Staff Publications 2011

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Articles are listed alphabetically by first author.

Abraham MB and Porter P
Clonidine in cyclic vomiting

Alessandri AJ
Parents know best: or do they? Treatment refusals in paediatric oncology
Journal of paediatrics and child health. 2011; 47(9): 628-631

Although treatment refusal is an infrequent occurrence in paediatric oncology, it is an important issue that threatens the ongoing therapeutic relationship between the health-care team and families. While there are good reasons to support the decision-making authority of parents in the medical setting, parents’ rights in this respect are not absolute. Fortunately, most disagreements between clinicians and parents regarding treatment decisions for children are resolved within the health-care team/family dyad or with the objective advice of other clinicians or clinical ethics services. The increasing appeal of ‘natural therapies’ and unsubstantiated confidence with which they are prescribed may lead to more frequent refusal of conventional, evidence-based oncology treatment in the future. The harm principle may assist paediatric oncologists in the difficult task of determining when it is justifiable to refer a case for judicial intervention.

Baker M and Borland M
Range of elbow movement as a predictor of bony injury in children
Emergency medicine journal : EMJ. 2011; 28(8): 666-669

Background: The aim of this study was to determine whether a normal range of elbow movement can be used as a rule out tool for significant injury after blunt trauma in the paediatric population. Methods: A prospective observational study was set up in an Australian tertiary paediatric emergency department. Patients from 3 to 16 years old were included. Active range of elbow movement (flexion, extension, supination and pronation) was recorded as either normal or abnormal. All participants received standard elbow x-rays. Range of movement (ROM) was compared to the radiologist's final x-ray report. An x-ray was considered abnormal if it showed a fracture, dislocation or isolated elbow effusion. Results: 177 patients were included in the study, of which all received elbow x-rays. 146 had a restricted ROM (82%). 106 x-rays were reported as abnormal (60%). An abnormal ROM had a sensitivity of 93.4% (95% CI 86.9% to 97.3%), specificity 33.8% (95% CI 23.0% to 46.0%) and negative predictive value of 77.4% (95% CI 58.9% to 90.4%) for an abnormal x-ray. There were seven false-negative results in this group. Clinical management was changed in four of these patients due to abnormalities seen on x-ray. Conclusion: In the setting of blunt trauma resulting in elbow injury in children, a normal ROM does not rule out a significant injury and should not be used as a screening tool.

Banerjee B, Ling K-M, Sutanto EN, Musk M, Yerkovich ST, Hopkins PMA, Stick SM, Kicic A and Chambers DC
The airway epithelium is a direct source of matrix degrading enzymes in bronchiolitis obliterans syndrome
The Journal of Heart and Lung Transplantation. 2011; 30(10): 1175-1185

Background: Long-term survival after lung transplantation is hindered by the development of bronchiolitis obliterans syndrome (BOS), and recent evidence suggests that dysregulated epithelial repair may underlie its development. Because matrix metalloproteinase (MMP) -2 and MMP-9 secretion is integral to repair, we
hypothesized that airway epithelial cells from patients with BOS would over-express these matrix-degrading enzymes.

Methods: Cells obtained from bronchial and bronchiolar brushings from patients with and without BOS (without acute rejection or infection) were analyzed via quantitative polymerase chain reaction and immunocytochemistry for MMP-2, and MMP-9 gene and protein expression. The expression of tissue inhibitor of metalloproteinase (TIMP)2 and TIMP1 was also assessed. MMP activity in bronchoalveolar lavage was determined via gelatinzymography.

Results: MMP-2 and MMP-9 production was significantly higher in bronchoalveolar lavage (3.85- and 11.59-fold, p<0.001) and airway epithelium (MMP-2 bronchial: 6.33-fold, bronchiolar: 3.57-fold, both p<0.001; MMP-9 bronchial: 32.55-fold, p<0.001; bronchiolar: 8.60-fold, p=0.01) in patients with BOS, but expression in patients without BOS was not different from healthy controls. TIMP expression was similar in patients with and without BOS. Immunostaining confirmed that the airway epithelium was a direct source of MMP-2 and MMP-9 expression in patients with BOS.

Conclusion: In patients with BOS, the airway epithelium over-expresses MMPs, even in the absence of acute rejection or infection. Dysregulated epithelial repair may be a key feature of BOS.

Baynam G, Claes P, Craig JM, Goldblatt J, Kung S, Le Souef P and Walters M

Intersections of epigenetics, twinning and developmental asymmetries: insights into monogenic and complex diseases and a role for 3D facial analysis


For decades the relationships of twinning and alterations in body patterning, such as laterality and asymmetry, have been investigated. However, the tools to define and quantify these relationships have been limited and the majority of these studies have relied on associations with subjectively defined phenotypes. The emerging technologies of 3-dimensional (3D) facial scanning and geometric morphometrics are providing the means to establish objective criteria, including measures of asymmetry, which can be used for phenotypic classification and investigations. Additionally, advances in molecular epigenetics provide new opportunities for novel investigations of mechanisms central to early developmental processes, twinning and related phenotypes. We review the evidence for overlapping etiologies of twinning, asymmetry and selected monogenic and complex diseases, and we suggest that the combination of epigenetic investigations with detailed and objective phenotyping, utilizing 3D facial analysis tools, can reveal insights into the genesis of these phenomena.

Bell LM, Curran JA, Byrne S, Roby H, Suriano K, Jones TW and Davis EA

High incidence of obesity co-morbidities in young children: A cross-sectional study

Journal of paediatrics and child health. 2011; Sep 9 [Epub ahead of print]

Aim: The prevalence of overweight and obesity in children is a public health problem because of future morbidity. However, the prevalence of medical complications in overweight and obese primary school children in Australia is not well documented. As part of the larger, prospective cohort Growth and Development Study, this report aimed to identify the medical complications of obesity in a population-based community sample of primary school-aged children. Methods: Two groups of primary school children were studied: a random community sample of overweight/obese children (not seeking treatment) and a matched community sample of normal weight children. Demographics, medical history, family history and symptoms of complications of overweight were collected. Children had a physical examination, oral glucose tolerance tests with insulins, fasting lipid profiles and liver function tests. Results: Data from 283 children are presented (6.1-13.4 years, mean 9.8 years). There were no differences in birth data, family composition, parental age or socio-economic status between groups. Overweight and obese children were more likely to complain of musculoskeletal pain, depression, anxiety and bullying, and had more adverse examination findings than control children. They also had more abnormal investigations: overweight children: impaired glucose tolerance (IGT) 1.3%, hyperinsulinism 19.5%, dyslipidaemia 63.8%, raised alanine transaminase (ALT) 9.0%; obese children: IGT 5.3%, hyperinsulinism 38.9%, dyslipidaemia 73.7%, raised ALT 31.6%. Conclusion: Overweight and obese primary school-aged children have significant medical complications of their weight status. Overweight children, in addition to obese children, should be screened for complications. A secondary finding is a high proportion of normal weight children with lipid levels outside desirable healthy ranges.

Association between human rhinovirus C and severity of acute asthma in children
The European respiratory journal : official journal of the European Society for Clinical Respiratory Physiology. 2011; 37(5): 1037-1042

A new and potentially more pathogenic group of human rhinovirus (HRV), group C (HRVC), has recently been discovered. We hypothesised that HRVC would be present in children with acute asthma and cause more severe attacks than other viruses or HRV groups. Children with acute asthma (n = 128; age 2-16 yrs) were recruited on presentation to an emergency department. Asthma exacerbation severity was assessed, and respiratory viruses and HRV strains were identified in a nasal aspirate. The majority of the children studied had moderate-to-severe asthma (85.2%) and 98.9% were admitted to hospital. HRV was detected in 87.5% and other respiratory viruses in 14.8% of children, most of whom also had HRV. HRVC was present in the majority of children with acute asthma (59.4%) and associated with more severe asthma. Children with HRVC (n = 76) had higher asthma severity scores than children whose HRV infection was HRVA or HRVB only (n = 34; p = 0.018), and all other children (n = 50; p = 0.016). Of the 19 children with a non-HRV virus, 13 had HRV co-infections, seven of these being HRVC. HRVC accounts for the majority of asthma attacks in children presenting to hospital and causes more severe attacks than previously known HRV groups and other viruses.

Blyth CC

Antifungal azoles: old and new
The Pediatric infectious disease journal. 2011; 30(6): 506-507

Blyth CC, Booy R and Dwyer DE

Point of care testing: diagnosis outside the virology laboratory

Numerous point-of-care tests (POCTs) are available to diagnose viral infections in both hospital and community settings. The ideal POCT is rapid, sensitive, specific, and simple to perform. This chapter will describe the benefits of POCTs, factors that can influence the accuracy of POCTs and highlight some limitations of POCT strategies. The sensitivity, specificity, and turn-around time of available POCTs are included for common conditions including respiratory viral infections (e.g. influenza, RSV) and blood-borne viral infections (e.g. HIV).

Blyth CC, Currie AJ, Wiertsema SP, Conway N, Kirkham LA, Fuery A, Mascaro F, Geelhoed GC and Richmond PC

Trivalent influenza vaccine and febrile adverse events in Australia, 2010: clinical features and potential mechanisms
Vaccine. 2011; 29(32): 5107-5113

INTRODUCTION: Increased numbers of children presenting with febrile adverse events following trivalent influenza vaccine (TIV) were noted in Australia in 2010. We describe the epidemiology and clinical features of the adverse events and explore the biological basis for the adverse events using an in vitro model. MATERIALS AND METHODS: Children presenting to a tertiary paediatric hospital in 2010 with adverse events within 72 h of TIV were retrospectively reviewed. Demographics, clinical features, physiological variables and outcomes were examined. Plasma cytokine and chemokine levels were examined in a subgroup of children with vaccine-related febrile convulsions. Peripheral blood mononuclear cells of age-matched children were stimulated with different TIV preparations. Inflammatory cytokine and chemokine analysis was performed on cultured supernatants. RESULTS: Vaccine-related febrile adverse events were identified in 190 children. Most occurred in healthy children (median age: 1.5 years) within 12 h of vaccination. Twenty-eight (14.7%) required hospital admission. High temperature >/=39.0 degrees C (101/190; 53%), vomiting (120/190; 63%) and convulsions (38/190; 20%) were common. All children presenting had received Fluvax((R)) or Fluvax Junior((R)). In the in vitro model, IFN-alpha, IL-1beta, IL-6, IL-10, IP-10 and MIP-1-alpha levels were significantly higher when measured at 6 and 24 h in cultures stimulated with Fluvax((R)) compared with alternative 2010 TIV preparations. CONCLUSIONS: Numerous febrile adverse events (including febrile seizures) were observed following Fluvax((R)) or Fluvax Junior((R)) in 2010. Clear differences in cytokine production were observed when peripheral blood mononuclear
cells were stimulated with Fluvax((R)) compared with alternate TIV preparations. Increased awareness of these potential adverse events is required to ensure earlier detection and prevention in the future.

Blyth CC, Gomes L, Sorrell TC, da Cruz M, Sud A and Chen SC
Skull-base osteomyelitis: fungal vs. bacterial infection
Clinical microbiology and infection: the official publication of the European Society of Clinical Microbiology and Infectious Diseases. 2011; 17(2): 306-311

Skull-base osteomyelitis (SBO) occurs secondary to invasive bacterial and fungal infection. Distinguishing between fungal and bacterial aetiologies of SBO has significant therapeutic implications. An 18-year (1990-2007) retrospective review of patients with SBO presenting to Westmead Hospital was performed. Epidemiological, clinical, laboratory and radiology data were collated. Twenty-one patients (median age 58 years) with SBO were identified: ten (48%) had bacterial and 11 (52%) had fungal SBO. Diabetes mellitus (57%) and chronic otitis externa (33%) were the most frequent co-morbidities; immunosuppression was present in five cases (24%). Cranial nerve deficits occurred in ten (48%) patients. The commonest pathogens were Pseudomonas aeruginosa (50% bacterial SBO) and a zygomycete (55% fungal SBO). Compared to bacterial SBO, fungal SBO was more frequently associated with underlying chronic sinusitis, sinonasal pain, facial/peri-orbital swelling and nasal stuffiness or discharge and the absence of purulent ear discharge (all p <0.05). Bacterial SBO was more frequently associated with deafness, ear pain or ear discharge (all p <0.05). Median time to presentation was longer in patients with bacterial SBO (26.3 weeks vs. 8.1 weeks, p 0.08). Overall 6-month survival was 88% (14/18 patients). All four deaths occurred in patients with fungal SBO. Immunosuppression was a risk factor for death (p <0.05). Early diagnostic sampling is recommended in patients at increased risk of fungal SBO to enable optimal antimicrobial and surgical management.

Blyth CC, Markus TY, Effler PV and Richmond PC
Ensuring safety of the 2011 trivalent influenza vaccine in young children
The Medical journal of Australia. 2011; 195(1): 52

Borland M, Milsom S and Esson A
Equivalency of two concentrations of fentanyl administered by the intranasal route for acute analgesia in children in a paediatric emergency department: A randomized controlled trial
Emergency Medicine Australia. 2011; 23(2): 202-208

Objective: Intranasal fentanyl's (INF) effectiveness is established using highly concentrated INF (HINF). Standard concentration INF (SINF) is more widely available. We aimed to illustrate the equivalence of SINF to HINF. Methods: Double-blinded randomized controlled trial was used within a children's hospital ED. Children aged 3-15 years with fractures were randomized to SINF or HINF. Outcome measures included pain scores at time zero and every 10 min until 30 min. Additional analgesic agents were noted. Results: Data in 189 children (91 HINF, 98 SINF) were obtained. Pre-analgesia median VAS was 80.0 mm (interquartile range [IQR] 60.0-95.5) in SINF, 77.5 mm (IQR 60.0-100) in HINF. At 10 min median VAS was 49.5 mm (IQR 26.5-68.5) and 43.0 mm (IQR 15.2-66.0), respectively, at 20 min 27.5 mm (IQR 18.5-56.5) and 35.0 mm (IQR 9.0-57.0) and at 30 min 20.0 mm (IQR 10.0-46.0) and 21.5 mm (IQR 4.75-51.0). Each agent demonstrated significant decrease in pain scores (median decrease 40 mm, P = 0.000). Additional analgesia was given in 67 (42 SINF, 25 HINF) (P = 0.028). The decrease in pain scores between children < and >/=50 kg in SINF was significant both overall (P = 0.005) and between 10 and 20 min (P = 0.003). There was no difference in HINF at any time by weight. Conclusions: The two concentrations of INF were equivalent in reducing pain, with a trend to increased oral additional agents in the more dilute solution. The widespread use of this readily available analgesic in the standard concentration can be supported, particularly in patients <50 kg.

Broadbent K and Lovegrove M
Not just another sore throat
Australian family physician. 2011; 40(8): 605-606

Case study A man, 26 years of age, presented to a hospital emergency department complaining of a sudden onset of a sore throat 6 hours previously while consuming a carbonated drink at work. The pain commenced about lunchtime, after he had been mixing concrete powder, and since then had been intermittent and was becoming more severe.
Burgess S, Sly P and Devadason S
Adherence with preventive medication in childhood asthma
Pulmonary medicine. 2011; Epub ahead of print

Suboptimal adherence with preventive medication is common and often unrecognized as a cause of poor asthma control. A number of risk factors for nonadherence have emerged from well-conducted studies. Unfortunately, patient report a physician's estimation of adherence and knowledge of these risk factors may not assist in determining whether non-adherence is a significant factor. Electronic monitoring devices are likely to be more frequently used to remind patients to take medication, as a strategy to motivate patients to maintain adherence, and a tool to evaluate adherence in subjects with poor disease control. The aim of this paper is to review non-adherence with preventive medication in childhood asthma, its impact on asthma control, methods of evaluating non-adherence, risk factors for suboptimal adherence, and strategies to enhance adherence.

Campanella SD, Rapley P and Ramelet AS
A randomised controlled pilot study comparing Mepitel(R)(R) and SurfaSoft(R)(R) on paediatric donor sites treated with Recell(R)(R)
Burns : journal of the International Society for Burn Injuries. 2011; 37(8): 1334-1342

This randomized controlled pilot study examined the effects of a silicone net dressing (Mepitel(R)(R)) and a monofilament polyamide woven dressing (SurfaSoft(R)(R)) on the rate of epithelialisation and epidermal maturation, pain, and ease of dressing removal on paediatric donor sites treated with epithelial cell suspension (ReCell(R)(R)). Fifteen children (1-15 years) admitted for acute or reconstructive burns procedures in a tertiary referral hospital in Australia were randomly assigned to the experimental group, Mepitel(R)(R) (n=8) and to the control group, SurfaSoft(R)(R) (n=7). All donor sites were treated with ReCell(R)(R) and covered with the assigned dressing. Measurements of rate of epithelialisation and epidermal maturation, pain, and ease of dressing removal were recorded every two days until the wound was healed. Results showed that there was no difference in the rate of epidermal maturation between the two groups. Less pain and force to remove the dressing was shown in the Mepitel(R)(R) group when compared to SurfaSoft(R)(R). The rate of epithelialisation was found to be an unreliable measure. Although additional research is required to support the results of this study, these results suggest that Mepitel(R)(R) pliable, self-adhesive and atraumatic properties may improve healing of ReCell(R)(R) treated donor sites with less pain at dressing changes. This pilot study provides a strong base for further research in this area.

Chapman R, Watkins R, Zappia T, Nicol P and Shields L
Nursing and medical students' attitude, knowledge and beliefs regarding lesbian, gay, bisexual and transgender parents seeking health care for their children

Background. Little research has been conducted to investigate students' attitudes, knowledge and beliefs regarding lesbian, gay, bisexual and transgender parents seeking health care for their children. Design. Descriptive, comparative study. Validated scales were used to assess students' attitudes, knowledge and beliefs and gay affirmative practice. Three open ended questions assessed beliefs regarding lesbian, gay, bisexual and transgender parents accessing health care for their children. Method. Nursing and medical students completed questionnaires about attitudes to homosexuality. Associations between variables were assessed using chi-square tests of independence, and differences between nursing and medical student groups were assessed using the Mann-Whitney U-test or the Kruskal-Wallis one-way analysis of variance test. Responses to the open ended questions were evaluated, coded and described. Results. Knowledge and attitudes about homosexuality were significantly associated with students' race, political voting behaviour, religious beliefs and having a friend who is openly lesbian, gay, bisexual and transgender. Conclusions. It is important to develop strategies to address the existence of prejudicial attitudes among student health professionals and prevent discriminatory practices towards lesbian, gay, bisexual and transgender parents when seeking health care for their children. Relevance to clinical practice. Educators can develop programs that provide students with knowledge and skills to ensure lesbian, gay, bisexual and transgender families receive effective health care when they access services for their children.
Chapman R, Zappia T and Shields L
An essay about health professionals’ attitudes to lesbian, gay, bisexual and transgender parents seeking healthcare for their children
Scandinavian Journal of Caring Sciences. 2011; 14 Nov, [Epub ahead of print]

Scand J Caring Sci; 2011 An essay about health professionals’ attitudes to lesbian, gay, bisexual and transgender parents seeking healthcare for their children Background: This paper is a polemic essay about an important but sometimes controversial subject. Lesbian, gay, bisexual and transgender (LGBT) clients can be reluctant to reveal their sexual orientation to health professionals from whom they may be seeking health care for their children. Family-centred care (FCC), where care is planned around the whole family not just the individual child, is widely used across the world, but unless all aspects of the families who present for care are respected, care delivery is compromised. This is particularly important for minority groups and potentially vulnerable families such as LGBT. Aim: This descriptive essay discusses the use of health services by LGBT parents, how seeking health care is influenced by perceived perceptions of LGBT people held by health professionals, and examines factors affecting such seeking of health care. Discussion: We show that LGBT people may be unwilling to disclose sexual identity to health professionals when seeking health care for their children. Health professional’s attitudes can be affected by factors such as gender, age, religious and political affiliations, education level and previous interactions with LGBT people. Conclusion: We conclude our argument with the assertion that all parents, including those from minority groups such as LGBT, who bring their children for health care need supportive family-centred care, and only by ensuring that the health professionals delivering care are well educated about all aspects of sexuality will care be family-centred.

