in one of the poorest region of Lima City; complications were low, mortality was as in developed world; the rate of bacterial associated pneumonia did not justify the use of antibiotics in children with ALRI unless a clear associated underlying health problem exist. RSV and Influenza Virus are very important etiology. It is necessary to manage ALRI as a Public Health Problem and develop a strategy because the burden of viral respiratory diseases is huge.

PERTUSSIS: MORBIDITY RISK FACTORS

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Introduction: There has been a rising incidence of pertussis in the young infant, which has conditioned an increase in morbidity and mortality.

Objective: To describe pertussis cases admitted to our hospital, risk factors for PICU admission and mortality rate.

Patients and methods: A retrospective and prospective observational study was designed. Patients affected by whooping cough with microbiological confirmation admitted in our hospital from January 2001 until December 2008 were collected.

Results: We collected 84 cases. The mean age was 65 days (15-437) without differences in gender distribution. Clinical presentation was paroxysmal cough (96.4%), cyanosant cough (75%) and vomiting (36.9%). 31% had apneas after cough and 11.9% primary apnea. Any patient had completed the vaccination regimen. Microbiological confirmation was performed by immunofluorescence or PCR in 68 cases (81%) and/or by culture in 65 (77.4%). Erythromycin was the drug of choice for treatment (60.7%). Twenty-four patients were admitted in PICU (28.6%). Risk factors for PICU admission were: leukocytosis (p 0.003), primary apnea (p 0.002, OR 7.8), respiratory distress (p 0.001, OR 9.5), infiltrates in x-rays (p 0.001, OR 12) and sepsis (p 0.005, OR 8.5). Noninvasive ventilation was applied in 11 cases (46%) (7 exclusively). Ten patients required mechanical ventilation, 5 HFOV and 2 ECMO. Five patients died (20.8%), all had pulmonary hypertension and were treated with nitric oxide. One exchange transfusion was carried out.

Conclusions: Pertussis is an ongoing and potentially fatal health problem. Presence of primary apnea, leukocytosis, respiratory distress, infiltrates in x-rays and sepsis are risk factors for morbidity.

**NASOPHARYNGEAL BACTERIAL COLONISATION WITH STREP PNEUMONIAE AND
HAEMOPHILUS INFLUENZAE IS QUANTITATIVELY ASSOCIATED WITH SYMPTOMS OF
NASAL CONGESTION**

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Background and aims: Bacterial nasal colonisation is generally called “asymptomatic”.

Methods: 439 children (4-75 months, 233 males) attending 6 nurseries each had alginate nasal swabs taken in February 2009 and stored in STGG broth. At sampling, nurses obtained a single symptom score for nasal discharge, nasal blockage and sneezing from parents as follows: 0-none; 1-mild-slight; 2-moderate-definite; 3-severe-bad. Swabs were cultured & bacteria identified using standard methods. For pneumococcus, density was scored as 1-5(1), >20(2), >50(3), >100(4), >100(5) colonies/50µl broth.

Results: 231(52.6%) 134(30.5%) and 62(14.1%) swabs were positive for Pnc, Hflu & S aureus, respectively. Among 428 children for whom scores were available, the proportion of children colonised with Pnc & Hflu rose progressively with rising symptom scores (χ^2 for trend: all $P < 0.00023$; < 0.00001). S aureus showed the opposite trend (NS). Symptom scores and Pnc colonisation density were strongly correlated ($P=0.00021$).

Symptom score	0	1	2	3
Total	104	224	89	11
Pnc pos (%)	41(39.4)	118(52.7)	55(61.8)	9(81.8)
Hflu pos(%)	22(21.2)	51(22.8)	50(56.2)	8(72.7)
S aureus pos (%)	23(22.1)	32(14.3)	7(7.9)	0(0)

[Table]

Conclusion: These results show that uncomplicated nasopharyngeal colonisation in healthy children with Pnc and Hflu but not *S. aureus* is strongly associated with nasal symptoms which are correlated to carriage density at least for Pnc and are likely to influence transmission. The cause-effect relationships and role of viral infections in this setting require further investigation.

INFLUENZA IN CHILDREN

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Background and aims: Every year during the epidemic period from 5.1 to 17.8% of the population in Belarus develop a flu meanwhile children constitute from 36 to 56%.

Methods: There were 80 patients age 1 - 17 years under supervision (70% type A и 30% flu B). The diagnosis was based on immunofluorescence reaction in 63 % of cases, PCR-diagnostics - in 29% and by means of two methods - in 8% of patients.

Results: The main clinical sign was fever for 76% of patients with median 4,0days (3,5 - 5,5). Moreover, the children complained about general weakness, malaise, headache, pain in muscles and eyes (most children are older than 5). Among respiratory syndromes were affection of nasopharynx in 37 patients (46, 2%), larynx - 18, 8%, trachea and bronchus - 35% (6 patients of them with flu A had manifestations of obstructive bronchitis). The following changes in the general analysis were determined: leucocytosis $13,4 \pm 0,58 \cdot 10^9/\mu\text{l}$ (32%), lymphocytosis in 22, 5% of patients from 50 to 81%, $(65 \pm 2, 3\%)$, stab neutrophil from 6 to 34% (in 50% of observations) and leucopenia $4,2 \pm 0,16 \cdot 10^9/\mu\text{l}$ (21.2%). Complications (acute otitis media, tonsillitis, pneumonia, suppurative rhinopharyngitis) were registered in 15% of patients with influenza.

Conclusions: Clinical sign of influenza has typical signs, presence of inflammatory changes (leukocytosis, stab neutrophil) and absence of specific changes (lymphocytosis, leukopenia) in the blood picture at the early stages of the illness are not the main diagnostic criteria to prescribe an antibacterial therapy.

EARLY DIAGNOSTIC MARKERS OF SEVERE INFECTIOUS DISEASES IN CHILDREN WITH RESPIRATORY TRACT INFECTIONS

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The aim of study was to compare the levels of HMGB1, LBP, IL-6 and CRP in children with respiratory tract infections.

Methods: 30 children with variable respiratory tract infections admitted to the UCH during 2008 /2009 were included. LBP, IL-6, HMGB1 and CRP levels were analyzed. Patients were distribute into two groups according to severity of infection: SIRS negative (n=8) and sepsis patients (n=22).

Results: In 13,6 % bacteriemia had been detected. There was no statistically significant difference in HMGB1 levels between children with sepsis or without. The levels of LBP, IL-6 and CRP were statistically significantly higher among patients with sepsis compared to SIRS negative ($p < 0.001$). Median values of LBP, IL6 and CRP were significantly higher in children with bacteriemia compared to those without bacteriemia. The area under the receiver operating curve for detecting bacteriemia was 0.87 for both IL6 and CRP and 0.82 for LBP. 95% confidence interval (CI) for IL6 was 0.78 - 0.96, for CRP- 0.79 - 0.95. AUC for LBP was 0.82 (95% CI 0.73 - 0.91). Sensitivity with cut-off levels 26.6 $\mu\text{g/ml}$ (LBP), 58.7 pg/ml (IL6) and 97 mg/l (CRP) was 80% for all three markers.

Conclusion: Severe infections of respiratory tract were associated with elevated levels of IL-6, LBP and CRP. LBP, IL-6 and CRP levels may be used as good biomarkers for identifying children with sepsis and bacteriemia, while HMGB1 seem to be less importance.

INTRODUCING PCR TESTING FOR VIRAL RESPIRATORY INFECTIONS IN A PAEDIATRIC UNIT**N. Hallam, L. Hesketh***Virology, Royal Preston Hospital, Preston, UK*

Background and aims: To assess the introduction of respiratory PCR testing for a busy paediatric unit.

Methods: Nasopharyngeal aspirates (NPA) from those under 2 years of age with clinical respiratory disease and requiring admission were tested.

Tests

On-site (Oct-Mar only): Immunofluorescence (DIF) - detects adenovirus, influenza viruses A and B, parainfluenza viruses 1-3 and RSV, and Immunochromatography (IC) - detects RSV.

Off-site (all year): Respiratory PCR - detects adenovirus, influenza viruses A and B, metapneumovirus, parainfluenza viruses 1-3, rhinovirus and RSV.

Oct-Mar: negative on-site specimens were sent for PCR testing, *April-Sept:* all specimens were sent for PCR testing only.

Results: 273 NPAs were received between 1st October 2007 and 31st March 2008. 183 were tested on-site, of which 93 were positive for RSV (only). The 90 on-site negatives and 90 others not tested on-site were sent for PCR testing, of which 177 were actually tested. 109 of these (62%) were positive, of which 91 (51% of specimens tested) were single infections (39 rhinovirus, 33 RSV, 10 metapneumovirus, 4 influenza A, 3 parainfluenza, 2 influenza B) and 18 (10% of specs) were dual infections (15 included rhinovirus, 6 adenovirus, 5 parainfluenza virus, 5 metapneumovirus, 4 RSV, 1 influenza A). The commonest dual infection was rhinovirus and parainfluenza virus (5 cases).

Conclusions: PCR testing is more sensitive than traditional methods but is less rapid, especially if performed off-site.

We will also present results for the winter of 2009-10 which will include pandemic H1N1 influenza (swine-flu) testing.

**EXTENDED-SPECTRUM BETA-LACTAMASES OR AMPC PRODUCING *ESCHERICHIA COLI*
ISOLATES COLLECTED IN CHILDREN WITH PNEUMONIA IN CHINA**

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Background and aims: Pneumonia is a common and fatal infection in children. In this study, we characterized the molecular and clinical features of extended-spectrum beta-lactamases or AmpC producing *Escherichia coli* (*E.coli*) pneumonia in Chinese children.

Methods: Between January 2005 and December 2006, 180 children confined in five hospitals were found to be afflicted with ESBLs or AmpC *E.coli* pneumonia, while 180 strains from them were analyzed by *Bla* gene detection and sequence analysis. Antimicrobial susceptibility testing was been operated too.

Results: Overall, 91.7% children were less than one year old and nineteen children were newborn infants. Nineteen children were manifested with complication; 44.4% of the children had been used the third generation of cephalosporin before one month; 15.6% children lived in the ICU, and six children had used the mechanical ventilation or endotracheal intubation. The resistance rate against cefotaxime, cefepime, ceftazidime were 64.4 %, 46.7%, and 25.0%, respectively. 161 isolates were positive for the *Bla*_{CTX-M} group, in which, 56.1% had the CTX-M-14, 24.4% with the CTX-M-15, 3.9% had the CTX-M-3, 4.4% both had CTX-M-14 and CTX-M-15, 1 with the CTX-M-24. Two new sequences of CTX-M were detected, with the GenBank accession numbers GU226838 and GU226840. In six *Bla*_{SHV} genes, two with SHV-1, two with SHV-12 and two were new sequences with the GenBank accession number EU350512.

Conclusions: Young infants are the major population of ESBL or AmpC *E.coli* pneumonia in China. The resistances to cephalosporins in those isolates are very high, while the CTX-M-14 is the predominant type of *bla* genes.

PERTUSSIS IN NON-VACCINATED INFANTS WITH BRONCHIOLITIS

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The aim was to evaluate *Bordetella pertussis* involvement in < 6 months old infants hospitalized for bronchiolitis.

During the 25-month study period in 2001-2004, 207 infants less than 6 months of

age were hospitalized due to bronchiolitis, and after viral studies in nasopharyngeal aspirates (NPA), 142 good-quality NPA samples were available for *B. pertussis* identification by polymerase chain reaction (PCR). In Finland, vaccinations against pertussis were given at 3, 4 and 5 months of age before the year 2005, and the coverage of vaccinations was almost 100%.

Cough classification	Pertussis + (n=12)	Pertussis - (n=130)
Cough with attacks	5 (42%)	19 (15%)
Cough without attacks	7 (58%)	104 (80%)
No cough	0	7 (5%)

[Results

(p=0.048)]

Pertussis-PCR was positive in 12/142(8.5%) infants (4 boys and 8 girls). Six were less than 3 months old (non-vaccinated) and six were 3 to 5 months old (partially vaccinated). Viral infection was found in 11/12(92%) cases (RSV in 8 cases). One of the authors (PK) checked the patient cards and classified retrospectively the cough histories into three categories.

Only 2/12 infants were treated with macrolides; 5 received penicillin or amoxicillin and 5 no antibiotics.

All infants with *B. pertussis* involvement in connection with viral bronchiolitis had cough but only half had cough attacks. Thus, the only way to diagnose pertussis in non-vaccinated infants at risk for severe disease is to study pertussis by PCR in NPA samples of all infants with cough symptoms.

PLEURAL EMPYEMA IN CHILDREN: THORACOSCOPIC APPROACH (117 CASES)

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Aim: To evaluate indications and results of thoracoscopy in empyema.

Method: Retrospective multicentric study (2001-2006), 117 patients (71% males) from 5 paediatric surgical departments in France. Median age: 4,5 years old (5,6 +/- 4,1). Staging anatomic lesions with thoracoscopic aspect (4 stages).

Results: Presentation: delay between first symptoms and surgical treatment (61,3%).

Treatments before surgery: antibiotics (94,4%), thoracocentesis (34,2%), chest tube (11,7%).

Etiology: bacterial infections (53,8%), viral and/or mycotic (4,3%), unknown (41'9%).

Efficiency of thoracoscopy (more than 75% of pleural space cleaned) in 94%, depending of video-anatomic stages (I:5%, II:39%, III:55%, IV:1%).

Hospitalisation: 9,5 days (4-60 days). Apyrexia obtained in 4,3 +/- 3,2 days, drain removed after 4,6 +/- 2,5 days. Antibiotics administered during 15 days after surgery.

Complicated post-operative course in 8,5% of patients, with five second thoracoscopy and 3 thoracotomy.

Children under 4 years old were more concerned with bacterial infections and presented a delay at discovery. Delay between first symptoms and surgery was correlated with an higher staging at thoracoscopy.

Discussion: Parapneumonic effusion and empyema seem become more prevalent. Reasons of these evolution are not clear. Treatments are numerous with various results (simple antibiotherapy, fibrinolysis). The high rate of delay at diagnosis and its consequences on staging, confirm the necessity of a large medical information about pleural empyema in children.

Conclusion: Thoracoscopic approach is an efficient therapy for stage II and stage III pleural empyema. Morbidity is reasonable. Indication has to be discussed with other therapeutic approaches.

SURVEY OF PERTUSSIS IN PATIENTS WITH PROLONGED COUGH >7 DAYS**J.-T. Lee¹, B. Elvers², L.-M. Huang³**

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Background and aims: The aim of this study was to determine the percentage of pertussis in patients and healthcare workers with prolonged cough >7 days.

Methods: We recruited school age children (aged 6-18 years) and adults with prolonged cough >7 days from November 2007 through October 2009 and healthcare workers with cough illness >7 days in 2009. We collected a nasopharyngeal swab for real time polymerase chain reaction (PCR) for detection of *Bordetella pertussis*. Serum samples were also taken and frozen before specific immunoglobulins against pertussis toxin (IgG-PT) and a sonicate of the whole bacterium *Bordetella pertussis* (IgA-Bp) were measured with an enzyme-linked immunosorbent assay. A labcode was calculated in the reference lab in the Netherlands. The interpretation was positive when IgG-PT is ≥ 100 U/ml or a labcode ≥ 8 .

Results: Seventy six patients with prolonged cough >7 days were recruited in the study period. There were 50 school age children, 19 adults and 7 healthcare workers. Positive samples in a real time PCR were detected in 14/50 (28%), 3/19 (15.7), and 2/7 (28.5%), respectively. Overall positive rate for real time PCR was 25% (19/76). Serum samples were interpreted positive in 11/45 (24%), 2/18 (11%) and 0/6 (0%), respectively. Cough illness with evidence of pertussis infection was found in 19/50 (38%), 4/19 (21%) and 2/7 (28.5%), respectively. The majority of the cases with PCR-confirmed pertussis (13/19, 68.4%) were adolescents aged 12-18 years.

Conclusions: Pertussis is not uncommon in adolescents with prolonged cough, who were responsible for the transmission of the disease.

COMPARING INCIDENCE FIGURES OF ACUTE OTITIS MEDIA IN YOUNG CHILDREN IN FIVE EUROPEAN COUNTRIES WITH THE PUBLISHED LITERATURE

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Background and aims: Acute otitis media (AOM) is one of the most frequent infections in young children. There is a large variation in reported AOM incidence in Europe due to different case definitions, study design and age groups. We initiated a retrospective cohort study in five European countries to determine AOM incidence and compared the results with previously published data.

Methods: 5776 healthy children aged 0-5 years were randomly selected from 73 convenient medical practices in Germany, Italy, Spain, Sweden and the United Kingdom (UK). AOM incidence in the previous year was determined using documented physician-diagnosed AOM from medical files and was compared with reported incidences from articles in online databases and bibliographies on AOM published between January 1990 and October 2009.

Results: This European study reported an overall incidence of 268 AOM episodes/1000 patient-years (95% CI:254-283), ranging from 176 [95% CI:153-203] in Italy to 382 [95% CI:350-427] in Spain. We identified 27 publications on AOM: 16 had data suitable to calculate annual incidence of AOM; three presented data separately for children aged 0-4 or 0-5 years old. In the published literature, the incidence in 0-5 year-old children ranged from 154 (95% CI:152-158) to 400 (95% CI:397-403) episodes/1000 patient-years, with the highest figures in Spain and the lowest in France.

Conclusion: Similarly to published results our study confirms the high incidence of AOM during childhood with large differences across Europe. This may indicate differences between investigated populations with regard to social structure, health care access and diagnostic approach.

UNDERESTIMATION OF INFLUENZA VIRAL INFECTION IN CHILDHOOD ASTHMA EXACERBATIONS

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Background: Respiratory viruses, including influenza, bocavirus and respiratory syncytial are common agents of acute asthma exacerbation in children

Objective of the study: To compare the incidence of influenza and other respiratory viruses in ambulatory and hospitalized children with asthma exacerbation

Patients and methods: From November 2005 to May 2009, viral immunofluorescence and bocavirus PCR were performed on nasopharyngeal aspirates in children (2-15y) examined in an hospital emergency room for acute asthma attack during the winter seasons and hospitalised or not..

Results: Bocavirus was found in 11.6% of hospitalized and 13% of ambulatory patients with exacerbation of asthma, and respiratory syncytial virus in 13.5% and 17.7%, respectively. However, influenza A virus was detected in 2.6% of hospitalized and 14.1% ($p < .001$) of ambulatory-treated patients.

Conclusion: Influenza virus contributes to exacerbation of childhood asthma and is more often founded in ambulatory patients than in hospitalised, but other respiratory viruses had the same frequency in the two groups. The influenza burden in childhood asthma may be underestimated if only hospitalised patients are considered.

INCIDENCE AND DIAGNOSIS OF ACUTE OTITIS MEDIA IN ITALIAN CHILDREN

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Background and aim: Acute otitis media (AOM) is one of the most common infectious diseases in young children. As little is known on the epidemiology of AOM in Italy, we studied the incidence and clinical presentation of AOM among Italian children.

Methods: The retrospective study, using PEDIANET general-practice research-database, included 92,373 children aged up to 6 yrs during 01/2003-12/2007. AOM cases were identified and validated in patient diaries. Incidence rates/100 person-years (PY) were calculated for total AOM and for uncomplicated AOM (un-AOM), recurrent AOM (rAOM, ≥ 3 episodes) and AOM with spontaneous otorrhea (AOM-O).

Results: A total of 43261 AOM episodes (36180 un-AOM, 2061 rAOM, 5020 AOM-O) were identified in 23669 children. Incidence rates were: total AOM 19.0 (18.8-19.2), unAOM 15.9 (15.7-16.1), rAOM :0.9 (0.9-0.9), AOM-O: 2.2 (2.1-2.3)/100 PY respectively. Total AOM rate/100 PY varied with age, peaking in children 3-4 yrs old: 25.1 (24.7-25.6), with similar age trends in all AOM subgroups. Earache was the most common symptom (total AOM: 54.5%;un-AOM 55.6%;rAOM 50.4% AOM-O 48.3%) followed by fever (total AOM: 48.3%; un-AOM 49.9%;rAOM 39.4%;AOM-O 41.0%). Pneumatic otoscopy was used in 3.7% of total AOM (un-AOM 3.8%; rAOM 1.9%; AOM-O: 4.3%).

Conclusions: Even if incidence of AOM seems lower than in other European countries, AOM has a considerable impact on the Italian primary care system. Diagnosis is major challenge, as usefulness of symptoms is limited and the most appropriate diagnostic method, pneumatic otoscope, is used in a minority of cases. Educational programs concerning diagnosis of AOM should be implemented.

DRUG PRESCRIBING PATTERN IN ACUTE OTITIS MEDIA IN ITALIAN CHILDREN

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Background and aim: Acute otitis media (AOM) is one of the major reasons for antibiotic prescriptions in developed countries. As little is known on drug prescriptions for AOM in Italy, we conducted a retrospective study to evaluate prescribing patterns among Italian children.

Methods: The study, using PEDIANET general-practice research-database, included 92,373 children 0 - 6 yrs old during 01/2003-12/2007. AOM cases were identified and validated in patient diaries. Prevalence of drug use was calculated by therapeutic class for total AOM and for uncomplicated AOM (un-AOM), recurrent AOM (rAOM, ≥ 3 episodes) and AOM with spontaneous otorrhea (AOM-O).

Results: A total of 43261 AOM episodes (36180 un-AOM, 2061 rAOM, 5020 AOM-O) were diagnosed and at least one drug was prescribed in 81.2% of the cases. Antibiotics represented 94.2% of prescriptions (un-AOM 96.3%; rAOM: 95.6%; AOM-O: 71.4%, $p < 0.001$). Amoxicillin was the most prescribed drug, followed by amoxicillin-clavulanate, independently of AOM subgroups and age. Analgesics and antiinflammatory accounted for 9.5% prescriptions (un-AOM 9.2%; rAOM 7.9%; AOM-O 13.0% $p < 0.001$) and systemic steroids for 3.8% (un-AOM 3-4%; rAOM 3.9%, AOM-O 7.6%, $p < 0.001$) prescriptions.

Conclusions: Drug prescription pattern is likely to have a substantial impact on the costs and outcome of AOM. While the use of amoxicillin as first drug is valuable, the limited use of antibiotics in AOM-O and the utilization of steroids are questionable. The surprising scarce use of analgesics may be attributed to self-prescribing. Educational strategies to improve compliance with published recommendations should be implemented.

REP- PCR ANALYSIS OF PHENOTYPIC DIFFERENT PSEUDOMONAS AERUGINOSA STRAINS FROM CYSTIC FIBROSIS PATIENTS WITH DIVERSILAB®

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Objectives: *P. aeruginosa* is highly prevalent in cystic fibrosis (CF) patients, causing a chronic airway- disease. This study was conceived to answer the following questions:

1. Is one patient colonized by one specific genotype?
2. Are phenotypic different strains of one patient also genotypic dissimilar?
3. Are there epidemic strains colonizing two or more patients?
4. Are the results of rep-PCR comparable to pulsed-field gel electrophoresis (PFGE-Spe I)?

Methods: From July to October 2009 a total of 46 *P. aeruginosa* consecutive strains were collected from the sputum of 17 CF-patients. Extraction of DNA, rep-PCR and generation of genetic fingerprints were done following the manufacturer's instructions. To determine the strain relatedness the DiversiLab® software was used. To evaluate the rep-PCR data 25 strains were also analyzed by PFGE-Spe I.

Results: In most cases one patient was linked with only one specific genotypic pattern. A total of 30 strains from 12 patients showed at least one phenotypic difference concerning resistance pattern or morphology (mucus, colour). Nevertheless the major part of these strains is related to four main genotypic patterns. In regard to question three, we found that there are epidemic strains colonizing two up to six different patients. In comparison to PFGE the rep-PCR provided similar results in most cases.

Conclusion: We can conclude that there is an evidence for the presence of epidemic *P. aeruginosa* strains. As a consequence of our findings further investigations will focus on sources and possible transmission routes to avoid cross-contamination.

ACUTE OTITIS MEDIA (AOM) IN CHILDREN < 5 YEARS OF AGE IN SOUTHERN ISRAEL DURING 1999-2006: EPIDEMIOLOGIC AND MICROBIOLOGIC TRENDS

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Aims: To study the epidemiologic and microbiologic characteristics of AOM before pneumococcal (SP) conjugate vaccine introduction.

Methods: Middle ear fluid from 10,198 children was cultured. SP penicillin-nonsusceptibility (PEN-NS) was defined as MIC>0.1 µg/ml and multidrug resistance (MDR) by nonsusceptibility to ≥3 antibiotic classes. Multivariate regression analysis models determining the relative risk (RR) for being sick with antibiotic-resistant SP-AOM (adjusting for ethnicity, previous antibiotic treatment and AOM history) were used.

Results: There were 12,793 AOM episodes; 7,357 (57.5%) occurred in Moslem Bedouins. *H. influenzae* (HI), SP, *S. pyogenes* and *M. catarrhalis* were recovered in 24.3%, 20.3%, 2.4% and 1.3% episodes, respectively. SP susceptibility to penicillin was 35.1% and increased from 30.1% (1999) to 42.8% (2006), $P=0.002$. SP susceptibility to erythromycin decreased from 85.6% (1999) to 66.5% (2006), $P< 0.001$. MDR-SP isolates increased in both Jews (20.6% in 1999 to 29.2% in 2006, $P=0.008$) and Bedouins (13% to 29.3%, $P< 0.001$). 23.5% HI isolates produced beta-lactamase. Beta-lactamase positive HI-AOM decreased during study years among Jewish children ($P=0.003$) and remained unchanged in Bedouins ($P=0.09$). RR for PEN-NS and MDR SP-AOM was 3.6 and 2.3, respectively, for a child with >3 prior AOM treated with antibiotics during last month, compared with one having ≤3 episodes and not receiving antibiotics.

Conclusions:

- 1) A significant increase in penicillin-susceptible and decrease in erythromycin susceptible-SP were recorded;
- 2) MDR-SP increased significantly;
- 3) Recent therapy and rich AOM history represented significant risk factors for AOM caused by PEN-NS or MDR-SP;
- 4) Beta-lactamase positive HI-AOM cases decreased in Jewish children.

HUMAN BOCAVIRUS AND HUMAN METAPNEUMOVIRUS INFECTION AMONG CHILDREN HOSPITALIZED FOR COMMUNITY-ACQUIRED PNEUMONIA IN A TROPICAL REGION

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Background: Human bocavirus (HBoV) and human metapneumovirus (HMPV) are new human-pathogenic viruses associated with respiratory disease in children. Limited information is available on HBoV and HMPV acute infection among children hospitalized for community-acquired pneumonia (CAP) in tropical regions.

Methods: During a 21-month period, a prospective study was carried out in Salvador, Northeast Brazil. In total, 277 children below 5 years of age hospitalized for CAP were enrolled for virus studies. HBoV DNA and HMPV RNA were detected in nasopharyngeal aspirates (NPA) by quantitative polymerase chain reaction (PCR) and reverse-transcription (RT)-PCR, respectively. For a more reliable HBoV diagnosis, paired serum samples were tested by IgG and IgM enzyme immuno assays (EIA) using recombinant HBoV VP2 virus-like particles.

Results: HBoV DNA and HMPV RNA were detected in NPAs of 62 (23.1%) and 11 (4.1%) of 268 children, respectively. Acute HBoV infection was serologically diagnosed (i.e. positive IgM or increase in IgG) in 31 (11.4%) of 273 patients; 76% of the children with a serodiagnosis had HBoV DNA in NPA, 68% of whom with a high DNA load. Of all 26 children with a high load of HBoV DNA in NPA 16 (62%) were serodiagnoses. The difference in age between children with acute HBoV serodiagnoses and HMPV RNA was significant (19.3 ± 9.4 vs. 11.5 ± 11.4 months, $P=0.04$).

Conclusions: Both HBoV and HMPV infections were often detected in children with CAP. HBoV was more frequent among older and HMPV among younger children. Serology is important for accurate diagnosis of HBoV primary infections.

ANTIBIOTICS FOR ACUTE OTITIS MEDIA IN CHILDREN: A SYSTEMATIC REVIEW OF CLINICAL PRACTICE GUIDELINES IN 27 COUNTRIES

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Background and aims: Acute otitis media (AOM) in children is nowadays often not treated with antibiotics (ABX). Do clinical practice guidelines in different countries recommend observation (“watchful waiting”) of AOM?

Methods: National guidelines for AOM were reviewed systematically.

Results: Data from 27 countries, with over 52% of the world population, were compiled. National recommendations vary from no routine use of antibiotics (“watchful waiting”) to 30 doses or more of antibiotics to all children with AOM. ABX are optional at all ages in Brazil, Hungary, Japan, New Zealand, Poland, the UK. ABX are mandatory at age < 6 months, optional >6 months in Denmark, Germany, the Netherlands. ABX are mandatory < 12 months, optional >12 months in Australia, Italy, Norway, the USA. ABX are mandatory < 18 months or longer in Canada, China, Colombia, Cuba, Finland, France, Hong Kong, Iceland, India, Saudi Arabia, Singapore, South Africa, Spain, Sweden.

Conclusions: The physicians' and families' compliance to the new guidelines and the incidence of severe complications to AOM (e.g. mastoiditis) should be carefully monitored in countries with a watchful waiting policy. Guidelines should be more proactive if there is an increase of severe complications. If there is no such increase, a watchful waiting policy ought to be considered in other high income countries. There are insufficient data to support such a policy in middle and low income countries.

A COMPARISON OF SEVERE RESPIRATORY SYNCYTIAL VIRUS RISK FACTORS BETWEEN PREMATURE AND TERM INFANTS HOSPITALIZED FOR SEVERE RSV IN RUSSIA

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Background: RSV is a leading cause of lower respiratory tract infections (LRTI) in infants. Prematurity and other demographic and environmental factors increase the risk for the development of severe RSV infection.

Objective: To describe differences in risk and protective factors between premature (≤ 35 wGA) and term infants hospitalized for RSV in the Russian Federation during the 2008-09 RSV season.

Methods: Infants ≤ 2 years admitted to hospital for a LRTI at participating sites in Moscow, St. Petersburg and Tomsk were tested for RSV. Patient data including RSV risk and protective factors were captured at admission. Differences in these factors between premature and term patients were compared.

Results: 519 LRTI hospitalizations were included in the study; 197 had confirmed RSV (182 terms versus 15 premature infants). Of all hospitalizations, 51.7% of premature infants versus 37.1% of term infants had confirmed RSV ($p=0.118$). Compared to term infants, premature infants were more likely to be of a multiple gestation ($p < 0.001$); have more siblings ($p=0.013$); and have more rooms in their home ($p=0.016$). Premature infants were less likely to be breastfed ($p < 0.001$); and have older mothers ($p=0.050$).

Conclusion: Compared to term infants, RSV was a more prevalent cause for LRTI hospitalization in premature infants. Of infants hospitalized for RSV, premature infants were more likely to be exposed to additional risk factors for severe RSV. These findings suggest premature infants may have a higher likelihood to be exposed to other risks for severe RSV than term infants.

ADMISSION DIAGNOSES OF CHILDREN 0-16 YEARS OF AGE HOSPITALIZED FOR INFLUENZA-RELATED ILLNESSES

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Background and aims: Influenza is an important cause of hospitalization in children, among whom the admission rates are clearly highest among the youngest ones. We sought to determine the main admission diagnoses of influenza-positive children in different age groups.

Methods: This retrospective study comprised all influenza-related hospitalizations of children 0-16 years of age at Turku University Hospital, Finland, during a 16-year period of 1988-2004. To find out the primary admission diagnoses, the medical records of all children with a positive viral culture, antigen detection, or rapid test for influenza were carefully reviewed.

Results: Of a total of 401 influenza-positive children hospitalized during the study period, 88 (22%) were younger than 6 months, 169 (42%) were 0.5- < 3 years, and 144 (36%) were 3-16 years of age.

28% of all children had an underlying medical condition. Among children < 6 months of age, the primary reasons for admission were sepsis-like illness (52%), wheezing (15%), and dehydration (9%). In children aged 0.5- < 3 years, the most frequent diagnoses were pneumonia (18%), febrile convulsion (18%), and asthma/wheezing (14%). Children 3-16 years of age were primarily admitted for pneumonia (15%), sepsis-like illness (14%), dehydration (12%), or febrile convulsion (10%).

Conclusions: Our study demonstrates that the reasons for hospitalization of children with influenza vary substantially between different age groups of children. The leading role of sepsis-like illness in infants younger than 6 months of age is of great clinical importance because it usually results in sepsis work-up and initiation of unnecessary antibiotic therapy.

CORRELATION OF VIRAL LOAD OF RESPIRATORY PATHOGENS AND CO-INFECTIONS WITH DISEASE SEVERITY IN CHILDREN HOSPITALIZED FOR LOWER RESPIRATORY TRACT INFECTION

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This prospective clinical study was performed to evaluate the correlation of viral load as well as co-infections with disease severity in hospitalized children with lower respiratory tract infections (LRTIs). To determine viral and bacterial load of respiratory pathogens we performed multiplex real-time polymerase chain reaction and semiquantitative bacterial cultures on nasopharyngeal aspirates (NPA). The specimens and clinical data were obtained from 404 children between 0-16 years old during the period 2006-2008. Twohundredfourtyfour (60%) children were hospitalized for lower respiratory tract infection with acute virus-induced wheezing and 160 (40%) for pneumonia. In the first NPA, viruses were identified in 315 (78%) of the 404 samples and bacteria in 198 (63,3%) of 311 samples. The most frequently detected viruses were RSV in 160 (51%), rhinovirus in 87 (28%) and adenovirus and human bocavirus in 28 (9%) cases, respectively. Two or more viruses were found in 67 cases (17%). Viral load was inversely related to CRP in RSV infections, whereas a positive correlation was observed in adenovirus infections. Duration of hospitalization was significantly longer in RSV single infections compared to rhinovirus single infections whereas in the latter, leucocytosis and use of systemic steroids was more common. In RSV co-infections the presence of fever, leucocytosis, and the use of antibiotics was significantly more frequent. In RSV and rhinovirus single infections *Haemophilus influenzae* and in RSV co-infections *Moraxella catarrhalis* positive cultures dominated. Viral and bacterial co-infections contribute to disease severity in children with LRTIs, whereas viral load seems to be a less important marker.

RHINOVIRUS INFECTION BEFORE 3 MONTHS OF AGE

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Background and aims: Rhinovirus is a common cause of respiratory infections in children, but few data are available of very early rhinovirus infections in the community setting. We aimed to study the frequency and risk factors for rhinovirus infection in infants younger than 3 months of age.

Methods: 436 children of mothers recruited from maternity clinics were followed from birth to 3 months of age in a prospective cohort study. Whenever the child had symptoms of respiratory infection, a nasal swab was obtained at the study clinic. Nasal swab specimens were analyzed using a multiplex real-time RT-PCR for rhinoviruses, enteroviruses, and respiratory syncytial virus. Positive amplicons were identified as rhinoviruses, enteroviruses, or respiratory syncytial virus based on the melting temperatures. Background data was obtained by structured questionnaires.

Results: Symptomatic rhinovirus infection was detected by RT-PCR in 65 of 436 infants (15%). As rhinoviruses circulate actively in the autumn, early infections were more common in infants born in the summer (22%) or autumn (20%) than in those born in the winter (8%) or spring (6%) ($P < 0.001$). The risk of early rhinovirus infection was increased in families with 2 or more children ($P = 0.01$), in those with only basic educational level of mother ($P = 0.007$), and in those with less than average income ($P = 0.03$).

Conclusions: Symptomatic rhinovirus infections are frequent already before the age of 3 months. Risk factors for early rhinovirus infection include birth in the summer or autumn, siblings in the family, and lower than average socioeconomic status of the family.

CLINICAL AND EPIDEMIOLOGIC CHARACTERISTICS OF HOSPITALISED CHILDREN WITH CONFIRMED PERTUSSIS DIAGNOSIS AT THE HOSPITAL INFANTIL JOANA DE GUSMÃO, BRAZIL

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Background: Despite massive utilization of pertussis vaccines, pertussis still remains as a significant cause of morbidity and mortality among children, specially infants. The study aim was to analyze the clinical and epidemiologic characteristics of hospitalized children with confirmed pertussis disease.

Methods: A retrospective review was performed of all patients records with a pertussis diagnosis (International Classification of Disease, code A37) hospitalized at Hospital Infantil Joana de Gusmão (HIJG), Florianópolis, Santa Catarina State, Brazil, from January 1st 2003 to December 31st 2008.

Results: Forty-six patients with confirmed pertussis diagnosis were identified, one (2003), two (2004), five (2005), seven (2006), 12 (2007) and 19 (2008), of whom 42 (91,3%) were < 6 months of age. A predominance of cases was observed in summer (41,3%) and 24 patients (52,1%) had history of household contact carrier of cough. Twenty-one patients (45,7%) were unvaccinated (14 patients were < 2 months of age). Only four patients (8,7%) were fully vaccinated (3 or more doses). Symptoms included cyanosis (89,9%), paroxysmal cough (73,9%), post-tussive vomiting (30,4%), whoop (26%) and apnea episodes (17,3%). The mean duration of cough was 13,08 days. A total of 15 patients (33,4%) presented complications and nine patients (19,6%) required admission to an intensive care unit.

Conclusions: Infants represent the major of hospitalized pertussis patients, most of whom are < 6 months of age and have had no or less than three doses of vaccine. Frequently the presence of a household presenting cough was observed.

IS ROUTINE IMMUNOLOGICAL SCREENING BENEFICIAL IN CHILDREN WITH COMMUNITY-ACQUIRED PNEUMONIA?

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Background: Severe community-acquired pneumonia (CAP) can affect previously well children. Virulence of pathogen, early appropriate treatment and immunocompetency have impact on disease outcome.

Materials and methods: Prospective consecutive follow-up study included children with clinically and radiologically confirmed CAP, hospitalized since IX/2006 to X/2009 at the Department of Paediatrics of Motol University Hospital. Apart from routine laboratory examination, serum levels of IgG, IgA, IgM, IgE antibodies (Ab), complement compounds and specific post-vaccination Ab levels were determined.

Results: 254 cases of CAP (131 boys, 123 girls, age median 4.5 years) were involved and treated according to standard hospital protocol. The outcome was favourable with no death, 9 patients developed necrotizing pneumonia, 8 needed chest drainage, 8 assisted ventilation, 4 thoracoscopy and decortication. 34 children presented with IgA levels under age-specific limit, 6 of them having IgA deficiency, 33 presented with lower IgG levels, anti-tetanus Ab were lower in 12 patients. Atopy was confirmed in 111 cases (43.7%). Surprisingly X-linked agammaglobulinaemia was diagnosed in 2 boys (11M and 21M) with proven mutations in Bruton's tyrosinkinase genes. In both children CAP was the first symptom of their immunodeficiency. Clinical course in the younger boy was uncomplicated, the older boy after initial successful treatment of pneumonia experienced pseudomonas sepsis.

Conclusion: Our experience advocates performance of basic immunological evaluation of previously well children hospitalized with CAP. It may contribute to disclosure of immunodeficient patients and optimization of their treatment strategy.

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VIRAL PATHOGENS ASSOCIATED WITH ACUTE RESPIRATORY INFECTION IN VIETNAMESE CHILDREN

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Background: Viral pathogens are globally considered as major causes of acute respiratory tract infections (ARI) which are responsible for high morbidity and mortality among children and adults. However, their role in the developing countries like Vietnam has not been well characterized yet.

Methods: All children admitted to KHGH with ARI from the catchment area, Nha-Trang were enrolled in the study. The study was conducted from February 2007 through July 2009. Clinical data, chest Xray, laboratory data and nasopharyngeal (NP) samples were collected. Four multiplex polymerase chain reaction (PCR) assays were performed to detect 13 respiratory viruses in each NP sample.

Results: A total of 1766 were enrolled in the study. The majority of children hospitalized for ARI (85%) were less than 3 years of age and 23-28% had radiological confirmed pneumonia. Respiratory viruses were detected in 60-69% of the cases with 10% multiple viral infection. The commonest was Rhinovirus(23-28%) followed by respiratory syncytial virus (RSV)(20-23%), influenza-A virus(13-15%), Adenovirus(5%), human metapneumovirus (hMPV)(5%), parainfluenza virus type 3 (PIV3)(4%) and human bocavirus (HBoV)(2%) infections. Significant association were found between PIV3 with LRTI ($p=0.012$) and RSV with bronchiolitis ($p=< 0.001$) cases. Rhinovirus-associated ARI was seen throughout the year however seasonal patterns were observed for Influenza-A (cool dry months) and RSV (hot wet months).

Conclusions: Our study showed that rhinoviruses, RSV and influenza-A viruses are leading causes of ARI among hospitalized children while the identification of hMPV and HBoV suggest that these recently identified pathogens may play an important role in Vietnam.

CERVICOFACIAL LYMPHADENITIS CAUSED BY MYCOBACTERIUM LENTIFLAVUM**F. Baquero-Artigao¹, N. Marin¹, G. Lopez², M.J. Garcia-Miguel¹, F. del Castillo¹**¹*Paediatric Infectious Diseases, ²Microbiology Department, Hospital Universitario La Paz, Madrid, Spain*

Aims: Nontuberculous mycobacterial lymphadenitis is most often caused by *Mycobacterium avium* whilst *Mycobacterium lentiflavum* is considered a rare pathogen. We describe the epidemiological and clinical features associated with *M. lentiflavum* cervicofacial lymphadenitis in children.

Methods: Retrospective review of children with culture-confirmed *M. lentiflavum* lymphadenitis during a ten-year period (2000-2009). Data regarding clinical presentation, possible environmental exposure, mycobacterial resistance and outcome were studied.

Results: Seven cases of *M. lentiflavum* lymphadenitis were identified. The median age was 23.4 months, 5 were girls. Median time to diagnosis was 2.5 weeks. Spontaneous drainage was observed in 4 children. No child was immunocompromised. Submandibular (5 cases), preauricular (4), cervical (1) and cheek (1) nodes were affected. Involvement of multiple lymph nodes was observed in 4 patients. Three cases had a history of contact with climatized-swimming-pool. Tuberculin skin test was negative in 5 children and gave an induration between 5 and 10 mm in 2 cases. Histologically, 4 patients presents necrotizing granulomas, 2 noncaseating granulomas and 1 necrotic tissue. Acid-fast smears in biopsy samples were positive in 3 cases. Surgery was performed in all cases, with complete excision (6 cases) or drainage (1), 5 children received adjunctive antimycobacterial therapy. Resistance to commonly used antimycobacterial agents was studied in 3 isolates and all were resistant to 3 or more drugs. No recurrences were observed.

Conclusions: *M. lentiflavum* is an occasional pathogen in cervicofacial lymphadenitis in children. Treatment is often difficult due to the high incidence of multiple lymph node involvement, spontaneous drainage, and antimycobacterial resistance rates.

INTERFERON GAMMA RELEASE ASSAY DETECTS MORE NUMBER OF CHILDHOOD TUBERCULOSIS CASES THAN TUBERCULIN SKIN TEST

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Background and aims: Diagnosis of tuberculosis (TB) in children is still a challenge to the clinician, since the existing diagnostic tools are not sensitive enough. Hence, search for additional or alternative diagnostic methods for TB in children continues. Recently introduced QuantiFERON TB-Gold in tube (QFT-IT) assay seems to have brought significant advancement in diagnosis of TB infection. However, data on its role in active TB diagnosis among children is still limited. In this study, we estimated the sensitivity of QFT-IT and compared it with Tuberculin skin test (TST).

Methodology: This study was carried out in Chennai city, a TB endemic area. A total of 50 clinically suspected childhood TB cases were recruited. The cut-off point for TST was considered as 10mm induration. QFT-IT results were analyzed as per manufacture's instructions.

Results: In the 50 clinically suspected cases, active TB was confirmed in 15 subjects and the remaining 35 were classified as possible TB cases. In the 15 confirmed TB cases, QFT-IT and TST were positive in 12 (80%) and 9 (60%) subjects, respectively. One confirmed TB case was positive only for TST and 4 TB cases were positive only for QFT-IT. The combination of QFT-IT and TST detected 13 (87%) cases. Among the possible TB cases, QFT-IT and TST were positive in 12 (34%) and 10 (29%) subjects respectively.

Conclusions: Our study results suggest that QFT-IT is a sensitive method for childhood TB diagnosis. Along with TST, QFT-IT will improve the diagnostic potential of the existing tools in childhood TB.

SELECTED RD1 PEPTIDES FOR ACTIVE TUBERCULOSIS DIAGNOSIS: COMPARISON WITH A COMMERCIAL INTERFERON- γ RELEASE ASSAY AND TUBERCULIN SKIN TEST IN CHILDREN

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Background and aims: Differences in the pathophysiology and clinical presentation of tuberculosis (TB) in children make diagnosis more challenging than in adults and definitions of latent TB infection and active tuberculosis are less clear cut. In an effort to develop more accurate tools for immunological diagnosis of TB several studies have been performed to evaluate immunological response to early secreted antigenic target 6 (ESAT-6) and culture filtrate 10 (CFP-10) proteins. The aim of our study is to evaluate the performance of an interferon- γ whole blood enzyme-linked assay, using selected ESAT-6 and CFP 10 peptides that appears specific for active TB in children by comparing its result with the tuberculin skin test (TST) and QuantiFERON-TB Gold (QFT-G) and exploring possible discordances.

Methods: We carried out a prospective study in 50 children with a high risk of TB infection. All the children have been simultaneously tested with TST, QFT-G and RD1 selected peptides.

Results: The overall agreement between QFT-G and RD1 selected peptides was good ($k=0,85$), while the overall agreement between TST and RD1 selected peptides was low ($k=0,15$). The RD1 selected peptides were positive in 10 children (55.6 %) diagnosed with TB disease and the test became negative in all 10 children after 66 (range 45-95) days of therapy. The test was negative in all children with latent TB infection.

Conclusions: This assay appear more specific for active TB diagnosis than QFT-G, and thus it may represent a complementary tool to rule-out active disease.

EVALUATION OF QUANTITATIVE INTERFERON- γ RESPONSES FOR THE FOLLOW UP OF CHILDREN EXPOSED TO *MYCOBACTERIUM TUBERCULOSIS*

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Background and aims: Interferon- γ release assays (IGRAs) have been recently developed for the diagnosis of tuberculosis (TB) infection. The aim of the study is to evaluate the use of a commercial IGRA [QuantiFERON-TB Gold *In-Tube* (QFT-IT)] in the follow-up of children exposed to *Mycobacterium tuberculosis*.

Methods: A prospective study in 170 children at risk for TB infection was carried out. All children were tested with QFT-IT and tuberculin skin test (TST).

Results: One hundred and six children (62.4%) had taken therapy for active TB or latent tuberculosis infection (LTBI) and had undergone an end-of-therapy control with QFT-IT. The QFT-IT became negative in 9/56 (16.1%) children. Neither the age ($< \geq 48$ months) nor the diagnosis (active or LTBI) seem to be a risk factor for the results becoming negative. Quantitative interferon- γ (IFN- γ) values did not decline significantly at the end of the therapy. On the other hand, a lower baseline IFN- γ level was more often associated with values of QFT-IT becoming negative at the end of the therapy ($p=0.047$). Moreover, the medians of the baseline IFN- γ values resulted significantly different between the children with active TB [6.75 (3.67-10.00) UI/ml] and those with LTBI [3.25 (1.00-7.98) UI/ml] ($p=0.022$).

Conclusions: At present, on the basis of our results as well as from published data, we believe that QFT-IT can have an important role for the follow-up of children at risk of TB infection. The quantitative response of QFT-IT rather than the qualitative results turns out to be important.

RECOGNITION OF DISSEMINATED BCG DISEASE IN IMMUNE COMPROMISED INFANTS**H. Bruell¹, P. Gavin¹, R. Watson², K. Butler¹***¹Infectious Diseases, ²Dermatology, Our Ladies Children's Hospital Crumlin, Dublin, Ireland*

In Ireland, neonatal BCG is part of the national immunisation schedule. We present a case series of 4 infants; 3 with disseminated BCG as presentation of severe combined immune deficiency & 1 leukaemia. In all recognition of characteristic skin lesions facilitated rapid diagnosis.

Case 1: Twin 1, born at 33 weeks gestation, with a history of recurrent cough and failure to thrive, presented at 7/12 with respiratory symptoms, diarrhea and vomiting. He had a few non-specific papular skin lesions, biopsy of which rapidly yielded AFB and resulted in diagnosis of SCIDS. BCG was also recovered from bone marrow.

Case 2: Presented at 8/52 with suppurative axillary lymphadenopathy, severe failure to thrive, hepatosplenomegaly and similar papular rash. Bone marrow biopsy yielded sterile granuloma. BCG was isolated from lymph node tissue and a presumptive diagnosis of disseminated disease was made. A diagnosis of a severe combined immune deficiency was subsequently confirmed.

Case 3: Presented age 4/12 with severe failure to thrive and acute RSV infection. Skin biopsy of similar papular lesion rapidly confirmed disseminated BCG infection and led to a diagnosis of SCIDS.

Case 4: Was diagnosed with AML age 7/52 and she developed disseminated BCG, also diagnosed on biopsy of small papulo-nodular skin lesions 2 month into treatment.

These cases not only highlight the problem of neonatal BCG vaccination given to infants with underlying severe immune compromise but illustrate the clinical utility of skin lesion recognition, biopsy of which can facilitate rapid diagnosis.

CONTACT TRACING BASED ON INTERFERON-GAMMA RELEASE ASSAYS (IGRAS) FOR IMMUNODEFICIENT CHILDREN AFTER EXPOSURE TO A CONTAGIOUS TB CASE

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Background: Tuberculin skin testing (TST) is of limited usefulness for latent tuberculosis infection (LTBI) identification in immunocompromised patients; IGRAs might improve the specificity and the sensitivity of LTBI diagnosis in these patients.

Aim: To describe a contact tracing based on IGRAs in immunodeficient children.

Methods: In November 2009 the mother of a Pakistan child with malignant osteopetrosis was diagnosed with smear-positive, drug sensitive, pulmonary TB. During 8 weeks before TB diagnosis she attended the pediatric hemo-oncology ward and the dayhospital. People sharing the same airspace with the index case for more than eight hours were enrolled in the contact tracing with QuantiFERON-Gold TB (QFT) and T-Spot testing. TST and chest radiographs (CXR) were also done.

Results: 45 contacts were evaluated; 18 children and 27 adults. Children (11 males) had a median age of 7.4 years (range 1 - 18), the median total lymphocyte count was 880 cells/mm³ (range 40 - 8820). QFT resulted negative for 15 and indeterminate for 3 children; T-Spot was negative for 12 indeterminate for 3 and positive for 2 children (1 failed). The total agreement between IGRAs was 61%; 2 children with indeterminate TSpot were negative on QFT. All CXR were negative for primary TB as were the 5 TST done. Contacts were started on isoniazid while waiting for repeated IGRAs and TST two months apart.

Conclusions: IGRAs may represent a valuable tool to diagnose LTBI in immunodeficient children. In our study, T-Spot was more sensitive than QFT to identify LTBI among TB-exposed children with immunodeficiencies.

ROLE OF SURGERY IN MULTI-DRUG RESISTANT GANGLIONAR TUBERCULOSIS

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Background and aims: The increase of multi drug-resistant tuberculosis (MDR-TB) and extensively drug-resistant (XDR-TB) has become a worldwide problem. Its approach must be as wide as possible, being medical and surgical treatment susceptible to be used in order to eradicate the presence of Mycobacteria. We report a case of a child affected by ganglionar MDR-TB treated successfully by medical and surgical approach.

Methods: Retrospective review of clinical history.

Report: A 2 year-old, previously healthy, male patient was referred to our clinic with a 2 months history of bilateral inguinal adenitis without any other symptoms. Familial and personal antecedents: Born in Spain, parents from Maroc. Travel for first time to Maroc 2 months ago, where he was circumcised. Physical examination showed hard and no painful inguinal lymph nodes, with no inflammatory signs and up to 3.5 cm of diameter. Thorax X-ray was normal. Neck, abdomen and groin ultrasound scan revealed multiple inguinal and iliac lymphadenopathies. Mantoux 8 mm, positive QuantiFeron®. Excisional biopsy of one side showed caseum granuloma. Microbiological study of the specimen was positive for *Mycobacterium tuberculosis* resistant to isoniazid, rifampicin, pyrazinamide, ethambutol, streptomycin, ethionamide and rifabutin. MDR-TB treatment was started (linezolid, amoxicilina, amikacin, cycloserine and levofloxacin). After 6 weeks, ganglia of the other side were still pathological, so surgery was undergone, still revealing presence of Mycobacteria.

Conclusions: In selected cases of TB, medical treatment may be insufficient to eradicate Mycobacteria from their reservoir, so surgery may be beneficial and has to be strongly considered.

REVERSION AND CONVERSION OF M. TUBERCULOSIS IFN- γ ELISPOT ASSAY RESULTS DURING ANTI-TUBERCULOUS TREATMENT IN HIV-INFECTED CHILDREN

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Background: Recent interest has focused on the potential use of serial interferon gamma (IFN- γ) release assay (IGRA) measurements to assess the response to anti-tuberculous treatment. The kinetics of IFN- γ responses to Mycobacterium tuberculosis (MTB)-antigens in HIV-infected children during treatment have not been investigated.

Methods: IFN- γ responses to the MTB-antigens, ESAT-6, CFP-10 and PPD were measured by an IFN- γ -ELISpot assay at presentation and at one, two and six months after starting anti-tuberculous treatment in HIV-infected children with definite or probable TB.

Results: Of 102 children with suspected TB, 22 (21%) had definite TB and 24 (23%) probable TB. In children with definite or probable TB in whom the IFN- γ -ELISpot assay result was positive at presentation, anti-tuberculous treatment was accompanied by a significant decrease in both the magnitude of the IFN- γ response to MTB-specific antigens (ESAT-6 median 110 SFCs/1,000,000 PBMC (IQR 65-305) at presentation vs. 15 (10-115) at six months, $p=0.04$; CFP-10 177 (48-508) vs. 20 (5-165), $p=0.004$) and in the proportion of children with a positive IFN- γ -ELISpot assay result (ESAT-6 15/0 vs 5/11, $p=0.0002$, CFP-10 22/0 vs 8/17, $p=0.0001$). However almost half of the children had a positive IFN- γ -ELISpot assay result after six months of anti-tuberculous treatment. In addition, some children with negative results at presentation became positive during anti-tuberculous treatment.

Conclusions: The kinetics of IFN- γ responses to MTB-antigens during anti-tuberculous treatment are not consistent. This suggests that serial IFN- γ -ELISpot measurements have limited clinical utility in assessing a response to anti-tuberculous treatment in HIV-infected children.

INTERFERON-GAMMA RELEASE ASSAYS IN THE EVALUATION OF CHILDREN WITH TUBERCULOSIS INFECTION IN A COUNTRY WITH HIGH BCG COVERAGE RATE

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Background and aims: IFN-gamma release assays for diagnosis of *Mycobacterium tuberculosis* infection have been used in different countries, but their performance is still not well established and may vary according to exposure to other mycobacteria and prevalence of immunosuppressive conditions.

Methods: We retrospectively evaluated the use of T-SPOT.TB in a pediatric tertiary care center with a high prevalence of immune compromising conditions in Sao Paulo, Brazil. All patients had also a tuberculin skin test (TST) performed. All but one had previous BCG vaccination.

Results: From June 2007 through December 2009, 51 patients (F/M:31/20) with median age of 11.0y (Q1-Q3: 4.4-13.1) who were under investigation for tuberculosis disease (90.2%) or infection (9.8%) were included. Twenty-two children (43.1%) were immunocompromised. Agreement between TST and T-SPOT.TB results occurred in 36 children (70.6%), 11 with positive and 25 with negative results. T-SPOT.TB produced an indeterminate result in 5 children (9.8%), three of whom had severe lymphopenia; all 5 children had negative TST results. Disagreement between tests occurred in 10 children (19.6%): 1 patient with monoarthritis with ANA titres of 1/1280 had negative T-SPOT.TB and positive TST; among the other 9 who had a positive T-SPOT.TB and TST < 10mm, 2 had leukemia, 2 were in use of immunosuppressors and the other 5 had a clear tuberculosis exposure history and/or symptoms highly suggestive of tuberculosis.

Conclusions: T-SPOT.TB may be more sensitive than TST and may prove helpful in deciding when to start tuberculosis therapy, especially in children with immune deficiency conditions.

MILIARY TUBERCULOSIS IN CHILDREN: ABOUT 20 CASES**N. Elhafidi, I. Zouizouo, F. Benbrahim, C. Mahraoui***Pediatric Infectious Unit, Children University Hospital, Rabat, Morocco*

Introduction: Our study aims to understand the epidemiological, clinical, radiological and evolution features of miliary tuberculosis in children hospitalized in the infectious unit of the Children's Hospital in Rabat.

Materials and methods: This is a retrospective study during from January 1998 to December 2008. 20 children were hospitalized for miliary tuberculosis and in whom the diagnosis was made of anamnestic, clinical and radiological arguments.

Results: The average age is 2 years 2 months. The boys represents 60% of cases (12 patients), the sex-ratio 1.5. All patients received BCG at birth. 55% patients have massive tuberculosis contagion. 13 patients are malnourished. 90% of cases developed a cough, 8 patients presented dyspnea. On chest radiography, all cases showed micronodular opacities (100%). The bacilloscopy was negative in 15 cases (75%), and positive in 5 cases (25%). Five patients have associated ganglionic localisation (40%). 75% of patients were treated according (2 SRHZ / 7 HR). The evolution was marked by recovery in 12 cases, relapses in 2 cases . Evolution is not known in 8 patients.

Discussion: The miliary tuberculosis is a serious disease whose socio-economic low, malnutrition are contributing factors. The immunity was not explored in most patients of this series. 35% of patients have extrapulmonary-localisation. All cases have been cured. The non-observance of treatment is responsible of relapse and may cause anti bacillary agents resistance.

Conclusion: Miliary tuberculosis is a serious disease, a diagnostic and therapeutic

emergency. Evolution is often marked by recovery under treatment by well adapted antibacillary agents.

MULTIFOCAL TUBERCULOSIS: ABOUT FOUR CASES**N. Elhafidi**¹, S. Mkadmi², F. Benbrahim¹, M. Chafiq¹¹*Children Hospital,* ²*Children's University Hospital, Rabat, Morocco*

Introduction: Multifocal tuberculosis is a serious form of tuberculosis, it is classified in Category I. It is confined to the immunosuppressed mainly the HIV-infected subject. However, multifocal tuberculosis may occur in the absence of risk factors as is the case in our series.

We report four cases admitted in the PI unit of the Rabat Children's Hospital in Morocco.

Cases history: Our patients are aged respectively six, seven, eight months and thirteen years. We report two cases of tuberculosis of pulmonary and peritoneal localization, a case of tuberculosis of pleural and peritoneal localization and one case of pulmonary and ganglionic localization.

All patients are immunocompetent.

The diagnosis of multifocal is retained on anamnestic, clinical, radiological, and histological data.

Three cases are treated with corticosteroid treatment and antibiary and one case treated by antibiary only.

Conclusion: Multifocal tuberculosis is rare and may seriously affect the patient's survival prognosis. It often requires extensive and long treatment.

TUBERCULOSIS INFECTION IN SPANISH PAEDIATRIC POPULATION: HOSPITAL ADMISSIONS OVER AN ELEVEN YEAR PERIOD (1997-2007)

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Background and aims: To estimate the burden of hospitalizations due to tuberculosis in Spanish paediatric population (children up to 14 years old) during an eleven-year period (January 1st, 1997 through December 31st, 2007).

Methods: Data of hospital discharges in Spanish hospitals due to tuberculosis were obtained from the national surveillance system for hospital data (Conjunto Mínimo Básico de Datos, CMBD) maintained by the Ministry of Health and covering more than 98% of Spanish hospitals. All hospital discharges for tuberculosis using the 9th International Classification of Diseases (ICD: 010-018), in any listed diagnosis, were selected. The annual incidence of hospital admissions, average length of hospitalization, mortality and case-fatality rate were calculated by using municipal data of population as denominators.

Results: A total of 6289 hospitalizations due to tuberculosis infections in children up to 14 years old were reported during the study period. The mean age of the patients was 5.2 years old and the average length of hospital stay was 9.3 days. Annual hospitalization rate was 9.5 cases per 100,000 children.

Eighteen deaths were reported among these hospitalized children. Mortality and case-fatality rates were 0.03 per 100,000 children and 0.3%, respectively. Hospitalization incidence and mortality rate decreased significant with age and had their highest values in children up to 4 years old (16.7 and 0.05 per 100,000 children, respectively).

Conclusions: Although deaths for tuberculosis are exceptional in developed countries, hospital burden of tuberculosis infection is still important in paediatric population in Spain, especially in the youngest age group.

MYCOBACTERIUM TUBERCULOSIS SECRETES AN IMMUNOSUPPRESSIVE FACTOR THAT INHIBITS T-CELL ACTIVATION

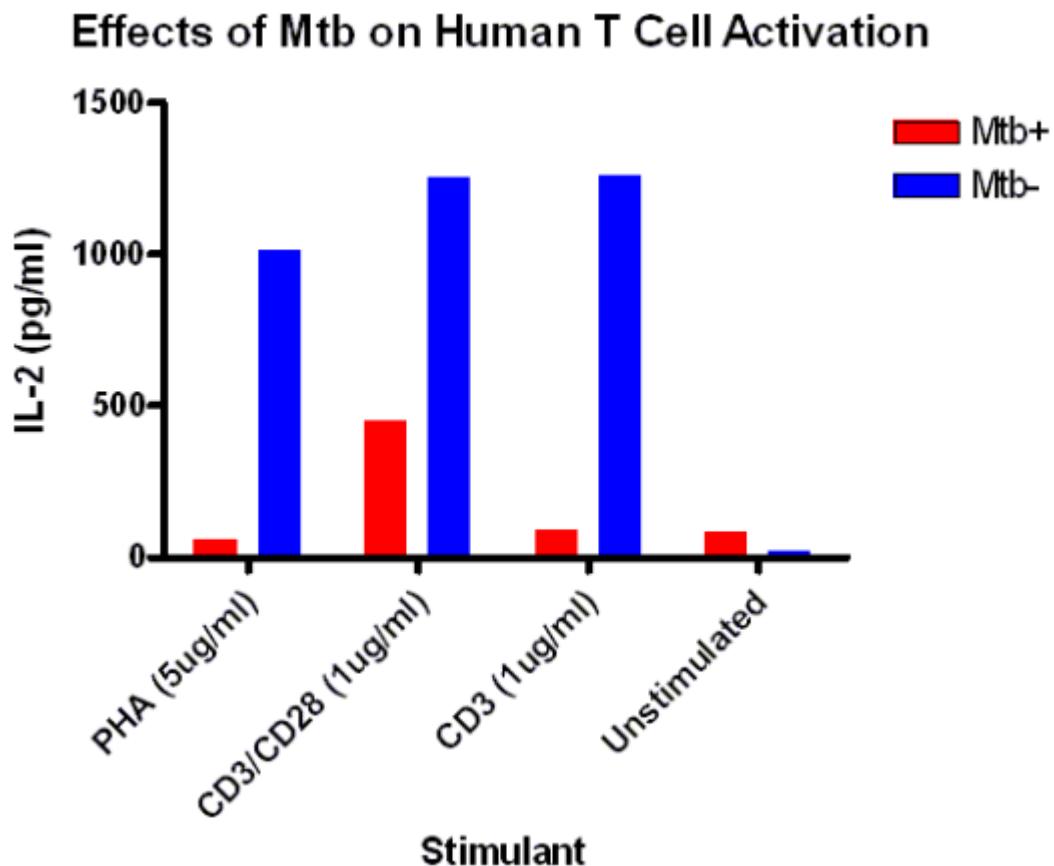
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Background and aims: T-cells play an essential role in controlling infection by *Mycobacterium tuberculosis* (*Mtb*). For example, HIV patients with low levels of functional T-cells have increased susceptibility to tuberculosis (TB). Patients with disseminated forms of TB, especially children, frequently exhibit cutaneous anergy, a false-negative tuberculin skin test, suggesting they may have an acquired defect in T-cell responsiveness.

We postulate that *Mtb* may release factors that inhibit T-cell activation, resulting in anergy and failure to contain the infection. We tested this hypothesis by examining T-cell activation after infection of human cells with *Mtb*.

Methods and results: We studied the effect of live *Mtb* and *Mtb* secreted factors on T-cell activation using healthy peripheral blood mononuclear cells stimulated with the antigen-nonspecific mitogen PHA, anti-CD3, and anti-CD3/anti-CD28. We found that exposure to live *Mtb* impaired IL-2 production, a measure of T-cell activation, in response to all three stimulatory proteins ($p < 0.001$) (**Figure**). We also observed that *Mtb* secreted factors suppress IL-2 production in response to PHA stimulation ($p < 0.02$), although less than with live *Mtb*, suggesting a dose-dependent secreted factor is partially responsible for the observed immunosuppression.



[Effects of *Mtb* on Human T Cell Activation]

Conclusions: Our results demonstrate that human blood cells exposed to live *Mtb* show impaired T-cell activation. Identification of the factor(s) responsible for this phenomenon may reveal a novel immunosuppressive mechanism of *Mtb*.

STEP BY STEP - TREATING MYCOBACTERIAL DISEASE IN A WISKOTT-ALDRICH PATIENT

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Background and aims: Wiskott-Aldrich syndrome is a rare X-linked recessive disease characterized by eczema, thrombocytopenia and immune deficiency. Immunoglobulin (Ig) M levels are typically low, IgA and IgE are elevated and IgG can be reduced or elevated. These patients present an increased susceptibility to infections, autoimmune diseases and malignancy.

Methods: The authors present a case report of an eleven year old boy with Wiskott - Aldrich Syndrome, manifested by severe thrombocytopenia, partially responsive to polivalent IVIg and awaiting bone marrow transplant.

Results: Admitted with a history of cough for the past 3 weeks and fever for the last 3 days. He had been diagnosed with right upper lobe pneumonia in the previous month and treated with amoxicillin. The chest x-ray showed atelectasis in the same location with compression of the right bronchium, and mediastinal enlargement. The pulmonary CT scan revealed mediastinal and mesenteric adenomegalies, some with calcifications (max. 34 mm). The tuberculin skin test was positive. Cultures of gastric aspirate specimens and sputum secretions were positive for *Mycobacterium tuberculosis* complex, susceptible to pyrazinamide, rifampicin, isoniazid and ethambutol. Quadruple therapy was initiated.

Seven months later he presented with an anterior mediastinal mass with extension to the neck. The CT scan was suggestive of lymphoma. The needle biopsy of the cervical mass revealed necrosis. Lymphoma was excluded.

Conclusions: The authors wonder about the duration of therapy, due to the urgency of bone marrow transplant, since there is a high risk of lymphoproliferative disease.

INTRAFAMILIAL CLUSTER OF PULMONARY TUBERCULOSIS DUE TO *MYCOBACTERIUM BOVIS*

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Background and aims: We report an intrafamilial transmission of human tuberculosis caused by *M. bovis*

Methods:

Case 1: In february 2002, a 3-year-old, born in Chad country had developed pulmonary tuberculosis due to *M. bovis*. The HIV antibody was negative. Therapy was initiated with association of isoniazid and rifampin during 6 month. A contact investigation (the patient's mother, father and sister) was considered as negative.

Case 2: In January 2003, the mother of the case 1, HIV infected, was hospitalized for pulmonary tuberculosis. Therapy consisted of an association of 4 antituberculous drugs during 9 months. To understand the mode of transmission, we compared the 2 *M. bovis* strains using spoligotyping and MIRU-VNTR.

Results: Our results confirmed the genetic link between the 2 isolates corresponding endemic genotype responsible for cattle TB in Chad.

Conclusions: Two hypotheses regarding the mode of transmission can be proposed:

(i) contamination of daughter in Chad and human-to-human transmission from the daughter to her mother;

(ii) contamination of these 2 patients from a zoonotic or human source of infection in Chad, followed by exogenous TB infection from daughter and endogenous reactivation TB infection from immunocompromised mother.

AN AUDIT OF THE DIAGNOSIS AND MANAGEMENT OF CHILDHOOD TUBERCULOSIS

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Background: Tuberculosis remains a significant cause of morbidity and mortality in children with an increasing incidence in certain UK populations.

Aims: To audit the management of paediatric TB and compare to the recently published NICE guidelines.

Method: All children diagnosed with active TB from 1999-2007 were identified from the local TB database. Data from medical records was analysed; standards were in accordance with The Management of Tuberculosis (NICE 2006).

Results: 39 children were identified and analysed: 32 from 1999-2005 and 7 from 2006-7. All had a CXR. 35(89.7%) had a mantoux test. 1 IGRA test was performed, which was negative. 12(30.8%) children were assessed for MDRTB.

	Sputum	Urine	Gastric Aspirate	Lymph Node	Abscess Fluid	Total
Number of Children That Produced Sample	10(25.6%)	3(7.7%)	6(15.4%)	2(5%)	1(2.6%)	19(48.7%)
Number of Positive Results	3(30%)	0(0%)	1(16.7%)	2(100%)	1(100%)	5(26.3%)

[Microbiological

Diagnosis]

	Double Therapy	Triple Therapy	Quadrupal Therapy	Not Documented
Number of Children Pre 2006 (n=31)	1(3%) (contact sensitivities known)	20(62.5%)	10(31.3%)	1(3%)
Number of Children Post 2006 (n=7)	0(0%)	2(28.6%)	4(57.1%)	1(14.3%)

[Treatment

Regimens]

Compliance was documented in 31(79.5%) of the childrens' records and was problematic in 3(9.7%). Only 1(2.6%) child was tested for HIV.

Conclusions: Children were commenced on quadruple therapy after 2006 as recommended by NICE. Further work will involve improving attempts to obtain microbiological diagnosis, to identify cases of MDRTB and to ensure that clinicians are aware that HIV needs to be considered and tested for in children with TB. NICE guidelines should help to standardise care to children with TB in the UK.

**TYPE-1 LEPROSY REACTION PRESENTING AS AN IMMUNE RECONSTITUTION
INFLAMMATORY SYNDROME IN A CHILD WITH AIDS**

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The immune reconstitution syndrome (IRS) is an exaggerated immune response to a latent antigen during the immune recovery period after highly active antiretroviral therapy (HAART) and has been infrequently reported in association with *M. leprae* infection.

We report the case of a 9-year old female resident in Mozambique who had been been diagnosed with HIV-1 infection 6 months earlier. She had also been treated two years earlier for multibacillary leprosy, having been discharged after 12 months of multi-drug therapy (MDT). At that time of diagnosis she had a blood CD4+ lymphocyte count of 91 cells/mL (the plasma virus load could not be determined because of the great distance between the village and the laboratory). HAART (zidovudine, lamivudine, and efavirenz) was started and the CD4+ lymphocyte count gradually increased to 324 cell/mL after 3 months. After 4 months, the patient reported the appearance of asymmetric skin lesions that first developed on her buttocks and legs and subsequently spread to her back and face. She also reported a burning sensation in hands and feet. The neurologic examination revealed loss of sensation to light touch in some skin lesions, and a thickened painful left popliteal nerve. As the skin and mucous bacteriological indices were negative and the patient had formerly undergone MDT for 12 months, type-1 leprosy reaction was considered as primary the hypothesis and prednisolone was started (1 mg/kg) for 4 weeks and gradually tapered for 3 additional months, with full remission of the lesions and the neurological deficits.

CLINICAL FACTORS ASSOCIATED WITH A DIAGNOSIS OF PULMONARY TUBERCULOSIS BY CHEST RADIOGRAPHY

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Background and aims: To analyze clinical factors associated with a chest radiograph (CXR) compatible with pulmonary tuberculosis (PTB) in a vaccine trial setting.

Methods: 1445 children (mean age 11.3, IQR 5.6-16.9 months) were investigated for suspected PTB during a Bacille Calmette Guerin vaccine trial (n=11680). Clinical, microbiological and radiological data were recorded. CXRs were reviewed blind by a panel of 3 pediatricians. Multivariate logistic regression assessed factors associated with a radiological diagnosis of PTB.

Results: CXR results were available for 1284 (88.9%) children and 18.8% (n=271) were compatible with PTB. In univariate analysis (OR, 95% CI), age (months) (1.07, 1.05-1.09), chest retractions (2.95, 1.08-7.99), crackles (1.87, 1.37-2.54), wheezing (1.4, 1.07-1.84), night sweats (1.35, 1.03-1.77), failure to thrive (2.39, 1.78-3.20), positive M. tuberculosis culture (2.26, 1.55- 3.30), HIV infection (2.95, 1.65-5.29), Mantoux diameter (mm) (1.03, 1.02- 1.04), and recently treated chest infection (1.54, 1.16-2.03), were associated with CXR compatible with PTB. In multivariate analysis (AOR, 95% CI), age (months) (1.09, 1.06-1.12), chest retraction (1.54, 1.13-2.10), crackles (1.96, 1.40-2.74), recently treated chest infection (1.54, 1.13- 2.10), HIV infection (5.01, 2.63- 9.56), failure to thrive (1.90, 1.39- 2.60), positive M. tuberculosis culture (2.30, 1.50- 3.51) and Mantoux diameter (mm) (1.03, 1.02- 1.05) remained positively associated

Conclusion: A clinical presentation that included features of lower airways obstruction and lung consolidation, or recent treatment for chest infection, was independently associated with CXR diagnosis of PTB, as was evidence of TB infection and confirmation of M. tuberculosis by culture. Odds of radiological diagnosis of PTB were five-fold higher in HIV infected children.

OPTIMIZING THE INTERPRETATION OF TUBERCULIN SKIN TEST (TST) RESULTS USING QUANTIFERON-TB GOLD TEST IN TUBE (QTF) AS “GOLD STANDARD”

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Aims: To analyze sensitivity and specificity of TST cutoff points using QTF as “Gold Standard”

Methods: Multicenter prospective study performed in immunocompetent children under 15 years. TST and QTF were performed on immigrants, tuberculosis (TB) contacts and suspected cases of tuberculosis. Sensitivity and specificity of TST were estimated using ROC curves and considering QTF as the reference standard.

Results: 459 children were included; 318 (69%) TB screening among immigrant children, 83 (18%) TB contact investigations and 58 (12%) suspected TB cases. Mean age was 4,73±3,68 years. 46% presented BCG scar. In children without BCG scar TST cutoff point of ≥10 mm presented a sensitivity of 95% (IC95% 88-98%) and a specificity of 95% (IC95% 91-97%), and a cutoff point of ≥ 5mm a sensitivity of 100% (IC95% 95-100%) and a specificity of 93% (IC95% 88-96%)(ROC curve 0,977;IC95% 0,95-0,99). In children with BCG scar TST cutoff point of ≥10 mm presented a sensitivity of 82% (IC95% 63-93%) and a specificity of 86% (IC95% 80-90%), and a cutoff point of ≥ 15 mm a sensitivity of 60% (IC95% 40-77%) and a specificity of 97% (IC95% 92-98%)(ROC curve 0,865; IC95% 0,76-0,96).

Conclusions: In children without BCG and with risk of TB (proceeding from endemic areas, TB contacts and suspected TB cases), TST cutoff point of ≥ 5 mm presents an excellent sensitivity and specificity.

In BCG vaccinated children the TST cutoff point of ≥ 15 mm improves the specificity but is associated with an important reduction in sensitivity, so cannot be recommended.

IMPACT OF AGE, MALNUTRITION AND INFECTIONS DIFFERENT FROM TUBERCULOSIS IN QUANTIFERON-TB GOLD TEST IN TUBE (QTF) RESULTS IN CHILDREN

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Aims: To study the impact of age, malnutrition and other infections different from tuberculosis (TB) in QTF's results.

Methods: Multicenter prospective study excluding immunocompromised children. QTF was performed in immigrants, TB contacts and TB. McLaren Nutritional Index (NI) was used to estimate nutritional state. Data regarding the presence of bacterial or viral infection were recorded. In immigrants three stool samples were collected for parasite investigation and thick smears were performed in children proceeding from malaria endemic areas.

Results: 434 children were included, 380 immigrants. Mean age was $4,6 \pm 3,6$ years (1 month-15 years). Mean NI was $98 \pm 21\%$, 156 children (35,9%) were malnourish (NI < 90%). Malnourished cases proceed mostly from India, China and EastEurope. Infections were diagnosed in 157 children (105 intestinal helminth infections, 54 viral infections, 17 bacterial infections and 2 plasmodium infections). All QTF indeterminate results (17/434; 3,9%) were due to low production of interferon-gamma (IFN-g).

Children with QTF indeterminate results were younger ($3,51 \pm 2,99$ years) than those with proper production of IFN-g ($4,78 \pm 3,7$ years), even this difference was not statistically significant ($p=0,12$). There were no differences in the NI of children with indeterminate results compare with those with proper production of IFN-g ($p=0,21$). There were no correlation between IFN-g production and age ($r=0,135$) or malnutrition ($r=0,05$). Children with infections different from TB did not present more indeterminate results than those without infections ($p=0,156$).

Conclusions: Infectious diseases and malnourish are frequent in immigrant children. Age, malnutrition and infections different from TB do not influence QTF's results.

UTILITY OF QUANTIFERON-TB GOLD TEST IN TUBE (QTF) IN THE DIAGNOSIS OF SUSPECTED MYCOBACTERIAL LYMPHADENITIS

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Background&Aims: Both tuberculous and non-tuberculous mycobacteria (NTM) can cause lymphadenitis in healthy children. Differential diagnosis with standard diagnostic tools is difficult. We evaluated the usefulness of QTF as a rapid supportive diagnostic method for suspected mycobacterial lymphadenitis.

Methods: Prospective study including immunocompetent children with subacute cervical adenitis and positive (>5 mm) tuberculin skin test (TST) or histological suspicion of mycobacterial infection. Evaluation included QTF, chest radiograph, TST, and fine-needle aspiration (FNA) cytology and culture.

Results: Sixteen patients with suspected mycobacterial lymphadenitis were included. Mean age was 3,5 years (range 1,5-12). Only one child was foreign-born, and none had received BCG vaccine. TST was negative in 7 children, gave an induration between 5 and 9mm in 6 cases and was ³10mm in 3 cases. After complete evaluation, 10 children were classified as probable NTM infection (compatible histology, normal chest radiograph, absence of known exposure to tuberculosis and negative TST reactions in family members), 2 as confirmed NTM infection (*M. avium* isolation in FNA culture), 1 as confirmed tuberculous infection (abnormal chest radiograph and *M. tuberculosis* isolation in FNA and gastric juice cultures), and 3 as no mycobacterial lymphadenitis (1 reactive adenitis, 1 lymphoma, 1 Rosai-Dorfman disease). Of the 10 children with no cultured-confirmed diagnosis, 9 were QTF negative and 1 gave indeterminate results. QTF was also negative in the 2 cases of confirmed NTM infection and positive only in the child with bacteriologically-confirmed tuberculosis.

Conclusion: QTF is useful as adjunctive test in the diagnostic work-up of children with suspected mycobacterial lymphadenitis.

TUBERCULOUS MASTOIDITIS: PRECOCIOUS VERSUS DELAYED DIAGNOSIS**S. Negre Policarpo**¹, M. Navarro Paterna², C. Otero Reigada¹¹*Pediatric Infectious Diseases,* ²*Pediatrics, Hospital Universitario La Fe, Valencia, Spain*

Background and aims: Tuberculosis of the middle ear and mastoid is uncommon. We report two cases in immunocompetent children, comparing their evolution and the precociousness of the diagnosis.

Methods: Retrospective review of two clinical cases.

Results:

Case 1: A 3 years-old girl presented a 1'5 months persistent middle ear infection. Intermittent fever, pain, exudation and weight loss were the most prominent signs. She had a right retroauricular erythema and swelling. Ceftriaxone and corticoid treatment were started, but 1 month later clinical signs persisted. Computerized tomography revealed a severe destructive lesion with a 17x7 mm abscess. Thorax tomography showed calcification in hilar and subcarinal lymph nodes. PPD produced 0 mm induration. After mastoidectomy, histopathological examination revealed granulomatous inflammation. Lowenstein-Jensen culture was positive for non-resistant *Mycobacterium tuberculosis* and triple therapy was started without recurrence.

Case 2: A 13 years-old girl with a left ear tympanoplasty 5 years ago because of a suspected cholesteatoma, presented 2 weeks intermittent fever and a left retroauricular painful erythema. Computerized tomography showed a mastoid abscess, without other complications. Despite empirical treatment, she required surgical drainage. Ziehl-Nielsen stained smears were positive. PPD showed no induration. Lowenstein-Jensen was negative. There was a good response to triple therapy and claritromicin, without mastoidectomy.

Conclusions: Clinical features of tuberculous mastoiditis may resemble common bacterial infections, delaying diagnosis with potentially serious results. Antibiotic resistance for common bacteria and/or destructive bone lesions should be considered as a sign of tuberculous infection. Surgical intervention is indicated in case of complications or recurrence despite drug therapy.

MILD PRIMARY INFECTIONS DOMINATE AMONG CHILDREN WITH TUBERCULOSIS IN SWEDEN

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Background and aims: Tuberculosis (TB) is nowadays rare in Sweden. Travel and migration has led to an increasing rate of the infection, but little is known about the severity of its manifestations.

Methods: During 2000 - 2009 we diagnosed 97 cases of childhood TB in northern Stockholm. We classified each case as mild, severe or indeterminate, depending on clinical and laboratory findings, and looked for predictors of having a severe or mild form.

Results: 70 of the children were born in or had parents from high-incidence (>100/100.000/yr) countries. 17 of 18 indigenous Swedes belonged to one day care center outbreak. 28 % of the cases were severe and 58 % were mild. Severe cases were typically older (median 12,5 yr) , born abroad, presented with symptoms more than a year after infection or immigration, and had an unknown source of infection. Mild cases were younger (median 7,4 yr), Swedish born, and found at active screening less than 6 months after infection or immigration.

Discussion: Cases of TB in industrialised countries have manifestations of disease that differ from those in resource-poor countries. Results from studies of most aspects of TB treatment and control in one setting may therefore not be applicable to the other. There is a lack of knowledge of how to best treat mild forms of primary TB, common in industrialised countries. Fewer drugs and/or shorter courses may be sufficient for these early cases with small bacterial populations.

TUBERCULOSIS IN INFANTS: A RETROSPECTIVE STUDY IN A LARGE FRENCH TERTIARY CARE CENTER

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Background and aims: There are only few population based data on tuberculosis (TB) in infants. Moreover, it is admitted that infants are at high risk to develop a severe form of the disease.

Methods: We analyzed retrospectively data from the children admitted for a TB disease in Robert Debré Hospital, Paris, France, between 1992 and 2007.

Results: One hundred forty three children with a median age of 9,7 years IQR [2,6-13,0] were included. Thirty children (21%) were less than 2 years old. At diagnosis, the infants were less symptomatic than the older children (50% vs 73%, $p=0,02$) ; tuberculin skin test (TST) was more often negative in infants (23% vs 9%, $p< 0,01$). Ninety percent of infants had pulmonary disease, without cavitary lesion but with 44% of the 27 bronchoscopy performed showing airway narrowing by enlarged lymph nodes. Extra pulmonary disease was less frequent in the infants (10% vs 29%, $p=0,03\%$). Twenty three percent of the infants had positive direct microscopy of gastric aspirate. Diagnosis was confirmed microbiologically in 40% of cases. Finally, side effects of the treatment were uncommon ($n=1/30$).

Conclusions: In our study, tuberculosis seemed not to be more severe in infants compare to the older children. However we confirm the difficulties of diagnosis in this specific population as half of the infants were asymptomatic and nearly a quarter had a negative TST. This highlights the importance of an early and strict management of the contact screening.

ARE BOOSTERS NECESSARY FOR TEENAGERS IMMUNIZED AGAINST HEPATITIS B IN INFANCY?

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Background: Duration of protection against hepatitis B afforded by vaccination remains unknown. However, no routine boosters are recommended. According to references, up to 50% of children lose the post-vaccination immune memory during 15 years after immunization. Aim of the study was to determine the immunity against hepatitis B in 10-12-year old children and to establish indications for routine booster doses.

Material and methods: In 130 children aged 10-12 years, immunized against hepatitis B with recombinant vaccine in infancy (10 µg, schedule: 0-1-2-12 months, first dose at birth) humoral immunity (anti-HBs antibodies) and cellular memory (anamnestic response to booster given in children without protective anti-HBs titers) were determined. Titers of anti-HBs ≥10 IU/l were considered protective. Anamnestic response was defined as increase in anti-HBs concentration from < 10 IU/l to ≥10 IU/l 4 weeks after booster dose. Moreover, markers of HBV infection - past (anti-HBc antibodies) and present (HBsAg) were determined.

Results: Protective level of anti-HBs was found in 102/130 (78%) children, 28/130 (22%) did not have humoral immunity, including 9/130 (7%) with undetectable antibodies. Immune memory was determined in 11 children - anamnestic response was revealed in 8/11 (73%). In total, immunity against hepatitis B was revealed in 110/113 (97%) of children. In 6/130 (4,5%) of participants HBV infection was confirmed according to positive anti-HBc, including 2 (1,5% of the study group) with positive HBsAg.

Conclusions: Most children in the studied group had seroprotection and immune memory against hepatitis B 10-12 years after vaccination. No routine booster seems to be necessary.

COMPARISON OF INTERFERON GAMMA AND INTERFERON GAMMA INDUCIBLE PROTEIN-10 IN THE DIAGNOSIS OF LATENT TUBERCULOSIS INFECTION IN CHILDREN

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Background and aims: One of the major hurdles in the implementation of preventive chemotherapy in *M. tuberculosis* infected children is lack of rapid and accurate test for tuberculosis (TB) infection. The measurement of TB antigens specific Interferon gamma (IFN-g) and IFN-g inducible protein (IP)-10 secretions is suggested to be potential marker of LTBI diagnosis. Nevertheless, the data on their performance are limited. Herey, we compared the levels of Interferon gamma (IFN- γ) and IFN-Y inducible protein (IP)-10 secretions in the whole blood culture.

Methodology: A total of 139 asymptomatic (for active TB) children included 56 healthy household contact (HCC) of adult smear positive TB patients and 83 healthy children (HC) who did not have any known contact with TB patients were recruited. QuantiFERON TB-Gold in-tube (QFT-IT) assay was employed to measure IFN- γ levels. IP-10 levels were measured in the supernatants collected from QFT-IT tubes.

Results: Of the 83 HC, two (1%) subjects were positive for QFT-IT. The ranges of IFN-g and IP-10 secretion in QFT-IT negative subjects were 0-0.21 IU/ml and 0-298 IU/ml. Hence, 300 pg/ml was set as cut-off point for TB antigens specific IP-10 response. For mitogen, we chose 200pg/ml based on earlier findings.

At this 300pg/ml, IP-10 was positive in 34 (61%) HHC; QFT-IT was positive in 29 (51.8%) HHC. The difference between QFT-IT and IP-10 did not reach statistical significance. The agreement between the tests was 80.1% (kappa=0.604).

Conclusions: Measurement of IFN- γ and IP-10 can be potential marker for the diagnosis of TB infection in children.

CENTRAL CATHETER BLOOD STREAM INFECTION DUE TO MYCOBACTERIUM CHELONAE IN AN ONE YEAR OLD GIRL

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Background and aim: We present a clinical case of central catheter blood stream infection due to *Mycobacterium chelonae*.

Case report: A one year old girl presents a multisystemic pathology of unknown etiology : iterative ischemic necrosis of guts, two episodes of tubulopathy systemic hypertension, resolutive hypertrophic myocardiopathy, cerebral ischemic accident and hypogammaglobulinemia. For her pathology she had a central venous catheter, Broviak Type. She presents some acute febrile access after each manipulation of catheter. Three blood stream cultures and catheter were positive for *Mycobacterium chelonae* confirmed by mycobacterium culture and ARN16s identification. She was first treated with clarithromycin and ablation of the central venous catheter. On the fifteen day of treatment she presents an ischemic necrosis of the gut of unknown origin. The in vitro antibiotic susceptibility of this isolate show a multiresistant pattern. Then clarithromycin was switched to piperacilline, amikacine and linezolid. When enteral nutrition was possible we change antibiotherapy for clarithromycin and linezolid. We stop antibiotic for a total duration of 2 month of treatment. At the end of the treatment technetium scintigraphy, cardiac echography, ocular examination were done to search dissemination all were negative.

Conclusion: *Mycobacterium chelonae* are rapid-growing ubiquitous mycobacterium that are relatively uncommon causes of systemic human infection. Catheter blood stream infection due to *M.chelonae* are rare but could be complicated. We discuss about the diagnosis, the duration of treatment and its adaptation for infant.

FREQUENCY OF MYCOBACTERIAL SPECIES AND THEIR ANTIBIOTIC RESISTANCE PATTERN IN CHILDREN IN IRAN

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Introduction: Tuberculosis remains one of the major disease involving children throughout the world. The world health organization has estimated approximately one million new cases and 400,000 deaths per year in children due to tuberculosis. There are reports of Mycobacterial infection in children in Iran in recent years. Here we determined the frequency and antibiotic resistance of mycobacterial infections children from 1 month to 12 years of age from various cities in Iran.

Material and Methods: During 2008, 118 suspected samples were collected from children. Majority of samples were collected from 65, 20, 5, and 28 from gastric washing, sputum, wound discharge and other sites. Samples preparation, direct smear, ziehl-neelsen and fluorescent staining, culture on Lowenstein-Jensen medium accomplished, biochemical testing and antibiotic sensitivity tests accomplished according to CDC guidelines.

Results: Out of the total 118 samples, 7 positive Mycobacterial species were collected. Three of which were *M. bovis*, 3 *M. tuberculosis* and 1 atypical mycobacterium. Four of the samples were from gastric washing and 2 from abscess, and one from bone. Two of *M. tuberculosis* isolates were found to be resistant to ethambutol, kanamycin and streptomycin and all 3 *M. bovis* isolated strains were only ethambutol resistant. None of the patients were HIV positive.

Conclusion: Overall, the results indicated an alarming rate of *M. bovis* in children in Iran. We will attempt to further analysis the high number of *M. bovis* in Iran.

OUTBREAK OF TUBERCULOSIS IN A PRIMARY SCHOOL: ROLE OF ROUTINE GASTRIC ASPIRATE

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Aims: To describe a tuberculosis outbreak happened in a primary school, from a teacher with tuberculosis, focusing on the role of routine gastric aspirate.

Methods: Active epidemiological and clinical study of exposed patients. Clinical management of infected children was recorded.

Results: 6 out of 17 (35%) exposed children (>6 hours/day for 3 months) had criteria for diagnosing tuberculosis. Four of them had symptoms. Notably, two children had a positive gastric aspirate for *M. tuberculosis* (susceptible to first line drugs, same strain) although were asymptomatic and had normal chest roentgenogram. Infection rate (latent infection + disease) was 94%. One child belonging to other group (1/82; infection rate 1.2%) was diagnosed of tuberculosis. Out of the index case, there were no other tuberculosis cases among the staff. Odds ratio of exposed children was 44.1 (95%CI: 4.8-402). One immunocompetent boy had initially a paradoxical worsening, and one girl developed alopecia and mild neutropenia on treatment, but eventually all the outcomes were good.

Conclusions: Prolonged exposure to a baciliferous patient may infect almost every child in closed groups. It can also cause a high rate of disease in these groups. In such a scenario, gastric aspirate may be considered even in asymptomatic patients with normal chest-X-ray, if they are infected.

AN OUTBREAK OF TUBERCULOSIS IN A NURSERY SCHOOL

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Background and aims: One of the main objectives to control TBC is prevention. In June-July 2008, the Epidemiology Department at the Public Health Centre of Valencia requested our collaboration to diagnose and treat an outbreak of tuberculosis which was detected in a nursery school in our Health Area.

Clinical observations: In June, one case of TBC was identified in a 2-year-old girl in a nursery school. Another TBC case was reported in a boy in the same classroom. The study of contacts identified a total of 15 children with a positive intra-dermal reaction of which 6(40%) presented alterations in the chest X-ray/CAT. Four of these 6 children were diagnosed in our A&E Unit: 3 boys/1 girl. Three were 3 years aged and 1 was 2 years aged. No clinical symptoms presented at the diagnosis. Radiology showed 2 parenchymatous cases, 1 mixed case (infiltrated and mediastinical or hilar adenopathies) and 1 ganglionic case. Nobody had anaemia, CBC count ranged between 8,200-17,000 mm³, VSG was 2-57 mm/h. Ziehl staining and culture of gastric washing samples were negative in all cases. PCR of *Mycobacterium tuberculosis* was positive in 1 case. The adult case identified was a Romanian childminder who had worked as an assistant in a classroom the year before.

