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Articles are listed alphabetically by first author.

**Abraham MB, Carpenter K, Baynam GS, Mackay DJ, Price G and Choong CS.**
Journal of paediatrics and child health. 2014.

Silver-Russell syndrome (SRS) and Mayer-Rokitansky-Kuster-Hauser (MRKH) syndrome are described in isolation. However, their co-occurrence has only been rarely reported. Here, we present a case report of an adolescent with SRS who was diagnosed with MRKH during the evaluation of primary amenorrhoea. Multiplex ligation-dependent probe amplification analysis showed a normal methylation pattern and normal dosage at 11p15.5. A PubMed search for all peer-reviewed publications (original articles and reviews) using the key words Silver-Russell syndrome, Mayer-Rokitansky-Kuster-Hauser syndrome, genetics, hypomethylation and reproductive anomalies identified three cases of SRS with MRKH, two of which were associated with significant hypomethylation of the H19 imprinting control region of the 11p15.5 locus. This report highlights the association between SRS and MRKH. The absence of hypomethylation and normal dosage at 11p15.5 suggests these two rare entities share alternative aetiopathogenic mechanisms.

**Abraham MB, Rao S, Price G and Choong CS.**
Efficacy of Hydrochlorothiazide and low renal solute feed in Neonatal Central Diabetes Insipidus with transition to Oral Desmopressin in early infancy.

**BACKGROUND:** The treatment of central diabetes insipidus (DI) with desmopressin in the neonatal period is challenging because of the significant risk of hyponatremia with this agent. The fixed anti-diuresis action of desmopressin and the obligate high fluid intake with milk feeds lead to considerable risk of water intoxication and hyponatremia. To reduce this risk, thiazide diuretics, part of the treatment of nephrogenic DI, were used in conjunction with low renal solute feed and were effective in a single case series of neonatal central DI. **AIM:** We evaluated the efficacy of early treatment of neonatal central DI with hydrochlorothiazide with low solute feed and investigated the clinical indicators for transition to desmopressin during infancy. **METHODS:** A retrospective chart review was conducted at Princess Margaret Hospital, Perth of neonates diagnosed with central DI and treated with hydrochlorothiazide, between 2007 and 2013. Four newborns were identified. Mean sNa and mean change in sNa with desmopressin and hydrochlorothiazide treatment were recorded along with episodes of hyponatremia and hypernatremia. Length and weight trajectories during the first 12 months were assessed. **RESULTS:** The mean change in sNa per day with hydrochlorothiazide and low renal solute feed was 2.5 - 3 mmol/L; on desmopressin treatment, the mean change in sNa was 6.8-7.9 mmol/L. There was one episode of symptomatic hyponatremia with intranasal desmopressin with no episodes of hyponatremia or hypernatremia during treatment with hydrochlorothiazide or following transition to oral desmopressin. Transition to oral desmopressin between 3 to 12 months of age was associated with good control of DI. Following introduction of solids, sNa remained stable but weight gain was slow. This improved following transition to desmopressin in one infant. **CONCLUSIONS:** Hydrochlorothiazide with low renal solute feed is a safe and effective treatment option in neonatal central DI. However, transition to desmopressin should be considered early in infancy following initiation of solids to facilitate growth.

Difficult airway equipment: a survey of standards across metropolitan Perth.

The importance of appropriate equipment to manage the difficult airway has been highlighted by the publication of the Australian and New Zealand College of Anaesthetists (ANZCA) guidelines in 2012. We set out to audit...
Delivering a Healthy WA

compliance with these guidelines in all public and private sites providing general anaesthesia in metropolitan Perth. Public and private health care websites identified 39 sites of which 37 were studied. Institutional and ethics approval was obtained. A tick-box design audit tool, based on the ANZCA guidelines, was used to collect information regarding the dedicated difficult airway container (DDAC) at each site. As recommended in the guidelines, only equipment within the DDAC was considered. Further data about each site, including the number of theatre suites, satellite anaesthetic areas, use of capnography and categories of patients treated (adult, obstetric and paediatric) were collected. An adult DDAC was found at 92% of all sites, but none of the sites had all the essential equipment listed in the ANZCA guidelines. There was limited provision of adult difficult airway equipment within private sites compared to public, and less provision of paediatric difficult airway equipment across all sites treating paediatric patients in metropolitan Perth. Capnography was available in 76% of post anaesthesia care units and used regularly in 27%. Adherence to the ANZCA guidelines regarding the DDAC could be improved. Standardised equipment across a metropolitan region would be of value in the management of the difficult airway.

Allen KL, Gibson LY, McLean NJ, Davis EA and Byrne SM.
Maternal and family factors and child eating pathology: risk and protective relationships.

BACKGROUND: Previous studies have found associations between maternal and family factors and child eating disorder symptoms. However, it is not clear whether family factors predict eating disorder symptoms specifically, or relate to more general child psychopathology, of which eating disorder symptoms may be one component. This study aimed to identify maternal and family factors that may predict increases or decreases in child eating disorder symptoms over time, accounting for children's body mass index z-scores and levels of general psychological distress.

METHODS: Participants were 221 mother-child dyads from the Childhood Growth and Development Study, a prospective cohort study in Western Australia. Participants were assessed at baseline, 1-year follow-up and 2-year follow-up using interview and self-report measures. Children had a mean age of 10 years at baseline and 46% were male. Linear mixed models and generalised estimating equations were used to identify predictors of children's eating disorder symptoms, with outcome variables including a global index of eating disorder psychopathology, levels of dietary restraint, levels of emotional eating, and the presence of loss of control (‘binge’) eating.

RESULTS: Children of mothers with a current or past eating disorder reported significantly higher levels of global eating disorder symptoms and emotional eating than other children, and mothers with a current or past eating disorder reported significantly more concern about their children's weight than other mothers. Maternal concern about child weight, rather than maternal eating disorder symptoms, was significant in predicting child eating disorder symptoms over time. Family exposure to stress and low maternal education were additional risk factors for eating disorder symptoms, whilst child-reported family satisfaction was a protective factor.

CONCLUSIONS: After adjusting for relevant confounding variables, maternal concern about child weight, children's level of family satisfaction, family exposure to stress, and maternal education are unique predictors of child eating disorder symptoms.

A decade of data from a specialist statewide child and adolescent eating disorder service: does local service access correspond with the severity of medical and eating disorder symptoms at presentation?

BACKGROUND: Eating disorders affect up to 3% of children and adolescents, with recovery often requiring specialist treatment. A substantial literature has accrued suggesting that lower access to health care services, experienced by rural populations, has a staggering effect on health-related morbidity and mortality. The aim of this study was to evaluate whether lower service access foreshadowed a more severe medical and symptom presentation among children and adolescents presenting to a specialist eating disorders program. METHOD: The data source was the Helping to Outline Paediatric Eating Disorders (HOPE) Project registry (N ~1000), a prospective ongoing registry study comprising consecutive paediatric tertiary eating disorder referrals. The sample consisted of 399 children and adolescents aged 8 to 16 years (M =14.49, 92% female) meeting criteria for a DSM-5 eating disorder.

RESULTS: Consistent with the hypotheses, lower service access was associated with a lower body mass index z-score and a higher likelihood of medical complications at intake assessment. Contrary to our hypothesis, eating pathology assessed at intake was associated with higher service access. No relationship was observed between service access and duration of illness or percentage of body weight lost.

CONCLUSIONS: Lower service access is associated with more severe malnutrition and medical complications at referral to a specialist eating disorder program. These findings have implications for service planning and provision for rural communities to equalize health outcomes.

A decade of data from a specialist statewide child and adolescent eating disorder service: does local service access correspond with the severity of medical and eating disorder symptoms at presentation?


Inborn errors of purine metabolism exhibit broad neurological, immunological, haematological and renal manifestations. Limited awareness of the phenotypic spectrum, the recent descriptions of newer disorders and considerable genetic heterogeneity, have contributed to long diagnostic odysseys for affected individuals. These enzymes are widely but not ubiquitously distributed in human tissues and are crucial for synthesis of essential nucleotides, such as ATP, which form the basis of DNA and RNA, oxidative phosphorylation, signal transduction and a range of molecular synthetic processes. Depletion of nucleotides or accumulation of toxic intermediates contributes to the pathogenesis of these disorders. Maintenance of cellular nucleotides depends on the three aspects of metabolism of purines (and related pyrimidines): de novo synthesis, catabolism and recycling of these metabolites. At present, treatments for the clinically significant defects of the purine pathway are restricted: purine 5’-nucleotidase deficiency with uridine; familial juvenile hyperuricaemic nephropathy (FJHN), adenine phosphoribosyl transferase (APRT) deficiency, hypoxanthine phosphoribosyl transferase (HPRT) deficiency and phosphoribosyl-pyrophosphate synthetase superactivity (PRPS) with allopurinol; adenosine deaminase (ADA) and purine nucleoside phosphorylase (PNP) deficiencies have been treated by bone marrow transplantation (BMT), and ADA deficiency with enzyme replacement with polyethylene glycol (PEG)-ADA, or erythrocyte-encapsulated ADA; myeloadenylate deaminase (MADA) and adenylosuccinate lyase (ADSL) deficiencies have had trials of oral ribose; PRPS, HPRT and adenosine kinase (ADK) deficiencies with S-adenosylmethionine; and molybdenylate cofactor deficiency of complementation group A (MOCODA) with cyclic pyranopterin monophosphate (cPMP). In this review we describe the known inborn errors of purine metabolism, their phenotypic presentations, established diagnostic methodology and recognised treatment options.


Inborn errors involving enzymes essential for pyrimidine nucleotide metabolism have provided new insights into their fundamental physiological roles as vital constituents of nucleic acids as well as substrates of lipid and carbohydrate metabolism and in oxidative phosphorylation. Genetic aberrations of pyrimidine pathways lead to diverse clinical manifestations including neurological, immunological, haematological, renal impairments, adverse reactions to analogue therapy and association with malignancies. Maintenance of cellular nucleotides depends on the three aspects of metabolism of pyrimidines: de novo synthesis, catabolism and recycling of these metabolites. Of the ten recognised disorders of pyrimidine metabolism treatment is currently restricted to only two disorders: hereditary orotic aciduria (oral uridine therapy) and mitochondrial neurogastrointestinal encephalomyopathy (MNGIE; allogeneic hematopoetic stem cell transplant and enzyme replacement). The ubiquitous role that pyrimidine metabolism plays in human life highlights the importance of improving diagnostic evaluation in suggestive clinical settings, which will contribute to the elucidation of new defects, future development of novel drugs and therapeutic strategies. Limited awareness of the expanding phenotypic spectrum, with relatively recent descriptions of newer disorders, compounded by considerable genetic heterogeneity has often contributed to the delays in the diagnosis of this group of disorders. The lack of an easily recognisable, easily measurable end product, akin to uric acid in purine metabolism, has contributed to the under-recognition of these disorders. This review describes the currently known inborn errors of pyrimidine metabolism, their phenotypic presentations, established diagnostic methodology and recognised treatment options.


This study analysed spatial and temporal variation in childhood incidence of type 1 diabetes mellitus (T1DM) among Western Australias 36 Health Districts from 1991 to 2010. There was a strong latitudinal gradient of 3.5% (95% CI, 0.2-7.2) increased risk of T1DM per degree south of the Equator, as averaged across the range 15-35 degrees south. This pattern is consistent with the hypothesis of vitamin D deficiency at higher latitudes. In addition there was a 2.4% (95% CI, 1.3-3.6) average increase in T1DM incidence per year. These effects could not be explained by population density, socioeconomic status, remoteness or ethnicity.


There are many current and evolving tools to assist clinicians in their daily work of phenotyping. In medicine, the term 'phenotype' is usually taken to mean some deviation from normal morphology, physiology and behaviour. It is ascertained via history, examination and investigations, and a primary aim is diagnosis. Therefore, doctors
are, by necessity, expert 'phenotypers'. There is an inherent and partially realised power in phenotypic information that when harnessed can improve patient care. Furthermore, phenotyping developments are increasingly important in an era of rapid advances in genomic technology. Fortunately, there is an expanding network of phenotyping tools that are poised for clinical translation. These tools will preferentially be implemented to mirror clinical workflows and to integrate with advances in genomic and information-sharing technologies. This will synergise with and augment the clinical acumen of medical practitioners. We outline key enablers of the ascertainment, integration and interrogation of clinical phenotype by using genetic diseases, particularly rare ones, as a theme. Successes from the test bed or rare diseases will support approaches to common disease.


We assessed IgA antibodies and polymerase chain reaction (PCR) for diagnosis of pertussis in nasopharyngeal aspiration (NPA) samples from outpatients in Australia. A total of 1700 patients (849 adults, 851 children) from Western Australia and the Northern Territory fulfilled the laboratory case definition for pertussis between 2004 and 2013: 732 specimens were positive by NPA IgA alone, 559 by PCR alone, and 409 by both tests. Overall, 968 cases (56.8%) were positive by PCR and 1141 cases (67.2%) by IgA [p < 0.00025]. Among pediatric patients, PCR was positive in 524 (61.3%) and IgA in 569 (67%). In 849 adult cases, the respective proportions were 52.3% and 67.4% [p < 0.00025]. The duration of cough in 507 patients was shorter in 262 pediatric cases (mean, 2.51 weeks; standard deviation [SD], 2.25) than 245 adult patients (3.27 weeks; SD, 2.79) [p = 0.0009].


Background: The NUT midline carcinoma (NMC) is a rare but fatal cancer for which systematic testing of therapy options has never been performed. Methods: On the basis of disease biology, we compared the efficacy of the CDK9 inhibitor flavopiridol (FP) with a panel of anticancer agents in NMC cell lines and mouse xenografts. Results: In vitro anthracyclines, topoisomerase inhibitors, and microtubule poisons were among the most cytotoxic drug classes for NMC cells, while efficacy of the bromodomain inhibitor JQ1 varied considerably between lines carrying different BRD4 (bromodomain-containing protein 4)-NUT (nuclear protein in testis) translocations. Efficacy of FP was comparable to vincristine and doxorubicin, drugs that have been previously used in NMC patients. All three compounds showed significantly better activity than etoposide and vorinostat, agents that have also been used in NMC patients. Statins and antimetabolites demonstrated intermediate single-agent efficacy. In vivo, vincristine significantly inhibited tumour growth in two different NMC xenografts. Flavopiridol in vivo was significantly effective in one of the two NMC xenograft lines, demonstrating the biological heterogeneity of this disease. Conclusions: These results demonstrate that FP may be of benefit to a subset of patients with NMC, and warrant a continued emphasis on microtubule inhibitors, anthracyclines, and topoisomerase inhibitors, especially those with a delayed presentation.