Chua KL, Ma S, Prescott S, Ho MH, Ng DK and Lee BW
Trends in childhood asthma hospitalisation in three Asia Pacific countries
Journal of paediatrics and child health. 2011; 47(10): 723-727

AIM: The study aims to examine recent childhood asthma hospitalisation rates in the Asia Pacific countries of Australia, Hong Kong and Singapore. On the background of reported decline in many countries with high asthma prevalence during late 1990s. METHODS: Annual asthma hospitalisation (ICD9-CM: 493 or ICD10-AM: J45-46)* and population data from 1994 to 2008, of children aged 0-14 years old, were obtained from the Australian National Hospital Morbidity Database, from the Hospital Authority in Hong Kong and from the Ministry of Health in Singapore. Data were stratified in two age groups: 0-4 and 5-14 years old, and also in different periods of calendar years. Time-series regression analyses were used to examine temporal trends. Diagnostic transfer was addressed by examining bronchitis hospitalisations. RESULTS: Significant decreases of up to 6.5% per annum in childhood asthma hospitalisation rates were found over the study period. However, the latter half of the study period showed increases in hospitalisation rates in all countries studied. No evidence of diagnostic transfer was found. CONCLUSION: Although there has been a decrease in childhood asthma hospitalisation rates since the 1990s, a modest increase was observed from 2003 to 2008. Ongoing monitoring is required.

Claes P, Walters M, Vandermeulen D and Clement JG
Spatially-dense 3D facial asymmetry assessment in both typical and disordered growth

Mild facial asymmetries are common in typical growth patterns. Therefore, detection of disordered facial growth patterns in individuals characterized by asymmetries is preferably accomplished by reference to the typical variation found in the general population rather than to some ideal of perfect symmetry, which rarely exists. This presents a challenge in developing an asymmetry assessment tool that is applicable, without modification, to detect both mild and severe facial asymmetries. In this paper we use concepts from geometric morphometrics to obtain robust and spatially-dense asymmetry assessments using a superimposition protocol for comparison of a face with its mirror image. Spatially-dense localization of asymmetries was achieved using an anthropometric mask consisting of uniformly sampled quasi-landmarks that were automatically indicated on 3D facial images. Robustness, in the sense of an unbiased analysis under increasing asymmetry, was ensured by an adaptive, robust, least-squares superimposition. The degree of overall asymmetry in an individual was scored using a root-mean-squared-error, and the proportion was scored using a novel relative significant asymmetry percentage. This protocol was applied to a database of 3D facial images from 359 young healthy individuals and three individuals with disordered facial growth. Typical asymmetry statistics were derived and were mainly located on, but not limited to, the lower two-thirds of the face in males and females. The asymmetry
in males was more extensive and of a greater magnitude than in females. This protocol and proposed scoring of asymmetry with accompanying reference statistics will be useful for the detection and quantification of facial asymmetry in future studies.

Clifford HD, Richmond P, Khoo SK, Zhang G, Yerkovich ST, Le Souef PN and Hayden CM

SLAM and DC-SIGN measles receptor polymorphisms and their impact on antibody and cytokine responses to measles vaccine
Vaccine. 2011; 29(33): 5407-5413

BACKGROUND: Despite the use of measles vaccine, measles virus continues to circulate and cause severe disease. Immune responses to the measles vaccine are variable between individuals, with up to 10% failing to produce a sufficient protective response post-vaccination. Signaling lymphocyte activation molecule (SLAM) and dendritic cell-specific intercellular adhesion molecule-3 grabbing nonintegrin (DC-SIGN; CD209) are specific measles receptors: SLAM binds and permits entry of the virus into the cell, DC-SIGN acts as an attachment receptor, increasing viral binding efficiency and transmission. Genetic variations in these receptor genes may alter measles vaccine antibody and cellular responses. METHODS: In 12-month-old infants from Perth, Western Australia after their first measles vaccine dose as part of the combination measles-mumps-rubella (MMR) vaccine, 7 SLAM and DC-SIGN polymorphisms were genotyped and associations were investigated with measles IgG antibody levels and in vitro measles cytokine responses. RESULTS: The DC-SIGN promoter variant -336C/T was associated with overall IFN-gamma responses after measles stimulation (P = 0.002) and three DC-SIGN polymorphisms (-336C/T, -139C/T and -871C/T) were associated with the proportion of cytokine non-responders to measles (P = 0.001, P = 0.021 and P = 0.036, respectively). However, no associations were found between the DC-SIGN or SLAM polymorphisms and measles IgG antibody levels. CONCLUSIONS: The results suggest that DC-SIGN -139C/T, -336C/T and -871C/T polymorphisms may modulate cytokine (but not antibody) responses to the measles component of MMR vaccine. Furthermore, contrasting previous studies, SLAM polymorphisms do not appear to affect measles antibody or cytokine responses in this cohort.

Clifford HD, Yerkovich ST, Khoo SK, Zhang G, Upham J, Le Souef PN, Richmond P and Hayden CM

Toll-like receptor 7 and 8 polymorphisms: associations with functional effects and cellular and antibody responses to measles virus and vaccine
Immunogenetics. 2011; [Epub ahead of print]

Successful defence against viral pathogens requires the rapid recognition of virus-specific “danger signals” and the activation of both innate and adaptive immunity. Toll-like receptors (TLR) 7 and 8 play a critical role in the elimination of viruses by recognising the common viral component, single stranded (ss)RNA. Measles virus, an ssRNA virus, continues to cause serious morbidity and mortality worldwide despite available measles vaccines. TLR7 and TLR8 genetic variation may cause functional alterations that result in impaired responses to measles. In a population of 12-month-old Australian infants, receptor protein expression was examined to assess the functionality of TLR7 and TLR8 polymorphisms, and the effects of these polymorphisms on cellular and antibody responses after the first measles vaccine dose were investigated. TLR7 Leu11Gln showed associations with TNF-alpha responses after ligand (imiquimod) stimulation in males only (P = 0.040), and non-responders were more likely to be Gln males (P = 0.044). TNF-alpha non-responders after imiquimod also had higher percentages of TLR8 -4284TT (69.6%) (P = 0.001) and TLR8 -558CC (69.6%) (P = 0.002) in females. Receptor protein expression after imiquimod or measles stimulation was not significantly altered compared with baseline, nor was it affected by genotype. None of the TLR7 or TLR8 polymorphisms studied were associated with measles-specific cytokine levels or with measles IgG levels. In conclusion, we report gender-specific associations with TLR7 and TLR8 polymorphisms and TNF-alpha cellular responses to its ligand. However, we found no evidence of any functional effects of TLR7 or TLR8 polymorphisms on receptor expression, measles-specific cellular responses or measles vaccine antibody responses.
Cole CH
Rapid update on childhood immune thrombocytopenic purpura
Journal of paediatrics and child health. 2011; [Epub ahead of print]

Most childhood immune thrombocytopenic purpura is benign, self-limiting and requires no therapy. However, questions remain: (i) to treat or not; (ii) bone marrow examination or not; and (iii) admit to hospital or not. These questions have dominated the literature and we still need a prospective large multi-centre study of these issues to determine a useful bleeding score, quality of life measure and a measure of parental anxiety.

Coyne I, O’Mathúna Donal P, Gibson F, Shields L and Sheaf G
Interventions for promoting participation in shared decision-making for children with cancer
Cochrane Database of Systematic Reviews. 2011; (2)
This is the protocol for a review and there is no abstract. The objectives are as follows: To examine the effects of interventions to promote shared decision-making (SDM) for children with cancer who are aged four to 18 years.

Preterm infants have deficient monocyte and lymphocyte cytokine responses to Group B Streptococcus Infection and immunity. 2011; 79(4): 1588-1596

Group B streptococcus (GBS) is an important cause of early- and late-onset sepsis in the newborn. Preterm infants have markedly increased susceptibility and worse outcomes, but their immunological responses to GBS are poorly defined. We compared mononuclear cell and whole-blood cytokine responses to heat-killed GBS (HKGBS) of preterm infants (gestational age [GA], 26 to 33 weeks), term infants, and healthy adults. We investigated the kinetics and cell source of induced cytokines and quantified HKGBS phagocytosis. HKGBS-induced tumor necrosis factor (TNF) and interleukin 6 (IL-6) secretion was significantly impaired in preterm infants compared to that in term infants and adults. These cytokines were predominantly monocytic in origin, and production was intrinsically linked to HKGBS phagocytosis. Very preterm infants (GA, <30 weeks) had fewer cytokine-producing monocytes, but nonopsonic phagocytosis ability was comparable to that for term infants and adults. Exogenous complement supplementation increased phagocytosis in all groups, as well as the proportion of preterm monocytes producing IL-6, but for very preterm infants, responses were still deficient. Similar defective preterm monocyte responses were observed in fresh whole cord blood stimulated with live GBS. Lymphocyte-associated cytokines were significantly deficient for both preterm and term infants compared to levels for adults. These findings indicate that a subset of preterm monocytes do not respond to GBS, a defect compounded by generalized weaker lymphocyte responses in newborns. Together these deficient responses may increase the susceptibility of preterm infants to GBS infection.

Davies K, Monterosso L and Leslie G
Determining standard criteria for endotracheal suctioning in the paediatric intensive care patient: An exploratory study
Intensive & Critical Care Nursing. 2011; 27(2): 85-93

Summary: This four-phase mixed method study developed an evidence based “Endotracheal Suction Assessment Tool” (ESAT) as a guide for nurses undertaking “endotracheal tube” (ETT) suction within “Paediatric Intensive Care” (PIC). Phase 1 involved a comprehensive literature review to determine the most commonly used criteria for assessing the need for ETT suction. In Phase 2 an “Endotracheal Suction Questionnaire” (ESQ) was developed to survey experienced PIC nurses in Australia and New Zealand regarding their ETT suction decision making process and validity testing of the ESQ. In Phase 3, the ESQ was administered to target group (n=104). In Phase 4, the empirical evidence generated from this study, based upon the criteria rated by nurses in this study as being most clinically important and essential during the decision making process, determined the ESAT design. Analyses of quantitative results showed a positive correlation between the perceived frequency of use of a criterion and the appropriateness of the assessment. Where a criterion was used less frequently as a clinical indicator for the requirement for ETT suction, participants had a lower regard for this when rating the criterion as a specific single indicator to perform suction. Findings from qualitative data identified six criteria not previously documented within the literature. Further testing and validation of the tool within the PIC setting will determine the clinical viability of the ESAT.
Deshpande G, Rao S, Kell A and Patole S
Evidence-based guidelines for use of probiotics in preterm neonates

BACKGROUND: Current evidence indicates that probiotic supplementation significantly reduces all-cause mortality and definite necrotising enterocolitis without significant adverse effects in preterm neonates. As the debate about the pros and cons of routine probiotic supplementation continues, many institutions are satisfied with the current evidence and wish to use probiotics routinely. Because of the lack of detail on many practical aspects of probiotic supplementation, clinician-friendly guidelines are urgently needed to optimise use of probiotics in preterm neonates. AIM: To develop evidence-based guidelines for probiotic supplementation in preterm neonates. METHODS: To develop core guidelines on use of probiotics, including strain selection, dose and duration of supplementation, we primarily used the data from our recent updated systematic review of randomised controlled trials. For equally important issues including strain identification, monitoring for adverse effects, product format, storage and transport, and regulatory hurdles, a comprehensive literature search, covering the period 1966-2010 without restriction on the study design, was conducted, using the databases PubMed and EMBASE, and the proceedings of scientific conferences; these data were used in our updated systematic review. RESULTS: In this review, we present guidelines, including level of evidence, for the practical aspects (for example, strain selection, dose, duration, clinical and laboratory surveillance) of probiotic supplementation, and for dealing with non-clinical but important issues (for example, regulatory requirements, product format). Evidence was inadequate in some areas, and these should be a target for further research. CONCLUSION: We hope that these evidence-based guidelines will help to optimise the use of probiotics in preterm neonates. Continued research is essential to provide answers to the current gaps in knowledge about probiotics.

Deshpande G, Rao S and Patole S
Progress in the field of probiotics: year 2011

Purpose of review: The interest and scope for research in the field of probiotics has significantly widened in recent years. This brief review covers the significant advances in the field of probiotics. Recent findings: These include conclusive evidence for the benefits of probiotics in preventing all cause mortality and necrotizing enterocolitis (NEC) in preterm very low birth weight (VLBW) neonates, understanding the role of probiotics as vaccine adjuvants, and in modulating inflammatory bowel diseases, bowel cancer, type 1 diabetes mellitus, obesity, high cholesterol levels, and bacterial resistance. Other areas of progress include understanding the role of probiotics in oral health and ageing. Summary: Current evidence will lead to routine probiotic supplementation to prevent all cause mortality and NEC in preterm VLBW neonates. Probiotics may also become novel agents as vaccine adjuvants, and in dealing with major public health issues such as obesity, type I diabetes mellitus, and poor oral health. Research in applications of probiotics in food products will rationalize product development, and health claims. As new frontiers continue to be explored the challenges to the basis of the hygiene hypothesis will influence further developments in the field of probiotics.

Dudman L, Rapley P and Wilson S
Development of a transition readiness scale for young adults with cystic fibrosis: face and content validity.

Mixed methods research in Australia to develop and validate a tool for assessing whether adolescents with cystic fibrosis are prepared to make the move from paediatric to adult health services. The Cystic Fibrosis Health Care Transition Readiness Scale was developed through a review of existing scales and interviews with adolescents/parents, and underwent expert content analysis.

A 26-year population-based study of burn injury hospital admissions in Western Australia
Journal of Burn Care and Research. 2011; 32(3): 379-386

The aim of the study was to use state-wide health administrative data to assess the incidence, temporal trends, and external cause of burn injury-related hospital admissions and mortality in Western Australia from 1983 to 2008. Linked hospital morbidity and death data for all persons hospitalized with an index burn injury in Western
Australia for the period 1983-2008 were identified. Annual age-specific incidence and age standardized rates were estimated. Poisson regression analyses were used to estimate temporal trends in hospital admissions and mortality. Zero-truncated negative binomial regression analysis was used to identify factors associated with hospital length of stay. From 1983 to 2008, there were 23,450 hospitalizations for an index burn injury. Hospital admission rates declined by an average annual rate of 2% (incidence rate ratio [IRR], 95% confidence interval [CI] = 0.983, 0.981-0.984), and burn-related mortality declined by an average annual rate of 2% (IRR, 95% CI = 0.98, 0.96-1.01). Aboriginal people while having significantly higher hospitalization rates than non-Aboriginal people experienced a greater 26-year decline in hospitalizations of 58% (IRR, 95% CI = 0.42, 0.37-0.48) compared with 32% (IRR, 95% CI = 0.68, 0.65-0.71) for non-Aboriginal people. Children younger than 5 years, 20- to 24-year-old men, and adults older than 65 years remain at high risk for burn injury, and males continue to be hospitalized twice as frequently as females. The results demonstrate declines in burn injury hospitalizations and mortality in both Aboriginal and non-Aboriginal populations. Continued research is required of the impacts of medical interventions and the burn pathway of identified high-risk populations.

Dunstan JA, Brothers S, Bauer J, Hodder M, Jaksic MM, Asher MI and Prescott SL
The effects of Mycobacteria vaccae derivative on allergen-specific responses in children with atopic dermatitis

The capacity of microbial products to inhibit allergic inflammation make them logical candidates for novel therapies in allergic diseases such as atopic dermatitis. To assess the effects of intradermal Mycobacterium vaccae derivative on allergen-specific immune responses in children with moderate to severe atopic dermatitis. Peripheral blood mononuclear cells were isolated from children aged 5-16 years who received intradermal injections of M. vaccae derivative AVAC(TM) (n = 26) or placebo (n = 34) three times at 2-weekly intervals, weeks 0, 2 and 4. Cytokine [interleukin (IL)-13, interferon (IFN)-gamma and IL-10] responses to allergen [house dust mite (HDM)], mitogen [phytohaemagglutinin (PHA)], Staphylococcal enterotoxin B (SEB) and Toll-like receptor (TLR) ligands were assessed. At week 8 (1 month after all injections given) children in the AVAC group showed a significant increase in IL-10 (P = 0.009), T helper type 1 (Th1) IFN-gamma (P = 0.017) and Th2 IL-13 (P = 0.004) responses to HDM compared with baseline (week 0). There were no significant changes in any cytokine production in the placebo. HDM-specific IL-10 responses remained significantly higher (P = 0.014) than at baseline in the AVAC group by week 12; however, the HDM-specific IL-13 and IFN-gamma responses were no longer significantly different from baseline. IL-13 (r = 0.46, P < 0.001) and IL-10 (r = 0.27, P = 0.044) responses to HDM were correlated with total immunoglobulin E but not with disease severity. There were no effects of AVAC on mitogen, SEB, TLR-2- or TLR-4-mediated responses. This M. vaccae derivative appeared to modulate responses to HDM selectively, suggesting the capacity for in vivo effects on allergen-specific immune responses.