Comments: The time which had passed until the contagious adult was identified enabled this disease to be transmitted. This outbreak reflects how one ill adult may transmit this disease during the months in which its diagnosis was delayed. Bacilloscope effectiveness was practically null.

SUCCESSFUL SUPPORTIVE MANAGEMENT OF EMPHYSEMATOUS PYELONEPHRITIS IN A PEDIATRIC RENAL ALLOGRAFT

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Background and aims: Emphysematous pyelonephritis (EPN) is a rare and life-threatening infection. Diagnosis is made on clinical and radiological grounds. We report the first case of EPN in 12 years - old boy with a renal transplant, and discuss the various diagnostic and management methods.

Methods: A case report of M.T who had end-stage renal disease secondary to neurogenic bladder and high-grade vesico-ureteric reflux in a solitary right kidney. He underwent successful preemptive living-related renal transplant from his mother and was maintained on immunosuppressant

Five months later he was admitted with high fever, chills, vomiting and abdominal pain. His allograft was diffusely tender, renal allograft ultrasound showed gas in the renal collecting system and renal biopsy showed of severe pyelonephritis and no sign of acute rejection.

Results: No surgical intervention was undertaken as the patient started to show improvement on clinical and biochemical grounds, . Urine culture became negative. The patient continued to do well 18 months after this episode. Disappearance of the gas within the collecting system was proved by us 3 months later.

Conclusions: This may be the first report of EPN in a pediatric renal transplant recipient. The diagnosis of EPN was made on clinical and radiological grounds. We were able to treat this problem without any surgical intervention by aggressive hydration, intravenous antibiotics, and continuous urinary drainage by an indwelling urinary catheter, adjustment of maintenance immunosuppressive therapy.

COMPLIANCE WITH NICE GUIDELINES FOR URINARY TRACT INFECTIONS: A SURVEY AMONG THE PAEDIATRIC TRAINEES OF THE LONDON DEANERY

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Background: The new National Institute of Health and Clinical Excellence (NICE) guidelines for management of urinary tract infection (UTI) in children were introduced in August 2007. We performed a survey to assess the awareness and compliance of these guidelines among paediatric trainees.

Methods: An online questionnaire was sent to all trainees in the Deanery. Some questionnaires were partially completed and this was accounted during final data analysis.

Results: 190 (20%) out of 930 trainees responded. 99% diagnosed UTI based on positive urine dipstick, as per the guidelines. 80% used clean catch as the primary collection method whereas 20% used urine-bag. Contrary to the guidelines, 53% used antibiotic prophylaxis for 1st UTI in children younger than 6 months.

94% were aware of the guidelines while 74% utilised it routinely for patient management. 44% used local hospital guidelines and for 40%, consultants made the decision (some trainees had multiple approaches).

90% learnt about the guidelines by self study, 28% by dedicated teaching sessions at their local hospital and 4% had received no teaching.

Conclusions: Majority of the trainees followed the NICE guidelines for diagnosis and specimen collections, but policies for treatment and prophylaxis varied widely despite existence of national guidelines.

Although 90% were aware of the guidelines, only a minority had any formal training in their implementation. Encouragingly, 82% felt that guidelines had changed their clinical practice.

We recommend local and national audits to be carried out with particular emphasis on treatment and prophylaxis, to ensure quality and equity of care.

BACTERIAL SPECTRUM OF COMMUNITY ACQUIRED UTI, CLINICAL SETTINGS AND ANTIBIOTIC RESISTANCE OF ISOLATES

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Background: Urinary tract infection (UTI) is one of the commonest bacterial diseases of childhood and a major health issue.

Objectives: To identify the bacteria causing community acquired UTI's, associated anomalies and to detect isolates antibiotics resistance.

Materials and methods: The retrospective study is based on data collected from the medical files of all children who were recommended urine cultures over 1 year period (2009) in a primary health care clinic in Bucharest.

Results: A total number of 1232 urine cultures collected from 859 patients were reviewed. Cultures were positive in 119 children (9,6 %). 98 children (11,40%) experienced at least one episode of UTI.

Positive cultures were obtained in 9,2 % (36 out of 390) of the total number of investigated boys and in 13,2 % (62 out of 468) of the girls.

Identified bacteria: Escherichia coli - 69 (57.9 %) of cultures, Klebsiella - 17 (14.2 %), Enterobacter - 9 (7,56 %), Enterococcus - 7 (5.88%), Proteus - 9 (7,56 %), Pseudomonas 5 (4,20 %), Enterobacter + Enterococcus - 2 (1,64%) , Providencia 1 (0,82%). During the studied period 16 children (16,32%) experienced more than 1 episode of UTI. In this group 6 children (6,1%) had various degrees of vesicoureteral reflux (VUR) and 2 (2%) were uncircumscised male infants. Antibiotic sensitivities of isolates were fairly good except in those children with multiple UTI and associated anomalies were multiresistant strains are isolated

Conclusions: UTI represent a diagnostic and a therapeutic challenge in children with VUR and in healthy children as well.

NEONATAL HYPERBILIRUBINEMIA RESULTING FROM URINARY TRACT INFECTIONS**H. Boskabadi, G.A. Maamouri***Mashad University of Medical Science, Mashhad, Iran*

Introduction: Urinary tract infections (UTI) are a common and serious clinical problem in newborn infants. The aim of this study was to evaluate the incidence, age presentation, and severity of jaundice, sign and complications of UTI in newborns with asymptomatic, unexplained indirect hyperbilirubinemia.

Methods: This was a cross sectional study conducted between May 2004 and April 2009, at the NICU, Ghaem Hospital, Mashhad- Iran. A total of 1487 infants with jaundice were recruited which, 1061 patients were evaluated for UTI. Among them, 629 infants were excluded and remain 74 patients with UTI and 358 infants with unknown etiology of jaundice as without UTI. Demographic data including prenatal, intrapartum, postnatal events and risk factors were collected by questionnaire. Serum fractionated bilirubin level, urinalysis and routine laboratory tests were measured.

Results: Age presentation, age admitted to hospital, age improved jaundice, serum bilirubin level and hospital stay in case group were significantly higher than control groups ($p < 0.05$). UTI was diagnosed in seventy four (7%) cases [Escherichia coli (44.4%), Klebsiella pneumoniae (22%)] Pyuria and or Bacteriuria were present in 58% of patients. Renal ultrasound showed urinary tract abnormalities in Twenty-three (32%) patient. Six infants had unilateral grade 1-3 reflux in voiding cysto urethrogram (VCUG).

Conclusion: A UTI was found in 7% of asymptomatic, jaundiced infants. Therefore, we recommend that testing for a UTI be included as part of the evaluation in asymptomatic, jaundiced infants presenting after five day of life. These infants should be evaluated for urinary tract abnormality by renal ultrasound and VCUG.

THE PREVALENCE OF VEROTOXIGENIC EHEC IN CLINICAL SAMPLES IN PATIENTS WHO REFERRED MOFID HOSPITAL

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Introduction: Urinary infection due to EHEC is one of the most important diseases in infants and children. If there would not be any useful diagnosis and followed treatment for them, may appear dangerous diseases such as HUS that including acute renal failure, Thrombocytopenia and Hemolytic Anemia. Thus, we considered methods for rapid diagnosis with high sensitivity and specificity.

Material and methods: We consider 12572 urine samples from children in Mofid hospital. We isolate 305 E.coli from urine samples that Only 9 EHEC strains were isolated from urine samples. E.coli strains that indicated beta hemolytic on sheep blood agar, negative fermentation of sorbitol on SMAC (sorbitol macconky agar) and negative motility on SIM were tested serologic test with VTEC-RPLA Seiken kit for consider production of toxin and PCR for detecting toxin genes.

Results: Five EHEC strains (56%) of nine isolated EHEC strains produced genes *vtx*. The prevalence of *vtx* -1 and *vtx* -2 and *vtx* -1&2 were 17.35%, 52.45%, 30.3% respectively.

Conclusion: The prevalence of urinary infections caused by EHEC strains is very significant because it causes aggravating pathologic effects. Thus we suggest rapid method for identification of this bacteria and proper treatment to inhibition of unwanted complications.

IS DMSA SCAN NECESSARY IN INFANTS WITH FEBRILE URINARY TRACT INFECTION WHEN RENAL ULTRASOUND AND VOIDING CYSTOURETHROGRAPHY ARE NORMAL?

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Introduction: Febrile UTI is a common pathology in infants. A minority of patients suffer from complications such as high blood pressure or chronic kidney disease. Imaging studies in this group of risk included renal ultrasound, voiding cystourethrography and dimercaptosuccinic acid scan. Recently, there is a tendency to minimize the number of imaging studies. The aim of this study is to evaluate the risk of renal scars, demonstrated by DMSA scan, in infants with normal renal US and VCUG.

Patients and methods: This prospective study includes 295 children less than 2 years old (61.4% females, 38.5% males) with a first episode of UTI. Renal US was performed within 1 week after diagnosis, VCUG within 6 weeks and DMSA scan after 6 months. Using DMSA scan as the gold standard for renal scars, we built up a diagnostic table to determine the value of a normal renal US and VCUG in excluding renal scars.

Results: 165 (55.9%) children had a normal renal US and VCUG. Renal scars were detected in 8 of these (4.8%). The negative predictive value for excluding renal scars in this group was 95%, with an odds ratio of 3.77 (95%CI: 1.60-8.89), and a likelihood ratio of 1.79 (95%CI: 1.36-2.37). The probability of finding renal scars when both renal US and VCUG are normal is only of 4.8%.

Conclusions: In children less the 2 years with a first episode of febrile UTI, DMSA scan could be delayed or even not done if renal US and VCUG are normal.

URINARY TRACT INFECTIONS IN CHILDHOOD: EPIDEMIOLOGY, DIAGNOSIS, TREATMENT AND IMAGING

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Background: Urinary tract infections (UTIs) are common during childhood. The aim of this study was to examine the epidemiology, treatment and imaging of UTIs in our setting.

Methods: We retrospectively examined the records of children, hospitalized at "Aghia Sophia" Children's hospital, a tertiary pediatric hospital, with UTI as final diagnosis, from January to December 2008.

Results: 436 children were identified with a median age of 6 months (0,2 - 168 months). Previous history of UTI was present in 20,2% of children and 11,2% were on chemoprophylaxis.

Urinalysis was found positive for pyuria (61,7%), nitrates (23,7%), leukocyte esterase (75,5%) or both (29,5%). Isolated pathogens included *E.coli* (73,9%), *K. pneumoniae*. (6,7%) and *P.mirabilis* (3,7%). Empirical treatment that included 3rd and 2nd generation cephalosporins (48,4% and 16,5% respectively) was modified after the antibiogram in 37,8% of cases.

The mean length of hospitalization was 5,75 days \pm 2,96. Regarding children with 1st episode of UTI, chemoprophylaxis was suggested for 92,5% until voiding cystourethrography (VUG), although 36,3% continued despite negative results. Positive findings in renal ultrasonography, VUG and renal scarring in DMSA were found in 11,1% (31/278), 31,7% (78/246) and 14,2% (8/56) respectively. A congenital anatomical urinary abnormality (e.g. posterior urethra valves, double pyelo-ureteral segments) was diagnosed in 4,6% (13/281) .

Except UTI, children had also final diagnosis bronchiolitis (3,7%) and gastroenteritis (6%).

Conclusion: Different strategies regarding chemoprophylaxis and imaging for UTIs exist in our setting. There is a need for commonly accepted guidelines regarding treatment, evaluation and follow up of children with UTI.

HIGH GENETIC DIVERSITY AMONG *ENTEROCOCCI* CAUSING CATHETER- ASSOCIATED URINARY TRACT INFECTIONS IN IRAN

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Background and aims: Urinary tract infection is one of the most common diseases in children. Precise and untimely diagnosis and comprehensive treatment can significantly decrease late serious complications. Among microorganisms causing UTI, *enterococci* are one of the most prevalent reported one. Microorganisms causing UTI are resistant to most of antibiotics which lead to increasing the duration of hospitalization, morbidity, mortality and there are medical and financial implications associated with UTIs. The aim of this study was to determine *enterococci* prevalence, its antimicrobial resistance and its genetic diversity isolated in children.

Methods: Urine samples were cultured by standard loop method. The 10⁵ CFU/ml cultures were assumed as positive. After identification of *enterococci* by biochemical tests, susceptibility of each isolate was assessed by disk diffusion method according to CLSI guidelines. In order to analyzing bacterial genotypic diversity, pulsed- field gel electrophoresis (PFGE) were performed using *Sma*I enzyme in CHEF DRIII apparatus.

Results: Out of 500 urine samples, 50 were positive for *vancomycin resistant Enterococci*. Out of 50 VRE isolates, 3 were isolated from catheter- associated urinary tract infections from neonatal intensive care unit and Pediatric ward. All of 3 VRE isolates showed a high level vancomycin resistance (MIC≥128) and harbored *vanA* gene. Genotyping by PFGE using *Sma*I enzyme revealed the presence of two types.

Conclusion: The prevalence of VRE catheter- associated urinary tract infections among NICU patients and Pediatric ward has been rare in Tehran. PFGE results revealed that among *enterococci* isolates PFGE patterns were diverse.

PREVENTION OF RECURRENT URINARY TRACT INFECTIONS (UTIS) IN CHILDREN: CO-TRIMOXAZOLE (SXT) VERSUS SECOND-GENERATION CEPHALOSPORINS (2GC)

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Background and aims: UTI is a frequent cause of morbidity in childhood. Chemoprophylaxis is recommended when high risk for recurrent UTIs exists; however, breakthrough UTIs still occur. We aimed to compare the prophylactic efficacy of SXT and 2GC in children with UTIs.

Patients and methods: Children aged 1mo-6y were enrolled in a prospective multicenter study if they were considered eligible for chemoprophylaxis after the first UTI episode by their clinicians. The patients were randomly selected on 1:1 ratio to receive either SXT or 2GC. In each patient, antibiotics were switched to each other every 6mo, for as long as chemoprophylaxis was considered necessary by the clinicians. Children were followed during chemoprophylaxis period, or until the first UTI breakthrough recurrence.

Results: Ninety-two children [50 girls (54%), median age 5.25mo] were studied. Recurrent UTIs occurred in 8 of 67 SXT courses and in 4 of 65 2GC courses ($p=0.36$). All prophylaxis failures occurred during the 6mo-period following UTIs. 2GC failures occurred earlier than SXT failures (mean \pm SE: 0.81 ± 0.1 vs 2.37 ± 0.36 mo, respectively $p=0.028$). Five of 8 children with SXT failure had high grade (≥ 3) reflux compared to 1 of 4 children with 2GC failure ($p=0.54$). Among 28 children with high-grade reflux, recurrent UTIs occurred in 5 of 25 SXT courses and in 1 of 21 2GC courses ($p=0.19$).

Conclusions: There is no difference between SXT and 2GC in preventing UTIs in children. Recurrent UTIs occur earlier in children on 2GC than on SXT possibly due to faster acquisition of resistant uropathogenic strains.

EFFICACY OF THE ORAL PENTAVALENT ROTAVIRUS VACCINE IN AFRICA

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Background and aims: The efficacy of the pentavalent rotavirus vaccine (PRV) against severe rotavirus gastroenteritis (RVGE) was evaluated in a double-blind, placebo-controlled, multicenter Phase III clinical trial conducted in Ghana, Kenya, and Mali (April 2007 to March 2009).

Methods: 5,468 infants were randomized 1:1 to receive 3 doses of PRV/placebo at 6-, 10-, and 14-weeks of age. Breastfeeding and concomitant administration of EPI vaccines, including OPV, were allowed. HIV-infected infants were not excluded (HIV testing offered in Kenya). The study's primary endpoint was vaccine efficacy (VE) against severe-RVGE measured from ≥ 14 days following the third dose through 2 years of follow-up in the combined 3 African countries. Severe RVGE was defined using the 20-point Vesikari scale (score ≥ 11). Symptom data were solicited from parents upon presentation to healthcare centers and clinical data were collected prospectively by physicians. Stool samples were analyzed by rotavirus-specific EIA and RT-PCR to determine the G/P genotypes.

Results: 5,468 infants were enrolled (2,200 Ghana, 1,308 Kenya, 1,960 Mali). VE against severe-RVGE through nearly 2 years of follow-up was 39.3% (95%CI:19.1%-54.7%); country-specific VE was 55.5% (95%CI:28.0%-73.1%), 63.9% (95%CI:< 0%-89.8), and 17.6% (95%CI:< 0-45.0) in Ghana, Kenya, and Mali, respectively. Through the first year of life, VE against severe-RVGE in Africa was 64.2% (95%CI:40.2%-79.4%).

Conclusions: In African countries with high under-5 mortality rates, PRV significantly reduced severe-RVGE through nearly 2 years of follow-up. VE varied among countries. These data provide an estimate of the public health impact of incorporating rotavirus vaccines in the EPI schedules of African countries.

SUSTAINED DECLINE IN ROTAVIRUS GASTROENTERITIS PRESENTING TO THE CHILDREN'S HOSPITAL OF PHILADELPHIA (CHOP) IN THE NEW ROTAVIRUS VACCINE ERA

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Background and Aims: A dramatic decline in rotavirus gastroenteritis cases during the 2007-08 rotavirus season in the United States was attributed to uptake of an effective rotavirus vaccine for infants. The RV5 vaccine (RotaTeq, Merck) was licensed in February 2006, followed by the RV1 vaccine (Rotarix, GSK) in April 2008. To exclude the possibility that these findings represented chance variation, we examined the 2008-09 experience at CHOP.

Methods: Infants presenting to CHOP with acute gastroenteritis have been tested for rotavirus antigen in the stool by ELISA (followed by serotyping if ELISA-positive) since the 1994-95 epidemic season (1-December to 1-June of the following year) in Philadelphia.

Results: The number of community-acquired cases during the last full rotavirus season before vaccine licensure was 271 in 2005-06, followed by 167 in 2006-07 and 36 in 2007-08. In 2008-09, 73 community-acquired cases were identified. Almost half of the cases were seen among children older than 2 years. G9P[8] strains caused 64% of the cases.

Rotavirus Season	G1	G2	G3	G4	G8	G9	G12	Total VP7-typeable strains
2005-06	134	101	4	0	1	21	0	261
2006-07	153	3	7	0	0	0	1	164
2007-08	11	3	15	1	0	1	1	32
2008-09	9	1	8	1	2	47	2	70

[VP7-typeable strains at CHOP]

Conclusions: The sustained decline in community-acquired rotavirus gastroenteritis is likely related to rotavirus vaccination. Although G9 outbreaks have been recognized in the prevaccine era, the effects of the current vaccines on serotype replacement need to be carefully monitored moving forward.

IMPACT OF A VACCINATION CAMPAIGN IN INFANTS (*NOURRISSONS*) ON HOSPITALISATIONS FOR ACUTE ROTAVIRUS DIARRHEA IN FRANCE: THE IVANHOE STUDY

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Objective: Evaluate the impact of a vaccination campaign against rotavirus in infants on hospitalisations for acute rotavirus diarrhea (ARD) in Brest University Hospital paediatric units.

Methods: An active hospital-based surveillance system initiated 5 years before vaccine introduction (May 2007) enabled the occurrence of 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[®] offered to all children born in Brest by mother and child health centres, paediatricians and general practitioners from the Brest Urban Community (BUC). The principal endpoint was the number of hospitalisations for ARD in infants under 2 years old living in the BUC during 2008/2009 epidemic season.

Results: A total of 4684 infants received at least one dose. For the BUC, almost 51% of the population received at least one dose and 2,034 infants received a vaccine regimen involving 3 doses (vaccine coverage (VC) of 47%).

Modeling allows estimating that number of hospitalizations has been divided by 2.04 (95% CI: 1.56 - 2.66) during the last epidemic season (2008/2009); Observed number was equal to 30 whereas expected number was equal to 61. Relative risk reduction for rotavirus diarrhea hospitalization was 98% (95% CI: 83% - 100%).

No notable serious adverse events were reported; 2 cases of intussusception were notified, commensurate with the number expected in the absence of vaccination.

Conclusion: We observed a noticeable impact of vaccination on rotavirus diarrhea hospitalization as soon as two years after vaccine introduction despite modest VC

EFFECTIVENESS OF THE HUMAN ROTAVIRUS VACCINE AGAINST HOSPITALIZATION FOR SEVERE ROTAVIRUS GASTROENTERITIS IN BELÉM, BRAZIL

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Background and aims: In March 2006, Brazil initiated universal immunization of infants with two doses of the monovalent G1P[8] human rotavirus vaccine. This study evaluates vaccine effectiveness (VE) against severe rotavirus gastroenteritis (RVSGE) hospitalizations.

Methods: Matched case-control study at four hospitals in Belém (annual birth cohort ~24,000) from May 14, 2008-May 28, 2009. Cases were children age-eligible to have received both vaccine doses hospitalized with ELISA-confirmed RVSGE. For each case, one neighborhood and one hospital control without gastroenteritis was selected, matching by birth date (± 8 and ± 6 weeks, respectively). Vaccination status was confirmed by vaccination card review. Matched odds ratio (OR) of two-dose vaccination in cases versus controls was used to estimate VE ($1-OR \times 100\%$).

Results: 538 RVSGE cases, 507 hospital controls and 346 neighborhood controls were included in this analysis, with 54%, 61% and 74%, respectively, having received both vaccine doses. G2P[4] accounted for 82.0% of RVSGE cases. VE was 75.8% [95%CI: 58.1,86.0] using neighborhood controls and 40.0% [14.2,58.1] using hospital controls. Using neighborhood controls, VE in children aged 3-11 months and ≥ 12 months was 95.7% [67.8,99.4] and 65.1% [37.2,80.6], respectively; and 55.6% [12.3,77.5] and 32.1% [-3.7,55.5] using hospital controls. G2P[4]-specific VE was 75.4% [56.7,86.0] using neighborhood controls and 38.9% [11.1,58.0] using hospital controls.

Conclusions: Although fully heterotypic G2P[4] was the predominant RV strain, good vaccine effectiveness was demonstrated. VE was highest in children aged 3-11 months. However, protection in children aged ≥ 12 months, important for optimal public health impact, was significantly sustained based on estimates obtained using neighborhood controls.

REDUCTION IN PAEDIATRIC GASTROENTERITIS ADMISSIONS IN SOUTH AUSTRALIA IN BOTH VACCINATED AND UNVACCINATED CHILDREN POST INTRODUCTION OF ROTAVIRUS VACCINE

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Background and aims: Rotavirus is the leading cause of severe gastroenteritis in children under 5 years of age in Australia and is responsible for approximately 10,000 hospitalisations each year. Rotavirus vaccination was included in the National Immunisation Program (NIP) in Australia, commencing 1 July 2007. The aim of this study was to evaluate the effectiveness of rotavirus vaccine in preventing hospitalisation from rotavirus positive and all cause gastroenteritis.

Methods: A retrospective analysis of hospitalisations was conducted for rotavirus positive and all cause gastroenteritis in South Australia from 2005 to 2009. Hospitalisations for both rotavirus positive (including measure of severity of disease) and all cause gastroenteritis in children < 5 years of age were compared prior to and post introduction of rotavirus vaccine.

Results: For all cause gastroenteritis there was a 42% reduction in hospitalisations in South Australia from 1833 hospitalisations prior to (2005/2006) and 1067 hospitalisations following introduction of rotavirus vaccine (2008/2009). Over a twelve month period prior to inclusion of rotavirus in the NIP, there were 499 (2005/2006) hospitalisations for rotavirus positive gastroenteritis compared to 115 hospitalisations in the same period post introduction of rotavirus vaccine (2008/2009) giving a 77% reduction in rotavirus hospitalisations. In unimmunised children (3-4 years of age) there was a 60% and 46% reduction in rotavirus positive and all cause gastroenteritis hospitalisations respectively, during the same time period.

Conclusions: Data from this study confirm a marked reduction in severe rotavirus positive and all cause gastroenteritis with evidence of herd immunity following introduction of rotavirus vaccine in South Australia.

**ROTAVIRUS GASTROENTERITIS AFTER LAUNCHING ROTAVIRUS VACCINES:
EPIDEMIOLOGICAL DATA FROM A REGIONAL HOSPITAL IN BELGIUM**

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Introduction: In a regional hospital in Belgium, data on hospitalizations due to rotavirus gastroenteritis (RVGE) were collected during pre (06/2002-05/2006)- and post-vaccination (06/2006-05/2009) periods. Vaccine coverage was estimated at 30% at the end of 2006 and 80-90% at the end of 2008

Methods: Between June 2002 and June 2009, stool samples were collected from children who presented with moderate to severe acute gastroenteritis in private practice and in the emergency department. The percentages positive samples were calculated.

Results: Total number of stool specimens, % rotavirus positive samples and hospitalizations due to RVGE during different pre- and post vaccine seasons are presented (Table).

Season	06/2002 05/2003	06/2003 05/2004	06/2004 05/2005	06/2005 05/2006	06/2006 05/2007	06/2007 05/2008	06/2008 05/2009
Samples							
Total	243	369	324	460	410	316	203
Rota+(n)	75	131	95	157	90	38	15
%	30.8	35.5	29.3	34	21.9	12	7.3
Hospitalization due to RVGE							
Patients (n)	70	118	93	142	84	36	14
Total days	396	714	505	724	426	207	97

[Stool samples and hospitalization due to RVGE]

Conclusion: Compared with the mean number of hospitalization days during the four pre-vaccine seasons, an 65% and 83% reduction in hospitalization days due to RVGE was seen in the 2007-2008 and the 2008-2009 season, respectively.

A dramatic reduction in total hospitalization days for RVGE was seen after launching the rotavirus vaccine on the Belgian market, inversely proportional to the increasing vaccine coverage.

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

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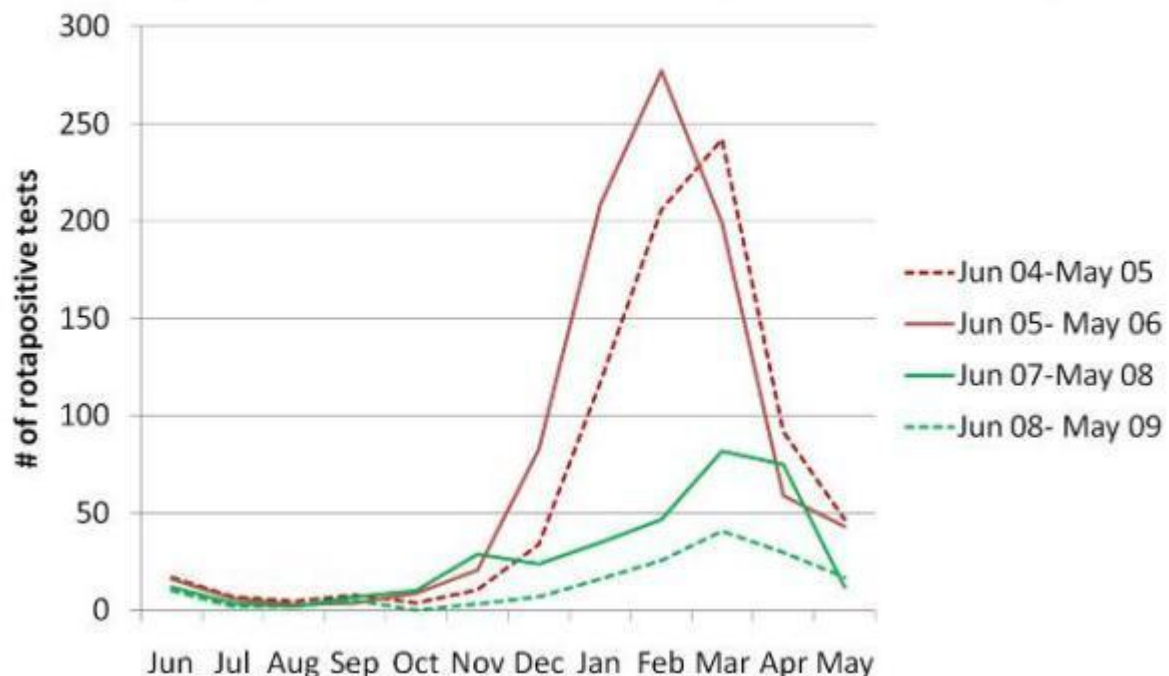
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Background and aims: Rotavirus vaccination is reimbursed in Belgium since November 2006. This study is a follow-up of last-year reported impact of 1st year post-vaccination on rotavirus-positive stool samples in 11 pediatric centers across Belgium.

Methods: Laboratory results of stool samples were now collected from hospitalized children, aged ≤ 5 y in the same centers. Two observation periods were compared: pre- (01/06/2004-31/05/2006) with post-vaccination period (01/06/2007-31/05/2009). Absolute numbers are reported with % reduction per year for ≤ 5 y and ≤ 2 y with chi-square-test for significance.

Results: In pre-vaccination period of 9 hospitals with complete data, 831 (25.9%) and 930 (29.9%) positive samples for ≤ 5 y and 735 (25.8%) and 829 (30.0%) for ≤ 2 y were observed in 1st and 2nd year respectively. Post-vaccination the number of positive samples decreased in 1st and 2nd year to 368 ($p < 0.0001$) and 199 ($p < 0.0001$) respectively for ≤ 5 y and to 293 ($p < 0.0001$) and 158 ($p < 0.0001$) for ≤ 2 y. In 2nd y post-vaccination, a decrease in number of positive samples of 46% for both ≤ 5 y old and ≤ 2 y old was seen compared with 1st y post-vaccination period.

Monthly distribution of the number of rota positive tests per year: in hospitalised children ≤ 2 years old (9 centers)



[Monthly distribution]

EFFICACY OF THE PENTAVALENT ROTAVIRUS VACCINE AGAINST ROTAVIRUS GASTROENTERITIS CAUSED BY MULTIPLE SEROTYPES IN AFRICA

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Background and aims: The efficacy of the pentavalent rotavirus vaccine (PRV) against severe rotavirus gastroenteritis (RVGE) was evaluated in a double-blind, placebo-controlled, multicenter Phase III clinical trial conducted in 3 low-income countries in Africa: Ghana, Kenya, and Mali (April 2007-March 2009).

Methods: 5,468 infants were randomized 1:1 to receive 3 doses of PRV/placebo at 6-, 10-, and 14-weeks of age; concomitant administration with routine EPI vaccines (including OPV) was allowed. HIV-infected infants were not excluded. Vaccine efficacy (VE) against severe-RVGE, defined using the 20-point Vesikari scale (score ≥ 11), by specific rotavirus-genotypes was calculated from ≥ 14 days following the third dose through a follow-up period of 2 nearly years in the combined 3 African countries. Stool samples were analyzed by rotavirus-specific EIA and RT-PCR to determine G/P genotypes.

Results: G1, G2, G3, G8, G9, G10, P1A[8], P1B[4], and P2A[6] were the rotavirus-genotypes detected during the follow-up period. VE against severe-RVGE caused by vaccine-contained G and P types (G1-G4, P1A[8]) was 34.0% (95%CI:11.2%-51.2%). VE against severe-RVGE caused by non-vaccine G types (G8, G9, G10) was 81.8% (95%CI:16.5%-98.0%), while VE against severe-RVGE caused by non-vaccine P types (P1B[4] and P2A[6]) was 40.7% (95%CI:8.4%-62.1%). VE against severe-RVGE caused by individual genotypes was: G1 (33.2% [95% CI: < 0.0%-55.4%]), G2 (27.1% [95%CI:< 0.0%-55.2%]), G3 (62.3% [95%CI:< 0.0%-93.6%]), G8 (87.5% [95%CI:6.5%-99.7%]), G9 (49.7% [95%CI:< 0.0%-99.1%]), P1A[8] (36.1% [95%CI:4.0%-57.9%]), P1B[4] (18.2% [95%CI:< 0.0%-63.8%]), and P2A[6] (47.7% [95%CI:10.4%-70.3%]).

Conclusions: PRV provides protection against severe-RVGE caused by diverse circulating rotavirus genotypes in Africa for a period of two years.

A CRITICAL REVIEW OF ECONOMIC MODELS OF ROTAVIRUS VACCINATION

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Background and aims: Economic evaluations play an important role in vaccination decision-making process. Published models on rotavirus vaccination have produced contradicting results. Our objective was to review and critically appraise existing economic models.

Methods: The literature search covered cost-effectiveness, cost-utility and budget impact models of Rotateq® and Rotarix® published or presented at conferences until October 2009. We extracted information on modeling approaches, input data (epidemiology, vaccine efficacy, utilities, vaccination costs) and results. Clinical evidence for the vaccines was also reviewed.

Results: We identified 36 relevant articles and 16 conference abstracts referring to distinct analyses, covering Europe (26 studies), US (3), Latin America (10), and Asia/Pacific (13). Results varied widely between studies. For the most studied countries, UK (5 studies) and France (6), incremental cost-utility ratios from societal perspective approached £74,000 and €140,000/QALY (quality-adjusted life-year) respectively, while other studies predicted cost-savings. Sources of variability included epidemiological inputs, indirect costs and assumptions for calculating QALYs. Clinical studies of Rotateq® and Rotarix® measured efficacy differently and no evidence of difference between vaccines was found. However 7 of 10 studies distinguishing the two vaccines used different efficacy assumptions. In addition, all these studies used different costs per vaccine course, which were based on hypothetical prices in 8/10 cases.

Conclusions: The basis for differentiating the two vaccines in economic analyses was often weak. The lack of consensus on methods for valuing health benefits for infants and productivity losses poses difficulty for cost-utility analyses of rotavirus vaccination.

PENTAVALENT ROTAVIRUS-VACCINATION IN GERMANY - AN ECONOMIC EVALUATION**B. Brüggengjürgen**^{1,2}, S. Schmitter³, N. Ezzat¹, S. Quilici⁴¹*Alpha Care GmbH, Celle*, ²*Steinbeis Hochschule Berlin*, ³*Sanofi Pasteur MSD GmbH, Berlin, Germany*, ⁴*Sanofi Pasteur MSD SNC, Lyon, France*

Background & aims: Rotavirus is a frequent cause of acute gastroenteritis in children younger than 5. Surveillance data of a rotavirus-vaccination program, initiated in the United States in 2006, indicates first signs of herd immunity. Aim of this study was to assess the medical and economic impact of pentavalent rotavirus-vaccination in Germany and exploring the impact of herd immunity (HI) effects.

Methods: A decision-analytic model was developed comparing the impact of vaccinating a birth cohort of 685,000 children (37% coverage) with a non-vaccination strategy. The cohort was followed from birth to the age of 5. Local epidemiological and cost data were taken from a prospective study, updated by an expert survey; vaccine efficacy was derived from a clinical trial. Extent of HI was estimated based on respective observations in the USA. Economic impact of pentavalent rotavirus-vaccination was assessed from societal perspective. Deterministic sensitivity analyses (DSA) were performed to test the robustness of the results.

Results: Rotavirus is responsible for about 362,620 symptomatic cases of rotavirus gastroenteritis (RVGE) within a time-period of 5 years and associated costs of about 142M€. Vaccination (37% coverage) could directly prevent 98,443 RVGE cases connected with substantial reduction in disease costs (40M€). 68% of related vaccination costs (46M€) are offset after 2 years. Cost savings could be realised for society if HI exceeds 5%. DSA supported the results.

Conclusions: Rotavirus-vaccination costs could be substantially outweighed by rapidly reducing cases and associated costs of RVGE. If HI exceeds 5%, vaccination could be cost-saving for society.

INTUSSUSCEPTION FOLLOWING ROTAVIRUS VACCINE ADMINISTRATION: POST-MARKETING SURVEILLANCE OF ROTATEQ AND ROTARIX IN THE NATIONAL IMMUNIZATION PROGRAM IN AUSTRALIA

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Introduction: National rotavirus vaccination commenced in Australia on 1 July 2007, with infants receiving RotaTeq or Rotarix vaccine depending on their state of residence. Active surveillance for intussusception (IS) was conducted.

Methods: Two active surveillance mechanisms (hospital-based case finding and monthly reports from paediatricians) ascertained IS cases between 1st July 2007 to 31st December 2008 in four regions. Linkage to vaccination records identified cases occurring within 1-7 and 1-21 days of rotavirus vaccination. These were compared with expected cases based on rates from 2000-2006 hospitalisations, coded as IS by age and region, applied to numbers vaccinated according to the Australian Childhood Immunization Register.

Results: There was no evidence of an increased risk of IS following vaccination combining across all doses to 9 months of age for either vaccine. In infants 1-< 3 months, there was suggestive evidence of more IS cases 1 to 7 and 1 to 21 days following dose 1 (1-7 days relative risk [RR]: RotaTeq 4.8, 95%CI 1.0,14.1; Rotarix 3.7, 95%CI 0.8,10.8 / 1-21 days RR: RotaTeq 3.2, 95%CI 1.2, 7.0; Rotarix 1.7, 95%CI 0.5, 4.2). No differences in clinical outcome were found in cases occurring within 21 days of vaccination.

Conclusion: Although we found no overall increase in IS following rotavirus vaccine in Australia, there was some evidence suggestive of an elevated risk following the first dose. Limitations include small case numbers and uncertainties deriving from historically based background incidence rates. More data from settings with varying background IS incidence and vaccine use is needed.

SEQUENCE ANALYSIS OF HUMAN ROTAVIRUS STRAINS: COMPARISON OF CLINICAL ISOLATES FROM NORTHERN AND SOUTHERN ITALY

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Background and aims: The objective of the present study was to compare rotavirus (RV) strains isolated in Northern (Ferrara) and Southern (Galatina-LE) Italy.

Methods: During 2008, eighty-two rotavirus positive stool samples were collected from children with diarrhoea admitted to Pediatric Department, "Arcispedale S. Anna" Hospital, Ferrara and also to "S. Caterina Novella" Hospital, Galatina (LE). The specimens were genotyped for VP7 (G-type) and VP4 (P-type) gene by reverse transcription (RT) and multiplex PCR using different type specific primer, as described in Iturriza-Gómara et al (2004). A subset of 10 G1, 6 G2, 2 G4, and 3 G9 RV strains was randomly selected and characterized by sequence analysis of the VP7 genes. Sequence similarity was detected using BLAST (www.ncbi.nlm.nih.gov/blast), multiple sequence alignment was conducted with ClustalW programs (www.ebi.ac.uk/clustalw) and phylogenetic analysis was performed on partial VP7 nucleotide sequences using version 4 of the MEGA software package.

Results: The 86.6% of stool samples was detected positive by RT-multiplex PCR. Totally, four G-type (G1, G2, G4 and G9), two P-type (P[8] and P[4]), four G/P combinations (G1P[8], G2P[4], G4P[8] and G9P[8]) and two co-infections (G1+G2 and G2+G4) were identified.

Phylogenetic comparison of the VP7 encoding gene of selected strains belonging to G1, G2, G4 or G9 showed that there was similarity of RV strains circulating in Northern and Southern Italy.

Conclusions: The observation of nucleotide sequence diversity contributes to a better understanding of rotaviruses spreading and helps to characterise the various antigenic shifts that could reduce vaccine efficiency.

PREVALENCE OF PERTUSSIS IN LATIN AMERICA

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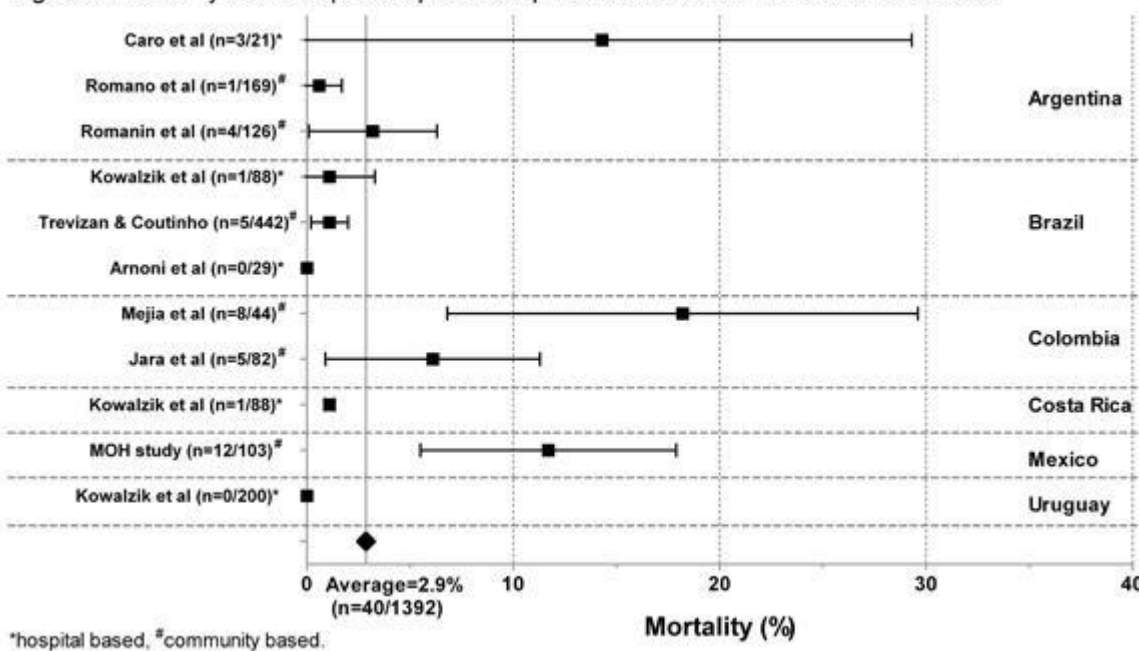
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Background: Widespread DTP vaccination has not eliminated pertussis in Latin America and pertussis has re-emerged as a health problem in the last five years. Evaluating the epidemiology of pertussis provides valuable insight into the current regional medical situation.

Methods: Retrospective literature review since 1990 focusing on disease incidence, mortality rate, number of hospitalisations and case confirmation in epidemiological publications.

Results: Data are scarce for many countries with most information obtained from Argentina, Brazil, Colombia, Costa Rica and Mexico. Twenty studies involving 3515 patients were identified; 11/20 gave information on mortality.

Figure 1. Mortality from suspected pertussis patients in six Latin American countries.



[Figure 1]

Pertussis was identified most frequently in paediatric patients < 1 year of age, and this group was most likely to be hospitalised. Hospitalisation rates from three community-based studies showed a dependency on age with rates of 9.4% (median age, 9 years), 62% (median age, 3 months) and 72% (median age, unreported). In hospital-based studies, laboratory case confirmation was reported at rates of 10.2-78.4%, whilst an overall rate of 28.4% was seen in all patients with suspected pertussis.

Conclusions: Mortality is predominantly in infants < 1 year with the rising prevalence of pertussis attributed to waning immunity in adolescents and adults. Laboratory confirmation was made only in approximately 25% of suspected cases, making accurate estimates of disease burden problematic and contributing to the under-reporting of pertussis in all age groups.

ROTAVIRUS GENOTYPES DIVERSITY AT THE FRENCH PAEDIATRIC EMERGENCY DEPARTMENTS

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Background and aims: Rotaviruses are the major cause of acute gastroenteritis (AGE) in young children, and require a careful surveillance, especially in the context of vaccination program. This study was designed to evaluate the strains circulation and to detect the emergence of potentially epidemic strains in France.

Methods: This prospective study was conducted from 2006 to 2009 in children under 5 years old consulting for acute diarrhea at the pediatric emergency units of 13 French University Hospitals. Rotaviruses were detected in stools by rapid tests and genotyped by RT-PCR on the basis of their outer capsid proteins VP4 (P type) and VP7 (G type).

Results: The genotyping of 1981 rotaviruses showed that G1 strains (59.8%) were predominant, followed by G9 (25.9%), G2 (4.3%), G3 (3.0%) and G4 (2.0%). Most strains were associated with P[8] (90.5%). Mixed infections, mostly G1/G9 associations, were found in 3.6% of stool samples. The distribution of genotypes was heterogeneous, regional frequencies regarding G1 and G9 ranged from 31.6% to 87.8% and 5.1% to 41.1%, respectively. Finally, 26 atypical reassortant strains were detected of which several G8 and G12 rotaviruses.

Conclusions: The G1P[8] and G9P[8] strains are the main rotaviruses circulating in France and account for 85.5% of AGE. The surveillance of rotavirus infections should be maintained to document strains distribution and their clinical expression, and to assess the emergence of new reassortants that may be likely to cause severe gastroenteritis and not respond to current rotavirus vaccines.

ROTAVIRUS INCIDENCE AND GENOTYPE FLUCTUATIONS IN THE GASTHUISBERG UNIVERSITY HOSPITAL, THREE YEARS AFTER NATIONAL ROTAVIRUS VACCINE INTRODUCTION IN BELGIUM

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Background and aims: Since 1999, the genotype incidence of circulating rotavirus strains has been monitored in the Gasthuisberg University Hospital, Leuven, Belgium. In 2005, we published the genotyping results for the period 1999 and 2003. Here we describe the following 6 rotavirus seasons between 2003 and 2009. Rotarix™ was introduced into the Belgian market in 2006 and RotaTeq™ in 2007, and currently more than 80% of newborns in Belgium are being vaccinated against rotavirus.

Methods: Rotavirus genotypes were determined by sequence analyses.

Results: In the three seasons preceding the introduction of vaccination (2003-2006) the number of ELISA positive cases of rotavirus gastroenteritis cases was respectively 193, 188 and 185. In the three seasons after vaccine introduction (2006-2009) the number of cases dropped to 99, 66 and 42 respectively, representing an approximate 30-50% decline in each season post vaccination, or a cumulative decrease of approximately 75%. As Rotarix™ contains an attenuated G1P[8] rotavirus strain, we were interested to see if genotype fluctuations would be influenced by the vaccine. The prevalence of the G2 genotype strongly increased in the 2006-2007 rotavirus season compared to the previous seasons and remained high (30-40%) in the 2007-2008 and 2008-2009 seasons.

Conclusions: Vaccination has strongly reduced the number of rotavirus positive cases in the Gasthuisberg University Hospital. It is unclear if the increased prevalence of G2 is related with the vaccine introduction, or if this is attributable to normal genotype fluctuations. Continuing surveillance will be pivotal to be able to answer this question in the future.

LARGE VARIATIONS IN ROTAVIRUS (RV) DISEASE AND STRAIN DIVERSITY DURING LOW-LEVEL VACCINE USE IN PORTUGAL

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Background and aims: RV vaccine became available in Portugal in May 2006. Although, to date, it is not included in the National Immunisation Program, the estimated coverage increased from 15% in 2007 to 35% in 2009. The aim of this study was to identify trends in RV disease and strain diversity over this period.

Methods: From 2006 to 2009, during the epidemic season (January-June), all children < 3Y, attending our Emergency Service, with acute gastroenteritis (AG) and available stool samples had them tested for RV. Genotyping was performed in positive samples.

Results: A total of 1565 children were studied (2006=475, 2007=467, 2008=267, 2009=356). The proportion of RV+ tests was: 2006=45%, 2007=36%, 2008=22%, 2009=31%. G9P[8] the most frequent type in 2006(90%) went down to very low proportions in 2008(1.9%) and 2009(10%). The opposite trend was observed for G1P[8] which increased progressively to become the predominant type in 2009(62%). G3P[8] was the predominant type in 2008(41%) and not detected in 2009. G2P[4] undetected in 2006, was found in a significant proportion of cases in 2007(22%) and 2008(31%). G4P[8] was found for the first time in 2009(18%).

Conclusions: Differences in proportion of AG cases attributable to RV in the different seasons were seen, with a trend suggestive of diminishing cases of RVAG. Also, co-circulation of different strains in the same geographic region and marked inter-seasonal fluctuations in the strain distribution were observed even with relatively low vaccine coverage. Attribution of changes in RV epidemiology to vaccine usage should be done with caution.

VACCINE FAILURE IN THE 2006 UNITED STATES MUMPS OUTBREAK AND IMPLICATIONS FOR PREVENTING FUTURE OUTBREAKS

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Background and aims: In the United States two doses of MMR vaccine have been routinely recommended for children since 1989. Despite that, in 2006 the US experienced a large mumps outbreak among highly vaccinated individuals. Other areas, including the Czech Republic, Ireland, and the United Kingdom, have also reported mumps outbreaks among highly vaccinated populations, bringing into question the effectiveness of current vaccination strategies.

Methods: We reviewed US national vaccine coverage estimates, case surveillance data, and military vaccination policy and disease rates.

Results: Since 1995 national one-dose MMR coverage has been $\geq 90\%$, and two-dose coverage has risen from 68% to 89% between 1997 and 2008. Following years of little mumps disease, 6,584 cases were reported in 2006. Where vaccination status was known, 76% of case-patients had received ≥ 1 dose, and 57% had received 2 doses. Among the most highly affected group, 18-24 year-old college students in the rural Midwest, 89-99% received 2 doses. In the United States, an unknown number of military recruits had received a 3rd vaccine dose. Incidence averaged 2.2/100,000, and no outbreaks were reported since data were available in 1998.

Conclusions: The key to preventing mumps outbreaks is to reduce the build-up of susceptibles in the population through high MMR vaccination coverage. During periods of low disease, immunity to mumps may wane, and susceptible individuals may accumulate. Serologic and vaccine coverage surveys may be useful to assess population immunity. Observations on the military may suggest a 3rd dose could play a role in preventing and/or controlling outbreaks.

INDIVIDUALLY-BASED DYNAMIC MODELING OF PERTUSSIS: THE EPIDEMIOLOGICAL IMPACT OF ADOLESCENT PERTUSSIS BOOSTER VACCINATION FOR THE NETHERLANDS

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Background: Despite widespread immunization programs, many developed countries are now considering the implementation of additional immunization strategies due to an increase in pertussis incidence. The epidemiological consequences of adolescent pertussis booster vaccination were evaluated within the Netherlands.

Methods: We designed a discrete event simulation model to pertussis transmission in the population. Three types of infection were considered: primary, recidive and asymptomatic. We used national age-specific notification data over the period 1996-2000 -corrected for underreporting- to calibrate the model assuming an endemic equilibrium. Thereafter adolescent vaccination was introduced. Other input parameters were obtained from literature (e.g. vaccine effectiveness: 90%) and expert opinions. As there is no consensus on the duration of immunity acquired by natural infection, we considered two scenarios with different durations (i.e. 8y and 15y). Duration of protection after vaccination was assumed at 8 years.

Results:

Table. Mean differences* in absolute incidence numbers between the current situation and the situation with adolescent pertussis booster vaccination over a 15 year period for a population of 150,000 people. Negative numbers indicate an increase in incidence numbers as a result of adolescent vaccination. Reduction in percentages are given between brackets.

Age	R _a = 8 years			R _a = 15 years		
	I ₁	I ₂	I ₃	I ₁	I ₂	I ₃
0 yr	2.7 (12.1)	≈0 (0)	≈0 (0)	3.8 (18.4)	≈0 (0)	≈0 (0)
1-3 yrs	9.7 (3.2)	19.0 (5.0)	55.3 (6.1)	17.1 (10.4)	21.9 (6.1)	74.2 (8.3)
4-9 yrs	33.2 (11.5)	475.6 (13.8)	1282.9 (15.1)	38.9 (14.2)	523.1 (16.6)	1555.5 (19.0)
10-19 yrs	140.2 (41.1)	7454.8 (29.4)	6540.4 (11.3)	142.7 (41.6)	6040.0 (32.0)	9435.7 (14.4)
20-49 yrs	≈0 (0)	-1184.8 (-2.9)	6752.2 (2.4)	≈0 (0)	-1015.9 (-5.2)	7646.3 (2.6)
50-74 yrs	0 (0)	-384.6 (-1.0)	4158.1 (2.2)	0 (0)	-372.3 (-2.0)	5353.6 (2.6)

R_a = Duration of protection after a disease episode.

I₁ = primary infection, I₂ = recidive infection and I₃ = asymptomatic infection.

≈ 0 refers to the situation where: -1.00 < incidence < 1.00.

*Due to the extensive running time of the model -related to the high complexity- only 20 runs per scenario were performed.

[Table]

In the population as a whole, implementation of adolescent booster vaccination reduced the absolute incidence of all infection types. A relatively large decrease in primary and recidive infections in 0-19 year old children was observed. However, concurrently, the relative number of milder recidive infections in the older age classes slightly increased (i.e. age shift).

Conclusions: Adolescent pertussis vaccination is likely to reduce the number of primary infections in children in the Netherlands, which has the biggest impact in terms of public health.

**SEROPREVALENCE OF HEPATITIS A IN MIGRANT AND FRENCH CHILDREN LIVING IN PARIS:
IMPLICATIONS FOR VACCINATION**L. Bourbotte, J.-F. Merittet, P. Lebon, **D. Gendrel***St Vincent de Paul Hospital / Paris 5 University, Paris, France*

Hepatitis A (HAV), in France as in other European countries, shows a seasonal peak in autumn due to import of HAV by young travelers returning from family visits in endemic areas who spread the disease in families and schoolmates. Recently (2009), preventive vaccination was recommended in France, not only in travellers, but also in children at risk of contact with persons returning from endemic areas. We have performed a systematic study, after approbation of ethical committee, on seroprevalence of HAV in children (1y-15y) never immunized and living in Paris area, according to their familial origin.

A total of 207 children were born in France (mean age 5.8y), and had never travelled. In the 81 children with a family of French origin HAV serology was negative, and in 5/126 (3,9%) with a father or a mother born in an endemic area, HAV serology was positive. Out of 59 (mean age 7.2 y) children born out of France, 17 (28.8%) had positive HAV serology. Among the 14 children born in a country of high endemicity (mean age 9.2 y) , 64.3 % had a positive HAV serology.

In France, more than 6 millions of residents (15 % of children) are travelling each year in countries of high endemicity for hepatitis A. Our data, showing the very low rate of positivity in children born in France, emphasize the importance of preventive vaccination before travel but also children staying in France and at risk of familial contact with a traveler.

2006-2009: PERTUSSIS PAEDIATRIC SURVEILLANCE, IN PRIVATE PRACTICE, IN FRANCE

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Background and aims: Between 1966 and 1995, French children received a primo-vaccination and one booster, with a highly efficacious pertussis whole cell (Pw) vaccine. In 1998, pertussis acellular (Pa) vaccines introduction allowed the administration of a second booster at 11-13 years of age. This age was chosen because the duration of protection of children immunized with Pw vaccine was estimated to be ~ 8-10 years. Between 2002 and 2006 pertussis surveillance in private practice (ACTIV) confirmed this duration of protection induced by Pw vaccines (Guiso, EID, 2008). ACTIV surveillance continued in order to evaluate the duration of protection induced by Pa vaccines.

Methods: Pediatricians enrolled suspected children (cough without fever, with whoops and /or cyanosis and/or vomiting) and completed standardized data form between 2006 and 2009. Biological confirmation of pertussis is obtained using either real time PCR or detection of anti-PT antibodies by the reference ELISA technique (>100IU/ml).

Results: Fifty-four pediatricians enrolled 166 suspected children. The ages of total number of confirmed cases, of vaccinated cases according to French recommendations and of non-vaccinated children are presented.

Conclusion: These preliminary data confirm the usefulness of the surveillance in the field in order to adapt vaccine schedule in accordance with epidemiological features of the disease now observed and the need of biological diagnoses to confirm the disease, particularly real time PCR.

	<i>Confirmed cases</i> <i>N = 60</i>	<i>Confirmed cases</i> <i>4 vaccinations with</i> <i>Pw and/or Pa</i> <i>N = 34</i>	<i>Confirmed cases</i> <i>Non vaccinated</i> <i>N = 11</i>
<i>Biological</i>			
<i>Diagnosis</i>			
<i>Culture</i>	4	3	1
<i>PCR</i>	27	10	8
<i>Serology ELISA</i>	23	19	1
<i>Epidemiological cases</i>	6	2	1
<i>Mean Age (years)</i>	6,6+/-5,1	8,5+/-3,6	3,2+/-5

<i>4 Pa</i> <i>n=10</i>	<i>4 Pw</i> <i>n=7</i>	<i>4 Pw+Pa</i> <i>n=17</i>
5,3+/-1,8	10,3+/-1,5	9,7+/-3,8

[Age of confirmed cases]

INCIDENCE OF PERTUSSIS IN CHILDHOOD AFTER PRIMARY AND BOOSTER VACCINATIONS

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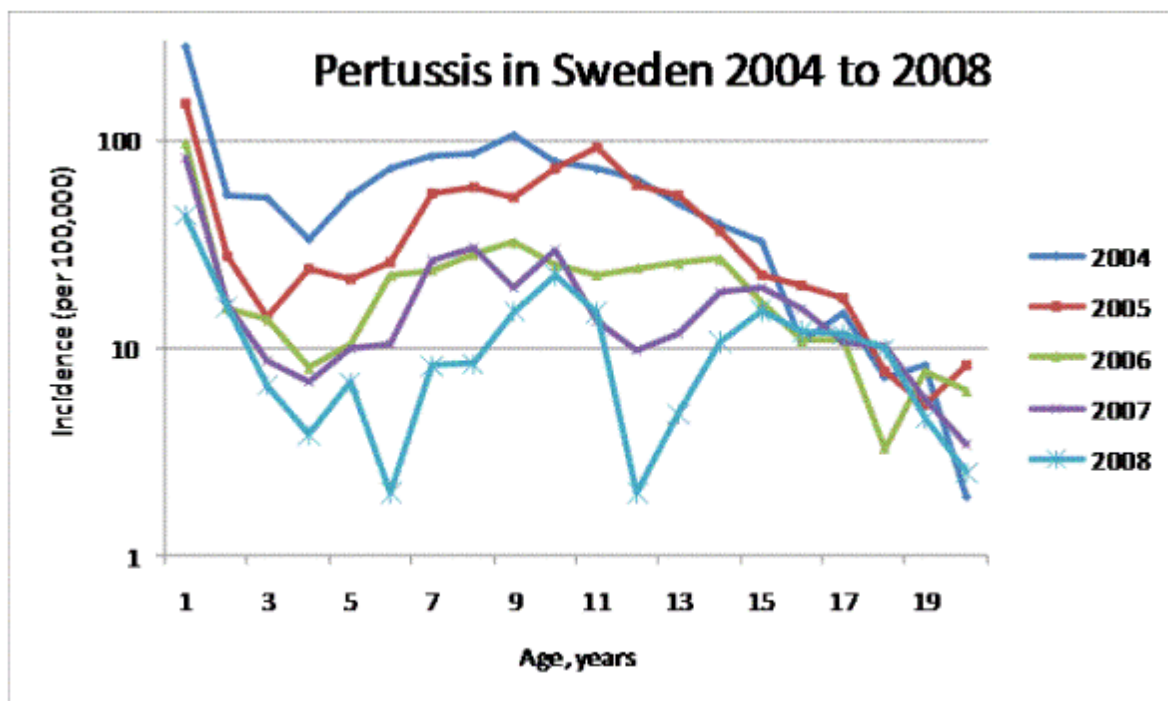
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Background: Acellular pertussis vaccination in infancy was introduced in Sweden in 1996. However, in spite of more than a decade of pertussis vaccination in childhood, pertussis is still an endemic disease in adults.

Aims: To describe the year-by-year incidence of pertussis since vaccination was introduced in 1996.

Methods: The overall incidence of laboratory confirmed pertussis has been documented in reports from the Swedish Institute of Infectious Disease Control. An Age-Period-Cohort (APC-) model was fitted to the reported data to estimate trends as well as the effect of a 5-6 year booster.

Results: The overall incidence in children from 1996 to 2008 has decreased from 96 to 4 cases and 100,000 children. The APC-model showed a significant effect for the booster at 5-6 years of age.



[Pertussis incidence 2004-2008]

Conclusion: We have shown that a booster dose at 5-6 years of age is an effective measure for reducing pertussis incidence. While the childhood incidence is decreasing, experiences from several countries show that resurgence in older ages pose a real risk. Our data show that pertussis booster doses can be used to keep the incidence under control.

MUMPS OUTBREAK IN JERUSALEM AFFECTING MAINLY MALE ADOLESCENTS**C. Stein-Zamir**, H. Shoob, N. Abramson, G. Zentner*Jerusalem District Health Office, Jerusalem, Israel*

Background: Mumps outbreaks, mainly involving adolescents and young adults, have emerged recently in several countries.

Methods: We performed an epidemiologic study of a recent mumps outbreak in Jerusalem.

Results: From mid-September 2009 to 25 November 2009, 107 cases of mumps have been reported in Jerusalem. The patients are mainly students (93/107 - 86.9%) in religious boarding schools; 87/107 males. The epidemic curve demonstrates a pattern compatible with person-to-person transmission. The median age -15 years; mean 15 ± 7.7 years. Altogether, 40 schools have been affected. Secondary cases in the household occurred in 24.3%. The clinical picture included unilateral and bilateral parotitis. One patient (a 19 year-old) was hospitalized with orchitis, 3 were admitted to ENT departments. Mumps IgM antibody test was positive in 12 patients, real-time reverse transcription-polymerase chain reaction (PCR) in urine was positive in 4 patients. The virus was classified as genotype G5. 70/107 patients (65.4%) had received 2 doses of MMR, 17 (15.8%) had received 1 dose (8 were age-appropriate), 12 (11.2%) - unimmunized and in 6 patients (5.6%) the status was unknown. Several patients reported contact with students from the United States (NY); some of whom were reported to have recently had mumps.

Conclusions: The two main characteristics of the current outbreak in Jerusalem are the predominance of male adolescents in religious boarding schools and the fact that most cases (74%) are appropriately vaccinated. Possible explanations include a combination of primary and secondary vaccine failure, waning immunity, inadequate vaccine effectiveness and specific living conditions.

DEVELOPMENT OF AN OPSONOPHAGOCYtic ASSAY TO *STREPTOCOCCUS PNEUMONIA* SEROTYPE 6C: DEMONSTRATION OF CROSS-FUNCTIONAL RESPONSES TO 6C IN PREVENAR-13 IMMUNE SERA

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Background and aims: Since the introduction of a 7-valent pneumococcal conjugate vaccine (PCV7), which includes serotype 6B conjugate, serotype 6B carriage and invasive pneumococcal disease (IPD) in the US has been largely eliminated. The incidence of serotype 6A IPD has also decreased, suggesting that serotype 6B conjugate provides cross-protection against serotype 6A. The recently identified serotype 6C is now recognized as a common carriage strain in the US and Europe. A 13-valent pneumococcal conjugate vaccine (PCV13) containing serotype 6A and 6B conjugates that has recently been approved in Europe was evaluated for its ability to elicit functional responses to serotype 6C.

Methods: The ability of serotype 6A and 6B conjugates to elicit OPA responses against a serotype 6C strain was assessed in subsets of sera collected post-infant vaccination from a clinical trial assessing the immune responses of PCV7 compared to PCV13.

Results: OPA responder rates were high (96%) for both serotype 6A and 6B in PCV13 immune sera. In PCV7 immune sera, responder rates were high (99%) for serotype 6B, and moderate (72%) for serotype 6A. In the subset of sera tested for serotype 6C, OPA responder rates were high (100%) in PCV13 immune sera, but low (< 20%) in PCV7 immune sera, suggesting that serotype 6A conjugate elicits cross-functional OPA responses to serotype 6C, while serotype 6B conjugate elicits minimal responses to serotype 6C.

Conclusions: The high OPA responder rate to serotype 6C elicited by PCV13 immunization suggests that PCV13 will protect infants against serotype 6C carriage and disease.

IMPACT OF TRAVELS ON CHILDREN HEPATITIS A SEROPREVALENCE IN FRANCE

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Background and aims: To determine the impact of travels in endemic areas on hepatitis A (HA) seroprevalence in children. Secondary objectives were to estimate the global HA seroprevalence in children in France and to identify risk factors for a positive HA serology.

Methods: A multicenter hospital-based seroprevalence study was performed in 8 paediatric emergency units in France. Specific HA antibodies (IgG) were measured in the serum of 4 children's age groups. Demographic, socioeconomic data and travels were prospectively collected within a standardized questionnaire. The main statistical analyses consisted of HA seroprevalence determination (with confidence intervals [CI]) and of uni and multivariate analyses of variables associated with a positive HA serology, including the role of travels in endemic areas.

Results: 487 children were included. The data of 430 children could be analysed. The HA seroprevalence was higher in the group of travellers (12% [95%CI, 6-18] vs. 2% [95%CI, 0-3], OR=7.0 [95%CI, 2.6-18.8]). 20 patients had a positive HA serology. The global seroprevalence was of 5% (95%CI, 3-7). After adjustment the variables associated with a positive HA serology were the age >14 years (OR=7.7; 95%CI, 1.6-38.3; p=0.01), to have a parent born outside metropolitan France (OR=5.2; 95%CI, 1.8-14.8; p< 10⁻³) and a previous travel in an endemic area (OR=4.3; 95%CI, 1.5-12.0; p< 10⁻³).

Conclusion: There is a statistical strong evidence in children of the role of travels in endemic areas on the HA serology. This study also confirms the low HA seroprevalence in children in France.

PNEUMOCOCCAL IMMUNISATION OF CHILDREN WITH CHRONIC RENAL DISEASES: IMMUNE RESPONSES TO CONJUGATE VACCINE AND POLYSACCHARIDE CHALLENGE

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Background/aims: There are few data on pneumococcal immunisation in high-risk children with chronic renal diseases.

Methods: We immunised PCV7-naïve children with 7valent conjugate vaccine(PCV7) and 6m later with (0.1ml)23valent polysaccharide vaccine(challenge). Serum collected before(V1&3) and 28-42days after(V2&4) each dose had IgG antibody to PCV7 serotypes(ST) measured(Luminex).

Results: 67 children(44 male) in 3 centres, aged 2.6-18.7y(median 11.7) had V1-2 serology; 63(42) 3.1-18.7y(11.9) V3-4. 38 were post-renal transplant; 15 chronic renal failure of whom 7 had renal replacement therapy and 2 pre-transplant. 2 had glomerulonephritis with low C3 and/or C4; 12 nephrotic syndrome (steroid resistant and/or frequently relapsing). GMCs are in the table.

ST	V1 n=67	V2 n=67	V3 n=63	V4 n=63
4	0.12	1.62	0.69	1.50
6B	0.25	3.16	2.07	2.31
9V	0.23	2.52	1.06	1.74
14	0.19	3.70	2.52	3.63
18C	0.19	2.92	1.42	2.19
19F	0.81	4.15	2.93	6.28
23F	0.26	5.13	2.60	3.80

[Geometric mean concentrations(GMC)($\mu\text{g/ml}$)]
 PCV7 antibody responses showed mean 13.9-fold rises (range 5.1-19.8 for the 7 serotypes). 82%(ST4&6B) to 90%(ST19F&23F) achieved $\geq 0.35\mu\text{g/ml}$.

Conclusions: After falling to mean 0.6 of post immunisation, a mean 1.6-fold titre rise (range 1.1-2.2) occurred after challenge, suggesting immunological memory. Children (n=11) who had received PPV23 prior to the study had lower responses to 6/7 PCV7 STs (p=0.006) suggesting hyporesponsiveness but similar fold-rises (p=0.1) on PPV23 challenge.

LONG-TERM IMMUNOGENICITY AFTER 2-DOSES OF THE ADULT FORMULATION COMBINED HEPATITIS A AND B VACCINATION IN CHILDREN AGED 1-11 YEARS

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Background and aims: A combination-vaccine (HAB) against viral hepatitis A and B (HAV and HBV) infections is indicated according to a simplified two-dose schedule in 1-15 year-old children and adolescents (with adult composition). This study assessed the long-term antibody-persistence and immune-memory induced by this vaccine 10-years after vaccination of children aged 1-11 years.

Methods: In the open-label primary vaccination study, 237 children received a HAB combination-vaccine (*Twinrix*TM Adult, GlaxoSmithKline Biologicals, 720EL.U HAV/20µg HBsAg) according to a 0-6-month schedule and were followed-up for 10-years. Yearly blood samples were collected and analysed to measure anti-HAV and anti-HBs antibody concentrations. A challenge dose of monovalent HBV vaccine was administered 6-12 months after the Year-10 visit to those with anti-HBs antibody concentrations < 10mIU/mL.

Results: One-month after the second dose of the primary vaccination course, 100% of subjects had anti-HAV antibody concentrations ≥15mIU/mL, while 98.5% had anti-HBs titres ≥10mIU/mL. At Year-10, 100% of the subjects had sustained seropositivity for anti-HAV, while 81.7% remained above 10mIU/mL for anti-HBs. The geometric mean concentrations (GMCs; mIU/mL) were 601.6 and 80.7 for anti-HAV and anti-HBs antibodies, respectively. 25 subjects received a challenge dose of HBV-vaccine. Post-challenge dose, all subjects demonstrated an anamnestic response, indicating the persistence of immune memory. The HBV-vaccine challenge dose was well tolerated.

Conclusions: In healthy children, the immune response to HAV and HBV induced by the two-dose primary vaccination schedule of adult formulation combined-HAB vaccine persists for at least 10-years after primary vaccination, conferring dual protection against hepatitis A and B disease.

SUSTAINED IMMUNOGENICITY AND EFFICACY OF THE HPV-16/18 AS04-ADJUVANTED VACCINE: FOLLOW-UP TO 8.4 YEARS

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Background and aims: We report efficacy and immunogenicity of the HPV-16/18 AS04-adjuvanted vaccine up to 8.4 years.

Methods: Healthy women, 15-25 years, DNA-negative for oncogenic HPV types, HPV-16/18 seronegative and with normal cytology at baseline received vaccine or placebo in a double-blind study (NCT00689741). Subjects were followed in extension studies NCT00120848 (full cohort) and NCT00518336 (Brazilian cohort; N=436). HPV-16/18 antibodies were measured annually by ELISA and pseudovirion-based neutralising assay (PBNA), in the according-to-protocol cohort (ATP). Cervical samples were tested 6-monthly for HPV DNA; gynaecological and cytopathological examinations were performed every 12 months. Vaccine efficacy (VE) is presented in the ATP for virological endpoints and in the total vaccinated cohort for cytohistological endpoints.

Results: Up to 8.4 years after first vaccination, all women were seropositive for HPV-16 and -18 antibodies by ELISA and PBNA, reaching a plateau ~18 months following first vaccination, with titres several-fold above natural infection levels. In extension NCT00518336 (2 years of follow-up), 5 incident infections and 1 \geq LSIL associated with HPV-16/18 occurred in the placebo group. VE (95% CI) against HPV-16/18-associated endpoints up to 8.4 years was 95.1% (84.6, 99.0), 100% (79.8, 100), 100% (56.1, 100), 94.6% (65.7, 99.9) and 100% (< 0, 100) for incident infection, 6-month persistent infection, 12-month persistent infection, \geq LSIL and CIN2+, respectively. There was no evidence of a difference in safety profile between groups.

Conclusions: The HPV-16/18 AS04-adjuvanted vaccine demonstrated high and sustained immunogenicity and efficacy against HPV-16/18-associated endpoints and a clinically acceptable safety profile, up to 8.4 years after first vaccination.

MEMORY B CELL DEVELOPMENT IN DIFFERENT PRIMARY DOSE SCHEDULES BEFORE AND AFTER NATIONWIDE INTRODUCTION OF THE PNEUMOCOCCAL CONJUGATE VACCINE

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Introduction: The CRM197-conjugated pneumococcal vaccine (PCV7) has been introduced in many national immunization programmes (NIP) worldwide, however with differences in the number and timing of primary and booster doses. Disappearance of circulating vaccine strains after widespread vaccination may implicate the loss of natural boosting of the immune system. Therefore, data on long term protection after different PCV7 schedules and the consequences of decreased natural boosting are important for further vaccination strategies.

Methods: We assessed plasma- and memory B cell responses in a cohort of children born in 2005 who received either a 2+1-dose PCV7 schedule or no vaccine (controls), well before implementation of PCV7 in the Dutch NIP in 2006. Secondly, we included a cohort of children between April-July 2009, previously receiving a 3+1-dose schedule, 3 years after nationwide implementation. All children were challenged with PCV7 at 24 months of age and blood was obtained before or one week after re-vaccination. PBMCs were plated in a direct and cultured ELISPOT to measure plasma and memory B cell numbers.

Results: After revaccination at 24 months, higher plasma and memory B cells could be found in infants receiving a 2+1-dose schedule in comparison to non-primed controls. B cell responses were comparable between the 2+1-dose schedule before PCV7 implementation and the 3+1-dose schedule after PCV7 implementation.

Conclusion: Both PCV7 schedules proved development of a memory response in comparison to non-primed controls. Adding a third primary dose of PCV7 did not result in higher memory, possibly due decreased natural boosting after implementation of PCV7.

SUCCESSFUL IMMUNE RESPONSE TO AEROSOL MEASLES VACCINE IN 9 MONTH OLD CHILDREN. A RANDOMIZED CONTROLLED TRIAL

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Aerosol measles vaccination is immunogenic and nonreactogenic as a booster among school-age children and as primary immunization in 12 month-olds; using the same dose immunogenicity is lower in 9 month-olds. We immunized 9 month-old children with aerosol measles vaccine using a higher dose than previous studies.

Methods: 113 healthy 9 month old children from Mexico city were enrolled; 58 received EZ measles vaccine by the aerosol route(A)($10^{3.85}$ TCID₅₀/0.5ml) and 55 subcutaneously(S)($10^{3.85}$ TCID₅₀/0.5ml). Blood samples were collected prior to vaccination, 3 and 6 months after immunization. Cellular immunity assays and neutralizing antibodies were performed. Clinical symptoms after vaccination were recorded.

Results: The percentage of children with a stimulation index (SI)>3 was 45% and 60% in A vs. 55% and 59% in S at 3 and 6 months (p=ns). After measles vaccination, the mean±SE SI was 4.38 ± 0.63 and 7.91 ± 2.05 in A vs 5.76 ± 0.87 and 6.74 ± 1.65 in S at 3 and 6 months (p=ns). CD8 memory cells increased in the aerosol group at 3 months (25.48 ± 2.95 in A vs 18.56 ± 1.72 in S, p=0.04). Mean±SE IFN γ levels after vaccination were equivalent. Seroconversion was 95% in A vs. 91% in S (p=0.43). Geometric mean titers were 373(441-843) and 1528(1470-2398) in A vs. 306(367-597) and 1214(1160-2193) in S at 3 and 6 months (p=ns). Side effects were comparable in both groups.

Conclusion: Using a higher dose than previous studies by the aerosol route, the cellular and humoral immune response and side effects are equivalent in 9 month old infants receiving measles vaccine by aerosol and subcutaneous route.

EFFECTIVENESS OF VACCINES FOR HEPATITIS B, CHECKING TITLE OF ANTIBODIES 1-6 YEARS LATER

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Background-aims: To check the effectiveness of HepatitisB (HBV) vaccine, based on the antibody title (a.t), of the commercially available vaccines: Engerix (E) and Recombivax (R).

Methods: 111 records of children and young persons, were collected based on their health books (70 girls between 0-23 years old that have been seen and vaccinated at the Health Center of Velestinos). 96.3% of the vaccinated people belonged in the Health region of Velestinos. The a.t that was considered protective was ≥ 10 iu/ml and was recorted based on the same method that was contacted in the local laboratories of Velestinos (79%) and Volos (21%) also. a.t value was checked 5 years (71%), between 5-6 years (24.5%) and between 1-5 years (4.5%), after the 3rd dose.

Results: More girls were vaccinated in total. 90% were vaccinated with Engerix and 10% with Recombivax vaccine. We checked the a.t of the persons (107) vaccinated at the Velestino Health Center only and find a range of a.t values and median value (m.v) of 103==>997 (m.v: 476) and 95 ==>446 (m.v: 264) respectively for "E" and "R".

Conclusions: Both vaccines lead to protective a. t, but the a.t value range and the median value is larger in the vaccine "E" and among girls. Despite the fact that our study population-group is of average size and statistically sufficient, in order to draw more objective conclusions, we need to study a larger sample size and other epidemiological factors.

EFFICACY OF THE ORAL PENTAVALENT ROTAVIRUS VACCINE IN ASIAN GAVI-ELIGIBLE COUNTRIES

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Background and aims: The efficacy of the pentavalent rotavirus vaccine (PRV) against severe rotavirus gastroenteritis (RVGE) was evaluated in a double-blind, placebo-controlled, multicenter Phase III trial conducted in 2 GAVI-eligible countries in Asia: Bangladesh and Vietnam (March 2007-March 2009).

Methods: 2,036 infants were randomized 1:1 to receive 3 doses of PRV/placebo at 6-, 10-, and 14-weeks of age along with routine EPI vaccines, including OPV. HIV-positive infants were not excluded; breastfeeding was not restricted. The primary vaccine efficacy (VE) endpoint was VE against severe-RVGE across Asia, defined using the 20-point Vesikari scale (score ≥ 11), from ≥ 14 days following the third dose through 2 years of follow-up. Gastroenteritis cases were assessed by clinic-staff assessments and parental-recollection reports. Stool samples were analyzed by rotavirus-specific EIA and RT-PCR to determine G/P genotypes.

Results: 2,036 infants were enrolled (1,136 Bangladesh; 900 Vietnam). VE against severe-RVGE was 48.3% (95%CI:22.3%-66.1%) through nearly 2 years of follow-up and 51.0% (95%CI:12.8%-73.3%) through the first year of life. Although VE against severe-RVGE through nearly 2 years of follow-up was numerically lower in Bangladesh (42.7% [95%CI:10.4%-63.9%]) than in Vietnam (68.1% [95%CI:7.6%-90.9%]), the number of severe-RVGE cases prevented per 100 vaccinated infants was greater in Bangladesh (4.4) than in Vietnam (2.3).

Conclusions: This was the first study to assess efficacy of a rotavirus vaccine in Asian GAVI-eligible countries. PRV significantly reduced severe-RVGE in Asia. These data support WHO recommendations for global use of rotavirus vaccines and provide a first estimate of the anticipated public health impact of rotavirus vaccines in Asia.

VACCINATION PROGRAM AND VARICELLA INCIDENCE IN AN ITALIAN POPULATION (SICILY)

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Background: In January 2003 Sicilian Health Authorities launched an universal vaccination program in all Sicilian Vaccination centers (VCs). To evaluate the impact of the vaccination program, two studies were implemented.

Methods: A coverage study involving local VCs started in 2003 and included all children 12-23 months of age and susceptible adolescents (18% of resident population of birth cohort 1993). A Surveillance study started in March 2005 to describe annual age-specific varicella incidence rates among children and adolescents 0 to 14 yrs, complications and hospitalization by vaccination status; age-specific incidence of herpes zoster by vaccination status. 30 Family Paediatricians (FPs) were randomly selected to participate, 30 monitoring visits were performed monthly and the database was audited (4 audits yearly).

Results: Coverage study: Data show mean coverage rates for the 12-23 month cohort increased from about 20% in 2003 to 35.4% in 2004, 49.7% in 2005, 62.4% in 2006 and 67.6% in 2007 (1st semester) (range between 52.9 and 87.4%). The target set up for this vaccination program was attained by 84.5% for children 12-23 month and by 57.6% for adolescents. Surveillance study: data were obtained from a total of 27,231 children (84.5% of the 32,235 eligible children). Annual varicella incidence rates declined from 97.2 (95% CI 90.1 ,102.6) for 1,000 PY in 2004 to 10.2 (95% CI 8.2, 12.6) for 1,000 PY during the 1st semester of 2007. Incidence declined in all age groups.

VACCINATION AGAINST NEISSERIA MENINGITIDIS GROUP C IN ICELAND

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Preventive measures such as vaccinations have decreased the incidence of life-threatening infections in children and are cost-effective. We evaluated the effect of vaccination against *Neisseria meningitidis* group C (MenC) in Iceland.

All positive bacterial blood cultures from children (0-18 years) at The Department of Clinical Microbiology, Landspítali University Hospital from September 1994 to March 2005 were evaluated. Over 90% of all blood cultures in Iceland are processed by The Department of Clinical Microbiology. The blood samples were mainly obtained at The Children's Hospital Iceland, but also from a few district hospitals. In some cases bacteria were obtained from spinal fluid only without blood cultures. We considered this to be equivalent to a positive blood culture.

Vaccination against MenC started in Iceland in 2002 (NeisVac-C®; Baxter). All children 0-18 years of age were vaccinated that year and the vaccine was included in the general childhood vaccination program at 6 and 8 months of age.

Neisseria meningitidis was isolated from 72 children during the study period with 42 strains being serogroup B (58,3%) and 30 serogroup C (41,7%). Prior to the introduction of the vaccine MenC was isolated on the average from 3,8 children per year (4,6/100.000/year). Since 2002 MenC has been isolated from only one unvaccinated child. Invasive MenC infections have also decreased in older age groups.

We conclude that MenC vaccination in Iceland has been very successful with no vaccine failures observed so far.

THE POTENTIAL PUBLIC HEALTH BENEFIT OF PNEUMOCOCCAL CONJUGATE VACCINES. EXAMPLE OF TURKEY

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Background & Aims: To define the potential public health benefit of vaccinating birth cohorts with pneumococcal conjugate vaccines: PHiD-CV, 7-valent (PCV-7) and 13-valent (PCV-13).

Method: A steady state model with a one-year time horizon was developed to project the impact of vaccination on the incidence of pneumococcal and non-typeable *Haemophilus Influenzae* (NTHi) infections in children aged 0-10 years. Data Sources: Turkey-specific epidemiological and demographic data. Model inputs: Payer perspective, 86% vaccine coverage, no herd protection and (3+1) vaccination schedule. One-way sensitivity analyses performed to assess the impact of changes in key model assumptions.

Results: PHiD-CV, PCV-7 or PCV-13 are projected to prevent more cases of invasive disease (978, 813, 997 respectively) and pneumonia hospitalizations (1,358, 1,039, 1,470 respectively) compared to no vaccination. PHiD-CV, PCV-7 or PCV-13 are projected to prevent additional myringotomies (11,179, 3,260, 5,470 respectively) and GP visits due to acute otitis media (AOM) (773,914, 225,675, 378,673 respectively) compared to no vaccination strategy. Vaccinating a birth cohort with PHiD-CV, PCV-7 and PCV-13 is expected to generate 11,311, 6,811, and 9,667 more QALYs compared to no vaccination. At price parity per dose, estimated total savings for healthcare system in 1 year post-vaccination of \$20.1M and \$14.2M for PHiD-CV compared to PCV-7 and PCV-13 respectively. Sensitivity analyses indicate that AOM efficacy and GP visits have biggest impact on results.

Conclusions: Overall, Synflorix would generate more QALYs and greater potential healthcare cost savings. Assuming vaccine price parity, Synflorix dominates both PCV-7 and PCV-13 because it has larger potential QALY gain and larger cost offset.

SEASONAL AND PANDEMIC A (H1N1) INFLUENZA VACCINATION COVERAGE AMONG HEALTHCARE WORKERS IN A SPANISH MATERNITY AND CHILDREN'S HOSPITAL

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Introduction: Although annual influenza immunization of healthcare workers (HCWs) is an important measure to prevent hospital transmission of influenza, vaccination rates remain low.

Objective: The aim of this study is to know vaccination coverage of seasonal and pandemic A (H1N1) influenza among HCWs in a tertiary maternity and children's hospital.

Material and methods:

Setting: Maternity and children's area of the Hospital Universitario Vall d'Hebron. Subjects: Medical staff, residents, nurses and nurses assistants (n=1439).

Methods : Active vaccination campaigns have been performed using mobile carts system. Seasonal influenza campaign has been initiated September 15, and the pandemic one, November 16. Logistic regression models have been performed to assess the association between pandemic A H1N1 influenza vaccination and sex, age, professional category and previous seasonal influenza vaccination.

Results: Pandemic A (H1N1) vaccination rate has been 13.3% (CI 95% 11.63-15.21) and seasonal vaccination 28.3% (CI 95% 25.97-30.69). Only 8% of HCWs received both vaccines. Professional group with highest coverage are doctors (38.1% pandemic vaccine and 44.2% seasonal). Resident physicians (OR: 13.4; 95% CI: 6.2-29.3) and previous seasonal vaccination (OR: 3.8; 95% CI: 2.7-5.4) are associated to pandemic vaccination.

Conclusion: Influenza immunization rates among HCWs in our centre are low, specially for pandemic vaccine. Educational programs are necessary for improving HCWs vaccination rates.

SEVERE OUTCOMES ATTRIBUTED TO INFLUENZA AND RESPIRATORY SYNCYTIAL VIRUS (RSV) IN ENGLAND, THE NETHERLANDS AND SPAIN

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Background: The necessary health impact data needed for decision making about paediatric influenza vaccination in Europe is lacking. We examined the burden of disease in children using rates of admission for primary cause pneumonia or influenza (P & I) as the main outcome measure in England, the Netherlands and Spain.

Methods: Weekly virological data for influenza and RSV, along with age-specific, hospitalization data from England, the Netherlands and Spain from three seasons (2002-2005) were used in a regression model, the EPIA model, where P & I hospitalization rate = $b_0 + b_1 * RSV + b_2 * Influenza + b_3 * \sin(2\pi t / 52.2) + b_4 * \cos(2\pi t / 52.2) + b_5 * t$. We controlled for the effect of RSV, another significant and co-circulating respiratory pathogen in children.

Results: In an average season, across the 3 countries, the EPIA model attributed 10 to 122 hospitalizations to influenza and 67 to 202 hospitalizations to RSV, per 100,000 children aged 0-4 years. For children aged 5-14 years, 0 to 6 admissions were attributed to influenza and between 0 and 7 admissions to RSV per 100,000 children.

Conclusions: We found that young children aged 0-4 years were at a 7-20 fold higher risk for influenza-related pneumonia hospitalization compared to older children. Differences within age groups as well as the patterns and magnitude of the burden between the countries will be discussed. Next we plan to consider a broader set of primary causes of hospitalizations, to obtain a more complete picture of disease burden attributable to influenza.

RATE OF VACCINATION WITH IMMUNOBIOLOGICAL AVAILABLE IN PRIVATE SECTOR OF HEALTH IN CHILDREN . RIO DE JANEIRO, BRAZIL

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The pediatric vaccination schedule available on public health in Rio de Janeiro does not cover vaccines recommended by Brazilian Society of Pediatrics such as meningitis, pneumococcal, chickenpox, hepatitis A and influenza. They are only enjoyed by who can payed for them.

Objective: To evaluate the rate of vaccination with immunobiological not offered by public sector of 248 children (1 - 7 years old).

Methods: We evaluate 248 vaccines books to quantify the rate of vaccination for pneumococcal (3 doses), meningitis (2 doses), varicella (1 dose), influenza (doses 1 and 2) , hepatitis A (1 dose) of 248 children who attended private day care nurseries in Rio de Janeiro in 2008.

Results: 50.40% (125) were female, 59.25% (147) had between 1 and 3 years old.

88% (218) of parents had higher education. Family income was greater than 10 minimum wages by 60% (148) of families. 24.50 %(61) of children were vaccinated for pneumococcal(3 doses), 26.80% (64) for meningococcal (2 doses) ,

41.53% (103) for chickenpox and 33.06% for hepatitis A. For influenza, 14.91% (37) (1 dose) and 14.11% (35) (2 doses).

Conclusion: Brazil has high rates of involvement in diseases such as meningitis, IPD, hepatitis A and influenza. A prime plot population (economic and intellectual level) maintains a low coverage of this vaccines despite they can pay for it. Efforts should be made by medical societies in order to spread more information on these vaccines who have extreme importance for the individual and community health.

IMMUNOGENICITY AND SAFETY OF HEPATITIS A VACCINE IN PEDIATRIC PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: There are only a few studies on immune response to routine vaccinations in pediatric patients with inflammatory bowel disease (IBD), despite the fact, that these studies are strongly required. The aim of the study was to evaluate the immunogenicity and safety of an inactivated hepatitis A vaccine in these group of patients.

Methods: Hepatitis A vaccination using 720 Elisa units were administered at 0 and 6-12 months. Seroconversion and geometric mean titers were measured after each vaccine dose. An antibody response >20 mIU/ml was considered as protective. The evidence of local and systemic adverse effects for 3 days after the first and second dose of vaccine was registered.

Results: 134 subjects, 66 patients and 68 controls completed the study. There was no significant difference in the rate of seroconversion between IBD patients and controls if measured after the second dose of vaccine (97% vs. 100%, $p=0.2407$), but was statistically lower in IBD group if measured after the first dose (39% vs. 64%, $p=0.00001$). The mean geometric titers were statistically significant lower in IBD group than in control group at all of the measure time points (after the first vaccine dose: at 4th week $p< 0.00001$, at 12th week $p< 0.00001$, before the second dose $p< 0.00001$, 4 weeks later $p< 0.0001$, and 12 weeks later $p< 0.000001$). There were no serious adverse events related to hepatitis A vaccine during the study.

Conclusion: Hepatitis A vaccine is both immunogenic and safe in pediatric patients with IBD.

CHANGES IN VACCINATION COVERAGE AGAINST HUMAN PAPILOMA VIRUS AMONG GIRLS AGED 14 YEARS IN MADRID

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The recommendation for vaccination against the human papiloma virus of girls born in 1994 went into effect on September, 2008 in Madrid, while the vaccination of girls born in 1995 went underway in 2009. These girls are currently being vaccinated once they turn 14. The vaccine is fully publicly financed. The vaccine administered is the tetravalent HPV vaccine administered at intervals of 0-2-6 months. Distribution of a specific batch of this same vaccine was put on hold in Spain this past February.

We currently have access to a software programme based on the nominal data found in our vaccination databases. This programme allows us to analyse the data on administered vaccines according to such characteristics as number of doses, date of birth, place of vaccination, and according to the doctor who administered the vaccine. We can thus analyse the progression of vaccination coverage rates in great detail.

During the first 11 months of the vaccination campaign we reached the following coverage rates for the cohort of girls born in 1994: 91,3% for the 1st dose, 85% for the 2nd dose and 71% for the 3rd dose and in girls born in 1995 we've reached the following coverage rates: 62.6% for the 1st dose, 54.4% for the 2nd dose, and 25.9% for the 3rd dose.

Significant differences in coverage rates may be observed between the two age cohorts we've analysed. Consequently, an active recruitment campaign will take place amongst the unvaccinated girls in order to improve the current results.

SAFETY OF 2-DOSE REGIMEN WITH COMBINED MEASLES, MUMPS, RUBELLA AND VARICELLA LIVE VACCINE (PROQUAD®) MANUFACTURED WITH RECOMBINANT HUMAN ALBUMIN (RHA)

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Background and aims: ProQuad® manufactured with recombinant human albumin (rHA) combines 2 well-established vaccines; measles, mumps and rubella (M-M-RVAXPRO®) and varicella (VARIVAX®). The aim of this single-arm, open-label study was to describe the safety of a two-dose schedule of ProQuad rHA administered to children in their second year of life.

Methods: Healthy children received 2 doses of ProQuad, 4 weeks apart. The primary objective was to document the safety of the second dose and the secondary objective, the safety of the first dose. General safety was evaluated on Day 0-28 following each dose and serious adverse events (SAEs) for the whole study.

Results: 3,388 infants were vaccinated and 3,346 received 2 doses. Mean age at Dose 1 was 14.6 months (range 11.5-23.8 months). After Dose 2, the frequency of infants experiencing solicited injection-site reactions (erythema 30.5%; swelling 13.2%; pain 11.5%), rashes of interest (2.8%), vaccine-related non-serious systemic AEs (13.4%) and temperature equal or above 39.4°C (12.1%) was consistent with previous studies. A total of 16 febrile seizures were reported following Dose 1 (10 subjects) or Dose 2 (6 subjects) and for all cases except one, infectious disease was reported concomitantly by the investigator. Neither serious allergic-type adverse events nor anaphylactic reactions were reported after either dose.

Conclusions: ProQuad rHA was well tolerated after both first and second dose, and the results of this study support the safety of M-M-RVAXPRO and ProQuad vaccines manufactured with rHA.

IMMUNOGENICITY AND SAFETY OF A 2-DOSE REGIMEN OF PROQUAD® ADMINISTERED TO HEALTHY CHILDREN FROM 9 MONTHS OF AGE

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Background and aims: WHO and some European countries recommend a first dose of measles or measles, mumps and rubella (MMR) vaccination under 12 months of age. To comply with those recommendations, this study evaluated the immunogenicity and safety of a two-dose regimen of ProQuad®, which combines MMR (M-M-RVAXPRO®) and varicella (VARIVAX®), in healthy children from 9 months of age.