Mould species represent the pathogens most commonly associated with invasive fungal disease in patients with haematological malignancies and patients of haemopoietic stem cell transplants. Invasive mould infections in these patient populations, particularly in the setting of neutropenia, are associated with high morbidity and mortality, and significantly increase the complexity of management. While Aspergillus species remain the most prevalent cause of invasive mould infections, Scedosporium and Fusarium species and the Mucormycetes continue to place a significant burden on the immunocompromised host. Evidence also suggests that infections caused by rare and emerging pathogens are increasing within the setting of broad-spectrum antifungal prophylaxis and improved survival times placing immunosuppressed patients at risk for longer. These guidelines present evidence-based recommendations for the antifungal management of common, rare and emerging...
mould infections in both adult and paediatric populations. Where relevant, the role of surgery, adjunctive therapy and immunotherapy is also discussed.

Effectiveness of trivalent flu vaccine in healthy young children.
BACKGROUND: There are few studies evaluating the effectiveness of trivalent influenza vaccination (TIV) in young children, particularly in children <2 years. The Western Australian Influenza Vaccine Effectiveness Study commenced in 2008 to evaluate a program providing TIV to children aged 6 to 59 months. METHODS: An observational study enrolling children with influenza-like illness presenting to a tertiary pediatric hospital was conducted (2008-2012). Vaccination status was determined by parental questionnaire and confirmed via the national immunization register and/or vaccine providers. Respiratory virus polymerase chain reaction and culture were performed on nasopharyngeal samples. The test-negative design was used to estimate vaccine effectiveness (VE) by using 2 control groups: all influenza test-negative subjects and other-virus-detected (OVD) subjects. Adjusted odds ratios were estimated from models with season, month of disease onset, age, gender, indigenous status, prematurity, and comorbidities as covariates. Subjects enrolled in 2009 were excluded from VE calculations. RESULTS: Of 2001 children enrolled, influenza was identified in 389 (20.4%) children. Another respiratory virus was identified in 1134 (59.6%) children. Overall, 295 of 1903 (15.5%) children were fully vaccinated and 161 of 1903 (8.4%) children were partially vaccinated. Vaccine uptake was significantly lower in 2010-2012 after increased febrile adverse events observed in 2010. Using test-negative controls, VE was 64.7% (95% confidence interval [CI]: 33.7%-81.2%). No difference in VE was observed with OVD controls (65.8%; 95% CI: 32.1%-82.8%). The VE for children <2 years was 85.8% (95% CI: 37.9%-96.7%). CONCLUSIONS: This study reveals the effectiveness of TIV in young children over 4 seasons by using test-negative and OVD controls. TIV was effective in children aged <2 years. Despite demonstrated vaccine effectiveness, uptake of TIV remains suboptimal.

Blyth CC, Pereira L and Goire N.
New Delhi metallo-beta-lactamase-producing enterobacteriaceae in an Australian child who had not travelled overseas.

Blyth CC, Richmond PC, Jacoby P, Thornton P, Regan A, Robins C, Kelly H, Smith DW and Effler PV.
The impact of pandemic A(H1N1)pdm09 influenza and vaccine-associated adverse events on parental attitudes and influenza vaccine uptake in young children.
INTRODUCTION: Parental attitudes towards vaccination significantly influence vaccine uptake. The A(H1N1)pdm09 influenza pandemic was followed in 2010 by an unprecedented increase in febrile reactions in children receiving trivalent inactivated influenza vaccine manufactured by bioCSL. Uptake of TIV in children <5 years in Western Australia (WA) decreased in 2010 and has remained low. The impact of pandemic A(H1N1)pdm09 and adverse events on parental attitudes towards vaccination is uncertain. MATERIALS AND METHODS: A parental attitudes survey towards influenza illness and vaccination was conducted as part of the West Australian Influenza Vaccine Effectiveness study. Vaccination status was assessed by parental interview and confirmed by the national register and/or vaccine providers. Parental attitudes from vaccinated and unvaccinated children and attitudes in 2008-2009 and 2010-2012 were compared. Principal Component Analysis was conducted to determine core attitudes that influenced vaccine uptake. RESULTS: Vaccination history and parental attitude surveys were available from 2576 children. Parents of fully vaccinated children less frequently stated that influenza was a mild disease, more frequently stated that influenza vaccine was safe and were less frequently worried about vaccine side effects. Uptake of influenza vaccine decreased significantly from 2010 onwards. From 2010, parents were less concerned about severe influenza, but more concerned about vaccine side effects and safety. Despite this significant shift in attitudes towards influenza vaccine, parental acceptance of vaccines on the national immunisation program did not change. Principal Component Analysis revealed that attitudes around vaccine safety and efficacy were the most important attitudes impacting on vaccine uptake. CONCLUSIONS: Parental attitudes to influenza vaccine changed from 2010. Confidence in the WA preschool influenza vaccination program remains low yet appeared unchanged for other vaccines. Restoring public confidence in childhood influenza vaccination is needed before uptake can be improved.

Neisseria meningitidis porA, fetA and fHbp gene distribution in Western Australia 2000 to 2011.
Boulter EL, Rogers JR and Borland ML.

Improving junior doctors' confidence in paediatric musculoskeletal assessment.

AIM: Musculoskeletal symptoms are a common cause for presentation of children and adolescents to health-care settings. Junior doctors report lack of confidence in assessment of the paediatric musculoskeletal system. Our aim was to assess the confidence of junior medical officers (JMOs) working in the emergency department (ED) with paediatric musculoskeletal assessment and determine if a readily available teaching module would improve confidence. METHODS: JMOs rostered to the paediatric ED were surveyed regarding their confidence in paediatric musculoskeletal assessment at the start and end of their ED rotation. A subgroup of these JMOs received formal teaching on paediatric musculoskeletal assessment using the paediatric gait, arm, leg and spine examination as part of their protected teaching time during their rotation. RESULTS: Forty-three JMOs were considered in the final analysis. Of those, 27 received teaching (intervention group), and 16 received no teaching (non-intervention group). In the intervention subgroup, there was a trend towards an increase in confidence in paediatric musculoskeletal assessment with the commonest response prior to the teaching intervention being 'some confidence' (11/27 41%) and the commonest response after teaching being 'fairly confident' (14/27 52%) without achieving statistical significance (P = 0.068). Of the JMOs in the intervention group, 26/27 (96%) found the teaching session useful, and 25/27 (93%) considered it relevant to their future practice. CONCLUSIONS: A clinical examination teaching intervention resulted in a trend towards an increase in confidence for JMOs in paediatric musculoskeletal assessment. Formal evaluation of a teaching module was feasible within the ED.
asthma and allergy, (4) pulmonary development, and (5) harmonization of existing birth cohorts. This article presents the workgroup reports and provides Web links (AsthmaBirthCohorts.niaid.nih.gov or www.medall-fp7.eu), where the reader will find tables describing the characteristics of the birth cohorts included in this report, the type of data collected at differing ages, and a selected bibliography provided by the participating birth cohorts.

Bowen AC, Burns K, Tong SY, Andrews RM, Liddle R, IM OM, Westphal DW and Carapetis JR. Standardising and assessing digital images for use in clinical trials: a practical, reproducible method that blinds the assessor to treatment allocation. PloS one. 2014; 9(11): e110395. With the increasing availability of high quality digital cameras that are easily operated by the non-professional photographer, the utility of using digital images to assess endpoints in clinical research of skin lesions has growing acceptance. However, rigorous protocols and description of experiences for digital image collection and assessment are not readily available, particularly for research conducted in remote settings. We describe the development and evaluation of a protocol for digital image collection by the non-professional photographer in a remote setting research trial, together with a novel methodology for assessment of clinical outcomes by an expert panel blinded to treatment allocation.

Bradman K, Borland M and Pascoe E. Predicting patient disposition in a paediatric emergency department. Journal of paediatrics and child health. 2014; 50(10): E39-44. AIM: The aim of this study is to directly compare published prediction tools with triage nurse (TN) predictions within a defined paediatric population. METHOD: A prospective observational study carried out over a week in May 2010 in the Emergency Department (ED) at Princess Margaret Hospital for Children in Perth, Western Australia. TN predicted which patients would be admitted to hospital at the time of ED presentation. Data required for the other prediction tools (paediatric early warning score (PEWS); triage category and the Pediatric Risk of Admission Score (PRISA) and PRISA II were obtained from the notes following the patient's ED attendance. RESULTS: A total of 1223 patients presented during the study week, 91 patients were excluded and a total of 946 patients (83.6%) had TN predictions and were included in the analysis. TN predictions were compared against a PEWS >/= 4, triage category 1, 2 and 3, PRISA >/= 9 and PRISA II >/= 2. TNs had the highest prediction accuracy (87.7%), followed by an elevated PEWS (82.9%), triage category of 1, 2, or 3 (82.9%). The PRISA and PRISA II score had an accuracy of 80.1% and 79.7%, respectively. CONCLUSION: When compared with validated prediction tools, the TN is the most accurate predictor of need to admit. This study provides valuable information in planning efficient flow of patients through the ED.


Buratto E, McCrossan B, Galati JC, Bullock A, Kelly A, d'Udekem Y, Brizard CP and Konstantinov IE. Repair of partial atrioventricular septal defect: a 37-year experience. Eur J Cardiothorac Surg. 2014. OBJECTIVES: Partial atrioventricular septal defect (pAVSD) is routinely repaired with a low mortality. However, limited data are available on the long-term follow-up of these patients. The current study was designed to determine long-term survival and morbidity of a large cohort of patients operated on at a single institution. METHODS: From 1975 to 2012, 249 consecutive patients underwent pAVSD repair at the Royal Children's Hospital. The follow-up data were obtained from hospital records, correspondence with cardiologists and primary care physicians, patient surveys and the state death registry. RESULTS: The early mortality rate was 1.2% (3/249), while the long-term survival rate was 96% (95% CI: 93-98%) at 10 years and 94% (95% CI: 89-97%) at 30 years. Freedom from reoperation was 84% at 10 years and 75% at 30 years. The most common reoperations were left atrioventricular valve surgery (30/249, 12.1%), resection of left ventricular outflow tract obstruction (12/249, 4.8%) and closure of residual atrial septal defects (5/249, 2.0%). Implantation of a permanent pacemaker was required in 3.2% (8/249) of patients. Despite a substantial reoperation rate, only 43% of patients older than 18 years of age were seen by a cardiologist within the most recent 2 years of the
study period, compared with 80% of those younger than 18 years (P < 0.001). CONCLUSIONS: Repair of pAVSD is performed with a low mortality and excellent long-term survival. However, a substantial reoperation rate warrants close follow-up into adulthood.

Charles A and Khong YT.
Stillbirth and intrauterine growth restriction.

Chen BC, Balasubramaniam S, McGown IN, O’Neill JP, Chng GS, Keng WT, Ng LH and Duley JA.
Treatment of Lesch-Nyhan disease with S-adenosylmethionine: Experience with five young Malaysians, including a girl.
Brain Dev. 2014; 36(7): 593-600.
Background: Lesch-Nyhan disease (LND) is a rare X-linked recessive neurogenetic disorder caused by deficiency of the purine salvage enzyme hypoxanthine phosphoribosyltransferase (HPRT, EC 2.4.2.8) which is responsible for recycling purine bases into purine nucleotides. Affected individuals have hyperuricemia leading to gout and urolithiasis, accompanied by a characteristic severe neurobehavioural phenotype with compulsive self-mutilation, extrapyramidal motor disturbances and cognitive impairment. Aim: For its theoretical therapeutic potential to replenish the brain purine nucleotide pool, oral supplementation with S-adenosylmethionine (SAMe) was trialed in 5 Malaysian children with LND, comprising 4 related Malay children from 2 families, including an LND girl, and a Chinese Malaysian boy. Results: Dramatic reductions of self-injury and aggressive behaviour, as well as a milder reduction of dystonia, were observed in all 5 patients. Other LND neurological symptoms did not improve during SAMe therapy. Discussion: Molecular mechanisms proposed for LND neuropathology include GTP depletion in the brain leading to impaired dopamine synthesis, dysfunction of G-protein-mediated signal transduction, and defective developmental programming of dopamine neurons. The improvement of our LND patients on SAMe, particularly the hallmark self-injurious behaviour, echoed clinical progress reported with another purine nucleotide depletion disorder, Arts Syndrome, but contrasted lack of benefit with the purine disorder adenylosuccinate lyase deficiency. This first report of a trial of SAMe therapy in LND children showed remarkably encouraging results that warrant larger studies.

Connective tissue growth factor is expressed in bone marrow stromal cells and promotes interleukin-7-dependent B lymphopoiesis.
Hematopoiesis occurs in a complex bone marrow microenvironment in which bone marrow stromal cells provide critical support to the process through direct cell contact and indirectly through the secretion of cytokines and growth factors. We report that connective tissue growth factor (Ctgf, also known as Ccn2) is highly expressed in murine bone marrow stromal cells. In contrast, connective tissue growth factor is barely detectable in unfractionated adult bone marrow cells. While connective tissue growth factor has been implicated in hematopoietic malignancies, and is known to play critical roles in skeletogenesis and regulation of bone marrow stromal cells, its role in hematopoiesis has not been described. Here we demonstrate that the absence of connective tissue growth factor in mice results in impaired hematopoiesis. Using a chimeric fetal liver transplantation model, we show that absence of connective tissue growth factor has an impact on B-cell development, in particular from pro-B to more mature stages, which is linked to a requirement for connective tissue growth factor in bone marrow stromal cells. Using in vitro culture systems, we demonstrate that connective tissue growth factor potentiates B-cell proliferation and promotes pro-B to pre-B differentiation in the presence of interleukin-7. This study provides a better understanding of the functions of connective tissue growth factor within the bone marrow, showing the dual regulatory role of the growth factor in skeletogenesis and in stage-specific B lymphopoiesis.

Cole CH.
Siegfried: the one who does not know fear.

Cooper MN, de Klerk NH, Jones TW and Davis EA.
Clinical and demographic risk factors associated with mortality during early adulthood in a population-based cohort of childhood-onset Type 1 diabetes.
AIMS: To calculate standardized mortality ratios and to assess the association between paediatric clinical factors and higher risk of mortality during early adulthood in a population-based cohort of subjects with Type 1 diabetes. METHODS: Subjects with Type 1 diabetes were identified through the Western Australian Children's
Diabetes Database and clinical data for those who reached 18 years of age (n = 1309) were extracted. An age- and sex-matched (without diabetes) comparison cohort (n = 6451) was obtained from the birth registry. Mortality records were obtained from the death registry. Participants were followed up until 31 January 2012. Associations of clinical factors (from clinic visits before 18 years of age) with mortality were assessed using Cox proportional hazard models. RESULTS: The standardized mortality ratio for all-cause mortality was 1.7 (95% CI 0.7-3.3) for male and 10.1 (95% CI 5.2-17.7) for female subjects with Type 1 diabetes (median age at end of study 25.6 years). The adjusted hazard ratio was 1.5 (95% CI 1.1-2.1) for a 1% increase in mean paediatric HbA1c level, 3.8 (95% CI 0.9-15.3) for four episodes of severe hypoglycaemia relative to zero episodes, and 6.21 (95% CI 1.4-28.4) for a low-level socio-economic background relative to a high-level background. CONCLUSIONS: People with childhood-onset Type 1 diabetes have higher mortality rates in early adulthood. At particularly high risk are women, those with a history of poor HbA1c levels, those with recurrent severe hypoglycaemia during paediatric management, and those from a low socio-economic background. These groups may benefit from intensified management during transition from paediatric to adult care facilities.