The relationship between maternal folate status in pregnancy, cord blood folate levels, and allergic outcomes in early childhood
Allergy. 2011; E[pub ahead of print]

ABSTRACT: Background: Dietary changes may epigenetically modify fetal gene expression during critical periods of development to potentially influence disease susceptibility. This study examined whether maternal and/or fetal folate status in pregnancy is associated with infant allergic outcomes. Methods: Pregnant women (n = 628) were recruited in the last trimester of pregnancy. Folate status determined by both food frequency questionnaires and folate levels in maternal and cord blood serum was examined in relation to infant allergic outcomes at 1 year of age (n = 484). Results: Infants who developed allergic disease (namely eczema) did not show any differences in cord blood or maternal folate levels compared with children without disease. Although maternal folate intake from foods was also not different, folate derived from supplements was higher (P = 0.017) in children with subsequent eczema. Furthermore, infants exposed to >500 mug folic acid/day as a supplement in utero were more likely to develop eczema than those taking <200 mug/day (OR [odds ratio] = 1.85; 95% CI 1.14-3.02; P = 0.013), remaining significant after adjustment for maternal allergy and other confounders. There was a nonlinear relationship between cord blood folate and sensitization, with folate levels <50 nmol/l (OR = 3.02; 95% CI 1.16-7.87; P = 0.024) and >75 nmol/l (OR = 3.59; 95% CI 1.40-9.20; P = 0.008) associated with greater sensitization risk than levels between 50 and 75 nmol/l. Conclusion: Fetal levels between 50 and 75 nmol/l appeared optimal for minimizing sensitization. While folate taken as a supplement in higher doses during the third trimester was associated with eczema, there was no effect on other allergic outcomes including sensitization. Further studies are needed to determine the significance of this.
Elliott CM, Reid SL, Alderson JA and Elliott BC
Lycra arm splints in conjunction with goal-directed training can improve movement in children with cerebral palsy
NeuroRehabilitation. 2011; 28(1): 47-54

OBJECTIVES: To investigate the effects of lycra(R) arm splint wear on goal attainment and three dimensional (3D) kinematics of the upper limb and trunk in children with cerebral palsy (CP). DESIGN: Randomised clinical trial whereby participants were randomised to parallel groups with waiting list control. PARTICIPANTS: Sixteen children with CP (hypertonia) aged 9 to 14 years. INTERVENTION: Three months lycra arm splint wear combined with goal directed training. MAIN OUTCOME MEASURE: Goal attainment scale, and 3D upper limb and trunk kinematics across four upper limb movement tasks. RESULTS: 17/18 children achieved their movement goals following three months of splinting. Selected joint kinematics improved on immediate splint application. Further improvements in joint kinematics were demonstrated following 3 months of splint wear, particularly in elbow extension, shoulder flexion and abduction and in thorax flexion. Only improvements in movement compensations at the thorax remained following removal of the splint. CONCLUSIONS: The lycra(R) arm splint, made a quantifiable change to the attainment of movement goals of importance to the child. Furthermore, improvements were demonstrated in selected maximum range of movement and joint kinematics during functional tasks at the elbow and shoulder joints and thorax segment in children with CP.

Fehr S, Bebbington A, Ellaway C, Rowe P, Leonard H and Downs J
Altered attainment of developmental milestones influences the age of diagnosis of rett syndrome

The early developmental history prior to the manifestation of Rett syndrome features is of clinical interest. This study describes the attainment of gross developmental milestones and regression, and assesses the relationships between genotype and age at diagnosis. The Australian Rett Syndrome Database and International Rett Syndrome Phenotype Database were used to source a total of 293 confirmed female subjects. Most girls learned to sit, were able to babble or use words, and approximately half learned to walk. Altered milestone attainment was associated with earlier diagnosis. There was variation in the acquisition of milestones, the age of regression, and the age of diagnosis by genotype. Most parents expressed concerns about unusual behaviors or development during infancy, and a more subtle atypical development during infancy was reported for most girls. It is important for clinicians to be aware of variable early development in Rett syndrome and that timely genetic testing is not precluded on this account.

Fehr S, Bebbington A, Nassar N, Downs J, Ronen GM, De Klerk N and Leonard H
Trends in the diagnosis of Rett syndrome in Australia
Pediatric research. 2011; 70(3): 313-319

 Modifications to diagnostic criteria and introduction of genetic testing have likely affected the pattern and timing of Rett syndrome diagnosis. The trends in incidence and prevalence of Rett syndrome in Australia were examined; the cumulative risk of a female being diagnosed was determined; and the impact of changes to diagnostic criteria and availability of genetic testing on these frequencies was investigated. The population-based Australian Rett Syndrome Database was used to identify a total of 349 verified Rett syndrome females born 1976-2006 and diagnosed 1982-2008. The proportion of female cases born and diagnosed per year and the cumulative risk of a diagnosis were determined. The median age of Rett syndrome diagnosis decreased from 4.5 y if diagnosed before 2000 to 3.5 y if diagnosed after 1999. The cumulative risk of diagnosis had almost doubled by 32 y of age [1/8,905 or 11.23 per 100,000 person-years (95% CI, 10.03-12.45)] in comparison with 5 y of age [1/15,361 or 6.51 per 100,000 person-years (95% CI, 5.65-7.39)]. Earlier age of diagnosis may result in families experiencing less stress and emotional strain compared with those with delayed diagnosis.

Finley JP, Ramsay JM, Bullock A, Chen RP, Warren AE and Wong KK
Benefits of an international working exchange in pediatric cardiology
Pediatric Cardiology. 2011; 32(1): 59-62

This report describes a 1-year exchange between members of two pediatric cardiology centers: one in Canada and one in Australia. Five cardiologists participated in sequence, fully engaging in the activities of the host
Delivering a Healthy WA
department. The motivation of the exchange was broadly educational including clinical experience, shared expertise, teaching, and research collaboration. Structured debriefing confirmed the value of the exchange. In addition to the experience of working in a different medical system, eight research papers were developed, with two research projects ongoing as well as subsequent exchanges of nursing and technical personnel. Interchange between two academic departments can add strength to both and allow development of new skills and research activity.

Forbes DA
The case for boosting infant male circumcision in the face of rising heterosexual transmission of HIV . . . and now the case against

Editorial reply to an article in the 20 September issue of the Journal that suggested circumcision of infant boys could be considered a “surgical vaccine” against future sexually transmitted HIV has attracted strong criticism from many of our readers.

Foster RS and Halbert AR
What is your diagnosis? An 18-month-old child with ornithine transcarbamylase deficiency and a rash
Pediatric dermatology. 2011; 28(4): 457-458

Gallagher-Swann M, Ingleby B, Cole C and Barr A
Improving transfusion practice: ongoing education and audit at two tertiary speciality hospitals in Western Australia
Transfusion Medicine. 2011; 21(1): 51-56

BACKGROUND: Institutions undertaking transfusion have a responsibility to ensure safe and appropriate practice. The hospital transfusion committee (HTC) plays a major role in monitoring all aspects of transfusion. Dedicated staff with the responsibility of undertaking transfusion education and audit have been employed at many hospitals. The question is ‘Do these positions improve practice?’. STUDY DESIGN AND METHODS: In 2005, a transfusion coordinator was employed by the King Edward Memorial Hospital (KEMH) and Princess Margaret Hospital (PMH) in Perth, Western Australia. After an initial audit to collect baseline data on transfusion documentation and compliance with national guidelines, a series of interventions was undertaken. In addition, the transfusion protocols were rewritten and published electronically. Further audits were undertaken in 2006, 2007 and 2009. RESULTS: Sequential audits show measured improvements in transfusion documentation. Baseline, hourly and completion observations are now correctly recorded in >94% of records at KEMH and >96% of records at PMH. Compliance with recording of 15 min observations has shown a 23% magnitude increase at KEMH and 36% at PMH. Compliance with recording of consent has increased by 20% at KEMH and 31% at PMH. Promotion of positive patient identification, when collecting specimens and administering blood, has been undertaken. CONCLUSION: The initiatives implemented by the transfusion coordinator and endorsed by the HTCs have improved the standard of transfusion documentation and practice at both institutions.

Inflammatory responses to individual microorganisms in the lungs of children with cystic fibrosis

BACKGROUND: We hypothesized that the inflammatory response in the lungs of children with cystic fibrosis (CF) would vary with the type of infecting organism, being greatest with Pseudomonas aeruginosa and Staphylococcus aureus. METHODS: A microbiological surveillance program based on annual bronchoalveolar lavage (BAL) collected fluid for culture and assessment of inflammation was conducted. Primary analyses compared inflammation in samples that grew a single organism with uninfected samples in cross-sectional and longitudinal analyses. RESULTS: Results were available for 653 samples from 215 children with CF aged 24 days to 7 years. A single agent was associated with pulmonary infection (≥10(5) cfu/mL) in 67 BAL samples, with P. aeruginosa (n = 25), S. aureus (n = 17), and Aspergillus species (n = 19) being the most common. These microorganisms were associated with increased levels of inflammation, with P. aeruginosa being the most proinflammatory. Mixed oral flora (MOF) alone was isolated from 165 BAL samples from 112 patients, with
97 of these samples having a bacterial density $\geq 10^{5}$ cfu/mL, and was associated with increased pulmonary inflammation ($P < .001$). For patients with current, but not past, infections there was an association with a greater inflammatory response, compared with those who were never infected ($P < .05$). However, previous infection with S. aureus was associated with a greater inflammatory response in subsequent BAL. CONCLUSIONS: Pulmonary infection with P. aeruginosa, S. aureus, or Aspergillus species and growth of MOF was associated with significant inflammatory responses in young children with CF. Our data support the use of specific surveillance and eradication programs for these organisms. The inflammatory response to MOF requires additional investigation.

Goldblatt J, Hyatt J, Edwards C and Walpole I

Further evidence for a marfanoid syndrome with neonatal progeroid features and severe generalized lipodystrophy due to frameshift mutations near the 3' end of the FBN1 gene

We report on a 20-year-old man who presented in infancy with severe generalized lipodystrophy with a progeroid appearance and some Marfanoid features. He subsequently was diagnosed with bilateral lens subluxations at the age of 16 years which prompted analysis of the FBN1 gene. This analysis showed him to have a novel heterozygous, de novo, c.8156_8175del, p.Lys2719ThrfsX12, frameshift mutation in exon 64 of his FBN1 gene. His phenotype is similar to a patient described by Graul-Neumann et al. [2010] who was found to have a de novo, heterozygous, c.8155_8156del deletion in exon 64 of FBN1. Both mutations result in a truncated protein with an extremely charged C-terminus, containing two positive and four negative charges in the last eight amino acids. This most likely has a profound impact on protein-protein interactions, which are very important in the extracellular matrix. The similarities in the phenotypes, and overlapping molecular defects, provides further evidence that the phenotype with features of Marfan syndrome with neonatal progeroid syndrome-like lipodystrophy is a distinct clinical entity due to frameshift mutations in exon 64 of the FBN1 gene.

Hall GL, Annese T, Looi K and Devadason SG

Usage of spacers in respiratory laboratories and the delivered salbutamol dose of spacers available in Australia and New Zealand
Respirology. 2011; 16(4): 639-644

Background and objective: Purchase and disinfection costs together with medication delivery factors may influence the choice of drug delivery options. This study assessed salbutamol delivery habits used in respiratory laboratories and quantified the delivered salbutamol dose of locally available spacers. Methods: An online survey was used to obtain data on disinfection processes, costs and delivery device choices. The delivered dose of six commercial spacers was assessed. Particle size distribution of salbutamol (Ventolin, GSK, 100 microg/actuation) from six spacers of each type was measured by quantifying the amount of drug (microg) deposited on each stage of an Anderson Cascade Impactor (ACI) using UV spectrophotometry. Clinical conditions were simulated using a flow volume simulator (FVS) and delivery of salbutamol via a pressurized metered dose inhaler and spacer to a low-resistance filter was measured. Results: Fifty survey responses were obtained, with 37 (74%) using $\geq 1$ type of spacer of which 92% processed single use spacers. The most commonly used spacers were Volumatic (n = 24), Breath-a-tech (n = 8) and Space Chamber (n = 7). The median disinfection cost was $2.45. Delivered salbutamol dose varied significantly and ranged from 16.98 to 38.28 microg with the ACI and 22.56 to 58.82 microg with the FVS. Using the FVS, small-volume spacers delivered similar doses (22.56 to 28.46 microg), while large-volume spacers delivery was more varied (24.31 to 58.82 microg). Conclusions: The majority of respiratory laboratories had not updated re-processing policies to comply with new regulations. The delivered salbutamol dose varied significantly and this might effect the choice of preferred spacer type.


Air trapping on chest CT is associated with worse ventilation distribution in infants with cystic fibrosis diagnosed following newborn screening
PloS one. 2011; 6(8): e23932

BACKGROUND: In school-aged children with cystic fibrosis (CF) structural lung damage assessed using chest CT is associated with abnormal ventilation distribution. The primary objective of this analysis was to determine the relationships between ventilation distribution outcomes and the presence and extent of structural damage.
as assessed by chest CT in infants and young children with CF. METHODS: Data of infants and young children with CF diagnosed following newborn screening consecutively reviewed between August 2005 and December 2009 were analysed. Ventilation distribution (lung clearance index and the first and second moment ratios [LCI, M(1)/M(0) and M(2)/M(0), respectively]) chest CT and airway pathology from bronchoalveolar lavage were determined at diagnosis and then annually. The chest CT scans were evaluated for the presence or absence of bronchiectasis and air trapping. RESULTS: Matched lung function, chest CT and pathology outcomes were available in 49 infants (31 male) with bronchiectasis and air trapping present in 13 (27%) and 24 (49%) infants, respectively. The presence of bronchiectasis or air trapping was associated with increased M(2)/M(0) but not LCI or M(1)/M(0). There was a weak, but statistically significant association between the extent of air trapping and all ventilation distribution outcomes. CONCLUSION: These findings suggest that in early CF lung disease there are weak associations between ventilation distribution and lung damage from chest CT. These finding are in contrast to those reported in older children. These findings suggest that assessments of LCI could not be used to replace a chest CT scan for the assessment of structural lung disease in the first two years of life. Further research in which both MBW and chest CT outcomes are obtained is required to assess the role of ventilation distribution in tracking the progression of lung damage in infants with CF.

Harun A, Blyth CC, Gilgado F, Middleton P, Chen SC and Meyer W
Development and validation of a multiplex PCR for detection of Scedosporium spp. in respiratory tract specimens from patients with cystic fibrosis
Journal of Clinical Microbiology. 2011; 49(4): 1508-1512
The emergence of Scedosporium infections in diverse groups of individuals, which are often treatment refractory, warrants timely and accurate laboratory diagnosis. Species- or group-specific primers based on internal transcribed spacer (ITS) sequence polymorphisms were designed for Scedosporium aurantiacum, Scedosporium dehoogii, Scedosporium prolificans, Pseudallescheria boydii species complex (former clade 5)/Pseudallescheria apiosperma (formerly classified as S. apiospernum sensu lato) and Pseudallescheria minitidispora. Primers for S. aurantiacum, S. prolificans, and P. boydii species complex/P. apiosperma were incorporated into a multiplex PCR assay for the detection and identification of the three major clinically important Scedosporium species and validated using sputum specimens collected from patients seen at a major Australian cystic fibrosis clinic. The multiplex PCR assay showed 100% specificity in identifying the three major clinically relevant Scedosporium species from pure culture. When evaluated using DNA extracts from sputa, sensitivity and specificity of the multiplex PCR assay were 62.1% and 97.2%, respectively. This highly species-specific multiplex PCR assay offers a rapid and simple method of detection of the most clinically important Scedosporium species in respiratory tract specimens.

Hewson ID, Daly J, Hallett KB, Liberati SA, Scott CL, Spaile G, Widmer R and Winters J
Consensus statement by hospital based dentists providing dental treatment for patients with inherited bleeding disorders
Australian dental journal. 2011; 56(2): 221-226
Avoidance of dental care and neglect of oral health may occur in patients with inherited bleeding disorders because of concerns about perioperative and postoperative bleeding, but this is likely to result in the need for crisis care, and more complex and high-risk procedures. Most routine dental care in this special needs group can be safely managed in the general dental setting following consultation with the patient's haematologist and adherence to simple protocols. Many of the current protocols for dental treatment of patients with inherited bleeding disorders were devised many years ago and now need revision. There is increasing evidence that the amount of factor cover previously recommended for dental procedures can now be safely reduced or may no longer be required in many cases. There is still a need for close cooperation and discussion between the patient's haematologist and dental surgeon before any invasive treatment is performed. A group of hospital based dentists from centres where patients with inherited bleeding disorders are treated met and, after discussions, a management protocol for dental treatment was formulated.

Heyes C, Chan J, Halbert A, Clay C, Buettner P and Gebauer K
Dermatology outpatient population profiling: indigenous and non-indigenous dermatopidemiology
BACKGROUND: Little is known about the population using Australian dermatology outpatient services, in particular, Indigenous patients. This information is important to direct the strategic planning of dermatology
services. METHODS: This study is a multicentre, retrospective audit of all patients attending public, outpatient dermatology clinics over 7 months across four Perth tertiary hospitals. The patient population (4873 patients) was profiled by age, gender, Indigenous status and rural/urban status. Medical records of the Indigenous patient population (104 patients) were reviewed to reveal the most common skin conditions. RESULTS: The population using public, outpatient services had a median age of 48 years, 51.4% were male and 13.6% were from rural areas. Male patient median age was 50 years compared to 45 years for female patients (P = 0.002). Indigenous patients had a median age of 22 years, a female to male ratio of 3:2 and 26.9% were from rural areas. Over 50% of Indigenous patient appointments were missed. Skin infections, eczematous conditions and naevi were the most common skin conditions in Indigenous patients. CONCLUSIONS: This data can guide strategies towards improving the provision of dermatology services for the Australian population. Particular attention is required towards improving Indigenous Australians' capacity to access dermatology services.

Hill CP, Damodaran O, Walsh P, Jevon GP and Blyth CC

Balamuthia amebic meningoencephalitis and mycotic aneurysms in an infant

Pediatric neurology. 2011; 45(1): 45-48

Balamuthia amebic encephalitis is rarely reported in infants. To the best of our knowledge, amebic encephalitis complicated by a mycotic aneurysm was only described once. We report on an 8-month-child with laboratory-confirmed Balamuthia mandrillaris meningoencephalitis, complicated by a mycotic aneurysm of the middle cerebral artery.