Methods: In this open-label, randomised, 3-arm comparative (1:1:1 randomisation), multi-centre study a total of 1,620 healthy children received ProQuad; first dose at the age of 9 months (Group 1), 11 months (Group 2) or 12 months (Group 3) and second dose 3 months later. Primary outcome: seroprotection rates (SPR) to MMRV (Day 42 following the second dose); safety criteria (Days 0–28 following each dose).

Results: Following the second dose of ProQuad the SPR in Group 2 (mean age 11.2 months) for mumps, rubella and varicella ($\geq 99.3\%$) and measles (98.0%) were non-inferior to Group 3 (mean 12.3 months) being $\geq 99.5\%$ and 98.8%, respectively. The SPR in Group 1 (mean 9.5 months) for mumps, rubella and varicella ($\geq 99.2\%$) were non-inferior to Group 3. Non-inferiority for measles was not observed, but SPR was almost 95% (94.9%). ProQuad was generally well tolerated in the 3 groups.

Conclusions: A two-dose regimen of ProQuad with a 3-month interval between doses could be given from 9 months of age if early protection is deemed necessary.

KNOWLEDGE,BELIEVES AND PRACTCES SURVEY CONCERNING IMMUNIZATIONS AMONG ALGERIAN PARENTS

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Vaccines have demonstrated an efficacy against viruses diseases.

Aim: To evaluate knowledges, believes and practices concerning immunizations among algerian parents.

Methodology: Survey by interviewing algerian parents from 29/11/09 to 03/12/09.

Results:

248 parents were interviewed.

Sex ratio:0,5.

Median age: 28 years

91% of parents were afraid from hepatitis,tuberculosis,menigitis.

11% of parents were afraid from influenzae.

11% of the parents thought that their children will have infectious diseases.

30% of the parents thought that immunizations protect against infectious diseases.

70% believe that washing hands can prevent from infectious diseases.

95% of parents thought that immunizations have side effects.

83% of parents give antipyretics to their children after immunizations.

Conclusion: A program of information concerning immunizations has been established and destined to the parents.

ROTAVIRUS VACCINATION EFFECTIVENESS IN CASTELLÓN (SPAIN). PRELIMINARY RESULTS USING DATA FROM A SPECIFIC DIARRHOEA STUDY AND THE REGIONAL VACCINE REGISTRY

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Background and aims: Since 2006 two rotavirus vaccines have been licensed in Spain. We have evaluated the rotavirus vaccination effectiveness (rVE) among children between 1 month and 3 years of age.

Methods: Case-control study. All children which tested positive to faecal samples in a public laboratory during the first six months of 2009. Cases were positive for rotavirus, and controls were positive for other causes. We accept as vaccinated a child with at least one dose of vaccine. We also did a comparative study using pneumococcal vaccination as exposure factor instead of rotavirus vaccinations to evaluate pneumococcal vaccination effectiveness against rotavirus diarrhoea, (in this case we expected no effect). We calculated odds ratios (OR) with 95% confidence intervals (CI), and VE (=1-OR) adjusted by age, sex, hospitalization and immigration.

Results: 189 children were included, 79 cases with rotavirus diarrhoea, and 110 controls. The proportion of rotavirus vaccinated among cases and controls were 2.5% and 22.7% respectively. Crude rVE=91.2% (61.5-80.0), adjusted rVE=92.6 (65.6-98.4). When we carried out the same analysis using pneumococcal vaccination, the proportion of vaccinated children was 50.6% among cases and 53.6% among controls, with no differences (crude p value=0.683, and adjusted p value=0.734).

Conclusions: This analysis supports the effectiveness of rotavirus vaccination in children in Castellón. There are some limitations, as we do not know rotavirus serotypes and have not performed differential analysis by type and doses of rotavirus vaccines. Counterpart analysis using pneumococcal vaccine serves to evaluate potential bias in our study.

TITLE: CAN INTRODUCTION OF ROTATEQ® IMPACT ON TIMELINESS OF OTHER SCHEDULED VACCINES?

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RotaTeq® (Rotavirus vaccine, live, oral, pentavalent) is a three dose vaccine that has been funded since July 2007 under the National Immunisation Program in Victoria to protect infants against Rotavirus gastroenteritis.

The purpose of this study is to determine the impact of timeliness pre- and post- introduction of RotaTeq® vaccination on paediatric vaccines (using DTPa or Infanrix® as proxy):

- pre-RotaTeq® defined as January to June 2007
- post-RotaTeq® defined as January to June 2009

No supply issues or events that may skew data were defined in the periods to be analysed.

Comparison of timeliness of RotaTeq® with the timeliness of Infanrix® will be made across 4 divisions of General Practice in the Eastern Region of Melbourne who are members of the Eastern Region Immunisation Committee

Timeliness is defined as the dosing windows specified in the RotaTeq® product information:

- Dose 1 : 6-12 weeks of age
- Dose 2 : 10-28 weeks of age
- Dose 3 : 14-32 weeks of age

Infants who have not had timely RotaTeq® immunization will be excluded from this analysis.

Interim data analysis shows that the inclusion of a vaccine that has defined dosing windows into the National Immunisation Program has a significant effect on the timeliness of other scheduled vaccines and the completion of the primary immunization schedule.

Analysis of immunization provider type (General Practitioner or Local Government) and timeliness will also be undertaken to identify potential areas for education and quality improvement

SAFETY OF MF59[®]-ADJUVANTED SEASONAL AND PANDEMIC INFLUENZA VACCINES IN PEDIATRIC POPULATIONS AND PREGNANT WOMEN - PROSPECTIVE AND RETROSPECTIVE ANALYSES

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Background: The recent A/H1N1 influenza pandemic has highlighted the importance of adjuvants in enhancing immune responses and antigen sparing. Lack of efficacy of established alum adjuvants with some antigens has led to development of novel adjuvants. The oil-in-water emulsion, MF59[®], has been successfully used both in a seasonal influenza vaccine for the elderly (Fluad[®]), and recently developed A/H1N1 vaccines used from 6 months of age.

Methods: We performed prospective clinical studies of MF59 safety in 8883 children from 6 months to 18 years, and retrospectively examined the Novartis Vaccines clinical safety database for adverse events in adult and pediatric subjects exposed to MF59, including a sub-analysis of outcomes of pregnancies occurring in the course of studies involving MF59-containing vaccines.

Results: In completed and ongoing pediatric trials there is statistical evidence for a higher risk of mild or moderate, transient, local and systemic solicited reactions after exposure to MF59-adjuvanted than to non-adjuvanted vaccines, most typically increased tenderness. There was no general trend for an increased reactogenicity with subsequent vaccinations. Otherwise, unsolicited AEs, SAEs and premature withdrawals from studies are balanced between vaccines with or without MF59, and typical of pediatric vaccines. Although data on pregnancies are limited, they do not indicate any evidence of risk associated with receipt of MF59-vaccine. Ongoing experience with A/H1N1 vaccines confirms these findings.

Conclusion: Experience in pediatric populations confirms the general safety and tolerability of MF59-containing vaccines, consistent with data obtained in adults subjects and experience after over 45 million doses of MF59-influenza vaccine distributed.

ASSESSING CROSS PROTECTION FROM 2009 PANDEMIC H1N1 INFLUENZA THROUGH ABSENTEEISM OF SCHOOL TEACHERS INCLUDING COMPARISON WITH 2007 EXPERIENCE

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Background and aims: The 2009 pandemic influenza A (H1N1) virus has been necessarily novel, at least in those pre-retirement. To assess the cross protection to 2009 pandemic H1N1 influenza, a study was conducted in secondary school teachers. End point was staff absenteeism.

Methods: We performed a retrospective cohort study in a Queensland school. Data were obtained on a total of 122 junior and senior staff in 2007 and 67 senior in 2009. Seventy-two staff in 2007 and 38 in 2009 received seasonal trivalent inactivated influenza vaccine before the influenza seasons. The school closed for three-week mid-year holiday which allowed an assessment of absenteeism before and after the holiday. Cross protection was determined by comparing absenteeism (all causes) in staff who were vaccinated with those not.

Results: No significant difference in absenteeism (all causes) was detected between vaccinated and non-vaccinated groups in 2009 when the novel influenza A (H1N1) was circulating, whereas those given seasonal influenza vaccine in 2007 had lower absenteeism in 2007 than those non-vaccinated (1.5% compared with 2.2%, $p=0.05$) during the peak month for absenteeism when background rates of influenza were peaking (Absenteeism in other months was identical). School closure (mid-year holiday) did not obviously reduce absentee rates in 2007 or 2009.

Conclusions: We found no evidence that vaccination with 2009 seasonal inactivated influenza vaccine induced cross protection to pandemic H1N1 influenza among senior teaching staff as measured by absenteeism.

ADJUVANTED AND NON-ADJUVANTED INACTIVATED 2009 A/H1N1 INFLUENZA VIRUS VACCINE IN HEALTHY CHILDREN

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Background and aims: The 2009 A/H1N1 pandemic influenza virus has high morbidity in children. Vaccines that rapidly induce immune responses in this population are a medical priority. Adjuvanted influenza vaccines may offer a solution.

Methods: Two multicenter randomized, dose-ranging studies evaluated adjuvanted and non-adjuvanted egg-derived (NCT00971542) and cell culture derived (NCT00971100) 2009 influenza A/H1N1 vaccines in healthy children 6 months to 17 years of age. Subjects received two vaccinations of MF59[®]-adjuvanted vaccine containing 3.75- μ g or 7.5- μ g HA antigen or non-adjuvanted vaccine containing 15- μ g HA antigen 21 days apart. Children 7-19 years of age received only the adjuvanted vaccines. Serologic analysis was done 21 days after each vaccination. This interim analysis presents the results in subjects 3-8 and 9-17 years of age.

Results: After the first vaccination in each trial, both adjuvanted vaccines met the European regulatory (CHMP) criterion for seroprotection (>70% subjects with HI titre \geq 1:40). Seroprotection rates for the nonadjuvanted vaccine were 60% in children 3-8 years of age. All vaccines met the CHMP seroconversion (>40%) and GMR (>2.5) criteria in 3-8 and 9-17 year old children. Three weeks after the second vaccination all three CHMP criteria were met in all study groups. In both trials, solicited reactions were reported more frequently after adjuvanted compared with non-adjuvanted vaccines. Reactogenicity was generally lower after the second vaccination than after the first.

Conclusion: Adjuvanted egg- and cell culture-derived 2009 H1N1 influenza vaccines provided rapid immune responses at a lower HA dose than required for a vaccine without adjuvant.

LIVE ATTENUATED MEASLES, MUMPS, RUBELLA AND VARICELLA VACCINES FOR PEDIATRIC SOLID-ORGAN TRANSPLANT RECIPIENTS: SYSTEMATIC REVIEW

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Background and aims: Vaccine-preventable diseases like measles, mumps, rubella and varicella can cause serious complications in immunosuppressed children following solid-organ transplantation, but the opportunities for vaccination before the transplantation are usually limited. The aim of this review is to assess the immunogenicity and clinical outcomes of live attenuated measles, mumps, rubella and varicella vaccines in pediatric solid-organ transplant recipients.

Methods: We searched for english and spanish published articles using MEDLINE. Search terms included measles, mumps, rubella, varicella, vaccines, immunosuppression, transplantation and graft.

Only original studies of any design that reported administration of live attenuated viral vaccines in children aged 0 - 18 years after solid-organ transplantation were included. 2 authors selected the articles independently.

Relevant data and quality indicators of the studies were extracted independently by 2 authors. The quality assessment was performed using the MINORS instrument.

Results: Search retrieved 324 articles; of them, 7 case series with 130 participants met the inclusion criteria. Types of transplantation included were: liver (n=106), kidney (n=23) and small bowel (n=2). The percentages and proportions of vaccinees that developed serologic response for each type of vaccine were: measles-mumps-rubella (MMR): 56,7% (21/37); measles: 77,5% (31/40); mumps: 75% (15/20); rubella: 100% (17/17); and varicella: 72,8% (67/92). 4 studies reported clinical outcomes : 4 vaccinees of 51 developed varicella; no cases of measles, mumps or rubella were reported. 1 child had an acute rejection after the measles vaccine.

Conclusions: Live attenuated viral vaccines are safe and immunogenic in pediatric solid-organ transplant recipients.

THE ORAL PENTAVALENT ROTAVIRUS VACCINE: A SUMMARY OF SAFETY, IMMUNOGENICITY, AND EFFICACY CLINICAL TRIALS AND ONGOING ACTIVITIES

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Background and aims: Phase III pre-licensure clinical trials showed that the pentavalent rotavirus vaccine (PRV) was efficacious, immunogenic, and well-tolerated.

Methods: >70,000 healthy 6- to 12-week-old infants were randomized (1:1) to receive 3 doses of PRV/placebo at 2-, 4-, 6-months of age. Vaccine efficacy was measured against rotavirus gastroenteritis (RVGE) and RVGE-associated healthcare encounters (HCE), defined as hospitalizations and emergency department visits.

Results: PRV was efficacious against severe RVGE (98%) and RVGE of any severity (72%), regardless of serotype. Reductions in RVGE-associated HCE, for up to 2 years postvaccination, were 95% (Europe), 97% (US), and 90% (Latin American/Caribbean), with a 94% overall reduction for up to 3.1 years of follow-up after completing vaccination. Post-hoc analyses indicated that PRV provides high protection against RVGE-attributable HCE starting ≥ 14 days Postdose-1; the early protection afforded by PRV may be beneficial to infants vaccinated during rotavirus epidemic seasons. PRV elicited high (>93%) seroresponse rates (≥ 3 -fold rise from Predose-1 to Postdose-3) across pre-licensure studies without interfering with the immunogenicity of routine pediatric vaccines. Robust postlicensure evaluation of PRV confirmed the safety profile with 100% and 96% effectiveness against RVGE-attributable HCE/physician-visits in the US, respectively. Several locations in the US showed 85-95% reduction in RVGE-associated HCE in 2-2.5 years of routine use.

Conclusions: Merck and PATH recently completed clinical trials to evaluate the efficacy, immunogenicity, and safety of PRV in GAVI-eligible countries in Africa and Asia. These activities are important steps toward rotavirus vaccine introduction in the developing world, where burden of disease is substantial.

ENHANCING PASSIVE SURVEILLANCE OF ADVERSE EVENTS (AE) FOLLOWING VACCINATION BY INTEGRATION WITH CLINICAL SERVICES: THE MODEL OF SAEFVIC, AUSTRALIA

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Background: The state based Australian adverse events following immunisation (AEFI) reporting system has marked regional differences. To improve the AEFI services in Victoria, Australia, SAEFVIC commenced enhanced passive surveillance in May 2007. SAEFVIC comprises a central reporting surveillance system integrated with clinical immunisation nurse follow-up of all reports. There is associated physician review of reported cases and supervised vaccination where appropriate. The Brighton Collaboration, Australian Immunisation Handbook and in-house case definitions are used to categorise AEFI reported.

Aim: To describe SAEFVIC service model and summarise outcomes for the first two financial years of operation.

Methods: Service utilisation and data for AEFI reported between 01 July 2007 and 30 June 2009 were reviewed.

Results: Reports for 1680 persons were received, detailing 3138 AEFI. Each person had received from one to five vaccines (median = two). Forty per cent (n=1258) of AEFI met one of 31 established case definitions: the remainder were recorded verbatim. 687 (22%) of reported AEFI were considered severe. Clinical consults were attended by 643 persons: 392 (61%) were revaccinated on-site, of which 144 were day-stay or overnight inpatients. Reporting rates increased from 2.6 per 10⁵ in 2003 to 7.7 per 10⁵ per annum in 2009.

Conclusion: SAEFVIC provides a comprehensive surveillance system integrated with clinical support. The AEFI data are robust, however there are limitations, particularly when determining rates that require detailed vaccination coverage data. Enhanced passive AEFI surveillance using integrated clinical services improves adverse event reporting as well as clinical support for vaccinees and their health-care providers.

SERA FROM MACAQUES IMMUNIZED WITH 13-VALENT PNEUMOCOCCAL CONJUGATE VACCINE PROTECTS INFANT RATS AGAINST CHALLENGE WITH SEROTYPE-1, 3 AND 5 STRAINS

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Background and aims: *Streptococcus pneumoniae* serotypes 1, 3 and 5 are medically important pathogens not covered by the licensed 7-valent pneumococcal conjugate vaccine (PCV7). A 13-valent pneumococcal conjugate vaccine (PCV13), which contains serotype 1, 3 and 5 conjugates, has recently been approved in Europe. PCV13 immunization has been shown to induce functional opsonophagocytic killing responses in people to all 13 serotypes including serotypes 1, 3 and 5. To further support the protective responses of PCV13 to serotypes 1, 3 and 5, these serotypes were evaluated in an infant rat challenge model using passive transfer of sera from macaques immunized with PCV13.

Methods: Sera were collected from rhesus macaques prior to immunization and two weeks after a third dose of PCV13. Infant rats received interperitoneal (IP) injections of 100 μ L of pooled immune or preimmune sera followed by lethal IP challenges of serotype 1, 3 or 5 strains after 18 hours. Bacteremia was evaluated by enumeration of blood CFU three hours post-challenge.

Results: Immunization of macaques elicited OPA killing responses to serotypes 1, 3 and 5 (OPA titer = 560, 772, 400, respectively). Passive transfer of undiluted or 1:5 diluted immune sera, but not preimmune sera, significantly reduced bacteremia in the infant rats.

Conclusions: Immunization of macaques with PCV13 generated immune sera that protected infant rats from challenges with strains of serotypes 1, 3 and 5 in a passive transfer model. These data suggest that PCV13 will be highly protective against these pneumococcal serotypes in human populations.

AN AUSTRALIAN AUDIT OF VACCINATION STATUS IN CHILDREN AND ADOLESCENTS WITH INFLAMMATORY BOWEL DISEASE

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Background: Patients with inflammatory bowel disease (IBD) are increasingly treated with immunosuppressive therapies and are at higher risk of vaccine preventable diseases (VPDs). The aim of this study was to review the current immunisation status of children and adolescents with IBD, including additional recommended pneumococcal and influenza vaccines.

Procedures: A multi-faceted retrospective review of children and adolescents on the Victorian IBD database, aged 0-18 @ diagnosis. Immunisation status was reviewed through four sources:

- (1) hospital records
- (2) telephone survey
- (3) Australian Childhood Immunisation Register (ACIR) and
- (4) family practitioners immunisation records.

Results: The study was conducted between July -November 2007 with 101 participants, 50% female, median age at diagnosis 12.1 years. 74% had Crohn's disease, 23% Ulcerative Colitis and 50% were on active immunosuppressive therapy. The review included hospital patient records (101); telephone immunisation surveys (42); ACIR records (51) and primary care immunisation records (33). 91% (38/42) were up-to date with routine immunisations. Reviewing all sources, 10% had 'ever received' an influenza vaccine and 5% a pneumococcal vaccine booster. 18% (17/94) had documented serology for VPD (e.g. varicella; hepatitis B) and/or conditions which may flare with immunosuppressive therapies (e.g. hepatitis C, tuberculosis, HIV).

Conclusion: This study highlights a high level of vaccination coverage with routine scheduled vaccinations, but poor compliance with current guidelines for influenza and pneumococcal vaccination. Improving serological work-up prior to commencing immunosuppressive therapies may be of benefit. A multi-faceted approach is required to maximise protection from vaccine preventable diseases in this vulnerable population.

SYNCOPE AND SYNCOPAL SEIZURES FOLLOWING HUMAN PAPILLOMAVIRUS VACCINE

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Background: The Australia human papillomavirus (HPV) vaccination program commenced in May 2007 for females aged 12-26 years. Syncope and syncopal seizures can occur with any painful stimulus. High rates of both have been documented post HPV vaccination in the United States.

Aim: To describe cases of 'syncope' and 'seizures' post quadrivalent (4v)HPV vaccination notified to SAEFVIC (Surveillance of Adverse Events Following Vaccination in the Community) in Victoria, Australia.

Methods: All reports of adverse events following immunisation (AEFI) received by SAEFVIC between May 2007 - April 2009 were selected for analysis. AEFI following 4vHPV vaccine coded as seizure or syncope were reviewed.

Results: During the study period, 6% (97/1653) of all SAEFVIC reports met the criteria: afebrile seizures (3), syncopal seizures (31) and syncope alone (63). Median age at vaccination was 15 yrs (range 8-30 years). 23% (7/31) of syncopal seizures had associated urinary incontinence. An injury was sustained in seven cases, including one vertebral (T5/T6) fracture. After clinical review, further 4vHPV vaccine doses were given under supervision whilst lying down for 20 minutes to 21 women with no recurrences. The rate of syncopal seizures in the state of Victoria, Australia was 2.6 per 100,000 doses of 4vHPV vaccine distributed.

Conclusion: A high rate of syncope and syncopal seizures was seen post 4vHPV vaccination in Victoria. Clinical follow-up allows for clarification of the diagnosis, a physical examination and investigations as appropriate. Effective strategies to minimise the risk recurrent syncope post vaccination include lying down before and 20 minute post vaccination.

COSTS OF AN INVASIVE MENINGOCOCCAL DISEASE (IMD) OUTBREAK IN CAMPINAS, A CITY IN SAO PAULO, BRAZIL

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Background: Outbreak control, usually through chemoprophylaxis of index case contacts and vaccination of the surrounding community, is the sole intervention for IMD in many countries. A cost analysis of a small community outbreak (9 cases) within Campinas (population ~1,000,000) was performed

Methods: Administrative costs for epidemiological surveillance (Municipal Government data), direct costs for treatment of confirmed cases (National Health Service data), and indirect costs related to productivity impairment were collected through medical chart review, interviews and administrative documents for the time period beginning with the occurrence of the first case (7/10/2009) and ending 10 days after the last case (8/17/2009).

Results: The total expenditure to manage the outbreak was R\$ (Brazilian Real) 269,305.73 (approx. US\$ 158,415.13); of this, control strategies accounted for 86.9%. Treatment of confirmed cases averaged R\$ 3,570.93 per patient, and hospitalization accounted for 92.5% of this amount. Indirect costs totaled R\$ 3,220.44, for all nine patients.

Discussion: The cost to manage this small outbreak was significant, even if done in only a small part of the city. Several outbreaks occur annually in countries like Brazil and outbreak control will follow a similar pattern, with supposedly similar costs. Current official estimates only consider hospitalization costs.

The total cost of outbreak control for the country should be taken into consideration in the cost-benefit equation to include a vaccine in the routine schedule.

H1N1 VACCINE IN IMMUNOCOMPROMISED CHILDREN. REPORT FROM A SINGLE ONCOLOGY DEPARTMENT

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Background-aims: The emergence of the pandemic H1N1 swine-origin influenza-A virus has generated an additional need to become concerned with vaccinating immunocompromised children. We evaluate the compliance with vaccination against H1N1 in an Oncology department.

Methods: In our department around 80 new patients with hematological malignancies or solid tumors are treated every year. According to guidelines, we scheduled to vaccinate all patients on treatment as well as children during the first 12 months after the end of treatment. The available doses in our country were adjuvanted-inactivated vaccine. Immunocompromised children were scheduled to receive two half doses of the vaccine given 3-4 weeks apart holding chemotherapy the following week.

Results: A total of 169 patients were scheduled to be vaccinated. Ninety three of them were vaccinated in our department and 29 in other health center. Eighteen parents refused to have their children vaccinated whereas 8 children had already recovered from H1N1 infection. Twenty one children excluded since they were on intensive chemotherapy or radiotherapy. No major complications were detected except for local swelling resolving within a few days. None of the vaccinated patients experienced H1N1 flu for at least one month after having had their first dose, although Greece was experiencing the peak of the pandemic. Furthermore, a total of 107 parents or relatives were vaccinated at the same time in our department.

Conclusions: A remarkable compliance (88%, 122/140) was documented among parents of immunocompromised children eligible for vaccination. The vaccine was well tolerated and was proven effective for such a high risk population since no cases of H1N1 flu were detected so far among vaccinated children.

COMPARISON OF 0,6,14 WEEK AND 6,10,14 WEEK SCHEDULE OF HEPATITIS B VACCINE: A RANDOMIZED CLINICAL TRIAL

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Background: Although Hepatitis B vaccine administered by 0,1,6 months schedule has proven efficacy, it has been proposed that it can also be given by a variety of schedules; however this remains to be proven through a randomized controlled trial.

Objective: This randomized, controlled trial was carried out to compare the sero-efficacy of Hepatitis B vaccine administered to healthy infants by either of two schedules- birth (0 weeks), 6 weeks, 14 weeks or 6, 10, 14 weeks.

Methods: Ninety infants born to HBsAg negative mothers were randomized to receive recombinant hepatitis B vaccine at birth, 6 weeks, 14 weeks (Group A) or 6 weeks, 10 weeks, 14 weeks (Group B). Serum anti-HBs antibody titer was measured prior to the first dose of vaccine and six months after the third dose by laboratory personnel blinded to the intervention. All participants received other vaccines as per the national immunization schedule at different site.

Results: At 6 months after the third dose sero-conversion was 100% in both groups. 97.3% of subjects in Group A was sero-protected (>10 mIU/ml) with GMT of 113.78 mIU/ml and 94.6% in Group B (GMT 107.04 mIU/ml) [p=0.8].

Conclusion: Hepatitis B vaccine administered by 0, 6, 14 weeks and 6, 10, 14 weeks schedules are comparable in terms of sero-efficacy.

INFLUENZA IN VACCINATED CYSTIC FIBROSIS PATIENTS

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Background: For CF-patients annual influenza vaccination (InV) is recommended. InV efficacy in CF is not well documented but the immunogenic effect of InV in CF is thought to be comparable to that in healthy individuals.

Aims: To evaluate the impact of influenza infection in well-vaccinated CF-patients, using commercial trivalent inactivated influenza vaccine (TIV).

Methods: During 4 winter seasons, we prospectively collected nasal secretions by nasal wash for PCR and culture and/or blood for serology, for detection of influenza viruses in all CF-patients presenting with an acute pulmonary exacerbation. All CF-patients from the age of 6 months were vaccinated against influenza, according to ACIP recommendations.

Results: Influenza viruses were detected in 21/170 (12.4%) acute pulmonary exacerbations in 75 CF-patients (median age = 17y7m; sex ratio: F/M = 38/37). Influenza was mainly found in adolescent and adult patients, with a median age of 20y 7m in the infected group. Influenza A was found in 19 and influenza B in 2 episodes. In 13/19 influenza A and 1 influenza B infections the patient was febrile (body temperature >38.5°C) and in 8/19 influenza A infections the patient needed (prolonged) oxygen supplements. Hospitalisation was needed in 17/21 influenza episodes (mean stay: 11.7 days). Treatment with Oseltamivir was well tolerated.

Conclusions: Influenza is frequent in CF-exacerbations, especially in adolescents and adults, despite correct vaccination. Influenza in CF-patients is associated with a high morbidity. More data are needed to evaluate the effect of Oseltamivir on the bad course.

REASSESSMENT OF PRIMARY VACCINE FAILURE FOLLOWING VACCINATION WITH ONE OR TWO DOSES OF VARICELLA-ZOSTER-VIRUS CONTAINING VACCINES

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Background and aims: Further evaluation of the immunogenicity conferred by one or two doses of varicella-zoster-virus (VZV)-containing vaccines is warranted. In order to improve data quality and throughput, a commercial ELISA assay (B-ELISA, *Enzygnost*[™], Dade Behring) was selected to titrate anti-VZV antibodies after vaccination, and was used to reassess the immunogenicity of live attenuated (OKA strain) varicella-containing vaccines (*Priorix-Tetra*[™] and *Varilrix*[™], GlaxoSmithKline Biologicals) in six clinical trials (NCT00568334/00127010/00406211/00126997/00127023/00352898).

Methods: Anti-VZV IgG geometric mean concentrations (GMC) were measured by B-ELISA with a technical cut-off established at 25 mIU/ml. Correlation with well-established assays (immunofluorescence, FAMA, gpELISA) was explored. Seroresponse thresholds of 50 mIU/ml, 75 mIU/ml and 100 mIU/ml were explored for their relevance in describing primary vaccine failure (PVF).

Results: The B-ELISA assay correlated well with other assays. Based on comparison with historical data, a seroresponse threshold of 75 mIU/ml seemed to best account for PVF after one dose, and indicated response levels >98% post-dose 2. GMC post-dose 1 ranged 97-143 mIU/ml, GMC post-dose 2 ranged 999-2393 mIU/ml, across studies. GMC post-dose 2 were at least in the range of 1000 mIU/mL across all studied age groups (11 months to 6 years) and regardless of the studied interval between doses (4 weeks to several years).

Conclusions: A second dose of VZV-vaccine given to children up to 6 years in a broad range of intervals leads to minimal PVF and a significant booster response. These high antibody levels should provide additional protection against breakthrough varicella.

EFFECTIVENESS OF SEROGROUP C MENINGOCOCCAL CONJUGATE VACCINE: A 7-YEAR FOLLOW-UP IN QUEBEC, CANADA

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Background: In 2001, a mass immunization campaign was implemented to control an outbreak caused by serogroup C meningococcus and routine immunization (one dose at 12 months) was implemented thereafter.

Purpose: To assess the effectiveness of the campaign and of meningococcal C-CRM₁₆₉ conjugate vaccine over a 7-year period.

Methods: The study population includes residents in the province of Quebec and, specifically, individuals targeted in the 2001 mass campaign. Cases were confirmed serogroup C meningococcal disease (C-MD) notified to public health authorities or reported to the reference laboratory in 2002-2008. Vaccination status of cases was ascertained through telephone interview and review of immunization records. Vaccination registry and census data were used to estimate age-specific vaccination rates.

Results: In the whole population, C-MD incidence decreased from 7.8/million in 2001 to 0.6/million in 2008 and currently, C-MD is only seen in adults. In the cohort targeted by mass immunization, 11 C-MD cases had been vaccinated and 22 not vaccinated. The seven-year vaccine effectiveness was 90% (95%CI: 74%-96%). There was a tendency for increased protection according to the age at vaccination: 3 C-MD cases among 56,433 individuals vaccinated before one year of age and zero case among 3,705 non-vaccinated individuals in the same age-group; 85% protection for individuals vaccinated during the second year of life and 92% protection for those vaccinated ³ 2 years of age.

Interpretation: Seven years after the mass immunization campaign, the incidence of C-MD remains low in the population and vaccine effectiveness seems to persist to some extent.

CLINICAL DEVELOPMENT OF PANDEMIC (H1N1) 2009 VACCINES IN EUROPE AND THE UNITED STATES

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Recent pandemic preparedness efforts focused on A/H5N1 influenza viruses. Sanofi pasteur developed a non-adjuvanted H5N1 vaccine with high haemagglutinin (HA) content and a low dose adjuvanted vaccine. The 2009 pandemic involved a new swine origin A/H1N1 virus requiring new clinical studies and a separate clinical development plan to produce candidate A/H1N12009 vaccines. The US FDA approved a pandemic H1N1 vaccine modeled after seasonal influenza vaccines. Clinical trials of a 15µg HA/dose non-adjuvanted H1N1 vaccine started in August 2009. In contrast to unadjuvanted H5N1 vaccines, a single dose of the non-adjuvanted vaccine induced high levels of antibodies in adults exceeding the US and European criteria for influenza vaccines. A parallel trial in children helped to define the optimal HA doses for pediatric vaccines. Safety results of the pediatric trial showed similar rates of local and systemic reactions after either vaccine or placebo. In Europe, regulatory authorities expected low dose pandemic H1N1 vaccines to be developed through formulation of these vaccines with adjuvants, modeling H5N1 vaccines. Therefore, sanofi pasteur initiated the clinical evaluation an AF03-adjuvanted vaccine (3.8µg HA/dose), in parallel with a 15µg HA/dose non-adjuvanted vaccine. A single injection of either vaccine was highly immunogenic and a second injection further increased antibody most markedly in children than in adult or elderly subjects. Interestingly, a single injection of the AF03 adjuvanted vaccine was found to induce protective antibody levels in children less than 3 years. The safety profile of the AF03-adjuvanted vaccine was similar to the non-adjuvanted vaccine except for injection site pain.

RISK FACTORS FOR DELAYED UP-TO-DATE IMMUNIZATION STATUS OF PRETERM INFANT BEFORE TWO YEARS OF AGE**S. Denizot¹, J. Fleury¹, G. Caillaux¹, V. Bureau², J.-C. Rozé¹, C. Gras-Le Guen¹**¹*Perinatology, ²Réseau Grandir Ensemble en Pays de Loire, CHU de Nantes, Nantes, France*

Vaccinations of preterm infants are often delayed despite an increased risk of vaccine-preventable infections. We evaluate the vaccinal coverage of a population of preterm infants hospitalized between January 2003 and July 2005 in Nantes NICU. Sociodemographic data and vaccinal status were collected through a parental questionnaire constructed in collaboration with INSERM unit INED 822. Vaccines including Diphtheria/ Tetanus/ Polyovirus/ Pertussis and Haemophilus meningitis named DTCoqPolioHib and pneumococcal meningitis administered during the first two years of life were evaluated. Immunization status was observed at 5 and 24 months of chronological age. Up-to date immunization status was defined based on the recommendations of the Conseil Supérieur d'Hygiène Publique de France.

602 infants < 36 WG were included. Median age of the primary vaccination was 3 months and 5 days. We observed an initial vaccinal delay: 38.9% (CI 95% [35.06-42.82]) of children were up-to-date for DTCoqPolioHib and 22.2% (CI 95% [19.1-25.7]) for pneumococcus at 5 months. At 20 months, 67 % (CI 95% [63,6-70.7]) were up-to-date for DTCoqPolioHib and 36 % (CI 95% [32.36-39.9]) for pneumococcus. After multivariate analysis, a primary vaccine before discharge was strongly associated with a better vaccinal coverage at 5 months (OR=5[2.9-8.5] for DTCoqPolioHib, OR=4.5[2.6-7.8] for pneumococcus) and an unemployed mother have a better vaccinal coverage for her children at 20 months in our study (OR=1.7 [1-2.9] for DTCoqPolioHib, OR=1.6 [1-2.5] for pneumococcus). With an ever-increasing number of prematurely born infants continuous parental and health care providers information about vaccine recommendations are necessary.

EFFECTIVENESS OF A DEDICATED HEPATITIS B IMMUNISATION SERVICE IN THE PAEDIATRIC DEPARTMENT IN A DISTRICT GENERAL HOSPITAL SETTING

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Background: Hepatitis B infection can be transmitted vertically or horizontally in babies. Vertical transmission in infants bear 90% chance of becoming chronic carrier. Effective immunisation at birth can prevent this up to 95%.. All infants born to hepatitis positive mothers receive immunisation at 0, 1, 2 and 12 months of age. Our previous audit demonstrated that only 10% of infants completed the full immunisation schedule in a non-hospital based primary care, which led to introduction of multidisciplinary guideline for hepatitis B immunisation in hospital.

Aim: To determine the outcome of a dedicated Hepatitis B Immunisation service in a district hospital.

Methods: Retrospective review of maternal and infant medical records over a 32 months period ((April 2006- December 2008).

Results: A total of 10393 deliveries were recorded in the study period. 33(0.3%) mothers were positive for Hepatitis B. All infants received the first and second dose as recommended. 97% babies aged 2 months received the 3rd dose. All infants aged 12 months received the 4th dose. All babies underwent serology testing at 14 months. 95% of babies were HBsAg negative with HBsAb titres >100 and were discharged after serology. 1 baby had HBsAb titres < 10 and underwent a further course of immunisation. 3(8%) babies moved out of the area before completion of course.

Conclusions: There has been significant increase in immunisation coverage (100% in this audit) for all eligible infants born to Hepatitis B positive mothers. A dedicated hospital-based immunisation service can prevent development of chronic carrier state and hence its long term complications.

DETERMINANTS OF PAEDIATRICIANS INTENTIONS TO GET VACCINATED AGAINST A(H1N1)P INFLUENZA? PRELIMINARY RESULTS OF A SURVEY

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Background and aims: Physicians own behaviours are known to be strongly associated with their recommendations to patients. In the context of A(H1N1) 2009 influenza pandemic, we assessed knowledge, attitudes and practices of paediatricians regarding A(H1N1)p influenza and its prevention by vaccination.

Methods: A self-administered anonymous mail-based questionnaire was sent to 1852 Canadian paediatricians.

Results: All 714 questionnaires received by October 29th 2009 were included in the analysis (response rate 39%). More than 80% of respondents perceived A(H1N1)p infection as a serious disease, that occurs frequently and generates significant economic burden in the absence of vaccination. Respectively 79% and 74% of respondents considered the A(H1N1)p vaccine to be safe and effective. Most paediatricians (83%) intended to received A(H1N1)p vaccine. Intention to be vaccinated with the A(H1N1)p vaccine was significantly associated with: intention to recommend A(H1N1)p vaccine to patients (OR=7.48); perceived safety of A(H1N1)p vaccine (OR=2.37); perceived usefulness of seasonal influenza vaccine (OR=2.06); belief that A(H1N1)p influenza is severe enough to take special precautions to prevent it (OR=1.84) and number of hours spent in outpatient consultation (OR=3.58).

Conclusions: Most Canadian paediatricians intended to be vaccinated against A(H1N1)p influenza. A strong association existed between intentions to receive the vaccine and intentions to recommend it to patients.

**DETERMINANTS OF CANADIAN PARENTS' DECISION REGARDING ROTAVIRUS
IMMUNIZATION OF THEIR CHILD: PRELIMINARY RESULTS OF A LONGITUDINAL STUDY**

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Background and aims: Rotavirus disease is a common cause of health care utilization and almost all children are affected by the age of 5. In the context where rotavirus immunization is recommended, but not publicly-funded, main objective of this study was to examine the determinants of parent's acceptance to have their child immunized.

Methods: The survey instruments were based upon the theories of planned behavior and interpersonal behavior. Data were collected by telephone interviews. Main outcome measures were parents' intention to have their child immunized against rotavirus (phase I) and the children's immunization status (phase II).

Results: As of November 15 2009, 370 and 315 parents have completed respectively Phase I and II. Most parents (67%) intended to immunize their child against rotavirus. Factors significantly associated with parental intentions were: perceptions of the moral correctness of having their child immunized (partial $R^2=0.62$, $p < 0.0001$); perceptions that significant others will approve the immunization behaviour (partial $R^2=0.07$, $p < 0.0001$); perceived capability of having their child immunized (partial $R^2=0.02$, $p < 0.0001$); and household revenue (partial $R^2=0.01$, $p=0.0003$). In Phase II, 156 parents (49.5%) reported that their child was immunized against rotavirus. Perceived uselessness of the rotavirus vaccines (58%); belief that the children received too many vaccines (58%) and cost of the rotavirus vaccines (41%) were the most frequently reported barriers by parents of children not immunized against rotavirus.

Conclusion: The majority of surveyed parents held positive attitudes toward rotavirus vaccines. Most parents with strong intention to have their child immunized effectively did it.

DETERMINANTS OF CANADIAN PHYSICIANS' INTENTION TO RECOMMEND ROTAVIRUS VACCINES: PRELIMINARY RESULTS OF A PAEDIATRICIANS' AND PHYSICIANS' SURVEY

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Background and aims: Almost all young children are affected by rotavirus and more than half of cases seek medical care. In the context where rotavirus immunization is recommended, but not publicly-funded, vaccine uptake depends largely upon whether health professionals recommend it to parents. We assessed paediatricians' and family physicians' knowledge, attitudes and intentions regarding rotavirus vaccines.

Methods: A self-administered anonymous mail-based questionnaire based upon the Health Belief Model was sent to a sample of 1182 family physicians and 1852 Canadian paediatricians.

Results: Between 79% and 90% of respondents agreed with the statements regarding the health and economic burden of rotaviral disease and 77% had had experience with severe cases in their medical practice. Consequences of rotavirus infection among patients under the age of 3 were rated as mild (48%) or moderate (41%). Respectively 96% and 93% of the physicians perceived the rotavirus vaccines as safe and effective, and 80% estimated that their knowledge on rotavirus vaccines was sufficient. The majority of respondents (80%) intended to recommend rotavirus vaccines to their patients. Intention to recommend rotavirus vaccines was independently associated ($p < 0.0001$) with: perceived benefits of vaccination (partial $R^2=0.55$); perceived acceptability of the vaccine by vaccinators (partial $R^2=0.05$); self-estimated sufficiently of knowledge about rotavirus vaccines (partial $R^2=0.01$); perceived severity of rotaviral diseases (partial $R^2=0.01$).

Conclusion: Most paediatricians and family physicians manifested willingness to recommend the rotavirus vaccine. Although consequences of rotavirus gastroenteritis were perceived as mild or moderate, immunization against rotavirus was seen as beneficial for young children.

SETTING PRIORITIES FOR NEW VACCINATION PROGRAMS BY USING PAEDIATRICIANS AND FAMILY PHYSICIANS OPINIONS

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Background and aims: In Canada, several new vaccines were or will be soon approved and many new candidate public vaccination programs are in ongoing discussion. Health professionals' opinion toward new vaccines is well recognized to influence future decisions concerning immunization programs. We assessed paediatricians' and family physicians' perceived priority ratings for 7 new immunization programs implementation.

Methods: A self-administered anonymous mail-based questionnaire was sent to 3034 Canadian physicians. Basic Priority Rating System (BPRS) approach was used. Responses to 8 statements regarding frequency and severity of the diseases, efficacy and safety of the vaccines and feasibility of immunization programs were used to calculate the BPRS scores (minimal score 0; maximal score 100).

Results: 921 physicians participated (30%). Perceived usefulness of different new public immunization programs varied from 29% to 67%. The BPRS scores were: 77 for the quadrivalent measles-mumps, rubella and varicella vaccine (MMRV); 75 for the hexavalent vaccine (DTaP-Polio-Hib-Hepatitis B); 72 for the conjugate pneumococcal vaccine (PCV-10); 69 for the quadrivalent meningococcal vaccine (ACYW135); 68 for the combined hepatitis A and B vaccine; 63 for the HPV vaccine and 56 for the rotavirus vaccine. BPRS scores were not influenced by respondents' sociodemographic or professional characteristics or by self-estimated level of knowledge on the vaccines. Between 0.24% and 2% of respondents considered that a given immunization program would not be feasible.

Conclusion: Physicians' opinions regarding usefulness and feasibility of new immunization programs varied greatly depending on the vaccine. As shown in previous studies, combined vaccines received the highest ratings.

ACUTE OTITIS MEDIA AND ITS PREVENTION BY IMMUNIZATION: PRELIMINARY RESULTS OF A SURVEY ON PHYSICIANS KNOWLEDGE, ATTITUDES AND PRACTICES

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Background and aims: Acute otitis media (AOM) is one of the most common bacterial infectious diseases among children and is a leading cause of children healthcare visits and antibiotics prescription. A new 10-valent pneumococcal vaccine (PCV-10, Synflorix™) with a larger spectrum of protection against AOM was approved in Canada in 2008. We assessed paediatricians' and family physicians' opinions regarding AOM and its prevention by immunization.

Methods: A self-administered anonymous mail-based questionnaire based upon the Health Belief Model was sent to a sample of 1182 family physicians and 1852 Canadian paediatricians.

Results: All 921 questionnaires received by October 29th 2009 were included in the analysis. Between 94% and 98% of respondents agreed with the statements regarding the health and economic burden of AOM. Consequences of AOM among patients under the age of 3 were rated as mild (52%) or moderate (43%). Almost all physicians (99%) considered the PCV-10 vaccine to be safe and effective and 53% strongly intended to recommend new PCV-10 vaccine to their patients. In multivariate analysis, intention to recommend PCV-10 vaccine was associated ($p < 0.0001$) with: perceived benefits of vaccination (partial $R^2=0.40$); perceived acceptability of the vaccine by vaccinators (partial $R^2=0.10$); perceived acceptability of the vaccine by the population (partial $R^2=0.03$) and self-estimated sufficiently of knowledge about the vaccine (partial $R^2=0.02$).

Conclusion: AOM was perceived as an important health problem and physicians were favourable to its prevention by immunization. The reduction of antibiotic administration and post-AOM complications were seen as the main benefits of AOM prevention by immunization.

PHASE III FORMULATION DEVELOPMENT OF RECOMBINANT MENINGOCOCCAL B VACCINE (RMENB) CONTAINING FHBP, NHBA, NADA, AND NEW ZEALAND (NZ98/254) OUTER MEMBRANE VESICLES (OMV)

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Background: An OMV vaccine against NZ98/254 is licensed in New Zealand. Reverse vaccinology identified antigens included in rMenB: fHBP and NHBA and NadA.

Methods: Five studies were conducted. In Phase 1 studies, 3- and 4-dose regimens and a booster of rMenB±OMV from Norwegian (NWOMV) or New Zealand (NZOMV) strains were evaluated in 19-40 year-olds. HepB and MPSV4 were used as comparators. In a Phase 2 study, adolescents 11-18 years of age received rMenB±NWOMV or placebo. Immunogenicity was evaluated via hSBA titers ≥4 and GMTs against serogroup B strains (15 for Phase 1; 4 for Phase 2) and ELISA against vaccine proteins. Solicited injection site and systemic reactions were recorded for 7 days.

Results: Overall, 176 adults and 203 adolescents enrolled. In Phase 1, most participants receiving an rMenB vaccine had vaccine responses to most strains. Recipients of OMV vaccines had hSBA responses to more strains than rMenB-only recipients. ELISA showed robust responses to all proteins in the vaccines administered. Results following 3 or 4 doses of rMenB±NWOMV were generally similar. rMenB vaccines were more reactogenic than controls. Most participants reported injection-site pain after the first vaccination; fewer reported pain with subsequent doses or a booster. In early Phase 1 studies, increases in C-reactive protein were observed; increases were not observed in the study in which NZOMV-containing vaccine was administered or in the Phase 2 study in adolescents.

Conclusions: All formulations of rMenB containing vaccines were well-tolerated and immunogenic. The rMenB with NZOMV provided an optimal immunogenicity and safety profile.

INFLUENZA VACCINATION OF ASTHMATIC CHILDREN AGED 5-14, LOOKING AT THE REGULARITY OF VACCINATION OVER THE PAST 3 YEARS

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Background: Routine annual influenza vaccination is recommended for asthmatic children. The proportion of asthmatic children in age groups 5-9, and 10-14 vaccinated against influenza in each year of a 3 year period was analysed and the regularity of influenza vaccination was evaluated for years 2006-2008.

Methods: Vaccination and asthma prevalence data were taken from the RCGP Weekly Returns Service (WRS) database. The prevalence of asthma (defined as asthmatic patients with diagnosis/monitoring code between 01/01/2003 and 01/10 of the year in question, the latest being 01/10/2008) was analysed by age group and gender. The proportions of children vaccinated in each year were then determined. The proportions of children vaccinated in the third year who had received a vaccination for 3 consecutive years were obtained. The frequency of vaccination of asthmatic children was then analysed.

Results: The average annual prevalence was higher in males- aged 5-9 8.1% and 10-14 10.7% compared with 5.0% and 7.6% in females. Vaccine uptake data was similar in all 3 years; 16% in children aged 5-9 and 19% aged 10-14. Of those vaccinated in the third year 33% in age group 5-9, and 47% aged 10-14 had been vaccinated in 3 successive years. Of all asthmatic children 5.4% aged 5-9, and 8.7% aged 10-14 were vaccinated 3 years consecutively. Vaccination uptake was similar in both genders.

Conclusions: These results provide evidence that asthmatic children are not being adequately vaccinated against influenza. These results also indicate that < 10% of asthmatic children return annually for influenza vaccination.

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Background

Routine annual influenza vaccination is recommended for asthmatic children. The proportion of asthmatic children in age groups 5-9, and 10-14 vaccinated against influenza in each year of a 3 year period was analysed, the regularity of influenza vaccination was evaluated for years 2006-2008.

Methods

Vaccination and asthma prevalence data were taken from the RCGP Weekly Returns Service (WRS) database (years 2006-2008). Asthmatic prevalence (defined as an asthma Read code entry between 01/01/2003 and 01/10 of the study year) was calculated age and gender specifically. The proportions of children vaccinated in each year were determined. The uptake of vaccination in asthmatics was analysed in each year. The three year data set was examined to determine the frequency of vaccination.

Results

The average annual prevalence was higher in males- aged 5-9 12.8% and 10-14 15.0% compared with 8.7% and 11.4% in females. Vaccine uptake was similar in all 3 years; 15.9% in children aged 5-9 and 17.3% aged 10-14. Of those vaccinated in the third year 56.8% in age group 5-9, and 50.8% aged 10-14 had been vaccinated in 3 successive years. Of the total asthmatic children (5-14 years) 9.3% had been vaccinated in one of the three years, 6.1 % in two years and 8.6% in all 3 years but 76% of them had not been vaccinated in the three years.

Conclusions

These results provide evidence that asthmatic children are not being adequately vaccinated against influenza. These results also indicate that < 10% of asthmatic children return annually for influenza vaccination.

IMMUNE RESPONSE OF UNPRIMED CHILDREN YOUNGER THAN 3 YEARS OF AGE TO AN INCREASED AMOUNT OF VIROSOME-ADJUVANTED INFLUENZA VACCINE

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Background and aims: Immune response of children < 3 yrs to influenza vaccine is not always adequate. To increase immunogenicity, use of adjuvants or administration of an increased amount of antigens have been suggested. This study evaluated the immune response of younger children to a double dose of the virosome-adjuvanted influenza vaccine.

Methods: Unprimed healthy children < 3 yrs were blindly, randomly assigned 1:2 to receive 2 doses 4- week apart of 0.25 mL (standard dose, SD) or 0.50 mL (double dose, DD) of Inflexal V (Crucell). Blood samples collected pre-vaccination, 4 weeks after each dose and 6 months after the second dose were analyzed by hemagglutination inhibition test. Safety assessments were made at baseline and during 14 days after each vaccination.

Results: Among the 66 children enrolled, 25 received the SD and 41 the DD. Seroprotection rates for H1N1, H3N2 and B viruses after the first dose and 6 months after the second dose were significantly higher in children vaccinated with the DD than with the SD (73.2%, 75.6% and 56.1% vs 32%, 48% and 24%, $p < 0.05$; 92.7%, 92.7% and 52.1% vs 72%, 72% and 52%, $p < 0.05$). Antibody GMTs were always higher in children receiving the DD, with differences statistically significant one and six months after the first and the second dose, respectively. No significant difference was observed in adverse events.

Conclusions: Administration of a double dose of virosome-adjuvanted influenza vaccine permits to significantly increase the short and long term antibody response to influenza in unprimed young children.

IMMUNOGENICITY OF ONE DOSE OF VARICELLA VACCINE AND TWO DOSES OF MMRV VACCINE

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Background and aims: To evaluate the immunogenicity of the varicella component in measles-mumps-rubella-varicella (MMRV) vaccine (*Priorix-Tetra*[™], GlaxoSmithKline Biologicals) and varicella vaccine (*Varilrix*[™], GlaxoSmithKline Biologicals) using commercially available B-ELISA assay in an efficacy trial.

Methods: Observer-blind, randomised (1:3:3, controlled, multicentre study in 10 European countries. 12-22 month-old children (N=5803) received either two doses of measles-mumps-rubella (2xMMR), two doses of MMRV (2xMMRV) or one dose of MMR and one dose of V (MMR,V), 42 days apart. Varicella antibodies were measured at Days 0, 42 and 84 using the *Enzygnost*[™] Anti-VZV/IgG (Dade Behring) B-ELISA assay. Seroresponse technical cut-off was 25 mIU/ml and thresholds were set at 50, 75 and 100 mIU/ml for exploratory purposes.

Results: Antibody concentrations at Day 84 are shown in the Figure.

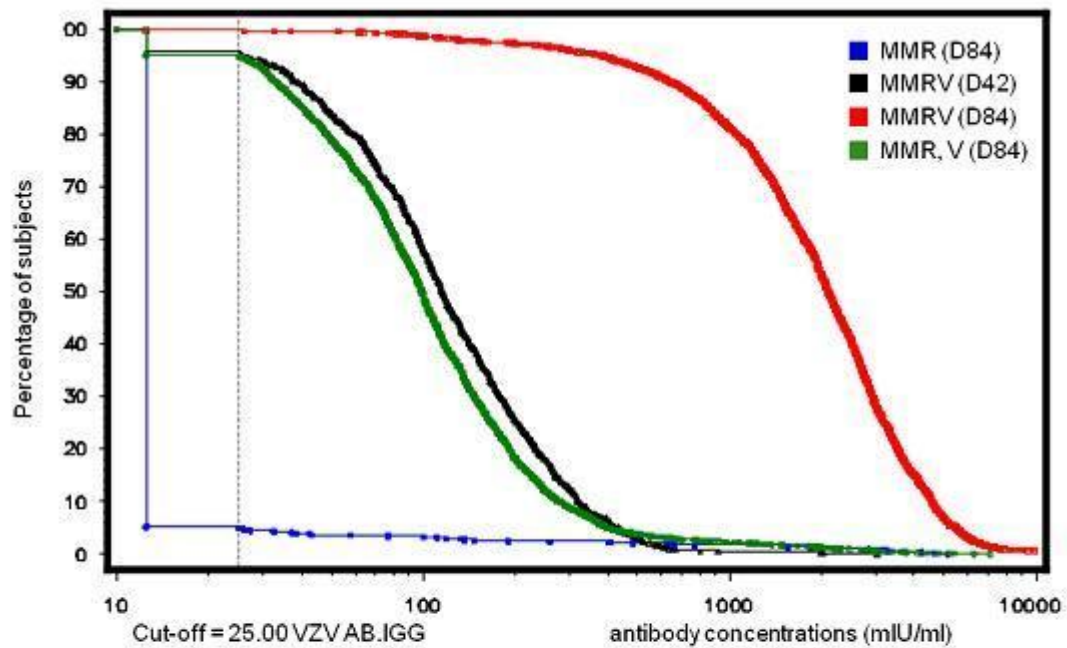


Figure. Reverse cumulative distribution curve (ANTI-VARICELLA antibody concentrations by B-ELISA) Post-vaccination Day 84 for one dose of varicella (MMR,V) and two doses of MMR and MMRV, and Post-vaccination Day 42 for MMRV (post-dose 1 of MMRV vaccine) on initially seronegative subjects (ATP cohort for immunogenicity, subset for Day 42, all for Day 84)

[Figure]

Seroresponse rates post-dose 1 were 79.2% [≥ 50 mIU/ml]; 64.8% [≥ 75 mIU/ml]; 49.7% [≥ 100 mIU/ml] in the MMR,V group; and 84.3% [≥ 50 mIU/ml]; 71.7% [≥ 75 mIU/ml]; 58.1% [≥ 100 mIU/ml] in the 2xMMRV group. Seroresponse rates post-dose 2 were 99.6% [≥ 50 mIU/ml]; 99.3% [≥ 75 mIU/ml]; 98.8% [≥ 100 mIU/ml] in the 2xMMRV group.

Conclusion: Data suggest a strong booster effect induced by the second dose of MMRV. This confirms historical data and further supports the need for a second dose of varicella-containing vaccine for optimal protection.

IGG RESPONSES AFTER AN EXTRA ACELLULAR PERTUSSIS BOOSTER VACCINATION IN DUTCH CHILDREN AT 9 YEARS OF AGE

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Background and aims: After introducing the acellular pertussis (aP) booster vaccine to 4 year old children, the peak incidence of whooping cough has shifted to 9-10 years old children. We investigated the effect of an extra aP booster vaccination in children 9 years of age on antibody responses and compared these with those found in 4 year olds.

Methods: Whole cell pertussis (wP) primed children (N=88), received an extra aP booster vaccination at 9 years of age (ISRCTN64117538). Blood samples were taken before and at 28 days after vaccination. IgG levels to pertussis toxin (PT), filamentous haemagglutinin (FHA), pertactin (Prn) and fimbriae type 2 and 3 (Fim2/3) were measured using a multiplex immuno assay. Antibody responses were compared with those found in aP and wP primed 4 year old children, a subset of a cross-sectional study (ISRCTN65428640).

Results: Pre booster IgG levels to all pertussis antigens were low. The post booster IgG-PT and IgG-FHA levels increased and were comparable in the 4 year old aP primed and the 9 year old wP primed children, but lower in the 4 year old wP primed children. The 4 year old aP children showed higher post booster IgG-Prn levels than the 4 and 9 year old wP primed children. Only in wP primed children IgG-Fim2/3 levels slightly increased.

Conclusions: An extra aP booster vaccination in wP primed children 9 years of age seems effective. The additional vaccination might reduce the incidence of *Bordetella pertussis* in this age group.

CD4+ T CELL RESPONSES TO CANDIDATE PNEUMOCOCCAL FUSION PROTEIN VACCINES IN PAEDIATRIC ADENOIDAL AND PALATINE TONSILS

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Background and aims: Previously, we have shown that T cell responses to pneumolysin (Ply) are strong in children, and that in mice, both Ply and a non-toxic variant ($\Delta 6$ Ply) have adjuvant effects on antibody responses when fused to pneumococcal surface adhesin A (PsaA). As the use of existing conjugate vaccines is limited, new vaccines are urgently needed. Thus, our aim was to examine whether an adjuvant effect, which would be potentially valuable in new vaccines, is also seen in paediatric mucosal T cell immunity.

Methods: Individual, mixed or fused proteins were used to stimulate mononuclear cells from paediatric adenoids (AMNC) and palatine tonsils (TMNC) and proliferative responses of CD4+ T cells were detected by flow cytometry.

Results: Significantly different responses were observed in AMNC (ANOVA $p < 0.001$), but not TMNC. Proliferation in response to $\Delta 6$ Ply was significantly higher than to Ply ($p = 0.0043$), but was no different whether it was fused to or mixed with PsaA or used alone. Responses to fused PsaAPly were significantly higher than responses to PsaA mixed with Ply ($p = 0.02$), which was the same as responses to the individual proteins.

Conclusions: These results suggest that immune responses towards pneumococcal antigens are affected by fusion, and confirm that both Ply and $\Delta 6$ Ply induce CD4+ T cell responses in the child's nasopharynx. Whether the effect of Ply in this model is non antigen-specific (adjuvant-like) remains to be determined, but this protein or the non-toxic $\Delta 6$ Ply are potentially valuable for use in future vaccines. This work was funded by PATH.

THE NUMBER OF CHILDREN TO BE VACCINATED TO AVERT A HOSPITAL ADMISSION FOR INFLUENZA/RSV

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Background: National data on influenza related hospital admissions are needed to determine vaccination policy. In some countries, healthy children 6-23 or 6-59 months are recommended for vaccination. We aimed to estimate admissions averted by this policy.

Methods: We examined 1.3 million respiratory hospital admissions for acute respiratory infections (coded to ICDX J02-06; J10.11;J12-18;J20-21,J45) in England over 11 years (1996-2006) in age groups (0-2, 3-5,6-11, 6-23, 6-59months) in seven 5 week winter periods (week 38 week 20 the following year). Excess winter admissions over summertime equivalents were attributed proportionately in each 5 week period to influenza and respiratory syncytial virus (RSV) based on national virology reports.

Results: The average annual admission rate for respiratory illnesses studied was 800-900 per 10,000 in all age groups up to 24 months, and 277 in age 6-59m. Excess admissions in each 5 week period were allocated to influenza/RSV as shown in the table.

5 Week Periods	38-42	43-47	48-52	1-5	6-10	11-15	16-20
Influenza	5	10	20	40	20	10	10
RSV	10	40	60	30	20	10	10

[Table 1 Percentage of excess admissions]

Excess admission rates/10,000 attributable to influenza were- age 0-2m 127; 3-5m 106; 6-11m 81; 6-23m 94; 6-59m 45: and to RSV, 252; 218; 192; 207; 151 respectively.

Conclusion: Influenza vaccination of all children aged 6-23 months with 70% efficacy against hospital admission would require 152 children to be vaccinated to avert one admission; and for children 6-59 months, 317 children.

THE NUMBER OF CHILDREN TO BE VACCINATED TO AVERT A HOSPITAL ADMISSION FOR INFLUENZA/RSV

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Background: National data on influenza related hospital admissions are needed to determine vaccination policy. We examined hospital admissions for acute respiratory infections in England over 11 years (1996-2006) in children < 59 months separately by year and age groups in seven 5 week winter periods.

Methods: 1.4 million admissions (coded to ICDX J02-06; J10.11; J12-18; J20-21, J45) were studied. Excess admission rates in 5 week periods were calculated for winter weeks 38-20 over summer weeks 21-37; and midwinter weeks 43-15 over periseasonal weeks 38-42, 15-20. The excesses were attributed between influenza and respiratory syncytial virus (RSV) based on the temporal distribution of national virology reports assuming that these viruses accounted for 70-90% of the total excess.

Results: The relative proportions of influenza/RSV reports were used to attribute the impact of each virus in each 5 week period (table). The midwinter over periseasonal excess admission rates/10,000 attributed to Influenza were:- age 0-2m 141-182; 3-5m 117-152; 6-11m 80-104; 6-23m 40-52: and to RSV 193-247, 158-202, 131-167 and 63-80 respectively. Excesses were minimal in children aged over 36 months.

5 Week Periods	38-42	43-47	48-52	1-5	6-10	11-15	16-20
Influenza	1.2	9.7	19.5	33.4	23.8	9.4	3.1
RSV	2.2	17.6	47.6	23.0	6.9	2.1	0.7

[Distribution (%) of total Influenza and RSV]

Conclusion: Influenza vaccination of all children aged 6-23 months using a vaccine with 70% efficacy would require 274-357 children to be vaccinated to avert one admission.

CHANGES IN CARRIAGE OF *STREPTOCOCCUS PNEUMONIAE* (SP) IN CHILDREN ATTENDING DAY CARE CENTRES (DCCS)

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Background and aims: Since 2007 we have conducted surveillance of Sp colonisation in DCCs. PCV7 became available in Portugal in 2001 and despite not being included in the recommended immunisation programme, rates of vaccination are now high. This study aims to monitor the carriage rates in this population in order to assess changes that may be attributable to vaccination.

Methods: A cross-sectional study of children aged 4-75 months from DCCs in Coimbra, Portugal was performed in February 2009. A nasopharyngeal swab was taken and serotyping and susceptibilities obtained for Sp positive samples. Results were compared with previous years.

Results: Of 586 samples, Sp was isolated from 300 (51%; 55.4% in 2008 and 61.3% in 2007); 84% had received PCV7. 8% (25) of the pneumococci were vaccine types (VT) (7.3% in 2008, 20.7% in 2007). Only 2 VT were detected (3 in 2008, 4 in 2007): 14 (1) & 19F (24) of which 18 were in age-appropriately vaccinated children. 56 (19%; 24% in 2008, 16% in 2007) isolates were penicillin non-susceptible (PenNS) (19A-18, 19F-18, 6C-6, 15A-6). The carriage of vaccine related types was common (19A, 23A, 23B, 6A and 6C: 29%), with 30% showing PenNS, mainly 19A.

Conclusions: With increasing vaccination rates, a corresponding decrease in carriage rate of VT was observed. However the fall in carriage rates of VT and apparent rises in rates of carriage of PenNS strains seen between 2007 and 2008 have not continued this year. Despite vaccination, 19F is still frequently carried and is frequently PenNS.

VACCINATION COVERAGE AT EARLY TEENAGE

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Background and aims: The quintessence of Pediatrics is the prevention mainly expressed by vaccines. The study's objective was assessing vaccination schedule's level in preteens and teens.

Methods: 230 children, 10-15 years old, examined as outpatients during 2008 were studied. Sex, age and vaccinations against Measles-Mumps-Rubella (MMR), Diphtheria-Tetanus-Pertussis(DTP), Hepatitis A,B, poliomyelitis (IPV), Varicella(VZV) and Meningitidococcus C, were recorded from health books.

Results: MMR immunization (Full: 2 doses, inadequate: 1dose). Fully immunized children: 188 (81.7%), inadequately immunized children: 37 (16.1%), not immunized: 5 (2.2%). HAV immunization: (Full: 2 doses, inadequate: 1 dose). Fully immunized children: 135 (58.7%), inadequately immunized: 38 (16.5%), not immunized: 57 (24.8%). HBV immunization: (Full: 3 doses, inadequate : < 3 doses). Fully immunized children: 205 (89.1%), inadequately immunized: 21 (9.1%), not immunized: 4 (1.8%). DTP-IPV immunization: (Full: 5 doses). Fully immunized: 208 (90.4%), inadequately immunized: 19 (8.3%), not immunized: 3 (1.3%). VZV immunization (Full: 2 doses, inadequate: 1dose). Fully immunized children: 58 (25.2%), inadequately immunized children: 48 (20.9%), not immunized, without reference of sickness: 124 (53.9%). Sickness: 67 (29.1%). Vaccination against Meningitidococcus C: Immunized children: 82 (35.7%), not immunized: 148 (64.3%).

Conclusions: The percentage of inadequately immunized preteens and teens is not inconsiderable. Empowerment of activities for the formation of this population's right attitude towards immunization is needed.

Bibliography: CDC. General recommendation on immunization. MMWR SS (RR-15) : 1- 46, 2006

DO WE KNOW HOW TO 'CATCH-UP' MISSED MMR VACCINATIONS: LONDON EXPERIENCE

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Background and aims: MMR immunisation rates have declined in London and England since 1997 following media concerns regarding vaccine safety, with only limited recovery. This paper reviews the effectiveness of two diverse catch-up campaigns in London, and considers emerging issues relating to design of effective interventions.

Methods: The 'Capital Catch-up' campaign (2004/05) worked with schools to identify and vaccinate eligible primary school age children. The Chief Medical Officer's campaign (2008/09) offered catch-up vaccination through general medical practices for all children 13months -18 years. Campaigns were evaluated for their effectiveness in increasing the number of vaccinated children, and for estimated effect on community epidemic risk.

Results: The campaigns were partly successful in identifying and vaccinating susceptible children, but achieved only modest reduction in community epidemic risk. Parental consent rates were inversely related to age for the school based programme. The primary care based programme was moderately successful in increasing the prevalence of vaccinated children of primary schedule age, but appeared less effective in vaccinating eligible school-age children.

Conclusions: Various interventions including two catch-up campaigns with divergent methodologies have been implemented over the past decade to try and ameliorate the effects of the prolonged decline in MMR vaccination uptake in London. The school based catch-up campaign was more effective overall with school aged children, but encountered significant consent refusal rates for younger children in this age group. Design of effective public health interventions for catching up vaccination among children above schedule age in a western metropolitan setting remains uncertain.

ACCEPTANCE OF SWINE FLU (H1N1) VACCINE AMONG HEALTH CARE WORKERS: A U.K TERTIARY NEONATAL UNIT SURVEY

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Background: Swine flu, a new strain of influenza A virus subtype H1N1, was declared a global pandemic by WHO in June 2009. In Oct 2009, swine flu vaccination programme was introduced in the U.K for frontline health care workers, on a voluntary basis. But there were concerns from chief executives about the anticipated low rate of acceptance for the vaccine.

Aim: To evaluate the awareness, perception and acceptance of vaccination among frontline health care workers in a large tertiary referral neonatal unit in South East England.

Method: A 12 point tick box questionnaire was used to interview and collect information about awareness and acceptance of the vaccine. The data were anonymised and analysed further using ME2007.

Results: 21 doctors and 51 nurses were interviewed. The overall acceptance rate was 33.3% (24/72). Protecting patients and family were the main reason for acceptance in 66% (16/24) and 79% (19/24) respectively. At least 45% felt that the vaccine was not beneficial and 10% were unsure about its safety. Of those who had the vaccine, none had significant reaction and 75% recommended it to others. 44% felt they did not get adequate information from trust and interestingly 35% felt more information would help them accept the vaccine.

Conclusions: Nearly 66% in our study group were reluctant to accept the vaccine, nurses significantly more than doctors. More effective means of spreading information like e-learning module might help in increasing the awareness and acceptance. It is reassuring that none had significant reaction to the vaccine.

ESTIMATING THE TOTAL DISEASE BURDEN CAUSED BY ROTAVIRUS IN LATVIA**D. Gardovska**¹, I. Grope¹, L. Kozlovska², V. Kūse³, I. Vingre⁴, J. Perevoščikovs³¹*Riga Stradins University*, ²*Latvian Rural Area General Practitioner`s Association*, ³*Infectiology Centre of Latvia*, ⁴*Riga Stradins University and Infectology Center of Latvia, Riga, Latvia*

Background and aims: Studies on Rotavirus disease frequency in children < 5 years old can help in estimating the burden of disease in countries with scarce data and evaluate the cost-effectiveness of vaccination.

Methods: The decision tree model used was: children with acute gastroenteritis (AGE); seek medical advice or not; GP recommend hospitalization or not. Hospitalizations data came from hospitals labs. Knowing that 1/ 7 to 1/ 5 GP-visit for rotavirus AGE is sent for hospitalization, total number of GP-visits per year can be calculated. Only 1 /3 to 1/2 children visits a GP because of rotavirus AGE. Unit cost-estimates for GP-visit and hospitalization came from official financial databases. The QALY impact for a diarrhea event at home care, GP-visit and hospitalization came from literature review.

Results: Birth cohort is 20,000 infants, 2500 hospitalizations for rotavirus infection are reported each year. Unit costs for 1 hospital case of rotavirus diarrhea and for 1 GP visit are estimated at 315 € and 12 €, respectively. The QALY impact per event is at -0.00243, -0.00356, and -0.00889 for one diarrhea event, one GP-visit and one hospitalization, respectively. A range of 25,000-52,500 diarrhea events, and 12,500-17,500 .GP-visits are observed per year. The cost burden varies between € 937,500 and € 997,500 per year and QALY-loss in children less than 5 years old is between -127 and -212 each year.

Conclusion: Simple calculations based on birth cohort, hospital events and unit costs related to rotavirus disease, can estimate the total disease burden in Latvia.

A COMMUNITY TRIAL TO ASSESS THE INDIRECT EFFECTIVENESS OF VACCINATING SCHOOLCHILDREN AGAINST INFLUENZA: PRELIMINARY DATA ON INCIDENCE OF INFLUENZA-LIKE ILLNESS

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Background and aims: Evidence of effectiveness of vaccinating schoolchildren against influenza is not yet conclusive. This study aims to assess the direct and indirect effectiveness of vaccinating schoolchildren against influenza in the prevention of the disease among vaccinated children and their unvaccinated household contacts.

Methods: A community trial was undertaken in São Paulo, Brazil, in 2009 flu season. A sample of 9 elementary schools located in the Western Region of São Paulo municipality was selected. Schools were randomly allocated to the experimental (seasonal influenza) or control (meningococcal C and varicella) vaccination groups. The study was presented to parents in meetings at each school. The ones that agreed to participate were asked to sign the Informed Consent Form. Influenza like illness (ILI) and laboratory confirmed influenza occurrence among children and their household contacts were actively monitored in the following 6 months after vaccination. We report here ILI's incidence.

Results: A total of 1,746 children were allowed by their parents to participate (44.8 % of enrolled children), with their 6,544 household contacts. As blinding has not yet been opened, we describe the data in groups A and B. ILI's incidence was 14.1% among children in group A, and 11.6% in group B ($p=0.08$). Among household contacts, incidence was 7.5% in group A and 6.3% in group B ($P=0.01$).

Discussion: Data suggest a reduced ILI incidence in one of the groups. The emergence of the A/H1N1 pandemic virus during the first month of follow up after vaccination might have influenced the trial results.

HIGH PUBLIC HEALTH BENEFIT OF ROTAVIRUS VACCINATION IN DEVELOPED COUNTRIES**C. Giaquinto¹, V. Spoulou²***¹University of Padova, Padova, Italy, ²Ethniko and Kapodistriako Panepisthimio, Athens, Greece*

Background: Since the introduction of rotavirus (RV) vaccines in developed countries in 2006, a number of studies have examined the potential public health benefits of vaccination against RV. Here we review the results of published RV vaccination impact studies to provide a preliminary overview of their impact on disease burden in developed countries.

Methods: Studies were identified by Medline search from 2006 to December 2009. Abstracts presented to international congresses were included. The impact on RV disease burden was defined as change in hospitalisation rates, emergency visits, and laboratory data before and after introduction of vaccination.

Results: A total of 19 studies were included: 13 from US, 5 from Europe, 1 from Australia. In the US Rotateq was the only vaccine available until August 2008. By late 2007, the vaccination coverage rate in the US was 18-32% in children 13 months of age (full course). During the two RV seasons 2007-08 and 2008-09 in the US, the rates of RV-related hospitalisations and/or ED visits decreased by 66-95% in vaccine eligible age-groups compared to the prevaccine period. The median RV-positivity rates decreased by 69-76% over this period. The significant reduction was also observed in non-vaccine eligible age-groups, and with sub-optimal vaccine coverage suggesting herd-immunity. Similar results were observed in Europe and Australia.

Conclusions: Rotavirus vaccination has already an important positive impact in developed countries, being associated with a marked and consistent reduction in RV disease burden. These data from a real-world setting demonstrate the high public health benefits of RV vaccination.

TOLERABILITY AND SAFETY OF MENVEO® QUADRIVALENT MENINGOCOCCAL GLYCOCONJUGATE VACCINE AGAINST SEROGROUPS A,C,W-135, AND Y IN 2-10 YEAR-OLD CHILDREN

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Background: Menveo® (MenACWY-CRM₁₉₇) was developed to protect all age groups against invasive disease caused by meningococcal serogroups A, C, W-135, and Y. We present safety and tolerability results from a Phase 3 study of the safety and immunogenicity of MenACWY-CRM₁₉₇ compared with Menactra® (sanofi pasteur; MCV4).

Methods: At 68 clinical centers in Canada and the United States, children 2-10 years of age were randomized to receive: one dose of MenACWY-CRM₁₉₇ or MCV4 or 2 doses of MenACWY-CRM₁₉₇ (2- to 5-year-olds only). Reactions within 30 minutes of vaccination were recorded as were: solicited injection site reactions of pain, erythema, and induration; systemic reactions including nausea, malaise, headache, and fever; and all adverse events for 7 days postvaccination. Any adverse event occurring within 28 days postvaccination or any event requiring medical intervention, including SAEs, within six months postvaccination were evaluated.

Results: Both MenACWY-CRM₁₉₇ and MCV4 were well tolerated in 2- to 10-year-old children. The safety profile was generally similar between the two age cohorts, for each vaccine administered and for participants receiving 1 or 2 doses of MenACWY-CRM₁₉₇. Most participants (60%-70%) experienced one or more solicited reactions; these were primarily mild and self-limited. The most common solicited reactions in both vaccine groups were injection site pain and erythema. The most common adverse events were upper respiratory tract infections and cough.

Conclusions: In this study, Menveo® and Menactra® were generally well tolerated when administered to healthy 2- to 10-year-olds. Favorable safety outcomes were observed in recipients of both vaccines.

PERSISTENCE OF BACTERICIDAL ACTIVITY IN ADOLESCENTS 12 AND 21 MONTHS FOLLOWING RECEIPT OF MENINGOCOCCAL VACCINES AGAINST SEROGROUPS A,C,W-135, AND Y

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Background: Serum bactericidal assays(SBA) using human complement(hSBA) are the basis for established correlates of protection against invasive meningococcal disease. Many regulatory agencies also consider data from SBAs using rabbit complement(rSBA) as meaningful.

Methods: Sera from adolescent recipients of Menveo[®] (MenACWY-CRM₁₉₇) or Menactra[®] (sanofi pasteur; MCV4) glycoconjugate or polysaccharide(Menomune[®] sanofi pasteur; MPSV4) vaccines in two randomized trials originally tested using hSBA were evaluated by rSBA. Sera collection from MenACWY-CRM₁₉₇ and MPSV4 recipients (n=140;1:1)12 months postvaccination and MenACWY-CRM₁₉₇ and MCV4 recipients (n=200;1:1)21 months postvaccination were planned.

Results: One month postvaccination, 90-100% of vaccinees had rSBA titers ≥ 128 . Twelve and 21 months postvaccination, 100% and 97% MenACWY-CRM₁₉₇ vaccinees, respectively, had rSBA titers ≥ 8 for serogroup A; as did 84% and 72% for serogroup C; 97% and 92% for serogroup W; and 97% and 90% for serogroup Y. At 12 months, rSBA GMTs for MenACWY-CRM₁₉₇ or MPSV4 recipients, respectively, were 2462 vs. 1127(P = 0.002) for serogroup A; 161 vs. 67(P=0.067) for serogroup C; 1627 vs. 157(P < 0.001) for serogroup W-135; and 1389 vs. 105(P < 0.001) for serogroup Y. At 21 months, rSBA GMTs for MenACWY-CRM₁₉₇ or MCV4 recipients, respectively, were: 1075 vs. 739(P=0.2) for serogroup A; 91 vs 44(P=0.05) for serogroup C; 792 vs. 280(P=0.002) for serogroup W-135; and 564 vs. 115(P=0.001) for serogroup Y.

Conclusions: A high percentage of Menveo[®] recipients maintained rSBA titers for 21 months postvaccination. Twelve and 21 months postvaccination, Menveo[®] recipients had evidence of higher levels of bactericidal antibodies than did recipients of comparator vaccines.

SAFETY AND IMMUNOGENICITY IN CLINICAL TRIALS OF MENVEO® QUADRIVALENT MENINGOCOCCAL GLYCOCONJUGATE VACCINE, IN ADULTS UP TO 65 YEARS OLD

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Background: Invasive meningococcal disease is a risk in areas with hyperendemic or epidemic disease or the Hajj. The only option for broad meningococcal disease protection for adult travelers outside of North America is the quadrivalent polysaccharide vaccine MPSV4 (Menomune® sanofi pasteur).

Methods: 19 to 65 year olds in two multicenter, observer-blind, controlled trials were randomized to receive Menveo® (MenACWY-CRM₁₉₇) or comparators MCV4 (Menactra® sanofi pasteur; 19-55 year-olds) or MPSV4 (56-65 year-olds); predefined noninferiority and superiority criteria for immunogenicity were assessed in subgroups. Solicited injection site and systemic reactions for 7 days postvaccination and adverse events for 6 months postvaccination were evaluated.

Results: Overall, 4190 adults (3864 19-55-year-olds and 326 56-65 year-olds) enrolled. MenACWY-CRM₁₉₇ met noninferiority criteria for all immunogenicity endpoints for all serogroups against MCV4. MenACWY-CRM₁₉₇ was statistically superior to MCV4: in study 1 for serogroup Y (all endpoints) and W-135 (seroresponse and hSBA titer \geq 8); and in study 2 for all end points for serogroups C, W-135 and Y. In 56-65 year-olds MenACWY-CRM₁₉₇ induced GMTs 1.4 to 5-fold higher than did MPSV4. In all vaccine cohorts, up to half of participants reported injection site reactions and somewhat fewer reported systemic reactions. The 56-65-year olds were somewhat less likely to report injection site or systemic reactions than younger vaccinees.

Conclusions: MenACWY-CRM₁₉₇ was immunogenic and well tolerated in 19-65 year-olds. MenACWY-CRM represents an important potential option to protect persons aged 56 and older from meningococcal disease caused by serogroups A, C, W-135, and Y.

ACCEPTABILITY OF H1N1 VACCINATION IN NURSES IN A PROVINCIAL HOSPITAL IN NORTHERN GREECE

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Introduction: Vaccination is one of the most effective and economically efficient ways to eliminate infectious diseases.

Aim: To investigate the beliefs of nurses in a provincial hospital in Northern Greece on the H1N1 infection and the extent they are informed.

Materials and methods: An anonymous questionnaire was randomly given to 150 nurses. It included demographic information and there were questions on:

1. Their intension to take up with the H1N1 and H5N1 vaccination for themselves and their families
2. Their beliefs on safety and side effects of the vaccines and
3. The factors influencing their decision.

Results: The response rate was 95.3%, mostly women (92.1%) aged 30-50 (75.28%). Their intension to accept the H5N1 vaccination for themselves was only 20.2% and 32.6% for their families. Their intension to accept the H1N1 vaccination for themselves was 7,8% and 10,1% for their families. The most important reason for not accepting both vaccinations was side effects, 68.5% for the H5N1 and 75.2% for the H1N1. The decision for the vaccination is influenced by media (30.3%), by the family doctor (22.5%) and by a doctor from their department (10.1%). 51.6% of the participants believe that the virus is moderately contagious. 56.2% of the participants believe that the disease caused by the H1N1 virus is moderately serious, 27.5% serious and 21.3% not very serious.

Conclusion: Side effects are decisive in accepting the vaccination. Media as well as the family doctor are determinant factors for their decision. The negative influence by the doctors should be examined.

AWARENESS OF RABIES AND KNOWLEDGE ABOUT MANAGEMENT OF ANIMAL BITES IN TURKISH PHYSICIANS

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Introduction: Rabies is an endemic infectious disease and one of the most important cause of human mortality in especially underdeveloped and developing countries. In this study we investigated awareness of rabies and knowledge about management of animal bites in Turkish physicians in country where every year 100.000 people applied with suspected animal bites to health-care units and 75 % of them are children.

Methods: 75000 Turkish physicians who enrolled as a member of Turkish Medical Association were asked to complete an Internet-based questionnaire by email.

Results: 1541 physician answered our internet- based questionnaires. Among them 43% recommend only rabies vaccine, 4% recommend only human rabies immunoglobulin (HRIG) and only 54% of them recommend rabies vaccine and HRIG together to patients with rabies prone animal bites. Of the 1541 physicians 46% of them did not know correct 5 dose regimen rabies vaccination schedule and 55% of them did not know correct dose of HRIG and 89% of them did not know correct application site and route of HRIG. On the other hand 75% of physicians know correct 10 days observation period for rabies if animal was captured.

Conclusion: Although the participants of this study were well aware of basic knowledge of rabies, the correct assessment of specific situations which like management of animal or human bite and postexposure rabies prophylaxis were not enough. Our findings provide important signals to governmental officials. We noticed a professional postgraduate training for physicians is needed.

PREVENTION METHODS' EFFICACY OF MOTHER TO CHILD TRANSMISSION OF HEPATITIS B INFECTION

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Background: More than 40% of the world population has contact with hepatitis B infection - one of the important infections which chronization in about 30% of cases ends with the carcinoma or cirrhosis of liver. 90% of newborns infected at birth become chronic patients and have high risk of developing liver diseases. The risk of acquiring Hepatitis B infection is much higher among newborns to HBsAg positive mothers.

Prevention of newborns from being infected at birth is highly important in eliminating Hepatitis B infection within society. Vaccination of newborns at birth is primary tactics for countries in the high and intermediate HBsAg prevalence zones.

Industrialized countries widely use passive immunization (with HBIG) together with Hepatitis B vaccine to protect such babies from the infection. Georgia is the first country in Caucasus that started immunizing of newborns to HBsAg positive mothers using the above method.

Goal/purpose: Assessing the efficacy of prevention methods of mother to child transmission of hepatitis B infection in Georgia

Methods: 243 children born to HBsAg positive mothers were screened on HBsAB and HBsAg in 12-18 of age. All these babies received hepatitis B vaccine and HBIG within 12 hours of birth and were followed 2 shot vaccination series (1&6 months).

Results: The beneficiaries were HBsAg negative and were protected from becoming chronically infected with Hepatitis B infection at birth.

Conclusions: Immunizing newborns to HBsAg positive mothers with HBIG and hepatitis B vaccine gives almost 100% efficacy in protecting these babies from acquiring HBsAg from their mothers.

LOW BCG VACCINATION COVERAGE AFTER THE END OF COMPULSORY VACCINATION IN FRANCE

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Background: In January 2006, BCG multipuncture was withdrawn from the market, leading to an estimated 54% decrease in BCG coverage. In July 2007, mandatory BCG vaccination for all children was replaced by a recommendation to vaccinate those at high risk of tuberculosis, among whom all children of Ile-de-France, the only region with an incidence rate $>10/10^5$. We used several methods to evaluate the impact of this policy change on BCG coverage.

Methods: We analyzed vaccine sales trends (2005-2008) in Ile-de-France. We performed a national cross-sectional survey (February 2008) in a sample of doctors working in private medical practices. We conducted a national random sampling survey (May 2009) in Maternal and Child Health Clinics (MCH).

Results: A decrease in vaccine sales of 35% was observed between 2005 and 2008 in Ile-de-France. Among a sample of 259 at risk children (2-7 months) born after the end of compulsory vaccination and followed by private practitioners, 68% had been vaccinated. Among a sample of 856 at risk children (2-23 months) born after the end of compulsory vaccination and followed in MCH clinics, 72.6% (66.3-78.0) had been vaccinated [Ile-de-France: 89.8%, other regions: 61.7%].

Conclusions: With the exception of the public sector in Ile-de-France, vaccination coverage remains insufficient in high risk children. Emphasis given in 2007 to vaccinate those children did not allow to catch-up for the decrease in coverage created by the disappearance of the multipuncture device. Training of doctors in intra-dermal vaccination and strengthening communication concerning the new vaccination policy should be prioritized.

A PHASE IV IMMUNOGENICITY STUDY OF THE HIB VACCINE, GIVEN AS PART OF THE ROUTINE IMMUNISATION SCHEDULE TO NEPALI INFANTS

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Background: The *Haemophilus influenzae* type b (Hib) conjugate vaccine is effective in preventing invasive Hib disease in children under five, however immunogenicity and efficacy of conjugate vaccines is not uniform across different populations. Hib is an important cause of meningitis and pneumonia in Nepali children. We determined the immunogenicity of the Hib conjugate vaccine (Act-Hib ®) in Nepali infants, prior to the introduction of the vaccine into the routine immunisation schedule.

Methods: Infants aged 40-60 days were recruited at Patan Hospital, Kathmandu (n= 90) and received 3 doses of the Hib vaccine with routine immunisations (DTP-HBV+ OPV) according to EPI schedule, and a Hib booster at 52 weeks. Anti-PRP, tetanus and diphtheria concentrations were measured at 18, 52 and 56 weeks, and the persistence of antibody at 52 weeks was compared with antibody levels in unimmunised controls (n=32).

Results: After 3 doses of primary immunisations, at 18 weeks of age (n=74), geometric mean antibody concentrations for Hib, tetanus and diphtheria were 12.42 mcg/ml (95% CI 9.63-16.02mcg/ml), 1.70 IU/ml (95% CI 1.37-2.10IU/ml) and 1.42 IU/ml (95% CI 1.11-1.81IU/ml) respectively. 100% of infants had anti-PRP concentrations above the accepted short and long-term protective thresholds (0.15mcg/ml and 1.0 mcg/ml). Data on antibody persistence and response to booster will be available shortly.

Conclusion: The Hib conjugate vaccine elicits an excellent anti-PRP response and should provide protection against invasive Hib disease in Nepali infants. Introduction of the vaccine into the routine schedule from mid-2009 is an important public health intervention for Nepal.

OUTCOME OF INFANTS BORN FROM CHRONIC HEPATITIS B VIRUS INFECTED MOTHERS

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Background and aims: Infants born from chronic hepatitis B virus infected mothers are predisposed for developing of HBV infection. The purpose of this study was to assess the outcome of infants born from chronic HBV infected mothers.

Methods: From April 2004 to September 2009, infants born from chronic HBV infected mothers were received Hepatitis B Immune Globulin 0.5 cc and the first dose of hepatitis B vaccine at birth. The second and third doses of HBV vaccine were administered at 1 and six months of age. Post-vaccination tests to detect hepatitis B surface antigen (HBsAg) and anti- HBs were performed at 12 months of age. Those who had anti- HBs titers < 10 mIU/ml received the second series of HBV vaccine.

Results: Thirty- four and 201 infants born from chronic HBeAg or anti-HBe+ mothers, respectively. HBsAg was detected in 6 (17.6%) cases born from HBeAg positive mothers and in 3 (1.5%) born from anti-HBe+ mothers ($p=0.0001$). Anti-HBs levels > 10 mIU/ml were developed in 204 (86.8%) cases. The mean anti- HBs levels in infants born from HBeAg+ mothers was 284.23 ± 257.2 and from anti HBe+ mothers was 367.2 ± 322.8 mIU/ml ($p=0.213$). Twenty-two (9.4%) infants were not responder and among them 11 cases responded to the second series of HBV vaccine.

Conclusion: The results show that infants of HBeAg positive mothers have higher risk of developing of HBV infection due to the higher viral load. Reduction of the viral load in this group of mothers is recommended.

VACCINE SAFETY: ATTITUDES, TRAINING AND COMMUNICATION (VACSATC)

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Background and aims: Infectious agents and rumours and concerns about vaccine safety cross borders. The problems cannot be resolved by action in one country. The aim of the VACSATC project is to improve confidence in vaccination programs through collaboration building on the experiences from many countries.

Methods: Guidelines developed by centres of excellence with implementation at national level.

Participation: 15 institutions in 12 EU member states and Norway and Turkey

Funding: European Commission DG SANCO and project partners

Website: www.vacsatc.eu

Results:

Attitudes

A collection of guidelines on methods was developed by the Department of Health, UK. Studies on attitudes to immunisations were conducted in 8 countries.

Training

A survey of pre-service training was conducted in 7 countries. A prototype curriculum on vaccinology has been developed and tested at the University of Antwerp (www.ua.ac.be/cev/summerschool).

Websites

Websites have been built or improved in 9 partner countries.

Linked databases

A survey was sent to 10 European public health agencies with responsibilities for immunisation programs. The results show that personal identifiers can be used to link data on vaccinations in 5 countries.

Conclusions:

- Sharing of best practices is a useful approach for EU collaborations.
- Collaboration can reduce duplication of work and is a rational use of resources.

· To further improve attitudinal studies, pre-service training on vaccinology, websites with information on vaccine safety and linked database studies the collaboration should be extended.

AN ADJUVANTED AND NON-ADJUVANTED EGG-DERIVED, INACTIVATED A/H1N1 MONOVALENT SUBUNIT INFLUENZA VACCINE IN CHILDREN 3 TO < 9 YEARS OF AGE

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Background and aims: Influenza vaccines with increased immune protection are a medical priority. Adjuvanted vaccines may offer a solution.

Methods: This single-blind, dose-ranging study enrolled 1357 healthy children 3 to < 9 years of age to evaluate a monovalent pandemic 2009 influenza A/H1N1 vaccine in both MF59[®]-adjuvanted and non-adjuvanted forms. Children were randomized equally to eight groups given intramuscular vaccine injections on Day 1 and Day 22. Vaccines were formulated with 3.75, 7.5, 15 or 30 µg antigen and), 50 or 100% MF59.

Interim immunogenicity (HI assay) relative to CBER seroprotection rate (95% CI lower bound ≥70%) and seroconversion rate (95% CI lower bound ≥40%) criteria was evaluated on Day 22.

Results: Baseline seropositivity (HI titer ≥10) rates in each group were comparable (18-27%). All adjuvanted groups and no non-adjuvanted group satisfied the seroprotection (HI titer ≥1:40) criterion. Subjects in all vaccine groups except 7.5 µg A/H1N1 antigen without adjuvant satisfied the seroconversion (pre-vaccination HI titer < 1:10 and post-vaccination titer ≥1:40 or pre-vaccination HI titer ≥1:10 and ≥4-fold rise in post-vaccination titer) criterion. Pairwise group comparisons of GMTs at Day 22 using two-sided 95% CIs shows that all adjuvanted vaccines at 3.75, 7.5 and 15µg antigen content were superior to all non-adjuvanted vaccines. No noteworthy differences in adverse events reporting was observed between the vaccine groups.

Conclusions: In this interim analysis, all MF59-adjuvanted influenza A/H1N1 vaccines generated antibody responses likely to be associated with protection (exceeding CBER criteria) within 3 weeks after a single dose. (clinicaltrials.gov: NCT00972816)

THE IMMUNOGENICITY AND SAFETY OF 3RD INACTIVATED JAPANESE ENCEPHALITIS VACCINE IN CHILDREN

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Background and aims: As the JE vaccination schedule in Korea has been reformed since 2000, reliable data by a prospective study on the immunogenicity and safety of the inactivated vaccines is required.

Methods: As a continuous project of the previous year, children were enrolled among the previous study. We measured the neutralizing antibody (NTAb) values of normal healthy children during 4-6 weeks after the 3rd dose (1 year after 2nd dose) of Mouse brain-derived Nakayama strain (inactivated) JE vaccine. According to the NTAbs values obtained, the positive rate and titer values of NTAbs tests were evaluated. Active monitoring of localized and systemic reactions were done through phone calls 7 days after vaccination, and the safety of vaccination was assessed. Adverse reactions were also recorded on the diary cards by parents for 4 weeks.