Cooper MN, McNamara KA, de Klerk NH, Davis EA and Jones TW.
School performance in children with type 1 diabetes: a contemporary population-based study.
Pediatr Diabetes. 2014.
AIMS: Our aim was to examine the school performance of children with type 1 diabetes in comparison to their peers, exploring changes over time, and the impact of clinical factors on school performance. METHODS: The study included data on 666 children with type 1 diabetes from the Western Australia Children's Diabetes Database (WACDD), a population-based registry, and 3260 school and school year matched non-diabetic children. Records from the National Assessment Program - Literacy and Numeracy (NAPLAN) (2008-2011), which examines four educational outcome domains and is administered annually to all years 3, 5, 7, and 9 children in Australia, were sourced for both groups. Clinical data were obtained for the children with diabetes from the WACDD. RESULTS: No significant difference was observed between those with type 1 diabetes and their peers, across any of the tested domains and school years analysed. No decline over time was observed, and no decline following diagnosis was observed. Type 1 diabetes was associated with decreased school attendance, 3% fewer days attended per year. Poorer glycaemic control [higher haemoglobin A1c (HbA1c)] was associated with a lower test score [0.2-0.3 SD per 1% (10.9 mmol/mol) increase in HbA1c], and with poorer attendance [1.8% decrease per 1% (10.9 mmol/mol) increase in HbA1c]. No association was observed with history of severe hypoglycaemia, diabetic ketoacidosis or age of onset and school test scores. CONCLUSION: These results suggest that type 1 diabetes is not associated with a significant decrement in school performance, as assessed by NAPLAN. The association of poorer glycaemic control with poorer school performance serves as further evidence for clinicians to focus on improving glycaemic control.

Cox DW and Le Souef PN.
Rhinovirus and the developing lung.
Human rhinovirus (HRV) infections are now widely accepted as the commonest cause of acute respiratory illnesses (ARIs) in children. Advanced PCR techniques have enabled HRV infections to be identified as causative agents in most common ARIs in childhood including bronchiolitis, acute asthma, pneumonia and croup. However, the long-term implications of rhinovirus infections are less clear. The aim of this review is to examine the relationship between rhinovirus infections and disorders of the lower airways in childhood.

d’Udekem Y, Galati JC, Rolley GJ, Konstantinov IE, Weinstein RG, Grigg L, Ramsay JM, Wheaton GR, Hope S, Cheung MH and Brizard CP.
Low risk of pulmonary valve implantation after a policy of transatrial repair of tetralogy of Fallot delayed beyond the neonatal period: the Melbourne experience over 25 years.
OBJECTIVES: The study sought to evaluate the late outcomes of a policy of transatrial repair delayed beyond the neonatal period. BACKGROUND: Long-term outcomes of transatrial repair of tetralogy of Fallot are unknown. METHODS: The records of 675 consecutive patients undergoing a transatrial repair of tetralogy of Fallot between 1980 and 2005 were reviewed, their follow-up updated and survival confirmed from national death registries. One-third (220 of 675) had undergone previous palliation. Median age at repair was 2 years in the first 8 years, and 1 year from 1988 onward. A transannular incision was performed in 75% of cases and autologous pericardium was the material used to patch this incision in 92% of cases. RESULTS: There were 7 hospital deaths (1%). Eight patients died during follow-up (2 sudden unexpected and 6 noncardiac deaths). Mean follow-up was 11.7 +/- 6.3 years. Twenty-five years’ freedom from implantation of a valved conduit was 84.6% (95% CI: 77.8% to 89.5%). By multivariable analysis, prior palliation and younger age at repair were predictive of implantation of a valved conduit (hazard ratio: 2.4, 95% CI: 1.3 to 4.6, p = 0.008; hazard ratio: 0.70, 95% CI: 0.50 to 0.96, p =...
0.03, respectively). CONCLUSIONS: During long-term follow-up, transatrial repair of tetralogy of Fallot was associated with a minimal risk of sudden death and low rate of reintervention for right ventricular dilation and residual outflow tract obstruction.

Redefining expectations of long-term survival after the Fontan procedure: twenty-five years of follow-up from the entire population of Australia and New Zealand.

BACKGROUND: The life expectancy of patients undergoing a Fontan procedure is unknown. METHODS AND RESULTS: Follow-up of all 1006 survivors of the 1089 patients who underwent a Fontan procedure in Australia and New Zealand was obtained from a binational population-based registry including all pediatric and adult cardiac centers. There were 203 atrioventricular connections (AP; 1975-1995), 271 lateral tunnels (1988-2006), and 532 extracardiac conduits (1997-2010). The proportion with hypoplastic left heart syndrome increased from 1/173 (1%) before 1990 to 80/500 (16%) after 2000. Survival at 10 years was 89% (84%-93%) for AP and 97% (95% confidence interval [CI], 94%-99%) for lateral tunnels and extracardiac conduits. The longest survival estimate was 76% (95% CI, 67%-82%) at 25 years for AP. AP independently predicted worse survival compared with extracardiac conduits (hazard ratio, 6.2; P<0.001; 95% CI, 2.4-16.0). Freedom from failure (death, transplantation, takedown, conversion to extracardiac conduits, New York Heart Association III/IV, or protein-losing enteropathy/plastic bronchitis) 20 years after Fontan was 70% (95% CI, 63%-76%). Hypoplastic left heart syndrome was the primary predictor of Fontan failure (hazard ratio, 3.8; P<0.001; 95% CI, 2.0-7.1). Ten-year freedom from failure was 79% (95% CI, 61%-89%) for hypoplastic left heart syndrome versus 92% (95% CI, 87%-95%) for other morphologies. CONCLUSIONS: The long-term survival of the Australia and New Zealand Fontan population is excellent. Patients with an AP Fontan experience survival of 76% at 25 years. Technical modifications have further improved survival. Patients with hypoplastic left heart syndrome are at higher risk of failure. Large, comprehensive registries such as this will further improve our understanding of late outcomes after the Fontan procedure.

Davey RJ, Paramalingam N, Retterath AJ, Lim EM, Davis EA, Jones TW and Fournier PA.
Antecedent hypoglycaemia does not diminish the glycaemia-increasing effect and glucoregulatory responses of a 10 s sprint in people with type 1 diabetes.

Davidoss N, Ha J, Banga R and Rajan G.
Delayed Presentation of a Congenital Cholesteatoma in a 64-year-old Man: Case Report and Review of the Literature.
Introduction Congenital cholesteatomas of the temporal bone are epidermoid cysts of embryologic origin that result in progressive desquamation and trapping of squamous epithelium behind an intact tympanic membrane. They are benign, slowly progressive lesions that can be found in various areas of the temporal bone. We report a case of a patient with a massive cholesteatoma first detected at the age of 64 years, causing significant destruction of the mastoid and petrous temporal bones, and adjacent occipital bone. Methods We reviewed the literature and a case report of a patient seen in our institution recently. The Medline database was used to search multiple terms including “congenital” and “cholesteatoma.” Results The patient's congenital cholesteatoma was detected incidentally on a computed tomography scan when the patient's only symptoms were unilateral conductive hearing loss with a family history of hearing loss. It was subsequently successfully operated on with minimal postoperative complications. Conclusions Congenital cholesteatomas of mastoid origin can often exist for many years in a subclinical state and develop into a massive size before causing symptoms. A high index of suspicion is necessary to detect congenital cholesteatomas in patients with unilateral conductive hearing loss who are otherwise asymptomatic and have a normal tympanic membrane.

de Dassel JL, Ralph AP and Carapetis JR.
Controlling acute rheumatic fever and rheumatic heart disease in developing countries: are we getting closer?
Curr Opin Pediatr. 2014.
PURPOSE OF REVIEW: To describe new developments (2013-2014) in acute rheumatic fever (ARF) and rheumatic heart disease (RHD) relevant to developing countries. RECENT FINDINGS: Improved opportunities for the primary prevention of ARF now exist, because of point-of-care antigen tests for Streptococcus pyogenes, and clinical decision rules which inform management of pharyngitis without requiring culture results. There is optimism that a vaccine, providing protection against many ARF-causing S. pyogenes strains, may be available in coming years. Collaborative approaches to RHD control, including World Heart Federation initiatives and the development of registers, offer promise for better control of this disease. New data on RHD-associated costs
provide persuasive arguments for better government-level investment in primary and secondary prevention. There is expanding knowledge of potential biomarkers and immunological profiles which characterize ARF/RHD, and genetic mutations conferring ARF/RHD risk, but as yet no new diagnostic testing strategy is ready for clinical application. SUMMARY: Reduction in the disease burden and national costs of ARF and RHD are major priorities. New initiatives in the primary and secondary prevention of ARF/RHD, novel developments in pathogenesis and biomarker research and steady progress in vaccine development, are all causes for optimism for improving control of ARF/RHD, which affect the poorest of the poor.

de Dassel JL, Ralph AP and Carapetis JR.
Controlling acute rheumatic fever and rheumatic heart disease in developing countries: are we getting closer? Current Opinion in Pediatrics. 9000; Publish Ahead of Print: 10.1097/MOP.0000000000000164.
Purpose of review: To describe new developments (2013-2014) in acute rheumatic fever (ARF) and rheumatic heart disease (RHD) relevant to developing countries. Recent findings: Improved opportunities for the primary prevention of ARF now exist, because of point-of-care antigen tests for Streptococcus pyogenes, and clinical decision rules which inform management of pharyngitis without requiring culture results. There is optimism that a vaccine, providing protection against many ARF-causing S. pyogenes strains, may be available in coming years. Collaborative approaches to RHD control, including World Heart Federation initiatives and the development of registers, offer promise for better control of this disease. New data on RHD-associated costs provide persuasive arguments for better government-level investment in primary and secondary prevention. There is expanding knowledge of potential biomarkers and immunological profiles which characterize ARF/RHD, and genetic mutations conferring ARF/RHD risk, but as yet no new diagnostic testing strategy is ready for clinical application. Summary: Reduction in the disease burden and national costs of ARF and RHD are major priorities. New initiatives in the primary and secondary prevention of ARF/RHD, novel developments in pathogenesis and biomarker research and steady progress in vaccine development, are all causes for optimism for improving control of ARF/RHD, which affect the poorest of the poor. (C) 2014 Wolters Kluwer Health | Lippincott Williams & Wilkins

Germ-line RB-1 mutations predispose to pineoblastoma (PinB), but other predisposing genetic factors are not well established. We recently identified a germ-line DICER1 mutation in a child with a PinB. This was accompanied by loss of heterozygosity (LOH) of the wild-type allele within the tumour. We set out to establish the prevalence of DICER1 mutations in an opportunistically ascertained series of PinBs. Twenty-one PinB cases were studied: Eighteen cases had not undergone previous testing for DICER1 mutations; three patients were known carriers of germ-line DICER1 mutations. The eighteen PinBs were sequenced by Sanger and/or Fluidigm-based next-generation sequencing to identify DICER1 mutations in blood gDNA and/or tumour gDNA. Testing for somatic DICER1 mutations was also conducted on one case with a known germ-line DICER1 mutation. From the eighteen PinBs, we identified four deleterious DICER1 mutations, three of which were germ line in origin, and one for which a germ line versus somatic origin could not be determined; in all four, the second allele was also inactivated leading to complete loss of DICER1 protein. No somatic DICER1 RNase IIIb mutations were identified. One PinB arising in a germ-line DICER1 mutation carrier was found to have LOH. This study suggests that germ-line DICER1 mutations make a clinically significant contribution to PinB, establishing DICER1 as an important susceptibility gene for PinB and demonstrates PinB to be a manifestation of a germ-line DICER1 mutation. The means by which the second allele is inactivated may differ from other DICER1-related tumours.

Deshpande G, Simmer K, Deshmukh M, Mori TA, Croft KD and Kristensen J.
Fish Oil (SMOFlipid) and Olive Oil Lipid (Clinoleic) in Very Preterm Neonates. Journal of pediatric gastroenterology and nutrition. 2014; 58(2): 177-182.

Dewar R, Love S and Johnston LM.

Ditcham W, Murdzoska J, Zhang G, Roller C, von Hollen D, Nikander K and Devadason SG.
Lung deposition of 99mTc-radiolabeled albuterol delivered through a pressurized metered dose inhaler and spacer with facemask or mouthpiece in children with asthma. Journal of aerosol medicine and pulmonary drug delivery. 2014; 27(S1): S-63-S-75.
Background: Research on the use of a pressurized metered dose inhaler (pMDI) with spacer (pMDI/spacer) in children has indicated oral inhalation via the spacer mouthpiece is more efficient than the combination of oral and nasal inhalation that occurs when a pMDI/spacer is used with a facemask. Changes in pMDI formulations and developments in spacer and facemask designs have highlighted the need for new comparative studies of spacer use, particularly focusing on the age at which children can be taught to transition from use of a pMDI/spacer with facemask to use of the spacer mouthpiece.

Methods: Twelve children aged 3–5 years (7 males) with stable asthma were recruited. Of these, 10 children (6 males) completed both arms of the study. A transmission scan of each compliant subject was taken using a 37 MBq 99mTc flood source. Actuations (2–3) of a 99mTc-radiolabeled albuterol pMDI were administered through an antistatic spacer (OptiChamber Diamond) via either a facemask (medium LiteTouch facemask), or the spacer mouthpiece. The subject's inhalation pattern was simultaneously recorded using a pMDI Datalogger, and narrative data relating to tolerance and compliance were documented. Anterior and posterior planar scintigraphic scans were taken immediately after aerosol administration.

Results: Mean (SD) lung deposition (% total dose) was 18.1 (9.1)% with the facemask and 22.5 (7.9)% with the spacer mouthpiece (p>0.05). Peripheral lung deposition (expressed as peripheral:central (P:C) ratio) was higher in 7 out of 10 children with the facemask compared with the spacer mouthpiece: 1.3 (0.26) vs. 1.2 (0.35); (p=0.11). Head and neck deposition was higher with use of the facemask compared with the spacer mouthpiece: 19.7 (10.6)% vs. 10.8 (5.3)% (p=0.011).