Houlston L, Nolan R, Noble V, Pascoe E, Hobday J, Loh R and Mallon D

Honeybee venom immunotherapy in children using a 50-mug maintenance dose


The clinical efficacy and safety of the FVIII/VWF concentrate, BIOSTATE((R)), in children with von Willebrand disorder: a multi-centre retrospective review

Haemophilia. 2011; 17(3): 463-469

Summary. Factor replacement with BIOSTATE((R)), a factor VIII (FVIII)/von Willebrand factor concentrate, forms the mainstay of treatment for children with von Willebrand disorder (VWD) in Australia and New Zealand. However, published data on the clinical efficacy and safety of BIOSTATE in the VWD paediatric population are limited. We retrospectively assessed the efficacy and safety of BIOSTATE in 43 children with VWD who received treatment for surgery, non-surgical bleeds or continuous prophylaxis at eight paediatric haemophilia centres in Australia and New Zealand. Data were collected on patient demographics, disease history, treatment history, dosage, administration, adverse reactions, concomitant medications and excessive bleeding events. BIOSTATE provided excellent/good haemostatic efficacy in 90% of surgical procedures (n = 42) with a mean daily FVIII dose of 47 IU FVIII:C kg(-1) and a median treatment duration of 3 days. Excellent/good haemostatic efficacy was achieved in 94% of non-surgical bleeding events (n = 72) with a mean FVIII dose of 45 IU FVIII:C kg(-1) day(-1) and a median treatment duration of 1 day. There were no bleeding events attributable to lack of efficacy. One case of nausea, possibly related to BIOSTATE administration, was reported. These results suggest that BIOSTATE is safe and effective for the treatment and prophylaxis of bleeding in children with VWD.

Hughes IP, Choong CS, Harris M, Ambler GR, Cutfield WS, Hofman PL, Cowell CT, Werther G, Cotterill A and Davies PS

Growth hormone treatment for Turner syndrome in Australia reveals that younger age and increased dose interact to improve response

Clinical endocrinology. 2011; 74(4): 473-480

OBJECTIVE: To investigate response to growth hormone (GH) in the first, second and third years of treatment in the total clinical cohort of Turner syndrome (TS) patients in Australia. CONTEXT: Short stature is the most common clinical manifestation of TS. GH treatment improves growth. DESIGN: Response was measured for each year of treatment. Stepwise multiple regression analyses were used to identify factors that significantly influenced response. PATIENTS: Prepubertal TS patients who completed 1 year (n=176), 2 years (n=148), or 3
years (n=117) of treatment and were currently receiving GH. MEASUREMENTS: Change in TS specific Height Standard Deviation Score (DeltaTSZ) was the main response variable used. Major influencing variables considered included dose, starting age and height, BMI, bone age delay, karyotype, parental height, and interactions between dose and starting age or height. RESULTS: Response was greatest in first year and declined thereafter (median DeltaTSZ: 1st year=+0.705, 2nd year=+0.439, 3rd year=+0.377) despite the median dose increasing [1st year= 5.5 mg/m(2) /week (0.23 mg/kg/week), 2nd year= 6.4(0.24), 3rd year= 7.2(0.26)]. An Age*Dose interaction was identified influencing first, second year, and total DeltaTSZ. The DeltaTSZ over 3 years was significantly influenced by first-year dose. Dose increments only attenuated the general decline in response. An acceptable first-year response (DeltaTSZ>1.01) was achieved by only 17.6% of patients. CONCLUSIONS: Growth response is greatest and most influenced by dose in the first year. Dose in first year is a major factor contributing to total response. A starting Age*Dose interaction effect was observed such that young girls on a high dose respond disproportionately better. Optimal GH treatment of short stature in TS thus requires early initiation with the highest safe dose in the first year.

Skin prick testing and peanut-specific IgE can predict peanut challenge outcomes in preschoolchildren with peanut sensitization
Clinical and experimental allergy : journal of the British Society for Allergy and Clinical Immunology. 2011; 41(7): 994-1000

BACKGROUND: The rise in peanut allergy is a source of considerable burden in the community. A growing number of preschool children have been identified as peanut sensitized in the course of investigation of other allergic conditions. Although many have never knowingly ingested peanuts and their clinical reactivity is not known, it has been common practice to place these children on avoidance diets for many years. OBJECTIVE: To determine the utility of skin prick tests (SPT) and fluorescent-enzyme immunoassays (FEIA) for identifying either peanut allergy or tolerance in preschool children with peanut sensitization. METHODS: Forty-nine preschool children (<5 years of age) with peanut sensitization (SPT >/= 2 mm or peanut-specific IgE >/= 0.35 kU/L) but unknown clinical reactivity had graded open peanut challenges reaching a total of 11 g. A positive challenge was defined as an objective IgE-mediated reaction during challenge or the 2-h observation. RESULTS: Forty-nine percent (24/49) of children had positive challenges. An SPT of >7 mm on the day of challenge predicted a positive challenge with a sensitivity of 83% and a negative predictive value (NPV) of 84%. An FEIA of >2.0 kU/L showed a sensitivity of 79% and an NPV of 80%. Predicting challenge outcome from a combination of SPT and FEIA (SPT >7 and/or FEIA >2 is positive) increased sensitivity to 96% and NPV to 95%. CONCLUSION AND CLINICAL RELEVANCE: At least half of preschool children with peanut sensitization and no antecedent history of peanut ingestion can tolerate peanuts. A SPT<7 mm and FEIA<2 kU/L identify children most likely to tolerate peanut, with only a 5% likelihood of failing an oral challenge. This study assists clinicians considering challenges in very young peanut-sensitized children.

Johnson SR, Nolan RC, Grant MT, Price GJ, Siafarikas A, Bint L and Choong CS
Sterile abscess formation associated with depot leuprorelin acetate therapy for central precocious puberty
Journal of paediatrics and child health. 2011; [Epub ahead of print]

We describe a case of an 8 year old girl with central precocious puberty. She was commenced on 3 monthly intramuscular depot Leuprorelin acetate therapy, as a result of which she developed sterile abscesses. She was converted to daily subcutaneous Leuprorelin acetate therapy with no recurrence of the abscesses. The possible mechanisms for this reaction are described in the article.

Kava MP, Bynevelt M, Lannigan F and Nagarajan L
Horner's syndrome in a child with otitis media: an unusual complication
Pediatric neurology. 2011; 45(3): 209-210
Keating M, Johnson J, Erb TO and von Ungern-Sternberg BS
Computed tomography changes of alveoli and airway collapse after laryngospasm

An eight-month-old girl underwent a computed axial tomographic study of the chest and neck for investigation of expiratory stridor. Following the scout scan, severe laryngospasm developed. While no cause for the laryngospasm was found, the computed axial tomographic chest study showed marked changes in the lungs consistent with absorption atelectasis which we postulate occurred secondary to laryngospasm.

Keith J, Fabian VA, Walsh P, Sinniah R and Robitaille Y
Neuropathological homology in true Galloway-Mowat syndrome

Galloway-Mowat syndrome is a rare condition that is likely hereditary though the underlying offending gene has not been identified, and is characterized by microcephaly and severe nephrotic syndrome culminating in childhood death. Some of the reported cases have abnormalities in neuronal migration and intractable seizures, but many of the described cases focus on the renal pathology and emphasize a diversity of clinical and pathological features. The case described herein includes a thorough neuropathological description, and when the neuroradiology and neuropathology of the previously published cases is scrutinized, a fairly consistent clinical and neuropathological phenotype emerges.

Knight DA, Stick SM and Hackett T-L
Defective function at the epithelial junction: a novel therapeutic frontier in asthma?

Kok J, Tudo K, Blyth CC, Foo H, Hueston L and Dwyer DE
Pandemic (H1N1) 2009 influenza virus seroconversion rates in HIV-infected individuals
Journal of acquired immune deficiency syndromes. 2011; 56(2): 91-94

The impact of pandemic (H1N1) 2009 influenza in HIV-infected individuals is unknown. Determining the prevalence of pandemic influenza in this at-risk group will guide vaccination programs. After the first pandemic wave, the seroprevalence rate of pandemic influenza in HIV-infected individuals in western Sydney, New South Wales, Australia, was 34.2%, similar to the rate observed in the general population. However, true seroprevalence is more accurately determined by seroconversion, defined as a 4-fold or greater rise between preexposure and postexposure antibody levels, which was 14.6% in the present study. Seroconversion rates were independent of CD4 T-lymphocyte count and HIV plasma load. Neither HIV infection, nor severe immunosuppression, was a significant risk factor for pandemic influenza during the first southern hemisphere pandemic wave.

Kotecha RS, Junckerstorff RC, Lee S, Cole CH and Gottardo NG
Pediatric meningioma: current approaches and future direction
Journal of Neuro-oncology. 2011 Jan 4, [Epub ahead of print]

With improvement in leukemia therapy, central nervous system (CNS) tumors are the leading cause of cancer mortality in children and the most expensive of all human neoplasms to treat. Meningiomas are rare intracranial tumors in childhood and adolescence arising from arachnoid cell clonal outgrowth in the meninges. There have been no collaborative prospective therapeutic trials for pediatric meningioma because of its rarity, and the best evidence for management comes from retrospective case analyses and extrapolation from the treatment of adult meningioma. However this may not be ideal, because the underlying biology of adult and pediatric meningiomas seems to be different, as is the case for other CNS tumors. In addition, treatment of pediatric brain tumors requires consideration of long-term quality of life. This review reflects on what is currently known about pediatric meningiomas and opportunities for future directions.
Kotecha RS, Murch A, Kees U and Cole CH
Pre-natal, clonal origin of t(1;11)(p32;q23) acute lymphoblastic leukemia in monozygotic twins
Leukemia Research. 2011 Apr 5, [Epub ahead of print]

AIM: Observation of identical genetic changes in leukemia cells from monozygotic twin pairs has provided evidence for the in utero single clonal origin hypothesis of leukemia, with intraplacental metastasis the basis for concordance. Investigation of this rare mixed lineage leukemia (MLL) cytogenetic abnormality aims to provide further evidence of the genetic changes that underpin this aggressive form of leukemia in infants. METHODS: The clinical features of a monozygotic infant twin pair with acute lymphoblastic leukemia (ALL) are reported. Banded chromosomal analysis and fluorescent in situ hybridization were used for cytogenetic characterization of the leukemic cells. Immunophenotype was determined by flow cytometry and polymerase chain reaction was used to determine the presence of FLT3-D835/I836 and FLT3-internal tandem duplication (ITD) mutations. RESULTS: The twins were seven weeks of age at diagnosis. Both had cytogenetic evidence for the t(1;11)(p32;q23) translocation. Trisomy X was present in a subpopulation of cells in one twin. Immunophenotypic profile at diagnosis was consistent with B precursor ALL (CD19, CD24, CD33 positive, weak CD13 positivity, CD10 negative) and both were negative for FLT3-D835/I836 and FLT3-ITD mutations. CONCLUSIONS: This is the first report of monochorionic monozygotic twins harboring the t(1;11)(p32;q23) translocation. Identification of this rare translocation in both twins, indicates a common stem line and provides further evidence for the intrauterine monoclonal origin for infant ALL with concordance explained by the shared circulation. Genetic diversity was observed in a subpopulation of cells from one twin at diagnosis. We must now utilize the sophisticated molecular biology tools available to capture changes at the genome-wide level to gain further insight into the complex events contributing to MLL leukemogenesis in infants.

Logie KM, Kusel MM, Sly PD and Hall GL
Exhaled breath temperature in healthy children is influenced by room temperature and lung volume
Pediatric pulmonology. 2011; 46(11): 1062-1068

BACKGROUND: Exhaled breath temperature (EBT) has been proposed for the non-invasive assessment of airway inflammation. Previous studies have not examined the influence of room temperature or lung size on the EBT. OBJECTIVE: This study aimed to address these issues in healthy children. METHODS: We assessed the effects of room temperature and lung volume in 60 healthy children aged 9-11 years (mean age 10.3 years, 33 male). Static lung volumes were assessed using multiple breath nitrogen washout. Questionnaire and skin prick tests were also used to establish respiratory health in the children. We obtained the EBT parameters of slope, end plateau temperature (PLET) and normalized plateau temperature (nPLET; plateau temperature minus inspired air temperature), and ascertained physiological factors influencing EBT. RESULTS: End plateau temperature was shown to be proportionally affected by room temperature (r = 0.532, P < 0.001) whereas slope and nPLET decreased with increasing room temperature (r = -0.392 P < 0.02 and r = -0.507 P = 0.002). After adjusting for room temperature, height and age, the total lung capacity (r(2) = 0.435, P = 0.006) and slow vital capacity (SVC; r(2) = 0.44, P = 0.005) were found to be the strongest predictors of end PLET in healthy children. When all factors were included in a multiple regression model, SVC and room temperature were the only predictors of plateau and nPLET. Slope was only influenced by room temperature. CONCLUSIONS: Exhaled breath temperature measurements are highly feasible in children with a 95% success rate in this healthy population. Room temperature and SVC significantly influence EBT variables in healthy children. Further studies are required to investigate the ability of EBT to assess airway inflammation in children with respiratory disease. Pediatr. Pulmonol. 2011; 46:1062-1068. (c) 2011 Wiley Periodicals, Inc.

Looi K, Sutanto EN, Banerjee B, Garratt L, Ling KM, Foo CJ, Stick SM and Kicic A
Bronchial brushings for investigating airway inflammation and remodelling
Respirology. 2011; 16(5): 725-737

Asthma is the commonest medical cause for hospital admission for children in Australia, affects more than 300 million people worldwide, and is incurable, severe in large number and refractory to treatment in many. However, there have been no new significant treatments despite intense research and billions of dollars. The advancement in our understanding in this disease has been limited due to its heterogeneity, genetic complexity and has severely been hampered particularly in children by the difficulty in obtaining relevant target organ tissue. This review attempts to provide an overview of the currently used and recently developed/adapted techniques used to obtain lung tissue with specific reference to the airway epithelium.
Dental arch relationship outcomes in children with complete unilateral cleft lip and palate, treated at Princess Margaret Hospital for Children, Perth, Western Australia
Cleft Palate-Craniofacial Journal. 2011 Jan 27, [Epub ahead of print]

Abstract Objectives: To a) audit dental arch relationships of all children born between 1982 and 1999 with complete unilateral cleft lip and palate (UCLP) treated at the Cleft Lip and Palate Unit, Princess Margaret Hospital for Children (PMH), Perth, Western Australia, b) assess the distribution of GOSLON ratings from dental casts taken at 9 years, c) compare the 9 year GOSLON ratings for “High” and “Low” caseload surgeons, and d) compare the 9 year PMH GOSLON ratings with published ratings from other Units. Design: Retrospective audit of dental casts and medical charts. Patients: Dental casts were retrieved for 71 children, 47 male and 24 female at 9 years of age. Main outcome measures: GOSLON rating ratings. Results: 68% of patients had an excellent to satisfactory dental arch relationship (GOSLON yardstick ratings 1-3) at nine years with a mean rating of 2.85. High caseload surgeons achieved statistically better mean GOSLON ratings than low caseload surgeons (2.72 and 3.33 respectively). Conclusions: PMH Cleft Unit’s dental arch relationship outcomes are comparable to published series of units using similar treatment protocols. High caseload surgeons achieved better dental arch relationships than low caseload surgeons. Key words: dental arch relationships, GOSLON yardstick, treatment outcome, unilateral cleft lip and palate, multi-center comparisons.

Ly TT, Anderson M, McNamara KA, Davis EA and Jones TW
Neurocognitive outcomes in young adults with early-onset type 1 diabetes: a prospective follow-up study
Diabetes Care. 2011; 34(10): 2192-2197

OBJECTIVE: The aim of this study was to reexamine the neurocognitive function of a cohort of young adults with early-onset type 1 diabetes and compare their cognitive function to a matched control group. We also examined whether cognitive function was related to prospectively obtained severe hypoglycemia history, long-term glycemic control, or severe diabetic ketoacidosis. RESEARCH DESIGN AND METHODS: Testing included Wechsler Intelligence Scale for Children and Adults, Wechsler Memory Scale, Cattell Culture Fair Intelligence Test (CCFIT), Wisconsin Card Sorting Test (WCST), youth and adult self-report, and Beck Depression Inventory. We tested 34 control subjects (mean +/- SE, age 19.5 +/- 0.5 years) and 33 type 1 diabetic subjects (age 19.3 +/- 0.5 years, age at type 1 diabetes onset 3.3 +/- 0.3 years, A1C from diagnosis 8.7 +/- 0.1%, and diabetes duration 16.0 +/- 0.5 years). RESULTS: There was no difference in full-scale IQ scores in type 1 diabetic and control subjects (100.7 +/- 2.0 vs. 102.5 +/- 1.4). There was no difference between groups in memory subtests or in reporting of emotional and behavioral difficulties. The type 1 diabetes group scored lower on the CCFIT for fluid intelligence compared with control subjects (P = 0.028) and also scored lower on WCST with more perseverative errors (P = 0.002) and fewer categories completed (P = 0.022). CONCLUSIONS: These data suggest no difference in general intellectual ability, memory, and emotional difficulties in our cohort of young adults with early-onset type 1 diabetes compared with control subjects and no deterioration over time. There were, however, findings to suggest subtle changes leading to poorer performance on complex tasks of executive function.

Ly TT, Hewitt J, Davey RJ, Lin EM, Davis EA and Jones TW
Improving epinephrine responses in hypoglycemia unawareness with real-time continuous glucose monitoring in adolescents with type 1 diabetes
Diabetes Care. 2011; 34(1): 50-52

OBJECTIVE: To determine whether real-time continuous glucose monitoring (CGM) with preset alarms at specific glucose levels would prove a useful tool to achieve avoidance of hypoglycemia and improve the counterregulatory response to hypoglycemia in adolescents with type 1 diabetes with hypoglycemia unawareness. RESEARCH DESIGN AND METHODS: Adolescents with type 1 diabetes with hypoglycemia unawareness underwent hyperinsulinemic hypoglycemic clamp studies at baseline to determine their counterregulatory hormone responses to hypoglycemia. Subjects were then randomized to either standard therapy or real-time CGM for 4 weeks. The clamp study was then repeated. RESULTS: The epinephrine response during hypoglycemia after the intervention was greater in the CGM group than in the standard therapy group. CONCLUSIONS: A greater epinephrine response during hypoglycemia suggests that real-time CGM is a useful clinical tool to improve hypoglycemia unawareness in adolescents with type 1 diabetes.
Ly TT, Jones TW, Griffiths A, Dart J, Davis EA, Stick S and Wilson A
Hypoglycemia does not change the threshold for arousal from sleep in adolescents with type 1 diabetes
Diabetes technology & therapeutics. 2011; [Epub ahead of print]

Abstract Background: Nocturnal hypoglycemia is a significant problem for children and adolescents with type 1 diabetes. The counterregulatory hormone response to hypoglycemia is blunted in both patients with type 1 diabetes and healthy subjects during sleep. It is not known whether the threshold for arousal from sleep is also modified by hypoglycemia. To address this question we compared the acoustic arousal threshold from sleep during hypoglycemia and euglycemia in adolescents with type 1 diabetes. Methods: Adolescents with type 1 diabetes were studied on two occasions: under hypoglycemic and euglycemic conditions. During the hypoglycemia night, subjects underwent a hyperinsulinemic hypoglycemic clamp with nadir glucose level of 2.8 mmol/L. Hypoglycemia was initiated during stage 2 sleep and maintained during slow-wave sleep. During the euglycemia night, blood glucose was maintained at 5.5 mmol/L using the same clamp technique. The acoustic arousal threshold was determined during the first cycle of slow-wave sleep. Results: Seven subjects (mean±SD: 14.2±0.8 years old, mean glycosylated hemoglobin 8.1±0.3%, duration of diagnosis 2.5±0.5 years) completed both study nights. Arousal was only noted during acoustic testing and did not occur during hypoglycemia alone. The acoustic arousal threshold during slow-wave sleep was similar under both conditions: 79±8 dB during euglycemia and 71±6 dB (P=0.353) during hypoglycemia. Conclusion: In adolescents with type 1 diabetes, hypoglycemia does not impair arousal from slow-wave sleep induced by an external auditory stimulus.