Result: NTAbs tests were performed among 73 children who received 3 doses of inactivated JE vaccines. Positive rate for NTAbs tests, which was defined as a serum titer greater than 1: 10, were 100%. The geometric mean titer value of the NTAbs tests were 276.8. Adverse reactions were investigated in 74 children. 13.5% showed localized reactions, and 8.1% showed systemic reactions.

Conclusion: Positive rate and titer values for NTAbs tests showed appropriate levels, and there were no difference of adverse reactions compared to previous studies. These results show that the current schedule of JE vaccination in Korea, performed in a 3 dose inoculation of inactivated JE vaccine is appropriate in preventing the disease.

EPIDEMIOLOGICAL CHANGES IN BACTERIAL MENINGITIS PREVALENCE IN SLOVAKIA

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Background and aim: Acute bacterial meningitis is one of the most severe and feared diseases of childhood. The most common etiological agents are *Haemophilus influenzae* type B (Hib), *Streptococcus pneumoniae*, and *Neisseria meningitidis*. The effective preventive approach is the vaccination against named pathogens.

We aimed to analyze the prevalence of bacterial meningitis in Slovakia from 1997 to 2007 using the etiological agents and their relationship to the newly introduced vaccination against Hib.

Methods: For our analysis, we used all the relevant data about the patients with bacterial meningitis reported in the Epidemiological Informative System of Communicable Diseases in Slovakia (EPIS) during the period 1997-2007, which was divided into 2 periods: 1997-2001 and 2002-2007 in relationship to the introduction of obligatory vaccination against Hib in 2000.

Results: During the period 1997-2007, 2067 patients were registered with bacterial meningitis. Children younger than 4 years represented 33.2% of the total number of reported cases. In this group, the most common etiological agents were *Neisseria meningitidis* (42.5%) and Hib (15.9%). Since 2002, we noticed significant decrease of meningitis caused by Hib. Analyzing two periods of time, we found the most dramatic decline of age-specific morbidity in the groups of infants younger than 4 years, especially due to evident reduction of the cases caused by Hib ($p < 0.001$).

Conclusions: Vaccines are the most promising and effective tools for preventing community-acquired bacterial meningitis. Our data on national level confirmed the expected effect of vaccination against Hib on Hib disease morbidity and mortality, especially among young children.

EFFICACY OF HUMAN ROTAVIRUS VACCINE RIX4414 IN JAPANESE INFANTS FROM 2 WEEKS POST DOSE 2 UP TO DATA LOCK POINT

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Background: Human rotavirus (G1P[8] strain) vaccine RIX4414 (Rotarix™, GlaxoSmithKline Biologicals) has been shown to be highly efficacious in preventing severe rotavirus gastroenteritis (RVGE) in diverse global settings. This Phase III, double-blind, randomised, placebo-controlled, multicentre study (NCT00480324/107625) assessed whether these results could be replicated in Japanese infants.

Methods: Healthy infants, aged 6-14 weeks, were randomised (2:1) to receive either two doses of RIX4414 or placebo, 1 month apart; routine vaccinations were given concomitantly. Vaccine efficacy (VE) against severe RVGE (RVGE requiring medical intervention and scoring ≥ 11 on the 20-point Vesikari scale) was calculated from 2 weeks post Dose 2 to data lock point (DLP). Diarrhoeal stool samples were tested for RV using ELISA and typed using RT-PCR and reverse hybridisation assays.

Results: 748 infants were included in the ATP cohort for efficacy (498 and 250 in the RIX4414 and placebo groups, respectively). From 2 weeks post Dose 2 to DLP (~1.3 years after Dose 2), significantly fewer subjects in the RIX4414 group reported severe RVGE compared with placebo (0.2% versus 4.4% for the RIX4414 and placebo groups, respectively). RIX4414 was 95.4% (95%CI: 68.6%; 99.9%) and 100% (95%CI: 24.0%; 100.0%) efficacious against severe RVGE caused by wild-type RV and wild-type G1 RV, respectively. VE against non-G1 types causing severe RVGE was 92.8% (95% CI: 44.2%; 99.8%).

Conclusions: VE of RIX4414 against severe RVGE from 2 weeks post Dose 2 up to DLP was high in Japan, and in line with results from developed countries. Administration of RIX4414 confers significant cross-protection.

PERSISTENCE OF ANTIBODY RESPONSE FOLLOWING A BOOSTER DOSE OF HIB-MENC-TT GLYCOCONJUGATE VACCINE: A PHASE IV OPEN RANDOMISED CONTROLLED TRIAL

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Aims: To assess persistence of seroprotection following a booster combination *Haemophilus influenzae* type b (Hib) and serogroup C *Neisseria meningitidis* (MenC) glycoconjugate vaccine (Hib-MenC-TT) administered at age 12-15 months.

Methods: In this open-label randomised controlled trial conducted in the UK and Poland, children immunised at age 2, 3 and 4 months with either DTPa-IPV-Hib (PediaceTM) and MenC-CRM₁₉₇ (MeningitecTM) (control group) or DTPa-IPV and Hib-MenC-TT (MenitorixTM) (Hib-MenC-TT group) received Hib-MenC-TT co-administered with MMR vaccine at 12-15 months of age. UK children immunised with three doses of a MenC conjugate vaccine and a Hib-containing vaccine before 8 months of age (no-boost group), were recruited separately (non-randomised). Anti-PRP Ig (Hib) and MenC bactericidal antibodies (rSBA) were measured at approximately 3.5 years of age.

Results: Sera from 379 participants at age 39-43 months were analysed. MenC seroprotection (rSBA $\geq 1:8$) was demonstrated in 147/219 of the Hib-MenC-TT group (67.1%, 60.5%-73.3%), 30/74 of control group participants (40.5%, 29.3%-52.6%) and 30/68 of no-boost participants (44.1%, 32.1%-56.7%). Hib seroprotection (anti-PRP Ig $\geq 1.0\mu\text{g/ml}$) was seen in 203/228 (89.0%, 84.2%-92.8%) of the Hib-MenC-TT group, 56/75 (74.7%, 63.3%-84.0%) of control group participants and 28/72 of no-boost participants (38.9%, 27.6%-51.1%).

Conclusion: A Hib-MenC-TT booster at 12 months helps sustain seroprotection against Hib at age 3.5 years. Antibody persistence against MenC is best when primed and boosted with Hib-MenC-TT; rates of seroprotection against MenC are significantly lower in children primed with MenC-CRM₁₉₇ and boosted with Hib-MenC-TT, consistent with results from other studies where CRM₁₉₇ is used as the protein conjugate for primary vaccinations.

PERSISTENCE OF ANTIBODY RESPONSE IN EARLY CHILDHOOD FOLLOWING 3 DOSES OF AN ACELLULAR PERTUSSIS VACCINE GIVEN TO INFANTS

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Aims: As part of a larger multi-centre trial comparing different primary immunisation schedules, this study assessed the persistence of anti-pertussis antibody in children prior to the administration of a pre-school booster.

Methods: This segment of an open-label randomised controlled trial (109666/NCT00454987) was conducted in the UK. Children previously immunised at 2, 3 and 4 months of age with either DTPa-IPV-Hib and MenC-CRM₁₉₇ (control group) or DTPa-IPV and Hib-MenC-TT (Hib-MenC group) received Hib-MenC-TT co-administered with MMR vaccine at 12-15 months of age. Antibody concentration against 3 pertussis antigens (FHA, PRN, PT) were measured on sera collected when participants were approximately 3.5 years of age.

Results: 93 participants were enrolled at 39-43 months of age. All participants had achieved antibody concentrations above the response threshold for all 3 antigens 1 month after the primary course of immunisations. Only 8/67 (11.9%, 5.3%-22.2%) of the HibMenC group and 3/23 (13.0%, 2.8%-33.6%) of control group participants had anti-PT antibody concentrations ≥ 5 EL.U/mL. 47/64 (73.4%, 60.9%-83.7%) of HibMenC participants and 13/22 (59.1%, 36.4%-79.3%) of the control group had anti-FHA antibody concentrations ≥ 5 EL.U/mL. 34/67 (50.7%, 38.2%-63.2%) of the HibMenC group and 7/23 (30.4%, 13.2%-52.9%) of control group participants had anti-PRN antibody concentrations ≥ 5 EL.U/mL.

Conclusions: Despite all participants achieving anti-pertussis antibody concentrations above the response threshold after the infant immunisation course, maintenance of seroprotection to preschool age is moderate for anti-FHA and poor for anti-PT and anti-PRN antibodies. This study confirms the need for a DTPa booster beyond the first year of life.

INVESTIGATION OF HEPATITIS B VIRAL INFECTION RATE BY AGE IN KOREA

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Objective: The Hepatitis B vaccine can reduce both acute and chronic hepatitis B viral infection. The positive rate of HBsAg was 7-10% in 1983 when vaccination had not been adopted in Korea, but the rate was reduced to 3.7% by 2005. This study investigates the hepatitis B vaccine effect against acute-chronic infection in Korea.

Subjects and methods: Samples were collected from August to October in 2006. The number of samples collected were 20 samples between age of 2 to 19 by one for each age, 20 samples between age of 20 to 49 by one for every 2 years of age, and 50 samples respectively from 50's and 60's regardless of age distribution.

Results: Anti-HBc positive rate by age was as follows; age of 2-4, 0%(0/73); 5-9, 8%(8/100); 10-14, 13.1%(13/99); 15-19, 9%(9/100); 20-29, 21%(21/100); 30-39, 58.6%(58/99); 40-49, 97.8%(91/93); 50s, 97.9%(46/47); 60s, 100%(49/49). The anti-HBc positive rate in the age between 2 to 33 was 11.9%(61/512) whereas the age between 34 to 69 was 94.4%(234/248).

Conclusion: The acute-chronic hepatitis B viral infection has been definitely decreased after the use of hepatitis B vaccine in Korea. It might be caused by the mass vaccination with approximately 600 million doses from 1984 to 1985 and immunization of school children from 1988. In addition, the lower infection rate among populations born after 1991 can be attributed to the inclusion of hepatitis B vaccine into the immunization guideline of the Korean Pediatric Society from 1991.

BCG VACCINE-ASSOCIATED INJURIES AND NATIONAL VACCINE INJURY COMPENSATION IN KOREA

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Background and aims: BCG-associated suppurative lymphadenitis is one of the most common injuries after live BCG vaccination, which is defined as the presence of fluctuation on palpation or pus on aspiration. This study was performed to evaluate the safety of BCG vaccines in Korea.

Methods: All data on BCG vaccination was collected based on the National Immunization and Vaccine Injury Reporting and Compensation System in Korea. We analyzed those data collected for 8 years from 2001 through 2008. Annual number of BCG vaccinees, strains of BCGs, methods of administration, BCG-associated injuries either notified and/or compensated were evaluated.

Results: Total number of BCG vaccinees were 2,875,029 (around 360,000 cases/year with average vaccination rate of 75% for 8 years). 1,083,354 cases (37.7%) were vaccinated intra-dermally with either Pasteur or Danish (after July 2007) strain, while 1,791,675 cases were vaccinated percutaneously with Tokyo strain. 1,868 cases of BCG-associated injuries were notified (6.5 cases/10⁴ vaccinees) during 8 years. Among them, 1,831 cases were vaccinated intra-dermally mostly with Pasteur strain, and only 37 cases received Tokyo strain. Finally 1,173 cases were diagnosed suppurative lymphadenitis (4.1/10⁴ vaccinees), and all of them were vaccinated intradermally with either Pasteur or Danish strain (10.8 cases/10⁴ intradermal vaccinees). All cases of suppurative lymphadenitis were compensated. Two cases of disseminated tuberculosis, one osteitis and one granulomatous hepatitis were also notified and compensated.

Conclusion: The incidence of BCG-associated suppurative lymphadenitis is higher in Korea. Pasteur strain was most commonly related to the occurrence of BCG-associated suppurative lymphadenitis. Further study will be needed using different BCG strains.

A REAPPRAISAL OF MMR VACCINES CURRENTLY USED IN KOREA**K.-H. Kim**^{1,2}, H. Lee^{1,2}

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Aim: We evaluated the immunogenicity and safety of two MMR vaccines in Korean children.

Methods: Children aged 12-23 months and 4-6 years were enrolled. All subjects received a single dose of either Priorix™ (GSK Biologicals, Rixensart, Belgium) or MMRII® (Merck & Co., Inc., West Point, PA). Antibody levels were determined by ELISA kits (Enzygnost®; Dade Behring, Schwalbach, Germany).

Results: A total of 160 Korean children were enrolled in the study. For the primary dose, 121 subjects were enrolled in the 12-23 months age group. For the second dose, 39 were enrolled in the 4-6 years age group. Among the prevaccine sera, 0.9% of the 12-23 months age group had anti-measles and anti-rubella IgG and none of the children had anti-mumps IgG. Among children 4-6 years, 96.3%, 88.9% and 96.3% of the children had antibodies for measles, mumps and rubella before vaccination. The seroconversion rate for previously seronegative subjects of 12-23 months age group was 100.0% for measles, 93.2-96.2% for mumps and 100.0% for rubella. There was no significant difference in geometric titers or seroconversion rates between the two study vaccines. In children 4-6 years of age who were previously seronegative, all children showed seroconversion for measles, mumps and rubella. There was no significant difference in reports of any adverse events between the two vaccines and between age groups.

Conclusion: The current MMR vaccines in Korea showed good immunogenic responses for measles, mumps and rubella in 12-23 months age and 4-6 year old children.

THE CANDIDATE MENACWY-TT CONJUGATE VACCINE IS IMMUNOGENIC AND HAS AN ACCEPTABLE SAFETY PROFILE IN CHILDREN 2-10 YEARS OF AGE

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Background and aims: This study compared the immunogenicity and safety of a candidate tetravalent meningococcal tetanus-toxoid conjugated vaccine (MenACWY-TT) with licensed CRM₁₉₇ conjugated meningococcal serogroup C (MenCCRM₁₉₇; *Menjugate*[®], Novartis) vaccine, in children aged 2-10 years.

Methods: In this phase III, open, randomised trial, 414 children received one dose of MenACWY-TT or MenCCRM₁₉₇ (3:1). Antibodies were measured pre- and 1 month post-vaccination; response to MenC was defined as rSBA-MenC titre $\geq 1:32$ for initially seronegative subjects (titre < 1:8) and ≥ 4 -fold increase for initially seropositive subjects (titre $\geq 1:8$). Solicited symptoms (stratified by age, 2-5 and 6-10 years) and SAEs were recorded.

Results: MenACWY-TT was non-inferior to MenCCRM₁₉₇ for vaccine response against MenC (Table). At least 99.3% of MenACWY-TT vaccines achieved rSBA titres $\geq 1:128$ against all 4 serogroups.

Table: Difference between groups in percentage of subjects with a vaccine response in terms of rSBA antibodies, one month after the vaccination (ATP cohort for immunogenicity); the lower limit of the 95% CI on the difference between groups for MenC was above the pre-specified non-inferiority limit of -10%.

		MenACWY-TT		MenCCRM ₁₉₇		Difference in vaccine response rate (MenACWY-TT minus MenCCRM ₁₉₇)	
Antibody	Pre-vaccination status	N	%	N	%	%	95% CI
rSBA-MenA	S-	121	99.2	41	9.8	89.42	-
	S+	105	89.5	26	15.4	74.14	-
	Total	226	94.7	67	11.9	82.75	72.43, 89.23
rSBA-MenC	S-	138	100	48	100	0.00	-
	S+	130	89.2	44	90.9	-1.68	-
	Total	268	94.8	92	95.7	-0.88	-5.25, 5.75
rSBA-MenW-135	S-	56	100	20	40.0	60.00	-
	S+	226	98.2	70	4.3	93.94	-
	Total	282	98.6	90	12.2	86.36	77.88, 91.80
rSBA-MenY	S-	39	100	16	37.5	62.50	-
	S+	246	95.9	72	1.4	94.55	-
	Total	285	96.5	88	8.0	88.54	80.69, 93.12

S-, seronegative; S+, seropositive

[rSBA titres]

Redness (2-5 years) and pain (6-10 years) were the most frequently reported solicited symptoms (both treatment groups). The most common solicited general symptoms were irritability and drowsiness (2-5 years) and fatigue (6-10 years). SAEs were observed in 6 MenACWY-TT subjects and 1 MenCCRM₁₉₇ subject; none were considered vaccine-related.

Conclusions: MenACWY-TT was non-inferior to MenCCRM₁₉₇ with respect to MenC vaccine response, induced robust immune responses against serogroups A, C, W-135 and Y and had an acceptable safety profile. This suggests that MenACWY-TT has the potential to broaden protection against meningococcal disease in children.

MENACWY-TT CONJUGATE VACCINE COADMINISTERED WITH DTPa-HBV-IPV/HIB IS IMMUNOGENIC AND HAS AN ACCEPTABLE SAFETY PROFILE, COMPARED WITH MENACWY-TT OR MENCCRM₁₉₇ ALONE

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Background and aims: Incidence of meningococcal disease is highest in young children. This study compared the immune response induced by MenACWY-TT when co-administered with DTPa-HBV-IPV/Hib (*Infanrixhexa*TM; GSK Biologicals), with MenACWY-TT or MenCCRM₁₉₇ (*Meningitec*[®]; Wyeth) alone in toddlers age 12-23 months.

Methods: In this phase III, open, controlled study, 793 children were randomised 2:2:2:1 to 4 groups: A) MenACWY-TT+DTPa-HBV-IPV/Hib (N=222), B) MenACWY-TT (+DTPa-HBV-IPV/Hib 1 month later) (N=220), C) DTPa-HBV-IPV/Hib (+MenACWY-TT 1 month later) (N=224), or D) MenCCRM₁₉₇ (N=127). Here we report antibodies measured pre- and 1 month post-first vaccination. Local/general solicited symptoms within 4 days of vaccination and SAEs up to 6 months after dose 1 were recorded.

Results: MenACWY-TT+DTPa-HBV-IPV/Hib immunogenicity was comparable to MenCCRM₁₉₇ for MenC and non-inferior to MenACWY-TT alone for all meningococcal serogroups (**Table**); for the percentage of subjects with antibody titres $\geq 1:8$, 95%CI lower limits (MenACWY-TT+DTPa-HBV-IPV/Hib minus MenACWY-TT) were $>-10\%$ (non-inferiority limit).

Table: Percentage of subjects with rSBA titres equal to or above the cut-off values of 1:8 and 1:128 and GMTs (ATP cohort for immunogenicity)

Antibody	Vaccine group	N	Subjects with titres $\geq 1:8$		Subjects with titres $\geq 1:128$		GMT	
			%	95% CI	%	95% CI	value	95% CI
rSBA-MenA	MenACWY-TT + DTPa-HBV-IPV/Hib	193	100	98.1, 100	100	98.1, 100	3152.9	2752.5, 3611.4
	MenACWY-TT	183	98.4	95.3, 99.7	97.8	94.5, 99.4	3169.9	2577.2, 3898.8
rSBA-MenC	MenACWY-TT + DTPa-HBV-IPV/Hib	191	100	98.1, 100	99.0	96.3, 99.9	879.7	763.1, 1014.0
	MenACWY-TT	183	97.3	93.7, 99.1	94.0	89.5, 97.0	828.7	672.4, 1021.4
	MenCCRM ₁₉₇	114	98.2	93.8, 99.8	89.5	82.3, 94.4	691.4	520.8, 917.9
rSBA-MenW-135	MenACWY-TT + DTPa-HBV-IPV/Hib	193	100	98.1, 100	100	98.1, 100	4147.0	3670.1, 4685.8
	MenACWY-TT	186	98.4	95.4, 99.7	96.8	93.1, 98.8	4022.3	3269.2, 4948.8
rSBA-MenY	MenACWY-TT + DTPa-HBV-IPV/Hib	192	100	98.1, 100	100	98.1, 100	3461.8	2990.1, 4007.9
	MenACWY-TT	185	97.3	93.8, 99.1	96.2	92.4, 98.5	3167.7	2521.9, 3978.9

[rSBA titres]

Redness, drowsiness and irritability were the most frequently reported solicited local/general symptoms in all groups. Ten MenACWY-TT+DTPa-HBV-IPV/Hib, eight MenACWY-TT and six MenCCRM₁₉₇ subjects reported SAEs; none were considered vaccination-related.

Conclusion: MenACWY-TT co-administered with DTPa-HBV-IPV/Hib was well tolerated, non-inferior

to MenACWY-TT alone in terms of immunogenicity to all four meningococcal serogroups and comparable to MenCCRM₁₉₇ for MenC. This suggests that MenACWY-TT may be co-administered with DTPa-HBV-IPV/Hib to offer broader meningococcal serogroup coverage in toddlers.

IMMUNIZATION COVERAGE OF THE GREEK PAEDIATRIC HEALTH-CARE WORKERS AGAINST A/H1N1 INFLUENZA DURING THE WINTER PERIOD 2009-2010

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Introduction: Influenza is a major cause of morbidity and mortality worldwide, affecting 5-30% of the population per year. To date, it has been well demonstrated that vaccination of health-care workers against influenza has considerable indirect effects on the health of patients, especially in patients, who are high-risk for influenza.

Material and Methods: During the winter 2009-2010, we conducted a questionnaire-based survey of the paediatric medical and nursing staff in two paediatric hospitals in Athens, Greece. Social-demographic variables, knowledge and attitudes about vaccination against A/H1N1 influenza were recorded.

Results: Twenty out of 93 (21.5%) health-care workers, who participated in the survey, received the vaccination against A/H1N1 influenza. Among nurses, the coverage rate was 12.7% (7/55), while among doctors the rate was 34.2% (13/38). In both hospitals the vaccine against A/H1N1 influenza was offered to the Staff at their work and at no cost. Only 24 out of 56 (42.9%) participants who were willing to be vaccinated against A/H1N1 influenza at the beginning of the winter 2009-2010 were aware about the significance of vaccination for their patients' protection.

Conclusions: In spite of the existing hospital-based influenza vaccination programme and the current recommendations, the uptake of A/H1N1 influenza vaccination among Greek paediatric health-care workers included in our study during the winter 2009-2010 was inadequate. Additional strategies such as better information about the indirect protection of patients at risk and education are necessary.

CHARACTERISTICS OF SIDE EFFECTS AT DTWP VACCINA

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Background and aims: Characteristics of postvaccinal reactions of DTwP (cellular) vaccine, and correlation between this vaccine and febrile convulsiones at early childhood.

Methods: We used descriptive and analytical method and data for the last 5 years from the Department of Public Helth, family doctors and General Hospital Veles, and reports of side effects of vaccines.

Results: From 14440 aplicated doses,119 children with postvaccinal reactions(0,82%) were registered. The most common are: temperature 83(69,7%), agitation 16(13,4%), local reaction 8(6,7%), cianosis 6(5%), dermatitis 1(0,84), convulsiones 5(4,2%), without information 23(19,3%). 40(33,6%) of them were coincided with infection of respiratory system.

We investigate 1000 parents whose children were vaccinated with 3306 doses of DTwP vaccine. 859(26%) of them had mild reactions and didn't need any medical help.

From 3934 children hospitalized at the pediatric department in our hospital at the same period, 73(1,8%) were with febrile convulsiones. Most representative age group is 0-3 years 62 (84,9%). For the first time were registrated 64(87,6%) and 9(12,3%) are recidivant. With respiratory infect were 69(94,5%) and 4(5,4%) like postvaccinal reaction.

Conclusions: The side reactions from DTwP vaccination, even they exist, are minimal in the most of cases.They do not result with letal exit or permanent damage.We do not have an exactly information whether vaccinae caused these negative effects. It is possible for accidental connection between reactions and aplicated vaccine which is used 5 times in the childhood. Anywhere, the benefit of vaccination with DTwP vaccine is more important than the risk of vaccination.

WOULD UNIVERSAL INFLUENZA VACCINATION BE COST-EFFECTIVE IN POLAND?

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Background: Flu epidemics occur in Poland yearly, usually during winter and early spring seasons leading to hundreds thousands of cases and many hospitalizations. The aim of our study was a pharmaco-economic analysis whether universal influenza vaccination of Polish population would be cost-effective.

Methods: We developed decision-analytical model to compare the costs associated with two opposite strategies: no vaccination and universal vaccination. Costs were calculated from societal perspective (including sick-leave and patient payments) in single year. We used epidemic and demographic data from 2007. Model inputs came from local epidemic data, published literature and expert opinions (when data missing only).

Results & discussion: The results of the analysis were particularly sensitive to influenza incidence rate and number of hospitalization. We think that the official figures (374.000 cases, 763 hospitalizations) are underestimated and inaccurate due to a passive monitoring system and only occasional use of diagnostic tests. Assuming that the influenza incidence in Poland is similar to that of western European countries, the decision-analytical model predicted that the universal vaccinations would cost less (approximately 1.1 billion zloty) than symptomatic treatment of outpatients (costing between 495 to 619million zloty) with sick leave payments (costing 2.2 to 4.7billion zloty) and hospitalizations (costing to 1 billion zloty). The results of the analysis were relatively non-sensitive to vaccine price, cost of medical visit and sick-leave payments.

Conclusions: Universal influenza vaccination in Poland would be cost-effective. The accurate pharmaco-economic analysis needs reliable data of influenza epidemicity obtained through active monitoring system and extensive use of confirmatory diagnostic tests.

SAFETY OF 13-VALENT PNEUMOCOCCAL CONJUGATE VACCINE IN INFANTS AND CHILDREN: META-ANALYSIS OF 13 CLINICAL TRIALS IN 9 COUNTRIES

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Aims: Summarize integrated safety analyses of 13-valent pneumococcal conjugate vaccine (PCV13) administered to infants and young children compared with 7-valent pneumococcal conjugate vaccine (PCV7).

Methods: Meta-analysis of integrated safety data from 13 infant studies (PCV13 n=4729 and PCV7 n=2760) was conducted in 9 North American, Europe, and Asian countries. Local reactions at the pneumococcal conjugate vaccine injection site and systemic events were collected for 4-7 days after each dose into electronic diaries. Unsolicited adverse events (AEs) were collected after each vaccination.

Results: Overall, rates of local reactions after any dose of the infant series were similar between PCV13 and PCV7 groups (tenderness [46.7 vs 44.8%], swelling [28.5 vs 26.9%], redness [36.4 vs 33.9%] respectively). After the toddler dose, tenderness was significantly higher ($p = 0.005$) among PCV7 (54.4%) subjects than PCV13 (48.8%) subjects. Frequencies of fever ($\geq 38^{\circ}\text{C}$) were similar in both groups, most were mild ($< 39^{\circ}\text{C}$); incidence of moderate fever ($39^{\circ}\text{-}40^{\circ}\text{C}$) with PCV13 was $\leq 2.8\%$ after any infant dose and 5% after the toddler dose compared to $\leq 2.6\%$ and 7.3% with PCV7. Fever $>40^{\circ}\text{C}$ was uncommon in both groups. Frequencies of decreased appetite, irritability, and sleep disturbances were similar in both groups. Reported AEs were types of conditions and symptoms expected in infants and children. Few subjects discontinued study vaccine because of AEs: 22 subjects (0.47%) in the PCV13 group and 17 subjects (0.62%) in the PCV7 group.

Conclusion: PCV13 has a favorable safety profile similar to that of PCV7, the standard of care for infants and young children.

AN INITIAL ASSESSMENT OF THE COST-EFFECTIVENESS OF THE NEW 13-VALENT PNEUMOCOCCAL CONJUGATE VACCINE FOR INFANT ROUTINE IMMUNIZATION IN HONG KONG

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Background and aims: Cost-effectiveness studies using local health data have supported the long-term health and economic benefits of the 7-valent pneumococcal conjugate vaccine (PCV-7) due to herd immunity leading to its inclusion in the routine immunization programme for infants in Hong Kong in 9/2009. The aim of the present study is to assess the clinical and economic impacts of the new PCV-13 vaccine on the whole population of Hong Kong.

Methods: A decision analytical model modified from the recent PREVENT model was used for the analysis of the outcomes of vaccination. The whole population of Hong Kong of around 7 million was analyzed with infants ≤ 2 either vaccinated or not vaccinated with PCV-13. Population data, incidence rates, serotype coverage, disease sequelae, mortality rates, vaccine effectiveness, duration of protection, herd effects, utilities, cost of vaccination, direct and indirect costs were adopted from local published studies, previous economic assessments of PCV-7/PCV-13 and local government sources to populate the model. Sensitivity analyses were performed to check the robustness of the results. The time horizon was one year and the study was performed from a societal perspective.

Results: Over 1 year, our analysis shows for a 4-dose regimen of PCV-13: a gain of 19 quality-adjusted-life-years (QALY), an avoidance of 1,534 related illnesses and 2 deaths, cost/life-year gained is US-177,259 and cost/QALY is -US174,229.

Conclusion: With GDP per capita of Hong Kong being US30,811 in 2008, our study results suggest PCV-13 vaccination is very cost-effective in providing protection to the people of Hong Kong.

A SUCCESSFUL INTERVENTION TO INCREASE IMMUNIZATION RATES IN LIVER TRANSPLANTED CHILDREN: TAILOR-MADE RECOMMENDATIONS BASED ON SEROLOGIES AGAINST VACCINE-PREVENTABLE DISEASES

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Background and aims: Despite well established vaccine recommendations for solid organ transplanted patients, children referred for orthotopic liver transplantation (OLT) in Switzerland were not vaccinated optimally. In 2002, new guidelines recommended to base catch-up immunization schedules on serum antibody titers against vaccine-preventable diseases assessed before and after OLT. We measure here the results of this intervention by comparing vaccine coverage in the pre- (1990-2002, P1) and the post- (2003-2008, P2) intervention cohorts.

Methods: P1 children (n=44, 57% female, mean age at OLT 4.4yr, range 0.6-16.8yr) and P2 children (n=30, 47% female; mean age 4.5yr, range 0.5-16.5yr,) were evaluated.

Results: Pre-transplant serologies were assessed more frequently in P2 compared to P1 children for DT, pneumococcus and MMR ($P < 0.001$, < 0.001 , and 0.004 , respectively). At time of OLT, more P2 patients were uptodate for DTaP (70% vs 43%, $P=0.023$) and MMR (74% vs 44%, $P=0.049$). More patients in P2 had received at least one dose of HBV, HAV, pneumococcus and VZV ($P < 0.001$, 0.012 , < 0.001 and 0.037 , respectively). At 1 year post-OLT, control serology was more frequently checked in P2 children for DT, pneumococcus, MMR and VZV ($P < 0.001$, < 0.001 , < 0.001 and 0.159 , respectively). These results were only explained by inclusion into the pre- and post-intervention periods and not by other differences (gender, age at OLT, diagnosis) among P1 and P2 patients.

Conclusion: Protection against vaccine-preventable diseases of high-risk children such as OLT patients may be significantly improved by tailor-made recommendations using serologies to vaccine-preventable diseases.

IMMUNOGENICITY AND SAFETY OF PNEUMOCOCCAL CONJUGATE VACCINE IN CHILDREN WITH IDIOPATHIC NEPHROTIC SYNDROME

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Aim: We evaluated pneumococcal conjugate vaccine(PCV) immunogenicity in children with INS in remission and we compared INS relapses in the following 12 months post vaccination with relapses occurred in the previous year.

Methods: 32(17 male) INS patients [median age(range):9(4-17)years] and 16(10 male) controls [14(7-20)years] with no history of pneumococcal vaccination received 1 dose of PCV(Prevenar, Wyeth Vaccines). Patients were on no treatment or low-dose alternate-day prednisone±mycophenolate mofetil (MMF) ± cyclosporine A (CyA). Sera obtained at baseline and 29±3.6 days later were analyzed by ELISA for detection of pneumococcal serotype (PS)-specific IgG antibodies.

Results: Patients and controls had similar antibody levels at baseline; protective PS titers $\geq 0.35\mu\text{g/ml}$ for ≥ 2 PS were detected in 8% of study subjects. Overall response defined as IgG $\geq 0.35\mu\text{g/ml}$ for ≥ 5 PS was lower in INS patients compared to controls(87% vs 100% respectively). Geometric mean antibody concentrations(GMC) at 1 month increased significantly for all PS in both groups however GMC for 5/7 PS were higher in controls compared to patients(GMC for PS4, 6B, 9V, 14, 18C: 5.43vs0.61, 17.68vs1.08, 5.01vs2.94, 17.16vs7.74, 4.09vs1.70 $\mu\text{g/ml}$ respectively, $p < 0.05$). Among patients, PCV immune response was lower for 3/7 PS in patients on MMF±CyA compared to subjects on low-dose or no steroids. There were 19vs11 INS relapses in 11vs7 patients pre and post vaccination respectively. All but 1 patients with relapse 3 months after PCV had a history of relapse in the 6-month period prior to vaccination.

Conclusions: PCV shows inferior immunogenicity in children with INS compared to controls. PCV-associated relapses are more frequent among subjects with history of recent relapses.

RESPONSES TO 2009 H1N1 VACCINE IN HEALTHY CHILDREN 3 TO 17 YEARS OF AGEA. Arguedas¹, C. Soley¹, U. Nicolay², K. Lindert³*¹Instituto de Atencion Pediatrica, San Jose, Costa Rica, ²Novartis Vaccines and Diagnostics, Marburg, Germany, ³Novartis Vaccines and Diagnostics, Cambridge, MA, USA*

Background and aims: Children are at increased risk for serious influenza illness. Experience with other pandemic vaccines indicates that two doses of 2009 H1N1 influenza vaccine might be needed to induce satisfactory immunogenicity. Adjuvants may permit a lower dosage than that needed for vaccines with non-adjuvanted antigens.

Methods: This randomized study in Costa Rica tested various doses of egg-based 2009 H1N1 vaccine in subjects 3-17 years of age (ClinicalTrials.gov NCT00973700). The vaccines were formulated with or without the MF59 adjuvant used in a European-licensed influenza vaccine (Fluad®). Children 3-8 (N=194) and 9-17 (N=196) years of age received (2:3:2 ratio) one 7.5-µg dose of adjuvanted vaccine; one 15-µg or two 15-µg doses of non-adjuvanted vaccine each on days 1 and 22. Serology was tested 21 days after each vaccination.

Results: After the first dose, all vaccines met the Center for Biologics Evaluation and Research (CBER) seroprotection criterion in children 9-17 years of age; but only the adjuvanted vaccine met the criterion in children 3-8 years of age. After the second dose, all children given adjuvanted vaccine had HI titers $\geq 1:40$. Seroprotection rates with the non-adjuvanted vaccines were 85-94% and 99-100% in children 3-8 and 9-17 years of age, respectively. Seroconversion rates with the adjuvanted vaccine in children 3-8 and 9-17 years of age were 95% and 83%, respectively; and 84-93% with the non-adjuvanted vaccine regimens.

Conclusion: The MF59 adjuvant provided adequate immune response after a single dose in younger and older children using lower hemagglutinin dose than non-adjuvanted vaccine.

MONITORING THE SAFETY OF THE ORAL VACCINE AGAINST ROTAVIRUS, PARANA-BRAZIL

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Background and aims: The widespread use of rotavirus vaccine (Rotarix ® GSK) in Brazil is important to control the disease and for assessment of adverse events, especially intussusception (IINT). The aim of this study was to evaluate possible association between the vaccine and IINT.

Methods: A case-control study was conducted in the region of Curitiba, Parana, Brazil. It is part of an international multicenter study coordinated by PAHO and the Ministry of Health. Children less than 1 year with IINT diagnosis performed during 2007 to 2009 were selected. The controls were matched (4:1) by age and region of origin.

Results: The study included 26 hospitalized cases, 92.3% underwent surgery, 84.6% underwent ultrasound, 23.1% a barium enema, 15.4% had histopathological material, 61.5% were male, 3 to 11 months of age (mean: 6.9 months, SD = 2.4), 69.2% had family income up to 3 minimum wages, 92.3% had received the 1st dose of vaccine rotavirus and 76.9% two doses, 84.6% were breastfed. The analysis showed an inverse association (OR = 0.21, 95% CI 0.06 to 0.74) between 2 doses of vaccine against rotavirus and IINT. There was no association with breastfeeding, low income, gender and 1st dose of vaccine.

Conclusions: Was no association between the Rotavirus vaccine and IINT, on the contrary, the 2nd dose showed a protective effect. It is important to await the outcome of the multicenter study to obtain more robust results.

COMMUNITY AND PARENTAL RESPONSE DURING THE H1N1 09 INFLUENZA PANDEMIC: AN EVALUATION OF COMPLIANCE IN PUBLIC HEALTH POLICY

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Background and Aims: An important step in future pandemic planning and response is to understand the views and experience of those affected by public health measures during a pandemic. This study aimed to evaluate the community's response to the H1N1 09 Influenza Pandemic.

Methods: A cross-sectional study was conducted by Computer Aided Telephone Interviews in rural and metropolitan South Australia. The survey assessed adult and parental knowledge, awareness and compliance with pandemic public health policy.

Results: 1961 interviews were conducted in metropolitan and rural households. 42% of respondents correctly identified the meaning of pandemic influenza with 0.7 % having never heard of pandemic influenza and 22.6% unaware of its meaning. At least one correct route of transmission was named by 93% of respondents. Almost all (94%) agreed they would stay home from work if they showed symptoms of H1N1 Influenza and 73% of parents would keep their children in home isolation for seven days if they had travelled to an area affected by H1N1. 57% of respondents intended to have the H1N1 vaccination when it became available. More respondents intended to have their children vaccinated against H1N1 (66%) than to be vaccinated themselves. Women (OR 0.54) and respondents with higher socioeconomic status (OR 0.53) were less likely to want children vaccinated.

Conclusions: Adults and parents reported high compliance with public health policy during the current H1N1 pandemic including acceptance of home isolation and intent to receive the H1N1 vaccine but actual behaviours, such as receiving the H1N1 vaccination, were much reduced for adults and children.

PROSPECTIVE ESTIMATION OF ROTAVIRUS VACCINE EFFECTIVENESS IN SPAIN

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Background and aims: Effectiveness data of available rotavirus vaccines (RVV) are mainly coming from USA and restricted to the pentavalent vaccine. We have estimated the effectiveness of RVV in Spain, where both rotavirus vaccines are available since 2007.

Methods: A prospective observational study was conducted from Oct-2008 through Jun-2009 including 682 children up to 5 years-old with AGE attended in primary care (n=18 centres), and ER and hospital settings (n=10), covering Galicia and Asturias regions(North-West Spain). A rapid stool immunochromatographic test for rotavirus antigen detection (test VIKIA, BioMerieux) was at least performed in all included patients. RVV global effectiveness was estimated as 1-OR after comparing the frequency of rotavirus vaccination in patients positive and negative to rotavirus etiology. RVV effectiveness to prevent hospital admission was also calculated.

Results: Of 682 enrolled children, 207(30.4%) were rotavirus positive and 152(22%) had received at least one dose of rotavirus vaccine. In 163 patients(24%) hospital admission was required, but patients with rotavirus AGE were admitted to hospital more frequently (47.8%vs14%)[p< .001]. RRVE (after at least one vaccine dose) to prevent rotavirus AGE was 90.5% (95% confidence interval: 82%-95%). RVVE to prevent hospital admission due to rotavirus AGE was 94.7% (83-98.4%). Once a child has an AGE, being vaccinated reduced the risk of admission by 44%, with a number needed to vaccinate(NNV) of 4, although these results were not statistically significant, probably due to the small number of rotavirus patients.

Conclusions: Rotavirus vaccines have showed an outstanding effectiveness in Spain despite low-medium coverage rates yet.

IMMUNOGENICITY AND SAFETY OF 13-VALENT PNEUMOCOCCAL CONJUGATE VACCINE GIVEN WITH MENINGOCOCCAL C TETANUS TOXOID CONJUGATE AND OTHER ROUTINE PEDIATRIC VACCINATIONS

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Aims: To compare immune responses to selected antigens in pediatric vaccines given as part of the Spanish calendar when administered concomitantly with 13-valent or 7-valent pneumococcal conjugate vaccine (PCV13 or PCV7), and to assess the immunogenicity and safety of PCV13 in infants and toddlers.

Methods: Healthy infants were randomized to receive either PCV13 (n=223) or PCV7 (n=226) with DTaP-Hepatitis B-IPV-Hib (ages 2, 4, 6 months), DTaP-IPV+Hib (age 15 months), and MnC-TT (ages 2, 4, 15 months). Antibody response to selected antigens in both groups was assessed 1 month after dose 2 and 3 of the infant series and 1 month after the toddler dose. Local and systemic events were reported for 4 days following vaccination. Demonstration of noninferiority for concomitant vaccines was set at >-10% (lower limit of 95% CI for the difference in proportions between PCV13 and PCV7).

Results: Infant and toddler immune responses induced by meningococcus, diphtheria, and tetanus antigens administered with PCV13 were all noninferior to those observed with coadministration of PCV7. After dose 3, ≥93% (PCV13) achieved pneumococcal anticapsular IgG concentrations ≥0.35 µg/mL for all serotypes except serotype 3 (86.2%). IgG GMCs for all serotypes were 0.85-4.51 µg/mL and 1.04-12.25 µg/mL after dose 3 and the toddler dose, respectively. Local and systemic reactions were similar between the two groups after the infant and toddler dose.

Conclusions: PCV13 can be given safely with routine infant vaccines without immunological interference. PCV13 has an acceptable safety profile and produces a strong immune response in both infants and toddlers.

EFFECTIVENESS OF ONE OR TWO DOSES OF THE PENTAVALENT ROTAVIRUS VACCINE (RV5) IN PREVENTING GASTROENTERITIS IN THE UNITED STATES

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Background and aims: The effectiveness of 3-dose administration of the pentavalent rotavirus vaccine (RV5) was previously demonstrated in a real-world setting. This study estimated the post-licensure effectiveness of one and two doses of RV5.

Methods: A national US health insurance claims database was used to assess reduced incidence of claims-based rotavirus-specific gastroenteritis and all-cause gastroenteritis resulting in hospitalizations, emergency department(ED) and physician visits. Infants vaccinated with RV5 were compared to infants who received diphtheria-tetanus-acellular pertussis(DTaP), but not RV5, over the 2007 and 2008 rotavirus seasons. Analysis included infants who received only 1 or only 2 doses and between doses among infants who eventually received three doses.

Results: 42,306 infants received the first RV5 dose and 28,417 received the first DTaP dose; 43,704 infants received the second RV5 dose and 31,810 infants received the second DTaP dose. The majority of follow-up was observed between doses among those who eventually received three doses. For prevention of hospitalizations or ED visits, one dose of RV5 was associated with 88% (95%CI:45%-99%) effectiveness against rotavirus gastroenteritis and 44% (95%CI:18%-62%) effectiveness against any gastroenteritis; two doses of RV5 were associated with 94% (95%CI:61%-100%) effectiveness against rotavirus gastroenteritis and 40% (95%CI:18%-56%) effectiveness against any gastroenteritis. For prevention of rotavirus gastroenteritis-related outpatient visits, one and two doses of RV5 were associated with 100% (95%CI:54%-100%) and 40% (95%CI:< 0%-88%) effectiveness, respectively. Limitations of the analysis include small numbers of cases and potential misclassification of exposure.

Conclusions: RV5 demonstrated effectiveness against rotavirus gastroenteritis, even when the 3-dose regimen was incomplete.

EFFECTIVENESS OF THE ORAL PENTAVALENT ROTAVIRUS VACCINE IN NICARAGUA

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Background and Aims: Since October 2006, the Merck & Co., Inc. and Nicaragua RotaTeq™ Partnership has provided over 1.3 million doses of the oral pentavalent rotavirus vaccine (RV5) to infants in Nicaragua. The partnership included an effectiveness evaluation of routine complete (3-dose) vaccination with RV5 to reduce severe rotavirus gastroenteritis (RVGE) associated hospitalizations and emergency department (ED) visits.

Methods: Between February 2007-October 2009, a case-control study enrolled inpatient and ED subjects at 6 hospitals in Nicaragua. Severe RVGE (Vesikari score ≥ 11) cases were age-eligible to have received RV5; presented to study sites within 72 hours of acute gastroenteritis onset; and were confirmed as rotavirus-positive by EIA. For each case, age-matched hospital controls with non-diarrheal infectious diagnoses, and community controls from the neighborhood of the case, were enrolled. Vaccination history was verified by card or health center records. Vaccine effectiveness was calculated using conditional logistic regression.

Results: 241 cases were eligible for this analysis and were matched to 791 hospital controls and 850 community controls. For the entire 32 month study period, vaccine effectiveness was 58% (95%CI 37%-72%) and 87% (95%CI 78%-93%) compared to hospital and community controls, respectively. For children < 12 months of age at disease onset, vaccine effectiveness was 88% (95%CI 74%-94%) for the combined control groups.

Conclusion: In Nicaragua, RV5 demonstrated high vaccine effectiveness for children under 1 year of age at highest risk for rotavirus disease and is expected to have a significant positive public health impact.

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CO-ADMINISTRATION OF MENACWY-TT CONJUGATE VACCINE WITH DTPA-HBV-IPV/HIB VACCINE DOES NOT IMPAIR IMMUNE RESPONSE TO DTPA-HBV-IPV/HIB, AND HAS AN ACCEPTABLE SAFETY PROFILE

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Background and aims: Incidence of meningococcal disease is highest in young children. This study assessed the impact of a candidate MenACWY-TT vaccine on the immune response induced by DTPa-HBV-IPV/Hib (*Infanrix-hexa*TM; GSK Biologicals), when co-administered in toddlers age 12-23 months.

Methods: In this phase III, open, controlled study, 793 toddlers were randomized 2:2:2:1 to 4 groups: A) MenACWY-TT+DTPa-HBV-IPV/Hib (N=222), B) MenACWY-TT (+DTPa-HBV-IPV/Hib 1 month later) (N=220), C) DTPa-HBV-IPV/Hib (+MenACWY-TT 1 month later) (N=224), or D) MenCCRM₁₉₇ (N=127). Here we report antibodies measured pre- and 1 month post-first vaccination (not sequential vaccinations). Local/general solicited symptoms within 4 days of vaccination and SAEs up to 6 months after dose 1 were recorded.

Results: The immunogenicity of DTPa-HBV-IPV/Hib co-administered with MenACWY-TT was non-inferior to DTPa-HBV-IPV/Hib alone for all antigens (**Tables 1 and 2**).

Table 1. Adjusted GMC values one month after vaccination (ATP cohort for immunogenicity); lower limits of the two-sided 95% confidence interval calculated on the GMC ratio were ≥ 0.67 (predefined non-inferiority limit)

Antibody	Adjusted GMC		Adjusted GMC ratio	
	MenACWY-TT + DTPa-HBV-IPV/Hib (N=194)	DTPa-HBV-IPV/Hib (N=188)	(MenACWY-TT + DTPa-HBV-IPV/Hib / DTPa-HBV-IPV/Hib)	95% CI
Anti-PT (EIU/ml)	83.6	86.6	0.97	0.83, 1.12
Anti-FHA (EIU/ml)	538.2	550.4	0.98	0.85, 1.13
Anti-PRN (EIU/ml)	439.9	476.1	0.92	0.78, 1.10

[Adjusted GMC values one month after vaccination]

Table 2. Proportion of subjects with antibody titres above the pre-specified limit, one month after vaccination (ATP cohort for immunogenicity)

Antibody (titre cut-off)	Proportion of subjects (%)		Difference in %	
	MenACWY- TT+DTPa-HBV- IPV/Hib (N=194)	DTPa-HBV-IPV/Hib (N=188)	(MenACWY-TT + DTPa-HBV-IPV/Hib minus DTPa-HBV-IPV/Hib)	95% CI
Anti-HBs* (10 mIU/ml)	99.4	98.2	1.22	-1.47 [†] , 4.60
Anti-PRP* (1 µg/ml)	99.5	98.3	1.19	-1.45 [†] , 4.50
Anti-Diphtheria (0.1 IU/ml)	100	99.4	0.57	-1.48, 3.19
Anti-TT (0.1 IU/ml)	100	99.4	0.57	-1.48, 3.19
Anti-Polio1 (1:8)	99.4	99.4	0.00	-2.76, 2.83
Anti-Polio2 (1:8)	99.4	98.8	0.63	-2.20, 3.83
Anti-Polio3 (1:8)	100	98.2	1.84	-0.44, 5.28

*Primary study objective: non-inferiority of MenACWY-TT+DTPa-HBV-IPV/Hib compared with DTPa-HBV-IPV/Hib; [†] lower limits of the two-sided 95% confidence interval calculated on the group difference were ≥ -10 (pre-defined non-inferiority limit)

[Antibody titres one month after vaccination]

Redness, drowsiness and irritability were the most frequently reported solicited local/general symptoms in both groups. Ten subjects in the MenACWY-TT+DTPa-HBV-IPV/Hib and 11 in the DTPa-HBV-IPV/Hib groups reported SAEs; none were considered related to vaccination.

Conclusion: MenACWY-TT co-administered with DTPa-HBV-IPV/Hib is well tolerated and does not impair DTPa-HBV-IPV/Hib immunogenicity in toddlers, facilitating the potential integration of MenACWY-TT into childhood vaccination schedules.

REDUCTION OF HOSPITALIZATION DUE TO RESPIRATORY DISEASES WITH THE USE OF VACCINES AND PALIVIZUMAB IN PREMATURES WITH CRONIC LUNG DISEASE

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Introduction: Lower respiratory infections (LRI) are the leading cause of hospitalisation and death during the first year of life in Panama. Premature and infants with chronic lung disease (CLD), are at increased risk of serious illness. The respiratory syncytial virus (RSV) is the common cause, frequently associated with bacterial pneumonia caused by *Streptococcus pneumoniae* (SP).

In 2005, Palivizumab, and 7 valent conjugated vaccine (PCV7) were introduced to our Follow up Program in CLD infants.

Objectives: To evaluate efficacy of Palivizumab and PCV7 reducing hospitalisation in infants with CLD.

Methods: Cohort study conducted over 3 RSV seasons (2005-2008), in CLD premature infants, less than 29 weeks gestational age. 130 infants follow in a 3 year period (2003-2005) before introduction of Palivizumab and PCV7, were used as historic control group. (group A).

79 infants received PCV7 and regular vaccines of the National Program, (group B). Another 79 infants (group C) received regular vaccines, PCV7 and Palivizumab (15 mg. per Kg. /month) during the RSV season. (June to November). Infants were follow up until December 2008, and data collected prospectively.

Statistical analyses were performed using Yates corrected chi-square test for numerical data.

Results: Group A have a hospitalisation rate of 36%, 25% group B, and 14% group C.

When compare with group A, group B presents a reduction of 30%, and group C of 62% ($p=0.0009$).

When compare with the Group B + C presents a significant reduction. ($p=0.003$)

Conclusions: Palivizumab and PCV7 significantly reduces hospitalisations caused by (LRI) in infants with CLD.

ATTITUDES OF PARENTS TOWARDS THE VACCINATION FOR PANDEMIC FLU IN ATHENS AREA BEFORE ITS OFFICIAL APPLICATION

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Background and aims: The efficacy and safety of H1N1 flu vaccine have been a focus of concern since its introduction. Purpose of this study was to evaluate parents' attitude towards the pandemic vaccine before its national implementation.

Methods: 235 self-administered questionnaires were given to 42 fathers and 193 mothers living in Athens area. The questionnaire included demographic characteristics of parents and their 398 children.

Results: There was unanimous (98.3%) acceptance of vaccinations in general without adopting uncritical attitude of doing any new vaccine without delay (89.8%) although a significant percentage (16.2%) preferred the natural disease. Conflicting opinions of doctors cause much confusion (35.9%) to parents. It's worth noticing parents' belief that the aim of developing new vaccines is profit (79.1%). Pediatricians were considered the most accurate source of information (98.3%) followed by government statements (48%) and the media (30%). Most parents (84.3%) were unwilling to vaccinate their children for pandemic flu. Correlation was found with the number of siblings and the age of the younger child ($p < 0.05$). Main reasons for vaccination were the fear of the potential the disease becoming serious (94.1%) and pediatricians' recommendation (44.1%). Among reasons to reject vaccination were: inadequate safety data (96.9%), efficacy skepticism (78.5%), lack of pediatricians' recommendation (73.1%) and the belief that H1N1 flu isn't a serious disease (37.2%).

Conclusions: Pediatricians are opinion leaders for parents regarding children's vaccination. Nevertheless, it seems that parents are unable to follow the evolution of knowledge step by step concerning a new issue as the H1N1 vaccination.

HIGH TETANUS ANTI-TOXIN CONCENTRATION IN THE NETHERLANDS; A SEROSURVEILLANCE STUDY

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Background and aims: Despite a low incidence of disease, it is important to evaluate the long term effect of routine vaccination. We aimed to assess if the Dutch population is sufficiently protected against tetanus, and which factors determine the tetanus anti-toxin level. Importantly, immunological protection against tetanus can only be obtained through vaccination.

Methods: Serum samples and questionnaire data from a population-based serosurveillance study were used for this study (N = 6385). Serum anti-toxin antibodies were assessed with a fluorescent bead-based multiplex immunoassay. Data were analyzed in SAS. Multivariable linear regression was used to study determinants of the tetanus anti-toxin antibody level.

Results: From all participants, 94% (CI 94-95) had a tetanus anti-toxin level above the minimal protective value (0.01IU/ml). The overall geometric mean titer for the Dutch population was 0.91 (CI 0.85-0.97) IU/ml. Born before 1951, being female, born in a non-Western country, non-participation in the national immunisation program (NIP) or having reported less than 4 vaccinations, no vaccination because of profession, not having travelled, longer time reported since last tetanus vaccination, and being religious (e.g. Protestant or Islam) were independently associated with lower tetanus antitoxin level.

Conclusions: Overall, the Dutch population is very well protected against tetanus due to high NIP participation and additional vaccinations because of tetanus toxoid-conjugated MenC mass vaccination, profession, travel or injury. However, individuals born before 1951, first generation migrants from non-Western countries and individuals from reformed protestant denominations remain at risk for tetanus and only they should be vaccinated after sustained injury.

EXPRESSION OF INFECTIOUS BOVINE RHINOTRACHEITIS VIRUS GLYCOPROTEIN D IN BACTERIAL CELL

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Background: Bovine Herpesvirus 1 (BHV-1) belongs to the genus of *Varicellovirus* and the family of *Herpesviridae* which contains three main *gB*, *gC* and *gD* genes and can cause different respiratory, reproductive and nervous system disorders in cows.

Aims and methods: In order to cloning of the coding region of *gD* gene of IBR Virus , PCR product of the open reading frame of the gene from IBR-MDBK cell line was amplified by PCR. A 1047bp PCR product of the *gD* gene with *EcoRI*, *HindIII* restriction sites were subcloned of pTZ57R/T and digested by the mentioned endonucleases. Digested insert cloned in to pET-32a and transfected in *E.coli* cells. For the expression of gD protein, the pET-32a recombinant vector was transformed and then induced in BL21(DE3) strain of *E.coli* competent cells using IPTG.

Results: The presence of gD expressed protein was shown in immunoblotting and SDS-PAGE system.

Conclusions: With respect to the remarkable frequency of infection to IBR in Iran and the necessity of controlling it through vaccination with recombinant vaccines of thymidine kinase, manufacturing and applying the recombinant gD protein are vital goals in recognition and distinction between infection and responses caused by vaccine.

Keywords: IBR virus, gD protein, pET-32a vector, protein expression, SDS-PAGE, immunoblotting.

COMBINED HAEMOPHILUS INFLUENZAE TYPE B-NEISSERIA MENINGITIDIS SEROGROUP C VACCINE (HIB-MENC; *MENITORIX*TM, GSK) IS IMMUNOGENIC AND WELL TOLERATED IN PRETERM INFANTS

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Background and aims: In preterm infants there is a trend for increased relative risk for invasive Hib disease and progressive reduction in anti-PRP immune response with decreasing gestational age. Primary vaccination of 163 pre-term (n=56, < 31 weeks; n=107, 31-36 weeks) and 150 full-term infants (>36 weeks), at 2-4-6 months of age with Hib-MenC, DTPa-HBV-IPV and 7vCRM₁₉₇ was assessed.

Methods: In this open, controlled, Spanish multi-centre study, blood samples were collected pre- and one month post-vaccination dose-3. Serum bactericidal activity was measured using baby rabbit complement assay (rSBA-MenC). Anti-PSC, anti-PRP and anti-HBs antibodies were measured by ELISA. Local/general symptoms were assessed for 3 days via diary cards, and AEs throughout the study.

Results: Post-dose-3, no differences between pre-term and full-term infants in seroprotection/seropositivity rates were observed (Table).

Table: Percentages of subjects with titres/concentrations greater than or equal to pre-defined cut-offs and GMTs/GMCs for anti-PRP, rSBA-MenC, anti-PSC and anti-HBs antibodies, one month post-dose 3 (ATP cohort for immunogenicity)

GA	Time-point	N	Anti-PRP			rSBA-MenC			Anti-PSC			Anti-HBS			
			% ≥0.15 µg/mL	% ≥1 µg/mL	GMC	N	% ≥1:8	GMT	N	% ≥0.3 µg/mL	GMC	N	% ≥10 mIU/mL	% ≥100 mIU/mL	GMC
<31 weeks	Pre	45	17.8 [8.0-32.1]	0.0 [0.0-7.9]	0.091 [0.080-0.104]	45	2.2 [0.1-11.8]	4.2 [3.8-4.5]	45	6.7 [1.4-18.3]	0.17 [0.15-0.19]	33	87.9 [71.8-96.6]	0.0 [0.0-10.6]	28.7 [21.0-39.1]
	Post	44	100 [92.0-100]	97.7 [88.0-99.9]	16.076 [11.080-23.527]	45	100 [92.1-100]	1098.6 [790.2-1527.3]	45	100 [92.1-100]	6.19 [4.84-7.92]	40	97.5 [86.8-99.9]	85.0 [70.2-94.3]	264.3** [180.2-387.8]
31-36 weeks	Pre	95	31.6 [22.4-41.9]	5.3 [1.7-11.9]	0.131 [0.108-0.158]	96	15.6 [9.0-24.5]	5.4 [4.6-6.2]	97	20.6 [13.1-30.0]	0.21 [0.18-0.24]	79	75.9 [65.0-84.9]	3.8 [0.8-10.7]	23.3 [17.4-31.3]
	Post	96	99.0 [94.3-100]	93.8 [86.9-97.7]	8.562 [6.590-11.125]	98	99.0 [94.4-100]	1036.8 [796.4-1349.8]	95	100 [96.2-100]	6.41 [5.49-7.49]	89	100 [95.9-100]	84.3 [75.0-91.1]	434.3 [334.9-563.1]
Full-term	Pre	138	31.2 [23.6-39.6]	6.5 [3.0-12.0]	0.140 [0.117-0.167]	137	16.8 [11.0-24.1]	5.9 [4.9-6.9]	137	26.3 [19.1-34.5]	0.25 [0.21-0.30]	118	66.1 [56.8-74.6]	6.8 [3.0-12.9]	16.7 [13.5-20.6]
	Post	142	99.3 [96.1-100]	94.4 [89.2-97.5]	10.473 [8.547-12.833]	140	100 [97.4-100]	1346.2 [1130.4-1603.1]	141	100 [97.4-100]	7.46 [6.67-8.34]	129	100 [97.2-100]	90.7 [84.3-95.1]	586.6 [473.8-726.2]

GA= gestational age; GMC/GMT= geometric mean antibody concentration/titre calculated on all subjects; N= Number of subjects with available results

* statistically significant difference between the indicated group and the full-term group, †between the two pre-term groups; Pre/post = prior to dose 1 and one month post-dose-3; [] = upper and lower limits of 95% CI

[Antibody titres]

Anti-HBs antibody GMCs were statistically significantly lower in the < 31 weeks group compared with other groups; there were no significant between-group differences for other GMC/Ts. Hib-MenC vaccine was well tolerated in all age strata. Apnoea occurred in one subject (< 31 weeks) on Day 24 and Day 42-post-dose-1; the subject recovered without sequelae. There was one death due to meningococcal serogroup-B sepsis (full-term). Neither these events, nor any other SAEs, were considered vaccine-related.

Conclusions: Hib-MenC vaccine was immunogenic and well tolerated in pre-term, compared with full-term, infants when co-administered with other recommended vaccines.

THE INFLUENCE OF MMR VACCINATION ON DEVELOPMENT OF INFANTS FOLLOWED OVER THE FIRST SIX YEARS OF LIFE

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Background and aims: A great deal of speculation exists concerning the possible associations of certain vaccines, particularly the measles-mumps-rubella (MMR) vaccine, with autism. The objective of this analysis was to determine the relationship between vaccination to measles (MMR and single measles vaccination) and cognitive and psychomotor development during the first 6 years of life.

Methods: The cohort recruited prenatally in Krakow, Poland, included 504 children. The Fagan test, Bayley Scales of Infant Development (BSID-II), Color Raven's Matrices, Bender-Koppitz and Wechsler tests, were administered to infants from 6th to 72nd month of life.

Results: Children vaccinated with MMR had significantly higher mental BSID-II scores than vaccinated with single measles vaccine in 24th (101.9±3.2 vs 96.0±13,9) and 36th month (103.7±10.3 vs 97.9±11.2). After standardization (gender, maternal education, maternal IQ and mercury level in cord blood) the relative risks of "delayed" score in "MMR" group in comparison with "single measles vaccine" were respectively 0.13 (95PU%:0.03-0,61) and 0.15 (95PU%:0.03-0,80). Similarly the result of Raven's test was better for MMR vaccinated (relative risk = 0.20; 95PU%:0.05-0.83):. Results of the other tests did not show any relation with measles vaccination.

Conclusions: Our study did not demonstrate that the MMR vaccine had an harmful effect on infants' development. On the contrary, children vaccinated with single measles vaccine had a tendency to display a higher risk of delayed mental development.

All studied children were a sample from cohort study on the susceptibility of fetus and child to environmental factors followed in Krakow with Columbia University in New York.

HEPATITIS B VACCINE NONRESPONSE: LINK BETWEEN GENOTYPE, GLUTEN-FREE DIET AND IMMUNITY

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Background and aims: A genetic predisposition to hepatitis B vaccine nonresponse has been characterized in multiple studies. Celiac disease has a strong association with the DQ2 particular human leukocyte antigen (HLA) genotype. We evaluated the achievement of protective antibody titers in relation to HLA genotype, disease activity and gluten-free diet accomplishment.

Methods: We studied 72 children with celiac disease and 67 age-matched control subjects, and reviewed their hepatitis B vaccine records, serological tests for anti-hepatitis B surface antigen antibody (antiHBs), disease activity and HLA genotypes. 23 patients with celiac disease were prospectively immunized after diagnosis, monitoring diet compliance and celiac disease activity by measurement of antibodies against transglutaminase and gliadin.

Results: All tested celiac subjects were either homozygous or heterozygous for DQ2. The seroconversion after hepatitis B vaccination was 95.5% in control group (64 patients). Of the newborn-vaccinated celiac subjects, 50 were non responders (69.4%) and 13 were low responders (18%). Response rate in patients immunized after diagnosis was 78.2% (18 patients) and correlated with gluten-free diet (100% of non-strict diet patients were non-responders), despite the presence of human leukocyte antigen DQ2.

Conclusions: Celiac disease patients have a significant genetically mediated predisposition to hepatitis B vaccine nonresponse. However, we showed an excellent vaccine response with an adequately gluten-free diet. Thus, DQ2 alleles do not seem to have a primary role in immune response. Nonresponse to hepatitis B vaccine may be a sign of undiagnosed celiac disease. Revaccination of these patients should be done during a gluten-free diet.

DESIGN A(H1N1) INFLUENZA VACCINATION IN CHILDREN UNDER 14 YEARS OF AGE

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Background and aims: One of the groups that were considered as having a higher risk of suffering an illness due to A(H1N1) influenza are children. During the monitoring of the pandemic wave in our community, children under 15 years of age have experienced higher rates of infection, consequently, the aim is to preventively influence this age group with risk factors associated to it due to its higher likelihood of morbidity.

Method: We analysed the associated risk factors. To facilitate recruitment activities, health centres will obtain listings of patients included in the following processes: diabetes; heart failure; asthma in adults and pediatrics; and COPD. Family nurses will be in charge of contacting their own patients. Records of both seasonal influenza and pneumococcal vaccination will also be used for pediatricians and family physicians to active uptake. During consultation, will capture those patients not included in previous listings. We have already started to bring together the heads of the Centres to inform them of rules and procedures regarding the use of the vaccines.

Results: Once the pandemic vaccine is available (GSK-Pandemrix® and Focetria®). The vaccination campaign begins targeting defined risk groups and especially children (the most affected group). We have already started training the heads of both Centres and Nursing Departments. Special emphasis has been placed on both patient safety and the monitoring of adverse reactions.

Conclusions: The epidemiological analysis, its monitoring and risk assessment, makes it possible to operationalise an active vaccination campaign which targets those most vulnerable to the A(H1N1)flu.

HAS THE PERTUSSIS INCIDENCE IN EARLY INFANCY DECREASED TO LOW LEVELS AFTER MORE THAN A DECADE WITH PERTUSSIS VACCINATION?

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Background: Pertussis is a severe disease in infancy with high risk of complications and a non-negligible mortality rate.

Aims: To estimate the incidence of pertussis in infants before one year of age.

Methods: The pertussis surveillance study in Sweden has been on-going since October 1. 1997 in children born from January 1. 1996. All laboratory-confirmed cases (PCR and culture) of pertussis have been included in the analyses. Vaccination was introduced at 3, 5 and 12 months of age in 1996 and booster immunisation at 10 years of age in 2005. The vaccination coverage in infancy is around 98.5%.

Results: Pertussis disease was verified by laboratory analyses in 1051 infants (less than 1 year of age) from October 1. 1997 to December 31. 2008. The incidence of pertussis in infants has decreased during these years to 41 (2008) cases per 100,000 infants/year. In 2008, 57% (23/40) of pertussis cases in infants occurred during the first three months of life. The hospitalisation rate in infants is 50% and the mortality around one infant/year.

Conclusions: From the pertussis surveillance study, the incidence in infants less than 3 months of age is still rather high, irrespective of 11 years of vaccination at 3, 5 and 12 months of age. However, the incidence in infancy is decreasing. A study concerning contact tracing of pertussis from the family and the environment of the infant is on-going.

PERCEPTION AND COVERAGE OF SEASONAL INFLUENZA VACCINE AMONG PROFESSIONALS TAKING CARE OF YOUNG CHILDREN

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Background and aims: Children younger than 5 years require protection against influenza because the course of disease in this group of patients may be severe, complications and hospitalizations are more often. These children, and professionals who take care of this children should be annually vaccinated against influenza. The aim of the study was to learn a perception and coverage of seasonal influenza vaccine among professionals taking care of children younger than 5 years.

Methods: A cross-sectional study was performed among 256 persons - professional staff of 2 orphanages and 3 day care facilities in Warsaw. They were asked to fulfill self administered survey containing questions about seasonal influenza vaccinations.

Results: We found that 93% of responders self estimated their knowledge concerning influenza and its prophylaxis as good and enough. 24% of responders was vaccinated against influenza last year and 22% of them declared they would be vaccinated next years. 51% of responders agreed that influenza vaccinations should be obligatory for medical professionals and persons taking care of young children. 56% of responders found themselves as persons especially predisposed to influenza contamination because of a close contact with young children. 63% of responders declared they know that influenza may be a severe disease for young children and that's way they should be protected.

Conclusions: The coverage of influenza vaccine among the professionals taking care of young children (22-24%) is low and it should be improved. The perception of influenza vaccine in this group of professionals should be also better.

INFLUENZA VACCINATION COVERAGE AMONG CHILDREN AGED 0-4 YEARS IN POLAND IN 2001-2008

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Background and aims: Influenza is an acute infectious disease with a high risk of complications, especially in patients belonging to risk groups. According to ACCIP recommendations healthy children aged 6-59 months and all children older than 6 months with accompanying diseases (mostly cardio-pulmonary disorders) are a group of higher risk of hospitalizations and complications due to influenza and should be annually vaccinated against flu.

The aim of the study was to estimate influenza vaccine coverage in children aged 0-4 years in Poland in 2001-2008.

Methods: Data collected in 2001-2008 by National Institute of Hygiene, National Institute of Public Health, Department of Epidemiology and Chief Sanitary Inspectorate, Department of Communicable Diseases Control, published yearly as a bulletin "Vaccinations in Poland", available on www.pzh.gov.pl, were analyzed. Demographic data were obtained from Central Statistical Office (www.stat.gov.pl).

Results: General number of vaccinations against influenza in children aged 0-4 years varied from 19834 (in 2007) to 34262 (in 2002). The coverage of vaccination against flu in these children ranged from 1,1% (in 2007 and 2008) to 1,9% (in 2005). Among vaccinations performed in persons at all ages, the percentage of vaccinations made in children aged 0-4 years varied from 1,6% (in 2008) to 2,5% (in 2002).

Conclusions: The coverage of vaccination against flu in children aged 0-4 years in Poland in 2001-2008 was extremely low (about 1% in 2007 and 2008). No positive increasing trend has been observed. It is necessary to find out reasons for this situation and to improve it.

THE OIL-IN-WATER EMULSION MF59[®] STRONGLY ACTIVATES INNATE IMMUNE REACTIONS UPON INTRAMUSCULAR INJECTION

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Background and aims: Vaccine adjuvants can be grouped in two classes: TLR-dependent, like CpG and MPL and TLR-independent, such as the licensed products alum and MF59[®]. Interestingly, combinations of these two classes of adjuvants represent often the optimal formulation for soluble protein antigens in preclinical studies. TLR-dependent adjuvants directly stimulate antigen presenting cells (APCs) and their mechanism of action has been described in great details. By contrast, TLR-independent adjuvants do not activate APCs directly and their mechanism of action is less understood and needs further investigation.

Methods: We analyzed the local and systemic reactions elicited by MF59, alum and CpG following intramuscular administration in mice by combining DNA microarray analysis, immunofluorescence techniques and (multiplex bead) ELISA.

Results and conclusions: We found that all adjuvants modulated a common set of innate immunity genes and MF59 was the stronger activator of most genes including cytokines and cytokine receptors. Accordingly, we found the release of chemokines acting on monocytes and granulocytes into the blood stream and therefore studied the recruitment of such cells into the muscle. We found that MF59 promoted a more efficient infiltration of blood cells compared to alum and CpG and studied the recruitment kinetics of monocytes/ macrophages, dendritic cells, neutrophils and eosinophils in great detail. All cells participate in antigen uptake as visualized by using a fluorescent model antigen. Interestingly, the ability of vaccine adjuvants to stimulate local innate immune reactions correlates with their potency in enhancing the adaptive immune responses to co-administered antigen.

ACCEPTABILITY OF INFLUENZA A/ H1N1 VACCINATION IN A PROVINCE REGION OF NORTHERN GREECE: A QUESTIONNAIRE CROSS SECTIONAL SURVEY

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Introduction: Vaccination is an effective measure to reduce morbidity and mortality rates. There are limiting data concerning the acceptability of the vaccine against influenza A/H1N1 in Greek population.

Aim: To investigate the intension of parents in a province region in Northern Greece to take up vaccination against influenza A/ H1N1 for themselves and their children.

Material and methods: A random sample of 95 parents were interviewed by an anonymous questionnaire from October-November 2009. The Questionnaire included demographical data of the parents and three sections: 1. Intention to take up vaccination with H5N1 vaccine and pandemic with H1N1 vaccine for themselves and their children, 2.Perception of safety and side effects, 3. Factors that have influenced their decision.

Results: The response rate was 91%. The overall intention to accept H5N1 vaccination for themselves was only 38.5% and for their children 59% and for H1N1 only 25.5% and 19%, respectively. The respondents who were willing to accept H5N1 vaccines were more likely to accept H1N1 vaccines as well (95%). Younger age, male sex, higher educational status were associated with greater intension to accept vaccination. The most common reasons for refusal was "worry about side effects,"(42%), "not yet the right time to be vaccinated,"(18%) and "simply did not want the vaccine (35%). The main factor that influenced their decision was media (84%).

Conclusion: Evidence about safety is critical in determining the prevalence of vaccination uptake. The negative influence of media should be controlled and health agencies need to provide more information to the public.

RUBELLA SEROPREVALENCE DURING A 2- YEAR PERIOD AMONG CHILDREN**K. Papavasileiou, I. Varzakakos, G. Kuriakopoulou, J. Loisiou, A. Voyatzi, E. Papavasileiou***Clinical Microbiology, Penteli Childrens Hospital, Athens, Greece*

Background: Rubella is traditionally considered a childhood, vaccine preventable, viral disease usually without complications. Rubella infection during pregnancy may result in the delivery of a child with congenital rubella syndrome (CRS). The aim of rubella vaccination is to eliminate occurrence of CRS. The objective of the study was to determine the seroprevalence of rubella virus in children during a 2 year period.

Methods: From Nov 2007 to Oct 2009 sera from a total of 394 children (Greeks and immigrants) aged 1-14years old were collected and screened for the presence of IgG, IgM antibodies to rubella virus. Specific antibodies were measured by an enzyme-linked immunosorbent assay ELISA (AxSYM,Abbott).

Results: The total of 394 children (48% boys, 52% girls) was tested for specific rubella antibodies. Immunization with IgG antibodies were found in 79% of children while in 21% no IgG antibodies were detected. Acute infection (positive IgM antibodies) was present in 1%. Lack of immunization was more frequently observed among girls (57%) and Greek children (67,5%vs 32,5%).

Conclusions: This study showed a high percentage for rubella specific IgG antibodies. Surprisingly, more females and Greek children resulted to be not immunized. We believe that the high prevalence of immunization among immigrants does not respect the real prevalence but represents the immunization status of well integrate immigrates. A continuous strong public health commitment is required to increase the proportion of vaccinated individuals and absolute priority must be given in women before fertile age.

PUBLIC VACCINATION SCHEDULE IN AUSTRIA: SEROPROTECTION RATES IN PRE-SCHOOL CHILDREN AGAINST DIPHTHERIA, TETANUS, PERTUSSIS, HEPATITIS, MEASLES, MUMPS AND RUBELLA

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Background: The Austrian Advisory Committee on Immunization Practices annually publishes recommendations for childhood vaccinations. This investigation aims to confirm the vaccination schedule by evaluating the status of seroprotection against diphtheria, tetanus, pertussis, hepatitis A and B, measles, mumps and rubella.

Methods: Antibody levels against diphtheria, tetanus, pertussis, hepatitis A and B, measles, mumps and rubella were evaluated in 350 sera of children between five and seven years of age who were vaccinated accordingly.

Results: Seroprotection rates against diphtheria, tetanus, measles and mumps were 81%, 96%, 90% and 88%, respectively. Protective antibodies against rubella were detected in 68% of female and 58% of male study participants. Protective antibodies against hepatitis B were present in 52% of the investigated sera. 73% of the children had no antibodies against pertussis. Hepatitis A, 4% of unvaccinated children showed asymptomatic acquired immunity against hepatitis A.

Conclusion: The immune status against tetanus, measles and mumps is at a satisfactory level, however postponing the second measles-mumps-rubella-vaccine to school age might be reasonable for longer lasting immunity against measles. The immune status against diphtheria, pertussis, rubella and hepatitis B seems insufficient for long-term protection. The results justify a booster vaccination against diphtheria, pertussis and hepatitis B during school age, as presently recommended in Austria. Determination of the immune status of females against rubella before childbearing age should be encouraged.

IMMUNISATION PRACTICES IN VERY PRETERM INFANTS: A NATIONAL OBSERVATIONAL PRACTICE SURVEY

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Aims: The purpose of the study was to identify the current immunisation policy for infants born before 33 weeks of gestation in France according to recommendations and cocooning strategy.

Methods: A questionnaire was sent to all level II and III neonatal units between March and September 2009. Focal points were the chronological time of vaccination initiation - before or after discharge - with or without monitoring, need for rehospitalisation and indirect protection from vaccination of their entourage with pertussis and flu vaccine.

Results: 134 responses were obtained. The response rates were respectively 88.7% (55/62) and 36.7% (79/215) for levels III and II. All centres except 3 performed vaccination. The majority of neonatologists were aware of the current guidelines and an institutional protocol was available in 35.1% of cases. During the initial hospitalisation, the immunisation program began on Day 42 (if early discharge was planned), D60 and D67 in 7.5%, 80.6% and 9.7% of centres, respectively, and at a weight more than 2000 g in 39.5%. Cardiorespiratory monitoring was conducted in 80.3%. Half (50.7%) of the centres required rehospitalisation for first vaccine administration after initial hospital discharge. Prophylactic paracetamol administration was used in 47% of centres. 83.6% of neonatologists offered parents a flu vaccination and 70.9% an up-to-date immunisation schedule for pertussis.

Conclusion: This declarative neonatology survey highlighted the good knowledge of immunisation guidelines and cocooning strategy. An ancillary study could be helpful in comparing declared vaccination practices with actual practice.

CONSISTENCY OF IMMUNISATION PRACTICES IN VERY PREMATURE INFANTS IN FRANCE WITH PAEDIATRIC VACCINE PRODUCT INFORMATION

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Background: The Committee for Human Medicinal Products (CHMP), in 2007, asked for the following warning to be included in the product information (SmPC) of paediatric vaccines: *"The potential risk of apnoea and the need for respiratory monitoring for 48-72 h should be considered when administering the primary immunisation series to very premature infants and particularly for those with a previous history of respiratory immaturity..."*

The purpose of the study was to evaluate consistency of current immunisation practices in premature infants with paediatric vaccine SmPCs.

Methods: A questionnaire was sent to level II and III neonatal centres between March and September 2009 to explore vaccination practice in < 33 Weeks Gestational(WG) preterm infants.

Results: 134 responses were obtained 55 (88.7%) from level III units and 79 (36.7%) from others. When the first administration of primary immunisation series of a vaccine is given after discharge, 49.3% of units do not require rehospitalisation. When hospitalisation is undertaken for monitoring purposes, this is for less than 48 h (median 24h) in 62.1% of units. For second and third administrations, only 1.5% of centres systematically hospitalised very preterm infants, in practice mainly in the event of safety issues during the previous administrations. Duration of hospitalisation is less than 48 h in 56.7% of units (median 36h).

Conclusion: Declared vaccination practices in very premature infants in France are different from the CHMP information required to be included in SmPc labelling. A study could be helpful to explore specifically the practices in < 28 WG preterm infants.

IMMUNOGENICITY AND SAFETY OF TWO TICK-BORNE ENCEPHALITIS VACCINES IN CHILDREN

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Data comparing FSME-IMMUN 0.25 ml Junior and Encepur 0.25 ml Children in randomized clinical trials are limited. This ongoing, single-blind, randomized, clinical Study in children 1 to 11 years of age investigated the immunogenicity and safety of both vaccines administered according to the conventional schedule.

A total of 150 and 152 subjects were enrolled in the FSME-IMMUN and Encepur group, respectively.

Four weeks after the second vaccination, 100% of subjects attained seropositive titers in NT¹ (NT \geq 1:10) in the FSME-IMMUN and 97.8% in the Encepur group. The GMT was 236.8 in the FSME-IMMUN and 118.8 in the Encepur group.

In the FSME-IMMUN group, 100% of subjects were seropositive in both the IMMUNOZYM-(>126VIEU/ml) and the Enzygnost ELISA² (>10.32U/ml) compared with 94.0% and 96.7% respectively, in the Encepur group.

Geometric mean concentrations (GMC) measured by IMMUNOZYM ELISA were 3026 in the FSME-IMMUN and 678 in the Encepur group. GMCs measured with the Enzygnost ELISA were 163.3 (FSME-IMMUN) and 93.7 (Encepur).

Local reactions occurred in 12.7% and 8.7% after the 1st and 2nd vaccination with FSME-IMMUN and in 28.9% and 22.4% with Encepur. The rate of systemic reactions was comparable: 9.3% and 4.7% (FSME-IMMUN) and 11.8% and 5.3% (Encepur).

After two vaccinations, both TBE vaccines showed high seropositivity rates in virus neutralization- and ELISA assays. FSME-IMMUN induced higher antibody levels both in the neutralization and ELISA assays. Overall, a trend towards higher antibody responses in the younger age groups was observed.

References:

¹NT according to Adner et al., 2001

²IMMUNOZYM FSME IgG, Progen; Enzygnost TBE, Dade Behring

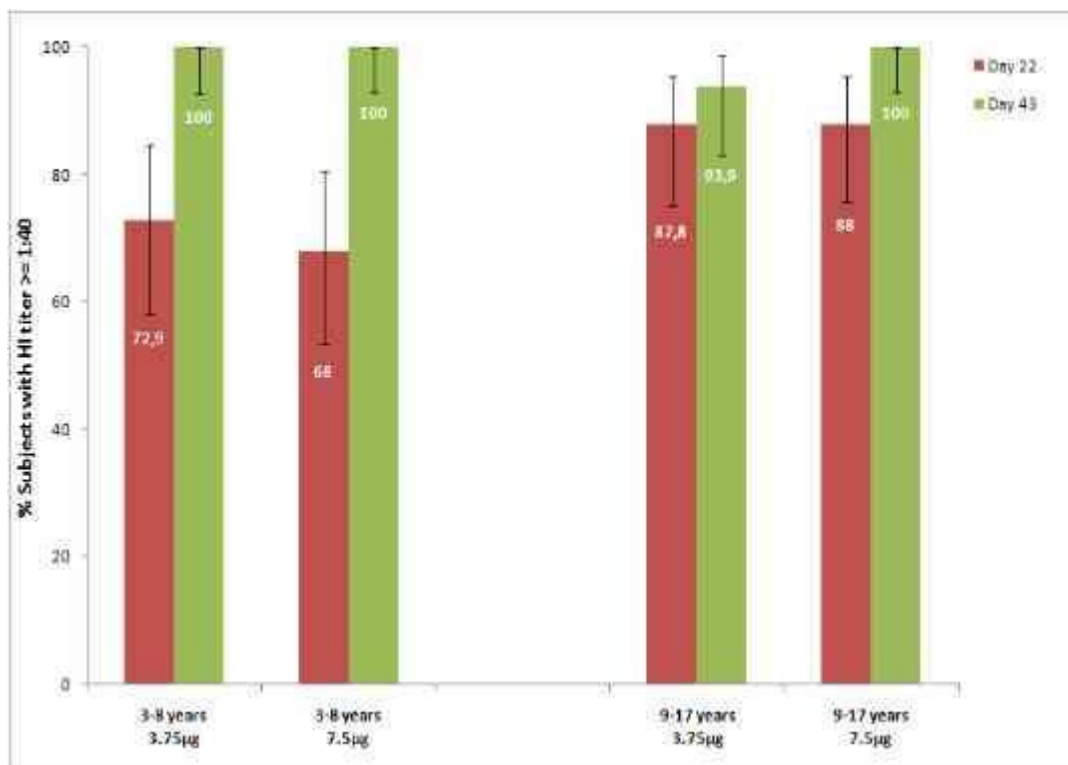
A WHOLE VIRUS CELL-DERIVED H1N1 PANDEMIC INFLUENZA VACCINE IS WELL TOLERATED AND HIGHLY IMMUNOGENIC IN CHILDREN

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This is an ongoing Phase 1/2 open-label, randomized clinical study investigating the safety and immunogenicity of 2 dose levels of a H1N1 pandemic influenza vaccine strain A/H1N1/California/07/2009 in healthy children and adolescents 6 months to 17 years of age. Four age strata (A: 9-17yrs, B: 3-8yrs, C: 12-35mo, D: 6-11mo) consisting of approximately 100 subjects each, were randomized (1:1) to receive two vaccinations of either the 3.75µg or 7.5µg vaccine dose 21 days apart.

Figure1 shows the seroprotection rates as determined by HI assay in the two oldest age strata. High seroconversion rates were observed after the 2nd vaccination: 85.4% and 96.1% in the 3-8 year age group and 81.6% and 98.0% in children aged 9-17 years with the 3.75µg and 7.5µg dose, respectively. GMT increases for the two dose levels were: 10.8 and 15.6 in the 3-8 year olds and 7.6 and 14.5 in the 9-17 years age group after the 2nd vaccination. MN assay results confirmed the immunogenicity of the vaccine in the investigated age groups.



[Fig1]

Safety data available so far (up to 8 days after the second vaccination) suggest that the vaccine was well tolerated. No dose effect was observed and no vaccine related SAEs were reported.

In summary this data confirms the suitability of Baxter's H1N1 pandemic vaccine for use in the pediatric population.

PROLIFERATE RESONSE TO PURIFIED *BORDETELLA PERTUSSIS* TOXIN ON MURINE SPLEEN LYMPHOCYTES

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Background and aims: Pertussis toxin (PT) produced by *Bordetella pertussis* (*B.pertussis*), causative agent of whooping cough is a major toxin involved in the pathogenesis of this highly contagious respiratory disease and it is generally believed to play an important role in the induction of protective immunity.

Methods: A purification procedure of pertussis toxin (PT) from submerged culture of *Bordetella pertussis* (*B.pertussis*) strain 134 using adsorption and affinity chromatography was discussed.

Results: The yield of the resulting PT was approximately 37.5mg/l of concentrated culture supernatant. The polypeptide pattern of the purified PT was investigated by SDS-PAGE and showed five bands between 11 to 26 KDa using low molecular weight marker. Since PT is the main component of acellular pertussis vaccine, obtaining a good yield of it would be essential for production of the new and safer vaccine generation. The other objective of this study was to determine the effects of PT on murine lymphocytes using MTT test. The effect of various doses of prepared PT on murine lymphocytes showed that the amount of 0.5µg/0.1ml had the highest proliferation. Furthermore comparison between the resulting PT and phytohemagglutinin showed much higher effect of PT on murine spleen cells.

Conclusions: These results indicate that *B.pertussis* strain 134 is a suitable strain for induction of PT in order to use it for development of acellular vaccine in Iran and also for *in vitro* studies on proliferation of murine lymphocytes.

EFFECTS ON SEROTYPE 6B AND 6A NASOPHARYNGEAL CARRIAGE FOLLOWING IMMUNISATION WITH 10-VALENT PNEUMOCOCCAL NON-TYPEABLE *HAEMOPHILUS INFLUENZAE* PROTEIN-D CONJUGATE VACCINE (PHID-CV)

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Background and aims: The 6B immune response after PCV vaccination tends to be among the lowest of all serotypes. PHiD-CV was shown to reduce overall nasopharyngeal carriage (NPC) of vaccine serotypes,¹ but no serotype-specific effects have been reported to date. We assessed the impact of PHiD-CV vaccination on 6B and 6A carriage and immunogenicity.

Methods: Immune responses and NPC were assessed in 209 children receiving PHiD-CV (at 3,4,5 months and 12-15 months) and in a control group (N=336). This descriptive analysis was restricted to children who did not receive prophylactic paracetamol (NPP) (as prophylactic paracetamol may impact the immunogenicity profile² and pneumococcal carriage³). Sampling timepoints are presented in Results.

Results:

Immune responses in children receiving PHiD-CV (ATP cohort for immunogenicity)

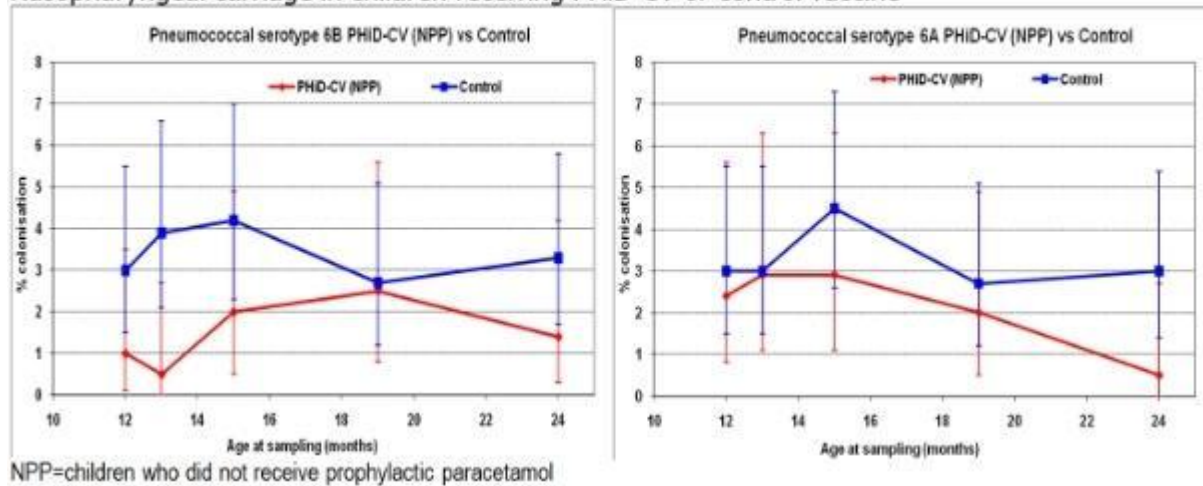
	Anti-6B* ELISA (N=203)		Opsono-6B (N=191)		Anti-6A* ELISA (N=202)		Opsono-6A (N=180)	
	%>0.2**	GMC**	%>8	GMT	%>0.2**	GMC**	%>8	GMT
1 month post-primary	75.2 (68.7-81.0)	0.45 (0.38-0.54)	93.1 (87.6-96.6)	728.2 (549.5-965.1)	36.3 (29.7-43.4)	0.12 (0.10-0.14)	64.1 (55.8-71.9)	60.4 (42.0-86.8)
1 month post-booster	99.0 (96.5-99.9)	2.41 (2.14-2.72)	98.4 (95.5-99.7)	931.7 (775.2-1119.9)	80.7 (74.6-85.9)	0.84 (0.68-1.03)	95.6 (91.4-98.1)	402.1 (327.8-493.1)

*22F-ELISA **µg/mL+95%CI

N=number of children with results available for ≥one timepoint

[Immune responses]

Nasopharyngeal carriage in children receiving PHiD-CV or control vaccine



[Nasopharyngeal carriage]

Conclusions: There was a trend towards lower carriage of serotype 6B pneumococci in children receiving PHiD-CV when compared to the control group, suggesting that the immune response to PHiD-CV was sufficient to impact 6B NPC. A comparable trend was observed for 6A after the booster dose.

This study was funded by GlaxoSmithKline Biologicals

References: Prymula et al: ¹WSPID 2009; ²Lancet 2009;374:1339-50; ³ISPPD 2010.

EFFICACY OF TWO-DOSE MMRV AND ONE-DOSE VARICELLA VACCINATION IN CHILDREN AGED 12-22 MONTHS IN 10 EUROPEAN COUNTRIES

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Background and aims: Measles-mumps-rubella-varicella (MMRV) vaccines are licensed in EU countries on a two-dose schedule. However, efficacy studies have been performed neither for the EU-registered schedule nor in European populations. The study aim was to demonstrate efficacy of two doses of MMRV (*Priorix-Tetra*[™], GlaxoSmithKline Biologicals) and/or one dose of varicella (*Varilrix*[™], GlaxoSmithKline Biologicals) vaccines in preventing varicella ≥2 years post-vaccination.

Methods: Randomised, controlled, observer-blind, multicentre study (N=5803) in 10 European countries. 12-22-month-old children received two vaccinations 42 days apart: MMR, then V (N=2487), 2xMMRV (N=2489) or 2xMMR (control, N=827). Suspected cases of varicella were described, varicella-like lesions photographed and cases confirmed by PCR or epidemiological link to an index case. Severity was defined by score table considering number/character of lesions/accompanying signs. Primary objective was reached if the lower limit of the 2-sided 97.5% CI for vaccine efficacy (VE) for MMRV and/or V was ≥60%.

Results: 481 cases were confirmed from 5285 subjects in total (mean follow-up 35 months 42 days post-dose 2). VE against any varicella was 94.9% (n=37, 97.5% CI [92.4, 96.6]; p< 0.0001) after two doses of MMRV and 65.4% (n=243, 97.5% CI [57.2, 72.1], p=0.127) after one dose of V. VE against moderate/severe varicella was 99.5% (n=2, 97.5% CI [97.5, 99.9]; p< 0.0001) and 90.7% (n=37, 97.5% CI [85.9, 93.9]), respectively.

Conclusion: Although statistically inconclusive, one dose of V appeared highly efficacious in preventing moderate/severe disease. However, this study demonstrated high efficacy of two doses of MMRV given 42 days apart in preventing any confirmed varicella.