Conclusions: Lung deposition achieved using the spacer with facemask was higher than previously reported, with a difference of only 4.4% of total dose measured compared to the deposition with mouthpiece. This may be due to a combination of factors including pMDI formulation, and use of an antistatic spacer with a flexible, well-fitting facemask.


Rett syndrome is one of many severe neurodevelopmental disorders with feeding difficulties. In this study, associations between feeding difficulties, age, MECP2 genotype, and utilization of gastrostomy were investigated. Weight change and family satisfaction following gastrostomy were explored. Data from the longitudinal Australian Rett Syndrome Database whose parents provided data in the 2011 family questionnaire (n=229) were interrogated. We used logistic regression to model relationships between feeding difficulties, age group, and genotype. Content analysis was used to analyze data on satisfaction following gastrostomy. In those who had never had gastrostomy and who fed orally (n=166/229), parents of girls<7 years were more concerned about food intake compared with their adult peers (odds ratio [OR] 4.26; 95% confidence interval [CI] 1.29, 14.10). Those with a p.Arg168 mutation were often perceived as eating poorly with nearly a 6-fold increased odds of choking compared to the p.Arg133Cys mutation (OR 5.88; 95% CI 1.27, 27.24). Couhing, choking, or gagging during meals was associated with increased likelihood of later gastrostomy. Sixty-six females (28.8%) had a gastrostomy, and in those, large MECP2 deletions and p.Arg168 mutations were common. Weight-for-age z-scores increased by 0.86 (95% CI 0.41, 1.31) approximately 2 years after surgery. Families were satisfied with gastrostomy and felt less anxious about the care of their child. Mutation type provided some explanation for feeding difficulties. Gastrostomy assisted the management of feeding difficulties and poor weight gain, and was acceptable to families. Our findings are likely applicable to the broader community of children with severe disability.

Children undergoing anaesthesia are prone to hypothermia. Perioperative monitoring of patient temperature is, therefore, standard practice. Postoperative temperature is regarded as a key anaesthetic performance indicator in Australian hospitals. Many different methods and sites of temperature measurement are used perioperatively. It is unclear to what degree these methods might be interchangeable. The aim of this study was to determine the relationships between temperatures measured at different sites in anaesthetised children. Two hundred children, 0 to 17 years, undergoing general anaesthesia for elective non-cardiac surgery, were prospectively recruited. Temperature measurements were taken in the operating theatre concurrently at the nasopharynx, tympanic membranes, temporal artery, axilla and skin (chest). Patient age and weight were documented. Temperatures varied according to site of measurement. The mean difference from nasopharyngeal temperature to temperatures at left and right tympanic, temporal and axillary sites were +0.24 degrees C, +0.24 degrees C, +0.35 degrees C, -0.38 degrees C and -1.70 degrees C, respectively. Levels of agreement to nasopharyngeal temperature were similar at tympanic, temporal and axillary sites. Tympanic and temporal temperatures were superior to axillary temperatures for detection of mild hypothermia (<36 degrees C). Skin temperature showed a large variation from nasopharyngeal measurements. Our findings indicate that measured temperatures vary between sites. Understanding these variations is important for interpreting temperature readings.


BACKGROUND: To date, no genome-wide association study (GWAS) has considered the combined phenotype of asthma with hay fever. Previous analyses of family data from the Tasmanian Longitudinal Health Study provide evidence that this phenotype has a stronger genetic cause than asthma without hay fever. OBJECTIVE: We sought to perform a GWAS of asthma with hay fever to identify variants associated with having both diseases. METHODS: We performed a meta-analysis of GWASs comparing persons with both physician-diagnosed asthma and hay fever (n = 6,685) with persons with neither disease (n = 14,091). RESULTS: At genome-wide significance, we identified 11 independent variants associated with the risk of having asthma with hay fever, including 2 associations reaching this level of significance with allergic disease for the first time: ZBTB10 (rs7009110; odds ratio [OR], 1.14; \( P = 4 \times 10^{-9} \)) and CLEC16A (rs62026376; OR, 1.17; \( P = 1 \times 10^{-8} \)). The rs62026376:C allele associated with increased asthma with hay fever risk has been found to be associated also with decreased expression of the nearby DEXI gene in monocytes. The 11 variants were associated with the risk of asthma and hay fever separately, but the estimated associations with the individual phenotypes were weaker than with the combined asthma with hay fever phenotype. A variant near LRRC32 was a stronger risk factor for hay fever than for asthma, whereas the reverse was observed for variants in/near GSDMA and TSLP. Single nucleotide polymorphisms with suggestive evidence for association with asthma with hay fever risk included rs41295115 near IL2RA (OR, 1.28; \( P = 5 \times 10^{-7} \)) and rs76043829 in TNS1 (OR, 1.23; \( P = 2 \times 10^{-6} \)). CONCLUSION: By focusing on the combined phenotype of asthma with hay fever, variants associated with the risk of allergic disease can be identified with greater efficiency.

Minor burns represent the majority of all burn patients in developed countries, yet little information regarding their outcomes is available in the literature. Minor burns at Royal Perth Hospital are provided routine outpatient clinic follow-up at 1 month postinjury resulting in increased ambulatory care demand and inefficiency due to high failure to attend rates. The authors hypothesized that improving patient education and using a posted quality-of-life survey in place of a 1-month outpatient clinic follow-up visit for minor burn patients would improve efficiency without compromising outcome compared to current standard practice. A sample of conservatively managed minor burn outpatients who healed within 14 days were administered a burn care education manual and discharged. Participants were assessed using postal Burn-Specific Health Scale-Brief and satisfaction surveys at 1 month postburn. Their responses were compared to those of patients who had received standard care. The intervention group had a higher, but not statistically significant, median BSHS-B score (156) than the comparison group (153) (P = .05). The intervention group also reported high levels of satisfaction with service. The new model of care is an appropriate strategy for management of minor burn. Its benefit over current hospital-based follow-up is that it saves one clinic appointment, improves efficiency related to nonattendance, and reduces patient burden.


Furlong E (2014). Reduced Macrophages IL-12 Production After Stimulation By BCG/INF-Gamma Suggestive Of Impaired INF-Gamma Pathway Signalling In a Child With Disseminated Atypical Mycobacterial Infection and History Of Chemotherapy For Langerhans Cell Histiocytosis. 2014 AAAAI Annual Meeting, Aaaai.


Gangell CL, Shackleton C, Poreddy S, Kappers J, Gaydon JE, Sloots TP, Stick SM, Ranganathan SC and Sly PD. Feasibility of parental collected nasal swabs for virus detection in young children with cystic fibrosis. Journal of Cystic Fibrosis. 2014; 13(6): 661-666. Abstract Background The detrimental role of viruses has been well described in CF, although the pattern of virus infections has not been investigated in a longitudinal study. The primary aim was to determine the feasibility of fortnightly parent collected swabs in young children with CF. Methods Children under three years with CF were recruited. Nasal swabs were collected by parents every fortnight and during periods of symptoms over 12 months. Nasal swabs were posted and virus detected using real-time PCR. Results Only 27% of the patients completed the study to 10 months, although 98% of the swabs returned were adequate for analysis. Mould was observed growing on 23% of the returned swabs. There was no evidence to demonstrate relationships with symptoms and viruses, prolonged symptoms, prolonged shedding or patterns of virus infections. Conclusions This study highlights the need to further investigate the role of viruses in children with CF using a robust method of frequent collection in children for a longitudinal study, with appropriate storage and shipping techniques to avoid mould growth or other potential contaminants.

Gardiner J, Wagh D, McMichael J, Hakeem M and Rao S.
Outcomes of hypoxic ischaemic encephalopathy treated with therapeutic hypothermia using cool gel packs - experience from Western Australia.
Therapeutic hypothermia is the standard clinical practice for neonates with moderate to severe hypoxic ischaemic encephalopathy (HIE). AIM: To describe the two year neurodevelopmental outcomes of neonates who were routinely cooled using cool gel packs for HIE in Western Australia. METHODS: Retrospective study. Cases were identified from the neonatal databases. Information was collected from chart review. RESULTS: 65 infants received therapeutic hypothermia, of which 13 had mild, 35 moderate and 17 had severe HIE. There were no serious adverse effects attributable to cooling. All 13 infants with mild HIE survived, of whom developmental outcomes were available on nine; none had severe disability. Among 52 infants with moderate to severe HIE, there were nine deaths (17%) and developmental outcomes were available on 39; the incidence of severe disability was 23%. The risk of death or severe disability was 40% in infants with moderate to severe HIE. Physical growth was adequate at two years of age. CONCLUSIONS: Neonates undergoing therapeutic hypothermia with cool gel packs had both good survival rates and long term neurodevelopmental outcomes and met international benchmarks.


Sickle cell disease can present with neurological manifestations. One such presentation is with posterior reversible leukoencephalopathy also known as reversible posterior leukoencephalopathy. The condition is classically described as reversible over time; it commonly presents with oedematous changes involving the white matter of the occipital and parietal regions. Only a few patients with the association between sickle cell disease and posterior reversible leukoencephalopathy have been described in the adult literature. We present two patients from our institutions to emphasise the association between the two conditions and summarise the published cases in the literature.

Georgiades M, Elliott C, Wilton J, Blair E, Blackmore M and Garbellini S.

Gibson N, Johnston K, Bear N, Stick S, Logie K and Hall GL.
OBJECTIVE: To investigate whether ventilatory factors limit exercise in overweight and obese children during a 6-min step test and to compare ventilatory responses during this test with those of healthy weight children. DESIGN: Cross-sectional, prospective comparative study. SUBJECTS: Twenty-six overweight/obese subjects and 25 healthy weight subjects with no known respiratory illness. Measurements: Various fatness and fat distribution parameters (using air displacement plethysmography and anthropometry), pulmonary function tests, breath-by-breath gas analysis during exercise, perceived exertion. RESULTS: Young people who are overweight or obese are more likely to experience expFL during submaximal exercise compared with their healthy weight peers [OR 7.2 (1.4, 37.3), P=0.019]. Subjects who had lower lung volumes at rest were even more likely to experience exercise-induced expFLs [OR 8.35 (1.4-49.3)]. Both groups displayed similar breathing strategies during submaximal exercise. CONCLUSION: Young people who are overweight/obese are more likely to display expFL during submaximal exercise compared with children of healthy weight. Use of compensatory breathing strategies appeared to enable overweight children to avoid the experience of breathlessness at this intensity of exercise.

Gilani SZ, Rooney K, Shafait F, Walters M and Mian A.
Gender score is the cognitive judgement of the degree of masculinity or femininity of a face which is considered to be a continuum. Gender scores have long been used in psychological studies to understand the complex psychosocial relationships between people. Perceptual scores for gender and attractiveness have been employed for quality assessment and planning of cosmetic facial surgery. Various neurological disorders have been linked to the facial structure in general and the facial gender perception in particular. While, subjective
Gender scoring by human raters has been a tool of choice for psychological studies for many years, the process is both time and resource consuming. In this study, we investigate the geometric features used by the human cognitive system in perceiving the degree of masculinity/femininity of a 3D face. We then propose a mathematical model that can mimic the human gender perception. For our experiments, we obtained 3D face scans of 64 subjects using the 3dMDFace scanner. The textureless 3D face scans of the subjects were then observed in different poses and assigned a gender score by 75 raters of a similar background. Our results suggest that the human cognitive system employs a combination of Euclidean and geodesic distances between biologically significant landmarks of the face for gender scoring. We propose a mathematical model that is able to automatically assign an objective gender score to a 3D face with a correlation of up to 0.895 with the human subjective scores.

Gill FJ, Leslie GD, Grech C, Boldy D and Latour JM.
Development of Australian clinical practice outcome standards for graduates of critical care nurse education.
AIMS AND OBJECTIVES: To develop critical care nurse education practice standards. BACKGROUND: Critical care specialist education for registered nurses in Australia is provided at graduate level. Considerable variation exists across courses with no framework to guide practice outcomes or evidence supporting the level of qualification. DESIGN: An eDelphi technique involved the iterative process of a national expert panel responding to three survey rounds. METHODS: For the first round, 84 statements, organised within six domains, were developed from earlier phases of the study that included a literature review, analysis of critical care courses and input from health consumers. The panel, which represented the perspectives of four stakeholder groups, responded to two rating scales: level of importance and level of practice. RESULTS: Of 105 experts who agreed to participate, 92 (88%) completed survey round I; 85 (92%) round II; and 73 (86%) round III. Of the 98 statements, 75 were rated as having a high level of importance - median 7 (IQR 6-7); 14 were rated as having a moderate level of importance - median 6 (IQR 5-7); and nine were rated as having a low level of importance - median 4 (IQR 4-6) (IQR 4-6). The majority of the panel rated graduate level of practice as 'demonstrates independently' or 'teaches or supervises others' for 80 statements. For 18 statements, there was no category selected by 50% or more of the panel. The process resulted in the development of 98 practice standards, categorised into three levels, indicating a practice outcome level by the practitioner who can independently provide nursing care for a variety of critically ill patients in most contexts, using a patient- and family-focused approach. CONCLUSION/RELEVANCE TO CLINICAL PRACTICE: The graduate practice outcomes provide a critical care qualification definition for nursing workforce standards and can be used by course providers to achieve consistent practice outcomes.

Gill FJ, Pascoe E, Monterosso L, Young J, Burr C, Tanner A and Shields L.
Parent and staff perceptions of family-centered care in two Australian children's hospitals.

Medulloblastoma Down Under 2013: a report from the third annual meeting of the International Medulloblastoma Working Group.
Medulloblastoma is curable in approximately 70% of patients. Over the past decade, progress in improving survival using conventional therapies has stalled, resulting in reduced quality of life due to treatment-related side effects, which are a major concern in survivors. The vast amount of genomic and molecular data generated over the last 5-10 years encourages optimism that improved risk stratification and new molecular targets will improve outcomes. It is now clear that medulloblastoma is not a single-disease entity, but instead consists of at least four distinct molecular subgroups: WNT/Wingless, Sonic Hedgehog, Group 3, and Group 4. The Medulloblastoma Down Under 2013 meeting, which convened at Bunker Bay, Australia, brought together 50 leading clinicians and scientists. The 2-day agenda included focused sessions on pathology and molecular stratification, genomics and mouse models, high-throughput drug screening, and clinical trial design. The meeting established a global action plan to translate novel biologic insights and drug targeting into treatment regimens to improve outcomes. A consensus was reached in several key areas, with the most important being that a novel classification scheme for medulloblastoma based on the four molecular subgroups, as well as histopathologic features, should be presented for consideration in the upcoming fifth edition of the World Health Organization's classification of tumours of the central nervous system. Three other notable areas of agreement...
were as follows: (1) to establish a central repository of annotated mouse models that are readily accessible and freely available to the international research community; (2) to institute common eligibility criteria between the Children's Oncology Group and the International Society of Paediatric Oncology Europe and initiate joint or parallel clinical trials; (3) to share preliminary high-throughput screening data across discovery labs to hasten the development of novel therapeutics. Medulloblastoma Down Under 2013 was an effective forum for meaningful discussion, which resulted in enhancing international collaborative clinical and translational research of this rare disease. This template could be applied to other fields to devise global action plans addressing all aspects of a disease, from improved disease classification, treatment stratification, and drug targeting to superior treatment regimens to be assessed in cooperative international clinical trials.