Martin AC, Besag FM, Berry DJ and Besag FP
The effect of lamotrigine on valproic acid concentrations

PURPOSE: To determine whether lamotrigine affects serum concentrations of valproic acid. METHODS: Premorning-dose serum valproic acid concentrations were measured in 76 subjects with epilepsy (48 M, 28 F, age range 6-20 years, mean age 14 years) in whom lamotrigine was added while the dose of valproate and other medication remained unchanged. In a comparison group, either acetazolamide or gabapentin was added to sodium valproate. RESULTS: Far more subjects (26/76 = 34%) had an increase of >25% in valproic acid concentration with lamotrigine than those who had a decrease of >25% (4/76 = 5.3%). The mean valproic acid concentration before starting lamotrigine was 61.0 mg/L and on lamotrigine was 67.1 mg/L; the difference in means was 6.1 mg/L (standard error 2.1, 95% confidence limits 2.0, 10.2, p=0.004, highly significant, paired sample t-test, two-tailed), a rise of 10%. The change in valproic acid concentration appeared to depend on the initial valproic acid concentration (Pearson r=-0.405, p<0.001). In 14.5% of the subjects the increase in valproate concentration was >50%, which could lead to toxicity, although the increase tended to occur with lower or intermediate initial valproic acid concentrations whereas a small overall decrease in valproic acid concentrations with lamotrigine was found with the higher initial valproic acid concentrations. One subject had abnormal bruising with the increased valproate level after lamotrigine was added, which resolved on decreasing the valproate dose. The changes in valproic acid concentrations in the comparison group were small (mean increase 2.6%) and were not statistically significant. CONCLUSIONS: Although there is a wide variation in the changes of valproic acid concentrations when lamotrigine is added, the concentrations tend to increase rather than decrease, especially with low or intermediate initial valproic acid concentrations. In some cases valproate toxicity, manifested by abnormal bruising, may result, although at higher initial valproic acid concentrations the valproic acid concentration usually tends to fall slightly with the addition of lamotrigine.

A national registry for juvenile dermatomyositis and other paediatric idiopathic inflammatory myopathies: 10 years' experience; the Juvenile Dermatomyositis National (UK and Ireland) Cohort Biomarker Study and Repository for Idiopathic Inflammatory Myopathies
Rheumatology. 2011; 50(1): 137-145

Objectives. The paediatric idiopathic inflammatory myopathies (IIMs) are a group of rare chronic inflammatory disorders of childhood, affecting muscle, skin and other organs. There is a severe lack of evidence base for current treatment protocols in juvenile myositis. The rarity of these conditions means that multicentre collaboration is vital to facilitate studies of pathogenesis, treatment and disease outcomes. We have established a national registry and repository for childhood IIM, which aims to improve knowledge, facilitate research and clinical trials, and ultimately to improve outcomes for these patients.
Methods. A UK-wide network of centres and research group was established to contribute to the study. Standardized patient assessment, data collection forms and sample protocols were agreed. The Biobank includes collection of peripheral blood mononuclear cells, serum, genomic DNA and biopsy material. An independent steering committee was established to oversee the use of data/samples. Centre training was provided for patient assessment, data collection and entry.

Results. Ten years after inception, the study has recruited 285 children, of which 258 have JDM or juvenile PM; 86% of the cases have contributed the biological samples. Serial sampling linked directly to the clinical database makes this a highly valuable resource. The study has been a platform for 20 sub-studies and attracted considerable funding support. Assessment of children with myositis in contributing centres has changed through participation in this study.

Conclusions. This establishment of a multicentre registry and Biobank has facilitated research and contributed to progress in the management of a complex group of rare musculoskeletal conditions.

Martino D and Prescott S
Epigenetics and prenatal influences on asthma and allergic airways disease
Chest. 2011; 139(3): 640-647

Uterine life is arguably the most critical time in developmental programming, when environmental exposures may have the greatest potential to influence evolving fetal structure and function. There has been substantial progress in understanding the epigenetic mechanisms through which environmental exposures can permanently alter the expression of fetal genes and contribute to the increasing propensity for many complex diseases. These concepts of "developmental origins" of disease are being applied across virtually all fields of medicine, and emerging epigenetic paradigms are the likely mechanism behind the environment-driven epidemic of asthma and allergic disease. Here, we examine the epigenetic regulation of immune development and the early immune profiles that contribute to allergic risk. In particular we review new evidence that key environmental exposures, such as microbial exposure, dietary changes, tobacco smoke, and pollutants, can induce epigenetic changes in gene expression and alter disease risk. Although most of these factors have already been clearly implicated in epidemiologic studies of asthma and allergic disease, new studies investigating the mechanisms of these effects may provide new avenues for using these pathways for disease prevention.

Evidence for age-related and individual-specific changes in DNA methylation profile of mononuclear cells during early immune development in humans
Epigenetics : official journal of the DNA Methylation Society. 2011; 6(9): 1085-1094

Environment induced epigenetic effects on gene expression in early life are likely to play important roles in mediating the risk of several immune-related diseases. In order to investigate this fully, it is essential to first document temporal changes in epigenetic profile in disease-free individuals as a prelude to defining environmentally mediated changes. Mononuclear cells (MC) were collected longitudinally from a small number of females at birth, 1 year, 2.5 years and 5 years of age and examined for changes in genome-scale DNA methylation profiles using the Illumina Infinium HumanMethylation27 BeadChip array platform. MC from two males were included for comparative purposes. Flow cytometry was used to define MC cell populations in each sample in order to exclude this as the major driver of epigenetic change. The data underwent quality control and normalization within the R programming environment. Unsupervised hierarchical clustering of samples clearly delineated neonatal MC from all other ages. A further clear distinction was observed between 1 year and 5 year samples, with 2.5 year samples showing a mixed distribution between the 1 and 5 year groups. Gene ontology of probes significantly variable over the neonatal period revealed methylation changes in genes associated with cell surface receptor and signal transduction events. In the postnatal period, methylation changes were mostly associated with the development of effector immune responses and homeostasis. Unlike all other chromosomes tested, a predominantly genetic effect was identified as controlling maintenance of X-chromosome methylation profile in females, largely refractory to change over time. This data suggests that the primary driver of neonatal epigenome is determined in utero, whilst postnatally, multiple genetic and environmental factors are implicated in the development of MC epigenetic profile, particularly between the ages of 1-5 years, when the highest level of inter individual variation is apparent. This supports a model for differential sensitivity of specific individuals to disruption in the developing epigenome during the first years of life. Further studies are now needed to examine evolving epigenetic variations in specific cell populations in relation to environmental exposures, immune phenotype and subsequent disease susceptibility.
Meldrum SJ, D’Vaz N, Dunstan J, Mori TA and Prescott SL
The Infant Fish Oil Supplementation Study (IFOS): design and research protocol of a double-blind, randomised controlled n-3 LCPUFA intervention trial in term infants
Contemporary clinical trials. 2011; 32(5): 771-778

STUDY DESIGN: The Infant Fish Oil Supplementation Study is a double-blind randomised controlled trial investigating whether the incidence of allergic disease can be reduced and developmental outcomes enhanced through supplementation with omega-3 fatty acids. Infants at high risk of developing allergic disease will be randomised to receive either fish oil or olive oil supplements until 6 months of age and followed up at six postnatal clinic visits to assess allergy outcomes and infant neurodevelopment. INTERVENTION: Study groups to consist of a treatment group allocated to receive 650 mg of fish oil daily (250-280 mg docosahexaenoic acid and at least 60 mg eicosapentaenoic acid) and a placebo group (olive oil) from birth to 6 months of age. OUTCOMES: Allergy outcomes will be assessed by clinical history, clinical assessments and allergen skin prick tests at the 12, 30 and 60 month visits. Neurodevelopmental assessments to be conducted at 18 months, and language questionnaires at 12, 18 and 30 months. Samples will be collected from mothers antenatally, from infants at birth, and at clinic visits from 6 months onwards for immunological assessments. Fatty acid composition to be measured in erythrocytes and plasma (at birth and after the supplementation period) to assess the effect of the intervention on fatty acid status. Information on medical history, diet and other lifestyle factors at an antenatal clinic visit and postnatal clinic visits will also be collected. CONCLUSION: This study is designed to examine clinically relevant factors of a novel, non-invasive and potentially low cost approach to reduce the incidence of allergic disease and facilitate neurodevelopment during early childhood.

Meldrum SJ, Smith MA, Prescott SL, Hird K and Simmer K
Achieving definitive results in long-chain polyunsaturated fatty acid supplementation trials of term infants: factors for consideration
Nutrition reviews. 2011; 69(4): 205-214

Numerous randomized controlled trials (RCTs) have been undertaken to determine whether supplementation with long-chain polyunsaturated fatty acids (LCPUFAs) in infancy would improve the developmental outcomes of term infants. The results of such trials have been thoroughly reviewed with no definitive conclusion as to the efficacy of LCPUFA supplementation. A number of reasons for the lack of conclusive findings in this area have been proposed. This review examines such factors with the aim of determining whether an optimal method of investigation for RCTs of LCPUFA supplementation in term infants can be ascertained from previous research. While more research is required to completely inform a method that is likely to achieve definitive results, the findings of this literature review indicate future trials should investigate the effects of sex, genetic polymorphisms, the specific effects of LCPUFAs, and the optimal tests for neurodevelopmental assessment. The current literature indicates a docosahexaenoic acid dose of 0.32%, supplementation from birth to 12 months, and a total sample size of at least 286 (143 per group) should be included in the methodology of future trials.

Nagarajan L, Ghosh S and Palumbo L
Ictal electroencephalograms in neonatal seizures: characteristics and associations
Pediatric neurology. 2011; 45(1): 11-16

The characteristics of ictal electroencephalograms in 160 neonatal seizures of 43 babies were correlated with mortality and neurodevelopmental outcomes. Neonatal seizures are focal at onset, most frequently temporal, and often occur during sleep. Twenty-one percent of babies with seizures died, and 76% of survivors manifested neurodevelopmental impairment during 2-6-year follow-up. A low-amplitude ictal electroencephalogram discharge was associated with increased mortality, and a frequency of <2 Hz with increased morbidity. Status epilepticus, ictal fractions, multiple foci, and bihemispheric involvement did not influence outcomes. Of 160 seizures, 99 exhibited no associated clinical features (electrographic seizures). Neonatal seizures with clinical correlates (electroclinical seizures) exhibited a higher amplitude and frequency of ictal electroencephalogram discharge than electrographic seizures. During electroclinical seizures, the ictal electroencephalogram was more likely to involve larger areas of the brain and to cross the midline. Mortality and morbidity were similar in babies with electroclinical and electrographic seizures, emphasizing the need to diagnose and treat both types. Ictal electroencephalogram topography has implications for electrode application during limited-channel, amplitude-integrated electroencephalograms. We recommend temporal and paracentral
Nagarajan L, Ghosh S, Palumbo L, Akiyama T and Otsubo H
Fast activity during EEG seizures in neonates
Epilepsy research. 2011; 97(1-2): 162-169

INTRODUCTION: Paroxysmal fast activity (FA) has been proposed as a marker for epileptic networks. We explore the presence and significance of ictal FA on scalp video EEG seizures (EEG Sz) recorded in neonates. METHODOLOGY: Forty two babies had 159 EEG Szs. The seizures were analysed for ictal FA, using a low frequency filter of 30Hz. We explored the relationship of ictal FA to the occurrence of electroclinical and electrographic seizures, the use of phenobarbitone and to neurodevelopmental outcomes. RESULTS: Ictal FA occurred in 62 (39%) of the 159 EEG Szs. In the 62 seizures with ictal FA, 34 (55%) were electroclinical seizures (ECSz) and 28 (45%) were electrographic (ESz). In the remaining 97 seizures without ictal FA, 27 (28%) were ECSz and 70 (72%) ESz. There was a significant correlation (p=0.0006) between ictal FA and electroclinical seizures. There was no relationship between phenobarbitone and presence of ictal FA. There was no significant difference in the background EEG, neuroimaging abnormalities, neurodevelopmental impairment or post neonatal seizures between those with and without ictal FA. CONCLUSIONS: Ictal FA is highly correlated to the occurrence of clinical features during an EEG seizure. The presence of ictal FA does not appear to influence neurodevelopmental outcomes.

Nagarajan L, Ghosh S, Palumbo L, Kohan R and Thonell S
Hydrocephalus in babies: a specific neonatal EEG pattern

Nagarajan L, Palumbo L and Ghosh S
Brief Electroencephalography Rhythmic Discharges (BERDs) in the neonate with seizures: their significance and prognostic implications

We aimed to explore the significance and prognostic implications of paroxysmal brief electroencephalography (EEG) rhythmic discharges (BERDs) in neonatal seizures. The 52 neonates in this study were divided into 3 groups: (1) BERDs only: 9 neonates, (2) BERDs + conventional EEG seizures: 11 babies, (3) Conventional EEG seizures only: 32 babies. We analyzed the BERDs and compared outcomes in the 3 groups: there was no significant difference in mortality and neurodevelopmental or background EEG impairment. Similar to conventional EEG seizures, BERDs are also associated with an increased mortality, morbidity, and EEG background abnormalities. Fewer babies with BERDS appear to develop postneonatal seizures suggesting their epileptogenic potential is less. In the appropriate clinical context, BERDs should be considered as miniseizures.

Naylor LH, Green DJ, Jones TW, Kalic RJ, Suriano KL, Shah M, Hopkins N and Davis EA
Endothelial function and carotid intima-media thickness in adolescents with type 2 diabetes mellitus
The Journal of pediatrics. 2011; 159(6): 971-974

OBJECTIVE: We assessed the effect of type 2 diabetes mellitus and obesity on flow-mediated dilation (FMD) and endothelial-dependent vasodilation and carotid intima-media thickness (cIMT) in young people. STUDY DESIGN: Adolescents were recruited in 3 groups: subjects with type 2 diabetes mellitus (n = 15), subjects who were obese and non-insulin resistant (n = 13), and lean control subjects (n = 13). Body mass index was similar in subjects with obesity and subjects with type 2 diabetes mellitus, but higher compared with that of lean control subjects (both P < .001). Brachial artery FMD and cIMT were assessed by using Duplex ultrasound scanning imaging. RESULTS: There were no significant differences in brachial or common carotid arterial diameters in the groups. cIMT was significantly greater in the group with type 2 diabetes mellitus (0.54 +/- 0.01mm) compared with both the lean control (0.46 +/- 0.02 mm, P < .001) and obese control (0.46 +/- 0.02 mm, P < .01) groups. FMD was significantly decreased in the group with type 2 diabetes mellitus (7.98% +/- 0.54%) compared with the lean group (10.40% +/- 1.00%, P < .05). CONCLUSIONS: Measures of vascular health were impaired in adolescents with type 2 diabetes mellitus compared with lean and obese adolescents who were not
O’Connell SM, Johnson SR, Lewis BD, Staltari L, Peverall J, Ly T, Martin AC, Jones TW, Price GJ, Murch A and Choong CS
Structural chromosome disruption of the NR3C2 gene causing pseudohypoaldosteronism type 1 presenting in infancy
Journal of pediatric endocrinology & metabolism : JPEM. 2011; 24(7-8): 555-559

Type I pseudohypoaldosteronism (PHA1) is a rare form of mineralocorticoid resistance presenting in infancy with renal salt wasting and failure to thrive. Here, we present the case of a 6-week-old baby girl who presented with mild hyponatraemia and dehydration with a background of severe failure to thrive. At presentation, urinary sodium was not measurably increased, but plasma aldosterone and renin were increased, and continued to rise during the subsequent week. Despite high calorie feeds the infant weight gain and hyponatraemia did not improve until salt supplements were commenced. Subsequently, the karyotype was reported as 46,XX,inv (4)(q31.2q35). A search of the OMIM database for related genes at or near the inversion breakpoints, showed that the mineralocorticoid receptor gene (NR3C2) at 4q31.23 was a likely candidate. Further FISH analysis showed findings consistent with disruption of the NR3C2 gene by the proximal breakpoint (4q31.23) of the inversion. There was no evidence of deletion or duplication at or near the breakpoint. This is the first report of a structural chromosome disruption of the NR3C2 gene giving rise to the classical clinical manifestations of pseudohypoaldosteronism type 1 in an infant.

O’Connor TE, Bilish D, Choy D and Vijayasekaran S
Laryngotracheoplasty to avoid tracheostomy in neonatal and infant subglottic stenosis
Otolaryngology Head and Neck Surgery. 2011; 144(3): 435-439

Objective. To outline the authors’ experiences with performing laryngotracheoplasty as an alternative to tracheostomy in neonates and infants with symptomatic subglottic stenosis (SGS). Study Design. Case series with chart review. Setting. A tertiary referral pediatric hospital. Subjects and Methods. Patients younger than 12 months undergoing single-stage laryngotracheoplasty for SGS at the authors’ institution over a 3-year period. Results. Ten patients (8 boys and 2 girls) underwent single-stage laryngotracheoplasty during the study period. There were 9 cases of acquired SGS and 1 case of congenital SGS. Eight patients had grade III SGS, and 2 patients had grade II SGS. In 9 of 10 patients, the procedure performed was an anterior cricoid split (ACS) and posterior cricoid split (PCS), with the placement of an anterior thyroid ala cartilage graft. One patient underwent ACS and PCS with the placement of a posterior rib cartilage graft, in combination with a right vocal cord lateralization. The mean period of intubation after surgery was 6.8 days (range, 5-9 days). Nine of 10 patients had a complete resolution of their airway symptoms following airway surgery, with a mean duration of follow-up of 305 days (range, 30-780 days). One patient required the placement of a tracheostomy tube 69 days postoperatively due to a failure to wean from ventilation in the setting of multiple comorbidities. Conclusion. Laryngotracheoplasty is a safe and effective alternative to long-term tracheostomy in infants and neonates with symptomatic SGS.

Omaoldomhnaigh C, Ramsay JM, Finley JP, Andrews D and Murray C
Bilateral aortico-atrial tunnels
Pediatric Cardiology. 2011; 32(8): 1199-1201

This report describes the investigation, diagnosis, and surgical correction of two aortico-atrial tunnels running from the noncoronary sinus of Valsalva to both the left and right atri in an asymptomatic 8-year-old boy.