IMMUNOGENICITY AND SAFETY OF A FULLY LIQUID DTaP₅-IPV-HIB VERSUS DTaP₃-IPV/HIB AT 3, 5 AND 12 MONTHS OF AGE

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Objective: A fully liquid DTaP₅-IPV-Hib vaccine (PEDIACEL[®], sanofi pasteur) or reconstituted DTaP₃-IPV/Hib vaccine (Infanrix[®]-IPV+Hib, GlaxoSmithKline) was administered to infants at 3, 5, 12 months of age. The vaccines were compared for immunogenicity and safety.

Design: Randomised, controlled, double-blind, 2-arm, multicentre phase 3 study in Finland and Sweden.

Results: Healthy infants (N=807) were randomised to receive either DTaP₅-IPV-Hib (PED group; n=402) or DTaP₃-IPV/Hib (INF group; n=405) on a 3-5-12-month schedule. Approximately 96% received all scheduled doses. A 3-dose vaccination series in PED or INF elicited seroprotection rates of, respectively, 93.2% versus 96.8% for PRP at ≥ 1.0 mg/mL, and did not achieve predefined noninferiority criteria (delta -5%), but were 99.1% versus 99.7% at ≥ 0.15 mg/mL. Seroprotection rates of 95.1% versus 90.3% for diphtheria (≥ 0.1 IU/mL), 100% versus 99.7% for tetanus (≥ 0.1 IU/mL), and $\geq 98.8\%$ versus 100% ($\geq 1:8$ 1/dilution) for poliovirus types 1-3 were also observed. Seroreponse rates against pertussis toxoid, filamentous hemagglutinin, and pertactin antigens were $\geq 96.9\%$ in PED and $\geq 99.1\%$ in INF. A response to fimbrial pertussis antigens (FIM) in PED was observed in 96.3% of participants; DTaP₃-IPV/Hib does not contain FIM. Cumulatively, fever ($\geq 38^{\circ}\text{C}$) was reported in 68.7% of PED and 70.4% of INF participants.

Conclusions: When administered following a 3-5-12-month schedule, vaccination with fully liquid DTaP₅-IPV-Hib elicited robust immune responses to all vaccine antigens. Anti-Hib responses were statistically lower than DTaP₃-IPV/Hib; however, the clinical significance of this difference is expected to be negligible. Similar safety profiles were observed in both groups.

IMMUNOGENICITY AND SAFETY OF A FULLY LIQUID DTaP₅-IPV-HIB VERSUS DTaP₃-IPV/HIB COADMINISTERED WITH PCV7: FOURTH DOSE AT 12-18 MONTHS OF AGE

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Objective: Evaluate a fourth dose of fully liquid DTaP₅-IPV-Hib vaccine (PEDIACEL®; sanofi pasteur) or reconstituted DTaP₃-IPV/Hib (Infanrix-IPV®+Hib; GlaxoSmithKline) coadministered with PCV7 (Prevenar®, Wyeth) at 12-18 months of age after a primary series of the same vaccines at 2, 3, and 4 months of age. Fourth-dose immunogenicity and safety were compared.

Design: Single-blind, randomised, controlled, 2-arm, multicentre phase 3 study in France and Poland.

Results: Healthy infants were randomised to receive a primary series of DTaP₅-IPV-Hib (PED group) or DTaP₃-IPV/Hib (INF group), each coadministered with PCV7; as toddlers, they received a fourth-dose booster (PED [n=267] and INF [n=264]) coadministered with PCV7. Seroprotection rates in PED or INF were, respectively, 99.1% versus 95.2% for Hib (≥1.0 mg/mL); 99.1% versus 100% for diphtheria (≥0.1 IU/mL); 100% versus 100% for tetanus (≥0.1 IU/mL). For poliovirus types 1-3, ≥99.5% in both groups achieved seroprotective levels (≥1:8 1/dilution). Pertussis booster response rates (4-fold increase in antibody concentration if prebooster dose < 4x lower limit of quantitation, otherwise 2-fold increase) for PED or INF were, respectively, 96.7% versus 95.0% (pertussis toxoid); 83.2% versus 96.0% (filamentous hemagglutinin); and 86.9% versus 98.0% (pertactin). A pertussis booster response to fimbrial antigens (FIM) was observed in 95.7% of PED; DTaP₃-IPV/Hib does not contain FIM. Pneumococcal responses as well as safety profiles were similar in both groups.

Conclusions: When coadministered with PCV7 as a fourth-dose booster at 12-18 months, vaccination with fully liquid DTaP₅-IPV-Hib elicited robust responses similar to DTaP₃-IPV/Hib for all antigens. The vaccines had similar safety profiles.

SAFETY AND IMMUNOGENICITY OF FULLY LIQUID DTaP₅-IPV-HIB VERSUS DTaP₃-HBV-IPV/HIB AS A BOOSTER AT 11-18-MONTHS OF AGE COADMINISTERED WITH PCV7

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Objective: Fully liquid DTaP₅-IPV-Hib (PEDIACEL[®], sanofi pasteur) or reconstituted DTaP₃-HBV-IPV/Hib (Infanrix[®] hexa, GlaxoSmithKline) was coadministered as a fourth dose booster with a first dose of PCV7 (Prevenar[®], Wyeth) to 11-18-month-olds: (DTaP₅-IPV-Hib + PCV7 [PED] versus DTaP₃-HBV-IPV/Hib + PCV7 [INF]). Safety and immunogenicity were compared in the study arms.

Design: Multicentre, double-blind, randomised, 2-arm, phase 3 study in Germany. All participants received a 3-dose hexavalent infant vaccination series. PED participants also received HBV vaccine (ENGERIX-B Kinder, GlaxoSmithKline) 28 days after DTaP₅-IPV-Hib.

Results: Participants (N=847) were randomised to PED (n=423) or INF (n=424). Rates of fever within 4 days of vaccination were similar: 59.4% (95%CI 54.5%-64.1%) for PED versus 62.5% (95%CI 57.7%-67.2%) for INF $\geq 38^{\circ}\text{C}$; 6.7% (95%CI 4.5%-9.5%) for PED versus 4.1% (95%CI 2.4%-6.4%) for INF $\geq 39.6^{\circ}\text{C}$. All participants achieved seroprotection levels for Hib ($\geq 1.0 \mu\text{g/mL}$), diphtheria ($\geq 0.1 \text{ IU/mL}$), tetanus ($\geq 0.1 \text{ IU/mL}$), poliovirus types 1-3 ($\geq 1:8 \text{ 1/dilution}$). Pneumococcal seroprotection rates ($\geq 0.15 \mu\text{g/mL}$) were similar: 75.0%-100% per serotype. Pertussis seroresponse rates (4-fold increase in antibody concentration if predose 4 < 4x lower limit of quantitation, otherwise 2-fold increase) for pertussis toxoid, filamentous hemagglutinin, and pertactin were similar for both groups. Hepatitis B seroprotection rates ($\geq 10 \text{ mIU/mL}$) were similar.

Conclusions: Fully liquid DTaP₅-IPV-Hib can be administered as a fourth dose booster in toddlers who received a hexavalent vaccine infant series. Similar immunogenicity with a comparable safety profile to DTaP₃-HBV-IPV/Hib was achieved. If required, a fourth dose of HBV can be administered after DTaP₅-IPV-Hib vaccination.

A SYSTEMATIC REVIEW ABOUT EFFICIENCY OF INFLUENZA VACCINE

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Background: Influenza is a common viral infection that causes annually many hospitalizations and deaths worldwide. Vaccination is recommended for its prevention among groups considered at risk. The safety, efficacy and effectiveness of this vaccine have been widely assessed in the literature but the decision-making process requires considerations about efficiency. The aim was to review the available scientific evidence regarding economic evaluations of influenza vaccination in adults.

Methods: Systematic review (August 2009) of economic evaluation studies. The databases used were Medline, Embase, Cochrane Library, CRD and Euronheed with MESH terms "influenza vaccines", "costs and cost analysis", and "quality-adjusted life year". Inclusion criteria were studies of cost-effectiveness(CEA), cost-utility(CUA) and cost-benefit(CBA) in adult populations. The intervention considered was annual influenza vaccination versus non-vaccination. The outcomes measured were the costs per life year gained(LYG), cost per adjusted life year (QALYs) and cost-benefit ratios. The quality of articles has been measured with the checklist of economic studies proposed by the working group CASP.

Results: 63 references were found after removal of duplicates. 43 of them were excluded by title and abstract. Finally 16 were included (5 ACE, 5 ACU and 6 ACB). A wide range of values were found for LYG (380\$-43,939\$) and for QALY gained (980\$-456,770\$). The quality of the studies was good, all studies included sensitivity analysis.

Conclusions: Influenza vaccine could be considered as an efficient intervention in terms of cost per QALY in most recent studies, although the influence of the value of the parameters on the models would modify the choices of decision-makers.

SAFETY OF A SECOND DOSE OF MMRV VACCINE IN A LARGE OBSERVATIONAL STUDY

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ProQuad™, a combined measles, mumps, rubella, varicella live vaccine (MMRV, Merck & Co., Inc., US) was licensed in the US in 2005. A post-licensure study was conducted in a U.S. managed care organization. Results on incidence of febrile convulsion after a first dose, the study primary endpoint, have been published [1]. We report here safety data following a second dose of MMRV.

69,237 children 12 months to 12 years of age received MMRV from February 2006-June 2007, of which 25,212 as a second dose of MMR and varicella (V) vaccines (95% were 4-6 years of age). Second dose MMRV recipients were matched on age, gender, and calendar date of vaccination to 24,788 children who received a second dose of MMR and V given at separate injection sites (MMR+V) from January 2004-January 2006 (comparison group), before MMRV availability. General safety was assessed by comparing rates of hospitalizations and emergency visits within 30 days of vaccination between the two groups for all possible individual health outcomes.

Of ~100 comparisons, only a few health outcomes had a slightly increased risk following MMRV, including fever and nausea/vomiting. During the 30 days post-vaccination, there were 5 cases with a convulsion/epilepsy code in each of the MMRV and MMR+V group, but no case of febrile convulsion in the 5-12 day period following MMRV as a second dose.

Data from this large post-licensure safety study do not suggest any specific safety concern with MMRV used as a second dose.

1. Jacobsen SJ *et al.* *Vaccine* 2009; 27(34):4656-61

ORAL SUCROSE SOLUTION FOR ANALGESIA IN NEWBORN INFANTS VACCINATION

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Background and aim: Routine vaccination of newborns during the first days of life is painfully procedures. The ability of neonates to perceive and react to pain has recently been acknowledged. Pain relief in the newborn is necessary because pain can lead to decreased oxygenation, haemodynamic instability, or increased intracranial pressure and other negative effects. This study was done to determine effect of oral sucrose for decreasing of intensity of pain during HB vaccination in newborns.

Material and method: This double blinded, prospective, randomised clinical study was designed to include normal full term newborn infants vaccinated in the normal nursery of Imam Reza hospital (Mashhad- Iran) from April 2007 until April 2008. 70 healthy full term neonates vaccinated with HB vaccine in the first day of birth were randomized in the experimental group (35 neonates) and control group (35 neonates).

Experimental group received 2 ml %25 sucrose solution, 2 minutes before vaccination and control group received 2 ml pure water, 2 minutes before vaccination. In both groups Pain responses estimated according to the NIPS score. Results were analyzed by t-student test and chi-2 test.

Results: In this study showed that there isn't any significant difference between pain scores in sucrose group compared to control group. ($p < 0.31$)

Conclusion: According to our study, 2 ml %25 sucrose before injection HB vaccina isn't enough for pain relief in newborns.

Keywords: Newborn, Pain, Sucrose

DOUBLE-BLIND, PLACEBO-CONTROLLED, RANDOMISED MULTICENTER STUDY OF OM-85 (BRONCHO-VAXOM®), AN IMMUNOSTIMULANT, IN PAEDIATRIC RECURRENT UPPER RESPIRATORY TRACT INFECTIONS

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Background and aims: The medical and socioeconomic burden of recurrent upper respiratory tract infections (URTIs) in children is substantial. The aim of this trial was to confirm and further investigate the efficacy and safety of Broncho-Vaxom®, an immunostimulant medication used to prevent recurrent URTIs, in infection-prone children.

Methods: This is a randomised, placebo-controlled, double-blind, multicenter study with Broncho-Vaxom® in 396 patients aged 2 to 6 years with recurrent URTIs, i.e. presenting a minimum of 4 such episodes during the year before study entry. Patients received one capsule/day during 1 month, followed by one capsule/day during the first ten days of months 3, 4 and 5.

Results: The mean rate of URTIs during the treatment period (150 days) was significantly lower in the Broncho-Vaxom® group than in the placebo group (1.97 vs 2.42; ANOVA: two-sided $p=0.0016$); the mean treatment effect was -0.45 (95% confidence limits: -0.71 to -0.18). The mean degree of severity and the mean duration of the URTIs were significantly reduced in the Broncho-Vaxom® group ($p=0.0029$ and $p=0.0002$). Antibiotic consumption was also significantly lower in the Broncho-Vaxom® group ($p < 0.0001$). Broncho-Vaxom® was well tolerated and the number of reported adverse events was higher in the placebo group compared to the active treatment group (136 in 74 patients vs 104 in 59 patients).

Conclusions: Broncho-Vaxom® treatment significantly reduced the rate, severity and duration of URTIs in infection-prone children. Safety and tolerance were excellent.

IGG ANTIBODY AVIDITY AFTER VARICELLA-ZOSTER-VIRUS (VZV) VACCINATION IN SOLID ORGAN TRANSPLANT RECIPIENTS

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Varicella-zoster-virus (VZV) vaccines induce both humoral and cellular immunity. Humoral immunity is a function of both antibody concentration and avidity (=chemical binding strength). The present study was aimed to answer the question whether solid organ transplant (SOT) recipients have sufficient IgG antibody avidity against VZV after vaccination.

The serum samples of 28 SOT recipients (20 liver, 3 heart, 5 kidney), who had received a single dose of Varivax prior to SOT, were evaluated for IgG antibody levels against VZV and IgG avidity. SOT recipients were compared to two control groups (36 patients who had had clinical and serological confirmed varicella infection after wild-virus contact; 14 patients who had had VZV vaccination with a single dose of Varivax).

Median IgG antibody levels were 630 U/ml in SOT recipients, 800 U/ml in wild-virus infected controls and 810 U/ml in vaccinated controls. Median relative avidity index (RAI) was 82% for SOT recipients, 89% for wild-virus infected controls and 94% for vaccinated controls (SOT compared to wild-virus infected controls: $p=0.01$; SOT compared to vaccinated controls: $p=0.002$).

The data showed that IgG avidity in SOT recipients may serve as a substitute marker to measure humoral immunity against VZV. However, the role of IgG avidity for protection against VZV has to be evaluated in long-term follow-up, since also cellular immunity may play a crucial role in defense against VZV.

4-YEAR FOLLOW-UP OF IMMUNOGENICITY AND SAFETY OF ADOLESCENT GIRLS VACCINATED WITH THE HUMAN PAPILLOMAVIRUS (HPV)-16/18 AS04-ADJUVANTED VACCINE

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Background and aims: We previously reported a phase III study of the HPV-16/18 AS04-adjuvanted vaccine in adolescent girls. Here, we present the follow-up study assessing antibody persistence and safety up to 4 years.

Methods: Girls (10-14 years) were randomised to vaccine or control at 0-1-6 months (104918/NCT00316706). Subjects in the vaccine group were invited to a 4-year extension phase. Anti-HPV-16/18 and anti-MPL (3-O-desacyl-4' monophosphoryl lipid A, in AS04 adjuvant system) antibodies were determined by ELISA. Immunogenicity data are presented in according-to-protocol cohort for girls in the extension phase (N=563 vaccine) and safety data in total vaccinated cohort for all girls (N=1035 vaccine; N=1032 control).

Results: At M48, all girls in vaccine group remained seropositive for both HPV-16/18 antibodies. Antibody levels (geometric mean titres; GMT) peaked at M7, then gradually declined to a plateau phase from M18 through M48 (Table). Levels were higher than the plateau in a phase IIB efficacy study (580299/007/NCT00518336). At baseline, 81.8% girls were seropositive for anti-MPL antibodies. In the vaccine group, anti-MPL levels increased to M7 then declined to just above baseline levels by M48. Incidence rates per 100,000 subjects per year of SAEs, medically significant AEs and potential NOCDs were similar between groups.

Conclusions: HPV-16/18 AS04-adjuvanted vaccine was generally well tolerated. High antibody levels sustained in adolescent girls through M48 may predict long-term protection.

Time point	GMT, EL.U/mL (95% CI)	
	HPV-16	HPV-18
Month 7	20726.3 (19372.1–22175.1)	8563.1 (7966.9–9203.8)
Month 18	4027.4 (3741.4–4335.3)	1599.3 (1473.2–1736.3)
Month 24	3275.8 (3038.5–3531.6)	1272.2 (1174.9–1377.5)
Month 36	2712.5 (2524.1–2914.9)	999.5 (921.3–1084.2)
Month 48	2395.8 (2230.5–2573.3)	885.6 (816.3–960.8)

[GMTs for HPV-16 and HPV-18]

MONITORING REGULAR IMMUNIZATION SERVICES IN KAILALI, NEPAL

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The expanded program on immunization is a priority and one of the most cost effective public health program of the Government of Nepal. The coverage of the routine immunization has been declining steadily each year since 2000 in Kailali District of Nepal. Such trend of coverage with varied fluctuations have been continuing since several years. The objective of the study was to determine the actual situation of the vaccination coverage of the district and to find the differences in immunization coverage of the local supervisory areas(lots) to compare with the National Standard coverage of 90%, and to explore the factors behind the failure of maintaining high coverage as well.

The Lot Quality Assurance Sampling(LQAS) method, was used with 19 samples from each of six supervisory areas of the district. A total of 114 samples were taken.

All routine immunizations coverage were found by the survey above the national standards of 90%. BCG coverage was 99.12%,DPTHib-3 99.12%, Polio-3 98.25%, and Measles coverage was 93.86%. The immunization card retaining was 74(64.04%) of the total of 114 sampled mothers. Fully immunized children out of the total 114 sampled children were 104 (91.23%) accepted at 95% confidence limits (86.04-96.42). The coverage of all six lots was accepted at 95% confidence limits (86.04-96.42). Chi-Square, Yetes Corrected value was 0.67(p,0.20). All the lots were homogenous, not heterogeneous, with the coverage of the vaccination.

Keywords: EPI coverage, immunization coverage, Lots , LQAS, vaccination coverage

MONITORING IMMUNIZATION SERVICES BY USING LOT QUALITY TECHNIQUE IN KAILALI, NEPAL, 2009**H. Shah^{1,2}**

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The objective of the study was to determine the actual situation of the vaccination coverage of the district and to find the differences in immunization coverage of the local supervisory areas (lots) to compare with the National Standard coverage of 90%, and to explore the factors behind the failure of maintaining high coverage as well. The Lot Quality Assurance Sampling (LQAS) method, was used with 19 samples from each of six supervisory areas of the district. A total of 114 samples were taken. All routine immunizations coverage were found by the survey above the national standards of 90%. BCG coverage was 99.12%, DPT/Hib-3 99.12%, Polio-3 98.25%, and Measles coverage was 93.86%. The immunization card retaining was 74 (64.04%) of the total of 114 sampled mothers. Fully immunized children out of the total 114 sampled children were 104 (91.23%) accepted at 95% confidence limits (86.04-96.42). The coverage of all six lots was accepted at 95% confidence limits (86.04-96.42). Chi-Square, Yates Corrected value was 0.67 (p, 0.20).

Keywords: EPI coverage, immunization coverage, Lots, LQAS, vaccination coverage.

THE PENTAVALENT ROTAVIRUS VACCINE PROTECTS AGAINST ROTAVIRUS-GASTROENTERITIS CAUSED BY DIVERSE ROTAVIRUS SEROTYPES OVER NEARLY TWO YEARS OF FOLLOW-UP IN ASIA

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Background and aims: The efficacy of the pentavalent rotavirus vaccine (PRV) against severe rotavirus gastroenteritis (RVGE) was evaluated in a double-blind, placebo-controlled, multicenter Phase III clinical trial conducted in 2 GAVI-eligible countries in Asia, Bangladesh and Vietnam (March 2007-March 2009).

Methods: 2,036 infants were randomized 1:1 to receive 3 doses of PRV/placebo at 6-, 10-, and 14-weeks of age with routine EPI vaccines, including OPV. Vaccine efficacy (VE) against severe-RVGE, defined using the 20-point Vesikari scale (score ≥ 11), by specific rotavirus-genotypes was calculated from ≥ 14 days following the third dose through a follow-up period of nearly 2 years in the combined countries. Stool samples were analyzed by rotavirus-specific EIA and RT-PCR to determine G/P genotypes.

Results: G1-G3, G6, G9, G12, P1A[8], P1B[4], and P2A[6] were the rotavirus genotypes detected during the follow-up period. In Bangladesh, the most common genotype combinations were G1P1A[8] and G9P1A[8]; the most common combination in Vietnam was G3P1A[8]. VE against severe-RVGE caused by vaccine-contained types (G1-G4, G6, and P1A[8]) was 49.4% (95%CI:22.2%-67.6%). VE against severe-RVGE caused by non-vaccine G (G9 and G12) and P (P1B[4] and P2A[6]) types was 50.9% (95%CI:1.0%-76.8%) and 50.9% (95%CI:< 0.0%-81.8%), respectively. VE against severe-RVGE caused by individual types was: G1 (46.2% [95%CI:< 0.0%-75.7%]), G2 (29.2% [95%CI:< 0.0%-82.3%]), G3 (67.0% [95%CI:< 0.0%-92.2%]), G9 (48.7% [95%CI:< 0.0%-76.8%]), P1A[8] (49.7% [95%CI:19.2%-69.3%]), P1B[4] (40.9% [95%CI:< 0.0%-82.4%]), and P2A[6] (60.5% [95%CI:10.4%-96.2%]).

Conclusions: PRV provides significant protection against severe-RVGE caused by diverse circulating rotavirus genotypes in a period of 2 years in two GAVI-eligible countries in Asia.

DECREASE IN VARICELLA-ASSOCIATED COMPLICATIONS AND HOSPITALISATION AFTER INTRODUCTION OF UNIVERSAL VARICELLA VACCINATION IN GERMANY

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Germany introduced universal varicella vaccination for children above 11 months in 2004 to reduce incidence, severe complications and economic burden of disease.

Using data from a countrywide varicella sentinel network and from the Federal Health Monitoring (FHM) we evaluated possible impacts of the vaccination programme.

Sentinel physicians reported monthly numbers of varicella cases by age and varicella-associated complications (VC) and submitted case-based questionnaires for patients with VC from April 2005 to September 2009.

Data on hospitalisation and health insurance sick-leave data published online by FHM were analysed if ICD10-coded with B01 (Varicella) or related subgroups from 2000 to 2007. Descriptive statistics were used to document trends and proportions.

Sentinel physicians reported 300 VC in total with declining trend in numbers and proportion on total reported varicella cases over time. FHM published an annual mean of n=975 hospitalised varicella cases with and n=1010 without complications between 2000 and 2004. Thereafter, cases decreased in both groups by ~35% until 2007. At age 0-4 years the decrease was 56%. This age-group was primarily affected with VC in sentinel sites (59%) and hospitals (50%), respectively. Varicella-related sick-leaves and workdays lost have decreased by 52 and 53.5% respectively, if 2007 compared to the annual mean of 2002-2004.

The decline in number and proportion of VC as well as of varicella-related hospitalisations and sick-leaves was observed in close temporal relation to the introduction of universal varicella vaccination. Whether this reflects an effect of the programme on the disease burden has to be verified by further monitoring.

PHASE 3, OPEN-LABEL TRIAL OF 13-VALENT PNEUMOCOCCAL CONJUGATE VACCINE (PCV13) AS A TODDLER DOSE IN HEALTHY CHILDREN

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Background/aims: PCV13 includes serotypes 1, 3, 5, 6A, 7F, 19A and the 7 serotypes in 7-valent PCV (PCV7) conjugated to CRM₁₉₇ to provide broader protection. This open-label, phase 3 study in Sweden evaluated immunogenicity and safety of a toddler dose of PCV13 following 2 infant doses of PCV7.

Methods: PCV13 was administered at age 12 months to healthy infants previously administered PCV7 at approximately 3 and 5 months of age as per the NIP.

Pneumococcal serotype-specific IgG ELISA response was measured before and 1 month after toddler dose. Local reactions and systemic events were monitored for 7 days following vaccination; adverse events were collected throughout.

Results: Enrollment totaled 116. Post-toddler IgG geometric mean concentrations (GMCs) ranged from 3.33 to 9.30 µg/mL for the common serotypes and from 1.34 to 13.16 µg/mL for the additional serotypes (Tables 1, 2). All serotypes showed substantial fold rises. Local reactions and fever were mostly mild or moderate.

Conclusions: PCV13 was well-tolerated and immunogenic when administered to toddlers who had received 2 infant doses of PCV7.

Serotype	4	6B	9V	14	18C	19F	23F
Pretoddler GMC (µg/mL) (95% CI)	0.61 (0.53, 0.72)	0.64 (0.50, 0.81)	0.69 (0.59, 0.80)	2.23 (1.85, 2.69)	0.44 (0.38, 0.50)	0.82 (0.67, 1.01)	0.40 (0.33, 0.47)
Posttoddler GMC (µg/mL) (95% CI)	5.06 (4.22, 6.06)	9.15 (7.06, 11.87)	3.33 (2.88, 3.84)	9.30 (7.90, 10.95)	3.87 (3.30, 4.53)	8.23 (6.32, 10.73)	4.40 (3.70, 5.22)
Geometric mean fold rise (95% CI)	8.23 (6.95, 9.75)	14.32 (11.27, 18.21)	4.82 (4.21, 5.50)	4.17 (3.46, 5.03)	8.88 (7.64, 10.33)	10.03 (7.98, 12.62)	11.08 (9.08, 13.52)

[Table 1. Geometric mean concentrations (GMCs) and geometric mean fold rises for PCV7 serotypes]

Serotype	1	3	5	6A	7F	19A
Pretoddler GMC	0.01 (0.01, 0.02)	0.05 (0.04, 0.07)	0.33 (0.26, 0.42)	0.24 (0.19, 0.31)	0.02 (0.02, 0.02)	1.53 (1.31, 1.78)

(µg/mL) (95% CI)						
Posttoddler GMC (µg/mL) (95% CI)	1.58 (1.30, 1.93)	1.34 (1.13, 1.58)	1.43 (1.19, 1.72)	2.46 (1.85, 3.26)	3.59 (3.12, 4.12)	13.16 (11.26, 15.38)
Geometric mean fold rise (95% CI)	107.65 (84.80, 136.65)	25.05 (19.57, 32.06)	4.30 (3.54, 5.22)	10.19 (7.81, 13.30)	177.31 (141.82, 221.68)	8.62 (7.47, 9.94)

[Table

2.

Additional

serotypes]

INFLUENZA VACCINE KNOWLEDGE AMONG PEDIATRICIANS IS A PREDICTOR TO HIGH VACCINATION RATES AMONG THE PEDIATRICIANS, AND AMONG THEIR PATIENTS

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Background: Influenza vaccination rates among Physicians and among the pediatric population in Israel is disappointingly low and variable.

We examined whether updated knowledge regarding the illness and its vaccine significantly influences the rate of vaccination.

Participants and Methods: During the winter of 2008 -09, we delivered a questionnaire including 12 questions regarding seasonal influenza to 32 Pediatricians working in Macabbi Healthcare Services (MHS).

The score was determined as high, low or very low according to the number of true answers.

Vaccination for influenza of these Pediatricians was recorded and vaccination rate of their patients was retrieved from the computerized data of MHS.

Results: 24/32 Pediatricians (75%) answered the questionnaires. 15 (62.5%) had high score, 5 (20.8%) had low score, and 4 (16.6%) had very low score.

The Pediatricians' scores were significantly associated with their and with their patients' vaccination rates: 14/15 (93%) Pediatricians with high score were vaccinated for influenza as compared with 40% of Physicians with low score and 25% of Pediatricians with very low score ($P = 0.002$).

In addition, vaccination rate $> 5\%$ was detected among 80% of the patients aged 6-60 months of Pediatricians with high score as compared to 35% of the respective patients of Pediatricians with lower scores ($P = 0.012$).

Conclusions: Knowledge about influenza and influenza vaccine is a significant factor influencing compliance with influenza vaccination among Pediatricians and among their patients. Therefore, intervention aiming at increasing influenza vaccination rates should also include steps for the improvement of Pediatricians' knowledge regarding this subject.

REVIEW OF ROTATEQ® VACCINE EFFECTIVENESS IN DEVELOPED COUNTRIES**V. Spoulou¹, C. Giaquinto²***¹Ethniko and Kapodistriako Panepisthio, Athens, Greece, ²University of Padova, Padova, Italy*

Background: Rotavirus vaccines have been in routine use in developed countries since 2006. Several recent studies have evaluated their performance in real life. The objective of this preliminary review is to provide a general overview of the efficacy in routine use (effectiveness) of RotaTeq®, pentavalent rotavirus vaccine, in developed countries.

Methods: Effectiveness studies were identified through Medline search from 2006 to December 2009. Abstracts presented to international congresses were also included. The primary outcomes analysed were RV-related hospitalisations, ED visits and office visits. Only studies where infants received a full course (3 doses) were included.

Results: The effectiveness of RotaTeq was assessed in 4 studies (case control and cohort) in the US from 2006-2009 and one cohort study in Europe conducted from 2007-2009. Vaccine effectiveness of RotaTeq full-course ranged from 79 to 100% against RV-related hospitalisations, 82 to 89% against RV-related emergency visits and 96% against RV-related office visits.

Conclusions: High vaccine effectiveness was consistently observed with a full-course of RotaTeq, confirming that the high and sustained efficacy already demonstrated during clinical development is seen in routine practice in developed countries.

BENEFITS OF A TWO VERSUS THREE DOSE VACCINE AGAINST ROTAVIRUS INFECTION IN CHILDREN: THE CASE OF PANAMA

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Background and aims: Two vaccines with different dosing schemes (two for *Rotarix*®, three for *Rotateq*®) are available for enhancing immunity against rotavirus infection in infants. Scenarios were tested to measure incremental benefit between them, with Panama as test case.

Methods: Markov model was developed detailing vaccine efficacy (VE) after each dose, following birth cohort of 70,000 infants until 5 years. Probabilities of events, disease management and costs were collected locally. VE after first doses follows exponential decrease. Three scenarios were tested. One follows literature review by M Jitt et al, 2009, Vaccine; Scenario 1. Two other scenarios follow recommendations of expert group: no difference in VE after 1st and last dose between vaccines, compliance and dose timing could be different. We tested same dose compliance and timing for 1st 2 doses but 50 (Scenario 2) to 90% (Scenario 3) compliance and 6th month timing for 3rd dose. Model outcomes are costs, mild, moderate, and severe events avoided.

Scenario	1	2	3
Mild events (N)	- 8300	- 6106	- 1121
Moderate events (N)	- 5012	- 4249	- 845
Severe events (N)	- 535	- 451	- 91
Total costs	- \$248 015	- \$182 797	- \$43 345
Costs without vaccine costs	- \$401 222	- \$335 509	- \$65 421

[Table

1]

Results: At vaccine price parity per course, cost savings with *Rotarix*® are high in 2 scenarios.

Conclusions: Favorable VE values for *Rotarix*® in scenario 1 have marginal benefit compared with scenario 2. Low 3rd dose compliance and 6th month timing are driving forces for improving cost savings of two-dose vaccine.

IMMUNIZATION COVERAGE AMONG 2 YEARS OLD TODDLERS IN JERUSALEM - BEFORE AND AFTER COMMUNITY-WIDE MEASLES OUTBREAKS

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Background: Recurrent community-wide measles outbreaks emerged in Jerusalem in 2003-2004 and in 2007-2008, mainly among unvaccinated children in Jewish ultra-orthodox communities. Despite the high national average coverage, specific sub-populations are under-immunized, as highlighted by these outbreaks.

Methods: We investigated the measles outbreaks and monitored immunization coverage in Jerusalem's neighborhoods. Routine childhood immunizations are provided at community public well-baby clinics. We evaluated the coverage of MMR vaccine (first dose- 12 months) versus other routine childhood vaccines - DTaP-IPV-Hib (4th dose- 12 months).

Results: The population of infants less than 1 year in Jerusalem increased from 22,000 in 2001 to 28,000 in 2009. The immunization coverage varied considerably within the various neighborhoods in Jerusalem. The average immunization coverage in Jerusalem at age two years (2001 data) was: DTaP-IPV-Hib4 (all 88%), HBV3 (95%), MMR1 (92%). The average immunization coverage at age two years (2008 data) was: DTaP-IPV-Hib4 (all 92%), HBV3 (95%), MMR1 (97%). The MMR1 vaccine coverage (2001 data) ranged from 78% to 95% ($p=0.01$) being lowest in the clinics in ultra-orthodox neighborhoods. About 8% of the families complied only with MMR vaccine during the outbreaks but did not attend the clinics later on to complete other routine childhood immunizations. About 1% did not wish to accept any preventive well baby services.

Conclusions: The improvement in MMR vaccination coverage in communities with less than satisfactory immunization coverage was not accompanied by a similar rise in the coverage of other routine vaccinations such as DTaP-IPV-Hib. Further health promotion activities aimed at increasing compliance are essential.

ACCEPTANCE AND COVERAGE OF VARICELLA VACCINATION IN GERMAN CHILDREN DURING THE FIRST FOUR YEARS AFTER GENERAL RECOMMENDATION

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Background and aims: In 2004, Germany was the first European country to recommend general varicella vaccination, with one dose at 11-14 months of age. We investigated coverage in children and factors associated with parent acceptance during 2006 to 2008.

Methods: In annual random samples (n=600) of children aged 18-36 months, child vaccination status, socio-demographic factors and paediatrician's recommendation on varicella vaccination were assessed by parent mail surveys in the area of Munich in 2006, 2007 and 2008.

Results: Between 59 % and 62% of the parents responded. Vaccination coverage increased from 38% in 2006 to 51% in 2007 and 53% in 2008. Recommendation of varicella vaccination by the paediatrician increased from 48% (2006) to 57% (2007) and 60% (2008), and was the main independent factor associated with parent acceptance (OR 12.8, 19.9 and 30.1, all p< 0.01). Median age at vaccination decreased from 15 months in 2006 to 12 months in 2008. One third of parents of unvaccinated children had not decided yet whether or not to vaccinate for varicella. A MMR-V combination vaccine was licensed in 2006 and was solely used in 29% of the children in 2008.

Conclusions: An initial increase of vaccination coverage up to 51% by 2007 was followed by stagnation in 2008, the 4th year of routine varicella vaccination. The coverage rate should exceed 85% to avoid a shift in disease epidemiology to older age groups. Programmes targeting paediatricians' and parents' acceptance of varicella vaccination are necessary to achieve a higher coverage in the future.

IMMUNIZATION COVERAGE IN LUXEMBURG IN 2007

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Background and aims: The aim of the study was to measure vaccine coverage. Vaccines are provided free of charge by the state. A major financial incentive is given by the state to the parents of children who fulfilled all the preventive health care visits scheduled for the first two years of live. Immunization is voluntary based

Method: A postal randomized sampling survey for 600 children 25-30 months of age was conducted in 2007. Immunization data were collected from immunization cards.

Results: Responds rate was 93.7%. 548 (91.3%) immunization cards were available.

IPV (4 dosis)	96.4 (94.8-97.9)
DTaP (4 dosis)	96.5 (95.0-98.1)
Hib (4 dosis)	95.3 (93.5-97.0)
VHB (3 dosis)	94.5 (92.6-96.4)
MMR (1 dose)	96.2 (94.6-97.8)
MenC	95.8 (94.1-97.7)
PCV7 (4 dosis)	67.75 (64.0-71.8)

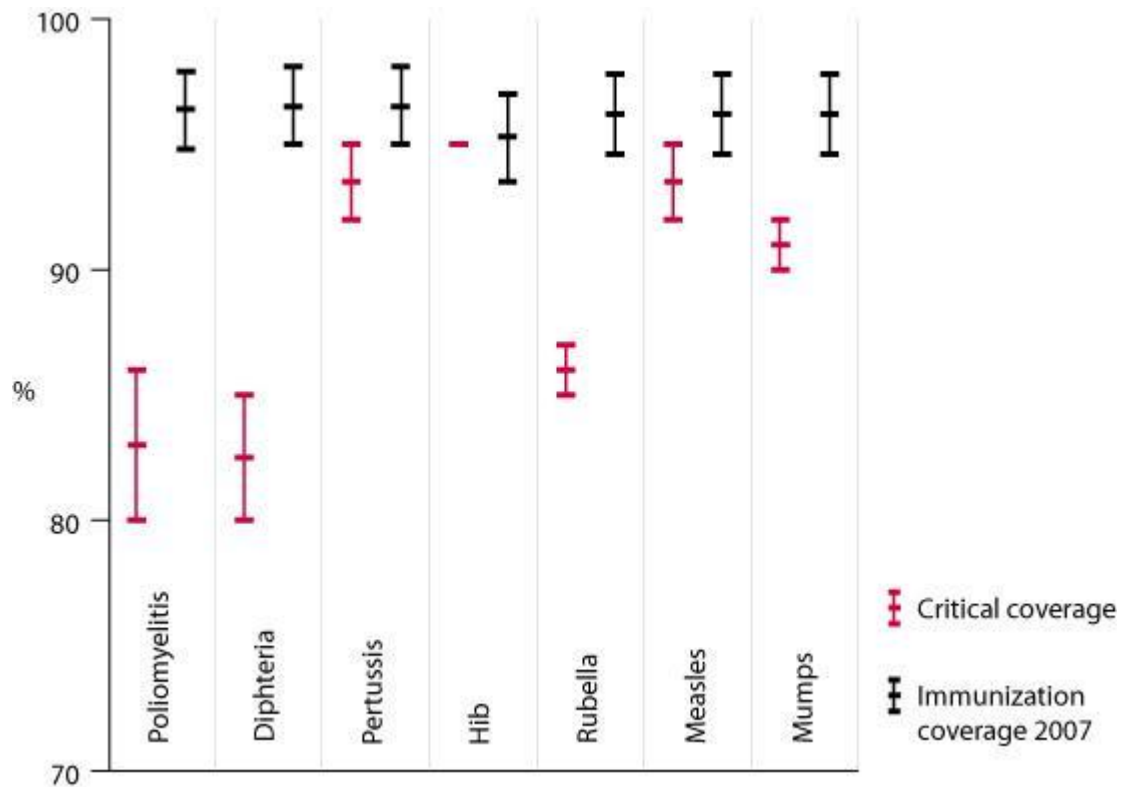
[vaccine

coverage

in

Luxemburg

2007]



[critical vaccine coverage]

Conclusion: In Luxemburg 2007, children Immunization coverage exceeded 94% for all vaccination except for PCV7.

Critical coverage was obtained for polio, diphtheria, pertussis, rubella and mumps. However for Hib and measles coverage remained borderline for collective protection (overlap of confidence intervals) but reached WHO-european target of 95%.

IMMUNIZATION COVERAGE IN FRENCH SPEAKING BELGIUM IN 2009

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Background and aim: The aim was to measure vaccine coverage.

Since 2007, completed immunization schedule includes: 4 doses DTaP-IPV-VHB/HIB, 3 doses PCV7, and one dose MMR and MenC. All vaccines are free of charge except for Rotavirus vaccine.

Method: A random cluster sample study according the EPI cluster sampling technique was conducted in 2009. 660 children 18-24 months of age were randomly selected in 48 municipalities. Immunization data were collected at home from his immunization card.

Results: On 576 established contacts 526 children participated to the survey (91.3%).

Vaccine (n=512)	dose 1	dose 2	dose 3	dose 4
IPV	99.6 (510) 99.1-100	99.6 (510) 99.1-100	98 (502) 96.8-99.2	90.4 (463) 87.9-93
DTP	100 (512)	100 (512)	98.6 (505) 97.6-99.6	90.6 (464) 88.1-93.1
Hib	99.0 (507) 98.2-99.9	99.0 (507) 98.2-99.9	97.5 (499) 96.1-98.8	90.2 (462) 87.7-92.8
VHB	98.8 (506) 97.6-99.8	98.8 (506) 97.6-99.8	96.9 (496) 95.4-98.4	90.4 (463) 87.9-93
MMR	92.4(473) 90.2-94.6			
MenC	91.2 (467) 88.7-93.7	0.2 (1) 0-0.2		
PCV7	97.1(497) 95.6-98.5	93.6 (479) 90.9-96.2	80.7 (413) 76.9-84.4	1.4 (7) 0.4-2.4
Rotavirus	82.0 (420) 78.7-85.4	77.3 (396)* 73.7-81.0		

[vaccine

coverage]

*Rotavirus 2 included completed schedules for both type of vaccines.

Conclusion: DTaP-IPV-VHB/HIB coverage is high for dosis before one year of age but drops 8% down for dose 4.

The WHO European objective of 95% for MMR is not yet reach.

Pneumococcal immunization, introduced in 2007, has dramatically increased from 30% in 2006 to 80.7%.

A complete schedule for Rotavirus, despite not being free of charge, reached 77%

POLIOVIRUS SERO-PREVALENCE OF INFANTS VACCINATED WITH IPV EXCLUSIVE PROGRAM

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Aims: Since 2005, Israeli infants are immunized against polio with 4 doses of IPV.

Since it is not clear whether the antibody titer achieved following an exclusive IPV is comparable to that achieved following a combined OPV/IPV program, we evaluated in this study the serologic response of infants immunized with the new, IPV based program and compared it to historical controls which were vaccinated with the previous IPV/ OPV combined program.

Patients and methods: Parents of infants aged 13-24 month arriving to the Emergency Room for any reason, who completed the 4 IPV vaccine dose program, were requested to be enroll in the study. The left out sera were analyzed for antibodies to polio serotypes.

Results: 57 infants, who received 4 doses of IPV were included. All had high titers against the 3 polio serotypes. The Geometrical Mean Titers (GMT) against these serotypes were: 17264, 15990 and 13163 respectively. These titers were comparable to historical titers achieved following the combined OPV/IPV program and indicate > 95% probability that a child vaccinated with 4 doses of IPV will to have protective level of antibodies to the 3 vaccine serotype. The sera of 5 other children who had only 3 doses of IPV were significantly lower than the titers of infants who received 4 doses of IPV.

Conclusions: Our findings support the decision to continue with exclusive IPV vaccination program. In addition, our results demonstrate the advantage of a 4 dose IPV program over a 3 dose program.

OPSONOPHAGOCYtic ACTIVITY INDUCED BY A NOVEL 13-VALENT PNEUMOCOCCAL CONJUGATE VACCINE (PCV13). A DOUBLE BLIND RANDOMISED ACTIVE CONTROLLED TRIAL (UK)

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Background: Serum opsonophagocytic activity might better correlate with protection against invasive pneumococcal disease (IPD) than serum IgG concentrations. We report serum opsonophagocytic assay (OPA) titres in infants immunised with PCV13, a CRM₁₉₇-conjugated vaccine against pneumococcal-serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F and 23F.

Methods: Healthy infants were randomized 1:1 to receive PCV13 or the 7-valent pneumococcal vaccine (PCV7) at age 2, 4 and 12 months with routine immunisations. Sera obtained at 5, 12 and 13 months were analysed by OPA (threshold of response set as $\geq 1:8$).

Results: Serotype-specific OPA analysis was performed on available sera from 65 to 80/139 and 46 to 62/139 of PCV13 and PCV7 recipients respectively. Following PCV13 immunisation at 2 and 4 months, 87 to 100% of participants had OPA titres $\geq 1:8$ for the PCV13-serotypes. Titres declined to < 50% for serotypes 4, 18C, 19F and 19A by 12 months of age but were $\geq 1:8$ in 93 to 100% of participants following the 12-month PCV13 dose. After 3 doses of PCV7, OPA titres were $\geq 1:8$ in 3.4% to 84.7% of participants for 5 of the 6 additional PCV13-serotypes and 96.7% for serotype 7F. However serotype 7F OPA-GMTs were 304 (95% C.I. 215 to 431) in PCV7 recipients compared to 6703 (C.I. 5260 to 8541) in PCV13 recipients.

Conclusions: A 2, 4 and 12 month course of PCV13 induced vaccine-serotype specific OPA titres $\geq 1:8$, in almost all recipients, indicating the potential for this vaccine to broaden protection against IPD.

ELEVEN-YEAR TREND OF OTITIS MEDIA AMONG CHILDREN AGED < 2 YEARS IN THE UNITED STATES, 1997-2007

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Background & aims: To examine trends in otitis media (OM) episodes among US children aged < 2 years during 1997-2007.

Methods: We conducted a retrospective database analysis and systematic literature review. The Impact Managed Care Benchmark National Database was used to identify OM visit claims from healthcare plans across the nine US census regions. OM episodes included consecutive OM visits within 30 days; person-years of observation (PY) included total time contributed by each subject. Annual incidence/1000PY was examined for three time periods according to pneumococcal conjugate vaccine (PCV) introduction: pre- (1997-1999), transition (2000-2002), post- (2003-2007). Results were compared with those from published clinical trials and US/Canadian database studies.

Results: Among children < 2y, 32,707PY in 1997 to 357,695PY in 2007 were available for analysis. Pre-PCV, OM rates decreased 19% from 1152/1000PY (95% CI 1141-1164) in 1997 to 931/1000PY (95% CI 926-935) in 1999. Rates continued to decline until the post-PCV period (average 688/1000PY in 2003-2007). Thus, compared to the year prior to PCV introduction (1999), rates decreased 26%. In clinical trials, AOM efficacy ranged from 6-23%. In previous database studies, reductions following PCV introduction ranged from 4-43%.

Author	Year	Country/Region	Data	Age Group	Outcome	Comparison	Reduction
Randomized Clinical Trials							
Fireman	2003	US	--	<3.5y	Episodes/Visits	PCV v. control arm	6-7% 6%
Eskola	2001	Finland	--	<2y	Episodes	PCV v. control arm	6%*
Palmu	2004	Finland	--	<5y	Episodes	PCV v. control arm	9%*
Non-Randomized Clinical Trials							
Esposito	2007	Italy	Observer blinded	<2.5y	Episodes	PCV v. control arm	17%
Adam	2008	Germany	Non-blinded	<2y	Children	PCV v. control arm	19-23%
US/Canadian Observational Database Studies							
Poehling	2004	Tennessee New York	Managed care	<2y	Visits	'98-'00 v. '01-'02	4%* 19%
Grijalva	2006	US	NAMCS/NHAMCS	<2y	Visits	'94-'99 v. '02-'03	20%
Zhou	2008	US	Employer insurance	<2y	Visits	'97-'99 v. '04	43%
de Wals	2009	Quebec	Physician claims	<5y	Visits	'01 v. '07	13%
Grijalva	2009	US	NAMCS/NHAMCS	<5y	Visits	'99-'00 v. '05-'06	15%
Our Analysis	2010	US	Healthcare claims	<2y	Episodes	'99 v. '03-'07	26%

*Not statistically significant

[Table 1]

Conclusion: Following PCV introduction in the US and Canada, only a single observational study has shown OM reductions above the 4-26% range, compared with 6-9% OM efficacy observed in randomized clinical trials.

KNOWLEDGE OF IMMUNISATION AMONG UNIPAROUS MOTHERS

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Background and aims: Irish immunisation uptake rates are 8% off target (95%) for MMR vaccine and 4% off target for remaining vaccines in the primary immunisation schedule. This study, designed to explore parental knowledge of the Irish Immunisation Schedule, includes specified information regarding diseases and vaccination contraindications, with the aim of optimising national immunisation uptake rates.

Methods: A prospective questionnaire-based study, June 1st to July 31st 2009, was conducted on the post-natal ward of University College Hospital, Galway (3,500 births/annum). Post-partum mothers (English speaking) were invited to participate. Information sought: demographics, vaccine knowledge, vaccine preventable diseases, contraindications and concerns; data analysed with SPSS (17).

Results: 386 were invited to partake, 355 (92%) questionnaires were completed. 81% were native Irish, 42% uniparous, 62% aged 31-40yrs, 68% rural dwellers. Overall, primiparous women were significantly less knowledgeable than their multiparous counterparts, regarding immunisation facts and schedule details (See P-values, Table 1). Notably, rural dwellers were less informed, with significantly more concerns regarding immunisation. Finally, 59% mothers would attend post-natal education, if vaccination information included.

Parity: Background Region:	Primiparous (Risk Factor Present)			Multiparous (Risk Factor Present)			Participants: incorrect selection (Risk Factor Absent)	P Value
	Rural	Urban	Total	Rural	Urban	Total		
No. of Participants:	104 (29%)	54 (15%)	158 (45%)	137 (39%)	60 (17%)	197 (55%)		
Exhibited ability to identify all vaccines in the schedule	8 (2%)	5 (1%)	13 (4%)	48 (14%)	18 (5%)	66 (19%)	276 (78%)	0.0001
Selected correct vaccination contraindication(s)	27 (8%)	13 (4%)	40 (11%)	13 (4%)	54 (15%)	67 (19%)	248 (70%)	0.082
Selected death as a complication of measles	27 (8%)	12 (3%)	39 (11%)	46 (13%)	18 (5%)	64 (18%)	252 (71%)	0.126
Selected meningitis as a complication of mumps	13 (4%)	3 (1%)	16 (5%)	26 (7%)	10 (3%)	36 (10%)	303 (85%)	0.035
Selected miscarriage as a complication of Rubella	37 (10%)	12 (3%)	49 (14%)	66 (19%)	30 (8%)	96 (27%)	210 (59%)	0.001
Selected pneumonia as a complication of Pertussis	26 (7%)	12 (3%)	38 (11%)	52 (15%)	23 (6%)	75 (21%)	242 (68%)	0.006
Knew influenza vaccine does not give flu symptoms	48 (14%)	23 (6%)	71 (20%)	60 (17%)	35 (10%)	95 (27%)	189 (53%)	0.593
Knew what PCV protects against	58 (16%)	40 (11%)	98 (28%)	50 (14%)	26 (7%)	76 (21%)	181 (51%)	0.0001

Table 1. Comparative knowledge of Primiparous vs. Multiparous (subcategories Rural vs. Urban)

Abb: GP General Practitioner, PCV Pneumococcal Conjugate Vaccine
P value, with 95% confidence interval: P compares total primiparous compared to total multiparous on knowledge exhibited

[Table 1]

Conclusions: Immunisation knowledge is lacking in a large percentage of Irish mothers, typically uniparous and rural, clearly indicating a need for education within these demographics. Both school curriculum and postnatal education should improve parental knowledge and ultimately impact upon immunisation uptake rates.

POTENTIAL RAPID AND SIGNIFICANT BENEFITS FOR NATIONAL HEALTH SYSTEM AND SOCIETY OF UNIVERSAL VACCINATION WITH ROTATEQ® IN GREECE

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Background and aims: In Greece, acute rotavirus gastroenteritis (RVGE) is estimated to cause 16.000 medical consultations, 10.000 emergency department visits, 2.000 hospitalisations, 1.200 nosocomial infections and 61.000 cases not seeking medical care on average in children under 5 years of age (8 million euros cost for National Health System). Aim was to evaluate the potential benefits of introducing universal rotavirus vaccination with RotaTeq® in terms of RVGE burden avoided and cost reduction.

Methods: A decision analytic model has been developed to compare the burden and cost of RVGE before and after the introduction of a routine vaccination programme with RotaTeq® (vaccination coverage 88%) for a cohort of children followed from birth until the age of 5 years.

Results: The National Health System benefit would be significant (more than 80% of hospitalizations and emergency department visits and 75% of medical consultations related to RVGE would be avoided, while the cost would be reduced by 6.5 million euros;-81%) and rapid (76% of cases and 84% of costs would be avoided in two years after RotaTeq® introduction). The society benefit would be also significant as the total annual number of RVGE cases and the parents work lost days would be reduced by 69%. Including societal costs the total saving would reach 10 million euros.

Conclusions: The introduction of routine vaccination with RotaTeq® in Greece could offer considerable benefits for National Health System and society. Potential herd immunity introduction in the model would have a positive impact on results in favour of the vaccination.

PARENTAL OPINIONS ON CHILDHOOD VARICELLA AND THE VARICELLA VACCINE: A UK MULTICENTRE QUALITATIVE INTERVIEW STUDY

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Background: Varicella-zoster virus can cause serious complications and require hospitalisation, even in healthy children. There is no universal varicella vaccination programme currently in the UK.

Aims: To explore the experiences and perceptions of childhood varicella and attitudes of UK parents towards a universal vaccination programme.

Methods: Face to face interviews were carried out at two hospitals (London and Manchester) in the paediatric wards, outpatients and in Accident and Emergency.

Results: Data was obtained from March to April 2009 on 454 children (age range 0.01 - 20.48, median 5.43 years) presenting to hospital and their siblings. The total number of parents surveyed was 388. 228 children (50.2%) had underlying medical conditions and 272 (59.9%) had chickenpox previously. 14 children (14/272, 5.1%) developed complications secondary to chickenpox.

59.2% (230/388) of parents surveyed regarded chickenpox as a potentially serious condition. For the children who had chickenpox, 201/272 (73.9%) of parents sought medical advice regarding diagnosis. Parents were most concerned about scarring (38/272, 14.0%) and high fever (13/272, 4.8%). Prior to the interview, only 101/388 (26.0%) of parents were aware of the existence of the varicella vaccine. However, 261/388 (67.3%) of parents surveyed would be in favour of a universal vaccination programme in the UK.

Conclusions: Parental experiences of childhood chickenpox vary but the majority of parents in this study would be in favour of a universal vaccination programme.

IMMUNOGENICITY OF THE REDUCED-ANTIGEN-CONTENT DTPA VACCINE (BOOSTRIX™) IN ADULTS ≥55 YEARS - A SUBANALYSIS OF 4 TRIALS

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Background: Older adults are at increased risk of severe pertussis and may pass the disease to very young unvaccinated infants. Both these risks could be reduced by a booster dose of reduced-antigen-content tetanus, diphtheria and acellular pertussis (dTpa) vaccine, but limited immunogenicity and safety data are available.

Methods: This sub-analysis pooled the immunogenicity results before and one month post-vaccination for adults aged ≥55 years in 4 clinical trials (dTpa-002, dTpa-003, dTpa-IPV-003, dTpa-034) of a single dose of either dTpa (*Boostrix*™, GlaxoSmithKline Biologicals) or dTpa-IPV (*Boostrix*™-polio). A pertussis booster response was defined as the proportion of subjects with reaching ≥5 EU/mL (if seronegative at pre-booster) or ≥2-fold increase in antibody concentration (if seropositive at pre-booster).

Results: Of the total of 293 subjects (mean age 64.4 years), a booster response for pertussis antigens was observed in 89.2% (pertussis toxoid), 95.8% (filamentous haemagglutinin) and 94.5% (pertactin). The vaccines were also immunogenic for diphtheria and tetanus toxoids in older adults; 82.8% (≥0.1 IU/mL ELISA or ≥0.016 IU/mL VERO) and 94.5% (≥0.1 IU/mL ELISA) respectively. Geometric mean concentrations increased substantially for all antigens.

Conclusions: Adults over 55 years are an important target group for control of pertussis. A single booster dose of dTpa or dTpa-IPV vaccine induced good immunological responses and could be readily integrated into existing programs.

COMPARATIVE COST-EFFECTIVENESS OF HUMAN ATTENUATED MONOVALENT VACCINE AND HUMAN-BOVINE PENTAVALENT VACCINE FOR PREVENTING SEVERE ROTAVIRUS-DIARRHOEA IN YOUNG CHILDREN IN MEXICO

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Background and aims: To conduct cost-effectiveness analyses of human attenuated monovalent vaccine (HAMRV) versus human-bovine pentavalent vaccine (HBPRV) for preventing severe rotavirus-diarrhoea in Mexican children.

Methods: The evaluation was from the public health-care perspective. The expected cost-effectiveness was estimated using a decision-analysis model for a 2-million infant cohort in 2006. The outcomes of the evaluation were disability-adjusted-life-years (DALY), deaths, hospitalizations and outpatients. Efficacy of severe events was assumed to be similar for the two vaccines: 85% varying from 70% to 94%. Efficacy of ambulatory events was assumed to be 70% (46-84%) for the HAMRV and 74% (67-80%) for the HBPRV. Efficacy rates of the HBPRV were adjusted by an uptake rate of 10% lower considering that completing a 3-doses schedule is expected to be more difficult than a 2-doses schedule for the HAMRV. The cost per course of vaccination was assumed to be the same for both vaccines (US\$ 30). The costs of vaccine administration were also assumed the same.

Results: Vaccine programme costs were estimated at US\$ 41.5 million. Deaths prevented by HAMRV are estimated at 419 meanwhile those estimated by HBPRV are slightly lower (378). The cost-effectiveness ratio was estimated at \$1,967 per DALY (ranging from \$1,388 to \$2,564) for HAMRV and US\$ 2,256 (ranging from US\$1,613 to US\$2,899) for HBPRV.

Conclusions: Considering the same cost for a vaccine programme for HAMRV or HBPRV, the lower uptake efficacy rate affects the effectiveness of HBPRV. Nevertheless, the range of cost-effectiveness does not predict significant differences between the two vaccines.

THE MENINGOCOCCAL TETRAVALENT TETANUS TOXOID-CONJUGATE VACCINE (MENACWY-TT) IS IMMUNOGENIC AND HAS AN ACCEPTABLE SAFETY PROFILE IN TODDLERS 12-23 MONTHS

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Background and aims: Conjugated meningococcal vaccines against serogroup C (MenC) are available, and currently used in toddlers and infants in many European countries. This study compared the candidate conjugate vaccine MenACWY-TT with the licensed conjugate MenC vaccine, MenC-CRM₁₉₇.

Methods: In this phase 3 study, toddlers (12-23 months) were randomised 3:1 to receive one dose of MenACWY-TT (n=374) or MenC-CRM₁₉₇ (n=125). Serum bactericidal (rabbit complement [rSBA], cut-off 1:8) antibodies were measured pre- and 42 days post-vaccination. Solicited and unsolicited adverse events (AEs) and serious AEs were reported up to 6 months post-vaccination.

Results: At least 99.7% of subjects had rSBA titres $\geq 1:8$ against A, C, W-135 and Y antigens following vaccination with MenACWY-TT vaccine. Immune responses to serogroup C were higher after MenACWY-TT than after MenC-CRM₁₉₇ vaccine (Table).

Table: Subjects with meningococcal rSBA titres $\geq 1:8$, $\geq 1:128$ and GMT 42 days post-vaccination (ATP cohort for immunogenicity).

Antibody	Group	% subjects with rSBA $\geq 1:8$	% subjects with rSBA $\geq 1:128$	GMT
MenA	MenACWY-TT (n=354)	99.7 [98.4-100]	99.7 [98.4-100]	2205.0 [2007.8-2421.6]
	MenC-CRM ₁₉₇ (n=51)	45.1 [31.1-59.7]	33.3 [20.8-47.9]	24.3 [13.4-44.1]
MenC	MenACWY-TT (n=354)	99.7 [98.4-100]	95.8 [93.1-97.6]	477.6 [437.3-521.6]
	MenC-CRM ₁₉₇ (n=121)	97.5 [92.9-99.5]	70.2 [61.3-78.2]	212.3 [170.0-265.2]
MenW-135	MenACWY-TT (n=354)	100 [99.0-100]	99.4 [98.0-99.9]	2681.7 [2453.1-2931.6]
	MenC-CRM ₁₉₇ (n=58)	50.0 [36.6-63.4]	25.9 [15.3-39.0]	25.1 [14.6-43.1]
MenY	MenACWY-TT (n=354)	100 [99.0-100]	99.7 [98.4-100]	2729.4 [2472.7-3012.8]
	MenC-CRM ₁₉₇ (n=59)	54.2 [40.8-67.3]	35.6 [23.6-49.1]	31.4 [18.4-53.6]

[] = lower and upper limits of 95% confidence interval

[Meningococcal rSBA titres and GMT]

In the 4-day follow-up, grade-3 (preventing everyday activity) solicited local symptoms were reported by $\leq 4.4\%$ of subjects in both treatment groups and fever ($\geq 38^{\circ}\text{C}$) was reported in 9.3% and 12.9% of subjects in MenACWY-TT and MenC-CRM₁₉₇ groups, respectively. No vaccine-related SAEs were reported in either treatment group.

Conclusions: The immune responses against all four vaccine serogroups and the higher responses against serogroup C compared with MenC-CRM₁₉₇ suggest that the MenACWY-TT vaccine has the potential to broaden protection against meningococcal disease in toddlers.

IMMUNOGENICITY AND SAFETY OF THE CO-ADMINISTRATION OF THE MENACWY-TT CONJUGATE VACCINE WITH MMRV IN TODDLERS

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Background and aims: Investigation of co-administration of the candidate meningococcal ACWY conjugate vaccine (MenACWY-TT) with a measles-mumps-rubella-varicella (MMRV) vaccine (GlaxoSmithKline Biologicals) in toddlers.

Methods: In the co-administration part of the phase 3 study, toddlers (12-23 months) were randomised to receive one dose of MenACWY-TT+MMRV (n=375), MenACWY-TT (n=374), or MMRV (n=126). Antibodies were measured pre- (meningococcal serum bactericidal [rabbit complement (rSBA)]), and 42 days post-vaccination (meningococcal serum bactericidal; MMRV [ELISA for M,M,R; immunofluorescence for V]). Solicited and unsolicited adverse events (AEs) were recorded up to 6-months post-vaccination.

Results: Non-inferiority was demonstrated for all seven antigens. rSBA-Men A, W-135 and Y responses were slightly lower in the co-administration group but rSBA-MenC responses were higher (Table1).

Table 1: Subjects with meningococcal rSBA titres $\geq 1:8$, $\geq 1:128$ and GMT 42 days post-vaccination (ATP cohort for immunogenicity).

Antibody	Group	% subjects with rSBA $\geq 1:8$	Difference in % subjects with rSBA $\geq 1:8$ (MenACWY-TT+MMRV minus MenACWY-TT)*	% subjects with rSBA $\geq 1:128$	GMT
MenA	MenACWY-TT+MMRV (n=360)	100 [99.0–100]	0.28 [-0.78– 1.58]	99.7 [98.5–100]	2085.9 [1905.3–2283.6]
	MenACWY-TT (n=354)	99.7 [98.4–100]		99.7 [98.4–100]	2205.0 [2007.8–2421.6]
MenC	MenACWY-TT+MMRV (n=357)	100 [99.0–100]	0.28 [-0.79– 1.58]	94.4 [91.5–96.5]	519.0 [470.9–571.9]
	MenACWY-TT (n=354)	99.7 [98.4–100]		95.8 [93.1–97.6]	477.6 [437.3–521.6]
MenW-135	MenACWY-TT+MMRV (n=360)	100 [99.0–100]	0.00 [-1.06– 1.07]	100 [99.0–100]	2055.8 [1871.0–2258.9]
	MenACWY-TT (n=354)	100 [99.0–100]		99.4 [98.0–99.9]	2681.7 [2453.1–2931.6]
MenY	MenACWY-TT+MMRV (n=359)	100 [99.0–100]	0.00 [-1.06– 1.07]	99.7 [98.5–100]	2282.4 [2051.3–2539.5]
	MenACWY-TT (n=354)	100 [99.0–100]		99.7 [98.4–100]	2729.4 [2472.7–3012.8]

[]= lower and upper limits of 95% confidence interval

*Non-inferiority defined as a lower limit of the 95%CI for the group difference (MenACWY-TT+MMRV minus MenACWY-TT) $\geq -10\%$.

[Meningococcal rSBA titres and GMT]

Responses to MMR antigens were generally lower but varicella responses were higher in the co-administration group (Table2).

Table 2: Subjects seropositive for MMRV antigens 42 days post-vaccination (ATP cohort for immunogenicity).

Antibody†	Group	% seropositive	Difference in percentage (MenACWY-TT+MMRV minus MMRV)*	GMC value
Anti-Measles ≥ 150 MIU/mL	MenACWY-TT+MMRV (n=361)	100 [99.0–100]	0.00 [-1.06–3.16]	4273.4 [4018.4–4544.6]
	MMRV (n=121)	100 [96.9–100]		4457.3 [3976.3–4996.6]
Anti-Mumps ≥ 231 U/mL	MenACWY-TT+MMRV (n=361)	87.7 [83.8–90.9]	4.06 [-2.81–12.45]	662.9 [598.4–734.4]
	MMRV (n=121)	83.6 [75.6–89.8]		710.1 [583.8–863.8]
Anti-Rubella ≥ 4 IU/mL	MenACWY-TT+MMRV (n=361)	100 [99.0–100]	0.00 [-1.06–3.16]	43.1 [40.0–46.5]
	MMRV (n=121)	100 [96.9–100]		53.2 [46.6–60.7]
Anti-Varicella ≥ 1:4	MenACWY-TT+MMRV (n=361)	97.9 [95.7–99.2]	3.30 [-0.28–9.32]	152.8 [133.5–174.8]
	MMRV (n=121)	94.6 [88.6–98.0]		128.8 [99.1–167.4]

[]= lower and upper limits of 95% confidence interval

*Non-inferiority defined as a lower limit of the 95%CI for the group difference (MenACWY-TT+MMRV minus MMRV) ≥ -10%.

†ELISA (Enzygnost™, Dade Behring, Marburg, Germany) immunoassays for measles (cut-off 150mIU/mL), mumps (231 U/mL) and rubella (4 IU/mL). Antibody levels against varicella were measured using indirect immunofluorescence assay (Virgo™, Hemagen Diagnostics, Columbia, MD, with modifications).

[Seropositivity for MMRV antigens]

Fever (≥38°C) was reported in 14.9%, 9.3% and 11.3% of subjects during days 0-3 and 75.5%, 31.9% and 75.8% during days 0-14 in MenACWY-TT+MMRV, MenACWY-TT and MMRV groups, respectively. No vaccine-related SAEs were reported in the study.

Conclusions: Non-inferiority of co-administration of MenACWY-TT+MMRV, compared with separate vaccinations, suggests suitability for integration of MenACWY-TT into current childhood vaccination schedules.

A PEDIATRIC TRIAL DEMONSTRATED HIGH IMMUNOGENICITY AND GOOD SAFETY OF AN MF59[®]-ADJUVANTED H5N1 INFLUENZA CANDIDATE VACCINE BOOSTER

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Background and aims: MF59-adjuvanted H5N1 influenza vaccines have demonstrated safety and immunogenicity in adults, elderly, children and adolescents. We report a 1 year MF59-H5N1 booster dose in a pediatric population.

Methods: Healthy toddlers (6-36 months), children (3-8 years) and adolescents (9-18 years) were randomized 3:1 to two doses three weeks apart of MF59-H5N1 (7.5 µg/dose) or MF59-seasonal (15 µg each antigen; half-dose in toddlers) influenza vaccines plus 12 months booster. Immunogenicity against the homologous A/Vietnam/1194/2004-like H5N1 vaccine strain was measured by hemagglutination inhibition (HI), single radial hemolysis (SRH) and microneutralization (MN). Solicited reactions were recorded for 7 days on diary cards.

Results: Antibody persistence was satisfactory; post-booster response was high.

H5N1 HI assay	6 to <36 mo. N=113	3 to <9 yr. N=83	9 to <18 yr. N=81
Baseline GMT (95% CI)	5.14 (4.87-5.43)	5 (5 -5)	5.17 (4.83-5.54)
Post-primary GMT (95% CI)	700 (598-819)	577 (450-740)	364 (260-510)
Pre-booster GMT (95% CI)	24 (18-33)	11 (8.18-14)	12 (8.92-16)
Post-booster GMT (95% CI)	1365 (1166-1598)	766 (613-958)	472 (335-667)
Post-/pre-booster GMR (95% CI)	55 (41-75)	73 (53-101)	39 (26-60)

[HI

titers]

HI titer ≥ 40 rates after booster were 99%, 98% and 91% for toddlers, children and adolescents. All subjects were seroprotected by SRH (GMA $\geq 25\text{mm}^2$). All toddlers and children and 99% of adolescents had MN titers ≥ 40 . Solicited reactions were similar after H5N1 or seasonal vaccine injection. No vaccine-related SAEs were reported.

Conclusions: The booster induced high levels of H5N1 antibodies, which might confer long-term protection, supporting use of this vaccine for pre-pandemic vaccination of toddlers, children and adolescents.

SAFETY AND IMMUNOGENICITY OF AF03-ADJUVANTED AND NON-ADJUVANTED PANDEMIC INFLUENZA A (H1N1) 2009 VACCINE IN CHILDREN 6-35 MONTHS OF AGE**T. Vesikari**¹, M. Denis², S. Pepin², I. Kusters³¹*Vaccine Research Center, University of Tampere, Tampere, Finland*, ²*Clinical Development*, ³*R&D, Sanofi Pasteur, Lyon, France*

Background: Vaccination is considered an essential measure in limiting the disease burden of pandemic influenza. Young children are vulnerable to pandemic influenza and constitute a primary vaccine target group. We investigated the safety and immunogenicity of AF03-adjuvanted and non-adjuvanted A/H1N1 vaccines in 400 children 6-35 months age to define optimal antigen and adjuvant dosage.

Methods: Phase II randomised, open-label, multicenter trial conducted in Finland: 8 groups of 50 children aged 6-11 months or 12-35 months received 2 intramuscular injections (21 days apart) of: 1) a half-dose or 2) a full dose of 3.8 µg HA A/H1N1 influenza vaccine adjuvanted with AF03 (an emulsion-based adjuvant); 3) a half-dose of a 7.5 µg HA A/H1N1 pandemic influenza vaccine adjuvanted with AF03; or 4) a half-dose of a 15 µg HA non-adjuvanted A/H1N1 vaccine.

Results: In all children, the EMEA immunogenicity criteria for influenza vaccines were met after 2 injections of the half-dose of the non-adjuvanted A/H1N1 vaccine or after a single injection of either dose of the AF03-adjuvanted vaccine. Seroprotection was seen in at least 95% subjects. Safety was satisfactory in both age and vaccine groups and no vaccine related serious adverse events were observed.

Conclusions: The A/H1N1 pandemic vaccines were well tolerated and induced excellent HI antibody responses in the 6-35 months age groups. The adjuvant effect of AF03 was clearly demonstrated in this age group since the EMEA criteria were met following a single dose of the AF03-adjuvanted vaccine while two doses of the non-adjuvanted vaccine were required.

**SAFETY AND EPIDEMIOLOGICAL EFFECTS OF MASS VACCINATION WITH A(H1N1)
INFLUENZA VACCINE PERFORMED IN SEPTEMBER, 2009 IN CHINA**

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Objective: To evaluate the safety and epidemiological effect of the first mass vaccination with A (H1N1) influenza vaccine in China.

Method: Subjects' information was collected by uniform tables at the immunization filed. Data on confirmed case of A (H1N1) influenza were collected from Information System for Disease Surveillance in Beijing. Data on side effects related to vaccination were collected from Beijing AEFI Management System. Descriptive epidemiology and cohort study design were used in this study.

Results: 95244 subjects were immunized with A (H1N1) influenza vaccine. 193 adverse events were reported through AEFI Management System. Reported rate of AEFI is 2.03‰. Most of the adverse events (137/193, 71.0%) happened during the first 24 hours after immunization. Of 81 adverse reactions confirmed to be related to immunization, 78(96.3%) were mild reactions. No Guillain-Barre Syndrome following vaccination was reported through the AEFI Management System. A (H1N1) vaccine's epidemiological protection rate could reach 65.3% when coverage rates without considering.

Conclusion: A (H1N1) influenza vaccine shows a similar safety profile as seasonal flu vaccine. The vaccine demonstrates a good epidemiological effect against A (H1N1) influenza virus infection.

**PRIMARY VERSUS SECONDARY FAILURE FOLLOWING VARICELLA VACCINATION:
IMPLICATIONS FOR INTERVAL BETWEEN TWO DOSES - LITERATURE REVIEW**

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Background and aims: A two-dose varicella vaccination schedule (administered at 12-15 months and 4-6 years) was established in the USA following outbreaks in vaccinated populations. Optimal timing of the second dose depends on whether breakthrough varicella (BV) results from primary vaccine failure (PVF) or secondary vaccine failure (SVF), defined as no protective immunity after vaccination and waning protective immunity, respectively. The literature on varicella PVF and SVF was thus reviewed to determine optimal timing of the second vaccine dose.

Methods: Published literature on live-attenuated vaccine failure (disease occurring >42 days post vaccination) associated with one and two doses of all varicella-containing vaccines, was systematically reviewed (1995-October 2009). Search terms included: primary OR secondary vaccine failure, waning immunity, seroconversion and breakthrough varicella.

Results: 48 relevant publications were identified; 25 determined the risk of BV with time, where an increased risk of BV is an indicator of SVF. Of these, 9 indicated an increased risk of BV with time (although 8 were outbreak analyses with limited power to detect differences); whereas 16 showed sustained protection after the first year with up to 20 years' follow-up. 23 publications showed seroconversion rates of 68-100% (assays were not standardised). 21 showed BV rates of 0-42%, with no consistent trend between BV rate and time since vaccination between publications.

Conclusions: Literature to date indicates a relatively high rate of PVF and limited evidence of SVF amongst one-dose varicella vaccine recipients, suggesting that a short interval between two doses might be preferable to reduce BV.

SAFETY OF THE COMBINED VACCINE MMR WITH STRAIN URABE, ON THE BASIS OF ITS TEN YEARS USAGE IN UKRAINE

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Purpose: To study safety of the vaccine against measles, mumps and rubella (MMR) with strain Urabe, on the basis of its ten years usage in Ukraine.

Methods: Clinical, epidemiological, statistical.

Results: In Ukraine the combined MMR vaccine was used for the planned vaccination since 1999. During this period more than 7 million (7025867) children aged 12 months and 6 years were vaccinated by the MMR. 1328481 children were vaccinated by the MMR with mumps culture Urabe.

According to clinical, pre-registration research results which was conducted in Ukraine (1998) the frequency of local adverse events following immunization (AEFI) ranged 2,55%-3,64%, general - 2,63%-5,78%.

During the period of the post-marketing surveillance after AEFI with the use of MMR, frequency of local and general AEFI ranged 0,1%-0,8% and 0,02%-0,1% accordingly. During this period 4 complications were registered - two allergic reactions of immediate type and two mumps associated with MMR vaccine. The development of allergic reactions is related to sensitization of vaccinated organism to some vaccine component. It is possible to consider that the particular qualities of mumps culture, contained in MMR, caused a development of mumps associated with MMR vaccination.

Conclusions: From data of the post-marketing monitoring after the AIFI of MMR it's possible to state that frequency of development of AIFI during the leadthrough of clinical research is significantly higher than during a planned vaccination. That is related to more thorough surveillance after patients. At the same time the combined vaccine with mumps culture Urabe is low reactogenic.

DECREASED ANTIBODY RESPONSE IN SOLID ORGAN TRANSPLANTED CHILDREN AFTER MENINGOCOCCUS C VACCINATION

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Objective: So far, no data exist on efficacy of Meningococcus C vaccination in pediatric solid organ transplant (SOT) patients. The study was aimed to determine whether or not children after SOT or with end-stage kidney failure are able to achieve protective meningococcal C specific antibody levels after vaccination.

Methods: Nine children after SOT and 1 child with end-stage kidney failure awaiting transplantation were vaccinated with a conjugated *Neisseria meningitidis* group C vaccine (NeisVac-C, Baxter, Vienna, Austria). Serum bactericidal antibody (SBA) titers were evaluated at time point 1, 3, 6, 12 and 18 months after vaccination. SBA titers ≥ 8 were defined to be protective.

Results: SOT patients showed an increase of SBA titers in the first half year after vaccination achieving protective levels. All patients showed protective SBA titers at 18 months. However, 18 months after vaccination a 50% decrease was detected in median SBA titers. When compared to SBA titers of 92 healthy children of the historical accreditation study, SOT patients showed significantly lower SBA titers 6 months after vaccination.

Conclusion: The data demonstrated that SOT patients have lower but still protective SBA titers after Meningococcus C vaccination. However, quickly waning humoral immunity in SOT patients should demand a close monitoring of SBA titers. Long-term studies may answer the question if there is a need for a second vaccination in these patients.

SURVEILLANCE OF 97 CONFIRMED PEDIATRIC CASES OF H1N1 INFLUENZA IN IRAN

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Background: After the first outbreak identified in Mexico in March 2009, influenza A sustained by a modified H1N1 virus rapidly spread to all continents. Here we report 97 pediatric patients with influenza A (H1N1) from some tertiary care hospitals in Tehran, Iran and evaluate clinical and epidemiological aspects and also complications of influenza A (H1N1) infection.

Methods: From June to November 2009, in a retrospective study in Department of Health, Shaheed Beheshti Medical University, Tehran, Iran, we evaluate confirmed cases of influenza A (H1N1) who were referred to several tertiary care hospitals in Tehran, Iran. Epidemiological data, signs and symptoms, mortality rate and cause of death were studied.

Results: Mean age of the patients was 9.78 (± 3.64) years; 43.3% male and 56.3% female. Mean duration of symptoms was 2.12 (± 1.73) days. 4.1% of patients had recent travel to other countries. Most frequent symptoms were fever (87.6%), cough (71.1%), and myalgia (54.6%). Thirty-three (34%) patients were hospitalized and 6 (6.2%) patients had died. All deaths were due to respiratory distress.

Conclusion: This study verifies the widespread of H1N1 influenza and showed that the youth are highly at risk and high spread was seen in school age children. Most frequent symptoms are fever, cough, and myalgia. Influenza A (H1N1) can result in severe complications and death. Respiratory problems are the leading cause of death in Iran.

INFLUENZA VIRUS MENINGOENCEPHALITIS WITH PARKINSONIAN SYNDROME

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We present a case of a 13-year old boy with normal physical and neuropsychological development, who had fever, cough and catarrhal symptoms in the beginning of February 2007. After a 7-day afebrile period his body temperature raised again and new symptoms appeared: headache, vomiting, intoxication, altered behavior, meningeal syndrome, and impaired consciousness deepening into coma. He was admitted at the Pediatric Ward with ICU, University Hospital of Infectious Diseases - Sofia. During the hospitalization he developed increased muscle tonus to rigidity, masked facies, anarthria, catatonic symptoms, memory impairments, seizures, and insomnia. Laboratory studies: complete blood count - neutrophil leucocytosis; CSF analysis - 620 cells/mm³, 0.81 g/l protein, PCR - negative for enteroviruses; serology - positive for influenza virus H3N2 (titer = 1:320). EEG was abnormal, while contrast MRI did not revealed involvement of the brain structures. Several syndromes were discussed: meningeal, extrapyramidal, psychoorganic with catatonic symptoms, mutism, pyramidal, epileptic, and Korsakoff syndrome. Treatment involved anti-edema, antiparkinson and anticonvulsant agents. The condition gradually improved and the boy fully recovered after 3 months. The case is demonstrative for influenza virus infection with meningoencephalitis and Parkinsonian syndrome that led to serious neurological manifestations and total recovery.

RETROSPECTIVE STUDY OF CNS VIRAL INFECTIONS IN CHILDREN

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Objectives: CNS viral infections contribute for one of the main parts of the infectious pathology in childhood.

Aim: To analyze etiological structure, laboratory constellation, clinical course and outcome of CNS viral infections in children.

Materials and methods: We analyzed retrospectively 111 children with CNS viral infection admitted at the Pediatric Ward with Intensive Care Unit, University Hospital of Infectious Diseases - Sofia in the period 1996 - 2008. By means of cerebrospinal fluid (CSF) analysis diagnosis of serous meningitis was confirmed in all cases.

Results: More than a half of the affected children were above 5-years old - 61 cases (54.80 %), and nearly 2/3 were boys - 71 cases (63.96 %). The etiological structure revealed the influenza virus as the most common cause for CNS infection - in 22 cases (19.82 %). Most frequent prodromal symptoms were fever, headache and vomiting - in 84 cases (75.68 %). Clinical manifestation of meningo-radicular syndrome was present in 103 children (92.79 %). CSF analysis showed: mean protein level - 0.43 g/l \pm 0.27; mean cell count - 488/3 \pm 611/3. CT scan was performed for 27 children - in 13 cases findings were abnormal, corresponding with the clinical manifestation. 93.69 % of all cases had favorable outcome. Seven children (6.31 %) developed permanent neurological impairments.

Conclusion: Typical profile of a pediatric patient with viral meningitis treated in University Hospital of Infectious Diseases - Sofia for the last 13 years is presented. Most severe and complicated were cases caused by influenza viruses.

NOROVIRUS AND ROTAVIRUS GASTROENTERITIS IN HOSPITALIZED CHILDREN, TURKEY**M. Altindis**¹, S. Yuksek¹, R. Koken², R. Kalayci^{3,4}, Y. Yoldas⁵

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Background and aims: Enteric viruses (especially rotaviruses and noroviruses) that have been reported as a cause of nonbacterial acute gastroenteritis. This study aims to determine the prevalence and the distribution of viruses 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 (range: 1 - 72 months) (negative for the presence of pathogenic bacteria by standard culture methods) were tested by ELISA (Ridascreen and Biomerieux) and RTPCR methods for detection of- Norovirus G1, G2.

Results: Noroviruses were detected in 22.8% of 92 children (< 6 years of age) and rotavirus were detected in 23.3 % of 150 hospitalized for gastroenteritis in Afyonkarahisar, Turkey, during 2009; predominant genotypes were GGIIb. Of children with viral enteritis, 6.5% had a mixed norovirus-rotavirus infection.

Conclusions: The severity of infection was lower for norovirus than for rotavirus but increased in co-infection.

THE EFFICIENCY OF GANCICLOVIR TREATMENT IN CHILDREN WITH CYTOMEGALOVIRUS INFECTIONS

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Objective: The aim of this study is to evaluate clinical and demographic features of CMV infections in children and to determine acute and long term effect of ganciclovir therapy.

Methods: Patients who were admitted to the Pediatric Infectious Disease Clinic during the period from December 2003 through December 2009 with the diagnosis of CMV infection were included in this study. The study was carried out in 40 children, aged between 1 months and 14 years of age. The diagnosis of CMV infection depended on clinical presentation, CMV-specific Immunoglobulin M and detection of viral DNA by polymerase chain reaction (PCR).

Results: Twenty-nine (72.5 %) patients were diagnosed as congenital CMV infection and 11 (27,5 %) patients had acquired CMV infection. Thirty (75,0 %) patients received ganciclovir treatment. The most common indications for ganciclovir treatment were CMV hepatitis (56,0 %) and CNS involvement (20%). All patients with hepatitis had full recovery(100%) while no recovery was observed in patients with CNS involvement. Nearly thirty percent of the patients suffered from moderate to severe hearing loss.

Conclusion: Although ganciclovir treatment lead to transient recovery such as in hepatitis, there were still relapses and morbidity due to complications of CMV such as hearing loss. Therefore the decision for the use of ganciclovir treatment should be evaluated individually and long-term follow-up of all patients should be considered in every patient.

NOVEL PAEDIATRIC SURVEILLANCE INFORMS PLANNING FOR SECOND WAVE PANDEMIC INFLUENZA A H1N1 (2009)

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Background and aims: During the 2009 Southern Hemisphere winter the Australian Paediatric Surveillance Unit (APSU) in collaboration with the National Centre for Immunisation Research and Surveillance (NCIRS) carried out influenza surveillance to identify and characterise children hospitalised with influenza, document the impact of influenza A H1N1 (2009), and compare outcomes of pandemic and seasonal influenza.

Methods: Use of a novel inpatient surveillance system (Paediatric Active Enhanced Disease Surveillance: PAEDS) to identify children < 15 years with laboratory-proven influenza. All three children's hospitals in NSW participated in this surveillance.

Results: 324 children were admitted to the children's hospitals (1802 hospital bed-days and 230 PICU bed-days) and most 237/324 (73.1%) had H1N1 (2009). Compared to 2007 (previous peak year), in 2009 at the Children's Hospital Westmead, admissions to hospital (226 versus 122) and PICU (22 versus 13) were increased. In 2009 the proportion aged < 6 months was lower than 2007 (15.5% versus 28.7%; $p=0.005$) and the proportion ≥ 5 years higher than in 2007 (33.2% versus 12.2%; $p=0.0001$). A similar proportion of children had pre-existing conditions in 2009 (43.4 %) and 2007 (49.1%). In 2009 vomiting was more frequent than in 2007 (38.5% versus 13.1%; $p=0.0001$) as were influenza complications (particularly neurological complications: 11.4% versus 2.4%; $p=0.0027$).

Conclusions: The H1N1 (2009) pandemic had a greater impact than seasonal influenza, placing increased demands on children's health resources. High admission and complication rates support universal influenza vaccination. Also needed are increased awareness of the presentation in children, reliable rapid diagnosis and more rational treatment.

A CHILD WITH RHABDOMYOLYSIS ASSOCIATED TO INFLUENZA A H1N1 VIRUS INFECTION**G. Bossi, M. Re, M. Pozzi, G.P. Noè***Pediatrics, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy*

Background: Myositis and rhabdomyolysis can rarely complicate an upper respiratory illness. Influenza viruses A and B are responsible for most cases. This rare syndrome is clinically defined as severe myalgia and elevated serum creatinine kinase (CK). To date, the full spectrum of complications of novel influenza A H1N1 virus remains unclear but it is assumed that only certain populations are considered at risk for complicated disease.

Case report: A 4 yr old previously healthy boy presented at the emergency department with painful calves and severe difficulty walking. His medical history was remarkable for an upper respiratory infection occurring some days before. No dark urine was reported. Full blood count and kidney function were normal, but CK was 822 mU/ml (normal < 190). Urine myoglobin at admission was 5 ng/ml. Aggressive hydration with 0.9% normal saline was started and the renal function remained stable throughout. CK peaked at 3490 mU/ml on day 2 of admission before the greatest part of the cases and gradually declining. Influenza A H1N1 was identified on a nasopharyngeal swab by PCR.

Discussion: As other influenza virus strains, also influenza A H1N1 virus causes myositis and rhabdomyolysis in previously healthy children. Although mild and self-limiting, a little number of patients develop renal failure and compartment syndrome. Recognition of this rare but distinct disease can spare a patient from potentially unneeded invasive testing. Prompt treatment is mandatory to prevent renal function impairment.

LESSONS FROM AN OUTBREAK: EPIDEMIC KERATOCONJUNCTIVITIS DUE TO ADENOVIRUS IN A NEONATAL INTENSIVE CARE UNIT

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Adenovirus is an agent which expresses as respiratory tract infections, gastroenteritis, cystitis and keratoconjunctivitis. Especially serotype 8, 10, 19 can cause epidemic keratoconjunctivitis characterized by lacrimal swelling, eye redness, and lacrimation in both eyes. Premature infants whom are immunologically at risk can be carriers of the virus for long periods of time and cause infection in other high risk infants. In such babies frequent ophtalmological examination is the major cause of infection. Here we present an epidemic nosocomial outbreak of keratoconjunctivitis due to adenovirus that occurred between July and August 2009 and affected 6 members of the hospital staff and 8 premature neonates. Of conjunctival swabs collected from 8 patients and 6 nurses, all were tested by virus isolation and direct fluorescent assay (DFA). Adenovirus was detected in 7/8 samples of infants by DFA and 3/8 samples of infants by DFA+ culture. None of the babies showed signs and symptoms of any other illness. All infants were discharged as soon as their prematurity related problems were resolved. Health workers were totally negative in terms of microbiological examination. However all obeyed clinical and epidemiological criteria of the infection. All affected personnel were suspended for 10 days after the onset of symptoms. By introducing rigorous infection control measures and avoiding unnecessary ophtalmologic explorations we controlled the outbreak in a much shorter period of time compared to literature. As a result, in newborns conjunctival symptoms especially after ophtalmologic examination should evoke suspicion of keratoconjunctivitis and strict infection control measures should be taken immediately.

COMPLICATIONS OF CHICKENPOX IN IMMUNOCOMPETENT CHILDREN

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Introduction: Chickenpox is a disease which severity depends rather of individual characteristics than changes in virus virulence.

Objective: Evaluation of complication in chickenpox cases hospitalised in a period of 2 years and 11 months (January 2007 - November 2009).

Material and method: Retrospective study about cases of chickenpox hospitalised between January 2007 and July 2008 in Children Infectious Diseases Clinic. We evaluate uncomplicated and complicated cases of chickenpox from demographic, clinic and therapeutic point of view.

Results: During years 2007, 2008 and 2009 in Children Infectious Diseases Department we hospitalised 116 patients with chickenpox. Majority of patients were from urban area (84/116). Sex ratio shown a preponderance of girls (65/116) affected by chickenpox. Median age was 6.47 years (ranges: 1 month and 18 years). Majority of cases were registered during cold months - 81 cases. From all cases hospitalised 62 (53.45%) children presented different complications: 6 with encephalitis (cerebellitis), 3 with arthritis, 7 cases with secondary hepatitis, one case of acute glomerulonephritis, 11 cases of persistent thrombocytopenia, 3 cases of acute bronchiolitis, in 12 cases bacterial pneumonia, one fluctuant collection of tight, in other 14 cases we registered bacterial infection of vesicles and in 4 cases we registered bacterial sepsis. Evolution was favourable, with no deaths.

Conclusions: During last two years we registered a decreased number of cases with chickenpox that required hospitalisation but an increased number of complicated cases (53.45%). We registered an increased number of complication rarely observed during the last years such as: arthritis, bronchiolitis, or hepatitis.

RISK FACTORS AND OUTCOMES AMONG CHILDREN ATTENDED TO IN A TERTIARY HOSPITAL WITH PANDEMIC A H1N1 INFLUENZA

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Introduction: Influenza causes significant morbidity and mortality in childhood. Limited data are available on epidemiological and disease characteristics of children with 2009 pandemic influenza A (H1N1) virus infection.

Objective: To describe demographic characteristics, risk factors and clinical features of pediatric patients with influenza A attended to in a tertiary hospital. To identify risk factors for severe disease by comparing hospitalized and no-hospitalized children.

Material and methods: We reviewed the charts of all children attended to in the emergency room and those hospitalized in the Hospital Universitari Vall d'Hebron, Barcelona, with laboratory-confirmed pandemic A H1N1 influenza, from July to November. We collected the following variables: age, sex, underlying medical conditions known to be risk factors for influenza-related complications, clinical features, hospitalization, requirement for intensive care and outcome. We conducted univariate and bivariate analysis to determine risk factors significantly associated with admission.

Results: We identified 422 children (52.6% boys and 47.4% girls). Seventy-five patients (17.8%) required hospitalization. Median age was 7 years old (range:0-19); the admitted children were significantly younger (5.8 y) than non-hospitalized (7.8 y) ($p:0.003$). Three-hundred and eleven children (73.7%) had underlying medical conditions (74.1% outpatients and 72% inpatients) ($p:0.71$). Asthma and chronic respiratory diseases were the most prevalent conditions (46.7%), followed by heart diseases (12.1%). Two children required admission to the ICU. No patient died.

Conclusion: Data on pandemic A H1N1 influenza in the children in our series are similar to those described recently. The rate of hospital admission was higher in younger children.

ACUTE PANCREATITIS AS ISOLATE FEATURE OF EPSTEIN-BARR VIRUS INFECTION IN A 13-YEAR-OLD BOY

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A 13-year-old boy was admitted to Department of Paediatric, Meyer Children's Hospital of Florence , with a 7-day history of abdominal pain radiating to the back and vomiting. Physical examination showed only mild hepatomegaly and splenomegaly and generalized abdominal tenderness. Laboratory features showed atypical lymphocytosis 11,179 / μ L (reference range, 4,110 to 9,590 / μ L), amylase 783 U/L (reference range, 10 to 220 U/L), lipase 1,170 U/L (reference range, 21 to 67 U/L), alanine transaminase 131 U/L (reference range, 10 to 45 U/L), aspartate transaminase 99 U/L (reference range, 10 to 45 U/L), C-reactive protein 8 mg/dL (reference range, < 0.3 mg/dl). Serum lipide profile was normal. Serological tests for hepatitis A, B, C viruses, Cytomegalovirus, and Mumps virus were all negative. Further serological examination revealed acute Epstein-Barr virus infection. Ultrasound of the abdomen confirmed hepatomegaly and splenomegaly and a swelling pancreas compatible with acute pancreatitis. Conservative treatment was started with nasogastric suction, analgesics, total parenteral nutrition, and empirical antibiotic therapy with ceftazidime. The patient recovered uneventfully and was discharged 10 days after admission.