Granich J, Hunt A, Ravine D, Wray J and Whitehouse AJ.

Ha J, Yu YC and Lannigan F.
INTRODUCTION: Lymphangioma is a rare benign cyst caused by congenital malformation of the lymphatic systems that often occurs in the cervicofacial region. There is no consensus on its management: Observation, aspiration, injection, cryotherapy, electrocautery, radiation, laser, ligation and excision. METHODS: We performed a literature search with the keywords "cystic hygroma", "lymphangioma", "management", "OK 432" and "picibanil" from Medline, Embase and PubMed databases. RESULTS: We present a review of the history, signs and symptoms, diagnosis, histology, classification and management options of cystic hygroma. CONCLUSION: There is no consensus on the treatment options. It should be individualised depending on the size of the lesion, anatomic localisation and complications.

Hakanson C, Douglas C and Robertson J.

Hansford JR, Phillips M, Cole C, Francis J, Blyth CC and Gottardo NG.
Bacillus cereus can cause serious infections in immunosuppressed patients. This population may be susceptible to B. cereus pneumonia, bacteremia, cellulitis, and rarely cerebral abscess. Here we report an 8-year-old boy undergoing induction therapy for acute lymphoblastic leukemia who developed multifocal B. cereus cerebral abscesses, highlighting the propensity for B. cereus to develop cerebral abscesses. A review of the literature over the past 25 years identified another 11 cases (3 children and 8 adults) of B. cereus cerebral abscess in patients undergoing cancer therapy. B. cereus cerebral abscesses were associated with a high mortality rate (42%) and significant morbidity. Notably, B. cereus bacteremia with concomitant cerebral abscess was associated with induction chemotherapy for acute leukemia in both children and adults (10 of 12 case reports). Our case report and review of the literature highlights the propensity for B. cereus to develop cerebral abscess(es). Therefore, early consideration for neuroimaging should be given for any neutropenic cancer patient identified with B. cereus bacteremia, in particular those with acute leukemia during induction therapy.

Harris EL, Minutillo C, Hart S, Warner TM, Ravikumara M, Nathan EA and Dickinson JE.
PURPOSE: To determine the progress, physical and metabolic outcomes of gastroschisis survivors. METHODS: Fifty children born with gastroschisis were assessed with a health questionnaire, physical assessment, bone density and nutritional blood parameters at a median age of 9 years (range 5-17). RESULTS: After initial abdominal closure, 27/50 (54%) required additional surgical interventions. Ten (20%) children had complex gastroschisis (CG). Abdominal pain was common: weekly in 41%; and requiring hospitalization in 30%. The weight, length and head circumference z-scores improved by a median 0.88 (p=0.001), 0.56 (p=0.006) and 0.74 (p=0.018) of a standard deviation (SD) respectively from birth; 24% were overweight or obese at follow up. However, those with CG had significantly lower median weight z-scores (-0.43 v 0.49, p=0.004) and body mass index (BMI) (-0.48 v 0.42, p=0.001) at follow up compared to children with simple gastroschisis. Cholesterol levels were elevated in 24% of children. Bone mineral density was reassuring. There were 15 instances of low blood vitamin and mineral levels. CONCLUSIONS: Although gastroschisis survival levels are
high, many children have significant ongoing morbidity. Children with simple gastroschisis showed significant 
catch up growth and a quarter had become overweight.

Hart J, Putsathit P, Knight DR, Sammels L, Riley TV and Keil A.
Clostridium difficile infection diagnosis in a paediatric population: comparison of methodologies.
The increasing incidence of Clostridium difficile infection (CDI) in paediatric hospitalised populations, combined 
with the emergence of hypervirulent strains, community-acquired CDI and the need for prompt treatment and 
infection control, makes the rapid, accurate diagnosis of CDI crucial. We validated commonly used C. difficile 
diagnostic tests in a paediatric hospital population. From October 2011 to January 2012, 150 consecutive stools 
were collected from 75 patients at a tertiary paediatric hospital in Perth, Western Australia. Stools were tested 
using: C. Diff Quik Chek Complete, Illumigene C. difficile, GeneOhm Cdiff, cycloserine cefoxitin fructose agar 
(CCFA) culture, and cell culture cytotoxin neutralisation assay (CCNA). The reference standard was growth on 
CCFA or Cdiff Chromagar and PCR on isolates to detect tcdA, tcdB, cdtA, and cdtB. Isolates were PCR 
ribotyped. The prevalence of CDI was high (43 % of patients). Quik Chek Complete glutamate dehydrogenase 
(GDH) demonstrated a low negative predictive value (NPV) (93 %). Both CCNA and Quik Chek Complete toxin 
A/B had poor sensitivity (33 % and 29 % respectively). Molecular methods both had 89 % sensitivity. Algorithms 
using GDH + Illumigene or GeneOhm reduced the sensitivity to 85 % and 83 % respectively. Ribotype 
UK014/20 predominated. GDH NPV and GeneOhm and Illumigene sensitivities were reduced compared with 
adult studies. Quik Chek Complete and CCNA cannot reliably detect toxigenic CDI. A GDH first algorithm 
showed reduced sensitivity. In a high prevalence paediatric population, molecular methods alone are 
recommended over the use of GDH algorithm or culture and CCNA, as they demonstrate the best test 
performance characteristics.

Hasselblatt M, Nagel I, Oyen F, Bartelheim K, Russell RB, Schüller U, Junckerstorff R, Rosenblum M, 
Alassiri AH and Rossi S.
SMARCA4-mutated atypical teratoid/rhabdoid tumors are associated with inherited germline alterations and 
poor prognosis.

Hawkrigg S, Johnson A, Flynn J, Thom G and Wright H.
Acute haemorrhagic oedema of infancy in a 5-week-old boy referred to the Child Protection Unit.
We describe the case of a 5-week-old infant boy presenting with purpura and oedema to both hands and torso. 
He was otherwise well, with no antecedent history of illness or trauma. Laboratory investigations were within 
normal limits. A review by the Child Protection Unit was organised during his admission for consideration of 
inflicted trauma as a cause of the lesions; this was felt most unlikely. A clinical diagnosis, following a 
dermatology consultation, of acute haemorrhagic oedema of infancy (AHO) was made.

Hawkrigg S and Payne DN.
Prolonged school non-attendance in adolescence: a practical approach.
Prolonged school non-attendance in adolescence poses a significant public health concern. Adverse outcomes 
for adolescents who have missed out on the social and academic benefits of high school include mental health 
disorders and economic, social and relationship difficulties that may persist into adulthood. Healthcare 
professionals are often consulted in cases of prolonged school non-attendance. Diagnosis and management of 
specific physical and mental health problems must be the health professional's initial priority, with the 
subsequent development of a management plan to assist with school reintegration. Using a specific framework, 
an understanding of the factors contributing to a young person's school non-attendance can be developed. 
Intervention leading to a successful return to school has the potential to lower the risk of associated long-term 
adverse health outcomes.

Haynes A, Cooper MN, Bower C, Jones TW and Davis EA.
Maternal smoking during pregnancy and the risk of childhood type 1 diabetes in Western Australia.
AIMS/HYPOTHESIS: The aim of this study was to investigate the association between maternal smoking during 
pregnancy and type 1 diabetes in the offspring, using complete population data sources available in Western 
Australia. METHODS: A prospective cohort study was undertaken with cases defined as children born in 
Western Australia between 1998 and 2008 who were diagnosed with type 1 diabetes at <15 years of age up to 
31 December 2010. Eligible cases were identified from the prospective, population-based Western Australian 
Children's Diabetes Database. Record linkage was performed to identify perinatal records of cases from the
Western Australian Midwives’ Notification System, which contains data on >99% of all births in Western Australia. Cox regression was used to analyse the data and adjust for recognised risk factors such as birthweight, gestational age, maternal age and socioeconomic status. RESULTS: The unadjusted HR for babies born to mothers who smoked during pregnancy being diagnosed with childhood type 1 diabetes was 0.70 (95% CI: 0.50, 0.97). After adjustment, the confidence interval widened but the point estimate remained relatively unchanged at 0.76 (95% CI: 0.54, 1.08). CONCLUSIONS/INTERPRETATION: Analyses of data from this population-based study indicate that maternal smoking during pregnancy may be associated with a reduced risk of childhood type 1 diabetes. Further investigation in larger populations with more detailed smoking data could lead to novel hypotheses regarding mechanisms that influence the immunopathogenesis of type 1 diabetes in early life.


Hernandez R. Seeking treasure beneath the ruins: Stories of narrative practice with children and their loved ones. The International Journal of Narrative Therapy and Community Work 2014; 4:24-34

Children with multiple challenges such as emotional, behavioural, mental, social, developmental, and educational difficulties, often experience constant hardship in their daily lives. These problems also impact their parents or carers. This paper shares stories of narrative practice with children and their loved ones. These stories include the use of externalising conversations, photographs, and the audio recording of outsider-witness responses.


Medulloblastoma is the most common form of malignant paediatric brain tumour and is the leading cause of childhood cancer related mortality. The four molecular subgroups of medulloblastoma that have been identified - WNT, SHH, Group 3 and Group 4 - have molecular and topographical characteristics suggestive of different cells of origin. Definitive identification of the cell(s) of origin of the medulloblastoma subgroups, particularly the poorer prognosis Group 3 and Group 4 medulloblastoma, is critical to understand the pathogenesis of the disease, and ultimately for the development of more effective treatment options. To address this issue, the gene expression profiles of normal human neural tissues and cell types representing a broad neuro-developmental continuum, were compared to those of two independent cohorts of primary human medulloblastoma specimens. Clustering, co-expression network, and gene expression analyses revealed that WNT and SHH medulloblastoma may be derived from distinct neural stem cell populations during early embryonic development, while the transcriptional profiles of Group 3 and Group 4 medulloblastoma resemble cerebellar granule neuron precursors at weeks 10-15 and 20-30 of embryogenesis, respectively. Our data indicate that Group 3 medulloblastoma may arise through abnormal neuronal differentiation, whereas deregulation of synaptic pruning-associated apoptosis may be driving Group 4 tumorigenesis. Overall, these data provide significant new insight into the spatio-temporal relationships and molecular pathogenesis of the human medulloblastoma subgroups, and provide an important framework for the development of more refined model systems, and ultimately improved therapeutic strategies.


AIM: (i) To compare the Centers for Disease Control and Prevention (CDC) reference and World Health Organization (WHO) standard/reference for height, particularly with respect to short stature and eligibility for growth hormone (GH) treatment by applying them to contemporary Australian children; (ii) To examine the implications for identifying short stature and eligibility for GH treatment. METHODS: Children from the longitudinal Raine Study were serially measured for height from 1991 to 2005 (2-15-year-old girls (660) and boys (702) from Western Australia). In the cross-sectional Australian National Children's Nutrition and Physical Activity survey (2-16-year-old boys (2415) and girls (2379) from all states), height was measured in 2007. Heights were converted to standard deviation scores (SDSs) based on CDC and WHO. RESULTS: Means and standard deviations of height-SDS varied between CDC and WHO definitions and with age and gender within each definition. However, both identified similar frequencies of short stature (<1st centile for GH eligibility),
although these were very significantly less than the anticipated 1% (0.1-0.7%) of the Australian cohorts. Mean heights in the Australian cohorts were greater than both the WHO and CDC means. CONCLUSIONS: Neither CDC nor WHO height standardisations accurately reflect the contemporary Australian child population. Australian children are taller than the CDC or WHO height means, and significantly less than 1% of Australian children are defined as being short using either CDC or WHO. This study suggests there may be a case for an Australian-specific standard/reference for height.


INTRODUCTION: Immature animals exposed to anesthesia display apoptotic neurodegeneration and neurobehavioral deficits. The safety of anesthetic agents in children has been evaluated using a variety of neurodevelopmental outcome measures with varied results. METHODS: The authors used data from the Western Australian Pregnancy Cohort (Raine) Study to examine the association between exposure to anesthesia in children younger than 3 yr of age and three types of outcomes at age of 10 yr: neuropsychological testing, International Classification of Diseases, 9th Revision, Clinical Modification-coded clinical disorders, and academic achievement. The authors’ primary analysis was restricted to children with data for all outcomes and covaried from the total cohort of 2,868 children born from 1989 to 1992. The authors used a modified multivariable Poisson regression model to determine the adjusted association of anesthesia exposure with outcomes. RESULTS: Of 781 children studied, 112 had anesthesia exposure. The incidence of deficit ranged from 5.1 to 7.8% in neuropsychological tests, 14.6 to 29.5% in International Classification of Diseases, 9th Revision, Clinical Modification-coded outcomes, and 4.2 to 11.8% in academic achievement tests. Compared with unexposed peers, exposed children had an increased risk of deficit in neuropsychological language assessments (Clinical Evaluation of Language Fundamentals Total Score: adjusted risk ratio, 2.47; 95% CI, 1.41 to 4.33, Clinical Evaluation of Language Fundamentals Receptive Language Score: adjusted risk ratio, 2.23; 95% CI, 1.19 to 4.18, and Clinical Evaluation of Language Fundamentals Expressive Language Score: adjusted risk ratio, 2.00; 95% CI, 1.08 to 3.68) and International Classification of Diseases, 9th Revision, Clinical Modification-coded language and cognitive disorders (adjusted risk ratio, 1.57; 95% CI, 1.18 to 2.10), but not academic achievement scores. CONCLUSIONS: When assessing cognition in children with early exposure to anesthesia, the results may depend on the outcome measure used. Neuropsychological and International Classification of Diseases, 9th Revision, Clinical Modification-coded clinical outcomes showed an increased risk of deficit in exposed children compared with that in unexposed children, whereas academic achievement scores did not. This may explain some of the variation in the literature and underscores the importance of the outcome measures when interpreting studies of cognitive function.