O’Neill TB, Rawlins J, Rea S and Wood F
Treatment of a large congenital melanocytic nevus with dermabrasion and autologous cell suspension (ReCELL((R))): A case report
Journal of plastic, reconstructive & aesthetic surgery : JPRAS. 2011; 64(12): 1672-1676

Congenital melanocytic naevi (CMN) are present at birth in between 1 and 6% of all neonates.(1) They are caused by malformations of the neuroectoderm that are comprised of melanocytes and occasionally neural elements, following dysregulated growth and arrest of melanocytes during migration from the neural crest to the
skin.(3) Most commonly they are sub-classified according to size.(5) They are at risk of malignant transformation, but the psychological impact of prominent CMN's is arguably of greater potential concern to the parent and child.(6,7) Treatment modalities to date have included complete surgical excision with defect reconstruction, as well as less invasive methods such as dermabrasion, curretage, chemical peels and laser therapy.(6) We present an illustrated case of a healthy, term, 4 week-old male neonate with a large CMN on his face. The lesion was dermabraded, and non-cultured epithelial autograft harvested from the right post-auricular area was applied. Dressings were no longer required by the 8th post-operative day, and excellent skin pigmentation and texture was achieved by 5 months post-op.

Fatal mycotic aneurysms due to Scedosporium/Pseudallescheria infection: case reports and literature review
Journal of Clinical Microbiology. 2011; Epub ahead of print

Angio-invasive complications of Scedosporium infections are rare. We report two cases of mycotic aneurysm, following apparent localized infection, due to Scedosporium apiospermum/Pseudallescheria boydii. The thoraco-abdominal aorta was affected in one patient, and cerebral vessels, in the other. Despite voriconazole therapy and surgical resection, the patients died. Previously-reported cases are reviewed.

O'Sullivan P, Beales D, Jensen L, Murray K and Myers T
Characteristics of chronic non-specific musculoskeletal pain in children and adolescents attending a rheumatology outpatients clinic: a cross-sectional study
Pediatric rheumatology online journal. 2011; 9(1): 3

BACKGROUND: Chronic non-specific musculoskeletal pain (CNSMSP) may develop in childhood and adolescence, leading to disability and reduced quality of life that continues into adulthood. The purpose of the study was to build a biopsychosocial profile of children and adolescents with CNSMSP. METHODS: CNSMSP subjects (n = 30, 18 females, age 7-18) were compared with age matched pain free controls across a number of biopsychosocial domains. RESULTS: In the psychosocial domain CNSMSP subjects had increased levels of anxiety and depression, and had more somatic pain complaints. In the lifestyle domain CNSMSP subjects had lower physical activity levels, but no difference in television or computer use compared to pain free subjects. Physically, CNSMSP subjects tended to sit with a more slumped spinal posture, had reduced back muscle endurance, increased presence of joint hypermobility and poorer gross motor skills. CONCLUSION: These findings support the notion that CNSMSP is a multidimensional biopsychosocial disorder. Further research is needed to increase understanding of how the psychosocial, lifestyle and physical factors develop and interact in CNSMSP.

Peake LJ, Grover SR, Monagle PT and Kennedy AD
Effect of warfarin on menstruation and menstrual management of the adolescent on warfarin
Journal of paediatrics and child health. 2011; Epub ahead of print

Aim: The aim of this study was to review a consecutive cohort of adolescent females on warfarin to determine the effect of warfarin on menstruation, management options and their perceived efficacy. Methods: All female patients on warfarin, over the age of 10 years, as of 31 August 2006, were identified using the Department of Haematology (Royal Children's Hospital) warfarin database. The presence of menorrhagia was defined by clinical indicators. Results: Of 81 adolescent females on warfarin, 24 (30%) were referred to gynaecology due to a concern about heavy periods and one for anticipatory guidance, on the basis of impending menarche. In 18 cases (22% of the cohort), menorrhagia could be substantiated on the basis of clinical indicators. Nineteen patients required treatment for menorrhagia with the options for treatment being the combined oral contraceptive pill, subdermal hormone administrations, tranexamic acid and the progesterone-only contraceptive pill. Significant adolescent psychosocial stresses were identified in those adolescents taking warfarin. Conclusions: Adolescent females on warfarin commonly suffer from menorrhagia. Adolescent review of all teenage girls receiving warfarin therapy is indicated.
Pharis CS, Conway J, Warren AE, Bullock A and Mackie AS
The impact of 2007 infective endocarditis prophylaxis guidelines on the practice of congenital heart disease specialists
American heart journal. 2011; 161(1): 123-129

BACKGROUND: the impact of the 2007 American Heart Association endocarditis prophylaxis guidelines on clinician practice has not been well established. Our objective was to evaluate how the American Heart Association endocarditis guidelines changed the practice of cardiologists who manage congenital heart disease and to ascertain the degree of practice variation among cardiologists. METHODS: a cross-sectional Web-based survey was e-mailed to Canadian (n = 134), Australian (n = 33), New Zealand (n = 9), and a random sample of American (n = 250) pediatric and adult congenital heart disease cardiologists in 2008. Nonrespondents received the survey 4 times by e-mail and once by regular post. RESULTS: the response rate was 59%. The lesions for which cardiologists were most evenly divided between recommending versus not recommending prophylaxis were "rheumatic mitral stenosis of moderate severity" (45% recommended prophylaxis) and "perimembranous ventricular septal defect (VSD) status post surgical patch closure with no residual shunt 3 months post-operatively" (54% recommended prophylaxis). The lesions for which the greatest proportion of cardiologists discontinued prophylaxis were "small muscular VSD, no previous endocarditis" (80% discontinued prophylaxis) and "small audible patent ductus arteriosus" (83% discontinued prophylaxis). Only 69% recommended prophylaxis for "VSD s/p surgical patch closure with small residual shunt" despite current guidelines recommending prophylaxis for this scenario. Twenty-eight percent of respondents felt that the new guidelines leave some patients at risk, and 6% would not recounsel any low-risk patients following these guidelines. CONCLUSIONS: the 2007 guidelines have resulted in a substantial change in endocarditis prophylaxis. There remains considerable heterogeneity among cardiologists regarding the prophylaxis of certain cardiac lesions.

Infection, inflammation, and lung function decline in infants with cystic fibrosis
American journal of respiratory and critical care medicine. 2011; 184(1): 75-81

RATIONALE: Better understanding of evolution of lung function in infants with cystic fibrosis (CF) and its association with pulmonary inflammation and infection is crucial in informing both early intervention studies aimed at limiting lung damage and the role of lung function as outcomes in such studies. OBJECTIVES: To describe longitudinal change in lung function in infants with CF and its association with pulmonary infection and inflammation. METHODS: Infants diagnosed after newborn screening or clinical presentation were recruited prospectively. FVC, forced expiratory volume in 0.5 seconds (FEV(0.5)), and forced expiratory flows at 75% of exhaled vital capacity (FEF(75)) were measured using the forced-volume technique, and z-scores were calculated from published reference equations. Pulmonary infection and inflammation were measured in bronchoalveolar lavage within 48 hours of lung function testing. MEASUREMENTS AND MAIN RESULTS: Thirty-seven infants had at least two successful repeat lung function measurements. Mean (SD) z-scores for FVC were -0.8 (1.0), -0.9 (1.1), and -1.7 (1.2) when measured at the first visit, 1-year visit, or 2-year visit, respectively. Mean (SD) z-scores for FEV(0.5) were -1.4 (1.2), -2.4 (1.1), and -4.3 (1.6), respectively. In those infants in whom free neutrophil elastase was detected, FVC z-scores were 0.81 lower (P=0.003), and FEV(0.5) z-scores 0.96 lower (P=0.001), respectively. Significantly greater decline in FEV(0.5) z-scores occurred in those infected with Staphylococcus aureus (P=0.018) or Pseudomonas aeruginosa (P=0.021). CONCLUSIONS: In infants with CF, pulmonary inflammation is associated with lower lung function, whereas pulmonary infection is associated with a greater rate of decline in lung function. Strategies targeting pulmonary inflammation and infection are required to prevent early decline in lung function in infants with CF.

Prescott S.
The allergy epidemic : a mystery of modern life
UWA Publishing, 2011

Why is allergic disease increasing so rapidly, especially in young infants? What are the environmental factors contributing to this? What is going wrong with the immune system and can we prevent it? When is it safe to give children peanut products? What are the current treatment options for allergies? What is epigenetics? Where is the research headed?
These are some of the many questions challenging not only parents and allergy sufferers, but whole societies now facing the global rise in immune diseases. Drawing on the latest research, The Allergy Epidemic provides clear, no-nonsense descriptions in the very personable style Susan's patients have come to expect.

Prescott S and Allen KJ
Food allergy: riding the second wave of the allergy epidemic
Pediatric Allergy and Immunology. 2011; 22(2): 155-160

Food allergy is a substantial and evolving public health issue, recently emerging over the last 10-15 yr as a 'second wave' of the allergy epidemic. It remains unclear why this new phenomenon has lagged decades behind the 'first wave' of asthma, allergic rhinitis and inhalant sensitization. In regions like Australia, which lead the respiratory epidemic, challenge-proven IgE-mediated food allergy now affects up to 10% of infants. Although their parents were among the first generation to experience the large-scale rise in allergic diseases, disorders of oral tolerance were previously uncommon. Of further concern, this new generation appears less likely to outgrow food allergy than their predecessors with long-term implications for disease burden. Allergic disease has been linked to the modern lifestyle including changing dietary patterns, changing intestinal commensal bacteria and vehicular pollution. It is not yet known whether the rise in food allergy is a harbinger of earlier and more severe effects of these progressive environmental changes or whether additional or unrelated lifestyle factors are implicated. New studies suggest environmental factors can produce epigenetic changes in gene expression and disease risk that may be potentially heritable across generations. The rising rates of maternal allergy, a strong direct determinant of allergic risk, could also be amplifying the effect of environmental changes. Preliminary evidence that non-Caucasian populations may be even more susceptible to the adverse effects of 'westernisation' has substantial global implications with progressive urbanization of the more populous regions in the developing world. Unravelling the environmental drivers is critical to curtail a potential tsunami of allergic disease.

Prescott SL
The influence of early environmental exposures on immune development and subsequent risk of allergic disease
Allergy. 2011; 66 Suppl 95: 4-6

Environmental exposures in pregnancy and the early postnatal period affect early immune development. Early immune function and future allergy susceptibility appear to result from a combination of maternal phenotype, infant genotype, and environmental exposures in utero that affect early gene expression. Furthermore, epigenetic changes in gene expression in one generation can also be inherited across subsequent generations, potentially amplifying heritable allergy risk.

Reduced placental FOXP3 associated with subsequent infant allergic disease

Priddis L and Shields L
Interactions between parents and staff of hospitalised children
Paediatric Nursing. 2011; 23(2): 14-20

The Platt report (Ministry of Health 1959) recommended that hospitals provide for parents to stay with sick children. This review, of how hospitals have or have not followed this guidance, assesses the literature and includes insights into research on the theory of attachment. The authors conclude that, although parents are commonly to be found on wards with sick children, this is not often systematically encouraged or even understood. However, recent initiatives to improve communication between staff and the parents of children admitted to hospital are encouraging.
INTRODUCTION: Improved nutrition is the major proven benefit of newborn screening programmes for cystic fibrosis (CF) and is associated with better clinical outcomes. It was hypothesised that early pulmonary inflammation and infection in infants with CF is associated with worse nutrition. METHODS: Weight, height and pulmonary inflammation and infection in bronchoalveolar lavage (BAL) were assessed shortly after diagnosis in infants with CF and again at 1, 2 and 3 years of age. Body mass index (BMI) was expressed as z-scores. Inflammatory cells and cytokines (interleukin 1beta (IL-1beta), IL-6, IL-8 and tumour necrosis factor alpha (TNFalpha)), free neutrophil elastase activity and myeloperoxidase were measured in BAL. Mixed effects modelling was used to assess longitudinal associations between pulmonary inflammation, pulmonary infection (Staphylococcus aureus and Pseudomonas aeruginosa) and BMI z-score after adjusting for potential confounding factors. RESULTS: Forty-two infants were studied (16 (38%) male; 39 (93%) pancreatic insufficient); 36 were diagnosed by newborn screening (at median age 4 weeks) and six by early clinical diagnosis (meconium ileus). Thirty-one (74%) received antistaphylococcal antibiotics. More than two-thirds were asymptomatic at each assessment. Mean BMI z-scores were -1.5 at diagnosis and 0.5, -0.2 and -0.1 at 1, 2 and 3 years, respectively. Neutrophil elastase and infection with S aureus were associated with lower BMI, whereas age (p=0.01) and antistaphylococcal antibiotics (p=0.013) were associated with increased BMI. On average, each log10 increase in free neutrophil elastase activity was associated with a 0.43 (95% CI 0.06 to 0.79) reduction in BMI z-score. DISCUSSION: Early nutritional status is associated with the underlying pulmonary pathophysiology in CF, and better understanding of these relationships is required. Studies are required to assess whether interventions can decrease pulmonary inflammation and improve nutrition. Early surveillance will enable such targeted interventions with the aim of improving these important clinical outcomes.

BACKGROUND: Standard surgical management of infants with perforated necrotizing enterocolitis (NEC) or spontaneous intestinal perforation in preterm low birth weight infants. Cochrane Database of Systematic Reviews. 2011; (6)

OBJECTIVES: To evaluate the benefits and risks of peritoneal drainage compared to laparotomy as the initial surgical treatment for perforated NEC or SIP in preterm infants. SEARCH STRATEGY: Cochrane Central Register of Controlled Trials (CENTRAL), (The Cochrane Library 2010, Issue 3), MEDLINE (1966 to July 2010), EMBASE (1980 to July 2010), CINAHL (1982 to July 2010), previous reviews and cross-references were searched. Abstracts of paediatric academic society meetings were also searched (online: 2000 to 2009; handsearching Pediatric Research: 1995 to 2000). SELECTION CRITERIA: All randomised or quasi-randomised controlled trials in preterm (< 37 weeks gestation), low birth weight (< 2500 g) infants with perforated NEC or SIP allocated to peritoneal drainage or laparotomy as initial surgical treatment. DATA COLLECTION AND ANALYSIS: Data were excerpted from the trial reports and analysed according to the standards of the Cochrane Neonatal Review Group. MAIN RESULTS: Only two randomised controlled trials (RCT) met the eligibility criteria. Overall, no significant differences were seen between the peritoneal drainage and laparotomy groups regarding the incidence of mortality within 28 days of the primary procedure (28/90 versus 30/95; typical relative risk (RR) 0.99, 95% CI 0.64 to 1.52; N = 185, two trials); mortality by 90 days after the primary procedure (typical RR 1.05, 95% CI 0.71 to 1.55; N = 185, two trials) and the number of infants needing total parenteral nutrition for more than 90 days (typical RR 1.18, 95% CI 0.72 to 1.95; N = 116, two trials). Nearly 50% of the infants in the peritoneal drainage group could avoid the need for laparotomy during the study period (44/90 versus 95/96; typical RR 0.49, 95% CI 0.39 to 0.61; N = 186, two trials). One study found that the time to attain full enteral feeds in infants <= 1000 g was prolonged in the peritoneal drainage group (mean difference (MD) 20.77, 95% CI 3.62 to 37.92). AUTHORS’ CONCLUSIONS: Evidence from two RCTs suggests no significant benefits or harms of peritoneal drainage over laparotomy. However, due to the very small sample size, clinically significant differences may have easily been missed. No firm recommendations can be made for clinicians. Large multicentre randomised controlled trials are needed to address this question definitively.
Maternal allergy modulates cord blood hematopoietic progenitor Toll-like receptor expression and function

BACKGROUND: Little is known regarding the prenatal determinants of innate immune responses in relation to infant allergic risk. Environmental exposures, including microbial stimuli, might predispose susceptible subjects to atopy and asthma in early infancy or even in utero. OBJECTIVE: Because Toll-like receptors (TLRs) recognize microbial products and because cord blood (CB) progenitor alterations have been observed in neonates at risk for atopy, we investigated the expression and function of TLRs on CB hematopoietic progenitors in relation to atopic risk, as defined by maternal allergic sensitization. METHODS: Thirty-two (15 with low and 17 with high atopic risk) infant CB samples were assessed for phenotypic and functional alterations in CD34(+) cells by means of flow cytometry and methylcellulose culture, respectively. CD34(+) hematopoietic progenitors were stained for TLR-2, TLR-4, TLR-9, GM-CSF receptor alpha, IL-5 receptor alpha, and IL-3 receptor alpha or cultured in methylcellulose assays for hematopoietic cytokine-stimulated eosinophil-basophil (Eo/B) colony-forming units (CFUs) with or without LPS. RESULTS: High-atopic-risk infants had significantly lower CB CD34(+) cell TLR-2, TLR-4, and TLR-9 expression (P = .009). High-risk infant progenitors gave rise to significantly more Eo/B CFUs (P = .002) with hematopoietic cytokine (IL-3, IL-5, or GM-CSF) stimulation ex vivo. Although LPS costimulation induced Eo/B CFUs from both low- and high-risk infant CB CD34(+) cells, this response was significantly (P = .020) muted in the high-risk CB progenitors. CONCLUSIONS: Neonatal CB CD34(+) hematopoietic progenitor cell TLR expression and functional responsiveness are altered in CB from atopic at-risk infants. Maternal allergic sensitization might modulate hematopoietic progenitor TLR expression and function in utero; specifically, Eo/B "lineage priming" at birth might be circumvented through engagement of TLR pathways in early life.

Rueter K, Bizzintino J, Martin AC, Zhang G, Hayden CM, Geelhoed GC, Goldblatt J, Laing IA and Le Souef PN
Symptomatic viral infection is associated with impaired response to treatment in children with acute asthma
The Journal of pediatrics. 2011; [Epub ahead of print]

OBJECTIVE: To examine the influence of viral respiratory infection (VRI) on treatment response in acute asthma in children. STUDY DESIGN: A total of 218 children (mean age, 6.6 years) with acute asthma were recruited. Symptoms were recorded, an asthma severity score was determined, and whenever possible, a per-nasal aspirate was obtained for detection of viruses. Each child's response to inhaled beta(2)-agonists was assessed after 6, 12, and 24 hours. RESULTS: The 168 children with VRI symptoms received more treatment with inhaled beta(2)-agonists after 6 hours (P = .010), 12 hours (P = .002), and 24 hours (P = .0005) compared with the 50 children without such symptoms. Asthma severity did not differ between the 2 groups. A per-nasal aspirate was obtained from 77% of the children. The most frequently identified virus was rhinovirus (61.4%). Among children with symptoms of a VRI, those with rhinovirus had an impaired response to beta(2)-agonists at 6 hours (P = .032). CONCLUSION: Children with acute asthma and symptoms of VRI respond less effectively to beta(2)-agonists after 6, 12, or 24 hours and thus may benefit from more intense therapy and monitoring.