Few data are available on the association between Epstein-Barr virus infection and pancreatitis. Generally the onset of the pancreatitis' symptoms occurs after the characteristic clinical features of mononucleosis (fever, adenomegaly, nasal obstruction, tonsillitis and periorbital oedema). At the best of our knowledge, this is the first report of a case of Epstein-Barr virus infection presenting with pancreatitis in the absence of clinical signs of infectious mononucleosis and suggests that Epstein-Barr virus is a pancreatotropic virus.

MYOSITIS ASSOCIATED WITH PANDEMIC INFLUENZA A- H1N1 VIRUS INFECTION**A. Cerqueira, H. Antunes***Serviço de Pediatria, Hospital de Braga, Braga, Portugal*

In 2009, cases of influenza like illness were reported in Mexico on March 18; the outbreak was subsequently confirmed as H1N1 influenza A. H1N1 Influenza tends to cause high morbidity but low mortality rates (1-4%). The first case was confirmed in Portugal on May 4, 2009. Were recorded 70 deaths, including 3 children (4.3%) at 4 months, 10, 11 and 14 years.

In our hospital 325 children were surveyed for H1N1 infection of which 165 (50.8%) were positive and 15 were hospitalized (9.1% of H1N1 positive). Only one had myositis. There were no deaths.

We report the case of a 9 years old boy with no personal or family relevant history who was admitted to the emergency room at the convalescent phase of a upper respiratory tract infection with a severe lower-extremity myalgia and reluctance to walk. On exam showed broad-based gait and calf pain. Creatine Kinase 13808 (38-190 U/l) and AST/ALT 333/64 (< 35/28 U/l) levels were elevated. Diagnosis of H1N1 was established by viral isolation (reverse transcriptase Polimerase Chain Reaction). He made intravenous fluids and was discharged the 2nd day.

Influenza-associated myositis is a complication of influenza among children. This case demonstrates the novel virus capacity for causing significant disease. Even so has an excellent prognosis.

EPIDEMIC INFLUENZAE H1N1 IN SOUTHEASTERN OF BRAZIL

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It is a report the experience of health care team at reference hospital during the influenzae H1N1 in southeastern Brazil.

Survey data of cases assisted at the Pediatric Emergency and notification at Center for Epidemiological Surveillance. It was creating a local protocol flow of assistance and to access to virus test: quick test for influenza A and RSV, for others virus used immunofluorescence and PCR test for laboratory reference.

Results: 82 suspected cases of H1N1 influenza in children under 12 years of age who were evaluated in service from 01 June to 31 October 2009. The seasonality was 2 cases occurred in June and 6 July in that were strong epidemiological link to contact people from traveling northern hemisphere abroad after the case was already local, 30 cases in August, 31 cases in September and 12 in October.

By sex: 37 female and 45 male. By age: 31 are less than a year old, 24 between one and five years old and 27 six to twelve years of age.

Have been confirmed for H1N1 testing by 31% (28/82 suspects) and 7/31 are < 1 year, 5/24 are 1-5 years and 16/27 are 6-12 years. Only one death was in girl 7 years old with morbid obesity. Virus circulation was RSV and influenza H1N, after parainfluenza viruses and all time together with seasonal influenza

The epidemic of influenza A H1 N1 in a referral hospital brought an important lesson to work on and the care in viral diseases in diagnosis, notification and preventions.

MOLECULAR EPIDEMIOLOGY AND GENETIC VARIABILITY OF THE FUSION PROTEIN GENE OF HUMAN RESPIRATORY SYNCYTIAL VIRUS IN NORTHERN TAIWAN

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Background and aims: Both the G and F protein of HRSV had genetic variability but few studies looked at the F protein genes. The aim is to characterize the molecular epidemiology of the F gene and correlation to G gene in Taiwan.

Methods: HRSV isolated from children with acute respiratory symptoms July 2000 to June 2008 were analyzed. Sequences of F protein gene were aligned with the BioEdit software followed by minimal manual editing. Phylogeny construction and evaluation were performed using the Phylip software package with the neighbour-joining method (NJ) and the maximum likelihood method (ML).

Results: A total of 278 HRSV were studied. There were 182 group A, 60 group B and 31 dual infections according to G protein gene. A consistent tree topology was obtained with both NJ and ML methods and 2 RSV genotypes were observed. The 2 monophyletic groups are corresponding to the genotypes A and B of G protein gene classification. The phylogenetic analysis of the variable region of F gene (nt 110-869) revealed 6 sub-clusters within genotype A and 4 sub-clusters within genotype B. Some genotype A isolates formed sub-clusters within the A group occurred in some specific consecutive seasons, e.g. one of the sub-cluster contained isolates only from 1992-1997.

Conclusions: Our results showed the F protein gene can be used for RSV genotyping as well as G protein gene. The F genotype predominating shift with the season and this suggested that there might be some specific strains circulating in Taiwan in certain years.

ENTEROVIRUS REMAINS AN IMPORTANT CAUSE OF CENTRAL NERVOUS SYSTEM INFECTION IN DUTCH CHILDREN

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Background and aims: Enteroviruses (EV) and Human Parechoviruses (HPeV) are an important cause of childhood infection, with various clinical spectra, from gastroenteritis to meningo-encephalitis. Moreover, there are reports of motor and developmental delay in children after EV meningo-encephalitis. The influence of EV/HPeV infection on motor and developmental delay in Dutch children after EV and HPeV infections has never been studied. The aim of the present study is to investigate the burden of EV/HPeV infection in children. Preliminary results are presented.

Methods: This study is part of an ongoing multicenter hospital-based prospective study, involving children 0-16 years visiting three major general hospitals in the Netherlands. Children with clinical suspicion of an EV or HPeV infection were included, starting in 2008 and finishing in 2010/2011. Children with other cause of illness are excluded.

Results: From 121 included patients, 48 (40%) and 15 (12%) had an EV and HPeV infection, respectively. Patients' characteristics are shown in the table. Half of the patients with an EV or HPeV had meningitis. The most frequent clinical symptoms were fever (98% in EV and 87% in HPeV) and malaise.

Conclusions: These results show that EV and HPeV are still an important cause of morbidity, including meningitis in Dutch children and the need for a nationwide registration and follow-up.

Table. Patients characteristics

	Total Group (n=116)	EV positive (n=48)	HPeV positive (n=15)
Median age (range)	90 days (2 days-14.8 years)	53.5 days (3 days-8.0 years)	41 days (8 days-9.1 months)
Male/female ratio	1.6 (72/44)	1.3 (27/21)	6.5 (13/2)
Median duration of symptoms [days] (range)	1 (0-14)	1 (0-14)	1 (0.5-5)
Diagnosis			
Meningitis	31	25	6
Gastro-enteritis	44	13	6
Other organ involvement			
Respiratory infection	5	2	0
No specific organ involvement	22	4	3
Unknown	14	4	0
No. admitted (%)	93 (80%) ^A	43 (90%) ^D	15 (100%)
Median duration of admission [days] (range)	3 (1-12)	3 (1-5)	4 (1-10)
No. patients receiving antibiotics (%)	40 (32%) ^B	23 (48%) ^E	7 (47%)
No. patients' antibiotics stop (%)	30 (75%) ^C	15 (65%) ^D	6 (86%)

^A 8 patients unknown, ^B 14 patients unknown, ^C 3 patients unknown, ^D 1 patient unknown, ^E 7 patients unknown.

[Table. Patients characteristics]

REAL-TIME POLYMERASE CHAIN REACTION IS THE MOST RELIABLE METHOD IN DETECTING ENTEROVIRUS-INFECTION

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Background and aims: Enteroviruses (EV) and Human Parechoviruses (HPeV) are an important cause of childhood infection. EV and HPeV can be diagnosed with culture, polymerase chain reaction (PCR) or serology. The aim of this study is to compare the value of serology by the complement binding assay (CBA), viral culture and real-time PCR in the diagnosis of EV/HPeV infection.

Methods: In this multicenter prospective study, children 0-16 years, visiting three Dutch major general hospitals with clinical suspicion of an EV or HPeV infection were included. Faeces, throat swab, urine, blood and if indicated cerebrospinal fluid (CSF) were collected for examination. Real-time PCR specific for EV or HPeV, viral culture and serology were performed.

Results: Of 121 included patients, 48 (40%) and 15 (12%) had an EV and HPeV infection, respectively. The results of the diagnostic tests are shown in the table. Real-time PCR detects more EV/HPeV than viral culture does. Serology by CBA is the least sensitive. It detected EV infection in only 1 of the 23 children with an EV infection.

Conclusions: The results of this ongoing research show that real-time PCR is more sensitive than viral culture in the detection of EV and HPeV infection in children. Serology (CBA) is not reliable for the detection of EV infection in children.

Table. EV and HPeV detection in patients with infection

Examination	EV positive (n=48)	HPeV positive (n=15)
Faeces PCR	100% (43/43)	93% (14/15)
Faeces culture	77% (33/43)	14% (2/14)
Throat PCR	72% (33/46)	53% (8/15)
Throat culture	46% (21/46)	0% (0/12)
CSF PCR	78% (25/32)	100% (6/6)
CSF culture	44% (11/25)	0% (0/6)
Urine PCR	63% (27/43)	62% (8/13)
Blood PCR	62% (18/29)	89% (8/9)
Serology (CBA)	4% (1/23)	0% (0/6)

[Table. EV and HPeV detection in patients]

A RARE ENTITY IN PEDIATRICS: CYTOMEGALOVIRUS-ASSOCIATED MENETRIER'S DISEASE

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Background: Menetrier disease is a protein-losing gastroenteropathy, characterized clinically by nonspecific gastrointestinal symptoms and generalized edema, biochemically by hypoalbuminemia, and pathologically by enlarged gastric folds.

Case: A 7 year-old boy who was previously healthy was presented with sudden onset anasarca type edema after 3 days of vomiting and abdominal pain. Laboratory data showed hypoalbuminemia, hypoproteinemia and hypogamaglobulinemia. Urinalysis was negative. Upper gastrointestinal endoscopy was macroscopically normal. However, histologic examination showed cystic elongation of gastric glands with mononuclear and eosinophilic cell infiltration and was concordant with the diagnosis of Menetrier's disease. CMV inclusion bodies were detected by staining and CMV DNA in both tissue and serum by polymerase chain reaction was positive. In the course of the disease, patient suffered from respiratory difficulty due to pleural effusion and was treated with albumin infusions in two separate occasions. At the end of the 2nd week of admission, his clinical condition was stabilized and edema started to disappear. Edema was completely resolved at the end of the 4th week.

Conclusion: Hypoproteinemia beside hypoalbuminemia is an important finding in Menetrier's disease. It may be beneficial to differentiate Menetrier's disease from protein losing enteropathy in clinical ground. So, this findings may lead us to perform upper gastrointestinal endoscopy and biopsy early in the course of the disease.

PULMONARY COMPLICATIONS IN PAEDIATRIC PATIENTS AFFECTED BY H1N1 PANDEMIC FLU. FREQUENCY AND RADIOLOGIC FEATURE

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Background and aims: Analysis of pulmonary complications in H1N1 pandemic flu. Patients hospitalized in Paediatric Infectious Diseases Department, Parma Hospital. Description of some radiologic frames.

Methods: Patients hospitalized according to Italian Influenza Guidelines 2008. Virus recognition via PCR-RT on pharynx tampon. Chest X-ray where appropriate.

Results: 105 hospitalized patients (pandemic analysis as of week 52, 2009, 7 weeks after pandemic peak). All patients subjected to tampon, of which 30 positive (28,5%). 20 positive patients subjected to Chest X-ray (66,6% of positives):

-10 simple pneumonia (50%)

- 2 bronchiolitis (10%)

- 2 pneumonia with pleural effusion (10%), among which 1 with left pleural effusion associated with Pneumococcus co-infection, treated with thoracentesis and streptokinase. Male patient, 7 y, no risk factor. Not moved to ICU.

- 1 pneumonia with pneumomediastinum (5%) and subcutaneous emphysema of the neck and left thorax. Female patient, 10 y, with history of unspecified broncho reactivity. Moved to ICU due to respiratory failure, treated with CPAP.

- 1 ARDS (5%). Female patient, 6 y, with asthma, Moved to ICU due to respiratory failure, treated with CPAP.

- 2 acute bronchitis (10%).

- 2 negative x-ray performed during sepsis (10%).

Conclusions: Data confirm frequent pulmonary respiratory complications in patients with H1N1 infection. Our case history reports 53% incidence. Most affected categories are subjects at risk - asthmatic especially - and subjects with bacterial super infection.

H1N1 PANDEMIC FLU, THE CASE OF PARMA PAEDIATRIC HOSPITAL, NORTHERN ITALYI. Dodi¹, M. Verna¹, V. Raggi¹, S. Lacava¹, D. Vignali¹, M.A. Bandello¹, G.C. Izzi¹, M.L. Tanzi²¹*Pediatric Infectious Disease Unit - Department of Pediatrics, University Hospital of Parma, ²Public Health Department, University of Parma, Parma, Italy***Background and aims:** Analysis of patients hospitalized in Parma Paediatric Infectious Diseases Department: number, typology, complications, hospitalization duration.**Methods:** Pandemic flu analysis as of week 49, 2009 - 4 weeks after pandemic peak. Case selection based on Italian Influenza Guidelines, 2008. Virus recognition via PCR-RT on pharynx tampon.**Results:** 101 patients (hospitalization rate, age 0-4: 118/100,000, age 5-14: 70/100,000)

M=51, F=50; Age range: 19d-26y;

Age distribution: ≤ 4y: 59 (58%); 5-14y: 35 (35%); >14y: 7 (7%)

Tampon total positivity: 29 (29%)

Age distribution: ≤ 4y: 12 (41%); 5-14y: 15 (52%); >14y: 2 (7%)

Average Hospitalization time: 5.4d

Average fever duration: 3.3d

Positive with Complications: 19 (66%), 3 moved to ICU (10% of positive patients)

- Pneumonia: 10 (53%), 1-15y, 1 S.Pneumoniae positive
 - Pneumonia with pleural effusion: 2 (10.5%), 7-11y, 1 S.Pneumoniae positive
 - Bronchiolitis: 2 (10.5%), 2m
 - Pneumonia with pneumomediastinum: 1 (5%), 10y
 - ARDS: 2 (10.5%), 6-9y
 - Sepsis: 2 (10.5%), 1m-2y
- Risk factors among positive patients: 11/29 (38%)
- Cardiopathy: 2 (18%), 2-12m
 - Broncolability: 1 (9%), 10y
 - AIDS: 1 (9%), 20y
 - Asthma: 4 (36%), 2-6y
 - Autoimmune disease: 1 (9%), 6y
 - Lissencephaly: 1 (9%), 9y
 - DMD: 1 (9%), 5y

Therapy

Oseltamivir, 5 days to all positive patients

Side-effects: 1 gastroenteritis (3%), 1 skin rash (3%)

Conclusions: Pandemic impact in Parma lower than expected. Higher rate complications in patients with assessed risk factors. Low incidence side effects with antiviral therapy.

ENCEPHALOPATHY AND APHASIA ASSOCIATED WITH NOVEL INFLUENZA A (H1N1) VIRUS INFECTION

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Background and aims: In a limited number of reports encephalopathy/encephalitis has been associated with novel influenza A (H1N1) virus infection. The aim of this report is to raise awareness of this complication.

Methods: We reviewed the hospital records of two children with novel influenza A (H1N1) infection, who were admitted to the University hospital of Patras, Greece, with neurologic manifestations, in November 2009.

Results: The first patient was a 13 year-old girl with a three-day history of fever, headache sore throat and cough, who developed altered mental status, disorientation and irritability, which lasted for 24 hours. Electroencephalogram showed generalized continuous delta slowing consistent with encephalopathy. Brain MRI was normal. CSF was normal and negative by polymerase chain reaction for influenza, cytomegalovirus, Epstein-Barr, Herpes-simplex virus and for mycoplasma. Urine toxicology and blood culture were negative. She received oseltamivir for 5 days. She recovered completely and was discharged 7 days after admission. The repeated EEG was normal. The second patient was a 10 year-old boy with a one-day history of fever, coryza, headache and vomiting, who experienced transient short-lasting expressive aphasia having full recollection of the event. The boy recovered quickly from his symptoms and was discharged 3 days after admission. Neither patient had focal neurologic signs. Both patients had positive nasopharyngeal swab specimens for novel influenza A (H1N1) virus by reverse-transcription PCR. Neither of the two had any sequelae.

Conclusions: Novel influenza A (H1N1) infection should be considered in children with mental status or speech changes during the current pandemic.

LUNG FUNCTION OF PREMATURELY BORN INFANTS FOLLOWING VIRAL LOWER RESPIRATORY TRACT INFECTIONS

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Background and aim: RSV lower respiratory tract infection (LRTI) in prematurely born infants is associated with reduced lung function at follow up. The aim of this study was to determine whether other viral LRTIs were associated with a similar adverse outcome.

Methods: Twenty eight infants born at less than 36 weeks of gestational age and prior to the RSV season were prospectively followed. A nasopharyngeal aspirate (NPA) was obtained every time the infants had a LRTI regardless of whether this was in hospital or in the community. NPAs were tested by RT-PCR for RSV A and B, Rhinovirus, human Metapneumovirus, Parainfluenza 1-3, Influenza A and B and Adenovirus. Lung function (functional residual capacity [FRC] by the helium gas dilution, lung clearance index, compliance [CRS] and resistance [RRS] of the respiratory system and plethysmographic measurements of FRC and airways resistance [Raw]) was assessed at one year of age.

Results: Eleven infants had "other" (ie not RSV) viral LRTIs (other virus group) and four infants developed RSV LRTIs (RSV group). Both the other virus group and the RSV group had higher RRS ($p=0.04$, $p=0.03$ respectively) and Raw ($p=0.02$, $p=0.04$ respectively) than the infants who did not have an LRTI. There were no significant differences in the lung function of the other virus group and the RSV group.

Conclusion: Prematurely born infants who have viral LRTIs in infancy have reduced lung function at follow up.

PRESENCE OF HBV-DNA IN CORD BLOOD IS ASSOCIATED WITH SPONTANEOUS PRETERM BIRTH IN PREGNANT WOMEN WITH CHRONIC HEPATITIS B

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Background: Spontaneous preterm birth (SPB) is the leading cause of perinatal morbidity and mortality. In our study we evaluated the SPB rates in a group of HBeAg (-) chronic HBV infected pregnant women without several known risk factors for preterm delivery. Moreover we examined the role of maternal laboratory data during perinatal period as well as the role of HBsAg and/or HBV-DNA presence in the cord blood in respect to preterm labor.

Methods: Haematological, biochemical and serological parameters were calculated using automated techniques. Serum HBV-DNA was determined by using the Cobas Amplicor HBV Test in both maternal and cord blood samples.

Results: 102 women were finally evaluated and fifteen of them (14.7%) exhibited SPB. The presence of SPB was not related with any maternal parameter except of maternal absolute lymphocyte count ($p=0.006$). A significant association between SPB and HBV-DNA presence in cord blood was observed ($p=0.007$). HBV-DNA positivity in cord blood was significantly associated with maternal HBV-DNA levels (147.543 copies/ml vs 1.646 copies in women with HBV-DNA positive or negative cord blood respectively, $p=0.002$). The relative risk of HBV-DNA presence in cord blood was 6.43 times higher among women with serum HBV-DNA ≥ 10.000 copies/ml and lymphocyte count < 1500 compared to those with all the other combinations of both parameters ($p=0.001$).

Conclusions: The presence of HBV-DNA in cord blood is associated with SPB in chronic HBV infected pregnant women. Women with HBV-DNA ≥ 10.000 copies/ml and lymphocyte count < 1500 during perinatal period have the higher probability of HBV-DNA presence in their cord blood.

BURDEN OF ROTAVIRUS GASTROENTERITIS IN THE MIDDLE EASTERN PEDIATRIC POPULATION

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Background and aims: Rotavirus (RV) is the most common cause of severe childhood diarrhea worldwide. Objectives were to estimate the burden of rotavirus gastroenteritis (RVGE) among children less than five years old in the Middle East.

Methods: A systematic literature search was conducted in major databases on the epidemiology and burden of rotavirus among children less than five years old in the Middle East during the last ten years. Data from each country was extracted and compared.

Results: The search identified 43 studies for 16 countries. RV was identified in 16-61% of all cases of acute gastroenteritis, with a peak in the winter. Hospitalization rates for RVGE ranged from 14% to 57%, compared to 14.4%-28.4% for non-RVGE. Annually, RVGE caused up to 112 fatalities per 100,000 in certain countries in the region. Hospitalization costs ranged from \$1.8 to \$4.6 million annually, depending on the country. G1P[8] was the most prevalent genotype combination in 8 countries (range 23%-68%). G2P[4] was most prevalent in 4 countries (24.5%-48%). G9P[8], and G4P[8] were also frequently detected. Variability and changes in genotype combinations among countries and over time were reported.

Conclusions: RVGE is a common disease associated with significant morbidity, mortality and costs. The pentavalent rotavirus vaccine, which covers the majority of types in the region, is expected to be efficacious and will help decrease the burden of RVGE in the Middle East.

ROTAVIRUS INFECTION AMONG CHILDREN WITH ACUTE DIARRHEA IN ASSIUT PEDIATRIC UNIVERSITY HOSPITAL: GENOTYPING AND COMPARISON BETWEEN STRIP AND EIA AND RT-PCR

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Objective: The aim of this study is to investigate the role of group A rotavirus in acute diarrhea among infants and children under three years of age attending or admitted to Assiut Pediatric University Hospital and to compare between the strip test and Enzyme Immune Assay (EIA) in diagnosis of rotavirus infection using the Reverse Transcriptase-Polymerase Chain Reaction (RT-PCR) as a gold standard, beside defining the genotype of the detected strains using multiplex-PCR.

Patients and methods: Eighty-eight children under the age of three years, presenting with acute diarrhea were examined for group A rotavirus antigen in stools by a quick strip test and EIA. RT-PCR was also performed as a reference test. Twelve children of matched age and sex, without diarrhea, were also included (control group). All rotavirus positive samples by RT-PCR were also subjected to genotyping by multiplex PCR (G1, G2, G3, G4, G8 and G9).

Result: The sensitivity and specificity of strips versus RT-PCR were 70.5% and 95.5% respectively whereas those of EIA were 86.4% and 91% respectively. Genotyping by multiplex PCR revealed that all the detected strains belong to G3 genotype.

Conclusion: The rate of infection with group A rotavirus among children with acute diarrhea differs according to the method used for detection (37.5% by strips, 47.5% by EIA and 50% by RT-PCR). The strips are more rapid, simple and specific than EIA, yet the EIA remains more sensitive in detecting rotavirus antigen in stools. All rotavirus strains detected belong to G3 genotype.

PREDICTORS OF PERSISTENT HEPATITIS C VIRUS (HCV) INFECTION IN EGYPTIAN CHILDREN

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Hepatitis C virus (HCV) has lower prevalence in children. There is limited knowledge of the natural outcome of HCV infection acquired at early ages of life.

Aim: To study the predictors of persistence of HCV infection in a cohort of Egyptian children.

Materials and methods: Ninety six out of 146 anti-HCV positive children were followed for 36 months. These children attended two pediatric hepatology units in Cairo, Egypt. Regular clinical and biochemical assessment was carried out at 3-monthly intervals; virological and imaging studies were carried out at 12-monthly intervals. Spontaneous clearance of HCV was defined as ≥ 2 positive anti-HCV antibody tests with negative HCV-RNA.

Results: The rate of spontaneous clearance was achieved in 31 (32%) patients. In univariate analysis, persistence of infection was associated with parenteral transmission (blood transfusion) ($P=0.03$), dental treatment ($P < 0.01$), male gender ($P < 0.01$), elevated alanine transaminases (ALT) ($P=0.01$), aspartate transaminases (AST, $P=0.008$) at baseline. After 36 months follow up, multivariate regression analysis, in which outcome of the study was the dependent variable, male gender (OR 7.5, $P=0.002$), dental treatment (OR 16.9, $P=0.001$), elevated baseline ALT (OR 4.9, $P=0.027$) and fluctuation of AST levels (OR 8.1, $P=0.024$) were significant predictors for the persistence of HCV infection.

Conclusion: HCV infected male children with elevated ALT levels at baseline and fluctuation of AST levels are unlikely to clear the virus spontaneously and deserve consideration for treatment.

RESISTANCE TO OSELTAMIVIR OF SEASONAL A/H1N1 INFLUENZA VIRUS DURING WINTER SEASONS 2007-2008 AND 2008-2009 IN ITALIAN CHILDREN

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Background and aims: Oseltamivir is the drug of choice to treat influenza in children aged < 7 years. Recently, oseltamivir-resistant influenza viruses due to neuraminidase mutations have emerged. Monitoring of incidence and clinical relevance of oseltamivir resistance is critical to evaluate the need for different schemes of therapy. This study evaluates these problems in Italian healthy children during two consecutive influenza seasons.

Methods: On nasopharyngeal samples collected in healthy children with influenza-like illness attending the Pediatric Departments of Milan, Bari, Padua, Naples and Genoa during winter seasons 2007-2008 and 2008-2009 RT-PCR for identification of A/H1N1, A/H3N2 and B influenza viruses was performed. On A viruses positive samples, influenza genome analysis using pyrosequencing method for identification of mutations H275Y and N294S in A/H1N1 and E119V, R292K, and N294S in A/H3N2 was applied. Mutations were evaluated in association with clinical data.

Results: Among 4,726 samples, 662 samples (14.0%) were positive for influenza A, 150 (126 H1 and 24 H3) and 512 (17 H1 and 495 H3) collected during the seasons 2007-2008 and 2008-2009, respectively. Of these, 2/126 in 2007-2008 (1.6%) and 17/17 in 2008-2009 (100.0%; $p < 0.0001$) H1N1 strains with H275Y mutation were found. No other mutation was identified. No child infected by mutated viruses had received oseltamivir. No difference in clinical course was observed between children infected by susceptible or resistant virus.

Conclusions: Incidence of oseltamivir resistance among seasonal influenza viruses is significantly increasing in Italy. This resistance does not seem drug-induced and appears without any clinical relevance in healthy children.

PROSPECTIVE CLINICAL AND VIROLOGICAL COHORT STUDY ON THE IMPACT OF SEASONAL INFLUENZA IN PEDIATRICS

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Background and aims: Many health authorities consider seasonal influenza of healthy children a mild disease for which vaccine prevention is not needed. However, the real incidence of seasonal influenza in children is not precisely defined. This study was planned to evaluate the clinical and socioeconomic consequences of seasonal influenza of healthy children in the community.

Methods: A total of 42 primary care pediatricians following 21,986 children younger than 5 years were asked to collect all the data regarding the visits made to their patients for influenza-like illness (ILI) between November 1st, 2008, and April 30th, 2009. Moreover, during each visit, they had to collect a nasopharyngeal swab on which identification of influenza viruses was performed by specific RT-PCR.

Results: Incidence rate of influenza was 96.4 x 1,000 children (influenza A 78.4 x 1,000 children and influenza B 17.5 x 1,000 children). Among 7,031 ILI-episodes, 2,143 (30.7%) had laboratory-confirmed influenza (influenza A, 81.7%; influenza B, 18.3%). Children with influenza had significantly more often fever higher than 39°C, general discomfort, cough, rhinitis, vomiting and diarrhea than children without influenza ($p < 0.001$). More than 50% of children with influenza received antibiotic therapy and 1,265 (23.7%) needed 2 or more visits. Parents of children with influenza suffered from ILI and lost work days significantly more often than parents of children without (46.8% vs 24.6% and 24.6% vs 15.9%, respectively; $p < 0.001$).

Conclusions: Clinical and socioeconomic consequences of seasonal influenza appear significant in the community. All these data support the recommendation of universal influenza vaccination in pediatrics.

OSELTAMIVIR-INDUCED RESISTANT PANDEMIC A/H1N1 INFLUENZA VIRUS IN A CHILD WITH CYSTIC FIBROSIS

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Background and aims: Oseltamivir is the preferred neuraminidase inhibitor as zanamivir is contraindicated in people with underlying respiratory conditions. However, it is still unclear how oseltamivir-resistant pandemic A/H1N1 influenza viruses emerge and what the clinical consequences may be.

Methods: An 8-year-old boy with cystic fibrosis was hospitalized because of fever and respiratory symptoms during a period in which the circulation of pandemic A/H1N1 influenza virus was widespread. The clinical and laboratory findings led to a diagnosis of pandemic A/H1N1 influenza due to a virus without the H275Y mutation accompanied by pulmonary exacerbation due to *Pseudomonas aeruginosa*. Oseltamivir and ceftazidime plus tobramycin were administered.

Results: During the first five days of hospitalisation, his clinical condition progressively worsened, peripheral oxygen saturation in room air decreased to 88%, chest radiography revealed the presence of atelectasis with pleural effusion in the lower part of the right lung, and his white blood cell count significantly increased, although C reactive protein always remained in normal range. His nasopharyngeal secretions remained positive for pandemic A/H1N1 and in the fifth day sample showed H275Y mutation. On the basis of these findings, oseltamivir was replaced by zanamivir and vancomycin added. This change was associated with a rapid improvement in the patient's general condition, respiratory findings and laboratory data in the absence of any adverse event.

Conclusions: Infection due to pandemic virus with the H275Y mutation can be highly pathogenic when it occurs in high-risk patients. In these cases, zanamivir appears an effective and safe treatment even in presence of chronic respiratory disease.

SEVERITY OF DISEASE IN INFANTS UNDER ONE YEAR OF AGE INFECTED BY 2009 PANDEMIC INFLUENZA A/ H1N1 VIRUS

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Background and aims: In spring 2009, a new pandemic influenza A/H1N1 virus emerged. Infected infants aged less than two years are considered at high risk for severe progressive pneumonia (WHO). We describe our clinical experience in East Midlands (U.K.) of infected infants under one year between May and December 2009.

Methods: Respiratory samples from 310 children, whose parents sought hospital paediatric review due to severe symptoms, were tested for 2009 influenza A/H1N1 virus by real-time reverse-transcriptase-polymerase-chain-reaction assay. 29 infants under one year were confirmed positive.

Results: No deaths were recorded. Three infants had radiographic evidence of pneumonia. Two required conventional intensive care support; one, a 6-month old female without underlying medical conditions, progressed to respiratory failure. She recovered after ten days extracorporeal membrane oxygenation (ECMO) supplemented by oseltamivir and zanamivir therapy.

In our limited experience in this group, lack of severe complications is the norm; neither lymphopenia nor monocytopenia was noted. Common symptoms were pyrexia and cough; common signs were tachypnoea, bilateral crackles and ronchi. Infants, even with underlying medical conditions such as chronic lung disease secondary to prematurity, did not always require antiviral treatment or hospital admission.

Conclusions: Our data which includes referrals to our paediatric ECMO unit, does not support the contention that infants under one year, infected with pandemic influenza A/H1N1, represent a high-risk group for refractory hypoxaemia.

Infants suspected to be infected, manifesting severe progressive pneumonia, should be offered immediate treatment with neuraminidase inhibitors.

Normal or raised monocytes represent a good prognostic feature.

HERPES SIMPLEX ENCEPHALITIS IN CHILDREN

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Background and aims: Although the use of acyclovir therapy decreased its mortality and morbidity, herpes simplex encephalitis (HSE) still remains the most frequent cause of sporadic fatal encephalitis in children under 6 months in the Western countries. Its estimated incidence is 1/250 000-500 000 per person per year, one third of the cases is noted in children. 30 % of confirmed cases are primary infections while the rest is caused by reactivation of the latent viral infection. The study aimed to analyze clinical presentation, diagnostic process and final outcome of HSE cases in children.

Methods: The authors analyzed cases of confirmed HSE in 23 patients - 6 males and 3 females age between 1 month and 15years. The diagnosis was based on the clinical presentation, laboratory findings, neuroimaging.

Results: Most patients presented with symptoms typical for neuroinfections: fever (n=17), vomiting (n=12), altered consciousness (n=17), 16 children presented with convulsions (partial, generalized tonic-clonic, myoclonic). Physical examination revealed labial herpes in 5 children. 10 of the group had contact with infected person. The most common finding in neurological examination was hemiparesis (18 children). Neuroimaging (MRI or CT) showed abnormalities of different extend in all patients. Laboratory findings confirmed herpes etiology by positive PCR results or presence of IgG and IgM antibodies in serum or CSF. In all cases, the acyclovir therapy was conducted. A relapse of herpes encephalitis was observed in 3 patients.

Conclusions: Proper diagnosis and early antiviral treatment is an important factor contributing to the remission of clinical symptoms.

PUTTING THE PANDEMIC INTO PERSPECTIVE: A COMPARISON WITH 10 SEASONAL INFLUENZA EPIDEMICS

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Background and aims: We wanted to extract the experience gathered from virologically proven, epidemic influenza during the last decade and compare it to prospectively gathered data from children admitted with virologically proven H1N1 influenza.

Methods: Data on risk factors, complications and need of intensive care were analyzed.

Results: 81 children with virologically confirmed H1N1 influenza were admitted, compared to 506 admissions of 503 children with confirmed seasonal influenza in the previous 10 seasons. The number admitted varied from 19 to 111 per season. For seasonal influenza, the mean age was 3,7 years, 50% had underlying risk-factors, 50% had complications and the median hospital stay was 2 days. For the pandemic influenza, the mean age was 4,5 years, 40% had underlying risk-factors, 38% had complications and the median hospital stay was 3 days. As with seasonal influenza, preterm infants and children with neurological disorders more frequently needed observation in the ICU. In seasonal influenza seasons, influenza was included among diagnoses at discharge in only half of the cases.

Discussion: The proportion of previously healthy children admitted was larger during pandemic influenza, most likely due to caution by the clinicians as the severity of the pandemic was unknown. The main difference of the pandemic influenza is that the children admitted to the hospital were older than in seasonal epidemics. The risk-pattern of the pandemic remained similar to the seasonal influenza with the most common risk factor for admission being neuromuscular disease, and the most common complications are obstructive respiratory symptoms and convulsions.

Q-PCR SCREENING FOR POLYOMA VIRUS IN PAEDIATRIC RENAL TRANSPLANT PATIENTS**K. Harvey-Wood**¹, A. Balfour¹, C. Williams¹, J. Beattie²¹*Microbiology Dept,* ²*Renal Unit, Royal Hospital for Sick Children, Yorkhill, Glasgow, UK*

Background: Primary infection with polyoma BK virus (BKV) occurs early in childhood and leads to latency. BKV can reactivate and cause nephropathy (BKN) during immunosuppression in renal transplant recipients. BKN affects up to 10% of renal transplant patients, and is a significant cause of graft loss. Routine screening for BKV is recommended so that early diagnosis and appropriate treatment can be commenced.

Aims:

- To develop and implement an algorithm for screening paediatric patients post-transplant for BKV to complement our current screening strategy for EBV, CMV and Adenovirus
- Analysis of first 6 months use of this algorithm

Methods: A commercial BKV Q-PCR kit (Alert, Nanogen) had previously been validated in our laboratory using EDTA blood and urine samples, and the optimal number of amplification cycles determined. We developed an algorithm which incorporated BKV analysis into our current regimen for screening for EBV, CMV and Adenovirus, using the same EDTA sample.

Results: From 01/06/09-30/11/09, 206 samples (172 EDTA blood, 34 urines) from 48 renal transplant patients were tested for BKV by PCR. 14/172 (8 %) EDTA samples and 14/34 (41%) urines were positive. 5/48 patients tested positive for BKV - 2 positive in blood, 2 positive in urine, and one symptomatic patient positive in both was treated with Cidofovir.

Conclusions: Recent studies indicate detectable virus in blood is more predictive of BKN than viraemia alone. We have developed and implemented a cost-effective algorithm for screening for BKV which complements our established regimen for screening for other viruses.

FEASIBILITY OF DIAGNOSING INFLUENZA DURING THE FIRST 24 HOURS OF SYMPTOMS IN CHILDREN 1-3 YEARS OF AGE

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Background and aims: Diagnosing influenza at an early stage of illness is important because it enables the initiation of effective antiviral treatment. However, especially in young children, influenza often commences with an abrupt onset of fever, with full-blown respiratory symptoms developing only later. We sought to determine the feasibility of diagnosing influenza in young children already during the first signs of the illness.

Methods: During confirmed influenza activity, we obtained nasal swabs from children aged 1-3 years who presented as outpatients within 24 h of the onset of fever ($\geq 38.0^{\circ}\text{C}$). The specimens were tested for influenza viruses with viral culture, antigen detection, PCR, and a rapid point-of-care test (Actim Influenza A&B). In addition, follow-up specimens were obtained from a proportion of children 3-7 days later.

Results: Influenza virus was detected already within 24 h of symptom onset in 56 of 61 (92%; 95% CI, 82-97%) children in whom influenza was eventually confirmed in the laboratory. A total of 158 rapid tests performed within 24 h of symptom onset yielded a sensitivity of 90% (CI, 74-98%) for influenza A viruses but only 25% (CI, 3-61%) for influenza B viruses, resulting in an overall sensitivity of 77% (CI, 61-89%) and specificity of 99% (CI, 95-100%) for any influenza.

Conclusions: In most young children, influenza can be accurately diagnosed already within 24 h of symptom onset. The rapid point-of-care test used was sensitive and specific for diagnosing influenza A, but its sensitivity for influenza B was limited.

HERPES SIMPLEX ENCEPHALITIS IN CHILDREN: EXPERIENCES AND CHALLENGES**T. Ho, Y. Le, D. Le, A. Pham***Infectious Diseases, National Hospital of Pediatrics, Hanoi, Vietnam*

Purposes: To describe the clinical, investigational characteristics and initial outcome of the patients who suffered from HSE at National Hospital of Pediatrics in 2007-2008.

Patients: 39 patients diagnosed with HSE were enrolled to the study. The crucial criteria of HSE diagnostics based on the acute encephalopathy syndrome and DNA of HSV detected in CSF by PCR method.

Methods: This is a case series report

Results:

1. It occurred sporadically and the ages varied from 1 month to 13 years old with predominant ages of 1 month to 5 years old (89.75%). Boy/girl ratio was 1.16/1
2. The most common signs and symptoms were: fever (92.31%), focal neurological signs (69.23%) and coma (58.97%).
3. CSF changes were mild elevated protein (69.13%) and leucocytosis (87.18%), with increased lymphocytes and monocytes predominately.
4. Cranial CT Scanner findings: the most common one was hypodense areas located at temporal lobes (66.67%). Hemorrhage was associated in 7 cases (17.9%).
5. Outcome with intravenous acyclovir: The recover rate was 7.95%, sequelae rate (76.92%) and mortality rate (5.13%).

Conclusions: HSE is a sporadic one whose fever, focal neurological signs, coma are frequently seen. Most patients have shown abnormalities at temporal lobes on cranial CT Scanner. Because of the treatable one, HSE is considered as a crucial diagnostic among patients suffering from acute encephalopathy syndrome with focal neurological signs. Further studies should be performed to improve the neurological impairment rate.

PROSPECTIVE STUDY OF THE BURDEN OF ROTAVIRUS GASTROENTERITIS IN CHILDREN UNDER 5 YEARS OF AGE

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Background and aims: Rotavirus (RV) is a major cause of gastroenteritis (GE) in children (1). Safe, effective RV vaccines are now available (2). Data on the burden of RVGE in Denmark (DK) needed for health authorities to evaluate the potential benefits of RV vaccination, are limited (3,4). The present study was designed to characterize the burden of RVGE in children aged < 5 years in DK.

Methods: During the 2008 and 2009 RV seasons, children attending general practitioners (GPs) in DK or the Department of Paediatrics, Hvidovre Hospital with symptoms of GE were included prospectively. A stool sample was obtained, and RV was detected by immunochromatography. Demographic data and clinical manifestations related to the child's illness were recorded.

Results: Of the 404 recruited children 315 met the inclusion criteria. RV was detected in 47 of the 96 (49%) patients attending hospital, and in 71 of the 219 (32.4%) patients attending GPs. Most cases of RVGE (70.3%) occurred in children > ½ and < 2 years of age. By multivariate analysis, the following odds ratios by RV status (+ vs.-) were: Vomiting 6.5, [3.53;11.93], $p < 0.001$; Dehydration 2.4, [1.23;4.59], $p = 0.01$; Weight loss 3.8, [1.84;7.70], $p < 0.001$; Fever 6.3, [3.23;12.19], $p < 0.001$; Change in behavior 9.1, [3.27;25.23], $p < 0.001$.

Conclusions: RV is a frequent cause of GE and RVGE is likely to be more severe than GE of other causes. This study supports that a substantial disease burden could be avoided by universal RV vaccination of infants in DK.

TRENDS IN SEVERE INFLUENZA AND PARAINFLUENZA ASSOCIATED PEDIATRIC ICU MORBIDITY: 2003-2009

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Aims: Respiratory viral infections cause significant morbidity and misery, affecting millions of children annually worldwide. We investigated if morbidity had increased in young children admitted to a pediatric intensive care unit (PICU) with a laboratory proven diagnosis of influenza or parainfluenza infection.

Methods: Retrospective study between January 2003 and December 2009 was carried out. Every child in the PICU with a laboratory-confirmed influenza or parainfluenza infection was included.

Results: 18 influenza (influenza A=13 and influenza B=5) and 17 parainfluenza admissions were identified over the 7-year period. Parainfluenza type 3 (n=9) was the commonest subtype of parainfluenza infection. The median age of children admitted with influenza was higher than parainfluenza (4.5 versus 1.7 years, $p = 0.044$). Admissions associated with proven influenza and parainfluenza infections accounted for 2% of PICU annual admissions. There was only one death in 2003. 51% of these patients required ventilatory support, 45% received systemic corticosteroids, and 91% received initial broad spectrum antibiotic coverage. Bacterial co-infections were identified in 25% of these patients. The incidence of influenza admissions had not increased significantly in 2009 (H1N1 pandemic) when compared with 2003 (SARS epidemic) ($p=0.3$). There were only two PICU cases of pandemic H1N1 in 2009 and both survived. The annual incidence of severe PICU cases of influenza and parainfluenza were 0.94 and 0.88 per 100,000 children per annum, respectively.

Conclusions: There is no evidence to suggest that PICU mortality and severe morbidity associated with the pandemic H1N1 and other influenza and parainfluenza viruses has increased dramatically in recent years.

NEONATES INVESTIGATED FOR INFLUENZA-LIKE ILLNESS DURING THE OUTBREAK OF PANDEMIC H1N1 2009: TRIVIAL INFECTIONS BUT MAJOR TRIAGE IMPLICATIONS

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Aim: The Pandemic H1N1/09 virus is a new swine-origin influenza A(H1N1) strain responsible for the 2009 flu pandemic. In hospital practice based on fever and contact history, we screen patients with symptoms compatible with an influenza-like illness (ILI), upper respiratory tract infection (URTI), or acute respiratory diseases. Nevertheless, the clinical presentations in neonates may be non-specific and fever or contact history is often absent.

Methods: We reviewed neonates admitted to a teaching hospital for the investigation of possible respiratory viral infections based on fever or respiratory symptoms or contact history during the outbreak of pandemic H1N1 2009 in Hong Kong.

Results: Eight neonates (from birth to 25 days; 6 Females, 2 Males) were admitted to the neonatal service of a teaching hospital with influenza-like illness during the outbreak of pandemic H1N1 between August and December 2009. Empirical antibiotics were often promptly initiated and timely stopped when sepsis was ruled out. There was no pandemic H1N1-09 but influenza A (H3N2, n=1), parainfluenza (type 3, n=3) and respiratory syncytial virus (n=1) have been isolated. The infants recovered spontaneously without any antiviral therapy. There was no outbreak of the respiratory infections in the neonatal service during the admissions.

Conclusions: Respiratory viral infections can occur in neonates although the clinical course may be milder and nonspecific. Emergency room and frontline staff must be vigilant of the non-specific clinical features of infections with respiratory viruses in the neonates so that prompt triage and isolation can be implemented to avoid outbreaks in the neonatal service.

VIRAL ETIOLOGY OF ASEPTIC MENINGITIS IN CHILDREN, SOUTHERN IRAN, 2007-2008**A. Hosseinasab¹, A. Alborzi², M. Zeyaeian²***¹Pediatrics, Kerman University of Medical Sciences, Kerman, ²Prof. Alborzi Clinical Microbiology Research Center, Shiraz University of Medical Sciences, Shiraz, Iran*

Background: Aseptic meningitis refers to a clinical syndrome of meningeal inflammation in which common bacterial agents cannot be identified in the cerebrospinal fluid. This study was conducted to determine the epidemiological, clinical, laboratory characteristics and viral etiology of aseptic meningitis in Shiraz, southern Iran in children aged 2 months to 15 years, using PCR method.

Methodology: From May 2007 to May 2008, 65 patients were hospitalized with aseptic meningitis. Having extracted nucleic acid from cerebrospinal fluid samples, we investigated the viruses which are commonly associated with aseptic meningitis in children (enteroviruses, mumps, CMV, HSV, VZV, EBV and HHV6) by commercially available PCR methods.

Results: The results of the study on 65 patients revealed that viruses were detected as responsible for aseptic meningitis in 30 (46.2%) patients of whom enteroviruses and mumps virus were detected in 13 (43.3%) and 11 (36.7%), respectively. The remaining 6 (20%) of the cases were caused by viruses including: herpes simplex, varicella zoster, cytomegalovirus and human herpes virus type 6. Haemophilus influenzae and enterovirus were detected in one patient simultaneously. Moreover, the viral meningitis was found more frequent during spring and summer. The majority (66.6%) of the patients, who were diagnosed as viral meningitis, had been hospitalized for 10 days and had received antibiotics. The age, gender, clinical features and routine laboratory findings have not been significantly different between the proven viral meningitis group and non-proven cases.

THE ROLE OF ENTEROVIRAL INFECTION IN YOUNG INFANT FEVER

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Background: Febrile illness in infants accounts majority of NICU admissions, most caused by viral infection, especially enterovirus. Rapid recognition of enterovirus infections is important to prevent unnecessary therapeutic interventions.

Methods: Through May to September 2008, we enrolled infants < 2 months with fever. Throat and rectal swabs for viral isolation were procured, and subsequently assayed by indirect immunofluorescence staining for the identification of serotype. The specimen was rapid detected by reverse transcriptase-polymerase chain reaction (RT-PCR). Serum of each subject was obtained for analyzing viral load by real time RT-PCR, measuring cytokines by Enzyme-linked immunosorbent assay (ELISA).

Results: Of 59 infants, only 14 (23.7%) subjects were detected enterovirus from RT-PCR, confirmed by viral isolation. Most were full term babies (GA: 37.77±2.20 weeks, BBW: 3001.08±629.45 gm). The mean postnatal age of disease onset was 36.64±22.63 days of life. All 14 cases were presented with fever, 4 had neurological symptoms, 2 had URI symptoms, 2 had skin rash. Their diagnosis were 10 for febrile illness, 4 for aseptic meningitis. Viral RNA could be detected in 3 patients and their viral loads were low (mean viral load: 9.226 copies/μl). Cytokines measured by using ELISA had no differences between groups with and without enteroviral infection.

Conclusions: 23.7% infants were isolated enterovirus indicated that enteroviral infection accounts one fourth of young infant fever in NICU. Use of RT-PCR during the first few days of illness offers potential benefits for early diagnosis, preventing unnecessary antibiotics treatment and reducing hospital stay for infants with mild enteroviral infection.

SYMPTOMATIC CMV PRIMAINFECTION IN IMMUNOCOMPETENT CHILDREN. NINE YEARS RETROSPECTIVE STUDY IN THE CHU OF MONTPELLIER

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Background and aims: Cytomegalovirus (CMV) is a common virus in human gender. Usually the primo infection is asymptomatic then the seroprevalence is about 43% between 1 and 4 years old infants in Europe. Symptomatic infection could be dangerous and happened usually in immunodepressive host and in maternofetal infection. Symptomatic CMV primo infection (SCPI) have been described in immunocompetent adult host but rarely in children.

Methods: We presented a retrospective study about SCPI in immunocompetent children except maternofetal infection between 1999/01 and 2008/12. The diagnostic of CMV primo infection status was made by specific IgG and IgM dosage, avidity test, antigenemia and quantitative PCR.

Results: During this study we identified 30 cases of SPCI. The sex ratio is 10 boys for 20 girls, the mean age is 4 years and 2 months. The most frequent clinical symptom was fever (11/30), it was isolated in 10 cases. Other clinical signs were rash, hepatomegaly, splenomegaly and adenopathy. C-Reactive Protein dosage was negative, there was anaemia (50%), lymphocyte activation (30%), and hepatic cytolysis (25%).

Conclusions: CMV primo-infection is probably underestimate. It could be symptomatic in immunocompetent children. Clinical manifestations are different than the adults. It could be evoked and have to be search in anaemia of unknown origin and in lymphoproliferative syndrome.

SEVERE CASES OF 2009 PANDEMIC INFLUENZA A(H1N1) INFECTION IN A TERTIARY HOSPITAL FROM BARCELONA

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Background and aims: Although 2009 H1N1 produce mostly banal infections, 665 severe cases with 37 deaths have been reported in Catalonia.

Aim: To report clinical data about 2009 H1N1 paediatric severe infection.

Method: We include prospectively patients with confirmed 2009 H1N1 infection by RT Real-Time PCR, admitted at Pediatric Intensive Care Unit from July to November 2009. We compare ICU-admitted patients with ward-ones.

Results: Twenty-four patients were recruited (62.5% males). Median age was 5.8 years (range: 2 months - 18 years). Thirteen had previously known diseases (neurological, mainly).

Main reason for admission was acute respiratory failure (18) (two of them had *S pneumoniae* coinfection, 1 RSV). Non invasive ventilation was effective in 14. Nine needed invasive mechanical ventilation (4 due to respiratory failure, 3 consciousness alteration, and 2 hemodynamic instability).

Extrapulmonar manifestations were meningoencephalitis (2), myopericarditis (2), and hepatorenal syndrome (1), who required renal replacement. LDH was increased in 10. Six patients received inotropic support.

Three patients died (2 limitations of life-sustaining treatments due to severe neurological disease and one previously healthy patient with fulminant myocarditis).

ICU patients were different that those admitted at ward in: higher inflammatory parameters, lower hemoglobin oxygen saturation before treatment. No differences were observed in: confirmed coinfection, age, and time from onset of symptoms to starting oseltamivir.

Conclusions: Many patients with severe 2009 H1N1 infection have not a previous recognizable disease and were not coinfectd. Hypoxemia is commonly observed at admission. Many had extrapulmonar manifestations. Non-invasive ventilation is used effectively and safely.

H1N1 INFECTION: CLINICAL SYNOPSIS IN 40 HOSPITALIZED CHILDREN

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Introduction: The first wave of new influenza A/ H1N1 infections reached Germany between September and November. Little is known yet on specific clinical courses in hospitalized children.

Methods: All children hospitalized at our tertiary teaching hospital with fever and respiratory symptoms PCR-positive for H1N1 were included and compared with a random sample of 27 children with respiratory symptoms tested negative for H1N1.

Results: We treated 40 children with H1N1-influenza, 25/40 had chronic diseases: 6 had asthma, 4 were immunosuppressed, 7 had neurological diseases, the others a broad range of chronic diseases. No child died; 2 needed intensive care treatment due to respiratory problems, but no mechanical ventilation was necessary. Of the 15 H1N1-positive children without chronic conditions 5 had a febrile seizure, 5 signs of bacterial pneumonia, one urinary tract infection, 2 infants were treated as suspected sepsis. 19/40 were treated with oseltamivir. 39/40 children with H1N1 presented with fever, all with cough, 5/40 with enteritis, 19/40 with vomiting, 7/40 with abdominal pain.

Inflammation parameters varied according to co-infection, but H1N1- infection was associated with leucopenia, low eosinophils and marked monocytosis.

1 child had received the H1N1 - vaccine 10 days prior to hospitalisation.

Conclusion: H1N1 influenza took different courses in the large spectrum of children with chronic diseases; severe disease with secondary bacterial pneumonia occurred also in otherwise healthy children. Some lab changes may be specific. Overall, H1N1-influenza took a benign course in the cases presented here.

HEPATITIS A IN CHILDREN

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Background and aims: Hepatitis A (HAV) is globally spread, with its frequency largely depending on the social-financial status. In developed countries it is seen either sporadically or in the form of microepidemics. Children and teenagers are mainly affected. Among the high risk groups belong the Romani dwelling in camps. Our purpose was to register a microepidemy of Hepatitis A in Romany children.

Methods: The 25 Romany children studied were infected by HAV and had been admitted to our department during December 2008 and January 2009. All were dwelling in the same camp.

Results: Among them, 11(44%) were girls and 14(56%) boys. One was under the age of 2 years, 14 were between 2-6 and 10 >6 years of age. All of them presented with malaise, abdominal pain, diarrhea and vomiting. 5 developed jaundice and had fever >38°C. All were positive for IgM HAV antibodies. ALT values were as presented below:

ALT U/L	until 40	40-100	100-200	200-600	600-1000	>1000
Number of children	4	5	5	5	4	2

[ALT

values]

The Prothrombin Time in all was normal. Total bilirubin in the 5 icteric children was between 2,4-3mg/dl, with a direct value ranging between 1,5-2mg/dl. None of the patients was vaccinated against HAV.

Conclusions: The clinical outcome in all children was good. The need for improvement of living conditions of this population and the urge for the vaccination against HAV to be implemented according with the National Program for Vaccination, should be stressed.

CLINICAL FEATURES OF PAEDIATRIC H1N1 ADMISSIONS IN A TERTIARY HOSPITAL IN SOUTH KOREA BEFORE VACCINE ERA

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Background and aims: Critical illness due to H1N1 swine-origin influenza (H1N1) is emerging threat to global children's health. This study is aimed to describe clinical data of first wave pandemic influenza for timely proper managements.

Methods: Retrospective study was performed with admitted patients under the age of 15 years who had H1N1 infection confirmed by reverse transcriptase polymerase chain reactions (RT-PCR) between August 1 and November 30, 2009 in Wonju Christian Hospital.

Results: Among a total of 2177 children who showed positive in RT-PCR, 120 patients (5.5%) were admitted and their diagnoses were pneumonia (73%), febrile convulsion (10%), asthma (9.5%), and croup (7.5%). Median age was 6 years of age (range: 0.25-15). Gender ratio was 2.75: 1. The median hospital stay was 5 days (range: 2-10). Oseltamivir was started before confirm results. Double dosage of oseltamivir was used in 20/120 patients. 29/120 (24%) needed oxygen therapy and 3/120 (2.5%) were treated with mechanical ventilation. The patients treated in intensive care unit have no underlying diseases. The median level of C-reactive protein (CRP) was 2.45 mg/dL (range 0.3-24). 44/120 patients showed elevated aspartate transminase levels, and 8/120 patients showed elevated creatinine kinase levels. All patients were completely recovered within 10 days. There was no significant difference in disease duration according to treatment modalities such as corticosteroid use, intravenous gammaglobulin, or double dosage of oseltamivir.

Conclusion: The overall clinical outcome of serious paediatric H1N1 infections seemed to be similar to those of other respiratory viruses which can cause severe respiratory tract infections.

EXPERIENCE OF NOVEL INFLUENZA A INFECTION AT THE NATIONAL MEDICAL CENTER OF SOUTH KOREA: FORCED CONFINEMENT IN A QUARANTINE FACILITY

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Background and aims: Initially, novel H1N1 influenza A infection was identified from Mexico and the United States in April 2009 and has spread very rapidly to many countries over several months. At that time, Korean government adopted a firm policy on laboratory-confirmed patients and strict isolation by hospitalization was performed from April to August 2009. Thus we investigated clinical and epidemiological characteristics of patients under 18 years of age hospitalized in the National Medical Center(NMC) during that period.

Methods: Clinical and epidemiological characteristics of 65 patients under 18 years old admitted to the NMC from May to August 2009 were investigated through retrospective review. New influenza A infection was confirmed by real-time RT-PCR.

Results: 39 were male among 65 patients and median age was 11 years(0.8-18 years). 50 patients(76.9%) were travelers mainly from North America(49.2%) or South-east Asia(18.5%). High-risk children under 59 months of age were 9(13.8%) and among 65 patients there were no underlying medical conditions. Clinical manifestations were cough(87.7%), fever(85.2%), rhinorrhea(67.7%), headache(60.0%), sputum(52.3%), soreness(47.7%), diarrhea(29.2%), vomiting(23.1%), myalgia(9.2%), and dyspnea(1.5%). The chest X-ray showed 3 infiltrations(4.6%). All patients took oseltamivir for 5 days.

Conclusions: All patients recovered completely, but one child had suffered from severe pneumonia. However, novel H1N1 influenza A infection was not a serious disease.

SEROPREVALENCE OF HEPATITIS A IN KOREA**K.-H. Kim**^{1,2}, H. Lee^{1,2}, J.-H. Kim^{3,4}

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Aim: After the introduction of the Hepatitis A vaccine, and decrease of disease incidence in Korea, there has been a shift in age groups of the target susceptible population. In this study, we aimed to evaluate the seroprevalence of anti-Hepatitis A IgG in Korea to assess the immune status of the Korean population and find the susceptible age groups to hepatitis A.

Methods: Residual serum samples from diagnostic laboratories throughout Korea were collected randomly from February to July, 2008 and stored at -70 °C until analysis. Among the samples recruited, 1,841 samples from all age groups were selected for analysis. Anti-HAV IgG antibodies were measured by Elecsys® (2010/Modular analytics E170, Roche Diagnostics GmbH, Indianapolis, IN, USA).

Results: Among the 1,841 samples, only 1,556 samples were analyzed due to lack of sera. The seroprevalence of anti-HAV IgG was 25.0% in infants < 1 years old, 57% in 1-4 years, 70.6% in 5-9 years and then started to decrease to 39% in 10-14 years, 21.7% in 15-19 years and was lowest in the 20-29 years age group by 11.2%. In the following age groups, increase in seroprevalence was seen with advancing age; 51.1% in 30-39 years, 82.9% in 40-49 years, 81.4% in 50-59 years, 93.2% in 60-69 years and 94.6% in 70-79 years.

Conclusion: The susceptible age for Hepatitis A proved to be between 10-29 years age, especially for those between 20-29 years age.

SEROPREVALENCE OF RUBELLA IN KOREA**K.-H. Kim**^{1,2}, H. Lee^{1,2}

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Aim: According to a systematic review which was done on studies of Rubella seroprevalence in Korea, although there have been several studies on the seroprevalence of Rubella in specific populations, no studies were done on all age groups. In this study, we aimed to evaluate the seroprevalence of anti-Rubella IgG in Korea to assess the population immunity against Rubella.

Methods: Residual serum samples from diagnostic laboratories throughout Korea were collected randomly from February to July, 2008 and stored at -70 °C until analysis. Among the samples recruited, 1,595 samples from all age groups were selected for analysis. Anti-Rubella IgG antibodies were measured by ELISA (Enzygnost®; Dade Behring, Schwalbach, Germany) and CLIA (Beckman Coulter, Unicel DxI).

Results: Among the 1,595 samples, only 1,493 samples were analyzed due to lack of sera. Overall rubella seropositivity rates in Korea were 90.5% for all ages. The seroprevalence of anti-Rubella IgG was 14.1% in infants < 1 years old, 95% in persons aged 1-3 years, 99.6% in persons aged 4-6 years, 99.5% in persons aged 7-12 years, 100% in persons aged 13-19 years, 96.6% in persons aged 20-29 years, 83.3% in persons aged 30-39 years and 92.3%, 97.1% and 92.9% for persons aged 40-49 years, 50-59 years and 60-69 years, respectively. The lowest rate was those of the age 30-39 years.

Conclusion: The overall rubella seropositivity rate is high in Korea

BENIGN ACUTE CHILDHOOD MYOSITIS ASSOCIATED WITH H1N1 INFECTION- A CASE REPORT

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Background and aims: Benign Acute Childhood Myositis (BACM) represents a self-limiting muscle syndrome occurring after upper respiratory tract viral infection, usually with Influenza A or B. Clinical presentation of BACM is characterised by severe calf pain, often causing difficulty walking and localised muscle tenderness. Laboratory findings include elevated muscle enzymes without myoglobinuria, as well as elevated hepatic enzymes.

Methods: We report a case of an 8 year old boy who presented with difficulty walking three days after an episode of upper respiratory tract infection. The patient could not dorsiflex lower feet and passive dorsiflexion was painful. There was marked calf tenderness and increased lower limb tendon reflexes but no clinical evidence of arthritis. Laboratory findings included a marked elevation of CPK, elevated LFTs but no myoglobinuria. Renal function tests and inflammation markers were normal. RT-PCR of nasopharyngeal swab was positive for the new pandemic influenza A (H1N1) virus.

Results: The patient recovered fully after three days of bed rest. No specific therapeutic intervention was required.

Conclusions: This case presents the typical clinical and laboratory characteristics of BACM and is the first known to us case associated with H1N1 infection in Greece.

It is important for the physician to be aware of this rare clinical entity in order to prevent unnecessary invasive testing and reassure the patient of the excellent prognosis.

INFLUENZA A AND B INFECTION IN GREEK CHILDREN DURING THE WINTER PERIOD 2008-2009

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Introduction: Influenza A and B is a highly contagious viral infection of the upper respiratory tract in childhood and its annual outbreaks are characterized by antigen annual variability and seasonality.

Material and methods: We examined the epidemiologic, clinical and radiological features of all cases with influenza-like symptoms, who examined in the 'Penteli' Children's Hospital in Athens from 30 November 2008 until 31 May 2009. Detection of Influenza A and B in pharyngeal swabs was performed using immunochromatography.

Results: Influenza A antigen was detected in 14 (7.4%) out of 190 children, while influenza B antigen was detected in 21 (11.1%) children. The median age of influenza-positive children was 7 years (age range: 2 to 13 years). The first positive case for influenza B was detected on the 19th February 2009. All patients had fever and influenza-like symptoms, while none had clinical or radiological evidence of pneumonia at presentation. Three children were admitted to the General Pediatric Ward and were discharged with full recovery after 1 to 3 days of hospitalization. No child was referred to the Pediatric Intensive Unit of our Hospital.

Conclusions: Our results demonstrate the late onset of influenza A and B infection in children with mild upper respiratory tract infection in Greece during the winter period 2008-2009.

PEDIATRIC CASE OF PANDEMIC H1N1 INFLUENZA IN ALBANIA

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Background: The 2009 A H1N1 influenza virus continues to be the dominant influenza virus in circulation in our country. It affects all age groups with a predominance of the age 15-24yrs among the laboratory confirmed cases. Pediatric cases presented 30% of all reported cases.

Objectives: To evaluate the updated epidemiological situation of pediatric pandemic influenza H1N1 cases in our country. To show the clinical characteristics, complications and follow up of this age group.

Material and methods: A **confirmed case** of influenza A (H1N1) virus infection is defined as a person with an influenza-like illness with laboratory confirmation of nasopharyngeal specimens collected by swabs detected by: real-time RT-PCR. A total of 795 pediatric specimens were examined. Study period included June - December 2009.

Results: 125 laboratory confirmed pediatric cases were reported for the study period. The most involved age group was 5-14 yrs with 83 cases, followed by children 1-4 years: 34 cases. Only 8 infants cases were reported. The male/female ratio was 1.8 and the greatest number of patients was registered during the second and third week of November. The clinical picture of pediatric cases was dominated by high fever and gastrointestinal signs. The most frequent reported complication was Pneumonia followed by other respiratory tract infections. One case with encephalitis by H1N1 was seen. antiviral treatment with Tamiflu was prescribed to all complicated cases. No fatal case was registered during this period.

Conclusion: The A H1N1 influenza virus was the most frequent viral respiratory tract infections during the last 6 months.

PANDEMIC (H1N1) 2009: A CLINICAL SPECTRUM IN THE PAEDIATRIC POPULATION IN COIMBRA, PORTUGAL

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Background and aims: The current pandemic (H1N1) 2009 is the world's first influenza pandemic in more than 40 years. Our aim was to characterize H1N1 positive cases.

Methods: Retrospective analysis of all paediatric H1N1 admissions, between July and November 2009, at a paediatric hospital. RT-PCR on combined nose and throat swabs was used for diagnosis.

Results: 241 children with pandemic (H1N1) 2009 were observed, 127 (53%) boys, with a median age of 6.5 years (16 days-17 years). 216 (90%) cases were diagnosed in October and November. The most common symptoms were: fever (96%), cough (84%), nasal discharge (61%) and headache (41%). Gastrointestinal symptoms were present in 33%. Laboratory tests were performed in 40 (17%) children. Median values were: leukocytes 6780/uL(1100-37800), neutrophils/lymphocytes 3600/1400/uL; and C-reactive protein 2,2mg/dL (0.2-36.8). Of the 56 (23%) chest X-ray performed, 25% had bilateral interstitial infiltrates and 29% had lobar pneumonia/effusion. 139 (58%) children had risk factors: 29 were < 1 year of age and 110 had underlying medical conditions mainly asthma. Oseltamivir was prescribed in 69 (29%). 39 (16%) children were admitted to the ward (42% had risk factors), of which 3 (8%; 0.3 overall) required ICU (2 needed mechanical ventilation and 2 had underlying conditions). The median length of stay was 3 days (1-27). There were no case fatalities.

Conclusions: The clinical features are broadly similar to other series. Approximately half of the cases had underlying medical conditions. Pneumonia was diagnosed in 10%. Overall 16% were hospitalized and 8% of those required care in ICU.

INFLUENZA A (H1N1) 2009 VIRUS INFECTION - EXPERIENCE OF A PAEDIATRIC WARD AT A GENERAL HOSPITAL IN PORTUGAL

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Background: The epidemiology of pandemic (H1N1) 2009 virus infection shows that overall attack rates are higher among children and young adults. Infants and children younger than 2 years old have the highest risk of severe illness.

Methods: A retrospective study was conducted on children with flu-like syndrome or lower tract infection admitted in the emergency department or hospitalised in a paediatric ward at a general hospital. In all cases Influenza A (H1N1) test by reverse transcriptase-polymerase chain reaction assay was requested. Data was collected on sex, age, reason for testing, use of antiviral therapy, adverse effects and complications, comparing outpatients and hospitalised population.

Results: Between September and December 2009, a total of 351 tests were performed. Out of these patients 52% were male, 30% were under 2 years old, 72% were outpatients and 54% had a positive test. Asthma and cardiovascular disease were the main comorbidities in both outpatients and hospitalised ones. The main reasons for testing in cohabitants were pregnancy, cardiovascular disease and asthma. Only a child had a severe form of disease with cardio-respiratory arrest. 27% of children received oseltamivir and 24.5% of contacts received prophylaxis. Only 4% of patients had adverse effects. Periods of increased influenza activity matched those of increased emergency department admissions. In this period, positive tests predominated over negative tests. An inverse relation was found when flu activity decreased.

Conclusion: Most children had relatively mild forms of disease. Influenza A (H1N1) test is a useful diagnostic method in clinical practice. Oseltamivir seemed to be safe in young patients.

VIRAL PATHOGENS ASSOCIATED WITH ACUTE RESPIRATORY INFECTION IN WHEEZY INFANTS**K. Matsuda**¹, N. Sera², H. Saito³

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Background and aims: Viral infections are closely linked to wheezing in infancy, and those children with recurrent virus-induced wheezing episodes are at great risk for chronic childhood asthma. By using nasal lavage, we studied the viral etiology of acute respiratory infection (bronchiolitis, acute asthma) in 90 children in outpatients settings.

Methods: Nasopharyngeal samples were tested for 9 respiratory viruses by multiplex reverse-transcriptase polymerase chain reaction (PCR). Sputum cultures and serological testing were performed and for some virus by direct immunofluorescent assay in nasopharyngeal samples.

Results: A potential causative viral agent was detected in 70% of the cases. Respiratory syncytial virus (RSV) (29%), rhinovirus(26%), parainfluenza virus(14%), human metapneumovirus (13%), nontypable rhino/enterovirus (10%) and adenovirus (8%) were found most frequently. Three (2 of RSV, 1 of rhinovirus) of 90 infants (3%) needed hospitalization.

Conclusion: To prevent and treat acute expiratory wheezing illnesses in wheezy infants under the age of 2 year, efforts should be focused on RSV, rhinovirus infections.

H1N1 DISSEMINATED INFECTION

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Although, H1N1 has a benign clinical course in healthy children, in the very young or in patients with chronic medical conditions it can be associated with severe complications.

Three-month old healthy boy that one week before admission presents an upper respiratory tract infection without fever. He was admitted in our Paediatric Intensive Care Unit with severe dehydration, irritability and bloody, watery diarrhea that started two days before. The initial laboratory evaluation showed thrombocytosis (1,259,000/ul) and severe coagulopathy (prolonged protrombin time (TP)- 143seconds, activated partial thromboplastin time(aPTT)- 75,3seconds). The blood gases, hematocrit, renal function and ionogram were normal.

Due to persistent irritability a lumbar tap was performed and the cerebrospinal fluid(CSF) examination showed 25 cells with polymorphonuclear predominance, a protein level of 65.9mg/dl and a glucose level of 82mg/dl.

Real-time reverse-transcriptase-polymerase-chain-reaction(RT-PCR) for H1N1 in nasopharyngeal, stool specimens and CSF were positive and oseltamivir was started. Stool and blood cultures, Rotavirus and PCR for Enterovirus and Adenovirus in CSF were negative.

Although clinically stable, he progressively developed a haemolytic coombs negative anaemia, the lowest value of haemoglobin was 6.8g/dl on day eleven, with schistocytes and thrombocytopenia (minimum 4000/ul). Fibrinogen was normal, with increased TP and aPTT. Transfusion of erythrocytes, fresh frozen plasma and platelets were necessary. The coagulation study, immunity and ADAMTS-13 activity were normal. The electrophoresis of haemoglobins revealed a sickle cell trait. He was discharged on day twenty-four.

The authors describe a case of severe H1N1 disseminated disease with respiratory, gastrointestinal and neurologic involvement, with coagulopathy and microangiopathic anemia

IS VIRAL SCREENING NECESSARY BEFORE CARDIAC CATHETERIZATION IN CONGENITAL HEART DISEASE?

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Backgrounds and aims: Homodynamic catheters are widely reused mainly in developing countries where the costs of new devices are very high. Although viral serology is routinely screened prior to angiography, the significance of it is not clear. This study aims to evaluate the necessity of such screening in patients with congenital heart diseases.

Methods: In the present cross sectional study, 442 cases with congenital heart diseases that underwent cardiac catheterization in Imam Reza Hospital, Mashhad, Iran during 2001-2006 were enrolled. The viral markers of hepatitis B surface antigen and antibodies against hepatitis C, HIV and HTLV1, 2 were detected in all patients undergoing cardiac catheterization.

Results: Out of 442 patients with congenital heart diseases undergoing cardiac catheterization, 220 patients were female. The patients aged between six months to 39 years (mean 7.8 years). Screening of these patients showed that 6 (1.3%) of them were seropositive for HTLV1, 2, four (0.9%) for HBs Ag, four (0.9%) for HCV. None of the screened patients were HIV positive.

Conclusion: Positive viral tests were seen in few patients in the study. Considering the above findings if the cleaning and sterilization procedures are carried out properly, these tests should be considered just for high risk patients.

Keywords: Congenital heart disease-Viral screening-Catheterization.

SEVERE MEDULLAR APLASIA WITH MYELOFIBROSIS 2ND TO ACQUIRED PARVOVIRUS B19 INFECTION IN INFANCY- A FIRST CASE REPORT**O. Neth¹, C. Marquez², B. Croche¹, M. Anchoriz¹, I. Obando¹***¹Paediatric Infectious Diseases, ²Paediatric Oncology, Hospital Universitario Virgen del Rocío de Sevilla, Sevilla, Spain*

Human Parvovirus B19 is predominantly a subclinical infection, known to cause red cell aplasia in chronic haemolytic anaemia or post BMT.

We present the case of a 3-month old girl, born to non-consanguineous parents with no previous family history of haematological disorder, who presented with a mild respiratory tract infection associated with marked hepatosplenomegaly (HSM; 8 and 4cm) and pancytopenia (Hb 7.5g/l, WCC $9.0 \times 10^9/l$ [lymphocytes 8.0, neutrophils 0.6], platelets $10 \times 10^9/l$). Imaging of the abdomen confirmed HSM with adenopathy. Coombs-test, anti-neutrophil and anti-platelet antibodies were negative. BMA and trephine revealed severe medular aplasia with myelofibrosis, no blasts, no signs of haemophagocytosis; normal cytogenetic studies. Immunoglobulin serum levels and lymphocyte subsets for age were normal in number and distribution (CD3 60%, CD4 36%, CD8 22%, CD19 34%, NK 2%), levels of double negative (CD4-/CD8-) T cells were slightly raised being 1% and 3% (normal < 1% of total lymphocytes) and an underlying autoimmune lymphoproliferative syndrome (ALPS) was initially suspected. ESR (56mm/h), LDH (666IU/l) and ferritin (300mcg/l) were raised. Serology was Parvovirus B19 IFI IgM positive whilst the mother was IgM and IgG negative. The infant was blood product dependent and treatment with 3 doses of 0.4g/kg IVIG resulted in good clinical (decrease of HSM and blood/platelet transfusions) and serological response (Parvovirus B19 IgM negative) and was discharged on low dose prednisolone. This is the first case of an infant with myelofibrosis 2nd to acquired Parvovirus B19 infection and should be considered as differential diagnosis in patients presenting with pancytopenia and HSM.

HYPOGLOSSAL NERVE PALSY SECONDARY TO INFECTIOUS MONONUCLEOSIS IN TWO ADOLESCENTS. A CASE REPORT

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Background and aims: Infectious Mononucleosis (IM) is a widespread viral disease caused by the Epstein-Barr virus (EBV). Primary infection occurs frequently in childhood or adolescence. Two children with infectious mononucleosis complicated by hypoglossal nerve palsy is described.

Methods: A case report.

Results: A seventeen-year-old boy was admitted to hospital with left deviation of the tongue. Four days previously, he had returned home after hospitalization due to infectious mononucleosis. The boy complained of tongue discomfort, dysarthria, and dysphagia. Clinical examination revealed isolated left hypoglossal nerve palsy. Meningeal signs were not present. Cerebrospinal fluid examination revealed mild pleocytosis (18 cells). Infectious mononucleosis was laboratory confirmed by positive heterophile antibody test. Tick-borne encephalitis was excluded by negative serology. False-positive IgM antibody to *Borrelia* in ELISA (not confirmed by Immunoblot) were found as a result of a polyclonal antibody response in IM. Neurological symptoms alleviated within three months without specific treatment. Another boy, fifteen years of age, was referred to hospital with lymph nodes enlargement. Lymphadenopathy, exudative pharyngitis and soon unilateral tongue writhing was noted on examination. Heterophil antibody test confirmed Epstein-Barr virus infection. Oral clarithromycin was started for secondary bacterial pharyngitis. Hypoglossal palsy persisted some four months from onset of symptoms and finally resolved entirely.

Conclusions: EBV infection should be considered with an isolated palsy of the hypoglossal nerve.

THE COMPARISON OF CLINICAL, LABORATORY FEATURES AND OUTCOMES OF H5N1 CASES WITH H1N1 CASES

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In this study, the clinical, laboratory findings and outcomes of eight patients with H5N1 and 37 patients with H1N1 those we managed outbreaks of 2006 and 2009 in Eastern Turkey, respectively, were compared. The ages of patients were 56.8 ± 55.8 and 121.5 ± 48.1 months in patients with H1N1 and H5N1, respectively. Between the groups, myalgia, headache, rash, bleeding from nose or mouth, tachypnea, retraction, needing for intensive care unit, congestive heart failure, disseminated intravascular coagulation, sepsis were found to be statistically significantly more common in H5N1 cases than H1N1 cases. When we compared these groups with regard to laboratory examinations, it was found that leukopenia, thrombocytopenia, elevated liver enzymes, prolonged prothrombine time, prolonged activated thromboplastine time, increased D-dimer test were found to be more common in H5N1 cases than H1N1 cases. Between the groups, there was also a statistically significantly difference with regard to treatment outcome. Of all patients, four (50 %) in H5N1 cases and three (8.1%) in H1N1 cases were died. Furthermore, it was observed that in H1N1 cases, 16 (43.2 %) patients had additional disease like Down syndrome and congenital heart disease, cerebral palcy, ALL, AML, Pompe disease which also could play a predisposing role for infections like influenza. No additional disease was found in H5N1 cases. In H1N1 cases, three patients were died, two of them had cerabral palcy and pompe disease. Our findings revealed that H5N1 had a worse clinical progress than H1N1. The H1N1 cases with additional disease may also represented more severe clinically condition.

ACUTE VIRAL GASTROENTERITIS AMONG CHILDREN IN MINSK CITY: PREVALENCE AND GENETIC DIVERSITY OF NOROVIRUSES

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Noroviruses (NoVs) are important etiological agents of gastroenteritis worldwide. To study prevalence of NoV gastroenteritis among children in Minsk City, 101 feces specimens were investigated for enteric virus (rota-, noro-, astrovirus) by RT-PCR. Fragments of NoV RNA polymerase gene were sequenced and analyzed to assess genetic diversity of circulating strains.

NoVs were the second most prevalent etiological agents of gastroenteritis: they were found in 21,8% of stool samples, whereas rotaviruses - in 31,7% and astroviruses - in 4,9%.

From 21 samples testing positive for NoV, 15 nucleotide sequences of a fragment of RNA polymerase gene were obtained. According to results of genetic analysis only 6,7% of NoV strains belonged to genogroup GI, whereas 93,3% of strains were NoVs of genogroup GII. Results of phylogenetic reconstruction revealed that most of NoV strains (86,7%) grouped in a single cluster with prototype strain Bristol (the maximum of nucleotide differences was 12,0%) and belonged to predominant over the last decade genotype GII.4. Within genotype cluster all NoV GII.4 strains grouped with GII.4/Nijmegen/90106-42472/2008/NLD and GII-4/Akita5/2006/JP strains (the maximum of nucleotide difference was 2,8%). Genotype identification of one of GII NoV strains was unsuccessful - its nucleotide sequence did not group with any of prototype NoV strain of different genotypes, but formed reliable cluster with Hu/GII/Goulburn Valley G5175 B/1983/AUS strain. The only strain of genogroup GI belonged to genotype GI.4.

The results revealed significant contribution of NoV genotype GII.4 in acute viral gastroenteritis among children in Minsk City.

SEROPREVALENCE AND DETERMINANTS OF CYTOMEGALOVIRUS ANTIBODIES DURING A TWO YEAR PERIOD (2007-2009) IN A PEDIATRIC HOSPITAL**K. Papavasileiou**, G. Kuriakopoulou, I. Varzakakos, K. Kalimerantzi, A. Voyatzi, E. Papavasileiou*Clinical Microbiology, Penteli Childrens Hospital, Athens, Greece***Aim:** The aim of this study is to determine the frequency of infection and the seroprevalence of CMV among children.**Methods:** From Nov 2007-Oct 2009 980 children aged 1-14 years were examined for CMV antibodies. They were either hospitalized or attended our outpatient clinic, presenting clinical symptoms of the infection. A pair of sera was collected from each patient during a 2 weeks period. All sera were tested for the presence of specific IgM, IgG antibodies using an enzyme-linked immunosorbent assay ELISA (AxSYM Abbott). The presence of both IgM, IgG antibodies or the quadruple title of the IgG antibodies at the 2nd sample was considered diagnostic of infection.**Results:** Out of 980 children tested for CMV antibodies, 53% (520) were found to be seronegative, while 47% (460) seropositive. Diagnosis of CMV infection was made in 232(50,4%): presenting 139(59,9%) initially specific IgM antibodies, 73(31,5%) both IgG and IgM, while 20(8,6%) only IgG with a quadruple title on the second sample. The rest 228(49,6%) children presented low titles of IgG antibodies in both samples. No significant difference was found between sexes. Epidemiological factors such as socio-economic status, day care centres attendance, or crowded living conditions were not associated with CMV seropositivity.**Conclusions:** This study showed that CMV infection among children is not rare. Due to the severe complications in infants the rapid and correct diagnosis of CMV infection is very important to advocate the right therapy and proper management of the case.

THE PREVALENCE OF HBV AND HCV AMONG STREET CHILDREN, TEHRAN, IRAN

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Introduction: Nowadays the issue of street children is one of the most important issues of societies from industrial city to developing cities.

Material and methods: 203 street children picked up from different places of Tehran and settled at welfare center, where provides shelter for street children, were chosen for this study. These children were clinically examined by pediatrician. In order to determine the existence of *Hepatitis B Virus* (HBV) and *Hepatitis C Virus* (HCV) infections, ELISA, PCR and RT-PCR methods were performed on serum samples.

Results: Among 203 street children, 196 children were boys and 7 children were girls. 6 cases (3%) were HBsAg positive, 54 cases were HBsAb positive (26.6%) and 16 cases were HBcAb positive (8%). 7 cases (3.5%) were HCV Ab positive. In HCV Ab positive cases there were 5 Iranian and 1 Afghanian kids. 3 children did not have family, 6 children did not smoke and one of them was addicted to crack and had tattoo on his body. The average age of this group in 3 cases was 14 > and in 4 cases 14 < years. 4 cases were HBV PCR positive and 6 cases were HCV RT-PCR positive.

Conclusion: According to this results, additional laboratory examination for screening of acquired infectious disease such as *Hepatitis* seem to be necessary. Although in this type of infection clinical symptom may appear a few months after exposure to the virus, it can be transmissible in this latent period.

CHARACTERIZATION AND CLASSIFICATION OF VP6 GENES FROM ROTAVIRUS STRAINS CIRCULATING IN PUNE, WESTERN INDIA DURING 2004-2007

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Background and aims: Rotaviruses are classified into seven groups (A-G) on the basis of major capsid protein VP6, and hence, VP6 gene is the primary target for molecular diagnosis of group A rotaviruses.

A study was carried out to characterize VP6 genes from rotavirus strains circulating in Pune, western India during 2004-2007.

Methods: Nearly full length VP6 genes from common (n=12, G1[8], G2P[4], G9P[8]) and reassortant (n=11, G1P[4], G1P[6], G2P[6], G2P[8], G2P[10], G4P[4], G9P[4], G9P[6], G10P[6], G9,G2P[8], G12P[4]P[8]) rotavirus strains recovered from children hospitalized for diarrhea were amplified by RT-PCR and sequenced. A phylogenetic dendrogram was constructed with nucleic acid sequences by neighbor-joining method and genetic distances were calculated using Kimura-2-correction parameter.

Results: Majority of strains (n=21) showed highest nucleotide identity (91-99%) with human rotaviruses. Only two strains shared 96-98% nucleotide identity with Indian porcine rotavirus HP140 (G6P[13]). Though a divergence of 0.1-21.4% was noted within the group (n=23), genes from reassortant rotavirus strains differed from that of the common strains by 0% - 8.1% at nucleotide level.

VP6 genes of the strains with types P[8] and P[4] in combination with either of the types G1, G2 or G9 clustered into genotype I 1 (Subgroup II) and I 2 (Subgroup I) lineages respectively, while those of G1P[6], G2P[6] and G9P[6] clustered with genotype either I 1 (Subgroup II) or I 2 (Subgroup I) lineages.

Conclusions: This data is useful to understand the diversity in VP6 genes of rotavirus strains from India and in the development of newer molecular diagnostic assays.

A(H1N1)V INFECTION IN PEDIATRIC SUBJECTS: INSIGHTS FROM A REGIONAL REFERENCE CENTER IN ITALY

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Background and aims: On 11th June 2009 the World Health Organization announced the start of the influenza A(H1N1) pandemic. The department of Public Health of the University of Parma is the regional coordination centre for the pandemic surveillance. This study reports data concerning incident cases over a six-month period focusing on the clinical features of paediatric cases.

Methods: Notification files of suspected cases were retrospectively analyzed. From April 2009 until September 2009, a total of 542 cases were notified, 242 of them \leq 18 year-old: 29.3% were positive for virus A(H1N1)v. Personal data (age/sex/nationality) as well as clinical features were explored. Continuous variables were analysed using t-Student test and categorical ones with χ -square test and calculation of RR and 95%CI.

Results: Paediatric cases had a not significantly shorter symptoms' duration (2.6 ± 4.3 days vs 3.6 ± 5.3 days, $p = ns$) than adult cases. Actually, A(H1N1)v+ cases were associated with headache (RR=2.1;95%CI=1.5-3.0), arthralgia (RR 2.0 95%CI1.4-2.9), myalgia (RR=2.3;95%CI1.7-3.3) and dry cough (RR=2.8;95%CI=1.9-4.0). On the contrary, they were at a lower risk of vomit (RR=0.3;95%CI=0.1-0.8). In contrast with adults, body temperature $\geq 38^{\circ}\text{C}$ was not significantly related to A(H1N1)v+ status.

Conclusions: The not significant association between fever and A(H1N1)v+ status could be explained by the clinician's higher degree of suspicion for influenza in pediatric subjects with high body temperature, with a higher number of improperly notified cases. Actually, our results suggests that fever by itself appears as a not significant sign for diagnosis of pediatric influenza.

VENOUS THROMBOSIS IN CYTOMEGALOVIRUS CONGENITAL INFECTION: A CASE REPORT**E.M. Ruga¹, E. Rizzardi²**

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Background and aims: An increasing evidence suggests that infections may play a role in atherosclerosis and thrombosis. Cytomegalovirus (CMV) can be found in vein or arterial walls, which present a site of latency for the virus. CMV induced thrombosis have been usually reported in immunocompromised patients. Few cases of venous thrombosis were reported in acutely infected immunocompetent adults and only one case in congenitally infected neonate.

Methods: To present a case report of a CMV congenitally infected patient with severe bacterial pneumonia that was complicated by deep venous thrombosis.

Results: A 4 year old boy CMV congenitally infected was hospitalized with a three day history of fever, productive cough and dyspnea. A chest radiograph showed total opacity of the left lung. *Klebsiella pneumoniae* grew from bronchoalveolar lavage fluid.

Four and fifteen days after admission he developed a marked edema with pain at the left arm and the right leg respectively. A vascular access had been placed three and four days before in both limbs. Doppler ultrasonography revealed a severe thrombosis in the left subclavian and axillary veins and an almost completely occlusive thrombosis in the common femoral vein. A coagulation screen performed before introduction of heparin therapy was negative. Antinuclear antibodies were negative and complement was normal. Factor V Leiden heterozygous mutation was found.

Conclusion: Our case report emphasizes the involvement of CMV induction of vascular thrombosis in patients with predisposing risk factors for thrombosis and suggests that a complete coagulation screen should be performed in CMV congenitally infected children.

PREVALENCE OF ADENOVIRUSES 40 AND 41 IN CHILDREN FEWER THAN 5 YEARS SUFFERING FROM ACUTE GASTROENTERITIS

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Introduction and objectives: Gastroenteritis, the inflammation of stomach and intestine is caused by variety of microorganisms including viruses. Especially adenoviruses type 40 and 41 of group F adenoviruses are 2 etiologies of gastroenteritis in newborns and infants of lower than 5 years old. The aim of this study was determination of prevalence of ad40 and Ad41 gastroenteritis in children hospitalized in Ahvaz Abuzar Hospital, Iran.

Materials and Methods: Fecal samples collected from the patients were tested first by an ELISA kit specific for adenovirus detection. All samples including positive specimens by ELISA method were subjected to 2 rounds of PCR test. Specific pair of primers for adenoviruses 40 and 41 was applied in PCR method.

Results: Out of 280 fecal specimens collected from diarrheic children, 7 (2.5%) were positive by ELISA test and 12 (4.3%) by PCR method. All of positive samples belonged to ad41.

Conclusion: From group F of adenoviruses, adenovirus 41 is the major etiology of gastroenteritis in Ahvaz area.

AUTOIMMUNE HEMOLYTIC ANEMIA: A SEVERE COMPLICATION OF EPSTEIN-BARR VIRUS INFECTION

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Background: Infection with Epstein-Barr virus (EBV) is common and frequently asymptomatic in small children. Autoimmune hemolytic anemia occurs in 0,5-3% of the patients.

Case report: An 8-month-old infant was admitted with fever since the day before. Physical examination revealed irritability, pallor and jaundice. Laboratory findings on admission: haemoglobin 3,1g/dL, white blood cell count (WBC) 29020/mm³ (35.8% neutrophils, 57.3% lymphocytes), platelets 310.000/mm³, total bilirubin 54,9 mg/L, direct bilirubin 6,5 mg/L, AST 102 U/L, ALT 24 U/L, LDH 1132 U/L, CRP 85,6 mg/L. Coagulation studies were normal. Abdominal ultrasound showed hepatosplenomegaly. There was clinical and laboratorial deterioration in the first 48 hours with elevation of WBC 62620/mm³ and LDH 2099 U/L. Autoimmune hemolytic anemia was confirmed by increased reticulocyte count and positive Coombs test. Bone marrow cytology showed marked erythroid hyperplasia. Positive EBV DNA (4,0x10⁵ copies/ml) revealed acute infection, specific EBV antibodies were negative. Acute infections by CMV, *Parvovirus B19*, *Mycoplasma pneumoniae* and *Chlamydia pneumoniae* were excluded. Treatment with glucocorticoids, RBC transfusion and IV immunoglobulin was administered, with gradual clinical improvement and haemoglobin raise to 9,7g/dL one week later.

Conclusions: In this case faced with severe haemolytic anemia and leukocytosis, after exclusion of neoplastic etiology, the diagnosis of autoimmune haemolytic anemia associated with acute EBV infection was confirmed.

Leukocytosis can be justified by the presence of circulating erithroblasts (automatically counted as WBC) and by corticosteroid therapy. Follow-up is necessary by the risk of lymphoproliferative disorders associated with this kind of haematological complications, which can appear in the 2nd decade of life.

FOCAL EPITHELIAL HYPERPLASIA: A REPORT OF TWO CASES OF HPV 13 DETECTED IN GUYANA

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Introduction: Focal epithelial hyperplasia (FEH) is a rare disease of the oral mucosa associated with the human papillomavirus (HPV). It affects mostly children and young adults, is chronic and is usually self-limited. FEH is characterized by multiple well-circumscribed papulo-nodular, soft, painless lesions on the mucosal epithelium of the lips and tongue. To date, there have been no published cases of FEH in Guyana. This study describes two cases of confirmed FEH from Amerindian communities in the Rupununi region of Guyana.

Methods: Children age 3-18 were screened for cutaneous lesions through physical examination at mobile medical clinics in southern Guyana. Initial diagnosis of FEH was based on the above clinical presentation. In two patients, intra-oral lesions were swabbed using Starswab Multitrans collection and transport system (Starplex Scientific Co., Etobicoke, Canada). The Linear Array HPV Genotyping Test (Roche) was used as well as specific primers for HPV 13 for DNA analysis.

Results: FEH was observed clinically by our group in 9 of 606 (1.5%) children aged 3-18. Swabs from lesions in two patients and subsequent DNA PCR analysis showed HPV 13 was present in both patients. Based on the clinical picture and DNA studies, both of these patients were diagnosed with FEH.

Conclusions: This is the first study to report FEH in Guyana. Given the concentration of disease previously reported within certain ethnic groups as well as in multiple family members, evaluation of a genetic predisposition and/or common environmental factors in the pathogenesis of FEH is warranted.

PANDEMIC INFLUENZA INFECTIONS IN HOSPITALIZED PEDIATRIC ONCOLOGY PATIENTSY. Mordish¹, I. Levy^{1,2}, E. Kazmirsky¹, S. Fischer³, I. Yaniv^{2,3}, I. Shalit^{1,2}

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Background and aims: Oncology patients are considered at higher risk for pandemic H1N1 influenza infections (PII). We studied all patients hospitalized with PII at our Pediatric Oncology Institute (POI).

Methods: Clinical, demographic, laboratory, imaging data and outcome were collected for POI in-patients diagnosed by PCR with PII between 1/8/09-30/11/09.