INTRODUCTION: Epidemiologic studies examining the association between anesthetic exposure and neurodevelopmental outcomes have primarily focused on exposures occurring under 3 years of age. In this study, we assess outcomes associated with initial anesthetic exposure occurring between 3 and 10 years of age. METHODS: We used data from the Western Australian Pregnancy Cohort (Raine) Study to examine the risk of cognitive deficit at age 10 in children with initial anesthetic exposure between 3 and 5 years and between 5 and 10 years of age compared with children unexposed at those ages. The cohort included 2868 children born from 1989 to 1992 evaluated using a range of neuropsychological tests. A modified multivariable Poisson regression model was used to determine the adjusted association of initial anesthetic exposure in each age group with outcomes. RESULTS: Exposed and unexposed children were found to have similar neuropsychological test results except for the McCarron Assessment of Neuromuscular Development (MAND) motor function scores. Even after adjusting for demographic and comorbidity differences, children exposed to anesthesia had a higher risk of motor deficit after initial exposure between ages 3 and 5 years (adjusted risk ratio, 2.32; 95% confidence interval, 1.42-3.79) and between 5 and 10 years (adjusted risk ratio, 2.33; 95% confidence interval, 1.21-4.48) compared with unexposed children. CONCLUSIONS: Initial exposure to anesthesia after age 3 had no measurable effects on language or cognitive function. Decreased motor function was found in children initially exposed after age 3 even after accounting for comorbid illness and injury history. These results suggest that there may be distinct windows of vulnerability for different neurodevelopmental domains in children.
AIMS: Umbilical hernias are a common finding in the paediatric community, with a preponderance to affect Afro-Caribbean and premature children. The rate of incarceration varies greatly between populations. Therefore, it is valuable to obtain some Australian data on this topic. METHODS: We undertook a retrospective study of the records of all patients who underwent umbilical hernia repair over a 12-year period of between October 1999 and May 2012 at Princess Margaret Hospital. From this group, all patients that had an umbilical hernia repair for reason of acute complication were identified and analysed for age, ethnicity and co-morbidities. RESULTS: Between October 1999 and May 2012, 433 umbilical hernias were repaired at Princess Margaret Hospital, five of which were as the direct result of an acutely complicated umbilical hernia. The mean age of hernia repair was 5 years old, and the mean age of acute complication was 5 years old. Out of the patients with acutely complicated umbilical hernia, there were no Afro-Caribbean patients, and one was premature complicated by hyaline membrane disease and broncho-pulmonary dysplasia. CONCLUSIONS: Western Australia has an incidence of acutely complicated umbilical hernia requiring operative intervention of 1:3000 to 1:11 000. On an international scale, this is low, and studies with similar incidence do not advocate for immediate repair of all identified umbilical hernias. The authors believe repair should be guided by patient and guardian, but if there is an episode of incarceration, acute repair is advised.

Trends in Fontan surgery and risk factors for early adverse outcomes after Fontan surgery: The Australia and New Zealand Fontan Registry experience.
OBJECTIVES: This study examined changes in practice and analyzed risk factors for adverse early outcomes after Fontan surgery through use of a binational, population-based registry. METHODS: Demographic, preoperative, and perioperative data were collected from all participating institutions of the Australia and New Zealand Fontan Registry. Patient and operative characteristics were analyzed with multivariable logistic regression for impact on early mortality, early Fontan failure (death, takedown, or mechanical support), effusions (prolonging hospital stay >30 days or requiring surgical reintervention), and stay longer than 30 days. RESULTS: Overall mortality was 3.5% (37/1071) and declined throughout the study period, from 8% (1975-1990) to 4% (1991-2000) and 1% (2001-2010). There were no differences between the extracardiac and lateral tunnel modifications for any outcome. After 2006, the extracardiac conduit was performed exclusively, with 1.3% mortality. The proportion of patients with hypoplastic left heart syndrome rose to 17% in the current era, and this group had more effusions (odds ratio, 3.0; 95% confidence interval, 1.4-6.6) and stayed on average 2 days longer in the hospital. Hypoplastic left heart syndrome was also an independent risk factor for composite adverse early outcome (death, failure, prolonged effusions, or prolonged stay >30 days; odds ratio, 2.6; 95% confidence interval 1.4-4.8 respectively). CONCLUSIONS: The extracardiac conduit is now the exclusive Fontan modification performed in Australia and New Zealand. Even with a higher proportion of high-risk cases, perioperative outcomes are excellent in the modern era. Hypoplastic left heart syndrome confers a higher risk of prolonged pleural effusion and early composite adverse outcome.

The extracardiac conduit Fontan procedure in Australia and New Zealand: hypoplastic left heart syndrome predicts worse early and late outcomes.
OBJECTIVES: To identify factors associated with hospital and long-term outcomes in a binational cohort of extracardiac conduit (ECC) Fontan recipients. METHODS: All patients who underwent an ECC Fontan procedure from 1997 to 2010 in Australia and New Zealand were identified, and perioperative, follow-up, echocardiographic and reintervention data collected. Risk factors for early and late mortality, failure and adverse outcomes were analysed. RESULTS: A total of 570 patients were identified, and late follow-up was available in 529 patients. The mean follow-up was 6.7 years (standard deviation: 3.5) and completeness of the follow-up was 98%. There were seven hospital mortalities (1%) and 21 patients (4%) experienced early failure (death, Fontan takedown/revision or mechanical circulatory support). Prolonged length of stay occurred in 10% (57 patients), and prolonged effusions in 9% (51 patients). Overall survival at 14 years was 96% (95% confidence interval [CI]: 93-98%), and late survival for patients discharged with intact Fontan was 98% (95% CI: 94-99%). The rates of late failure (late death, transplantation, takedown, New York Heart Association class III/IV
or protein-losing enteropathy) and adverse events (late failure, reoperation, percutaneous intervention, pacemaker, thromboembolic event or supraventricular tachycardia) per 100 patient-years were 0.8 and 3.8, and their 14-year freedoms were 83% (95% CI: 70-91%) and 53% (95% CI: 41-64%), respectively. After adjustment for confounders, hypoplastic left heart syndrome (HLHS) was strongly associated with prolonged effusions (OR: 2.9, 95% CI: 1.4-5.9), late failure (hazard ratio [HR]: 2.8, 95% CI: 1.1-7.5) and adverse events (HR: 3.6, 95% CI: 1.3-7.5). CONCLUSIONS: The extracardiac Fontan procedure provides excellent survival into the second decade of life, but half of patients will suffer a late adverse event by 14 years. Patients with HLHS are at higher risk of late adverse events than other morphological groups, but their survival is still excellent.


OBJECTIVES: This study sought to examine nevirapine hypersensitivity (NVP HSR) phenotypes and their relationship with differing major histocompatibility complex (MHC) Class I and Class II alleles and the associated CD4 and CD8 T-cell NVP-specific responses and their durability over time. METHODS: A retrospective cohort study compared HIV-positive patients with NVP HSR, defined by fever and hepatitis and/or rash, with those tolerant of NVP for more than 3 months. Covariates included class I (HLA-A, B, C) and class II (HLA-DR) alleles. Cellular studies examined NVP-specific CD4 and CD8 T-cell responses by interferon-gamma (IFNgamma) ELISpot assay and intracellular cytokine staining (ICS). RESULTS: NVP HSR occurred in 19 out of 451 (4%) NVP-exposed individuals between March 1993 and December 2011. HLA associations were phenotype dependent with HLA-DRB1*01 : 01 associated with hepatitis (P = 0.02); HLA-B*35 : 01 and HLA-Cw4 associated with cutaneous NVP HSR (P = 0.001, P = 0.01), and HLA-Cw*08 was associated with NVP HSR with eosinophilia (P = 0.04) and multisystemic NVP HSR (P = 0.02). NVP-specific INFgamma responses waned significantly more than 3 months from the original reaction and were diminished or completely abrogated when either CD4 or CD8 T cells were depleted from the peripheral blood mononuclear cells culture. CONCLUSION: The association of specific class I and II allele pairings with specific phenotypes of NVP HSR, and cellular studies showing both CD4 and CD8 T-cell NVP-specific responses suggest that specific combinations of NVP reactive class I restricted CD8 and class II restricted CD4 T cells contribute to the immunopathogenesis of NVP HSR.


Introduction Pain is a subjective experience. In children with limited understanding and communication skills, reliable assessment of pain is challenging. Self-reporting of pain is the gold standard of pain measurement. For children who are unable to self-report their pain, assessments made by their parents are often used as a proxy measure. The validity of this approach has not been conclusively determined. Aim To investigate differences in the assessment of pediatric pain between children, parents, nurses, and independent observers in the acute postoperative setting. Method Three hundred and seven children (207 verbal, 100 nonverbal) undergoing elective day-case surgery were asked to participate in this quality of care audit. Pain scores given by verbal children, their parents, nurses, and independent observers were collected. A numerical rating scale or the Wong-Baker Faces Pain Scale was used. All participants were blinded from other scorers. Results For verbal children, scores reported by patients and their parents did not differ significantly. Median [inter-quartile range (IQR)] scores by children, parents, nurses, and independent observers were, respectively, 2.0 (0–4.0), 2.0 (1.0–4.0), 0.0 (0–2.0), and 1.0 (0–2.0). In nonverbal children, median (IQR) scores by parents, nurses, and
Delivering a Healthy WA

Independent observers were 1.0 (0–3.0), 0 (0–1.0), and 0 (0–2.0), respectively. The agreement between the different scorers was statistically significant. Conclusion Children's pain self-reports should be used wherever possible to guide management, but in their absence, parental pain scores can be reliably used as a surrogate measure. Nurses and independent observers produce lower pain scores than parents or children, which may result in inadequate treatment of pain.

How is paediatric chronic fatigue syndrome/myalgic encephalomyelitis diagnosed and managed by paediatricians? An Australian Paediatric Research Network Study.
Journal of paediatrics and child health. 2014.

Kotecha RS, Buckland A, Phillips MB, Cole CH and Gottardo NG.

Kotecha RS, Gottardo NG, Kees UR and Cole CH.
The evolution of clinical trials for infant acute lymphoblastic leukemia.
Acute lymphoblastic leukemia (ALL) in infants has a significantly inferior outcome in comparison with older children. Despite initial improvements in survival of infants with ALL since establishment of the first pediatric cooperative group ALL trials, the poor outcome has plateaued in recent years. Historically, infants were treated on risk-adapted childhood ALL protocols. These studies were pivotal in identifying the need for infant-specific protocols, delineating prognostic categories and the requirement for a more unified approach between study groups to overcome limitations in accrual because of low incidence. This subsequently led to the development of collaborative infant-specific studies. Landmark outcomes have included the elimination of cranial radiotherapy following the discovery of intrathecal and high-dose systemic therapy as a superior and effective treatment strategy for central nervous system disease prophylaxis, with improved neurodevelopmental outcome. Universal prospective identification of independent adverse prognostic factors, including presence of a mixed lineage leukemia rearrangement and young age, has established the basis for risk stratification within current trials. The infant-specific trials have defined limits to which conventional chemotherapeutic agents can be intensified to optimize the balance between treatment efficacy and toxicity. Despite variations in therapeutic intensity, there has been no recent improvement in survival due to the equilibrium between relapse and toxicity. Ultimately, to improve the outcome for infants with ALL, key areas still to be addressed include identification and adaptation of novel prognostic markers and innovative therapies, establishing the role of hematopoietic stem cell transplantation in first complete remission, treatment strategies for relapsed/refractory disease and monitoring and timely intervention of late effects in survivors. This would be best achieved through a single unified international trial.

Identification Of Epithelial Phospholipase A2 Receptor 1 (pla2r1) As A Target In Asthma.

Rapid increase in pertactin-deficient Bordetella pertussis isolates, Australia.

Larcombe AN, Phan JA, Kicic A, Perks KL, Mead-Hunter R and Mullins BJ.
Route of exposure alters inflammation and lung function responses to diesel exhaust.

Leung M, Ozanne R, Smith L and Martin A.

Lung Function Decline In School-Age Children With A Neonatal Diagnosis Of Bronchopulmonary Dysplasia.
Love S and Blair E. 
The right interventions for each child with cerebral palsy. 

A cost-effectiveness analysis of sensor-augmented insulin pump therapy and automated insulin suspension versus standard pump therapy for hypoglycemic unaware patients with type 1 diabetes. 
OBJECTIVE: To assess the cost-effectiveness of sensor-augmented insulin pump therapy with "Low Glucose Suspend" (LGS) functionality versus standard pump therapy with self-monitoring of blood glucose in patients with type 1 diabetes who have impaired awareness of hypoglycemia. METHODS: A clinical trial-based economic evaluation was performed in which the net costs and effectiveness of the two treatment modalities were calculated and expressed as an incremental cost-effectiveness ratio (ICER). The clinical outcome of interest for the evaluation was the rate of severe hypoglycemia in each arm of the LGS study. Quality-of-life utility scores were calculated using the three-level EuroQol five-dimensional questionnaire. Resource use costs were estimated using public sources. RESULTS: After 6 months, the use of sensor-augmented insulin pump therapy with LGS significantly reduced the incidence of severe hypoglycemia compared with standard pump therapy (incident rate difference 1.85 [0.17-3.53]; P = 0.037). Based on a primary randomized study, the ICER per severe hypoglycemic event avoided was $18,257 for all patients and $14,944 for those aged 12 years and older. Including all major medical resource costs (e.g., hospital admissions), the ICERs were $17,602 and $14,289, respectively. Over the 6-month period, the cost per quality-adjusted life-year gained was $40,803 for patients aged 12 years and older. CONCLUSIONS: Based on the Australian experience evaluating new interventions across a broad range of therapeutic areas, sensor-augmented insulin pump therapy with LGS may be considered a cost-effective alternative to standard pump therapy with self-monitoring of blood glucose in hypoglycemia unaware patients with type 1 diabetes. 

Ly TT, Maahs DM, Rewers A, Dunger D, Oduwole A and Jones TW. 
Assessment and management of hypoglycemia in children and adolescents with diabetes. 

Febrile seizures following measles and varicella vaccines in young children in Australia. 
Vaccine. 2014.