Schultz A and Brand PL
Episodic viral wheeze and multiple trigger wheeze in preschool children: a useful distinction for clinicians?
Paediatric respiratory reviews. 2011; 12(3): 160-164

Accumulating evidence suggest that splitting preschool recurrent wheezing disorders into Episodic (Viral) Wheeze (EVW) and Multiple Trigger Wheeze (MTW) is an oversimplification. There is little evidence that the EVW and MTW phenotypes are related to the longitudinal patterns of wheeze, or to different underlying pathological processes. As the clinical response to inhaled corticosteroids and montelukast varies considerably between individual children with EVW, and between individual patients with MTW, the clinical usefulness of the EVW-MTW approach is doubtful. Based on the currently available evidence, we propose to describe preschool wheeze symptoms not only in terms of temporal pattern, but also in terms of frequency and severity, and age of onset. Relevant associated clinical parameters like atopy and eczema should be described with recognition of age of onset, pattern, and severity. Comparing these data to biomarkers and histopathology may help to improve our understanding of preschool wheezing disorders in the future. Until phenotypes can be described that are associated with different pathobiological process, are related to different longitudinal outcomes, or are clearly different in terms of response to therapy, clinicians are encouraged to take a trial and error approach of different therapeutic agents in preschool children with troublesome recurrent wheeze.
Schultz A and Brand PL
Phenotype-directed treatment of pre-school-aged children with recurrent wheeze
Journal of paediatrics and child health. 2011; [Epub ahead of print]

Wheeze in childhood may comprise different underlying diseases. Disease-specific treatment could potentially improve treatment efficacy. Various attempts have been made to differentiate between pre-school wheeze phenotypes. In this review, the results of clinical trials evaluating treatment of pre-school wheeze are discussed, with specific emphasis on the characteristics and phenotype of the study populations. Evidence suggests that systemic corticosteroids are not beneficial for the treatment of mild-to-moderate exacerbations of pre-school wheeze, irrespective of phenotype. The use of high-dose intermittent inhaled corticosteroid treatment cannot be recommended because of unacceptable side effects. Treatment with regular inhaled corticosteroids and leukotriene antagonists offer modest benefit, but neither treatment reduces hospitalisation rates. There is currently some evidence for a phenotype-specific effect of treatment. Phenotype-directed treatment of pre-school wheeze is currently limited by our ability to accurately differentiate between clinically useful phenotypes.

Schultz A, Sly PD, Zhang G, Venter A, Le Souef PN and Devadason SG
Incentive device improves spacer technique but not clinical outcome in preschool children with asthma
Journal of paediatrics and child health. 2011; [Epub ahead of print]

Aim: To investigate the influence of an incentive device, the Funhaler, on spacer technique and symptom control in young children with asthma and recurrent wheeze. Methods: Randomised controlled trial where 132 2-6 year old asthmatic children received regular inhaled fluticasone through Aerochamber Plus, or Funhaler. The setting was a research clinic at Princess Margaret Hospital for Children, Perth, Australia. Subjects were followed up for a year. The main outcome measure was asthma symptoms. Proficiency in spacer technique was measured as salbutamol inhaled from spacer onto filter. Quality of life was measured every three months. Groups were compared in terms of spacer technique, symptoms and quality of life. The relationship between spacer technique and clinical outcome was examined. Results: There was no difference between Funhaler and Aerochamber groups in wheeze free days, cough free days, bronchodilator free days or quality of life (P = 0.90, 0.87, 0.74 and 0.11 respectively). Spacer technique was better in the Funhaler group (P = 0.05), particularly in subjects younger than 4 years of age (P = 0.002). Drug dose on filter (as the mean of five 100 mg doses) ranged from zero to 136 mg. Conclusions: Use of Funhaler incentive device does not improve clinical outcome, but improves spacer technique in children younger than 4 years. Variability in drug delivery is large in young children using pressurised metered dose inhalers and spacers.

Shields L.

Shields L
Failing standards of education
The Queensland nurse. 2011: 22-23

Shields L.

Shields L
Family-centred care: effective care delivery or sacred cow?
Forum on Public Policy : a journal of the Oxford Round Table. 2011; (1): 10

Family-centred (The British spelling, centred, is used in this paper) care as a way to care for children in hospitals has become ubiquitous in the world of paediatrics. It evolved from work of pioneers in theories of maternal and child attachment, and paralleled the evolution of paediatric nursing as an academic (and evidence-generating) discipline. However, in the last decade, doubts have been sewn as to its efficacy and
workability, due to the lack of rigorous evidence about whether or not it works, or as to whether or not it makes a difference to the children and families for whom it is purported to care. This paper examines the historical evolution of family-centred care, discusses the current research about it, and poses questions around the ethics of continuing to use a model around which so many questions are generated.

Shields L
The head chef
Journal of the Royal Society of Medicine. 2011; 104(3)

Shields L

Shields L
Seeing is believing
The New Scientist. 2011; 209(2799): 28-29

Opinion letter

Shields L, Hall J and Mamun AA
The 'gender gap' in authorship in nursing literature
JRSM. 2011; 104(11): 457-464

Objectives Gender bias has been found in medical literature, with more men than women as first or senior authors of papers, despite about half of doctors being women. Nursing is about 90% female, so we aimed to determine if similar biases exist in nursing literature. Design Taking the eight non-specialist nursing journals with the highest impact factors for that profession, we counted the numbers of men and women first authors over 30 years. Setting We used nursing journals from around the world which attract the highest impact factors for nursing publication. Participants Eight journals qualified for entry, three from the United Kingdom, four from the United States of America, and one from Australia. Main outcome measures Using Chi-square and Fisher exact tests, we determined differences between the numbers of men and women across all the journals, between countries (USA, UK and Australia), changes over the 30 years, and changes within journals over time. Results Despite the small proportion of men in the nursing workforce, up to 30% of first authors were men. UK journals were more likely to have male authors than USA journals, and this increased over time. USA journals had proportions of male first authors consistent with the male proportion of its nursing workforce. Conclusions In the UK (though not in the USA) gender bias in nursing publishing exists, even though the nursing workforce is strongly feminized. This warrants further research, but is likely to be due to the same reasons for the gender gap in medical publishing; that is, female nurses take time out to have families, and social and family responsibilities prevent them taking opportunities for career progression, whereas men's careers often are not affected in such ways.

Shields L, Mamun AA, Pereira S, Nions P and Chaney G.
Measuring family centred care: working with children and their parents in a tertiary hospital

Rationale and aim: Family-centred care (FCC) is widely used in paediatrics, though no rigorous evidence for it exists. A growing body of qualitative research raises concerns about FCC, and health professionals' attitudes to it. We measured attitudes to working with children and working with parents of hospitalised children held by nurses, doctors, allied health and ancillary staff at an Australian children's hospital, using a validated questionnaire with two scores, one for working with children, one for working with parents, and demographic characteristics, and compared responses. Method: we recruited a randomized sample, and compared means of working with children and working with parents scores, using a Wilcoxon signed rank test p<0.0001. Mean differences by categories of demographics were estimated using ANOVA and median test compared the median scores. Results: respondents gave significantly more positive scores for working with children than parents. These were influenced by level of education, whether respondents were parents...
themselves, if they held senior positions, had worked with children for a long time, and held a paediatric qualification. Conclusions: paediatric health professionals view working with children in a more positive light than working with parents. However, if FCC was being implemented effectively, given its emphasis on the whole family as the unit of care, there would be no difference between working with children or their parents. This quantitative study supports the increasing body of qualitative research which highlights problems with this model. In addition, this study provides a way to measure FCC.

Shields L, Morrall P, Goodman B, Purcell C and Watson R
Care to be a nurse? Reflections on a radio broadcast and its ramifications for nursing today
Nurse Education Today. 2011; [Epub ahead of print]

Shields L, Purcell C and Watson R
It's not cricket: the Ashes of nursing education

The aim of this short discussion paper is to engender debate about the downturn in intellectual standing of nursing courses in Australia, where entry standards to nursing courses, and pass marks are being lowered to cater to the needs of health services for pairs of hands. We give examples of indicators of declining standards and reference them to the state of nursing education in the United Kingdom. We hope for debate and argument, and critical discussion, that might lead to a reassessment of nursing education in both countries.

Simpson SJ, Straszek SP, Sly PD, Stick SM and Hall GL
Clinical investigation of respiratory system admittance in preschool children
Pediatric pulmonology. 2011; Epub ahead of print

INTRODUCTION: The upper airway shunt attenuates measurements of respiratory system impedance (Zrs), with greater impact in young children. Changes in respiratory system admittance, Ars (or Zrs(-1) ), are theoretically independent of the shunt. This study compared the ability of Ars, to standard oscillatory outcomes, to determine respiratory disease and differentiate responses to inhaled bronchial challenges in the clinical setting. METHODS: The forced oscillation technique (FOT) was used to establish reference equations for Ars in healthy preschool children, compare the change in Ars to standard oscillatory outcomes during bronchial challenge with inhaled adenosine-5'-monophosphate (AMP) and to inhaled bronchodilator in healthy children and those with respiratory disease. RESULTS: Children with respiratory disease had lower baseline Ars than healthy children (P < 0.05). However, there was no improved ability for Ars to differentiate between bronchodilator responses in healthy and disease populations. In contrast, the response to inhaled AMP occurred at a lower concentration, [25 (3.12-400) mg ml(-1) ; median (10th-90th centile)], as measured by Ars when compared to respiratory system resistance [225 (6.25-400) mg ml(-1) ; P = 0.016]. CONCLUSION: This study supports the use of Ars during inhaled challenges, but not in response to bronchodilation. Pediatr Pulmonol. (c) 2011 Wiley-Liss, Inc.

Sims C and Johnson C.
Your guide to paediatric anaesthesia
McGraw-Hill Australia, 2011

This first Australian book on paediatric anaesthesia in 20 years is practical, descriptive and exam focused. It gives safe, experience-based ‘how-to’ approaches to common and rarer paediatric and neonatal conditions. Assuming readers know about adult anaesthesia, it focuses on what is different about children. The key to paediatric anaesthesia is to learn the skills to be confident about managing a child’s airway, as everyone knows children go blue very fast. Once mastered, you can then start to enjoy working with children and learning the art of managing their anxiety and that of their parents. Written by clinical, full-time paediatric anaesthetists, this is the one book that gives both all the information for specialist exam preparation, and the knowledge of contemporary paediatric anaesthesia that will stand a consultant anaesthetist in good stead.
Sly PD, Ware RS, de Klerk N and Stick SM
Randomised controlled trials in cystic fibrosis: what, when and how?
The European respiratory journal : official journal of the European Society for Clinical Respiratory Physiology. 2011; 37(5): 991-993

Soszyn N, Fricke TA, Wheaton GR, Ramsay JM, d’Udekem Y, Brizard CP and Konstantinov IE
Outcomes of the arterial switch operation in patients with Taussig-Bing anomaly

BACKGROUND: The arterial switch operation (ASO) is associated with poorer outcomes in patients with Taussig-Bing anomaly (TBA) compared with transposition of the great arteries (TGA). We describe the outcomes after ASO in patients with TBA at a single institution. METHODS: Between 1983 and 2009, 57 patients with TBA underwent the ASO at the Royal Children's Hospital in Melbourne. RESULTS: Hospital mortality was 5.3% (3 of 57). Larger weight at operation (p=0.015), pulmonary artery banding prior to ASO (p=0.049) and concurrent pulmonary artery banding (p=0.049) were risk factors of early death. Actuarial survival was 94% at 15 years. Follow-up was 84% complete with a mean follow-up of 9.8+/−6.7 years (range, 6 days to 19.1 years). There was no late mortality. Reintervention was required in 24.4% (11 of 45). Longer cross-clamp time (p=0.027) was a risk factor for reintervention. Freedom from reintervention was 75.3% at 15 years. After ASO, 2.2% (1 of 45) presented with sub-neopulmonary obstruction and 13.3% (6 of 45) had moderate or more neo-aortic insufficiency (neo-Al). Surgery prior to ASO was a risk factor for sub-neopulmonary obstruction (p=0.049) and moderate or more neo-Al (p=0.016). Freedom from moderate or more neo-Al was 91.1% at 10 years. CONCLUSIONS: Early mortality has improved over time with no mortality occurring in the last decade. Although patients are doing well on late follow-up, many patients require reintervention and show progression of neo-Al. Close long-term follow-up is warranted as patients are likely to require further reintervention in the second decade after TBA repair.

Southall PJ, Walters MJ and Singer S
The influence of orthodontic treatment on the GOSLON score of unilateral cleft lip and palate patients
The Cleft palate-craniofacial journal : official publication of the American Cleft Palate-Craniofacial Association. 2011;[Epub ahead of print]

Abstract Objective: To assess the effect of orthodontic treatment on GOSLON yardstick outcome. Design: Retrospective study. Patients: A series of 66 consecutive patients born with a complete UCLP. Patients were sorted into a non treatment group (n=47) and a treatment group (n=19). Method: Three assessors trained in the use of the GOSLON yardstick ranked the dental arch relationships of study casts taken at 6 and at 9 years. Results: There was only a fair agreement (Kappa 0.33) between 6-and 9 year GOSLON yardstick scores for the cohort of 66 patients, with a significant (P< 0.05) difference in the mean score at 6 years (3.17+/−0.8) and at 9 years (2.88+/−1.0). Removal of 19 subjects who had orthodontic inventions prior to taking of 9 year old study cast improved the agreement to moderate (Kappa 0.52). There was no significant difference (P> 0.05) in mean scores at 6 and 9 years, at 3.13+/−0.9 and 3.17+/−1.03 respectively. The treatment group exhibited significant differences (P<0.001) with mean GOSLON yardstick scores of 3.0 +/-0.9 at 6 and 2.25+/−0.45 at 9 years Conclusions: The inclusion of patients who had received orthodontic treatment prior to taking of study casts being used for GOSLON yardstick scoring can result in a more favourable outcome. Patients who have received active orthodontic treatment prior to taking of dental casts should be excluded or accounted for in audits to assess primary cleft surgical outcome in patients with a UCLP. Key Words: GOSLON yardstick, longitudinal cleft audit, cleft outcomes, orthodontic treatment.

Stick SM and Sly PD
Exciting new clinical trials in cystic fibrosis: infants need not apply
American journal of respiratory and critical care medicine. 2011; 183(12): 1577-1578
Stutz MD, Gangell CL, Berry LJ, Garratt LW, Sheil B and Sly PD
Cyanide in bronchoalveolar lavage is not diagnostic for Pseudomonas aeruginosa in children with cystic fibrosis
European Respiratory Journal. 2011; 37(3): 553-558

Early detection of the cyanobacterium Pseudomonas aeruginosa in the lungs of young children with cystic fibrosis (CF) is considered the key to delaying chronic pulmonary disease. We investigated whether cyanide in bronchoalveolar lavage (BAL) fluid could be used as an early diagnostic biomarker of infection. Cyanide was measured in 226 BAL samples (36 P. aeruginosa infected) obtained from 96 infants and young children with CF participating in an early surveillance programme involving annual BAL. Cyanide was detected in 97.2% of P. aeruginosa infected and 60.5% of uninfected samples. Cyanide concentrations were significantly higher in BALs infected with P. aeruginosa (median 25th–75th percentile) 27.3 (22.1–33.3) µM) than those which were not (17.2 (7.85–23.0) µM, p<0.001). The best sensitivity, specificity, positive and negative predictive values were obtained with a cut-off concentration of 20.6 µM, and were 83%, 66%, 32% and 96%, respectively. Neutrophil number in BAL was a significant predictor of cyanide concentration (p<0.001). Cyanide concentration can distinguish between P. aeruginosa infected and uninfected BALs as a group, but not individually; therefore, cyanide is a poor diagnostic biomarker of P. aeruginosa infection. Cyanide levels in BAL are related to the level of neutrophilic inflammation.

Sutanto EN, Kicic A, Foo CJ, Stevens PT, Mullane D, Knight DA and Stick SM
Innate inflammatory responses of pediatric cystic fibrosis airway epithelial cells: effects of non-viral and viral stimulation
American Journal of Respiratory Cell and Molecular Biology. 2011 Feb 11, [Epub ahead of print]

RATIONALE: There is controversy regarding whether cystic fibrosis (CF) airway epithelial cells (AEC) are intrinsically pro-inflammatory. OBJECTIVE: To characterize the inflammatory profiles of AEC from children with CF compared with cells from healthy controls. METHODS: Lower airway epithelial cells were obtained from healthy children (12) and those with CF (27). Biochemical and functional characteristics were assessed by stimulating cells with IFN gamma, LPS, a cocktail referred to as cytomix which consists of IFN gamma, IL-1beta, TNF-alpha and LPS or with human rhinovirus (HRV). Cytokine production was assessed using ELISA. Apoptotic responses to HRV infection were measured via production of ssDNA. RESULTS: CF and healthy cells exhibited similar morphology in monolayer culture. CF cells constitutively produced greater amounts of IL-6, IL-1beta and PGE2 but similar levels of IL-8 and sICAM-1 compared to healthy cells, and this profile was maintained through repeated passage. Stimulation with LPS or cytomix elicited similar levels of IL-8 in CF and non-CF cells. In contrast, exposure to HRV1b resulted in a marked increase in IL-8 production from CF compared to non-CF cells. CF cells also exhibited reduced apoptosis and increased viral replication compared to non-CF cells following exposure to HRV1b. CONCLUSIONS: CF and healthy AEC have similar basal and stimulated expression of IL-8 in response to pro-inflammatory stimuli but elevated IL-8 release in response to HRV infection. The elevated IL-8 together with dampened apoptotic responses by CF cells to HRV could contribute to augmented airway inflammation in the setting of recurrent viral infections early in life.