Results: Overall, 35/240 patients treated in our POI were hospitalized with PII (14.5%; M/F 60/40). Peak hospitalization occurred at weeks 45-46. Peak age was 5-10y (63%). Hematological malignancies were the underlying disease in 27/35 (77%) compared to 77/240 (32%) in the entire cohort ($p < 0.001$). Clinical presentation included fever (91%), cough (71%), rhinorrhea (71%), pharyngitis (11%) and hypotension (3%). Only six patients (17%) had neutropenia ($ANC < 500$). Chest X-ray was normal in 48%. Alveolar infiltrates were found in 20%. CRP was normal in 48% and mildly elevated ($>0.5-5$) in 41%. LFT's were mildly elevated in 18 patients and creatinin was normal in all. Co-infections were detected in 5 patients. Time to defervescence was $< 2d$ in 68%, 3-5d in 23% and $>5d$ in 9%. One patient required assisted ventilation for 3d and recovered. Three patients developed a relapse with repeated positive PCR. All recovered uneventfully. AEs to oseltamivir included hallucinations (1) and diarrhea (2).

Conclusions: H1N1 in pediatric oncology patients was more prevalent in patients with hematological malignancies. Despite being a high risk group, the disease was mild with rapid recovery in the large majority of patients. Co-infections may occur and physicians should be aware of the possibility of H1N1 re-infection.

CLINICAL PRESENTATION OF NOVEL INFLUENZA A (H1N1) IN HOSPITALIZED CHILDREN ZAHEDAN, IRAN

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Background: Human pandemic Influenza H1N1 virus as the cause of febrile respiratory infection ranging from self-limited to severe illness has spread globally during 2009.

Signs and symptoms of upper & lower respiratory tract involvement, fever, sore throat, rhinitis, myalgia, malaise, headache, chills and fatigue are common.

Methods: Between September and October 2009, all children requiring hospitalization for confirmed or suspected H1N1 infection were transferred to Pediatrics' Infectious Diseases ward. For all patients the throat swab set up for PCR testing to confirm or exclude the diagnosis of H1N1 Influenza A.

Case patients were identified through the H1N1-positive patients. Age, sex, symptoms, signs, laboratory data, CXR changes, details of therapy, duration of admission and patient outcome were documented.

Results: Thirteen patients was H1N1 positive. Mean age of patients was 70.31 ± 53.39 months. Fever & coughs were the most commonly reported symptoms (53.8%). Other presentation included vomiting (46.2%), abdominal pain (23%), cyanosis & dyspeina (7.7%), Bodyache (30%), rhinorrhea (76.9%), Sore throat (38.5%), head stiffness (aseptic meningitis) (7.7%) and loss of conciseness (7.7%).

The mean temperature of our patients was 38.50 ± 0.80 °C. CXR changes were noted in 8 out of 13 patients (61.5%).

Mean leukocyte & palette were 7092.31 (2600-17900) & 185920 (70000-329000) respectively.

Twelve patients were treated with Oseltamivir, 2 patients had adjuvant antibiotics. The mean duration of admission was 3.9 days , except tow patients required intensive care support that both of them expired due to super infection.

Conclusion: Our data shows confirm that the presentation of influenza in children is variable.

CLINICAL AND EPIDEMIOLOGICAL CHARACTERISTICS OF PEDIATRIC PANDEMIC INFLUENZA A(H1N1) PATIENTS HOSPITALIZED IN ISTANBUL, TURKEY

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Background: The aim was to describe the clinical and epidemiologic characteristics of patients, who were admitted to the Pediatric Infectious Diseases Wards in Istanbul due to influenza A (H1N1) infection between 26 October and 26 November, 2009.

Methods: 114 patients with suspected pandemic influenza (H1N1)v infection were hospitalized, and nasal swabs were sent to National Influenza Reference Laboratory for confirmation of pandemic influenza A (H1N1)v infection by real-time rRT-PCR assay. Patient's data recorded from the day of hospitalization until discharge were evaluated.

Results: Forty-six (40%) female and 68 (60%) male patients were included to the study. Age of the patients ranged from 40 days to 16 years. Eighty-four patients had pneumonia, 16 had asthma attacks, two patients were epileptic and one patient had hepatitis at the time of admission. Sixteen patients required mechanical ventilation due to hypoxemia. Fifty patients (44%) were previously healthy children. Clinical and/or radiological pneumonia were detected in 96% of all patients. Previously healthy children required mechanical ventilation and oxygen therapy more than patients with chronic diseases. Pneumonic infiltrations were predominantly basal and bilateral with patchy alveolar opacities. Laboratory blood tests revealed that patients had elevated levels of CRP, 65%, LDH, 53%, creatinine kinase, 19%, and 30% were lymphopenic. Elevated levels of CRP and LDH in patients with respiratory distress and patients who required mechanical ventilation were statistically significant.

Conclusion: Our study showed that progress of pandemic influenza (H1N1)v infection in previously healthy children is as severe as their counterparts with chronic underlying diseases.

USAGE OF CYTOMEGALOVIRUS (CMV) ANTIGENEMIA ASSAY AND CMV PCR IN DIAGNOSIS OF CMV INFECTIONS IN PATIENTS WITH CONGENITAL IMMUNODEFFICIENCIES**A. Soysal¹, C. Kuzdan¹, E. Şenay¹, I. Barlan², M. Bakır¹***¹Pediatric Infectious Diseases, ²Pediatric Allergy-Immunology, Marmara University, Istanbul, Turkey*

CMV infection remains as an important cause of morbidity and mortality in children with immunodeficiencies. Here we reported performance of CMV antigenemia and CMV PCR assays in the diagnosis of CMV infections and effect of gancyclovir treatment on both assays results in children with congenital immunodeficiencies. A total of 8 children of whom 4 diagnosed as severe combined immunodeficiency, 2 as common variable immunodeficiency and 2 as other primary immunodeficiencies those whom age ranging between 6 to 120 months were involved. CMV pneumoniae were diagnosed in 7 children and CMV gastrointestinal disease -arthritis in 1 children. All children received either gancyclovir or gancyclovir plus intravenous immunoglobulin. CMV antigenemia were positive in 7 (87.5%) children and CMV PCR were positive in 5 (62.5%) children. Among CMV PCR negative 3 patients CMV antigenemia were positive and among CMV antigenemia negative 1 patients CMV PCR were positive. After gancyclovir treatment CMV antigenemia become negative in 4 patients and CMV PCR become negative in 3 patients (Table 1). Among 8 patients 5 were improved with gancyclovir treatment and 3 died. As conclusion we believed that usage of both CMV antigenemia and CMV PCR may help early diagnosis CMV infections especially in high risk patients. Also monitoring of CMV antigenemia and PCR may be used for follow-up of antiviral treatment.

CLINICAL EVALUATION OF CHILDREN WITH NOVEL INFLUENZA A (H1N1) VIRUS AT A UNIVERSITY HOSPITAL IN TURKEY

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Background and aims: To describe the primary experience of our pediatric department from Oct 20, 2009 to Dec 31, 2009 during the novel influenza A(H1N1) pandemic in Turkey.

Methods: Children with the diagnosis of influenza A (H1N1) confirmed by real-time reverse-transcriptase-polymerase-chain-reaction (RT-PCR) testing were analyzed retrospectively.

Results: There were 47 outpatient and 46 inpatient confirmed cases at our clinic during that period. Their median age were 85.9 (1-204) months and 48 (57.8%) were male. Fifty two (62.6%) of them had underlying conditions where as 31 (43.5%) children were otherwise healthy. Pneumonia was the leading cause of hospitalization existing in 36 children. Myositis (n=5), encephalopathy (n=2), sepsis (n=1), thrombocytopenia (n=1) and accelerated idioventricular rhythm (n=1) were the other complications. 4 (4.8%) patients were admitted to pediatric intensive care unit and 1 (1.2%) died because of acute respiratory distress syndrome and bacterial superinfection.

Conclusions: Complications of novel influenza A (H1N1) that require hospitalization are various and may be seen even in healthy children.

LONGITUDINAL FOLLOW-UP OF 2 YEARS OF NEW BORN CHILDREN FROM MOTHERS HEPATITIS C VIRUS POSITIVE (HCV+)

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Background: HCV in children is mainly acquired via maternal transmission. The aim of the study was to follow the clinical and biological evolution of these children from birth to 2 years old.

Methods: Mothers HCV-infected or HIV/HCV co-infected were included in a prospective study during 4 years in public hospitals in Southern France. Recorded data included mother's virological status, circumstances of the delivery and children characteristics with their virological and biological data (birth, M3, M6, M12, M18 and M24).

Results: Among 262 mother-and-child pair with a partial (48) or total follow-up (214), 59 mothers were HIV/HCV co-infected (23%) and 12 children had circulating HCV-RNA at birth. None of children was infected by HIV. Between birth and M3, the median level of ALT was not different for the 262 children. Compared to non-infected children, significantly increased ALT median values (as times the upper limit of normal) were observed after M3 and especially at M6: 2.53 [1.07-6.04] versus 0.54 [0.61-0.97], $p=0.003$. For 3 of the 12 infected children (25%) HCV-RNA levels became negative and their ALT returned to normal (M3: 2.39; M6: 1.85; M12: 4.10; M18: 0.70; M24: 0.53) between M18 and M24. ALT level of 9 children remained high: (M3: 1.48; M 6: 3.40; M12: 1.67; M18: 1.20; M24: 1.43). No mother or child factor was found to explain ARN VHC clearance.

Conclusions: After HCV maternal transmission, a clearance of HCV-RNA is possible after M18. High level of ALT at M6 and especially after M18 is correlated to HCV infection.

H1N1 INFLUENZA VIRUS INFECTION IN CHILDREN IN A TERTIARY HOSPITAL IN CRETE

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Background and aims: To study the epidemiological and clinical picture of children with confirmed H1N1 infection in Crete.

Methods: Clinical and epidemiological profile of children that visited the emergency department of a tertiary hospital during the enhanced surveillance and the pandemic period is retrospectively analyzed. H1N1 infection was confirmed by real-time-RT-PCR-assay from nasopharyngeal specimens.

Results: From July through December 2009, 102 children were identified with H1N1 infection, of which 20(19%) needed hospitalization. The median age of the overall population was 9 years (range 33 days to 14 years), whereas the median age of the hospitalized children was 2,5 years (range 33 days to 10,5 years). The median duration of the disease was 5 days (range 1,5 to 10). The most common symptoms were fever (96%; median temperature 39,3°C) and cough (89%). Fifty-two percent presented with soar throat and 13% with vomiting and/or diarrhea. Half of patients reported contact with confirmed H1N1 infection and 13% had an underlying cardiovascular or respiratory disease. Treatment with oseltamivir was prescribed to 8.5% of patients; antibiotic-treatment was provided to 25% for secondary bacterial-airway-infection. Among hospitalized children, 35% had pneumonia, 10% bronchitis or bronchiolitis, 20% febrile-seizures and 20% febrile-illness, 10% upper respiratory airway disease and 5% gastroenteritis. All patients recovered from the disease and none required transfer to the intensive care unit.

Conclusions: School-aged children were most commonly infected with H1N1 but younger children required hospitalization. The outcome of the disease was optimal in all children with H1N1 infection. Treatment with oseltamivir was limited.

INCIDENCE AND CLINICAL DATA OF RSV INFECTION IN CHILDREN WITH CANCER

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Introduction: RSV is an important cause of respiratory disease in the immunocompromised children with cancer.

Objectives: The purpose of our study is to investigate the role of RSV in respiratory infections in children with cancer compared to otherwise healthy ones (controls).

Material and methods: We reviewed the records of 139 respiratory tract infections in 84 children with cancer during chemotherapy versus 132 respiratory tract infections in 132 controls. The survey was carried out between January 2007 and December 2008. Pharyngeal swab was obtained from each child. RSV was isolated by PCR.

Results: The median age of children with cancer was 5 years and 87,1% suffered from hematological malignancies, while of controls was 2,5 years. The male/female ratio was 2,1/1 in cancer patients and 1/1,1 in controls. Upper respiratory infections occurred more frequently among children with malignancies (91,6%), while lower respiratory infections among controls (94,7%). RSV was detected in 8,6% of children with cancer (RSV-A type 5,8% and RSV-B type 2,9%), and in 14,5% of controls (RSV-A type 8,4%, RSV-B type 5,3%, RSV-A and RSV-B type 1,5%). Most infections were mild in both groups (80,6%). No death was recorded. Dual infections were detected only in controls (16,1%). RSV infections were significantly associated with spring ($p=0,04$). Age ≤ 2 years was significantly ($p=0,04$) and lymphopenia ($< 1.400/mm^3$) marginally significant associated with RSV infections in cancer patients.

Conclusions: Most RSV infections in children with cancer are mild upper respiratory infections, which occur at a younger age and are related with a low lymphocyte count.

SEVERE GUILLAIN-BARRÉ SYNDROME IN A 3 MONTH-OLD INFANT ASSOCIATED WITH 2009 H1N1 INFLUENZA VIRUS

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Aims: The majority of children with pandemic H1N1 influenza experience mild illness with full recovery without treatment. Guillain-Barré syndrome has not been described associated with H1N1.

Methods: Case report.

Results: A 2,5 month old baby girl, previously healthy, was admitted to another hospital in respiratory distress with a previous 5-day history of lethargy and moaning. Chest radiography showed bilateral infiltrates. Detection of H1N1 virus was positive and all other etiologic investigations were negative. She was transferred to our PICU with the diagnosis of H1N1 infection with respiratory failure, mechanically ventilated. Therapy with oseltamivir and antibiotics was started. Attempts made to extubate to non-invasive ventilation were unsuccessful despite normal chest radiological findings and fiberoptic bronchoscopy excluding airway malacia or obstruction. Episodes of cardiovascular instability were noted since day 7 as also as a progressive neurological deterioration after day 20 with marked hypotonia and absent deep tendon reflexes. Brain MRI and ophthalmic examination were unremarkable. Extensive neuro-metabolic investigation excluded inborn errors of metabolism and mitochondrial disorders. CSF examination demonstrated an albumino-cytologic dissociation: proteins 72 mg/dL and WBC 2/mm³. Nerve conduction studies showed no motor responses and absent sensory potential compatible with axonal form of Guillain-Barré Syndrome. Intravenous immunoglobulin (1g/kg/day) was administered with no clinical improvement. At day 81 the child had a tracheotomy and is still dependent on ventilatory support despite a slight improvement of the neurological status.

Conclusions: To our knowledge this is the youngest case of GBS acquired postnatally and the first associated with the novel H1N1 virus.

CHRONIC ENTEROVIRUS MENINGOENCEPHALITIS IN A BOY WITH X-LINKED AGAMMAGLOBULINEMIA; EVIDENCE FOR PLECONARIL AS EFFECTIVE TREATMENT

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Background and aims: Chronic enteroviral meningitis is a condition with extensive morbidity and high fatality rate in patients with X-linked agammaglobulinemia (XLA). Treatment options consist of intravenous immunoglobulin (IVIG) with various outcome.

An alternative treatment is the antiviral drug pleconaril with *in vitro* activity against enteroviruses. Effectivity of pleconaril in patients with CEMA has been described previously but only in a very small number of patients and always in combination with IVIG.

We treated a boy with chronic echovirus 13 meningoencephalitis and progressive neurologic symptoms with IVIG and pleconaril. To determine the effectivity of both pleconaril and IVIG we tested their *in vitro* activity.

Methods: In the two IVIG batches the patient received, the presence of neutralizing antibodies against the echovirus 13 of the patient and some control strains was tested by virus-neutralization assay. The 50% inhibitory concentration (IC₅₀) of pleconaril against the echovirus 13 of the patient was determined.

Results: *In vitro*, IVIG did not contain neutralizing antibodies against echovirus 13 while the strain was highly susceptible to pleconaril. In accordance, the boy had not improved after several gifts of IVIG, but 6 weeks after treatment with pleconaril the enterovirus PCR became undetectable in CSF and the boy recovered completely.

Conclusions: Our *in vitro* data show that in this patient pleconaril is the only active compound. These results suggest that pleconaril is important in the treatment of chronic enterovirus infections.

H1N1 VIRUS-ASSOCIATED RHABDOMYOLYSIS IN TAIWANESE CHILDREN**C.-T. Wu¹, J.-L. Huang²**

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Aim: H1N1-associated rhabdomyolysis is an infrequent and little-known complication of H1N1 virus infection in children. Diagnosis is made based on clinical presentation, the presence of laboratory data, and detection of virus. The aim of this study was to describe the clinical and laboratory manifestations, complications, and outcomes of H1N1 virus-associated rhabdomyolysis in Taiwanese children.

Methods: A retrospective analysis was conducted of patients aged < 17 years who had been diagnosed with H1N1 virus-associated rhabdomyolysis at a university children's hospital in North Taiwan during 2009. All children enrolled in the study had presented with rhabdomyolysis associated with laboratory-confirmed H1N1 virus infections. Demographic data, clinical manifestations, complications, and outcomes were included in the analysis.

Results: Overall, 4 H1N1 virus-associated rhabdomyolysis cases were analyzed. It occurred in young aged children with a 3:1 male: female ratio. The mean age was 3.2 ±1.9 yr. The median interval between the onset of H1N1 virus infection and onset of rhabdomyolysis was 3.4 days (range, 1-6). Laboratory tests indicated a mean initial blood creatine kinase (CK) of 7458 U/L. The median time to clinical recovery was 16 days (range 8-24). All patients had renal failure initially, and they all improved later and survived after dialysis. H1N1 virus-associated rhabdomyolysis tends to occur mainly in young children. This virus can induce some complications including death. So early detection and careful medical treatment with Tamiflu are necessary.

Conclusion: The results of this study indicate that outcomes of H1N1 virus-associated rhabdomyolysis are good with proper medical care.

NEUROBRUCCELLOSIS IN CHILDHOOD: FOUR NEW CASES AND A REVIEW OF THE LITERATURE

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Aim: Neurobrucellosis accounts for < 1% of cases of brucellosis in children . we describe our experience regarding the epidemiological, clinical, laboratory and therapeutic findings in four children with neurobrucellosis.

Patients & methods: During the past nine years we treated four children with neurobrucellosis in the Islamic Hospital (Amman_Jordan). Diagnosis was based on:epidemiological data, clinical manifestations, serum & cerebrospinal fluid (CSF) serology, quantitative changes in C.S.F and favorable response to treatment. Therapy consisted of combinations of two or three of the following drugs for three months: rifampin, gentamycin, streptomycin and trimethoprim-sulfamethoxazole.

Results: All patients had a history of exposure to a source of brucellosis. The mean age of children was 7.2 years, and the male: female ratio 3:1. The clinical signs were heterogeneous with high grade fever, vomiting, neck stiffness & seizures Neurologic signs appeared during the active phase in two patients and later in other two patients. The interval from onset of symptoms to diagnosis was from 3 days to 5 months.

CSF revealed lymphocytic pleocytosis (500 - 2160/ μ l), in all patients, high protein concentration in three and low glucose concentration in two patients. Reciprocal brucella agglutination titers were significantly elevated in serum (\geq 160) and in CSF (\geq 80) of all patients. *Brucella melitensis* was isolated both from blood and CSF in one patient, from blood only in two. No mortality, relapses or morbidity were noted in our patients after 12 months.

Conclusion: We suggest that neurobrucellosis should be considered when neurological manifestations ensue with unknown etiology in endemic areas.

SEROPREVALANCE RATE OF TOXOCARIASIS (TOXOCARACANIS INFECTION) IN PRIMARY SCHOOL CHILDREN OF URBAN & RURAL AREA IN AHVAZ, IRAN, 2008-2009**S.M. Alavi¹, S.A. Hussein²***¹Infectious Diseases, Joundishapour Infectious and Tropical Diseases Research Center, ²Infectious Diseases, Joundishapour University of Medical Sciences, Ahvaz, Iran*

Introduction: Toxocariasis is a worldwide zoonosis. Seroprevalance of toxocariasis vary with geographic regions. In this study, the sera of school children aged between 6 to 15 years were examined for the presence of anti T. canis antibodies.

Methodology: In this descriptive cross-sectional study the sera of 203 school children aged between 6 to 15 years from urban and rural regions in Ahwaz, south western of Iran was examined by means of ELISA with excretory- secretory antigen of infectious larva stage. CBC was performed for the presence of eosinophilia or hypereosinophilia. A short questionnaire interview was conducted to obtain data concerning their age, sex, history of pica, contact with dogs and living area (urban or rural).

Results: Of 203 students 90 (44.3%) were female and 113 (55.7%) were male. 86 (42.9%) were rural and 114 (57.1%) were urban, 67 (33%) had contact with dogs, 35 (17%) had history of recent cough, 5 (2.5%) had pica, non had hypereosinophilia but 21 (10.3%) had eosinophilia, 4 (2%) had positive ELISA for T.canis IgG, of them one was male and three were female, two were urban and two were rural, non had history of contact with dogs, pica, chronic cough or asthma, and also non had hypereosinophilia but all had eosinophilia.

Conclusion: Our study showed that toxocariasis in the school children of Ahwaz is lower than was expected and also lower than similar tropical regions.

**VISCERAL LEISHMANIASIS: A COMMON CAUSE OF PANCYTOPENIA IN CHILDREN:
EXPERIENCE OF A TERTIARY CHILDREN'S HOSPITAL**

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Visceral leishmaniasis (kala-azar) is caused by *Leishmania* spp, a parasite which is prevalent in Mediterranean countries. Leishmaniasis usually presents with fever, hepatosplenomegaly, lymphadenopathy and pancytopenia.

The aim of the study was to examine the possible causes of multiple cytopenia in children with febrile illness and to investigate the association of acquired pancytopenias with parasitic infections.

Material-methods: We studied 117 children, 4.0 ± 3.8 y old (range:0-14), who were admitted to a Pediatric Ward because of febrile cytopenia during a 2y period and were investigated with acute phase reactants, cultures of body fluids, and serological tests. All patients had a bone marrow aspiration.

Results: Of all patients pancytopenia was detected in 9/117 (7.7%) (5 males, 4 females), with a mean \pm SD age of 4.5 ± 3.0 years. The mean \pm SD values of WBC was 3827 ± 1455 /ml, ANC: 1229 ± 655 /ml, Hb: 8.3 ± 1.1 gr/dl and the mean \pm SD platelet count was 88200 ± 20186 /ml. All had fever (mean duration: 8.9 ± 8.7 days) (Tmax: $39.5\pm 0.6^\circ\text{C}$) and remarkable hepatosplenomegaly (9/9) while 2/9 had lymphadenopathy. In all nine children leishmania was detected in bone marrow examination. All patients were treated with liposomal Amphotericin B and had an excellent response rate. Pancytopenia resolved within a mean \pm SD of 17.6 ± 17.3 days (range 8-60d) and there was no relapse in two years' follow-up.

Conclusion: Children with febrile pancytopenia should be examined for all possible causes including malignancies. In Mediterranean countries leishmaniasis is the most common cause of febrile pancytopenia in otherwise healthy children. Nevertheless, a thorough examination must always be performed.

**MALARIA PROPHYLAXIS IN CHILDREN TRAVELLING TO THEIR PARENT'S HOME COUNTRY:
A SURVEY**E. Venturini, **E. Chiappini**, L. Galli, M. de Martino*University of Florence, Florence, Italy*

In industrial countries malaria is the most important cause of fever in travelers arriving from endemic areas. Children account for around 15-20% of all imported malaria cases. In previous reports, over 60% of travellers to endemic areas were reported to take no malaria prophylaxis (1). We carried out a survey on a sample of immigrated parents. A questionnaire was administered to parents of children consecutively referring to the Infectious Disease Unit, Department of Paediatrics, Florence, between August 1st, 2009 and November 1st, 2009. Overall, 101 questionnaires were collected. Median children's age was 4 years (interquartile range [IQR]:1-8), 51 (50.49%) were males. Seventy-eight children (77.23%) were born in Italy. The parents' origin continent were Asia (67; 66.34%), Africa (33; 32.67%) and South America (1; 0.99%). Seventy two children (71.29%) had travelled to their parent's home country (median stay duration: 1.75 months; IQR:1-2.5); 28 children (38.98%) had resided in a rural area. Ten children (13.89%) had received pharmacological malaria prophylaxis, the mostly used drug being mefloquine (8; 80%). Side effects to the drug were reported in 3 cases (30%). Seventy seven per cent of parents were aware of malaria risk in their native country. While abroad, 9 parents (8.91%) and one child (0.99%) had developed malaria. Our data highlight the need for educational actions in Italy about malaria prophylaxis, especially among immigrants.

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VISCERAL LEISHMANIASIS IN CHILDREN: A 10-YEAR EXPERIENCE IN NORTHERN GREECE

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Background and aims: Visceral leishmaniasis (VL) is endemic in the Mediterranean basin. We report cases of VL treated in two tertiary care pediatric hospitals in Thessaloniki, Northern Greece, during a 10 year period (2000-2009).

Methods: Epidemiological data, underlying diseases, clinical and laboratory findings, therapeutic interventions and clinical outcome were analyzed retrospectively.

Results: Twenty-five children (male 19), aged 6m-13yrs (median age: 2.5yrs) were identified. Two cases of VL were associated with acute lymphoblastic leukemia and one case was transmitted congenitally from mother to child. On admission, all patients presented with "prolonged fever-marked splenomegaly-anemia". Two children presented with Coombs positive hemolytic anemia. Hepatomegaly, pancytopenia and hyperglobulinaemia were found in 60-73% of patients. Bone marrow aspiration revealed intracellular parasites in 21/24 children. All children had positive IgG antibodies for *L. infantum* sp. Ten children received pentavalent antimonials (Glucantime®), 14 liposomal amphotericin B (L-AmB, Ambisome®) and one Amphotercin B lipid complex (AmB-LC, Abelcet®). Twenty-three patients had successful outcome. The single patient treated with AmB-LC experienced treatment failure, and one immunocompetent child treated with L-AmB had a relapse. They received a further course of L-AmB, with good response and no signs of relapse 1-2 years later.

Conclusion: VL is endemic in our region and therefore, especially in young children, should be included in the differential diagnosis of anemia and other blood disorders such as leukemia. The use of L-amB has proven to be safe and effective in children. In immunocompetent patients, disease relapse following L-AmB is rare and requires re-treatment.

INTENSIVE CARE ADMISSIONS FOR CHILDREN WITH IMPORTED MALARIA IN THE UNITED KINGDOM (2004-2008)

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Background and aims: Little is known about children with imported malaria diagnosed in non-endemic countries who require intensive care. This study describes the clinical presentation and management of children admitted to a paediatric intensive care unit (PICU) in the United Kingdom over a five-year period.

Methods: Data on children with malaria requiring intensive care between 2004 and 2008 were obtained from PICANET, which collects information on all children admitted to PICU in the United Kingdom (www.picanet.org.uk).

Results: Over the 5-year period, 29 children were admitted to PICU. Their median age was 4 years compared with 8 years for children with malaria who did not require intensive care. Over half the children (16/29 cases, 55%) were admitted in August, September and January and none had any other co-morbidities. Ten children (34%) had cerebral malaria, of whom 8 required mechanical ventilation and 1 required inotropic support. Four other children had severe hypotension requiring inotropic support and one other had concurrent septicaemia with enteropathogenic *Escherichia coli* and *Salmonella typhi*. The remaining 14 cases were admitted for close monitoring only. Most children (21/29, 72%) remained in PICU for ≤ 48 hours. One child developed cerebellar infarction, but none died.

Conclusions: In the UK, children with imported malaria rarely require intensive care. Of those who are admitted to PICU, a third had cerebral malaria, most of whom required mechanical ventilation. Younger children were over-represented among those admitted to PICU with malaria. While mortality remains very low, some children may develop severe long-term sequelae.

PERFORMANCE OF FOUR RAPID DIAGNOSTIC TESTS FOR DIAGNOSIS OF FALCIPARUM AND NON-FALCIPARUM MALARIA IN ENDEMIC AREAS OF GONDAR REGION

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One of the major obstacles of malaria control program in Ethiopia is the lack of accurate and rapid diagnostic tests (RDTs) in most resource poor settings where malaria is endemic. Very recently, efforts have been made to develop and implement various formats of malaria RDTs. In view of this, the performance of the OptiMAL, Paracheck, CareStart™ malaria pLDH 4 line test (CareStart 4 line) and CareStart™ malaria pLDH/HRP II combo test (CareStart 3 line) were investigated in comparison with microscopic examination blood film in malaria endemic areas of Gondar. In order to evaluate these assays the sensitivity and specificity values of each RDT were calculated in a total of 588 febrile patients. Paracheck was the most sensitive (100%) assay for the diagnosis of *P. falciparum* in comparison with OptiMAL (98.1%), CareStart 4 line (98.1%) and CareStart 3 line (96.2%). However, OptiMAL was the most specific (99.1%) as compared to Paracheck (97.9%), CareStart 3 line (96.4%) and CareStart 4 line (93.8%) for *falciparum* malaria diagnosis. For the diagnosis of *P. vivax*, both CareStart™ assays had better sensitivity (94.4% for CareStart 4 line and 94.2% for CareStart 3 line) as compared to OptiMAL 88.2%. But OptiMAL gave the higher specificity (99.8%) than CareStart 4 line (98.1%) and CareStart™ malaria pLDH/HRP II combo test (97.9%). Although microscopy remains the gold standard for malaria diagnosis, OptiMAL, Paracheck, CareStart 3 line and CareStart 4 line may prove a useful screening for malaria in Ethiopia where microscopic examination is not in place.

IMPORTED MALARIA IN CHILDREN DURING THE 9 LAST YEARS IN THE SOUTH EAST OF FRANCE

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Aim: To study epidemiological, clinical, and parasitological characteristics, as well as regimen received, of imported malaria cases in children hospitalised in Alpes Maritimes and East Var (South Est of France).

Methods: Retrospective study from 2000/01/01 to 2008/12/31 including children from 0 to 18 years old hospitalized for imported malaria. Severity of the disease is defined by the WHO criteria in 2000. Evaluation of adequacy of the treatment is based on the French Recommendations of 1999 for cases before 2008 then on the new recommendations of the SPILF from 2007.

Results: 101 children were included. Mean age was 6.2 years. 10% of them was diagnosed serious while 23 % were it according to the criteria of the WHO. All cases was acquired in Africa, specially in Comoros Islands (61%) and Ivory Coast (10%), and appeared mainly to African living in Africa (43%), Causasian (30%) and African resident in France (21%). *Plasmodium falciparum* was involved in 83% of cases (by QBC (60%), thickdrop and bloodsmear examination (20%), rapid test (30%)). 62% of children have been under prophylaxis but only 43% admit good compliance. Chemoprophylaxis was inadequate in half of cases. Halofantrine was prescribed inadequately in place of intravenous quinine in half of cases of serious disease. No death was observed.

Conclusion: Imported malaria in children is rare but not exceptional in South Est of France, Serious diseases are under estimated. A better education needs to be implemented both to practitioners and Comorian population, regarding malaria risks and prophylaxis.

ANALYSIS OF VACCINATION IN CHILDREN AGAINST TICK-BORNE ENCEPHALITIS IN THE SLOVAK REPUBLIC

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Background and aims: Analysis of vaccination coverage in children and current situation in vaccination against tick-borne encephalitis in the Slovak Republic in 1997-2008.

Methods: Group of 107 reported cases of tick-borne encephalitis from total number 849 reported cases of the disease, ICD code A84.1, registered in the Epidemiologic Information System (EPIS) and 75,269 vaccinated children from 1 to 15 years old, identified during annual administrative checks of vaccination in children, performed by the Public Health Authority. Processing by descriptive methods of statistical analysis (SPSS version 11.0, Excel).

Results: During study period 75,269 children from 1 to 15 years old were vaccinated in our country, 0.69% average vaccination coverage of the age group. The percentage of vaccinated children increases each year, in 2008 the vaccination coverage reached 1.83% of children. The age-related morbidity decreased from 1.41/100,000 in 1997 to 0.60/100,000 in 2008. In the Slovak Republic there are 2 vaccines available against the tick-borne encephalitis from Baxter and Novartis Vaccines and Diagnostics, currently they are not reimbursed from public health insurance.

Conclusions: The importance of the tick-borne encephalitis is large in relation to clinical seriousness of the disease. The active immunisation is a possible protection. The reimbursement of the vaccine is currently done through preventive programs of some healthcare insurance companies. Apollo offers vaccination free of charge till 18 years, Dôvera pays the 3rd vaccine to its clients from the first year of life and Union pays 50% of cost of each vaccine since 1.1.2010.

CHANGING PATTERNS OF TICK-BORNE ENCEPHALITIS OCCURRENCE DURING THE LAST THREE DECADES IN THE CZECH REPUBLIC

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Background and aims: TBE has been recognized in the Czech Republic (CR) since 1948 when, for the first time ever in Europe, the TBE virus was isolated from patients and *I. ricinus* ticks. In early 1990s a sharp increase in the number of registered cases occurred which remains nowadays with certain fluctuations every year.

Methods: TBE data were obtained from databases of the reporting systems EPIDAT since 1993,(and previous reporting systems prior to 1993) and analyzed.

Statistical processing was conducted by Epi-Info, Statcalc and ANOVA tests.

Results: Maximum incidence ever - 1029 cases (10,0/100 000) has been recorded in 2006. Current incidence in the year 2009 - 809 cases is suggesting that it will be the second highest. Both years were characterized by mild winter and unusually warm weather during the rest of the year. During last three decades the extension of the TBE season towards spring and autumn period is observed. Ticks infected by TBE virus have been detected at altitudes below 700 m a.s.l. in eighties, 1000 m during nineties and up to 1140m recently. Human cases get infected at 900 meters. Emergence of them in areas where never had been detected was notified in several parts of CR. Shift of the age specific incidence towards the higher age groups during the last decade is influenced by the change of life style of older population.

Conclusions: The current development of TBE occurrence is strongly influenced by changing meteorological conditions and by sport and leisure human activities.

FIRST CASE OF HUMAN SYSTEMIC INFECTION BY MORAXELLA CAPRAE, A GOAT BACTERIA

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We report the case of a 8 years old boy admitted for a 5 day persistent fever. He was otherwise at a high risk of endocarditis because of a complex congenital heart disease. This was formed by atrio-ventricular discordance and multiple inter ventricular shunts, and underwent twice surgery with implementation of materials and Dacron tubes. He also had ocular rosacea with no blepharitis, recently treated by local steroids. The fever was well tolerated, with erythema on the palms and neither septicaemia or heart failure signs. Biology showed CRP = 100mg/l and WBL= 7Giga/l. Blood cultures successively isolated a gram negative bacillus, susceptible to the tested antibiotics. The strains were identified as *moraxella caprae*, which belongs to the "*moraxella lacunata* group" and found in the nasal flora of healthy goats (Kodjo 1995). Face to this never described human infection, and regarding the rare but reported endocarditis related to *moraxella lacunata*, the identification was specified by molecular biology. In fact, the father was in contact with goats during the preceding weeks and might transmit the bacteria to his son. As regards previous association between ocular rosacea and *moraxella lacunata* infection, we could not exclude that the blood contamination occurred through the periocular lesions, despite the lack of obvious inflammation. The complete investigations did not allow determining other causal infections. The survey by echocardiography did not revealed endocardial or endomaterial vegetations and the outcome was good after a 6 weeks course of ceftriaxone.

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 intermitent diarrhea and steaturrhea which cause malabsorption are the main clinical signs.

The etiologic agent is Giardia lamblia which is found in the forms of trophozoite (pathogenic form) and cyst (infective form).

The infective form is Transmitted by water, direct contact, vegetables and flies.

Aims: In order to evaluate the efficacy of secnidazole and comparing with metronidazole, a study was undertaken over a 15 months period on 83 patients suffering from giardiasis in Emam Reza Hospital.

Methods: After the completion of a questionair for each patient, the patients were treated with secnidazole (30 mg/kg single dose) or 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.

Results: Examinations showed that secnidazole was effective in 94.4% and metronidazole was effective in 80% of infected children ($P < 0.05$).

Conclusions: Since secnidazole had milder side effects and was more effective in relation to metronidazole and it can be used in single dose, this drug can be recomend as a better drug than metronidazole for treatment of giardiasis in children.

Keywords: Giardia lamblia, Secnidazole, Metronidazole, Treatment, Side effects.

PEDIATRIC CASES OF MALARIA IN A TERTIARY HOSPITAL IN SPAIN, 2003-2009

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Background: Malaria cases continues being one of the important problems of Public Health; in spite of the fact that officially has been eradicate for more than forty years. International traveling and immigration from countries where the disease is endemic has caused an increase in the number of annual cases of imported malaria in the Valencian Community in recent years.

Objective: To describe characteristics of the cases of malaria detected in children from January 2003 to October 2009 in our hospital.

Materials and methods: Cases of malaria diagnosed between 01/01/2003 and 31/10/2009 in our hospital, were studied. Only one positive result per patient was included in the study. A rapid test of immunocromatography to Plasmodium antigens detection (Binax) was used as a screening test; the confirmation was realized by direct vision in a thin smear by Giemsa's tint.

Results: Fifteen cases of confirmed malaria were identified, nine girls and six boys. The age range was from 8 months to 14 years. Of these 9 (60%) corresponded to *P. falciparum*; 6 (40%) cases were mixed infection for *P. falciparum* and *P. vivax*. Fever 86% (13) was the most common symptoms; No cases of complicated malaria or death occurred. All patients had recently travelled to or from endemic countries without a correct quimioprofilaxis. More than 85% were proceeding from Guinea Equatorial.

Conclusions: The incidence of pediatric malaria is increasing at the Valencian Community. *P. falciparum* was the most frequently identified specie. It seems to be important to continue surveillance for malaria and its correct quimioprofilaxis in our country.

INFECTIOUS DISEASES IN FOREIGN-BORN CHILDREN OF IMMIGRANT FAMILIES

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Objective: To describe the prevalence of infectious diseases in immigrant children presenting at our tertiary care center.

Methods: Retrospective chart review of children evaluated at CHU Sainte-Justine, Montreal, Canada (98/01/01-08/12/31).

Results: 492 children were evaluated, 51.1% male. Median age: 5.3 years. Overall, 79.5% were seen in the first year after arrival, emigrating mainly from Africa (34.6%), Americas (19.9%), Europe (19.1%), and Mediterranean and Middle East (17.9%). BCG vaccine was documented in 208 children. TST was positive in 24.5%. Stool parasites in 35.7% and Malaria in 13/98.

N=492	N positive/tested	(%)	Comments
HBsAg	4/475	(0.8%)	
HBeAg	3/475	(0.6%)	1 patient Anti-HBeAg
Anti-HBs ≥10	261/476	(54.8%)	
Anti-HBc (IgG+IgM)	22/475	(4.6%)	1 patient IgM+
Hepatitis C (IgG)	1/471	(0.2%)	
Hepatitis A (IgM)	8/32	(25.0%)	
Syphilis (RPR)	0/433	(0.0%)	
HIV	3/462	(0.7%)	
<i>Strongyloides stercoralis</i>	4/31	(12.9%)	

[Serologies]

Conclusion: This study shows a significant prevalence of infectious diseases in 35.4% of patients. Overall, 25% of immigrant children had positive TST, 17% more than 1 pathogenic intestinal parasite, 1% hepatitis B, 0.7% HIV, 0.2% hepatitis C. Malaria, *Strongyloides stercoralis* and hepatitis A were found in smaller proportions. Screening for infectious diseases should be performed in all immigrant children.

THE PREVALENCE OF VANCOMYCIN RESISTANCE ENTEROCOCCI AND VRE GENES FROM THE STOOL OF HOSPITALIZED CHILDREN

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Background: Prevalence of Vancomycin resistance in Enterococci, (VRE) and its spread to other Gram positive organisms have lead to serious problems in patients.

The object of this study was to determine the prevalence of Vancomycin resistance Enterococci and VRE genes from the stool of hospitalized children.

Methods: Two Stool Samples were the day of admission and the 48 hours after were cultured on Bile Esculine agar containing 6 µg/ml Vancomycin and 64 µg/ml Ceftazidime was used to screen Enterococci. E-test was performed on VRE strains. Antibiotics, for E-test. Susceptibility level was reported on the basis of CLSI charts. Prevalence of *van* genes was determined by PCR method.

Results: Stool samples 780 patients were examined. enterococci were isolated from 739 (94.7%). specimens pattern of antibiotics resistance was as follows: vancomycin 16.9% ,Cefotetan 76%, Erythromycin 98.2%, Oxacillin 87.4%, Cefotaxim 79%, Clindamycin 97% , Ampicillin 93.3,Nafcillin 74.6%, Cephalosporin 89.5%. The prevalence of *van* genes was 69.1%, 27.4%, 3% and 0.5 % for *vanA*, *vanB*, *vanC* and *vanD* respectively.

Conclusion: Direct multiplex PCR assay using *vanA*, *vanB*, *vanC* and *vanD* primers, was more sensitive than culture for the detection of gastrointestinal colonization by Vancomycin-Resistant Enterococci. It is crucial for laboratories to provide accurate antimicrobial resistance pattern for Enterococci so that effective therapy and infection control measures can be initiated.

STREPTOCOCCI RESISTANCE TO ANTIBIOTICS. A STATISTICAL EVALUATION

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Background and aims: European Surveillance has reported resistance of group A streptococci to macrolides: 11% of isolates (Portugal), 32% (Italy). First clindamycin-resistant isolate was reported in 1999. Authors evaluate antibiotic resistance of pyogenic *streptococci* (serogroups A, C, G) for pediatric population in context of increased morbidity among children.

Methods: There were performed 714 throat cultures during 30 days period: 56 isolates (7,84%) were positive (large-colony streptococci). Inclusion criteria (antibiogram performing): beta-hemolytic streptococci group A (GAS), C (GCS) and G (GGS). Exclusion criteria: small-colony streptococci. 34 isolates were selected for diffusimetric method (Mueller Hinton medium 5% *sheep blood*; *S. pneumoniae* ATCC 49619 strain as quality control) using penicillin, erythromycin and clindamycin disks. The cases were reevaluated after 10 days penicillin therapy.

Results: 7 strains (20,58%) were erythromycin resistant (5 strains GAS, 1 GCS, 1 GGS), 2 strains (5,88%) clindamycin resistant (1 strain GAS, 1 GGS). One case wasn't cured after penicillin therapy (antibiogram revealed resistance just for erythromycin), justifying Clindamycin treatment with good evolution. The other cases were successfully treated with penicillin.

Conclusions:

1. The study confirmed macrolides resistance for streptococci pyogenes (1/5 strains);
2. It isn't recommended routine antibiogram;
3. Penicillin is first choice treatment for streptococcal pharyngitis;
4. One case was penicillin resistant, probably due to bacterial adaptive mechanisms: *streptococcal „internalisation”*, beta-lactamases produced by *saprophytic mouth bacteria*, streptococcus persistence (lingual tonsils);
5. Streptococcus pharynx persistence after penicillin treatment is different from concept of GAS resistance to penicillin;
6. Clindamycin resistance was revealed for 6% strains, justifying its use for penicillin resistant cases.

ETIOLOGY AND ANTIMICROBIAL SUSCEPTIBILITY OF BLOODSTREAM ISOLATES IN NICU

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Background and aims: Empiric antimicrobial therapy is frequently used for suspected sepsis in NICU. Knowledge of incidence and antimicrobial susceptibility patterns of bacterial pathogens is very important.

Methods: Retrospective analysis of microbiology records on causative bacterial isolates from blood cultures of neonates hospitalized in a NICU from 1/2007 to 12/2008.

Results: Among 226 isolates 80% were Gram-positive. Coagulase-negative staphylococci (CNS, 89.9%) were the most frequent Gram-positive bacteria followed by *Staphylococcus aureus* (2.8%), *Enterococcus faecalis* (2.8%), *E. faecium* (2.8%) and group B streptococci (GBS, 1.7%). More than 50% of CNS and 37.5% of *S. aureus* were resistant to methicillin. However, all staphylococci were sensitive to vancomycin. Additionally, while all GBS and *E. faecalis* isolates were susceptible to ampicillin and vancomycin, 80% of *E. faecium* were resistant to ampicillin and 60% to vancomycin. The most frequent Gram-negative isolates were *Klebsiella* spp., *Enterobacter cloacae*, *Escherichia coli* and *Acinetobacter baumannii*.

Bacteria (n)	Ampic	Amik	Ceftaz	Cipro	Imipen
<i>K. pneumoniae</i> (21)	0	80.6	23.8	100	100
<i>E. cloacae</i> (9)	0	66.7	55.6	66.7	88.9
<i>K. oxytoca</i> (6)	0	100	100	100	100
<i>E. coli</i> (5)	60	100	80	100	100
<i>A. baumannii</i> (4)	-	75	50	75	75

[Susceptibility

(%)]

Conclusion: Vancomycin is the first-choice antibiotic for neonatal nosocomial sepsis due to staphylococci. Imipenem, amikacin and ciprofloxacin are most appropriate for Gram-negative sepsis.

ANTIMICROBIAL SPECTRUM OF PROBIOTIC BACTERIAL STRAIN FROM PAEDIATRIC POPULATION AND COMMERCIAL SOURCES

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Background: Probiotics are nonpathogenic microbial food ingredient that exerts a positive influence on the health or physiology of the host. This study was conducted to evaluate commercial probiotic and isolated indigenous probiotic flora for antibiotic resistance with purpose of verifying their ability to survive if they are taken simultaneously with an antibiotic therapy.

Methods: Probiotic preparations and indigenous lactic acid bacillus isolated from stool samples of children. Samples inoculated on MRS medium for growth of all probiotic. Strains identified by API 50 CH. Antibiotic resistance carried out by disk diffusion method on MRS agar.

Results: Commercial probiotic possesses different resistance pattern(n=8). Of these two specified probiotic, 1st - resistant to five antibiotics including vancomycin and sensitive to five antibiotics like erythromycin, amikacin, gentamicin, ciprofloxacin and cefoperazone, 2nd - found resistant to 9 antibiotics tested except erythromycin. Of total 25 indigenous *Lactobacillus sp.* showed different antibiogram, where as in one baby three sequential sample cultured at different interval to see stability of endogenous probiotic bacteria (*L. salivarius*); showed similar antibiogram with resistance to 4 antibiotics. Antibiotic resistance among 25 isolates detected against amikacin (72% of the isolates), vancomycin (80%), augmntin (16%), cefotaxime (12%), cefuroxime(100%),ceftazidime (44%), cefoperazon(28%), ciprofloxacin(68%),erythromycin (12%) and gentamicin (60%). All isolates showed multiple antibiotics.

Conclusions: This is the first report on antibiogram pattern of indigenous flora (*LAB*) and commercial source of probiotic from India. The information resulting from the study may help clinicians to judiciously prescribe the right probiotic for preventive and therapeutic intervention in Indian population.

RESISTANCE OF UROPATHOGENIC BACTERIA IN CHILDREN ON PERITONEAL DIALYSIS IN LABBAFINEJAD AND MOFID CHILDREN HOSPITALS OF IRAN

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Growing antibiotic resistance demands reassessment of antimicrobial efficacy, particularly in countries with wide antibiotic abuse. Knowledge of resistance trends is important when prescribing antibiotics empirically, as the case for urinary tract infections (UTIs) especially in children on dialysis treatment. In IRAN, amoxicillin, cotrimoxazole (trimethoprim/sulfamethoxazole) and third generation cephalosporins are used as "first-line" antibiotic treatment for UTI. Appropriate management strategies designed for specific groups of patients with UTI can maximize therapeutic benefit. The aim of this study was to assess the kinds of isolated bacterial strains and their drug resistancy to commonly used antimicrobials in children with terminal renal failure on peritoneal dialysis (PD) treatment who suffer from UTI. In this study, bacterial isolates from urine samples collected from pediatric patients (6 months -17 years) on PD with acute UTIs in Tehran from March to September 2006. Samples were tested for susceptibility to 13 antibiotics by the disk- diffusion method. 36 bacterial isolates were derived from 34 culture positive UTI episodes (27 *Escherichia coli*). We found a high prevalence of resistance towards the drugs used as "first-line" when treating UTIs: amoxicillin and cotrimoxazole, (71.4%, 51.7%, resistance, respectively). The results showed that 70.4% of *E. coli* isolates were resistant to amoxicillin, whereas 55.6% of them were resistant to cotrimoxazole. Resistance towards thirdgeneration cephalosporins was also high (44.5% and 37% of *E. coli* to Cefixim and Ceftriaxone, respectively).

Conclusion: Resistance of *E. coli* isolates to first-line treatment (amoxicillin, cotrimoxazole) of UTI was high, whereas most *E. coli* isolates were susceptible to Amikacin and nitrofurantoin.

Keywords: Peritoneal dialysis-UTI-Antibiogram-Children.

UNUSUALLY HIGH PREVALENCE OF MULTI-DRUG RESISTANT COMMUNITY-ACQUIRED METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS (CA-MRSA) ISOLATES IN CHINESE CHILDREN

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Background and aims: CA-MRSA isolates are often considered susceptible to many non-beta-lactam antimicrobials, however few multi-resistant CA-MRSA have been reported recently. Our study was to investigate the antimicrobial resistance of CA-MRSA isolates from five pediatric hospitals in China from 2005 to 2009.

Methods: Susceptibility to eight non-lactam antibiotics was determined by the agar dilution method. The antibiotics tested were clindamycin(Cli), ciprofloxacin(Cip), chloramphenicol(Chl), erythromycin(Ery), gentamicin(Gen), tetracycline(Tet), trimethoprim-sulfamethoxazole(Sxt), and vancomycin(Van). The multi-drug resistance of CA-MRSA was defined as resistant to more than three non-lactam antibiotics.

Results: Among 127 CA-MRSA isolates, 96.7% were resistant to erythromycin, 83.5% to clindamycin, 57.5% to tetracycline, 46.5% to gentamicin, 43.3% to chloramphenicol, 33.9% to ciprofloxacin, and 23.6% to trimethoprim/sulfamethoxazole. All CA-MRSA isolates tested were susceptible to vancomycin. Of 127 CA-MRSA, 99(78.0%) were multi-drug resistance (MDR). The multi-drug resistant patterns were shown in the table.

	Kinds of antibiotics	The major MDR patterns
	Three(30)	Cli-Ery-Tcy (13)
MDR CA-MRSA (99)	Four(32)	Cli-Ery-Tcy-Chl(11)
	Five(14)	Cli-Ery-Tcy-Chl-Cip(4)
	Six(10)	Cli-Ery-Gen-Tcy-Chl-Cip(4)
	Seven(13)	Cli-Ery-Gen-Tcy-Sxt-Chl-Cip(13)

[Multi-drug resistant patterns of CA-MRSA isolates]

The Arabic numerals in parentheses were the number of isolates.

Conclusions: In China, there was a high prevalence of multi-drug resistant CA-MRSA isolates, so for children with putative CA-MRSA infection, a glycopeptide-containing regimen should be considered for initial empirical therapy.

DISSEMINATED BACILLUS CALMETTE-GUERIN INFECTION, DESCRIPTION AND REPORT OF SIXTEEN CASES

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Background and aims: There is some evidence that hematogenous dissemination of the bacilli does occur following BCG vaccination to many organs, a process that may lead to disseminated BCG infection in certain instances. The aim of this study was to assess the epidemiologic, clinical and laboratory characters of the patients with disseminated BCG infection.

Methods: Patients with the final diagnoses of disseminated BCG infection, admitted in Mofid Children Hospital, during a 5 yr period from mid-2003 to mid 2009, were studied.

Results: Sixteen patients, with the age range of 1 to 32 months were enrolled. Male to female ratio was 5:3. All were vaccinated with BCG at birth. The most common symptoms were fever, malaise and FTT, respectively in 90%, 75% and 75% of cases. Hepatosplenomegaly and various skin lesions, generalized and axillary lymphadenopathy were present in 50%, 62%, 95%, and 50% of patients respectively.

All the patients had anemia, elevated ESR and positive CRP and liver function tests were abnormal in half of them. Immunologic work up revealed a variety of deficiencies including humoral abnormalities, IL-12 deficiency, severe combined immunodeficiency and chronic granulomatous disorder. Microbiologic and histologic tests had 56.5% yield that reached to 68.7% after autopsy. Treatment strategy was to Prescribe at least four anti-mycobacterium drugs beside Gamma-Interferon, IVIG and GM-CSF in some instances.

Conclusions: Disseminated BCG infection should be considered in any child presenting with fever, malaise and hepatosplenomegaly.

THE PREVALENCE OF VEROTOXIN GENES IN EHEC ISOLATED FROM URINE SAMPLES IN MOFID CHILDREN HOSPITAL

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Introduction: Urinary infection due to EHEC is one of the most important diseases in infants and children .If there would not be any useful diagnosis and followed treatment for them, may appear dangerous diseases such as acute renal failure, Thrombocytopenia and Hemolytic Anemia. Thus, we must find a method for rapid diagnosis with high sensitivity and specificity.

Material and methods: Urine samples were collected from children with UTI. At first, we cultured urine on Blood agar and EMB media. then gram negative bacilli from EMB subcultured on TSI, IMVIC, urea. E.coli strains that indicated beta hemolytic on sheep blood agar, negative fermentation of sorbitol on SMAC (sorbitol macconky agar) and negative motility on SIM were tested. Serologic test with VTEC-RPLA latex agglutination kit production of toxin and PCR method for detecting toxin genes.

Results: We consider 12572 urine samples from children in Mofid hospital. 12.43% of urine culture was positive. Distribution of bacteria pathogens were: E.coli(47.2%), Pseudomona aeruginosa (8.9%), Staphylococcus epidermidis(14.9%), Proteus mirabilis(6.4%), klebsiella spp.(18.3%), Staphylococcus aureus(4.3%). 20.97% of E.coli was positive beta hemolysis, negative fermentation on SMAC-agar. The prevalence of EHEC was 2.3%. The prevalence of vtx-1, vtx-2 and vtx1&2 was 17.3, 52.4, 30.3 respectively.

Conclusion: The prevalence of urinary infections caused by EHEC strains is very significant because it causes aggravating pathologic effects. Thus we suggest rapid method for identification of this bacteria and proper treatment to inhibition of unwanted complications.

MYCOPLASMA PNEUMONIAE INFECTION: AGE AND CLINICAL PRESENTATION**J. Dias**¹, H. Antunes^{1,2}

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Background and aims: *Mycoplasma pneumoniae* (MP) infection in pediatric population presents with an extended spectrum of disease. Often thought to affect school aged children and adolescents, there is evidence that affects younger children. The aim of this study is to determinate the prevalence of MP infection in children and its relation with age and clinical presentation.

Methods: Retrospective study of population between 1 and 15 years old, admitted in Braga Hospital, with MP antibody IgM positive by enzyme linked immunosorbent assays ELISA, confirmed by polymerase chain reaction from January 2005 to July 2008.

Results: Were included 60 children from 2 to 14 years old (31 girls), 43% had less than 5 years old. The peak incidence occurred between January and May (67%). Fever was the predominant symptom (92%), followed by cough (85%), anorexia (22%) and vomiting (20%). The average duration of symptoms was 8 days. Pneumonia was the most common diagnosis followed by multiform erythema, acute pancreatitis, urtetrinitis, cholestatic hepatitis, ataxia, arthritis and prolonged fever. Most patients (53%) were discharged, 47% were admitted, and the median length of stay was 3 days (range 1 to 12 days). No correlation was found between age and clinical presentation ($p=0.08$) or duration of illness ($p=0.58$). Patients with leukocytosis and elevated reactive C protein value were more likely to be admitted ($p=0.04$).

Conclusion: MP infection is not related to gender and infection site, but to age and season. Children over 2 years old are vulnerable to MP infection.

BACTERIAL INFECTIOUS DISEASES IN TERM NEWBORN INFANTS**E. Lekic**

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Introductions: Maternal, environmental, and host factors determine which infant exposed to a potentially pathogenic organism will develop serious or other potentially invasive infections, causing significant mortality and long-term morbidity in neonates.

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

Results: 1391 term newborns (TNB) were treated at the Center of Neonatology in Podgoricaduring the period 2002-2004. In 528 TNB were proven infections. Most frequent infectious diseases were :omphalitis (44,9%), pneumonia (18,5%), sepsis (10,9%), cutaneus infections (8,7%), urinary tract infection (5,3%), conjunctivitis (5,5%), otitis media (3,8%), mastitis (1,7%), diarrhea (0,7%). Sepsis and / or meningitis were diagnosed in 58 term newborn (10,9%). The bacterial agents responsable for sepsis and / or meningitis were: Coagulasa -Negative Staphylococcus (41,3%) , Staphylococcus Aureus (19%), E.coli (5.3%) , then with equally frequency SGB, SGA, Streptococcus pneumoniae, Enterococcus , L.Monocytogenes, Klebsiella pneumoniae, Acinetobacter, Serratia, Pseudomonas , Klebsiella-Enterobacter (each one 1,7%).Meningitis were proven in 16 TNB or 27,6%.

Conclusions: Temporal and geograpgic differences of various neonatal patogens are well recognized. It is important to identifications the bacterial microorganismsims in our region, analysis of longitudinal trends assist in the formulations of strategies to treat and prevent neonatal serious infections.

MYCOPLASMA PNEUMONIAE INFECTION MANIFESTATING AS MULTIORGAN DYSFUNCTION SYNDROME: AN UNUSUAL PRESENTATION IN A CHILD

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Background and aims: *Mycoplasma pneumoniae* (Mp) is a well known cause of lower respiratory tract infection in childhood. Extrapulmonary manifestations include the central nervous system as well as the cardiovascular, gastrointestinal, urinary and hematological systems. We report a case of acute Mp infection presenting as multiorgan dysfunction syndrome, without pulmonary detection.

Methods: A 13-year-old boy was admitted due to a 4-day fever with headache, anorexia, abdominal pain, vomiting and gross hematuria. On admission the patient appeared sick. The liver was slightly enlarged and palpated 3cm below the right costal margin. Murphy's sign was positive. The spleen was palpated too. Other systemic examinations were normal. The laboratory results showed leucopenia, thrombocytopenia, liver and renal dysfunction and depression of multiple coagulation factors. Abdomen ultrasonography revealed hepatosplenomegaly, wall thickening of gallbladder, enlarged hyperechogenic kidneys and presence of liquid in the hepatorenal space.

Results: Further serologic workup revealed acute infection due to Mp. Other serologic findings, including hepatitis A, B, C, cytomegalovirus and Epstein-Barr virus, were negative. Clarithromycin was administrated for 14 days. A week after the admission all the clinical and laboratory findings were resolved.

Conclusions: A variety of extrarespiratory manifestations of Mp infection has been reported. Rarely, Mp may be responsible for multiorgan dysfunction syndrome presentation and it should be suspected even in cases without respiratory participation.

VALUE OF URINE ANALYSIS IN DIAGNOSIS OF URINARY TRACT INFECTION IN CHILDREN**M. Jafarzadeh***Pediatrics, Mashad University of Medical Science, Imam Reza Hospital, Mashad, Iran*

Background and aim: Because of high prevalence and morbidity of UTI in children , early diagnosis and on time treatment are essential; but confirmation of UTI diagnosis needs a urine culture which takes at least 48 hours . The aim of this study was to ascertain predictive values of urinalysis in the diagnosis of UTH.

Material and methods: In this descriptive study the recorded files of 59 febrile patients, 30 patients with positive urine culture and 29 patients with negative urine culture, hospitalized in Imam Reza Hospital in one year, were evaluated. Age, sex, results of U/A including pyuria, hematuria, urine nitrite test and urine culture were gathered and analyzed using descriptive statistics.

Results: In this study sensitivity and specificity of nitrite test in diagnosis of UTI were 46.7% and 89.7 respectively . Sensitivity and specificity of pyuria were 76.1% and 48.3% respectively . Sensitivity and specificity of U/A (nitrite test and pyuria) in diagnosis of UTI in children under 2 years old were 85% and 70% , but in patients older than 2 years old were 100% and 35% respectively.

Conclusion: This study indicted that non active U/A in children older than 2 years old rules out UTI in nearly 100% of cases.

Keywords: Urinary tract infection, pyuria, Nitrite test.

ILIOPSOAS MYOSITIS MIMICKING APPENDICITIS

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Background and aim: Pyomyositis is a primary bacterial infection of skeletal muscles. Almost 90% of pyomyositis cases in children are caused by *Staphylococcus aureus* and normally affect lower limb muscles. We present a case of primary pyomyositis affecting the iliacus muscle, which was unexpectedly associated with a surgical abdominal pathology.

Observation: An 11-year-old boy arrived at A&E with a 4-day-fever of 40°C, pain in the right hip and functional incapacity. Physical examination: generally affected state, pain-related position of the low right limb, intensely painful semi-flexion of the hip and knee and limited mobility. The right iliac fosse was very painful to palpation and with psoas sign positive.

Complementary exams: haemoglobin 12.9g/dl, haematocrit 38.5%, WBC count: 5000/mm³, neutrophils 3900/mm³, PCR 175 mg/L, Fibrinogen 713 mg/dl, blood culture: *staphylococcus aureus*. Hip ultrasound: asymmetric size of both iliacus muscles, the right being larger. Abdominal ultrasound: appendix size: 6mm. There were appendicoliths and an abnormal underlying muscle structure. Abdominal CT scan: alteration of abdominal fat in paracolic gutters near the iliacus muscle and the caecum. Retrocecal appendix, appendicoliths and inflamed iliacus muscle were compatible with myositis. During surgery, we observed an abscess-like retrocecal appendix with adenopathies in the ilium and the ascending colon, and myositis-type psoas. Treatment: meropenem iv for 7 days, cloxacillin iv for 6 days, to continue orally with clindamycine and cefalexin for 10 days.

Conclusions:

- Pyomyositis can mimic appendicitis and early correct diagnosis can help.
- The coincidence with appendicoliths makes the differential diagnosis between primary myositis and reactive myositis more difficult.

ANTIBIOTIC SENSITIVITY RATIOS IN COMMUNITY ACQUIRED E.COLI INFECTIONS

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Background and aims: Urinary system infections are one of the most frequent infections that increase the resistance towards the antimicrobials. The aim of this study is to determine the antimicrobial sensitivities of *Escherichia coli* that proliferate in the cultures of patients who have urinary system infections.

Methods: The microorganisms isolated between January 2008-February 2009 are analysed retrospectively. We studied the sensitivities of ampicillin, amoxicillin-clavulanic acid, cefuroxime, ceftizoxime, ceftriaxone, ceftazidime, cefotaxime, aztreonam, gentamicin, amikacin, tobramycin, netilmicin, trimethoprim-sulfamethoxazole, norfloxacin, ciprofloxacin, cefoperazone-sulbaktam and imipenem on uropathogen *E.coli*.

Results: It was found that the most effective antibiotic in all strains was imipenem(90,4%), the least effective antibiotic was amoxicillin(30%).The sensitivity ratios were 75% for nitrofurantoin, 60 % for seftriakson, 88.8% for amikacin. ESBL production among *E.coli strains* was found 18,1%.

Conclusions: These consequences show that antibiotic resistance is an increasing problem.The antibiotic usage and the antibiotic resistance should be carefully researched and all centers must use their own antibiotic guides. Beside that, ceftriaxone and ciprofloxacin resistance in the ESBL producing strains are important problems and the treatment should be followed closely.

UNILATERAL OPTIC NEURITIS AS A PRESENTATION OF NEUROBRUCELLOSIS**R. Marques**¹, C. Martins², I. Machado³, J.P. Monteiro², N. Campos³, P. Calhau¹¹*Pediatric, ²Neuropediatric Unit, Pediatric Department, ³Ophthalmology, Hospital Garcia de Orta, Almada, Portugal***Background:** Neurobrucellosis is a rare disease with a wide spectrum of clinical manifestations.**Case report:** A teenager was admitted with a headache and right eye visual impairment. She had no significant personal or family history, except for a vacation in the countryside and a consumption of unpasteurized dairy products. Physical examination only revealed sub-febrile temperature (37.7 C), mild edema of right tibiotarsic joint, afferent pupillary defect and a funduscopy with optic disc swelling

The initial diagnostic was a post-infectious optic neuritis so ev bolus of methylprednisolone (250 mg, 6/6h) was initiated.

Investigations showed a Brucella serum agglutination titer of 1/640. Lumbar puncture revealed a clear and colorless cerebrospinal fluid with 40.2 mg/dl protein, 97.1 mg/dl glucose and 7 polymorphonucleated cells. PCR for Brucella in the CSF was negative and MRI scan was normal. Oligoclonal bands were not performed and visual evoked potentials were abnormal.

Antibiotic therapy with Doxycycline (200mg/d) and Rifampicin (600mg/d) was started and a complete reversal of the visual and systemic symptoms was registered, with a 6 month follow-up.

Discussion: Neurobrucellosis has neither a typical clinical picture nor specific cerebrospinal fluid findings. Optic neuritis is a rare manifestation of neurobrucellosis.

PVL POSITIVE S. AUREUS SEPSIS WITH BILATERAL NECROTIC PNEUMONIA AND MULTIPLE OSTEOMIEELITIS IN PREVIOUSLY HEALTHY BOY

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

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: Previously healthy 15 years old boy with complains about sweating and pain in both knees for 4 days was admitted to Children Clinical University Hospital. Immediately after admission he was moved to intensive care unit due to severe respiratory insufficiency. He had bilateral necrotic pneumonia and multiple osteomyelitis. Invasive *S. aureus* isolated from blood, synovial fluid and pus was methicillin susceptible, Panton - Valentine leicocidin producing and belonged to *spa* type t435. Patient underwent repeatedly incisions and drainages, he received antibacterial therapy with clindamycin, oxacillin, ciprofloxacin, amikacin, cefuroxime and was discharged after 3 months without fully convalescence due to necrosis and collapse of femoral head.

Conclusion: Molecular investigation showed that PVL positive MSSA with *spa* type t435 can cause severe systemic infections with osteomyelitis and pneumonia.

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SEARCHING THE BEST METHOD (CULTURE, PCR, AG DETECTION, GRAM STAIN SMEARS) IN SYNOVIAL FLUID FOR DIAGNOSIS OF SEPTIC ARTHRITIS

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Objective: To determine the bacterial infection in synovial fluid by Culture, Ag detection, gram stain smears and PCR.

Methods & materials: A cross sectional study had done in pediatric and orthopedic ward of Rasoul/hospitals in Tehran, Iran 2006-2008. 62 patients with arthritis selected by continuous sampling. Aspirated Synovial fluid in all cases searched for direct gram stain smear, culture, latex (antigen) particle detection, bacterial PCR. Chi square values (CI 95%, $p < 0.05$) were calculated for all categorical variables.

Findings: Range of age: 6 months-14 years, Mean age=10.3±4.12 years with no sex prediction. Septic arthritis detected in 46% (31/62) cases, aseptic arthritis in 53% (36). Rheumatoid arthritis was the most common predisposing factor in 70% cases. 12 cases with positive culture: included staph aureus n=9, N.meningitis, pseudomonas. 5 cases had positive antigen test for N.meningitis (1); S. pneumonia (1), H.influenza (1). Staph super antigen detected in 73% of cases. No significant relation seen between positive culture and ESR>30 & CRP>2+.

No significant correlation seen between positive culture and latex antigen test with high ESR, but near significant relation seen between positive culture and superantigen Staph; $P_v=0.06$.

Conclusion: Adding the bacterial antigen test to conventional culture, gram stain smear and routine analysis in synovial fluid are helpful for diagnosis of septic arthritis. Detection the bacterial antigens is useful and rapid, cheap and not hard in compare with PCR as a complex and timeful method.

H1N1 INFECTION- A CAUSE OF KAWASAKI'S DISEASE ?

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Background and aims: In the setting of an influenza pandemic, pyrexia of unknown origin can be incorrectly ascribed to H1N1 influenza resulting in a delay in the diagnosis of other conditions including Kawasaki's Disease (KD). In addition, the two conditions might co-occur.

Methods: Case reports

1: A four year old boy was admitted to hospital with high fever for 9 days and all the major clinical criteria for diagnosis of KD. He was treated with intravenous immunoglobulin and Aspirin. His nasopharyngeal aspirate was positive for H1N1 influenza and he was treated with Oseltamivir. Echocardiogram did not show coronary artery aneurysms. He made a full recovery.

2: A two year old girl who was being treated with Oseltamivir for a presumed H1N1 infection was diagnosed with KD when she had progressive symptoms of red eyes, fever and reluctance to walk. She required two doses of Intravenous Immunoglobulin and Aspirin. Echocardiogram showed giant aneurysm and she remains under follow-up.

Results: The cause of KD is unknown and there is no confirmatory test. It is not clear whether H1N1 might have been a trigger in these cases.

Conclusions: We present two cases of Kawasaki's disease associated with H1N1 infection. The diagnostic features of Kawasaki disease may appear sequentially rather than simultaneously. Overlap between symptoms of KD and those attributable to influenza can present a diagnostic dilemma during the current pandemic.

ACUTE MYOSITIS ASSOCIATED WITH THE FIRST PHASE OF TICK BORNE ENCEPHALITIS (TBE)

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Background and aims: TBE is an emerging zoonotic infectious disease caused by TBE virus (TBEV) transmitted to humans by ticks. Western TBEV has a biphasic course. The first phase correlates with viremia and the second one with virus invasion of the CNS. Slovenia is endemic for TBE. We present a patient with clinically overt myositis during the first phase of TBE.

Methods: Since clinical picture and laboratory results of blood were nonspecific, the diagnosis of TBE was confirmed by microbiological investigations.

Results: A 10-years old boy started to complain about headache, nausea and fever five days after a tick bite. Two days later excruciating pain in calf muscles appeared. He refused to walk because of myalgia. The affected muscles were tender on palpation. Leukopenia ($2.6 \times 10^9/L$), increased AST (10.81 $\mu\text{kat/L}$), ALT (2.24 $\mu\text{kat/L}$), CK (233.18 $\mu\text{kat/L}$), LDH (11.16 $\mu\text{kat/L}$), aldolase (463 nkat/L) and pyruvat (122 mmol/L) concentrations were detected in blood. Values of serum lactate and troponin were normal. TBEV RNA was detected in serum by RT-PCR prior to development of serum TBEV antibodies. The condition resolved spontaneously within fourteen days when he returned to the hospital because the second phase of disease with meningitis, detectable serum ELISA TBE-IgM and -IgG and intrathecal production of TBE-IgG.

Conclusions: Clinically overt acute myositis is a rare manifestation of TBE. Serum RT-PCR is of great diagnostic help in the early diagnosis of TBE, mainly restricted to the first phase of infection prior to the development of serum TBEV antibodies.

PREVALENCE OF SALMONELLA AND SHIGELLA INFECTIONS IN PEDIATRIC POPULATION. A STATISTICAL EVALUATION

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Background and aims: Prevalence of Salmonella / Shigella infections vary due to inconsistent diagnosis techniques. Authors evaluate Salmonella / Shigella infections regarding epidemiological and evolution aspects for hospitalized children.

Methods: There were performed 585 stool cultures during 3 months period using mediums (agar-desoxycholate-citrate-lactose medium, selenite broth), biochemical tests (mobility-indol-urease, triple-sugar-iron), latex agglutination, serological somatic (O) *Salmonella* tests. Mueller-Hinton medium was chosen for diffusimetric antibiogram using disks for ampicillin(AMP), ceftazidime(CAZ), trimetoprim-sulfamethoxazol(SXT), nalidixic acid(NA) and colimycin(CT). Inclusion criteria for antibiogram: newly diagnosed Salmonella / Shigella cases. Exclusion criteria: positive stool culture for previously treated children.

Results: From 585 samples, 39 (6,67%) were positive: 34 Salmonella isolates (17 group B, 15 group D, 2 group C) and 5 Shigella isolates (4 samples *S. sonnei*, 1 sample *S. boydii*). From Salmonella samples, 13 represented post-therapeutic relapses (5 group B, 7 group D, 1 sample group C). There were performed 21 antibiograms: group B Salmonella -from 9 samples, 6 strains AMP resistant, 2 SXT resistant; group D Salmonella -from 7 samples, 2 strains NA resistant; group C Salmonella -1 susceptible strain; *Shigella sonnei* -3 AMP and SXT resistant strains; *Shigella boydii* -1 susceptible strain. All positive cases were treated according to antibiogram.

Conclusions:

1. Salmonella group B was most frequent detected;
2. Salmonella group D had higher relapse rate (7 relapses from 15 samples);
3. Higher resistance rate was reported for AMP and SXT;
4. As compare to Shigella, Salmonella cases had frequent relapses (13 from 34 samples).

**ACTIVE HOSPITAL-BASED SURVEILLANCE OF INVASIVE PNEUMOCOCCAL DISEASE (IPD),
CLINICAL AND CHEST X-RAY POSITIVE PNEUMONIA IN INFANTS/YOUNG CHILDREN IN
POLAND**

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Background/aims: *Streptococcus pneumoniae* (SP) is the leading cause of vaccine preventable disease in children under 5 years of age. IPD incidence data are limited. We prospectively estimated the incidence of IPD, clinical pneumonia and chest X-ray positive pneumonia (CXR+Pn), in infants and young children in Poznan City and Poznanski County.

Methods: One-year active, prospective, hospital-based surveillance (2/15/2008 - 2/14/2009), in children from 28d to 60m old. Eligibility criteria: children residing within the surveillance area with temperature $\geq 39.0^{\circ}\text{C}$ within 24 hours prior to screening and/or clinical suspicion of IPD or pneumonia.

Results: 1581 subjects were enrolled, mean age: 17.8m. SP was detected in 8 isolates from 7 subjects (source: 7 blood, 1 CSF). Final IPD diagnoses were: bacteremic pneumonia 3(42.9%); sepsis 2(28.6%); meningitis 2(28.6%). The incidence rate of IPD overall and in children from 28d to < 24m was 11.9/100,000 and 20.1/100,000. The highest IPD incidence rate was seen in children 6m to < 12m: 29.6/100,000.

Overall incidence rates of clinical pneumonia and CXR+Pn were 1888.7/100,000 and 657.3/100,000. The highest incidence rate of clinical pneumonia and CXR+Pn occurred in children 28d to < 6m: 5026.1/100,000 and 1721.7/100,000, respectively.

Serotype analyses, n: 1 each for **6B, 14, 23A, 23F, and 33F**; isolates not tested 2. Serotype coverage was 60.0% for PCV7 and PCV13.

Conclusions: IPD and pneumonia cause a demonstrable burden of vaccine preventable disease in Poland. Vaccines with demonstrated effectiveness against both IPD and pneumonia can have substantial impact on public health.

REGIONAL DIFFERENCES IN BACTERIAL FLORA OF DIFFERENT NEONATAL INTENSIVE CARE UNITS

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Aims: Neonatal sepsis is the most important problem that physicians encounter with working in a NICU. Microbial agents causing sepsis in NICU's changes in between developing countries and developed countries.

Methods: In this study we researched newborns with sepsis in a NICU for their clinical characteristics, positive culture results and antibiotic sensitivities and try to explain the differences between countries.

Results: We found that 46.1 percent of sepsis causing agents was methicillin resistant staphylococcus aureus, 15.4% E.coli, 15.4% Klebsiella pneumonia, 7.6% Candida albicans and 7.6% Klebsiella oxytoca.

Conclusions: Etiology of sepsis changes in between different regions of world mostly associated with the countries developmental status. We show this below in a table reviewed from recent studies. These differences are just because of the NICUs' own characteristics, societies' different economical statuses and different antibiotics usage.

DEVELOPED COUNTRIES	DEVELOPING COUNTRIES
group B streptococcus	klebsiella spp.
l. monositogenesis	enterobacter spp.
e. coli	serratia spp.
s. aureus	coagulase negative staphylococcus
coagulase negative staphylococcus	e. coli
gram(-) enteric bacilles	s. aureus

[regional

differences]

TURKEY	OUR NICU
coagulase negative staphylococcus	coagulase negative staphylococcus
klebsiella spp.	klebsiella spp.
enterobacter spp.	e. coli
serratia spp.	enterobacter spp.
e. coli	candida spp.
candida spp.	
s. aureus	
pseudomonas spp.	

[regional

differences

2]

CONTROL OF PERTUSSIS REMAIS A CHALLENGE

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Background and aim: *Pertussis* is a serious disease in infants and in spite of available vaccination continues to be high at various ages. The aim of this study was to analyze the profile of *pertussis* in children hospitalized in a referral hospital in Sao Paulo, Brazil.

Methods: The study was retrospective analysis of medical records of confirmed cases of *pertussis* in children 0 to 15 years old hospitalized from January 2000 to December 2008 at the Institute of Infectious Diseases Emilio Ribas, Sao Paulo, Brazil.

The criteria used to confirm *pertussis* were:

1. Clinical (clinical manifestations and leukocytosis over 20,000 cells/mm³, with absolute lymphocytosis),
2. Clinical and Epidemiological (transmission by suspected household or close contacts),
3. Positive Culture.

Results: From the 22 suspected cases, 16 were confirmed: 13 below 12 months (m) of age; 2 from 12 to 24m, 1 with 36m. Eight cases (50%) had clinical and epidemiological criteria, 7 cases (87.5%) below 12m. Two cases and one household contact (mother) were confirmed by culture. Nine children (56%) had adequate vaccination for age (7 below 12m), 4 incomplete vaccination, 2 with no vaccination, 1 vaccination status unknown. Two children with 2m complicated with convulsions, bronchospasms and atelectasis.

Conclusions: In spite of the high coverage of primary *pertussis* vaccination by the government (> 95%), the incidence of *pertussis* continues to be higher in the young children; the close contact (especially adult) was probably the main vehicle of transmission. The clinical diagnostic still prevail due to the difficulty of performing cultures.

COULD IMMUNIZATION AGAINST HEPATITIS A BRING OUTBREAKS UNDER CONTROL AMONG CHILDREN IN ORPHANAGES?

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Background and aims: Hepatitis A is an acute infectious disease of the liver that can cause mild to severe illness. Hepatitis A immunization in Macedonia is not obligatory, despite the intermediate level of transmission. The most affected target are children from 5 to 18 years of age. The aim of this study is to present Hepatitis A outbreaks among children in orphanages as well as our hygiene and sanitary procedures to prevent epidemic outbreaks.

Method: Active epidemiological research, elaborated initial and final Information by the Department for Epidemiology at the Centre for Public Health-Skopje, as well as laboratory examination samples.

Result: From 21.08.2009 until 26.10.2009, in an orphanage with 80 children, we registered 22 (27, 5%) cases of Hepatitis A. The disease was detected among children between 5 to 18 years of age. After the first two cases, in order to prevent the outbreaks of Hepatitis A, 130 blood samples were examined for AST-GOT (U/L) ALT-GPT (U/L) twice, during which 9 children (without symptoms) were detected. After a couple of days, 6 of them developed the symptoms, whereas 3 children were asymptomatic.

Conclusion: Outbreaks of Hepatitis A continue to occur, despite all epidemiological measures. The outbreaks could not be brought under control because of the close contact of the children and the three asymptomatic cases. After the first three cases, we suggested a Hepatitis A immunization for all children, but the experts were undecided whether children should be vaccinated during outbreaks of Hepatitis A.

IS RESPIRATORY PAPILLOMATOSIS - FOCAL DISEASE?**S. Bakanov***Clinic 'Snegiri', Chelyabinsk, Russia*

Respiratory papillomatosis (RP) and its most aggressive form of recurrent respiratory papillomatosis (RRP) is severe, incapacitating and poorly-predicted disease. Neither patients with RP nor medical professionals treating with this pathology are satisfied with the therapy outcomes. Thus, many medical, social, juridical and financial problems have arisen. We have charted Chelyabinsk region and Chelyabinsk city showing the incidence of RP disease. In accordance with our findings we consider that it is difficult to judge the incidence of RP diseases on the regional territory (too little cases). Nevertheless we have found out an interesting phenomenon while analyzing the incidence of disease in Chelyabinsk City, i.e. in the place of compact population residence. The cases of RP on the map of Chelyabinsk were spread compactly enough forming peculiar "foci". It's interesting that these "foci" were localized in the city areas with poor ecological environment. The incidence of RP in children is known to be the most informative criterion while assessment of ecological welfare. From the point of view of physiology the biological significance of the factors is determined not only by the amount of exposure but by the organism tolerance, the resources of its regulatory systems. The only effective way of prevention and preventive therapy of ecopathology is to form children's groups which are susceptible and resistant to xenobiotics. Ecopathogenic exposure was proved to be integral. A number of diseases are known to be the "markers" of the ecologically unfavourable territory (atopical dermatitis, bronchial asthma, malignant tumors, etc.). Is RP such a marker?

INFECTION WITH RESPIRATORY SYNCYTIAL VÍRUS OVER THE YEARS - HOSPITAL SANTO ANDRÉ, LEIRIA 2005-2009

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Background: Respiratory syncytial virus (RSV) is the leading cause of respiratory infection in the first 2 years of life. It has seasonal variation and greater prevalence in colder months. Prophylaxis with monoclonal antibody (Palivizumab) can prevent these infections in the most vulnerable population. Administration of Palivizumab in Hospital Santo André (HSA) is carried out monthly from September to March.

Aims: To relate local temperatures with RSV bronchiolitis and to determine whether this period coincides with the protection given to vulnerable groups by administering Palivizumab.

Methods: Retrospective descriptive study of children with bronchiolitis who had used HSA between October 2005 and April 2009. Relation with mean temperatures in each month. VSR season: period between October and April of the next year.

Results: There were 9233 bronchiolitis (7914 in RSV seasons). The greatest number of bronchiolitis was in 2006/2007 (2154 cases) but it was in 2005/2006 and 2008/2009 that we had the largest number of RSV positive - in those 2 seasons occurred the lowest temperatures. Most RSV positive bronchiolitis were in January. There was a considerable number of RSV positive in February, March and December, unlike October and November, with only a few cases. These 2 months are included in database administration Palivizumab.

Conclusions: As expected, the majority of bronchiolitis occurred in winter; it was January (with the lowest temperatures) that showed the highest number of RSV infections. There was little RSV bronchiolitis in October and November, which raises questions about whether the onset of Palivizumab should begin later.

MUCORMYCOSIS IN 2 YEAR OLD HEALTHY CHILD**D. Bhat¹, A. Gupta², R. Josan¹***¹Pediatrics, ²Plastic Surgery, Dayanand Medical College, Ludhiana, India*

Mucormycosis is an opportunistic infection. It is commonly found in diseased, debilitated, diabetic, immunocompromised patients. Early diagnosis is difficult and requires a very high degree of suspicion. Recommended mainstay of treatment has been amphotericin B and extensive surgical debridement. We share our experience of a case of mucormycosis in apparently healthy child.

A two-year old male child was referred to our hospital with ulcer on the right fore-arm since 25 days. He had a small (pea-sized) ulcer to begin with. The size of ulcer gradually progressed and started to ooze pus. Outside I & D was performed and IV antibiotics started but child kept on worsening. In our hospital debridement of the wound was done and sample was sent for histopathological examination, which showed mucormycosis. The patient was started on Amphotericin B lipid complex. However patient had to be ventilated and expired on day 9 of hospitalization.

In this child there was no history of any trauma in past.

PERSISTENT MULTI-RESISTANT STENOTROPHOMONAS MALTOPHILIA BACTEREMIA IN A CHILD WITH LEUKEMIA ON EXTRACORPOREAL MEMBRANE OXYGENATION

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Background: *Stenotrophomonas maltophilia*; an emerging multi-resistant nosocomial pathogen causes substantial morbidity and mortality in immunocompromised hosts. There are few reports of successful treatment in patients on extracorporeal membrane oxygenation (ECMO).

Method: Case report

Results: A 6-year old boy with acute myeloid leukemia (M4) developed neutropenic fever following chemotherapy from *Streptococcus mitis* septicemia with multi-system organ failure. He initially responded to supportive therapy but as his neutropenia resolved, developed ventilator-associated pneumonia and refractory acute respiratory distress syndrome requiring venovenous ECMO. *Stenotrophomonas maltophilia* was isolated from respiratory and blood cultures. The blood isolate was multi-resistant and only sensitive to trimethoprim-sulfamethoxazole (TMP-SMX) and polymyxin-B. He had persistent *Stenotrophomonas maltophilia* bacteremia (34 days) with the blood isolates becoming resistant to TMP-SMX. Multi-resistant isolates were also found from the ECMO circuit. With heparinisation on ECMO (target activated clotting time of 180 to 200 seconds), there was an unacceptably high risk of bleeding that prevented removal of CVCs. He was treated with combined TMP-SMX and polymyxin-B. He has since recovered. His blood cultures have remained negative after 49 days of polymyxin-B.

Conclusion: This case highlights the difficulties in managing multi-resistant nosocomial infections in patients on ECMO with its requirement for aggressive heparinisation and concomitant risk of removing potentially infected CVCs. The multi-resistant bacteremia in this immunocompromised child was controlled with combination therapy of TMP-SMX and polymyxin-B. Strategies have to be developed to prevent and treat these infections in our increasingly vulnerable patients.

FLUCONAZOLE AND AMPHOTERICIN-B RESISTANT CANDIDA CIFFERRI: AN UNKNOWN CAUSE OF SYSTEMIC MYCOSIS IN A CHILD

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Introduction: *Candida cifferri*, which was known as an agent of superficial yeast infection and onychomycosis, had been rarely reported to be isolated as an agent of candidemia.

Case: We report a rare candidemia case due to *Candida cifferri* in a 8- year-old child in which isolated *Candida* species were resistant to both to amphotericin-B, fluconazole and caspofungin but sensitive to voriconazole. Although *Candida cifferri* isolated in our case was sensitive to voriconazole in vitro, unfortunately we could not able to observe its in vivo activity , since our patient died before the yeast isolation in the culture.

Conclusion: Up to now, limited data about systemic infections due to *Candida cifferri* was present. Isolated *Candida cifferri* strains were reported to have different resistance features. In conclusion although compared to other non-*albicans* candidas such as *C. glabrata*, *C. parapsilosis*, and *C. tropicalis*, *Candida cifferri* is a rare cause of candidemia, it has greater importance with its resistance patterns to antifungal therapies.

RANGE OF CLINICAL FEATURES BETWEEN ROTA AND NON-ROTA GASTROENTERITIS IN CHILDREN UNDER 5 YEARS OLD: A RETROSPECTIVE STUDY

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Aim: To study the clinical features between Rota and non-Rota gastroenteritis in children under 5 years old.

Method and material: Children less than 5 years old who were admitted for symptoms of gastroenteritis were recorded from October 2008 to July 2009. The following fields were recorded: age, gender, duration of diarrhea, duration of hospital stay, fever, presence of vomiting, CRP, faecal test for Rotavirus, stool cultures for bacteria, presence of pathological elements in stools (blood, mucous), dehydration. Statistical analysis was performed using t-test and chi-squared test.

Results: 158 children were recorded (84 males and 74 females). 44.3% (70/158) were positive for rotavirus infection with negative stool cultures. Positive cultures were recorded in 18 cases (11.4%) with negative Rotavirus test (6 cases *Campylobacter spp.* and 12 cases *Salmonella spp.*). Significant difference was observed between Rotavirus gastroenteritis and non-Rotavirus gastroenteritis in age (18.8±12.7 months vs 28.6±16.4 months, $p < 0.001$) and duration of fever (2.26±1.6 days vs 1.4±1.3 days, $p = 0.001$). The presence of pathological elements in stools was correlated with non-Rotavirus gastroenteritis ($\chi^2 = 6.45$, $df = 1$, $p = 0.01$). Cases with positive stool cultures were associated with increased CRP (71.1±16.8 vs 15.3±14.5, $p < 0.001$) and greater maximum fever (39.1±0.5°C vs 38.2±1.0, $p = 0.01$).

Conclusion: Rotavirus gastroenteritis was associated with smaller age, shorter duration of fever and no pathological elements in stools. Bacterial gastroenteritis was associated with greater maximum fever, pathological elements in stools and increased CRP. State of dehydration, duration of hospital stay and the presence of vomiting were not associated with any type of gastroenteritis.

INFORMATION ON WHO RECOMMENDATIONS ON MANAGEMENT OF ACUTE GASTROENTERITIS IN MEDICAL STAFF OF GEORGIA

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Aim of this study was to determine the information on WHO recommendations on treatment of acute gastroenteritis in regions. The epidemiological study (one to one interview) was performed in randomly selected 5 regional hospitals and outpatient clinics. Special questionnaire was elaborated based on the WHO guideline, that covered issues of identifying diarrhea, causes, indications of antibiotic use, signs pointing severity of dehydration and rehydration therapy.

Total 460 interviews were analyzed (missed 27), 154 -from hospitals and 306 - from outpatient clinics (47, 8 % doctors, 52, 2 % nurses). Approximately 90 % of physicians from outpatient clinics followed WHO recommendations about using ORS for rehydration, but in case of moderate dehydration 43, 4% refer the patients to hospital. Only 67, 8 % of hospital staff correctly defined. In cases of moderate dehydration in hospitals was frequently (48, 7 %) used intravenous infusion instead of oral rehydration. In cases of oral rehydration only 19, 4 % of patients were rehydrated rapidly. In 39 % of hospitalized patients was used lactose free formula or diet. Study revealed that antibiotics are more widely used then it's recommended. In 43, 4 % antibiotics were used without indication.

The results of the study emphasized those basic principles of WHICH recommendations are followed, more in outpatient clinics. This may be explained by training of representatives of outpatient clinics on IMCI program. The results show that it is important further training of outpatient clinics and starting the training in hospitals to implement WHO recommendations into practice.

CARDIOPULMONARY COLLAPSE SECONDARY TO SUBCLINICAL ROTAVIRUS INFECTION**I.A.N. Teo¹, J.H. Lee²***¹Department of Paediatrics, ²Department of Intensive Care Unit, KK Women's and Children's Hospital, Singapore, Singapore*

Background: In the past, rotavirus infection is known to be the leading cause of acute gastroenteritis death in neonatal and children, which is thought to be secondary to severe dehydration leading to rapid circulatory collapse. Previous case reports have described rotavirus causing meningoencephalitis, pneumonitis and myocarditis. All these cases have clinical syndrome of diarrhoea. Till date, there are no reports with regards to subclinical rotavirus infection leading to cardiopulmonary collapse.

Methods: We report two cases of cardiopulmonary collapse secondary to subclinical rotavirus infection.

Results: Both cases were children less than 6 months of age. Both had cardiopulmonary collapse outside the hospital and required more than 45 minutes of resuscitation before return of spontaneous rhythm returned. Both patients did not have diarrhea prior to the cardiopulmonary collapse. A thorough infective screen showed presence of rotavirus antigen in the stools for both patients; with no other viruses or bacteria isolated. Both patients suffered severe hypoxic ischemic encephalopathy and medical care was withdrawn in view of medical futility.

Conclusive: These case reports add to the evidence that rotavirus infection may sometimes not be only isolated to the gastrointestinal tract; instead it may be a systemic illness which may lead to severe morbidity and mortality.

ACUTE ACALCULOUS CHOLECYSTITIS DUE TO SALMONELLA ENTERITIDIS IN A CHILD WITH INFLUENZA A H1N1V: A CASE REPORT

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Introduction: Acute acalculous cholecystitis is uncommon in pediatric age group and is a rare complication of nontyphoidal salmonella enterocolitis. Dual infection with influenza A H1N1v has not been previously described.

Case report: A 10-year-old previous healthy boy had a flu syndrome (fever, headache, myalgia and abdominal pain). RT-PCR for influenza A subtype H1N1v positive but oseltamivir was not performed. Five days later he was admitted by persisting symptoms and onset of vomiting and profuse diarrhea. He was mild toxic appearing, with severe dehydration, acute prerenal failure, oliguria and hypokalemia. Leukocytes count was $9400/\text{mm}^3$, with 84,8% neutrophils and C-reactive protein 32,14 mg/dL. Past medical history revealed ingestion of custard. Analgesics, antipyretics and fluidotherapy were started. Stool culture yielded Salmonella enteritidis.

On day 9 of disease he got worsened with tender upper abdomen and Murphy's sign. Abdominal ultrasound disclosed distended gallbladder with moderate thickened wall and an adenopathy in relation with neck gallbladder. Cefotaxime, gentamicin and metronidazole were started. Vomits and abdominal pain persisted for 5 days and he was discharged after 10 days with good evolution.

Discussion: The etiology of the acalculous cholecystitis was probably multifactorial resulting from fever, dehydration, analgesics and extended fasting. Compression by hyperplastic lymph node by Influenza A H1N1v was a probable additional factor and we question if oseltamivir treatment would have affected the prognosis.