Febrile seizures following measles and varicella vaccines in young children in Australia. 
Vaccine. 2014. 
BACKGROUND: Febrile seizures (FS) are common in childhood with incidence peaking in the second year of life when measles and varicella-containing vaccines are administered. This study aimed to examine the vaccine-attributable risk of FS following separate administration of MMR and monovalent varicella vaccines (VV) prior to a planned change to MMRV as the second dose of measles-containing vaccine at 18 months of age. METHODS: All FS cases in children aged <5 years from 1st January 2012 to 30th April 2013 were identified from emergency department (ED) and inpatient databases at five Australian tertiary paediatric hospitals participating in PAEDS (Paediatric Active Enhanced Disease Surveillance). Immunization records were obtained from the Australian Childhood Immunization Register (ACIR). The relative incidence (RI) of FS following MMR dose 1 (MMR1) and VV in children aged 11-23 months was determined using the self-controlled case series (SCCS) method and used to calculate attributable risk. RESULTS: There were 2013 FS episodes in 1761 children. The peak age at FS was 18 months. The risk of FS was significantly increased 5-12 days post receipt of MMR1 at 12 months (RI=1.9 [95% CI: 1.3-2.9]), but not after VV at 18 months (RI=0.6 [95% CI: 0.3-1.2]. The estimated excess annual number of FS post MMR1 was 24 per 100,000 vaccinated children aged 11-23 months (95% CI=7-49 cases per 100,000) or 1 per 4167 doses. CONCLUSIONS: Our study detected the expected increased FS risk post MMR1 vaccine at 12 months, but monovalent varicella vaccine at age 18 months was not associated with increased risk of FS. This provides baseline data to assess the risk of FS post MMRV, introduced in Australia as the second dose of measles-containing vaccine at 18 months of age in July 2013. 

Mace AO, Mulheron S, Jones C and Cherian S. 
Educational, developmental and psychological outcomes of resettled refugee children in Western Australia: a review of School of Special Educational Needs: Medical and Mental Health input.
AIM: There are limited data regarding the educational backgrounds and associated psychological and developmental outcomes of refugee children resettling in Western Australia (WA). The WA paediatric Refugee Health Service (RHS) revised its first consult questionnaire (August 2011) to increase educational and psychosocial documentation, concurrent with engagement of a School of Special Educational Needs: Medical and Mental Health (SSEN: MMH) liaison teacher. This study aims to utilise these data to increase understanding of this cohort's educational, developmental and psychological needs and to describe SSEN: MMH's role within the RHS. METHODS: Retrospective audit and analyses were performed on all initial standardised questionnaires for school-aged refugee children (4-18 years) and SSEN: MMH referrals between August 2011 and December 2012. RESULTS: Demographic data from 332 refugees are described (mean age 9.58 +/- standard deviation 3.43 years). Detailed educational information was available for 205 children. Prior education was limited (median 2 years), 64.9% experienced likely schooling interruption and 55.8% received education in their primary language. Language development concerns were significantly associated with previous education in a second language (odds ratio (OR) 4.55, P < 0.05). Other severe developmental and schooling issues were uncommon at presentation, with few correlations to prior education. In contrast, several migration factors, including family separation and mandatory detention, were significantly associated with psychological comorbidities such as post-traumatic stress disorder (OR 5.60, P < 0.001 and OR 14.57, P < 0.001, respectively). SSEN: MMH reviewed 59 complex cases. Referral was significantly associated with multiple educational, developmental and psychological concerns. CONCLUSIONS: Refugee children have varied migration, trauma and educational backgrounds, impacting on health and psychological outcomes. In-depth multidisciplinary history including prior education and psychosocial issues is recommended. Partnering with education services appears to play an effective, multifaceted role in aiding resettlement; however, longitudinal studies are required.

The national incidence and clinical picture of SLE in children in Australia--a report from the Australian Paediatric Surveillance Unit.
Lupus. 2014; 0961203314552118.

The national incidence and clinical picture of SLE in children in Australia - a report from the Australian Paediatric Surveillance Unit.
Lupus. 2014.
OBJECTIVES: The objectives of this paper are to prospectively determine the incidence of paediatric systemic lupus erythematosus (pSLE) in Australia as well as describe the demographics, clinical presentation and one-year outcome. STUDY DESIGN: Newly diagnosed cases of pSLE were ascertained prospectively from October 2009 to October 2011 through the Australian Paediatric Surveillance Unit (a national monthly surveillance scheme for notification of childhood rare diseases) as well as national subspecialty groups. Questionnaires were sent to notifying physicians at presentation and at one year. RESULTS: The annual incidence rate was 0.32 per 105 children aged less than 16 years. The incidence was significantly higher in children of Asian or Australian Aboriginal and Torres Strait Islander parents. Approximately one-third of children underwent a renal biopsy at presentation and 7% required dialysis initially although only one child had end-stage kidney disease (ESKD) at one-year follow-up. CONCLUSION: The incidence of pSLE in Australia is comparable to that worldwide with a significantly higher incidence seen in children of Asian and Australian Aboriginal and Torres Strait Islander backgrounds. Renal involvement is common but progression to ESKD, at least in the short term, is rare.

Early Atherosclerosis Relates to Urinary Albumin Excretion and Cardiovascular Risk Factors in Adolescents With Type 1 Diabetes: Adolescent Type 1 Diabetes cardio-renal Intervention Trial (AdDIT).
OBJECTIVE: The origins of cardiovascular and renal disease in type 1 diabetes begin during childhood. We aimed to evaluate carotid (cIMT) and aortic intima-media thickness (aIMT) and their relationship with cardiovascular risk factors and urinary albumin excretion in adolescents with type 1 diabetes in the Adolescent Type 1 Diabetes cardio-renal Intervention Trial (AdDIT). RESEARCH DESIGN AND METHODS: A total of 406 adolescents with type 1 diabetes, who were 14.1 +/- 1.9 years old with type 1 diabetes duration of 6.7 +/- 3.7 years, and 57 age-matched control subjects provided clinical and biochemical data and ultrasound measurements of vascular structure (cIMT and aIMT). Vascular endothelial and smooth muscle function was also measured in 123 of 406 with type 1 diabetes and all control subjects. RESULTS: In type 1 diabetic
subjects. Mean/maximal aIMT related to urinary albumin-to-creatinine ratio (multiple regression coefficient [SE], 0.013 [0.006], P = 0.03; 0.023 [0.007], P = 0.002), LDL cholesterol (0.019 [0.008], P = 0.02; 0.025 [0.011], P = 0.02), and age (0.010 [0.004], P = 0.004; 0.012 [0.005], P = 0.01), independent of other variables. Mean/maximal cIMT was greater in males (0.023 [0.006], P = 0.02; 0.029 [0.007], P < 0.0001), and mean cIMT related independently to systolic blood pressure (0.001 [0.001], P = 0.04). Vascular smooth muscle function related to aIMT and cIMT but not to urinary albumin excretion. CONCLUSIONS: aIMT may be a more sensitive marker of atherosclerosis than cIMT in type 1 diabetes during mid-adolescence. Higher urinary albumin excretion, even within the normal range, is associated with early atherosclerosis and should direct clinical attention to modifiable cardiovascular risk factors.

Mariyappa B, Barker A, Samnakay N and Khosa J.
Management of duplex-system ureterocele.
AIM: To analyse different treatment modalities, functional outcome and continence in children treated for duplex-system ureterocele and to review the relevant literature. METHODS: The medical records of patients with duplex-system ureterocele treated between 2001 and 2011 were reviewed retrospectively. RESULTS: Twenty-two cases were identified. Five patients underwent incision of the ureterocele as initial procedure. It was curative in only one patient. Seven patients underwent upper-pole nephroureterectomy. It was curative in 4 cases. Five patients underwent excision of ureterocele and common-sheath reimplant, and the remaining 5 patients had upper-pole nephroureterectomy and simultaneous excision of ureterocele with lower-moieties ureteric reimplantation. These surgeries were curative in all patients. Follow-up ranged from 4 to 84 months. Functional outcome was good in all patients. Fourteen patients were continent at follow-up, and continence was not assessed in the other 8 because of young age. CONCLUSIONS: Our data suggest a higher rate of secondary procedures if there is retained ureterocele. Data also suggest that complete reconstruction can be safely performed in a young infant without any adverse effect on continence.

Predictors of Disease Severity in Children Hospitalized for Pertussis during an Epidemic.
The Pediatric infectious disease journal. 2014.
BACKGROUND:: Australia recently experienced its worst pertussis epidemic since introduction of pertussis vaccine into the National Immunisation Program. This study aimed to determine factors associated with severe pertussis in hospitalized children during an epidemic using a novel pertussis severity scoring (PSS) system. METHODS:: This prospective, observational, multicenter study enrolled children hospitalized with laboratory confirmed pertussis from 8 tertiary pediatric hospitals during a 12 month period (May 2009 - April 2010). Variables assessed included demographics, clinical symptoms and relevant medical and immunization history. Cases were scored using objective clinical findings with cases classified as either severe (PSS >5) or not severe (PSS <=5). Logistic regression models were used to predict variables associated with severe disease. RESULTS:: 120 hospitalized children 0-17 years of age were enrolled with a median PSS of 5 (IQR 3-7). Most (61.7 %) were classified as not severe with 38.3% (46/120) severe. Most severe cases (54.3%) were <2 months of age. Presence of co-infection (OR: 4.82, CI 1.66-14.00), < 2 months old (OR: 4.76, CI 1.48-15.32) fever >37.5C (OR: 5.97, CI 1.19-29.96) and history of prematurity (OR 5.00, CI 1.27-19.71) were independently associated with severe disease. Of the 70 cases in children 2 months of age, almost a third (n=23) had not received pertussis vaccine. CONCLUSIONS:: Most severe pertussis occurred in young, unimmunized infants, although severe disease was also observed in children > 12 months of age and previously vaccinated children. Children admitted with pertussis with evidence of co-infection, history of prematurity or fever on presentation need close monitoring.

Martin L, Rea S, McWilliams T and Wood F.
Hot ash burns in the children of Western Australia: How and why they happen.
INTRODUCTION: Burns from hot ash are common in the paediatric population in Western Australia. Fifty children were admitted to the paediatric burn centre with hot ash contact burns to the feet in 2011 and 2012. It is important to examine the extent of the problem, seasonal variations, and identify those at risk to determine strategies for prevention campaigns. METHOD: Retrospective review of medical notes for all admissions to the paediatric burns unit was undertaken for 2011 and 2012. Data were collected for patient demographics, time, circumstance of injury, burn severity and treatment. RESULTS: Hot ash burns accounted for 8.6% of admissions but 16.1% of burns sustained in non-metro areas. Median age was just under 3 years, male or female. Median burn TBSA was 2%, and 44% of children required surgery. The burns were less common in summer, more common on non-school days and in children who were on camping trips away from home.
DISCUSSION: Previous work has shown the value of targeted campaigns. The group for targeted prevention campaigns are the carers of very young children who go camping. Information distributed at camping shows and stores about the principles of campfire safety would reach the people at risk.

Martinez FE and Hooper AJ. 
Drowning and immersion injury.

McGarry S, Elliott C, McDonald A, Valentine J, Wood F and Girdler S. 
Paediatric burns: from the voice of the child.

INTRODUCTION: Despite burns being common in children, research into the psychological experience and trauma remains limited. Improvements in the professional understanding of children's experiences will assist in improving holistic care. PURPOSE: This study uses phenomenology, a qualitative methodology to explore the psychological experiences following a burn injury in children. METHODS: In-depth interviews were conducted six months after burn with 12 (six girls and six boys) children who underwent surgery for a burn. The children were aged eight to 15 years. The interview examined the overall experience of children and included probing questions exploring participants' perceptions, thoughts and feelings. Transcripts were analysed according to the seven-step Colliazzi method. Relationships between themes were explored to identify core concepts. RESULTS: The findings demonstrated that trauma was central to the burn experience and comprised two phases: the burn trauma and the recovery trauma. Six themes emerged as a result of this experience: ongoing recurrent trauma; returning to normal activities; behavioural changes; scarring-the permanent reminder; family and adaptation. CONCLUSION: This research has clinical implications as its findings can be used to inform clinical care at all stages of the burn journey. These research conclusions could be used to develop comprehensive information and support management plans for children. This would complement and support the surgical and medical treatment plan, providing direction for comprehensive service delivery and improved psychosocial outcomes in children.

McLeod C, Morris PS, Snelling TL, Carapetis JR and Bowen AC. 

INTRODUCTION: Australian Indigenous children suffer a high burden of diarrhoeal disease. Nitazoxanide is an antimicrobial that has been shown to be effective against a broad range of enteropathogens. To date, its use has not been reported in the tropical Top End (northernmost part) of the Northern Territory, Australia. The objective was to describe the use of nitazoxanide at the Royal Darwin Hospital, Northern Territory, and to assess any association with the time to resolution of diarrhoea. METHODS: Eligible children (<13 years) were identified from dispensary records as having been prescribed nitazoxanide during the audit period, 1 July 2007 to 31 March 2012. Patient demographics, symptoms, diarrhoeal aetiology, treatment details and clinical outcomes were obtained by chart review. RESULTS: Twenty-eight children were treated with nitazoxanide, mostly for Cryptosporidium infection associated with prolonged diarrhoea. Dehydration was evident in 27 (96%) children on admission, and 11 (41%) were underweight. Diarrhoeal duration prior to treatment was 11.5 days (6.5 days pre- and 5 days post-admission). For children >12 months, nitazoxanide was prescribed according to guidelines stipulated by the Centers for Disease Control and Prevention (CDC). Resolution of diarrhoea occurred a median of 2.4 days (IQR: 1.4-7.3) after starting treatment. An increase in weight for length at discharge was found for all children. CONCLUSIONS: Prompt resolution of diarrhoea without adverse outcomes suggests nitazoxanide may be an effective treatment for Cryptosporidium infection in this setting. Its role in the treatment of other causes of infectious diarrhoea needs further investigation. Randomised trials will further direct its use and determine optimal dosing regimens.

McTaggart S, Danchin M, Ditchfield M, Hewitt I, Kausman J, Kennedy S, Trnka P and Williams G. 
Diagnosis and Treatment of Urinary Tract Infection in Children.
Nephrology. 2014.

McWilliams T, Hendricks J, Twigg D and Wood F. 
Burns education for non-burn specialist clinicians in Western Australia.
Burns : journal of the International Society for Burn Injuries. 2014.

Middleton B, Morris P and Carapetis J. 
Invasive group A streptococcal infection in the Northern Territory, Australia: Case report and review of the literature.
Journal of paediatrics and child health. 2014.
Moore HC, Jacoby P, Hogan AB, Blyth CC and Mercer GN.
Modelling the seasonal epidemics of respiratory syncytial virus in young children.
BACKGROUND: Respiratory syncytial virus (RSV) is a major cause of paediatric morbidity. Mathematical models can be used to characterise annual RSV seasonal epidemics and are a valuable tool to assess the impact of future vaccines. OBJECTIVES: Construct a mathematical model of seasonal epidemics of RSV and by fitting to a population-level RSV dataset, obtain a better understanding of RSV transmission dynamics.
METHODS: We obtained an extensive dataset of weekly RSV testing data in children aged less than 2 years, 2000-2005, for a birth cohort of 245,249 children through linkage of laboratory and birth record datasets. We constructed a seasonally forced compartmental age-structured Susceptible-Exposed-Infectious-Recovered-Susceptible (SEIRS) mathematical model to fit to the seasonal curves of positive RSV detections using the Nelder-Mead method. RESULTS: From 15,830 specimens, 3,394 were positive for RSV. RSV detections exhibited a distinct biennial seasonal pattern with alternating sized peaks in winter months. Our SEIRS model accurately mimicked the observed data with alternating sized peaks using disease parameter values that remained constant across the 6 years of data. Variations in the duration of immunity and recovery periods were explored. The best fit to the data minimising the residual sum of errors was a model using estimates based on previous models in the literature for the infectious period and a slightly lower estimate for the immunity period. CONCLUSIONS: Our age-structured model based on routinely collected population laboratory data accurately captures the observed seasonal epidemic curves. The compartmental SEIRS model, based on several assumptions, now provides a validated base model. Ranges for the disease parameters in the model that could replicate the patterns in the data were identified. Areas for future model developments include fitting climatic variables to the seasonal parameter, allowing parameters to vary according to age and implementing a newborn vaccination program to predict the effect on RSV incidence.