Interactions between acute lymphoblastic leukemia and bone marrow stromal cells influence response to therapy
Leukemia Research. 2011; [Epub ahead of print]

Thomas R, Lee S, Patole S and Rao S
Antibiotic-impregnated catheters for the prevention of CSF shunt infections: a systematic review and meta-analysis
British journal of neurosurgery. 2011; [Epub ahead of print]

Abstract Context. CSF infections are a serious complication of CSF shunts and external ventricular drains (EVDs). Antibiotic-impregnated catheters (AIC) have been tried in order to minimise the risk of such infections. Objectives. To conduct a systematic review and a meta-analysis comparing AICs versus non-AICs used as ventriculo-peritoneal (VP) shunts or external ventricular drains (EVDs) in the neonatal population. The secondary aim was to include data from a paediatric and adult population if insufficient information was available from neonatal studies. Data sources. PubMed (March 2011), EMBASE (March 2011), CENTRAL (1980-March 2011), and CINAHL (March 2011) were searched. Study selection. Both randomised controlled
trials (RCTs) and observational studies were included. Results. Only three observational studies reported on the use of AI-VP shunt catheters in the neonatal population. Meta-analysis found a statistically significant difference favouring AI shunts (RR: 0.37; CI: 0.16, 0.86; p = 0.02). Twelve studies (one RCT, 11 observational; n = 3284) compared AI versus non-AI VP shunts in a paediatric and adult population. The RCT showed a trend towards benefit using the AICs (RR: 0.38; 95% CI: 0.11, 1.30; p = 0.12). A meta-analysis of the 11 observational studies showed a significant benefit in the AI group (RR: 0.37; CI: 0.23, 0.60; p = 0.0001; n = 3149). Similar benefits were noted for AI-EVDs in RCTs (RR: 0.19; 95% CI: 0.05, 0.64; p = 0.01; n = 472, two studies) and observational studies (RR: 0.31; 95 CI: 0.13, 0.74; p = 0.009; n = 2415, five studies). Conclusions. A meta-analysis of mainly observational studies suggests that AICs may be an effective way of reducing the incidence of shunt and EVD infections. Well-designed multi-centre RCTs are urgently needed.


The all-age spirometry reference ranges reflect contemporary Australasian spirometry
Respirology. 2011 Mar 14, [Epub ahead of print]

SUMMARY AT A GLANCE: The 'All-ages' spirometry reference equations significantly advance the definition of the normal range of spirometry. The relevance of these equations for contemporary populations, and methods has not been tested. Using collated spirometry data from healthy Australasian subjects we demonstrated that the all-ages spirometry equations provide good estimates for contemporary populations. ABSTRACT: Background and objective: Advances in statistical modelling have allowed the creation of smoothly changing spirometry reference ranges that apply across a wide age range and better define the lower limit of normal. The objective of this study was to assess the agreement of the Stanojevic 2009 all-age reference ranges to contemporary lung function data to verify the appropriateness of this reference for clinical use in Australia and New Zealand. Methods: Spirometry data from healthy Caucasians measured between 2000-2009 in Australia and New Zealand were collected. Z-scores were calculated for the standard spirometry outcomes based on the all-age reference ranges. Results: Spirometry from 2066 subjects aged 4-80 years (55% male) from 14 centres were eligible. Statistically, the collated contemporary dataset differed from the all-age reference ranges, but these differences were relatively small, and clinically irrelevant representing differences of approximately 3% predicted. Significant differences were also observed between some centres and equipment, potentially indicating varying influence of equipment or subject selection. Conclusions: Spirometry from contemporary Australasian healthy subjects fits the all-age reference ranges well. While the current study supports the use of the all-age reference ranges, the between-centre differences highlight the need for spirometry to be used in conjunction with other clinical findings.


Differences in innate immune function between allergic and nonallergic children: new insights into immune ontogeny

BACKGROUND: Microbial products are of central interest in the modulation of allergic propensity. OBJECTIVE: We sought to explore whether allergic children show differences in microbial Toll-like receptor (TLR)-mediated responses over their first 5 years of life. METHODS: Mononuclear cells isolated from 35 allergic and 35 nonallergic children at birth and 1, 2.5, and 5 years of age were stimulated with TLR2-TLR9 ligands to study innate immune function and with allergens or mitogen to assess adaptive T-cell responses. Cytokine production was measured by using Luminex multiplexing technology. RESULTS: Nonallergic children show progressive and significant age-related increases in innate cytokine responses (IL-1beta, IL-6, TNF-alpha, and IL-10) to virtually all TLR ligands. This innate maturation corresponds with a parallel increase in adaptive T(H)1 (IFN-gamma) responses to allergens and mitogens. In contrast, allergic children show exaggerated innate responses at birth (P < .01) but a relative decrease with age thereafter, so that by age 5 years, TLR responses are attenuated compared with those seen in nonallergic subjects (P < .05). This early hyperresponsiveness in allergic subjects fails to translate to a corresponding maturation of T(H)1 function, which remains attenuated relative to that seen in nonallergic subjects but is associated with a characteristic age-dependent increase in allergen-specific T(H)2 responses (P < .01). CONCLUSION: Our findings suggest significant differences in the developmental trajectory of innate immune function in children with allergic disease that might contribute to the recognized differences in postnatal adaptive T-cell immunity.
von Ungern-Sternberg BS
Muscle relaxants are obligatory for pediatric intubation: Con.
Anaesthesist. 2011; 60(5): 476-478
Muskelrelaxanzien sind obligat für die Intubation bei Kindern: Kontra. Article in German

von Ungern-Sternberg BS and Habre W
Changes in lung volume during spells in children with Tetralogy of Fallot under general anesthesia
OBJECTIVE: To describe the changes in end-expiratory lung volume and ventilation inhomogeneity during spells in three children with Tetralogy of Fallot. DESIGN: After approval of the institutional Ethics Committee was obtained, children were included in a study protocol that included the assessment of end-expiratory lung volume and ventilation inhomogeneity, using a sulfur hexafluoride multibreath washout technique at different times before and during the surgical repair of congenital heart disease. Additional parental consent was sought to publish this subseries. SETTING: Operation theater in a tertiary-care university hospital. PATIENTS: We report the changes in end-expiratory lung volume and ventilation inhomogeneity in three children undergoing Tetralogy of Fallot repair who spilled before surgical incision. While starting the immediate treatment with phenytoin and increasing FiO2 to 1.0, we were able to measure respiratory function. During the spell, end-expiratory lung volume decreased and ventilation inhomogeneity increased significantly and only recovered slowly even after return of SaO2 to prespill values. CONCLUSIONS: These data show the deleterious effect of a spell on respiratory function, which may worsen hypoxemia. The loss in lung volume can have a deleterious additive effect in the presence of a spell, particularly because of the slow improvement after treatment.

Wei R, Claes P, Walters M, Wholley C and Clement JG
Augmentation of linear facial anthropometrics through modern morphometrics: a facial convexity example
Australian dental journal. 2011; 56(2): 141-147
BACKGROUND: The facial region has traditionally been quantified using linear anthropometrics. These are well established in dentistry, but require expertise to be used effectively. The aim of this study was to augment the utility of linear anthropometrics by applying them in conjunction with modern 3-D morphometrics. METHODS: Facial images of 75 males and 94 females aged 18-25 years with self-reported Caucasian ancestry were used. An anthropometric mask was applied to establish corresponding quasi-landmarks on the images in the dataset. A statistical face-space, encoding shape covariation, was established. The facial median plane was extracted facilitating both manual and automated indication of commonly used midline landmarks. From both indications, facial convexity angles were calculated and compared. The angles were related to the face-space using a regression based pathway enabling the visualization of facial form associated with convexity variation. RESULTS: Good agreement between the manual and automated angles was found (Pearson correlation: 0.9478-0.9474, Dahlberg root mean squared error: 1.15 degrees -1.24 degrees ). The population mean angle was 166.59 degrees -166.29 degrees (SD 5.09 degrees -5.2 degrees ) for males-females. The angle-pathway provided valuable feedback. CONCLUSIONS: Linear facial anthropometrics can be extended when used in combination with a face-space derived from 3-D scans and the exploration of property pathways inferred in a statistically verifiable way.

Whitehouse AJ, Maybery M, Wray JA and Hickey M
No association between early gastrointestinal problems and autistic-like traits in the general population
Aim The aim of this study was to determine whether gastrointestinal problems in early childhood relate to autistic-like traits in a general population sample. Method The parents of 804 children (442 females; 362 males) reported at 1-, 2-, 3-, and 5-year follow-ups whether their child had been taken to a hospital, general practitioner, or health clinic for any of five gastrointestinal symptoms: (1) constipation; (2) diarrhoea; (3) abdominal bloating, discomfort, or irritability; (4) gastro-oesophageal reflux or vomiting; and (5) feeding issues or food selectivity. Parents also reported whether their child had received the measles, mumps, and rubella vaccination. Autistic-like traits were measured when the children had reached early adulthood (mean age 19y 7mo; SD 0.63y) using a self-report questionnaire, the Autism Spectrum Quotient (AQ). Results There was no
statistically significant difference in AQ scores between those who had (n=133) and those who had not (n=671) experienced early gastrointestinal symptoms. chi(2) analyses revealed that the children with early gastrointestinal problems were no more likely to be represented in the upper quintile of scores on any of the AQ scales. The measles, mumps, and rubella vaccination was unrelated to gastrointestinal symptoms or AQ scores. Interpretation Parent-reported gastrointestinal problems in early childhood are unrelated to self-reported autistic-like traits in the general population.

Wibrow BA, Ho KM, Flexman JP, Keil AD and Kohrs DL
Eosinopenia as a diagnostic marker of bloodstream infection in hospitalised paediatric and adult patients: a case-control study

The objective of this study was to assess whether eosinopenia was a reliable diagnostic marker of bloodstream infection in hospitalised adult and paediatric patients. The design was a case-control study, set in a tertiary adult and paediatric hospital. A total of 157 adult and 85 paediatric patients with bloodstream infection (‘cases’) were compared to 195 and 94 randomly selected adult and paediatric patients who had clinical suspicion of bloodstream infection but with a negative blood culture (‘controls’) respectively. Patients with haematological or immunosuppressive disease and control patients who were treated with antibiotics within one week prior to the blood culture were excluded. Eosinopenia, or undetectable eosinophil count (<0.01 x 10(9) or <10/mm3), was more common among the cases than the controls (46.5% vs 21.5%, respectively). The specificity of eosinopenia to predict bloodstream infection in adult patients was reasonable (79%, 95% confidence interval [CI] 74 to 82), but its sensitivity was low (47%, 95% CI 41 to 52). The absolute eosinophil count only had a modest ability to discriminate bloodstream infections from controls in adult patients (area under receiver operating characteristic curve 0.349, 95% CI 0.288 to 0.411). Eosinophil counts had very little overall predictive ability (area under receiver operating characteristic curve 0.448, 95% CI 0.363 to 0.533, P=0.237), and the sensitivity (54%, 95% CI 47 to 61) and specificity (56%, 95% CI 49 to 63) of eosinopenia to predict bloodstream infection in paediatric patients were both low. In the multivariate analyses, only C-reactive protein concentrations and neutrophil counts, but not eosinopenia, were significantly associated with the presence of bloodstream infection in both adult and paediatric patients. The presence of eosinopenia can be considered as an inexpensive warning test for bloodstream infection in hospitalised adult patients so that further investigations can be initiated. An absence of eosinopenia is, however not sensitive enough to exclude bloodstream infection. C-reactive protein concentrations and neutrophil counts were both better markers of bloodstream infection than eosinopenia in hospitalised paediatric and adult patients.

Wiertsema SP, Chidlow GR, Kirkham LA, Corscadden KJ, Mowe EN, Vijayasekaran S, Coates HL, Harnett GB and Richmond PC
High detection rates of nucleic acids of a wide range of respiratory viruses in the nasopharynx and the middle ear of children with a history of recurrent acute otitis media

Both bacteria and viruses play a role in the development of acute otitis media, however, the importance of specific viruses is unclear. In this study molecular methods were used to determine the presence of nucleic acids of human rhinoviruses (HRV; types A, B, and C), respiratory syncytial viruses (RSV; types A and B), bocavirus (HBoV), adenovirus, enterovirus, coronaviruses (229E, HKU1, NL63, and OC43), influenza viruses (types A, B, and C), parainfluenza viruses (types 1, 2, 3, 4A, and 4B), human metapneumovirus, and polymaviruses (K1 and WU) in the nasopharynx of children between 6 and 36 months of age either with (n = 180) or without (n = 66) a history of recurrent acute otitis media and in 238 middle ear effusion samples collected from 143 children with recurrent acute otitis media. The co-detection of these viruses with Streptococcus pneumoniae, nontypeable Haemophilus influenzae, and Moraxella catarrhalis was analyzed. HRV (58.3% vs. 42.4%), HBoV (52.2% vs. 19.7%), polymaviruses (36.1% vs. 15.2%), parainfluenza viruses (29.4% vs. 9.1%), adenovirus (25.0% vs. 6.1%), and RSV (27.8% vs. 9.1%) were detected significantly more often in the nasopharynx of children with a history of recurrent acute otitis media compared to healthy children. HRV was predominant in the middle ear and detected in middle ear effusion of 46% of children. Since respiratory viruses were detected frequently in the nasopharynx of both children with and without a history of recurrent acute otitis media, the etiological role of specific viruses in recurrent acute otitis media remains uncertain, however, anti-viral therapies may be beneficial in future treatment and prevention strategies for acute otitis media.
Wiertsema SP, Kirkham LA, Corscadden KJ, Mowe EN, Bowman JM, Jacoby P, Francis R, Vijayasekaran S, Coates HL, Riley TV and Richmond P
Predominance of nontypeable Haemophilus influenzae in children with otitis media following introduction of a 3+0 pneumococcal conjugate vaccine schedule
Vaccine. 2011; 29(32): 5163-5170

In Australia the 7-valent pneumococcal conjugate vaccine (PCV7) is administered at 2, 4 and 6 months of age, with no booster dose. Information on bacterial carriage and the aetiology of recurrent acute otitis media (rAOM) after introduction of PCV7 using the 3+0 schedule is required to evaluate the potential impact of second generation pneumococcal vaccines. We found that 2-4 years after introduction of PCV7 in the National Immunisation Program, nontypeable Haemophilus influenzae (NTHi) was the predominant pathogen isolated from the nasopharynx and middle ear of children with a history of rAOM. Compared with healthy controls (n=81), NTHi and Streptococcus pneumoniae carriage rates were significantly higher in children with a history of rAOM (n=186) (19% vs. 56% p<0.0001 and 26% vs. 41%, p=0.02, respectively). Carriage of PCV7 pneumococcal serotypes was rare, whereas PCV7-related and non-PCV7 serotypes were isolated of 38% of cases and 24% of controls. Serotype 19A was the most common serotype isolated from the nasopharynx and middle ear and accounted for 36% (14/39) of total pneumococcal isolates with reduced susceptibility to cotrimoxazole. Of the 119 children carrying NTHi, 17% of isolates were beta-lactamase positive. The scarcity of PCV7 serotypes in children with and without a history of rAOM indicates that the 3+0 PCV7 schedule is preventing carriage and rAOM from PCV7 serotypes. Introduction of new vaccines in Australia with increased pneumococcal serotype and pathogen coverage, including 19A and NTHi, should decrease the circulation of antibiotic-resistant bacteria and reduce the burden of rAOM.

Williams BK, Guelfi KJ, Jones TW and Davis EA
Lower cardiorespiratory fitness in children with Type 1 diabetes

Aims: The present study aimed to compare cardiorespiratory fitness levels in children with and without Type 1 diabetes. In addition, the relationship between cardiorespiratory fitness and a range of physical and clinical factors was investigated. METHODS: Eighty-eight children with Type 1 diabetes aged 5-14 years completed a submaximal step test of cardiorespiratory fitness. Sixty-two of these children were successfully matched to control subjects without diabetes based on age, sex and anthropometrics for comparison. In addition, the relationship between cardiorespiratory fitness and a range of physical and clinical variables was assessed in the children with diabetes. RESULTS: The heart rate response to exercise was higher in children with Type 1 diabetes, indicating reduced cardiorespiratory fitness levels compared with control subjects. Both gender and glycaemic control (HbA1c) were significantly associated with cardiorespiratory fitness, with female sex and poorer glycaemic control associated with reduced fitness. CONCLUSIONS: Future research should investigate whether the reduced fitness in children with Type 1 diabetes is attributable to lower physical activity levels, or physiological changes resulting from the diabetes pathology itself.

Yim DL, Murray CP and Bullock AM
Computed tomography and occlusion of a right coronary artery to the left atrial fistula
Cardiology in the young. 2011; 21(5): 585-586

Young D, Bebbington A, de Klerk N, Bower C, Nagarajan L and Leonard H
The relationship between MECP2 mutation type and health status and service use trajectories over time in a Rett syndrome population

This study aimed to investigate the trajectories over time of health status and health service use in Rett syndrome by mutation type. Data were obtained from questionnaires administered over six years to 256 participants from the Australian Rett Syndrome Database. Health status (episodes of illness and medication load) and health service use (general practitioner and specialist visits and hospital stays) were summarized into composite scores with Principal Component Analysis. Linear and mixed regression models examined effects of mutation type and other variables on these scores over time. For some mutations (such as p.R255X, p.R168X) health status was poorer at a younger age and improved over time, while for p.R133C it was better at a younger age and deteriorated with time. For those with p.R133C health service use was lowest at a younger age and
highest at 25 years. With other mutations, such as p.R255X, p.R270X, p.R294X, C terminal and p.R306C, health service use was higher at a younger age, but dropped off considerably by 25 years of age. Health service use generally declined in parallel with deterioration in health status, although this pattern differed by mutation type, demonstrating important variability in the course of Rett syndrome.

Disparity of innate immunity-related gene effects on asthma and allergy on Karelia
Pediatric allergy and immunology : official publication of the European Society of Pediatric Allergy and Immunology. 2011; 22(6): 621-630

BACKGROUND: We investigated the interactive effects of 11 innate immunity-related genes (IL10, IL12b, IL8, TLR2, TLR4, CD14, IFNGR, CC16, IFNg, CMA1, and TGFβ) and four IgE response genes (IL4, IL13, IL4RA, and STAT6) with 'Western' or 'Eastern' environments/lifestyles on asthma and allergy in Karelian children. METHODS: Karelian children (412 Finnish and 446 Russian) were recruited and assessed for a range of allergic conditions, with 24 single-nucleotide polymorphisms genotyped in 15 genes. RESULTS: The genotype-phenotype relationships differed in Finnish and Russian Karelian children. The interaction between polymorphisms and the variable representing 'Western' and 'Eastern' environments/lifestyles was significant for IL10-1082 (p = 0.0083) on current rhinitis, IL12b 6408 on current conjunctivitis (p = 0.016) and atopy (p = 0.034), IL8 781 on atopic eczema (p = 0.0096), CD14 -550 on current rhinitis (p = 0.022), IFNgR1 -56 on atopic eczema (p = 0.038), and STAT6 2964 on current itchy rash (p = 0.037) and total serum IgE (p = 0.042). In addition, the G allele of IL13 130 was associated with a lower level of total serum IgE in Finnish (p = 0.003) and Russian (p = 0.01) children and overall (pooling the two populations together, p = 0.00006). After adjusting for multiple tests, the association between IL13 130 and IgE and the interactive effects of IL10-1082 on current rhinitis and IL8 781 on atopic eczema were significant by controlling a false-positive rate of 0.05 and 0.10, respectively. CONCLUSIONS: Living in an Eastern vs. Western environment was associated with a different genetic profile associated with asthma and allergy in the Karelian populations.