CHRONIC PANCREATITIS DIAGNOSED DUE TO ASCARIS LUMBRICOIDES INFECTION**O. Falup-Pecurariu**, M. Mitrica, C. Popa, S. Florian, C. Pascu, C. Otelea, C. Falup-Pecurariu*Department of Pediatrics, Children's Hospital, Faculty of Medicine, Transilvania University, Brasov, Romania*

Background: Chronic pancreatitis appears usually after an acute episode of infection in children that is due to parasites or viruses.

Aim of the study: Case report of chronic pancreatitis due to repeated ascaris lumbricoides infection.

Patient and method: Case report of a 6 years old girl admitted for vomiting, pain in the upper abdominal area, loss of appetite and failure to thrive.

She was twice admitted with acute gastroenteritis, at the second admittance stool culture was positive for ascaris lumbricoides and ultrasound showed splenomegaly. Third admittance for fever, general state poor, pallor with signs of dehydration, normal pulmonary and heart activity, tender abdomen, especially in the epigastric area, pain accentuated after meals, persistent vomiting. Stool culture positive for ascaris lumbricoides, amylase values were 524 U/l and after 334 U/l.

Abdominal ultrasound revealed an enlarged pancreatic area occupied by a inhomogenous mass. At the second one the pancreas had diameter of the head 1.26 cm, body 2 cm, tail 1.3 cm, having hyperechogenic and transonic images, dilated Wirsung, splenomegaly. The image suggested a chronic pancreatitis in an acute phase with portal hypertension. The abdominal CT revealed the same image as ultrasound. She underwent medical and surgical monitoring. MRI colangiopancreatography confirmed the diagnoses. Despite treatment the evolution was unfavorable. Complex treatment was started but every time feeding was started colicky pain restarted. She underwent surgical intervention.

Conclusion: This case report of chronic pancreatitis suggest a possible link to the ascaris lumbricoides infection.

ADENOVIRUS GASTROENTERITIS IN ROMANIAN CHILDREN - EVOLUTIVE CORRELATIONS

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Background and aim: There are multiple reports on rotavirus gastroenteritis (RGE) in Romanian children, but few on adenovirus enteric-infection (AVE). Our aim was to describe course and outcome of AVE in a Romanian tertiary referral unit.

Methods: Retrospective analysis of patients admitted or treated as outpatients in Emergency Unit (EU) of IMCC during five months (1st Oct 2008 -1st March 2009) in the cold season.

Results: 13.762 patients were EU-evaluated and 3432 were admitted. 23.9% of presented and 31% of admitted children had acute enteritis. 3282 stool samples were analyzed: 2204 stool cultures and 1078 rapid viral detection tests. For viral detection were used rapid immuno-chromatographic assays (Coris BioConcept and R-Biopharm).

91.1% were combi-tests and only 8.35% for rotavirus, alone.

Rotavirus tested positive in 35.25%, adenovirus in 3.46% (34 cases). 29.41% of positive tests for adenovirus were positive for both (rota&adenovirus). Clinical features of AVE were dominated by fever (94.12%), diarrhea (watery in 82.35% and bloody in 17.65%), vomiting (91.17%).

In spite of being more frequently admitted (24 of 34 positive tests - 58.82%), no significant clinical differences were noted versus RVE. Length of in-hospital stay was 3.8+/-1.5 days for AVE vs. 4.4+/-2.1 for RVE. No death occurred.

Conclusions:

1. Although rare (3.5%) AVE is the second most frequent cause of viral enteritis in children.
2. One third of AVE patients tested positive for both rotavirus and adenovirus.
3. Course and outcome of AVE were not different from RVE.
4. Extensive dual testing for RVE+AVE does not seem to be cost-efficient.

HIV/AIDS KNOWLEDGE AND RISK BEHAVIOR AMONG CHILDREN ACCOMMODATED IN INSTITUTIONS FOR CHILDREN WITHOUT PARENTAL CARE IN SERBIA

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Background and aims: Serbia, as a country in transition, faces not only socio-economic problems but also rapid changes in behavior, especially among adolescents. The aim of this study was to analyze difference in knowledge and behavior of children aged 12-14 and 15-19 years, accommodated in institutions for children without parental care, in relation to risk of HIV infection.

Methods: By the use of random sampling procedure in this cross-sectional study were included 483 children 12-19 years old (78% of all children without parents in Serbia, in 2007) who were accommodated, at least one month before interview, in institutions for children without parental care. In the statistical analysis chi square test was used.

Results: The mean age at first sexual intercourse was 11.8 for children aged 12-14 and 14.9 for children aged 15-19 years. The use of condom at last sexual intercourse with irregular sexual partner was reported by 70.8% of children 15-19 years old during the last year. Only two of younger children had irregular sexual partners and no one of them used condom. The difference between these two age groups was statistically significant. Correct answers to 5 questions about HIV transmission were significantly more frequent among children 15-19 years old (34.6%) than among younger children (15.5%). In previously HIV preventive programs were significantly more frequently included children 15-19 years old (45.4%) than younger children (12.2%).

Conclusions: It can be concluded that HIV/AIDS preventive programs are especially necessary for children without parents aged 12 to 14 years.

ANTIRETROVIRAL RESISTANCE IN HIV-1 INFECTED SAUDI CHILDREN FAILING HIGHLY ACTIVE ANTIRETROVIRAL THERAPY (HAART)

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Background: Limited data are available on antiretroviral resistance in pediatric HIV-infected children and no information existed from Saudi Arabia. The aim of the study was to analyze prevalence of HIV-1-drug resistance among HIV-1-infected Saudi children failing HAART.

Methods: Prevalence of genotypic resistance was estimated retrospectively between July 2006 and January 2009 in 22 treated children who experienced virologic failure (with HIV-1-RNA>1000 copies/ml) followed-up King Faisal Specialist Hospital and Research Center in Riyadh. All patients received 3-drug regimens that included protease inhibitors (PI) or non-nucleoside reverse transcriptase (RT) inhibitors (NNRTI).

Results: Among 22 children with resistance testing, prevalence of resistance to any drug was 86.4%.

Twenty four mutations were detected within PI and fourteen in the RT region. PI M36I was present in 80% of strains. RT M184V was present in 70% of strains and was associated with cross-resistance to at least two nucleoside RT inhibitors (Lamivudine and emtricitabine). RT K103N was found to confer clinically significant efavirenz resistant. Antiretroviral resistant were not associated with geographic region and CDC status.

The group of study children respond satisfactory to the genotype guided treated after long follow-up.

Conclusion: Antiretroviral resistance is common among HIV-infected Saudi Children. The frequent mutations were PI M36I and RT M184V. Resistance testing should be considered to help to guide the choice of new drugs for children who experience virologic failure.

EVOLUTION OF VASCULAR TUMORS WITH FAST METASTASIS IN A YOUNG OF HIV INFECTED DIAGNOSTIC PROBLEMS. CASES PRESENTATION

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Background: It is known that the frequency of tumors grow at the same time increase survival in patients with HIV can sometimes take unpredictable forms and evolutions

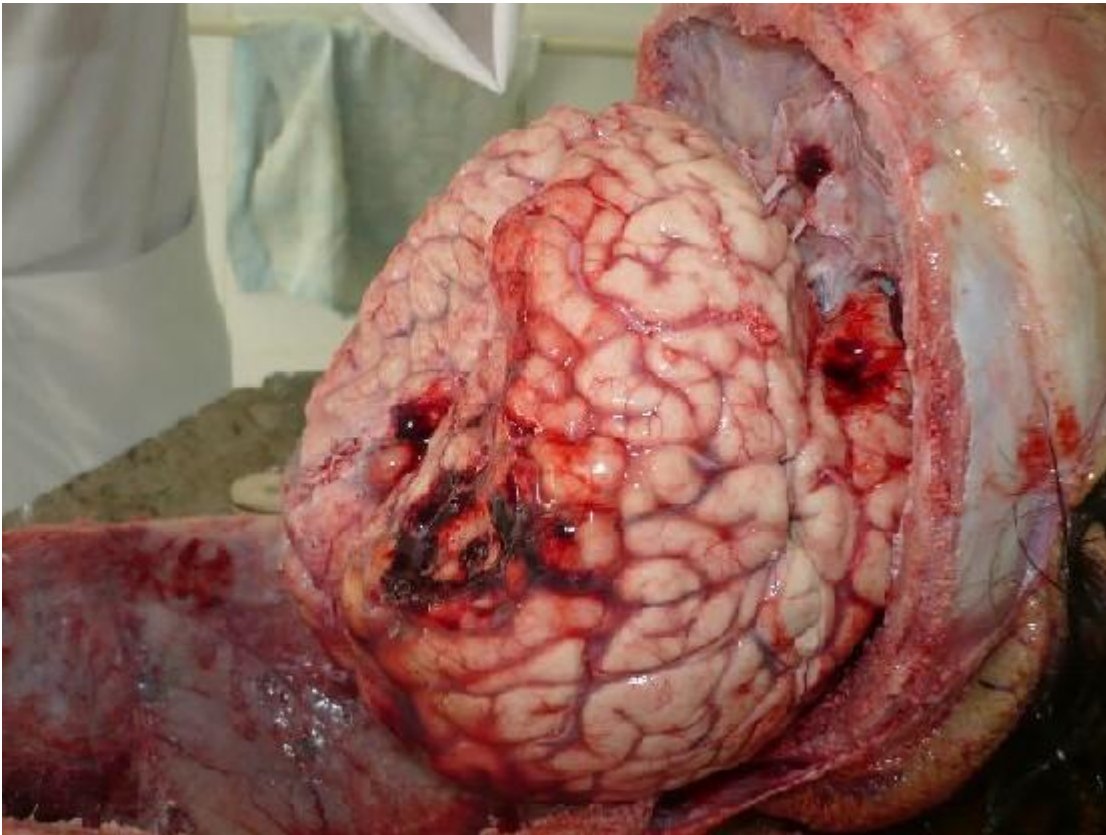
Objectives: We present the case of a young man with vascular tumor with visceral metastases fulminant onset Young person with AIDS C3 is hospitalizations for headache and convulsions. Appearance of subcutaneous nodules of low consistency in chest, nodule which the patient exercised pressure action of determining the occurrence of bruising break (fig1). After 2 days the patient developed paraplegia labeled as flaccid paraplegia, although clinical neurological examination has revealed ROT present bilaterally. Was required to make emergency MRI toracolombara column. In the next 2 days the patient's neurological status is degraded rapidly patient entering a coma and dies the next day anatomic pathological examination were observed macroscopic changes in the type of formations present pancreas vascular, liver, kidney.

Discussion: Tumor formation situated between the cranial cavity and duramater, compress cerebral hemispheresfig2. Note the same type of disseminated tumor in the liver fig3, pancreas, kidney was observed. Evolution fulminant vascular tumor with rapid metastasis did not allow rapid diagnosis and effective etiological treatment while the establishment Surgery did not get It should be helped not to reach such a compression of cerebral hemispheres with drastic consequences on the patient.

Conclusions: There is evidence in the literature that HAART therapy may interfere with the natural history of malignant. All HIV-infected patients with malignancy should be treated with HAART in combination with standard therapy of malignancy.



[fig1]



[fig2]



[fig 3]

MACROPHAGE ACTIVATION SYNDROME IN HIV INFECTION**N. Neves**¹, A. Pedro², R. Ferreira³, G. Rocha¹¹*Consulta Doenças Infecciosas, ²Hepatologia, ³Unidade de Gastroenterologia, Hospital Pediátrico, Coimbra, Portugal*

Introduction: Macrophage Activation Syndrome (MAS) is characterized by activation of macrophages and histiocytes with phagocytosis of blood cells and precursors. Should be evoked in febrile patient with hepatosplenomegaly and systemic involvement, excessive bleeding, increased ferritin, gamma globulins, triglycerides, and hypofibrinogenemia. The HIV and opportunistic infections are a classic combination.

Case report: Six year old child with HIV, short bowel secondary to bowel resection by Volvo in the 1st month of life, dependent on parenteral nutrition (PN). Cholestatic hepatitis in February 2008, accompanied by homogeneous hepatosplenomegaly, frequent epistaxis, normochromic anemia (6.6g/dl), thrombocytopenia (107000/uL), increased ferritin (854ng/ml), hypergammaglobulinemia (22.7g / dL) and hypofibrinogenemia (226mg/dl), hypertriglyceridemia (4 mmol / L). Decrease of NK-CD56 + (1/ μ L). Liver biopsy with lesions suggestive of toxicity of PN, no improvement with the usual measures. Bone marrow showed histiocytes with phagocytosed material not identified. Microbiological investigation in bone marrow and liver biopsy excluded infection by bacteria, fungi, mycobacteria, *Cryptococcus neoformans*, EBV, CMV and HHV6. Corticotherapy was performed with improvement of laboratorial parameters and resolution of hepatosplenomegaly, maintaining markers of cytolysis and cholestasis, so in March 2009, in spite of CD4 and HIV viral loads triple antiretroviral therapy was introduced. Favourable outcome, with negative viral load after 4 months of therapy and laboratory resolution of cholestatic hepatitis.

Comments: The combination of MAS and HIV infection occurs most often secondary to opportunistic infections and malignancies. Intermediate clinical histiocytic activation has been described associated with HIV infection alone. The response to steroids and afterwards to the antiretroviral therapy confirmed the diagnosis.

A VARIETY OF HIV-1 SUBTYPES AT CHILDREN ON HAART**V. Eremin**¹, E. Gasich¹, I. Karpov²¹*Clinical Virology, Research Practical Center for Epidemiology & Microbiology,* ²*Infection Diseases, Byelaratian State Medical University, Minsk, Belarus***Background:** The subtype And HIV-1 remains dominant at a HIV-infected children in Belarus.**Methods:** Plasma of a HIV infected patient underwent sequencing of the pol gene using the ViroSeq HIV-1 v2.0 genotyping system and the Stanford University Drug Resistance database for result interpretation, SeqScape, BioEdit, MEGA4.**Results:** 10590 cases of a HIV-infection (109,5 per 100th population) are registered for December, 1st, 2009 in Belarus. Majority of a HIV-infected are young men aged 15 - 29 years (67,1%). 1 490 children have been born to HIV-infected mothers during the period from 1987 to 01.12.2009. To 151 children the diagnosis "HIV-infection" is confirmed, 8 children have died. All children requiring therapy receive HAART. Unfortunately, because of available breaks in reception of preparations are resistant strains of HIV found out to different classes of preparations in some of children. Following mutations have been revealed:PI - M46I, L90M, I54V, V82F, I84V. NRTI resistance mutations - D67N, T69I,T69Xi, K70R, V75M, V118I, M184V, L210W, T215Y K219Q; NNRTI resistance mutations - K101H, G190A, K103NS. In 75% of cases the subtype A, and in 25% - G and CRF_A/B HIV-1 have been revealed at children.**Conclusion:** Introduction of a method of detection of HIV resistance to ARV preparations in Belarus has allowed us to optimize approaches to treatment of HIV infected patients, guiding changes in preparations and regimens for treatment. The resistance testing equipment has been obtained through means donated by the Global Fund.**Keywords:** HIV drug resistance; PI; NRTI; NNRTI, HIV subtypes

ANTIRETROVIRAL THERAPY IN CHILDREN WITH HIV INFECTION**A. Fernandes, M.J. Calix, L. Marques***Hospital Maria Pia, Centro Hospitalar do Porto, Oporto, Portugal*

Introduction: Combination antiretroviral therapy changed HIV infection to a treatable, chronic disease of childhood and adolescence. Adherence to a life-long therapy has become a major problem. The aim of this study is to assess the effectiveness of ARV treatment, the number of regimens used and the compliance in HIV-infected children followed in our Hospital.

Methods: Retrospective chart analysis of children and adolescents with HIV infection followed since 1998.

Results: Twenty-eight patients were included with a median follow-up of 7 years. The median age was 8 years (5 months at diagnosis). Before beginning treatment the majority presented a viral load over 100 000 copies/mL, 37% were in stage N1 and 18% in stage C3. 29% received only one regimen; 25% needed two regimens and 21% four. Only one received five. The majority switched therapy for virologic failure. Most children received an association with two NRTI and PI and adolescents received two NRTI and NNRTI. Toxicity was present in 30%. Gastrointestinal intolerance and hypercholesterolemia were the major side effects. Bad compliance was recorded in 37%, viral resistances in 39%. There was a correlation between bad compliance and regimen switching and between bad compliance and occurrence of viral resistances. There were no deaths and no new defining AIDS's diseases after beginning of treatment.

Discussion: The aims of antiretroviral therapy to achieve and sustain full HIV RNA viral load suppression, while minimising the development of drug resistance and drug toxicity are challenging. Adherence is a critical issue in the treatment of HIV patients.

ASSESSMENT OF KAWASAKI DISEASE PATIENTS FAILING TO RESPOND TO INTRAVENOUS IMMUNOGLOBULIN

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Background: Prediction of IVIG non-response before IVIG infusion has some limitations to assess the severity of ongoing inflammation in KD. We determined pre- and post-treatment characteristics of intravenous immunoglobulin (IVIG) non-responders in patients with Kawasaki disease (KD).

Methods: We evaluated 229 consecutive KD patients, treated with 2 g/kg of IVIG, at a single center over 8 years. Those who had persistent fever > 24 hours after IVIG infusion made up the 23 IVIG non-responders (10%); the remaining 206 cases defervesced without fever recurrence.

Results: Demographic and clinical characteristics were similar in both groups. The IVIG non-responders had a longer overall duration of fever ($P < 0.001$) and a higher incidence of coronary artery lesions (CAL) (14/23, 61% vs. 37/206, 18%, $P < 0.001$). Prior to IVIG treatment, non-responders had significantly higher neutrophil differential and CRP and lower cholesterol ($P \leq 0.002$, all comparisons). Of the laboratory parameters measured within 24 hours after the IVIG infusion, a WBC count of $> 13,100/\mu\text{L}$, neutrophil differential of $> 51\%$ and total protein value of < 7.2 g/dL showed reasonable sensitivity (91%, 91% and 64%, respectively) as independent characteristics of IVIG non-response on multivariate analysis.

Conclusion: IVIG non-response is correlated with both pre- and post-IVIG changes in inflammatory indices. Assessment of laboratory parameters before and shortly after IVIG may assist in identifying those with the greatest and most sustained inflammation who are at greatest risk of CA damage and may benefit from additional treatments.

POSTINFECTIOUS PURPURA FULMINANS SECONDARY TO VARICELLA INFECTION**G. Januário**¹, S. Ramroop², D.V. Shingadia², V. Novelli²¹*Pediatric Department, Hospital Pediátrico de Coimbra, Coimbra, Portugal,* ²*Infectious Diseases Department, Great Ormond Street Hospital, London, UK*

Background and aims: Varicella can be severe and life-threatening. We report a case of purpura fulminans (PF) following varicella infection in a healthy child and discuss its diagnosis, management and prognosis.

Methods: We describe a case of PF following varicella.

Results: A 6 year- old female presented to our hospital on the 7th day of varicella because of severe limb pain and ecchymotic patches in both her limbs. She was treated with fresh frozen plasma and platelets because of a clotting derangement. Protein C (PC) levels were normal but free protein S (PS) was very low. Anti-PS antibodies were detected in high levels while the anti-thrombin was normal and the dilute Russell viper venom test and the anti-cardiolipin autoantibodies were negative. Assays for factor VIII, XII and activated PC resistance were normal and common thrombotic mutations were negative. Diagnosis of PF due to an acquired PS deficiency secondary to varicella was made and plasmapheresis and IV heparin infusion were started. Due to the development of a compartmental syndrome she required fasciotomies of both lower limbs and remained on daily plasmapheresis for 7 days until PS levels were stable. Blood cultures were always negative and improvement in her legs was noticed on daily basis. Since discharge she received split-thickness skin grafts and her PS levels have been stable.

Conclusions: Although exceptionally rare, PF is one of the most spectacular and feared complications of varicella. Intensive care management and timely surgery can be successful in improving the outcome and prevent life-long morbidity.

PRIMARY IMMUNODEFICIENCY PRESENTING AS A SEVERE DISSEMINATED CMV INFECTION

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Introduction: Cytomegalovirus (CMV) is a human herpes virus that has a high worldwide incidence. It's one of the most important opportunistic pathogen in immunocompromised patients and is transmitted through contaminated body fluids, with either vertical or person-to-person transmission.

In newborns and immunocompromised patients, CMV infection is frequently symptomatic, with multiorgan involvement and even a fatal outcome.

Case report: We present a 4 month-old boy, who at 3 months of age, started a failure to thrive and diarrhoea. By 4 months he began fever, worsening diarrhoea and tachypnea without cyanosis, cough or auscultatory changes.

Blood analysis showed pancytopenia that progressively improved, although lymphopenia remained. The immunological study evidenced agammaglobulinemia and the study of lymphocyte populations showed a significant decrease in CD3+ (T cells) and CD19+ (B cells) and a increase in CD16+&56+ (NK cells), suggesting a severe combined immunodeficiency (B-T-NK+).

Chest X-ray revealed a hypoplastic thymus and bilateral interstitial infiltration suggestive of interstitial pneumonitis. Ganciclovir was prescribed for a possible CMV infection, which was later confirmed by a strongly positive PCR in blood (4.6×10^6 copies/ml), faeces, urine and bronchoalveolar lavage. Pneumocystis jiroveci investigation was negative.

Ophthalmological examination revealed a perivascular retinitis typical of CMV.

After ganciclovir and immunoglobulin intravenous treatment, there was a clinical improvement with tachypnea and eye lesions regression.

Genetic study showed a RAG2 mutation.

Conclusion: Although frequently founded in immunocompromised, CMV's initial infection in severe combined immunodeficiency is uncommon.

Beside Pneumocystis jiroveci, CMV investigation is also mandatory in an early evaluation.

UNENCAPSULATED *HAEMOPHILUS INFLUENZAE* STRAINS AS A CAUSE OF MENINGITIS - CASE REPORT

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Background and aims: Invasive bacterial diseases caused by unencapsulated types of *Haemophilus influenzae* (NTHI - nontypable *Haemophilus influenzae*) are rare. We present a case of a boy who twice went down with meningitis caused by NTHI.

Methods:

1. Analysis of two incidents of bacterial meningitis which occurred in 10th and 22nd months of the boy's life.
2. Culturing and molecular analysis (PCR) of NTHI strains obtained from cerebrospinal fluid (CSF) and blood.

Results: From early infancy the boy was suffering from recurrent otitis media then followed by otitis media with infusion. Neither humoral nor cellular immunodeficiency was found.

The first incidence of meningitis occurred in 10th month of the child's life. Until then the child had been vaccinated with 3 doses of anti-Hib vaccine. NTHI was isolated from CSF. After a year, at 22 months of age, the boy went down with bacterial meningitis for the second time (2 months after the 4th dose of anti-Hib vaccine). Again, NTHI was isolated both from blood and CSF. The isolates were compared using molecular methods (PCR). No affinity between them was found. After the second incidence of meningitis the boy was vaccinated with 10-valent pneumococcal vaccine (*Synflorix*), which may have positive impact on immunity against NTHI. 6-months of observation revealed no complications after treatment.

Conclusions: Unencapsulated *H. influenzae* etiology should be considered in childhood meningitis, even in children who received all doses of anti-Hib vaccines.

ACUTE MYELOID LEUKEMIA (AML) PRESENTING WITH ECTHYMA GANGRENOSUM AND FATAL PSEUDOMONAS AERUGINOSA SEPSIS

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Introduction: Almost every reported case of ecthyma gangrenosum (EG) in previously healthy children is associated with some type of immunocompromise.

Case report: A previous healthy 22-month old boy with unremarkable family history was admitted to the PICU with septic shock. Two days prior he had a fever of 40°C, a generalized maculopapular rash and a rapidly evolving ulcer on his left upper arm. On admission, he appeared lethargic, his BP: 60/40 mmHg, HR: 180/min, RR: 70/min, capillary refill time: 5secs. His results reflected pancytopenia (WBC: 1000/ul, Hgb: 9mg/dl, PLT: 155,000/ul), lactic acidosis and DIC. He was immediately intubated and mechanically ventilated and was given fluid resuscitation, inotropic support (intravenous adrenaline, dopamine and dobutamine), FFP, coagulation factors and blood transfusion. Empirical antibiotics were started with gentamycin and ceftazidime. All fluid cultures (blood, bronchial, CSF, skin lesion's) yielded *Pseudomonas Aeruginosa*, sensitive to the administered regimen. Due to the uncommon pathogen and the severe clinical presentation, a bone marrow biopsy was performed that established the diagnosis of AML (>80% atypical promyelocytes, M3 according to FAB classification). Within 2 days the necrotic lesions extended, occupying the face, trunk, upper and lower extremities, he developed MODS and was placed on a peritoneal lavage. Despite massive intensive care efforts the boy expired on the 4th day of hospitalization.

Conclusion: EG can be an early indication of an undetected malignancy. Prompt identification is crucial to initiate appropriate antipseudomonal therapy and to perform a thorough laboratory investigation, to rule out predisposing causes including congenital immunodeficiencies and cystic fibrosis.

SEROEPIDEMIOLOGICAL STUDY OF TOXOPLASMOSIS AMONG HIGH-SCHOOL GIRLS IN GONABAD -IRAN

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Background and aims: Toxoplasmosis is caused by the protozoan parasite *Toxoplasma gondii* and is frequently asymptomatic; in high risk population serological screening has been recommended to identify the non-immune individuals. Due to considerable prevalence of toxoplasmosis during childbearing age, identification of non-immune girls is necessary. The aim of this study was to determine the prevalence of toxoplasma-related IgG and IgM in high-school girls, and to detect factors that increase prevalence of the disease.

Methods: In this cross-sectional study, through cluster sampling method 240 blood samples were collected from high-school girls. A questionnaire which included demographic and some epidemiological factors were used for Data collection. IgG and IgM specific to toxoplasma gondii were detected using ELISA. The results obtained were analyzed using the chi-square to determine any relationship between the positive cases and the epidemiological factors.

Results: Out of 240 high-school girls 35 cases (%14.6) were positive for T.gondii specific IgG, none of the samples showed toxoplasma related IgM .

The statistical results showed a significant relationship between eating undercooked meat and raw vegetables.

There was no significant association between seropositive cases and other variables.

Conclusion: The findings of this study indicated that, to reduce toxoplasma gondii infection eating of well-cooked meat and avoid of eating fruits and vegetables if they are not cooked, washed, or peeled is necessary.

Keyword: Seroepidemiology, high-school girl , toxoplasma ,Gonabad.

VIRAL SCREENING BEFORE CARDIAC CATHETERIZATION IN CONGENITAL HEART DISEASE?

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Backgrounds and aims: Homodynamic catheters are widely reused mainly in developing countries where the costs of new devices are very high. Although viral serology is routinely screened prior to angiography, the significance of it is not clear. This study aims to evaluate the necessity of such screening in patients with congenital heart diseases.

Methods: In the present cross sectional study, 442 cases with congenital heart diseases that underwent cardiac catheterization in Imam Reza Hospital, Mashhad, Iran during 2001-2006 were enrolled. The viral markers of hepatitis B surface antigen and antibodies against hepatitis C, HIV and HTLV1, 2 were detected in all patients undergoing cardiac catheterization.

Results: Out of 442 patients with congenital heart diseases undergoing cardiac catheterization, 220 patients were female. The patients aged between six months to 39 years (mean 7.8 years). Screening of these patients showed that 6 (1.3%) of them were seropositive for HTLV1, 2, four (0.9%) for HBs Ag, four (0.9%) for HCV. None of the screened patients were HIV positive.

Conclusion: Positive viral tests were seen in few patients in the study. Considering the above findings if the cleaning and sterilization procedures are carried out properly, these tests should be considered just for high risk patients.

Keywords: Congenital heart disease-Viral screening-Catheterization.

ANNUAL RECORDING OF INFECTIONS AND INFECTIOUS DISEASES IN THE FRAME OF EPIDEMIOLOGIC MONITORING, GENERAL HOSPITAL OF VOLOS

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Background-aim: To detect and record individual cases, as well as epidemiologic elations during a period of one year, so that the appropriate measurements are taken both locally, and in the wider community.

Methods: Throughout 2004 we recorded all the-obligatory stated- diseases, in individuals of irrespective of age that visited or were admitted in the Ahiolopouleio General Volos Hospital (AGVH). A statement of illness was filled (transmitted aerogenically with droplets, anticipated by vaccination or transmitted through foods/water or from environmental source and animals).

Results: We recorded 539 cases of which 430 regarded massive infection from *Salmonella enteritidis* (s.e) (23-26/5/2004). The remaining cases: 28 (26%) regarded cases during the epidemiological monitoring for the 2004 Olympic Games, 81 (74%) regarded Infectious diseases during the rest of the year. The remaining recorded diseases were: Gastroenteritis from Salmonella (77), Brucellosis (13), Meningitis (7), Gastroenteritis from Shigella (3), Tuberculosis (3), Leishmaniasis (2) and (Mumbs, Rubella, Hepatitis B) (4). 36% of the cases were recorded during July-August, while 70% of the cases during July-October.

Conclusions: The medical services of the AGVH collaborated efficiently to face the extraordinary incident of food infection . The peak season of declared infectious diseases, coincides with the period of intensive epidemiologic monitoring, due to closer recording in view of the Olympic Games and due to seasonal or climatic conditions. The food-borne infections, referring mainly to Salmonella and Brucellosis, continue bothering our prefecture, drastic metres of prevention and strategies of intervention are needed for enlightenment of the population from experts and specialists.

STUDY OF 100 CULTURE RESULTS FROM DEVICE, SOLUTIONS AND HAND OF PERSONNEL IN EMAMREZA HOSPITAL MASHHAD IN NICU

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Background and aims: Infection is a common cause of neonatal death and nosocomial infection may increase neonatal death 11% at NICU. In this study we surveyed the result contamination of devices, solutions and personnel hands at NICU based on the type of bacteria. If there was contaminated device we take the serious steps for prevention of contaminating and its disinfection.

Methods: All devices and solutions which were related to neonates were studied during 2006 - 2007 at NICU of Emamreza hospital, neonatal research center of Mashhad University of medical science. Two samples were taken from all device and solutions and hand of personnel by head nurse weekly. Then the samples were transferred to laboratory and detecting kind of contamination. If the culture was positive, after disinfection of devices another's culture was taken.

Results: From 155 samples, 66 samples were sterile (42.6%) and 89 (57.4%) were contaminated. Common organisms were consisted of gram positive non pathogen organism (25/8%), staph Coagulate negative (12/9%) and staph Auras (6/5%). The most common contaminated samples were incubators, solutions and hand of personnel.

Conclusions: This study shows that the common contaminated organisms are the same as nosocomial organisms at NICU so hand washing of personnel and disinfecting of incubators are the main our policy in our hospital for decreasing nosocomial infection in NICU.

Keywords: Neonates, NICU, contamination, devices.

EVALUATION OF GROUP B STREPTOCOCCI COLONIZATION RATE IN PREGNANT WOMEN AND PREGNANCY OUTCOME (NEWBORN)

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Background: Group B streptococcus (GBS) is one of the most important bacteria in the majority maternal and neonatal infections. In addition this microorganism cause severe infections such chorioamnionitis, endometritis, bacteremia, septicemia and neonatal meningitis in mothers and neonates. GBS screening is one of the recommended strategies that has been mentioned by (CDC) during pregnancy.

Aim: Taking the importance of the issue in to our consideration, we decided to study the percentage of colonization of the microorganism in mother and neonate and its probable outcomes in order to show responsible factors and frequency of the colonization and its outcomes and more over to recommended practical approaches towards prevention of this infection.

Methods: 200 pregnant women who were admitted at the Ghaem Hospital, were involved in the study, the information of mother an neonate were mentioned in the questionnaire and cultures were taken from vaginal secretions of mother during delivery and secretions of umbilical cord in the post partum period.

Findings: The colonization in the pregnant women and neonates who studied was reported 6% and 5% respectively. All mothers of neonates who carried GBS were in the group of GBS carriers and all of them had premature rupture of membrane (PROM) 18 hours before delivery.

Conclusion: There is a meaningful relationship between maternal and neonatal GBS colonization and more over 80% of neonates among GBS carrier mothers were colonized by GBS. Colonization rate in mother an neonate were 11%.

Keywords: GBS-Vagina-colonization- partum, pregnant women.

ASSESSMENT NEONATAL SEPSIS IN BOSNIA AND HERZEGOVINA

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Background: Neonatal sepsis is an infection by any bacteria in an infant during the first seven days of life. The neonates may have decreased tone, lethargy, and poor feeding. Signs of neurologic hyperactivity are more likely when late-onset meningitis occurs.

Aims: Sepsis is a significant cause of morbidity and mortality in the newborn, particularly in preterm, low birth weight infants.

Methods: Diagnosis is clinical, with extensive laboratory testing. Levels of C-reactive protein (CRP), an acute phase protein associated with tissue injury, are elevated at some point in 90% of infants with systemic bacterial infections. Organisms were isolated from 118 blood cultures, 19 urine cultures, and 27 CSF cultures.

Results: The degree of reactive hyperemia was higher in the group with sepsis (median + 150% perfusion increase) than in that without (+30%). Neonatal sepsis occurs at an estimated rate of 2 to 3 cases per 1000 live births in the Bosnia and Herzegovina.

Discussion: Neonatal sepsis continues to be a significant cause of morbidity and death.

Conclusions: Neonatal sepsis is an infection that affects infants and it can be fatal, if treatment is not given early. Treatment is initially with ampicillin plus either gentamicin or cefotaxime, narrowed to organism-specific drugs as soon as possible. The mortality and morbidity for both early and late onset sepsis still remains high, despite the use of potent antimicrobials.

Keywords: Sepsis, Neonates, Management, Diagnostics.

NEONATAL INFECTIONS ARE THOSE WHICH ARE TRANSMITTED TO,OR ACQUIRED BY A NEWBORN IN THE FIRST 4 WEEKS OF ITS LIFE

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Neonatal infection can be acquired in utero transplacentally, through the birth canal during delivery (intrapartum), and from external sources after birth (postpartum).

In utero infection, which can occur any time before birth, results from overt or subclinical maternal infection. Consequences depend on the agent and timing of infection in gestation and include spontaneous abortion, intrauterine growth restriction, premature birth, stillbirth, congenital malformation (eg, rubella), and symptomatic neonatal infection (eg, toxoplasmosis, syphilis).

Intrapartum infection occurs from passage through an infected birth canal, by ascending infection if delivery is delayed after rupture of membranes. Common viral agents include herpes simplex, HIV, and hepatitis B; these can rarely be transmitted transplacentally. Bacterial agents include group B streptococci, enteric gram-negative organisms (primarily *Escherichia coli*), gonococci, and chlamydiae.

Postpartum infections are acquired from contact with an infected mother either directly (eg, TB, which also is sometimes transmitted in utero), by breastfeeding (eg, HIV, CMV) or contact with hospital environment.

Risk factors: Neonates are immunologically immature, with decreased PMN and monocyte function. Maternal IgG antibodies are actively transported across the placenta, but effective levels are not achieved until near term. IgM antibodies do not cross the placenta. Premature infants have decreased intrinsic antibody production hence are also more likely to require invasive procedures (eg, endotracheal intubation, prolonged IV access) that predispose to infection.

Antibacterial therapy: Drug selection is similar to that in adults, because infecting organisms and their sensitivities are not specific to neonates. However, numerous factors, including age and weight, affect dose and frequency are taken into account.

EVALUATION OF NEONATAL SEPSIS AGENTS AND FACTORS IN A NEONATAL INTENSIVE CARE UNIT

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Aims: Despite all intensive care applications and antibiotic usage, mortality and morbidity are still important problems in neonatal sepsis. Analysing microorganisms proliferating in neonatal intensive care centers and antibiotic sensitivity of them help us choosing the most appropriate empirical antibiotic. In this study, positive blood cultures and antibiotic sensitivities in newborns having sepsis are researched.

Methods: The clinical characteristics of newborns having sepsis, positive cultures and the antibiotic sensitivities are analysed retrospectively.

Results: According to the results in this study; 57,1% of the patients attending the study were preterms, proven sepsis ratio among 238 patients was 8,7%. The mortality rate due to sepsis was found 4%. Staphylococcus was the leading isolated microorganism with a percentage of 46%. *Klebsiella pneumoniae* (15,9%), *Esherichia coli* (13,9%), *Candida albicans* (7,8%), *Klebsiella oxytoca* (7,4%) following then.

Conclusions: Every neonatal intensive care unit should determine its own bacterial flora and antibiotic resistance profile for empirical treatment protocols for nosocomial infections.

SPONTANEOUS RESOLUTION OF HEPATITIS C VIRAEMIA AT 18 MONTHS IN AN INFANT WITH VERTICALLY ACQUIRED INFECTION

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Background and aims: Mother-to-child-transmission of HCV infection is well-recognized. However, the natural history of such infections is little known. While viraemia is usually persistent, it may be intermittent or even absent in seropositive children.

Methods: A seropositive 5-year-old child was vertically infected with HCV viraemia, documented by repeated testing until the age of 12 months. However, a test at 18 months showed no viraemia and this result has been confirmed by subsequent annual resting. There has not been any therapeutic intervention.

Results: A full-term boy was born to an HCV-infected mother by normal vaginal delivery. The child was followed up in accordance to Health Protection Agency guidelines. There were no apparent clinical manifestations of the infection. HCV RNA, genotype 1a, was detected throughout the first year of his life. The viral load fluctuated from 500,000 IU/ml at 3 and 6 months to 215,000 at 12 months; alanine transaminase and alkaline phosphatase were mildly raised. No hepatomegaly was recorded. At 18 months of age, HCV RNA became undetectable while alanine transaminase and alkaline phosphatase levels returned to normal. While the child remains seropositive, HCV RNA remained undetectable in two subsequent blood samples taken a year apart.

Conclusions: We confirm the absence of clinical signs and symptoms in this child vertically infected with HCV, and the spontaneous clearance of the virus by 18 months despite constantly high HCV RNA levels during the first year of his life, a finding which is usually associated with a high rate of chronic infection.

NEONATAL GROUP B *STREPTOCOCCUS* INVASIVE DISEASE: CASE SERIES

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Background and aims: Group B *Streptococcus* (GBS) is a leading cause of neonatal invasive disease. Different preventive strategies of early-onset disease (EOD) have been adopted. The aim was to evaluate epidemiological trends and clinical data of neonates with GBS infection.

Methods: Retrospective review of the medical records of neonates admitted to the NICU with GBS positive blood culture, between 1998-2009 (12y). Routinely GBS culture was not performed. A risk-based approach has been adopted since 2003: women's prophylaxis is performed when risk factors are identified.

Results: Fifteen children were admitted, 11 male. Median gestational age was 37w (26-41). The overall incidence of EOD was 0.31/1000 live births (0.38/1000 before 2003; 0.27/1000 after 2003). Three children had late-onset disease (LOD). EOD presented with lethargy (10), grunting (8) and apnoea (5), within 12h of birth. Diagnoses were sepsis (15), meningitis (2) and pneumonia (1). At least one risk factor was present in 9 cases: 6 were born prematurely, 2 had suspected chorioamnionitis and peripartum fever and 1 had membrane rupture >18h. Intrapartum antibiotics were known to have been correctly administered only to 1 mother with suspected chorioamnionitis. The median length of stay was 10d. The first line of treatment was ampicillin plus gentamicin/netilmicin. One child with LOD (meningitis) died. Developmental delay was noticed on follow-up in one child with EOD.

Conclusions: The incidence of EOD was lower than found in literature. Furthermore, low morbidity and the risk of increasing antibiotic resistance patterns from organisms other than GBS supports our institutional strategy, regarding prophylaxis.

HERPES SIMPLEX VIRUS TYPE 1 (HSV-1) PNEUMONITIS IN THE FIRST DAY OF LIFE**M. Fraser**¹, E.E. Yates¹, A.E. Currie², J.A. Fawke²¹*Clinical Microbiology*, ²*Neonatal Intensive Care Unit, University Hospitals of Leicester NHS Trust, Leicester, UK*

Background and aims: Most infants affected with neonatal herpes are born to asymptomatic mothers. Early neonatal pneumonia is mainly bacterial; HSV is the main, albeit infrequent, vertically transmitted viral agent causing significant morbidity and mortality.

Methods: A newborn male, born after uneventful pregnancy and term vaginal delivery, presented at twelve hours with tachypnoea requiring oxygen support. There were no other symptoms or mucocutaneous lesions.

Results: Blood cultures were taken and antibiotics commenced empirically. Chest X-ray showed right lobar consolidation, bilateral lung opacification and hyperinflation. Blood cultures revealed no microbial pathogens. Nasopharyngeal aspirate was negative for bacteria, viral pathogens and ureaplasmas. Two generalised seizures on day 7 prompted proactive acyclovir therapy. Later, HSV-1 DNA was detected in an EDTA blood sample. CSF showed pleocytosis and mildly raised protein; no bacterial pathogens, HSV or enterovirus were detected. High-dose acyclovir was continued for three weeks, with clinical and radiological recovery, although tachypnoea persisted for 22 days. Cranial ultrasound and MRI, EEG and echocardiography were normal. HSV-1 DNA was undetected in two consecutive blood samples before therapy was stopped. HSV-1 antibody was detected in maternal post-delivery serum, indicating recurrent rather than primary infection.

Conclusions: Neonatal persistent tachypnoea requires further investigation; pneumonitis is an uncommon presentation of neonatal HSV infection which in this case was unusually caused by HSV-1. Diagnosis may be difficult; early, proactive, initiation of acyclovir should be based on suspicion of HSV infection, before virological confirmation, in all neonates with relevant symptoms. In this case passive immunity may have hastened recovery.

SERRATIA MARCESCENS OUTBREAK IN A TERTIARY LEVEL NURSERY OF NORTHERN INDIA

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The outbreak occurred in the Nursery of SSK Hospital, New Delhi, India. This nursery has a capacity of 30 babies. Only intramural babies with no risk factors for sepsis are admitted.

The outbreak was spread over a span of 2 weeks in December 2006. The index case was a 34 week newborn, admitted in view of prematurity. On day 4 the baby became lethargic, developed abdominal distension and brownish gastric aspirates. The blood culture grew *Serratia marcescens*.

Within next five days 13 out of the total 21 babies admitted in the Nursery deteriorated with signs and symptoms suggestive of sepsis. All these babies were shifted to the isolation unit. Stable babies were transferred to mothers or shifted out to another neonatal unit.

Initial manifestations noted were brownish gastric aspirates or malena (9/14), petechie (4/14), lethargy (10/14), abdominal distension (7/14), respiratory distress (4/14) and sclerema (5/14). Pneumonia was seen in 8 and meningitis in 8 babies. All cases had platelet count < 20,000. *Serratia marcescens* could be isolated from the blood culture in all 14 babies.

Surveillance of the personnel and environment of nursery, labor room and maternity did not yield *Serratia* from any of the specimens. It was the index case which probably led to intra-unit spread of infection. Possible source of infection for the index case could not be identified.

Unusual observations about this outbreak were explosive onset and termination, higher incidence of secondary attack rates, meningitis, bleeding manifestations, bacteremia and lower mortality (3/14) from what has been reported.

NEONATAL SEPTICEMIA BY PSEUDOMONAS AERUGINOSA LEADING TO EXCESSIVE HEPATOCELLULAR DAMAGE AND CHOLESTASIS-A CASE REPORT

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Background and aims: Systemic infection by *Pseudomonas Aeruginosa* (PA) has been reported to cause cholestasis and increased serum concentration of liver enzymes in immunocompromised patients. A few cases in neonates have been previously reported.

Methods: This is a case of a neonate, who developed jaundice and hepatocellular damage in the course of septicemia, secondary to urinary tract infection caused by PA.

Results: A 16-day-old male was referred to our Department with clinical signs of shock. Prior to the admission, the baby had undergone a bladder catheterization, for voiding cystourethrogram, which had revealed vesicoureteral reflux grade V. Support of the circulation and antibiotic therapy with ampicillin, meropenem and cefepime was initiated. All urine, blood and cerebrospinal fluid cultures developed PA. Concentrations of liver enzymes rose up to maximum values on the third day, with alanine aminotransferase: 2120 U/L and aspartate aminotransferase: 2259 U/L. The baby also developed jaundice, with values of total bilirubin up to 20,6 mg/dl and conjugated bil:11,1 mg/dl. Coagulation studies revealed prolonged prothrombin time and partial thromboplastin time. Severe leukopenia WBC: 2500/mm³, (Neutrophils: 68%, Mononuclears: 19%) and thrombocytopenia was noted (Platelet count: 44.000/mm³). In the following days, laboratory values of liver enzymes and blood tests gradually improved and the baby recovered clinically from septicemia. He was discharged after 3 weeks of antibiotic therapy.

Conclusions: Extrahepatic bacterial infection and sepsis caused by *Pseudomonas aeruginosa* can produce cholestasis and liver damage, possibly due to decreased metabolic activity of liver cells in association with severe infection.

EFFECTIVENESS OF BACTERIOPHAGE THERAPY IN NEONATAL SEPSIS (PRELIMINARY DATA)

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Background and aims: Neonatal sepsis still remains a challenging problem, especially in low weight newborns. Very often pathogenic bacteria display resistance to antibiotics. The interest in bacteriophage therapy is raising up over the world. Nevertheless the data on its clinical effectiveness especially in infants are scarce.

Aim of the study was to reveal the possible effect of bacteriophage therapy on the clinical course of sepsis in newborns with low weight. Preliminary data are presented.

Methods: Double blind research design was used. From the first day of admission in addition to conventional treatment the neonates (weight 1500-2500 g) with sepsis were given orally commercially available phages (n=10) or placebo (n=10). Duration of the phage therapy was 7 days. Following outcomes were compared: scores for clinical condition, blood formula, CRP, number of hospital days.

Results: After 7 days of bacteriophage therapy the clinical condition has improved in 8/10 cases and stayed the same or worsened in 2/10 cases; 4/7 and 3/7 cases in the control group, correspondingly. 3 newborns from the placebo group were excluded from the study: one died on the third day, one vomited after every taking of the placebo, one was moved to another hospital. No differences in blood formula and CRP changes were pronounced. Hospital stay was shortened by 0.9 ± 0.6 for emergency unit and 1.9 ± 1.8 days in total.

Conclusions: Our preliminary data point to some positive effect of bacteriophage therapy on the course of neonatal sepsis. Study continuation seems to be reasonable to draw more definite conclusions.

MICROBIOLOGICAL STUDY CORRELATED WITH PATHOLOGICAL ASPECTS OF NEWBORN ENTEROCOLITIS

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Background: The enterocolitis is an important death cause for the newborn. We intended to determine the prevalence of the microbiological pathogens correlated with the pathological aspects and abnormal pregnancy and birth signs.

Methods: We studied the medical history, the antibiograms and the pathological slides from the necropsy for 27 newborns with enterocolitis from the total 368 newborns hospitalized and deceased in Neonatal Department of the Emergency Children Hospital, Timisoara, between 11.2004 - 11.2009.

Results: Incidence of the enterocolitis among the total cases with autopsy in the studied period (7,33%).

A great prevalence of the disease to the premature newborn 33,33% (9/27).

In abnormal pregnancy and birth : maternal infections 11,74%; premature rupture membrane 18,61%; co- loured amniotic liquid 26,56% ; APGAR less than 5 - 51,96%; intensive therapy needed to birth 20,16%.

The microbiological study revealed : Enterobacter 11,11%; Pyocianic 7,4%; Escherichia coli 3,7%; Sta- philococcus aureus 22,22%; Candida albicans 7,4%; Klebsiella 11,11%.

The main pathological forms of the enterocolitis were: pyo-haemorrhagical 77,77%; haemorrhagical 22,22%.

The most frequent pathological complications discovered were: peritonitis 29,62%; bowel perforation 14,81%.

Conclusions: We consider that the risk factors of the are: maternal infections during pregnancy, prema-turity, intensive therapy needs at birth, infectious factors. Enterocolitis remains one of the most common emergencies for the newborn because of the peritonitis and the bowel perforation.

Keywords: *Enterocolitis, newborn , microbiological study, pathological aspects, maternal infections*

**LACK OF MOTHER-TO-NEWBORN TRANSMISSION OF HEPATITIS C VIRUS IN IRAQI WOMEN:
A PROSPECTIVE STUDY WITH HEPATITIS C VIRUS RNA TESTING**

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Background: What has been published about the risk of mother-to-infant transmission of hepatitis C virus (HCV), shows variation according to the population studied and the test used. Polymerase chain reaction (PCR) was used for the first time in Iraq in a prospective study.

Aims: To assess the risk of vertical transmission in an unselected population of Iraqi pregnant women by using Polymerase chain reaction (PCR) was used for the first time in Iraq in a prospective study

Material & methods: HCV antibodies (Abs) were sought with third generation enzyme immunoassay (EIA-3) in 3491 pregnant women. A positive reaction was then confirmed by a third-generation immunoblot assay (LiaTek-III). This last test was confirmed positive in 112 serum samples. We followed 26 babies of 25 anti-HCV positive mothers at first month of life. Eight of these children could be followed for six months postnatally.

Result: All the 26 neonates were positive for HCV Antibodies (with EIA-3 and Lia Tek-III) during the first month of life and it completely disappeared within the following six months. HCV RNA was consistently negative in 22 sera (14 infants at first months and 8 of repeated at 6 months later) regardless of the hepatitis C virus polymerase chain reaction status of their mothers (9 of whom were positive for HCV RNA).

Conclusion: The study showed the absence of vertical transmission of HCV from pregnant Iraqi women to their offspring.

A RETROSPECTIVE EPIDEMIOLOGICAL STUDY OF INVASIVE PNEUMOCOCCAL DISEASE IN CHILDREN AGED 0-5 YEARS IN BAHRAIN

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Background and aims: Pneumococcal infections are associated with a high disease burden. Pneumococcal disease is preventable through vaccination. The objective of this study was to determine the incidence of pneumococcal diseases in children aged < 5 years in Bahrain.

Methods: Cases of pneumococcal infections in children aged < 5 years, recorded in hospitals from 1 January 1999-31 December 2003, were retrospectively reviewed. Case definition required isolation of *Streptococcus pneumoniae* from blood, cerebrospinal fluid, or any other normally sterile biological fluid, or a clinical diagnosis only.

Results: 371 eligible cases were reported. Patients were 57.7% male and 42.3% female, 83.9% were aged < 2 years, and 88.4% were Bahrain nationals. The Table shows the estimated incidence rates of invasive pneumococcal diseases (IPD).

Year	Population < 5 yrs old	Number of cases; annual incidence per 100,000				
		Meningitis	Septicemia/ Bacteremia	Pneumococcal Pneumonia	Lobar pneumonia, Streptococcus Pneumonia	Overall
1999	76,754	1; 1.30	2; 2.61	23; 29.97	6; 7.82	32; 41.69
2000	70,315	3; 4.27	12; 17.07	47; 66.84	15; 21.33	77; 109.51
2001	60,385	4; 6.62	8; 13.25	49; 81.15	17; 28.15	78; 129.17
2002	62,302	1; 1.61	9; 14.45	58; 93.09	12; 19.26	80; 128.41
2003	50,107	3; 5.99	52; 103.78	12; 23.95	37; 73.84	104; 207.56

[Table. Incidence of IPD]

During the study period, the annual incidence of IPD was 115 per 100,000 in children aged < 5 years, and 471 per 100,000 in children aged < 1 year.

Conclusions: The burden of IPD in children aged < 5 years in Bahrain was high compared with reported rates in European countries (7.6-34.5/100,000) and Arabian Peninsula countries (3.4-53.5/100,000).

A RETROSPECTIVE EPIDEMIOLOGICAL STUDY OF INVASIVE PNEUMOCOCCAL INFECTION IN CHILDREN AGED 0-5 YEARS IN OMAN

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Background and aims: Pneumococcal diseases caused by the bacterium *Streptococcus pneumoniae* (*S. pneumoniae*) are a worldwide public health problem. The World Health Organization estimates that in developing countries > 1 million young children die each year owing to pneumococcal pneumonia. The objective of this study was to determine the incidence of invasive pneumococcal disease (IPD) in children aged < 5 years in Oman.

Methods: Cases of pneumococcal infections in children aged < 5 years, recorded in four hospitals in Oman from 1 January 2006-31 December 2006, were retrospectively reviewed. Case definition required isolation of *S. pneumoniae* from blood, cerebrospinal fluid or any other normally sterile biological fluid, or a clinical diagnosis only. A summary of disease financial burden was compiled.

Results: 35 eligible cases were reported. Patients were 51% male and 49% female; 62% were aged < 2 years; 40% had a known concomitant medical condition.

The Table shows the estimated incidence of IPD. The highest incidence occurred in children aged < 2 years. 54% of cases were resistant to at least one antibiotic. Meningitis cases had the highest direct costs.

Age	Meningitis		Septicemia/bacteremia		Pneumococcal pneumonia		Overall	
	Number of cases	Incidence per 100,000	Number of cases	Incidence per 100,000	Number of cases	Incidence per 100,000	Number of cases	Incidence per 100,000
0-2 years	2	4.6	10	34.8	9	20.9	21	60.4
0-5 years	6	7.3	19	35.0	10	12.1	35	53.2

[Incidence of IPD]

Conclusions: The burden of IPD in children aged < 5 years in Oman was high compared with reported rates in Europe (7.6-34.5/100,000) and the Arabian Peninsula (3.4-53.5/100,000).

USEFULNESS OF PNEUMOCOCCAL ANTIGEN DETECTION FOR THE RAPID DIAGNOSIS OF INFECTION BY STREPTOCOCCUS PNEUMONIAE IN CHILDHOOD

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Background and aims: Streptococcus pneumoniae is a leading cause of infectious diseases. Diagnosis of pneumococcal infections still remains problematic and relies heavily on insensitive culture techniques. As the rapid immunochromatographic test (ICT) for the detection of C-polysaccharide antigen of S.pneumoniae is feasible, it is preferred to diagnose pneumococcal infections. We evaluated the usefulness of ICT in diagnosis of pneumococcal infection in the urine samples of children.

Methods: A total of pneumococcal infection suspected 50 children with sepsis, pneumoniae, otitis or meningitis as the patient group and 50 healthy children as the control group were enrolled in study. Urine samples and nasopharyngeal cultures were obtained from all cases. Blood, transtracheal aspirate, urine and cerebrospinal fluid cultures were taken from the patients whom are available. The Binax NOW S.pneumoniae Antigen test (Portland, USA) is used for the detection.

Results: We found urinary antigen positivity in 7/50 of control group and 10/50 of patient group. All of the 3 children (1 in control group, 2 in patient group) who carried *S.pneumoniae* in their nasopharynx, had positive ICT. We detected pneumococcus in 1 blood culture and 2 CSF culture of 3 patients. ICT was positive in all of them. There was no effect of antimicrobial treatment, vaccination and acute fase reactant levels on the urinary antigen detection test.

Conclusions: This test is not useful for diagnosis of pneumococcal infections in children as high carriage rates cause false positivity. This test can only be tried as a supplementary method with other conventional microbiological tests.

DEVELOPMENT OF A NOVEL PCR DIAGNOSTIC ASSAY OF RESPIRATORY SYNCYTIAL VIRUS IN YOUNG CHILDREN WITH SEVERE DISEASE

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Background: Respiratory syncytial virus (RSV) is the leading cause of severe lower respiratory infection (LRI) for young children worldwide. It is classified into two major antigenic groups (RSV-A and RSV-B). In this study, we have developed a novel "in-house" PCR diagnostic assay for further investigation of distribution patterns of RSV strains in Latvia.

Methods: Patients, in age of 2-24 months, were selected by WHO definition of LRI case. RNA from nasopharyngeal aspirate specimens was extracted with QIAamp Viral RNA kit (QIAGEN). Simultaneously, nasal swab was taken for IFA and used as a control.

Results: At first, cDNA was synthesized in reverse transcription reaction with primer F164_Rv specific for both RSV subgroups. For general screening of samples, intercistronic M-P gene locus was PCR-amplified with primers P_Fw/M_Rv. In parallel, defined G-gene fragments were amplified using subgroup specific primers Ga_Fw or Gb_Fw and F_Rv. Alternatively, subgroups can be detected in two-step PCR, with non-specific external primer Gab for the first reaction, followed by subgroup specific primers in heminested PCR. All positive samples belonged to subgroup A. We could not detect subgroup B, obviously, because of small number of samples tested.

Conclusion: The assay described is at least as sensitive as IFA and will be used for the study of the molecular epidemiology of RSV in tertiary level children's hospital in Latvia.

Primer	Gene	Positions based on RSV strain A2 (M74568)	Sequence (5'→3')	Reference
F164_Rv	F	173-151	GTTATRACACTRGTATACCAACC	Modified from Sullender et al., 1993
P_Fw	P	452-475	CATTAGTAGTTGCAAGTGCAGGAC	Original
M_Rv	M	46-25	CTGTGTATGTGGAGCCTTCGTG	Original
Gab_Fw	G	137-158	TGGCAATGATAATCTCAACYTC	Original
Ga_Fw	G	522-542	CATATGCAGCAACAATCCAAC	Original
Gb_Fw	G	328-347	CCAATCCACACAAATTCAGC	Original
F_Rv	F	6-(-15)	CTCCATTGTTATTTGCCCCAG	Modified from Peret et al., 1998

[Oligonucleotides used in this study]

SWINE INFLUENZA A(H1N1) INFECTION IN 2 NEWBORNS

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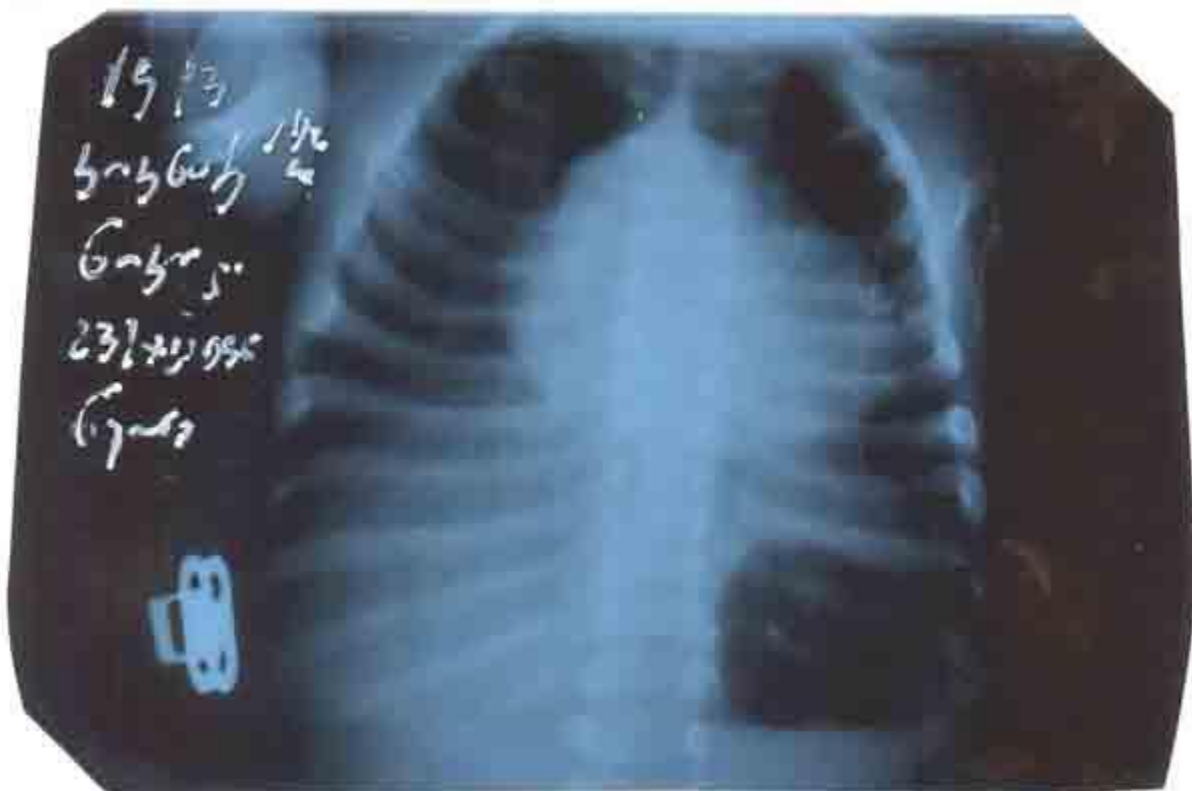
Background and aims: We represent two cases of Swine Influenza A(H1N1) Infection in newborns.

Methods: In November-December 2009, 66 patients were hospitalized in Neonatology Department with diagnoses acute respiratory infection. Were collected Nasopharyngeal secretions and Swine Influenza A(H1N1) virus was detected with the method of Polymerase Chain Reaction (PCR), which has a sensitivity of 99% and specificity of 92%. Research was made in the centers of Disease control and Public health.

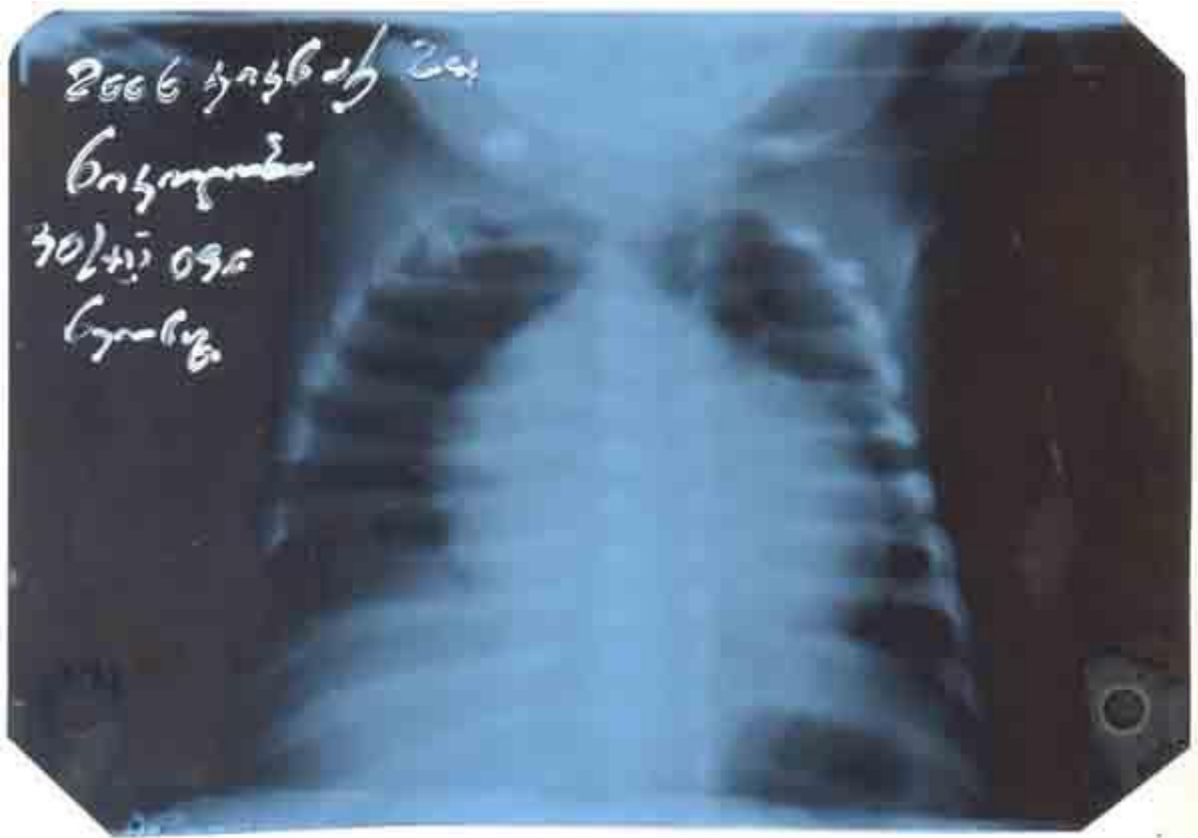
Results: Among 66 patients who have acute respiratory infection A(H1N1) virus was detected in 2 newborns. According epidemic anamnesis, both patients had contact with mother and other family members, who were infected with Swine flu. In both cases patients had symptoms: fever(40°), respiratory distress, vomiting, intoxication, wheezing, rhinorea, cough, tachipnea, tachycardia, abnormal cardiac examination results, abnormal chest x-ray-pulmonary infiltrate. They took Tamiflu (Oseltamivir) 2mg/kg weight every 12 hours, but despite of this pneumonia was developed in both newborns(see fig.1,2)

Conclusion:

- 1) Swine Influenza A(H1N1) Infection in newborns passed with serious results. Such as pneumonia and myocardioathy.
- 2) In the epidemic anamnesis the leading part is contact with the infected family members.



[Fig. 1]



[Fig. 2]

EVALUATION OF EPIDEMIOLOGIC, CLINICAL AND LABORATORY FACTORS OF HOSPITALIZED CHILDREN WITH PNEUMONIA AT ALI EBN-E ABITALEB HOSPITAL ZAHEDAN-IRAN

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Introduction: This study was done with objective of evaluation of epidemiologic, clinical and laboratory factors of hospitalized children with pneumonia.

Methods: This retrospective descriptive study, was evaluated file of patients that with diagnosis of pneumonia hospitalized in done on pediatric patients, between 1 month to 12 years who were hospitalized in pediatrics ward in Zahedan, Iran at 2005-2008. The diagnosis of pneumonia was based on physical examination, result of and laboratory findings and chest radiography. The results were analyzed by SPSS ver.15 and reported by distribution frequency and mean.

Results: Of 300 evaluated patients, 177 (59%) and 123 (41%) patients were male & female respectively. The mean age was not significant difference between male & female ($P>0.05$). Bacterial and viral pneumonia was 30% & 70% respectively. The most common clinical presentations were cough (93%), tachypnea (89%), dyspnea (73%) positive pulmonary auscultation (rales 71%, wheezing 33%, rhonchi 22%). The blood culture was positive in 11.11% of cases (total of blood culture was 162 cases), that most common bacteria was negative coagulase staphylococcus (8 cases) and streptococcus pneumoniae (5 cases). The most common underlying conditions in this study were failure to thrive (FTT) and congenital heart disease. The mortality rate of pneumonia in this study was 1%.

Conclusion: The most common pathogen of pneumonia in children was staphylococcus and streptococcus pneumoniae. High frequency of FTT in our study can be due to low socio-economic state of families. So for necessary educations to families, especially attention to nutritional state of children and more evaluations must be attempted.

HYPONATRIEMIA IN CASES OF CHILDREN WITH PNEUMONIA

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Background and aims: Hyponatremia is the most common electrolyte imbalance seen in clinical practice, and a common laboratory finding in children with community acquired-pneumonia (CAP). This study aimed to identify the incidence of hyponatremia in cases of CAP, to find predictive tools in order to classify the severity and outcome of CAP and to explore possible differences of clinical importance between two sexes.

Methods: The medical files of 54 children with pneumonia were retro-prospectively reviewed.

Results: 54 children (66.4% males) with pneumonia were recorded. They were 4.67 ± 2.88 years-old. 35/54 (64.8%) children with pneumonia had normal values of sodium at admission, 18/54 (33.3%) had mild hyponatremia and 1 child (1.9%) moderate hyponatremia. Increased heart rhythm and tachypnea at admission were correlated with lower values of sodium ($z=-2.664$, $p=0.007$ and $z=-1.705$, $p=0.089$ respectively). No differences were found between two sexes concerning the characteristics of pneumonia or the range of sodium in serum at admission. Correlation was found between sodium admission values' and:

a) C-reactive protein ($p=0.000$), and

b) leukocytes value ($p=0.006$). Sedimentation rate ($p=0.021$) was also considered as a possible risk factor affecting the value of sodium at admission to hospital.

Finally, negative association was also observed between the degree of hyponatremia and the duration of hospitalization ($z=-3.398$, $p=0.001$).

Conclusions: In our study increased heart rhythm, tachypnea, leucocytes counts, C-reactive protein, and also erythrocytes' sedimentation rate could be considered as possible risk factors influencing the degree of hyponatremia, and thus the outcome of hospitalized children with CAP.

CARDIAC TAMPONADE SECONDARY TO SUPPURATIVE PERICARDITIS IN AN 11-YEAR-OLD BOY

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Tuberculosis is a common infection in Portugal (incidence 34/100000 inhabitants). The incidence of tuberculosis as a cause of pericardial disease is related to its overall prevalence in a given population.

We describe a case of pneumonia with bilateral pleural effusion complicated by purulent pericarditis effusion with tamponade.

An 11-year-old boy was admitted to the Emergency Service with a 2-week history of weight loss and complaints of pain in the left shoulder and cough in the previous 2 days. Fever was denied. The exam showed subfebrile temperature, tachycardia, normal blood pressure, no need for O₂, jugular turgidity at 45°, deafened heart sounds, decreased breath sounds in both lung bases, hepatomegaly and no oedema. Analytically he presented with anaemia, without leukocytosis or neutrophilia, C-reactive protein-49.8mg/L and erythrocyte sedimentation rate-86mm/h. The imaging tests confirmed paracardiac lower right hypotransparency, small bilateral pleural effusion, large volume pericardial effusion, homogeneous hepatomegaly and medium volume ascites. Both pericardiocentesis and thoracocentesis fluids were exudative. Cultures for aerobes and mycobacteria (blood, pleural and pericardial fluids) were negative, IgM for *Mycoplasma pneumoniae* negative, PCR for enterovirus in the pericardial fluid negative, PCR for mycobacterium (pleural and pericardial fluids) negative and culture of Koch bacilli in the sputum negative. After 24 hours of treatment with ampicillin and given the clinical worsening, the antibiotic was changed. He had a good outcome with tuberculostatic drugs.

Acute purulent pericarditis is rare in children and is usually a complication of upper respiratory tract infection. Appropriate treatment with adequate surgical drainage and antimicrobial therapy are vitally important for the outcome.

DO LOW VITAMIN D LEVELS INDICATE CHILDHOOD TUBERCULOSIS WHEN THERE IS ACTIVE TRANSMISSION OF TUBERCULOSIS IN THE FAMILY?

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Introduction: It is well recognised that childhood tuberculosis is a difficult disease to diagnose and as a result a delay in diagnoses is not uncommon. Childhood tuberculosis disease indicates active tuberculosis transmission in the community and a large number of children with tuberculosis are picked up through contact tracing.

Low vitamin D levels are known to be associated with tuberculosis disease and infection.

We present 4 children who presented with a delay in diagnoses of tuberculosis disease in the midst of overwhelming active TB transmission within their families.

Methods: Children were contact traced; had Mantoux test/s [except were not indicated], chest Xray, FBC, ESR, LFT, Vitamin D levels.

Cases:

Patient 1; 7 year old boy presented with abdominal tuberculosis, 13 months after his 3 year old sibling was diagnosed with pulmonary tuberculosis.

Patient 2; 3 year old boy presented with pulmonary tuberculosis, 1 month after his 3 other siblings were diagnosed with pulmonary tuberculosis.

Patient 3; 4 year old girl presented with pulmonary tuberculosis, 2 months after her 13 year old sibling was diagnosed with pulmonary tuberculosis.

Patient 4; 12month old boy presented with pulmonary tuberculosis, 2 months after his 3 siblings were diagnosed with pulmonary tuberculosis.

There was at least one adult index case in all 4 families.

Conclusion: Three of the four children had low vitamin D levels at the time of contact tracing. A low vitamin D level in a child whose family profile shows overwhelming tuberculosis transmission may indicate that the child may have TB.

SCLERITIS AND ULCERATING CUTANEOUS LESION: DO YOU THINK ABOUT TUBERCULOSIS?

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Background and aims: Extra-pulmonary tuberculosis is notoriously difficult to diagnose on account of the polymorphism of the disease and the weak specificity of the clinical manifestations. A firm diagnosis always rests on histological or microbiological evidence.

Case report: A previously healthy 12 year-old black girl, immigrated from London one month before, was admitted with a three month isolated cutaneous ulcerating lesion (6x7cm) in the left leg and a six weeks red, painful right eye without fever or weight loss. Her father had a positive tuberculin skin testing six years before and no treatment was performed. Ophthalmologic evaluation revealed nodular scleritis of the right eye. Laboratory findings: Hb-12.3g/dL, 5000 WBC/ μ L (55.2% neutrophils, 32.1% lymphocytes), 250.000 platelets/ μ L, C-reactive protein-0.36 mg/dL, erythrocyte sedimentation rate-37mm. Tuberculin skin testing: positive (17mm of induration); HIV 1 and 2 negative. Other serologic markers as well as autoimmunity were negative. Three sputum specimens were negative for mycobacterium (Ziehl Neelsen and Lowenstein negative). Chest X-ray and abdominal ultrasonography were normal. A skin biopsy was performed: Ziehl Neelsen was negative and Lowenstein remain negative. However, the histological examination showed granulomatous infiltrates, with giant Langhans cells and caseous necrosis, compatible with cutaneous tuberculosis.

Antituberculous therapy, topical corticosteroids and cycloplegics were performed, with a favourable clinical evolution.

Comments: The diagnosis of non-pulmonary tuberculosis poses a particular challenge for clinicians. A high level of suspicion is required in order to avoid delays in diagnosis which may influence treatment outcome.

THE STUDY ON RELATION OF HUMAN PAPILLOMAVIRUS WITH BLADDER TRANSITIONAL CELL CARCINOMA

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Background: Carcinoma of bladder is one of the most common types of cancer in the world. Among different risk factors of bladder carcinoma, the role of genital Human Papillomavirus in TCC was the aim of this study.

Methods and materials: Formalin- fixed, paraffin embedded tissue samples of 147 patients with TCC and 39 non- neoplastic cases as a control group were tested for the presence of HPV DNA. In addition, HPV high risk typing was performed to all positive patients.

Results and conclusion: The positive rates of HPV DNA were 34.7% and 7.6% in case and control groups, respectively and HPV18 was the most common type in association with TCC. There is a meaningful relation between genital HPV infection and bladder carcinoma among Iranian patients. The ratio of male to female was the same in both case and control groups and it was about 6.4. Investigation of age classification showed that the highest number of case group patients aged 51-60 years old.

Keywords: HPV, cervical cancer, PCR, biopsy.

Abbreviations: Double Distilled Water, (DDW); human Papilloma virus, (HPV); sexually transmitted diseases, (STDs); Squamous Cell Carcinoma, (SCC).

TREATMENT DIFFICULTIES IN A CASE WITH URINARY TRACT INFECTION AND COMPLEX KIDNEY MALFORMATION

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Background and aims: The authors emphasize the diagnosis particularities and treatment difficulties in a child with urinary tract infection (UTI).

Methods: The authors present a 2 year-old girl admitted for fever. The clinical exam has revealed: fever, impaired nutritional status, skin pallor, a right-side abdominal mass, intermittent pyuria and dysuria.

Results: The blood investigations have shown: anaemia, augmented inflammatory markers and normal kidney function. The urine cultures have identified *E. Coli* extended-spectrum-beta-lactamases (ESBL). *According to* imagistic evaluations: abdominal ultrasonography has discovered on the right side a 2nd degree hydronephrotic kidney in contact with a large polycystic mass whereas the left kidney appears normal; the contrast CT scan and urography results were suggestive for complete right side ureteral duplication. The antibiotic treatment (carbapenems) was initiated based on bacteria susceptibility test, but without good clinical evolution and surgical therapy was considered the most efficient measure to treat this patient. During surgical intervention there was discovered a complex urinary tract anomaly: the ureter that drains the superior pole of right kidney inserts ectopically in uretra and appears as a megaureter with polycystic appearance. The megaureter has induced compression on the other homolateral ureter from right side explaining secondary hydronephrosis.

Conclusions: This patient has presented pyelonephritis caused by a very resistant strain *E.coli* (ESBL) in context of complex urinary tract malformation. The most efficient treatment was considered the surgical intervention (megaureter removing). The case peculiarities: the intermittent pyuria has represented a distinctive feature for urinary tract malformation background.

DETERMINING OF FREQUENCY OF THE BACTERIAL AGENTS IN CHILDREN WITH URINARY TRACT INFECTIONS AND THEIR ANTIMICROBIAL SUSCEPTIBILITY PATTERNS IN HAMADAN

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Background and aim: Urinary tract infections (UTIs) are most common urogenital disease and second common infections in childhood.

The aim of study was to determining the frequency of bacterial agents in children with UTI and detection of their antibiotics susceptibility pattern in children who referred to Ekbatan hospital in Hamadan, western Iran.

Methods: In a retrospective cross-sectional study 156 children with UTI were investigated for urine cultures and their antibiograms. Antibiogram for eleven antibiotics test was performed by method of Kirby-Bauer. The required data of patients were analyzed using spss system.

Results: Of 156 children with UTI, 74.7% were girl and the most common age group in boys was 1-24 month (40%) and in girls was 6-18 years (34.5%). The most common isolates were *Escherichia coli* (82%), *Kelebsiella sp* (10%) and *Staphylococcus aureus* (3.4%). The most effective antibiotics against isolates were nitrofurantoin, ciprofloxacin, naldexic acid, amikacin, ceftizoxime, co-trimoxazole and tobramycin while most of isolates showed high resistance against ampicillin, and tetracycline.

Conclusions: This study showed that Gram-negative bacilli in particular *E. coli* and *Kelebsiella sp.* are predominant causes of bacterial agents of UTIs in children in this region. Most species showed high sensitivity to routine antibiotics such as nitrofurantoin, ciprofloxacin, amikacin and tobramycin.

COVERAGE VPH VACCINE 14 YEARS OLD GIRLS FROM THE HEALTH DISTRICT BAHÍA DE CÁDIZ - LA JANDA (CÁDIZ, ANDALUSIA, SPAIN)

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Background and aims: The Cervarix® vaccine (which is immunogenic and effective in 10 to 25 year old girls and women) is the vaccine used by the Andalusian Health Service on its vaccination program against VPH. The goal of this study is to analyse the vaccine coverage reached, geographical distribution patterns and the negative effects noted in our district.

Methods: Descriptive observational environmental study. The unit of analysis is the aggregation of the cohort of supervised 14 year old girls, who have completed vaccination by basic health sector (territorial unit). The frequency of use of the service has been compared, seeking the detection of any certain geographical pattern. The type and frequency of the adverse reactions reported has also been compared.

Results: An active capture was not carried out. Once the vaccination of the 1994 cohort (2443 girls) was completed, the District's uptake rate was 81%, and the full vaccination 70%. The highest coverage occurs in rural areas with a capture rate higher than 83% and a vaccination rate higher than the District's average rate; it is lower in bigger cities, depressed areas and coastal areas. The District's global vaccination rate 87%. The adverse reactions reported were insignificant (0.0143%).

Conclusions: Once the vaccination of the first cohort was completed, it seems necessary to rethink active capture in order to obtain a full vaccination rate of at least 75% in low coverage areas. It is still a very safe vaccine with no significant adverse results.

ANTI- PNEUMOCOCCAL VACCINATION WITH 7- VALENT CONJUGATE VACCINE (PCV 7) IN PRESCHOOL CHILDREN: APPLICATION AND SIDE EFFECTS

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Background and aims: Pneumococcus is the commonest cause of severe bacterial infection in children. In Greece, is the first cause of pneumonia and acute middle otitis and the second, by frequency, cause of bacterial meningitis- after meningococcus. The aim of our research is vaccination's status recording against pneumococcal strains at children of preschool age and vaccination's side effects.

Methods: Health books of 815 children- 18 months- 5 years old- that were examined at outpatient clinics of our institutions for the period 11/2008- 11/2009, were checked. Children's vaccination coverage- against pneumococcus- and vaccination's side effects were recorded.

Results: 573 children (70.3%) were vaccinated - against pneumococcus-, while only 242(29. 7%) were unvaccinated. Higher vaccination coverage appeared at ages up to 4 years - 485 children (84.6%) - while lower vaccination coverage was observed at the age of 5 years (15.4%). Local side effects (ache, redness, oedema) were found at 17.3%. Moderate fever and muscle aches were found at 0.9%.

Conclusions:

1. Vaccination coverage of preschool children with PCV 7 is satisfactory.
2. Pneumococcal vaccine is safe and well tolerated. It may causes mild local reactions and rarely low fever.
3. Although antibiotics have decreased morbidity and mortality from pneumococcus, the antimicrobial resistance in drugs continuously increases.

Therefore, the necessity of pneumococcal's infection prevention using anti-pneumococcal vaccination is essential.

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ELIMINATION PLAN OF MEASLES IN CANARY ISLANDS. EVALUATION OF THE VACCINATION STRATEGICS (2001-2009)

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Background: Inside the strategics for the Elimination Plan of Measles in Canary Islands, we set up vaccination outlines to reach and keep the covering with MMR vaccine higher to 90% and made an especify catch-up wich first objective was to immunize in only a time a big poblation percentage, taking off a high number of suspicious. We present the coverings reached at 2001-2009.

Methods: For the coverings results with MMR vaccine we used as denominator the total number of children aged between one and two years, and as numerator the total of children aged between one and two yeras immunized with MMR vaccine.

Results: Meanwhile the years 2001-2009 the vaccination covering with MMR were highest to the 90%.

Conclusion: We can consider that the established object of the vaccination strategics enclosed in the Elimination Plan of Measles in Canary Islands, is going to get obtained.

THE STUDY OF RELATION BETWEEN BCG SCAR SIZE ,THELPER1/THELPER 2 WITH ASTHMA IN CHILDREN

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Object: The aim of this study is identifying the relations between the levels (INFY) of Thelper 1, Thelper 2 (IL4, IL13) with asthma also identifying the relations between the sizes of scar of BCG with the asthma in the children.

Method: The design of the study was in the manner of observation and in this study, 100 children with scar that from they , 60 persons were suffering from asthma and 40 person were not afflicted to Asthma were examined. INFY and 114, 13 and the size of scar of them were studied and tested with the analyses of k2 (if necessary fisher) and test.

Findings: The test of chi- square showed the plenitude of the cases with scare larger than 5mm in the patients with asthma is 43% and in the observer group was 70%. From statistique vision, this observed difference is meaningful. Also the test of T test showed:

1. The average of INFY in the patients with asthma is $6/95 \pm 3/83$ (Pg/MI) and this measure in the example group is $10/75 \pm 6/98$ (Pg/MI).
2. The average of IL4 in patients with asthma is $30/90 \pm 16/5$ and in the example group, its $9/95 \pm 7/44$ (Mg/ml).
3. The average of IL13 in the patients suffering from asthma was $48/85 \pm 13/66$ and at the example group, its $10/49 \pm 12/44$. ($P < 0/001$).
4. The average ration of INFY/IL13 in the group suffering from asthma is $0/3054$ and in the example group, its $1/9334$ and at the statistic vision, this difference is meaningful.

Conclusion: There are relation between the size of BCG scar, asthma and between the levels of (INFY) Thelper 1 and Thelper 2 (114, 13) with asthma.

DISSEMINATED BCG INFECTION DUE TO BCG VACCINATIONI. Sedighi¹, A. Amanati¹, **B. Borzouei**²

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Background: Bacillus Calmette-Guerin (BCG) vaccine is administered in developing countries to prevent tuberculosis, and considered safe. The most serious complication of BCG is disseminated disease.

Methods: A 6-month-old girl was admitted in our hospital due to change in mental status and have a two months history of multiple fistulous ulcers in right axillary, supra-clavicular and anterior upper arm. She was lethargic, febrile and very ill. Her ulcers had been treated with traditional care.

Results: Her vital signs were: RR=70/min, PR=150/min, T=38.5(Ax) and BP=110/40. In physical examination she had abdominal distention and huge hepatosplenomegally. Visible vessels in anterior upper chest wall were seen. The III/VI systolic murmur was detected in LSB and apex. In chest radiography bilateral hilar LAPs and right axillary soft tissue swelling were seen. She received appropriate fluid replacement therapy and wide spectrum antibiotics. She had not urinary output in first few hours after admission, and was clinically managed for prevention of septic shock. Due to tonic seizure, intravenous Phenytoin was started. In the case of severe abdominal distention NGT was inserted, after 8 hours secretions became bloody and she was managed for gastrointestinal bleeding. In bone marrow aspiration increase in monoblasts and myeloblasts with numerous acid-fast bacilli were seen. Wound discharge culture was negative. Ceftazidime and Vancomycin were continued and Rifampicin, Isoniazid and Clarithromycin were started. Unfortunately 5 days after admission she died.

Conclusions: In our country all newborns are received single dose BCG vaccine at the birth. Therefore the complications of vaccination should be considered exactly.

PATHOGENETICAL CHARACTERISTIC OF THE CLINICAL AND BIOCHEMICAL INDEXES AT CHRONIC VIRAL HEPATITIS IN CHILDREN

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Backgrounds and aim: To study the main clinical and biochemical indexes at children with chronic viral hepatitis (CVH) B and C with their pathogenetical analysis.

Methods: 35 children (from 1 till 18 y.o.) of Vinnitsia region with CVH were inspected. The biggest group of patients was school age (65,7%). CVHC was diagnosed in 65,7%, CVHB - in 28,6%, CVHB+C - in 5,7%. Bilirubin level, ALT, AST, specific markers of CVH by immune-enzyme analysis and polymerase chain reactions, virus genotype and loading were determined in blood.

Results: The 1b genotype was exposed at all children with HVHC, in 15,4% - simultaneously with 1a or 3a. The viral loading hesitated from 709 to $5,9\tilde{10}^7$ copy/ml. In 60,0% infectious process was in virus replication phase (RF), in 22,9% - integration phase (IF), in 5,7% (CVHB+C) - HBV was in RF and HCV in IF; in 11,4% viral activity is unknown. Clinical symptoms of CVH depend from virus replication phase. At RF asthenic syndrome develops in 91,3%, cholemia - in 39,2%, hemorrhagic syndrome - in 34,8%, hepatomegaly - in 26,1%, while in IF these syndromes are observed in 12,5%. Biochemical indexes of cytolysis at RF were in 2 times higher than at IF. Indexes of cholestatic syndrome like conjugated bilirubin (in 5 times) alkaline phosphatase and cholesterol level (in 1,5 times) were higher at patients with RF. Also RF characterized by hypoglycemia.

Conclusions:

1. The 1b genotype was exposed at all children with HVHC.
2. Clinical manifestations, indexes of cholestasis and cytolysis are more expressed at patients with RF.

ENCEPHALITIS DUE INFLUENZA A (H1N1) IN A SEVEN YEAR-OLD GIRL WITH GOOD RESPONSE TO OSELTAMIVIR

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Background and aims: Human infection with the novel H1N1 influenza virus, was first reported in April 2009. Novel Influenza A (H1N1) virus produces higher mortality in young people. Different clinical manifestation of Influenza A (H1N1) has been reported. We present encephalitis due influenza A (H1N1) with good response to oseltamivir.

Patient: The patient was a seven year-old girl presented with mood change and gait ataxia from 5 days before admission. She also had fever, delusion, and lethargy. She had history of common cold several days before admission. She was treated with acyclovir with impression of encephalitis without improvement. In physical examination (P/E) she was febrile, there was no nuchal rigidity. P/E of chest, abdomen and extremities were normal. Lumbar puncture was performed. Cerebrospinal fluid (CSF) was normal. CSF culture showed no growth after 48h. CBC, FBS, BUN, Cr, Na, K, ALT, AST, CRP and procalcitonin were all normal. HSV PCR was negative. Electroencephalography (EEG) was done that suggested encephalitis. Brain MRI was normal. Throat culture was obtained for the diagnosis of influenza A (H1N1) that was positive. The patient was treated with oseltamivir. The patient recovered after treatment and tests for equilibrium became normal.

Conclusions: Encephalitis due to influenza A (H1N1) should be considered in every patient with signs and symptoms of encephalitis during influenza A (H1N1) pandemy.

MYOSITIS ASSOCIATED WITH PANDEMIC INFLUENZA A- H1N1 VIRUS INFECTION**A. Cerqueira¹, H. Antunes^{1,2}**

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In 2009, cases of influenza like illness were reported in Mexico on March 18; the outbreak was subsequently confirmed as H1N1 influenza A. H1N1 Influenza tends to cause high morbidity but low mortality rates (1-4%). The first case was confirmed in Portugal on May 4, 2009. Were recorded 70 deaths, including 5 children (7.1%) (4 months, 10, 11, 14 and 17 years).

In our hospital 325 children were surveyed for H1N1 infection of which 165 (50.8%) were positive and 15 were hospitalized (9.1% of H1N1 positive). Only one had myositis. There were no deaths.

We report the case of a 9 years old boy with no personal or family relevant history who was admitted to the emergency room at the convalescent phase of a upper respiratory tract infection with a severe lower-extremity myalgia and reluctance to walk. On exam showed broad-based gait and calf pain. Creatine Kinase 13808 (38-190 U/l) and AST/ALT 333/64 (< 35/28 U/l) levels were elevated. Diagnosis of H1N1 was established by viral isolation (reverse transcriptase Polimerase Chain Reaction). He made intravenous fluids and was discharged the 2nd day.

Influenza-associated myositis is a complication of influenza among children. This case demonstrates the novel virus capacity for causing significant disease. Even so has an excellent prognosis.

SCREENING FOR TROPICAL AND GEOGRAPHICALLY-ENDEMIC INFECTIONS IN CHILDREN WITH HAEMATOLOGICAL AND ONCOLOGICAL DISEASES

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Background and aims: In recent years, immigration has led to major demographical changes in Spain, where 500,000 children under the age of 15 years are immigrants. These children may have diseases that are not common in our country and which may have severe consequences in immunodepressed patients.

Methods: All children from countries endemic for tropical diseases hospitalised in the Paediatric Oncology and Haematology Department between April and October 2009 were included. Specific screening for infectious diseases consisted of direct tests (parasites in faeces and urine, thick blood smear) and indirect tests (parasites and viral serologies).

Results: Twenty-five patients were included (11 girls, 14 boys). Median age was 7 years (range: 6 months-15 years). Patients were from South America (9 patients), North Africa and the Middle East (8), Sub-Saharan Africa (3), Eastern Europe (3) and the Indian Subcontinent (2). Five were diagnosed of infectious diseases: occult hepatitis B (2), leishmaniasis (1), ascariasis (1), and taeniasis by *Hymenolepis nana* (1). No patient had symptoms prior to onset.

Conclusions: The prevalence of tropical and geographically-endemic infections in immigrant patients was 20%.

Screening permitted these patients to be treated pre-emptively.

ENCEPHALITIS OF UNKNOWN ETIOLOGY IN 16 YEARS OLD BOY**T. Ahačič***Splosna Bolnisnica Jesenice, Jesenice, Slovenia*

16 years old boy was admitted to hospital after first epileptic seizure. After admission he had worsening headache with normal neurologic exam. On the second day he became aphasic, had paresis of facial nerve on the right side and progressively lost muscle strength on the right side of the body. CT of the brain showed no abnormality. CSF showed mild elevated proteins and pleocytosis. Empirical antibiotic treatment with acyclovir and ceftriaxon was started. MRI of the brain and EEG showed signs of encephalitis.

CSF was negative for TBE, HSV, Borelia Burgdorferi. Serology was negative for Toxoplasma gondii, Mycoplasma pneumoniae, Chlamidia psittaci, Chlamydia pneumoniae, EBV and CMV. Blood and CSF cultures were sterile, culture for Listeria was negative.

During treatment the boy was getting better and at discharge his neurological status was normal, but he had some behavioural and learning problems. After a month he had no neurological problems and his school performance was as before illness.

Conclusion: We treated 16 years old boy with encephalitis of unknown etiology. He was cured, but we are not sure that our treatment has had any affect on his improvement.

EPIDEMIC DROPSY IN DISGUISE OF DENGUE HEMORRHAGIC FEVER**D. Bhat, H. Singh, G. Dhooria, N. Mal***Pediatrics, Dayanand Medical College, Ludhiana, India*

An 11 year old female was referred to our hospital as a suspected case of dengue hemorrhagic fever. On examination general condition of the child was sick. There was a marked pallor, edema feet, facial puffiness, child was fully conscious, JVP was not raised. On systemic examination, chest examination showed intercostals retractions and bilateral crepts with decreased air entry in both inferior axillary areas. Blood investigations revealed severe anemia with thrombocytopenia. Xay chest showed right sided pleural effusion. As around this time we were having many cases of dengue hemorrhagic fever so first possibility was kept of the same. However on taking a detailed history it was learnt that both mother and father too were ill. Mother was hospitalized outside with complaints of respiratory problem and generalized edema over body. Father was also having edema feet. On further history taking it was learnt that they were consuming mustard oil for last few months. Samples of the oil tested positive for Sanguinarine (argemone oil). Patient was finally discharged on day 10th of hospitalization.