More K, Rao S, McMichael J and Minutillo C.
Growth and developmental outcomes of infants with hirschsprung disease presenting in the neonatal period: a retrospective study.
OBJECTIVES: To describe the presentation and progress over the first year of life of neonates with Hirschsprung disease, to describe their physical and developmental outcomes at 12 months of age, and to compare the outcomes of infants with short- vs long-segment Hirschsprung disease. STUDY DESIGN: A retrospective study of neonates born with Hirschsprung disease in Western Australia between January 1, 2001, and December 31, 2010, to review their presentation, progress, growth, and development at 12 months of age. RESULTS: Fifty-four infants were identified (40 with short and 11 with long segment and 3 with total colonic aganglionosis); 9 infants had a recognized syndrome and 1 infant died, unrelated to Hirschsprung disease. A primary pull-through procedure was performed in 97% and 21% of neonates with short- and non-short-segment Hirschsprung disease, respectively; 17 (31%) infants developed anal stenosis requiring dilatations. Enterocolitis occurred in 14 (26%) infants. Griffiths Mental Development Scale scores (1 year) were available in 31 of 45 nonsyndromic survivors: mean general quotient (94.2, SD 8.89) was significantly less than the population mean (P = .007), but the number of infants with developmental delay was within the expected range. Physical growth, except length, appeared adequate in nonsyndromic infants. There were no significant differences in the outcomes of infants with short- vs non-short-segment Hirschsprung disease. CONCLUSIONS: At 1 year of age, many infants with Hirschsprung disease have ongoing gastrointestinal problems. Their overall growth appears satisfactory, and most infants are developing normally; however, their mean general quotient appears shifted to the left. Longer-term studies will better define developmental outcomes.

Mortazavi S, O'Dea C, Le Souef P, Hall G and Wilson A.
The Clinical Utility Of The Forced Oscillation Technique In Children With Neuromuscular Disease.
Mutch RC, Watkins R and Bower C.
Fetal alcohol spectrum disorders: Notifications to the Western Australian Register of Developmental Anomalies. Journal of paediatrics and child health. 2014.
AIM: There is increasing attention on fetal alcohol spectrum disorders (FASD) in Australia, but there are limited data on their birth prevalence. Our aim was to report on the birth prevalence of FASD in Western Australia.
METHODS: Data on notified cases of FASD born in Western Australia 1980-2010 were identified from the
Western Australian Register of Developmental Anomalies. Tabulated denominator data were obtained from the Midwives Notification System. Prevalence rates per 1000 births were calculated by demographic variables. Prevalence ratios (PRs) and 95% confidence intervals (CIs) of Aboriginal compared with non-Aboriginal prevalence rates were calculated. PRs were also calculated to compare rates for births 2000-2010 with 1980-1989. RESULTS: Two hundred ten cases of FASDs were identified: a birth prevalence of 0.26/1000 births (95% CI 0.23-0.30). The majority of cases reported were Aboriginal (89.5%), a rate of 4.08/1000, compared with 0.03/1000 in notified non-Aboriginal cases, giving a PR of 139 (95% CI 89-215). The prevalence of FASD in 2000-2010 was over twice that in 1980-1989 for both Aboriginal (PR 2.37; CI 1.60-3.51) and non-Aboriginal (PR 2.13; CI 0.68-6.69) children. CONCLUSIONS: There has been a twofold increase in FASD notifications in Western Australia over the last 30 years. Population surveillance data such as these are valuable in advocating for and monitoring the effectiveness of preventive activities and diagnostic and management services.


OBJECTIVE: To determine the relationship between serum ferritin and malnutrition in newly assessed patients at a paediatric eating disorders clinic. DESIGN: This was a prospectively assessed clinical cohort study. SETTING: Intake assessment clinic of a tertiary eating disorders service for children and adolescents. METHODS: Clinical, anthropometric and laboratory features of children and adolescents were systematically measured. The relationship of serum ferritin to other clinical, anthropometric and laboratory measures was determined using linear regression. RESULTS: A total of 121 female patients aged 9.5-17.6 years were included, with body mass index (BMI) z score -5.7 to 1.9 (median -1.3). Using multiple regression, serum ferritin was inversely associated with BMI z score (regression coefficient (beta)=-0.234, 95% CI -0.413 to -0.055) and serum insulin-like growth factor 1 (IGF-1) (beta=-0.476, 95% CI -0.884 to -0.068) and positively associated with alanine aminotransferase (beta=0.357, 95% CI 0.055 to 0.659, controlling for age, pubertal stage and serum iron). CONCLUSIONS: In malnourished adolescents with eating disorders increased serum ferritin is associated with lower BMI z score and serum IGF-1.


Objective: To investigate the reproducibility and repeatability of digital models of patients with a unilateral cleft lip and palate (UCLP) using the GOSLON yardstick. Design: Reproducibility and repeatability study. Method: Two examiners used the GOSLON yardstick to assess the intermaxillary dentoalveolar relationship of 30 consecutive UCLP patients by analyzing their 9-year (±3 months) dental study casts and digital study models. The records were rated 1 week apart to avoid bias. The process was repeated 1 month later as a measure of reproducibility. Reliability was assessed by comparing the GOSLON score achieved between the two modalities. Patient dental study casts were sent to 3M Unitek Australia to be scanned using the 3M Unitek Lava™ system to produce digital study models. The accuracy of the dental study cast occlusal registration was assessed by both raters prior to sending the study models for scanning. Statistical analysis: The Linear Weighted Kappa statistic and Kendall's Coefficient of Concordance statistic were used to determine the levels of agreement within and between raters. Results: The linear weighted Kappa statistic for intrarater repeatability of digital study models scores were very high (0.89 and 0.97). This compared favorably to the intrarater repeatability of study model casts scores (0.86 and 0.97). There was very good agreement for interrater digital study model scores (0.80 and 0.87) and also for the interrater study model casts scores (0.80 and 0.90). Kendall's Coefficient of Concordance statistic (0.99) and Correlation Coefficient (0.86) support the weighted Kappa results of the digital study model scores. Conclusion: Digital models can be used for GOSLON scoring with a high degree of reproducibility and repeatability.


AIM OF THE STUDY: Sialorrhea and chronic salivary aspiration are a major problem in many neurologically impaired children causing embarrassment, skin issues and recurrent lower respiratory tract infections (LRTI). The aim of this study was to assess the efficacy of salivary gland surgery in the treatment of chronic salivary aspiration in such children. OBJECTIVES: To compare admission rates for LRTI per annum before and after surgical intervention. METHODS: Retrospective review of all patients who underwent salivary management surgery for chronic aspiration under Princess Margaret Hospital's (PMH) Otolaryngology department from 2006 until 2013. RESULTS: Twelve patients were included in this review. Their ages ranged from 3 to 21 years (mean=11.4). Their genders were equally distributed. Two patients had underlying congenital disorders; one had an acquired brain injury, while the majority (n=9, 75%) had cerebral palsy secondary to a sustained perinatal injury. Most patients (n=11, 91.7%) had bilateral submandibular gland excision and parotid duct ligation as a primary procedure. One patient had a laryngotracheal separation. Two patients went on to have a second procedure. The mean follow up time was five years. Using Wilcoxon Signed-Rank test we showed that the median rate of admission per annum for LRTI pre-operatively was 1.0. This was reduced to 0.5 post-operatively, which was statistically significant (p<=0.05). CONCLUSIONS: We hypothesize that the combination of bilateral submandibular gland excision and bilateral parotid duct ligation is effective in reducing admissions with aspiration pneumonia in neurologically impaired children, and therefore improves the quality of life in these patients.


Context: Intronic DNA frequently encodes potential exonic sequences called pseudoexons. In recent years mutations resulting in aberrant pseudoexon inclusion have been increasingly recognised to cause disease. Objectives: To find the genetic cause of Familial Glucocorticoid Deficiency (FGD) in two siblings. Patients: The proband and his affected sibling, from non-consanguineous parents of East Asian and South African origin, were diagnosed with FGD at the ages of 21 and 8 months respectively. Design: Whole exome sequencing was performed on gDNA of the siblings. Variants in genes known to cause FGD were assessed for causality. Further analysis of gDNA and cDNA was performed by PCR/RT-PCR followed by automated Sanger sequencing. Results: Whole exome sequencing identified a single, novel heterozygous variant (p.Arg71*) in nicotinamide nucleotide transhydrogenase (NNT) in both affected individuals. Follow up cDNA analysis in the proband identified a 69 bp pseudoexon inclusion event and Sanger sequencing of his gDNA identified a 4bp duplication responsible for its activation. The variants segregated with the disease: p.Arg71* was inherited from the mother, the pseudoexon change from the father and an unaffected sibling had inherited only the p.Arg71* variant. Conclusions: FGD in these siblings is caused by compound heterozygous mutations in NNT; pseudoexon inclusion in combination with Arg71*. Discovery of this pseudoexon activation mutation highlights the importance of identifying sequence changes in introns by cDNA analysis. The clinical implications of these findings include: facilitation of antenatal genetic diagnosis, early institution of potentially life-saving therapy and the possibility of preventative or curative intervention.


OBJECTIVE: To report the results of a study conducted on voiding function in children who have undergone intravesical trans-trigonal Cohen ureteric reimplantation surgery before the age of one year. SUBJECTS: Twenty-eight children (18 males, 10 females) had surgery at a mean age of 4.9 months (range 8-352 days). METHODS: Bladder function was assessed at a mean age of 7.3 years using questionnaires, the dysfunctional voiding scoring system, PinQ quality of life tool, uroflowmetry and post-void residuals. RESULTS: Of the total children, 72% had normal lower urinary tract (LUT) function. Eight children (28%) had evidence of LUT dysfunction, two had urge incontinence, two had giggle incontinence, two had voiding postponement, one had dysfunctional elimination syndrome and one had evidence of dysfunctional voiding. Five of the eight children were managed with continence physiotherapy (urotherapy) and one required ongoing anticholinergic therapy.
CONCLUSION: When compared to the published rates of LUT dysfunction in the general paediatric community, no evidence was found to suggest an increased incidence of bladder dysfunction in children undergoing intravesical Cohen ureteric reimplantation surgery under one year of age.


OBJECTIVES: To describe antimicrobial use in hospitalised Australian children and to analyse the appropriateness of this antimicrobial use. DESIGN: Multicentre single-day hospital-wide point prevalence survey, conducted in conjunction with the Antimicrobial Resistance and Prescribing in European Children study. SETTING: Eight children's hospitals across five Australian states, surveyed during late spring and early summer 2012. PATIENTS: Children and adolescents who were inpatients at 8 am on the day of the survey. MAIN OUTCOME MEASURES: Quantity and quality of antimicrobial prescribing. RESULTS: Of 1373 patients, 631 (46%) were prescribed at least one antimicrobial agent, 198 (31%) of whom were < 1 year old. The highest antimicrobial prescribing rates were in haematology and oncology wards (76% [95/125]) and paediatric intensive care units (55% [44/80]). Of 1174 antimicrobial prescriptions, 550 (47%) were for community-acquired infections, 175 (15%) were for hospital-acquired infections and 437 (37%) were for prophylaxis. Empirical treatment accounted for 72% of antimicrobial prescriptions for community-acquired infections and 58% for hospital-acquired infections (395 and 102 prescriptions, respectively). A total of 915 prescriptions (78%) were for antibacterials; antifungals and antivirals were predominantly used for prophylaxis. The most commonly prescribed antibacterials were narrow-spectrum penicillins (18% [164 prescriptions]), beta-lactam-beta-lactamase inhibitor combinations (15% [136]) and aminoglycosides (14% [128]). Overall, 957 prescriptions (82%) were deemed appropriate, but this varied between hospitals (range, 66% [74/112] to 95% [165/174]) and specialties (range, 65% [122/187] to 94% [204/217]). Among surgical patients, 65 of 187 antimicrobial prescriptions (35%) were deemed inappropriate, and a common reason for this was excessive prophylaxis duration. CONCLUSION: A point prevalence survey is a useful cross-sectional method for quantifying antimicrobial use in paediatric populations. The value is significantly augmented by adding assessment of prescribing quality.


neonatal period. RESULTS: Over 26 years, 80 neonates were transferred interstate for ASO surgery. Twelve infants required ventilation, 36 needed prostaglandin (prostaglandin E1) infusion and 3 inotropic support. There was no mortality during transport and there was a single early post-operative death. This early mortality of 1.2% compares favourably with the RCH mortality of 2.8% from a recently published review of early outcomes for ASO. CONCLUSIONS: When in utero transport is not possible, long-distance transport of neonates with TGA can be safely undertaken, with no evidence of increased transport mortality/ major morbidity or higher early surgical mortality.


Human rhinovirus is a key viral trigger for asthma exacerbations. To date, murine studies investigating rhinovirus-induced exacerbation of allergic airways disease have employed systemic sensitisation/intranasal challenge with ovalbumin. In this study, we combined human-rhinovirus infection with a clinically relevant mouse model of aero-allergen exposure using house-dust-mite in an attempt to more accurately understand the links between human-rhinovirus infection and exacerbations of asthma. Adult BALB/c mice were intranasally exposed to low-dose house-dust-mite (or vehicle) daily for 10 days. On day 9, mice were inoculated with human-rhinovirus-1B (or UV-inactivated human-rhinovirus-1B). Forty-eight hours after inoculation, we assessed bronchoalveolar cellular inflammation, levels of relevant cytokines/serum antibodies, lung function and responsiveness/sensitivity to methacholine. House-dust-mite exposure did not result in a classical TH2-driven response, but was more representative of noneosinophilic asthma. However, there were significant effects of house-dust-mite exposure on most of the parameters measured including increased cellular inflammation (primarily macrophages and neutrophils), increased total IgE and house-dust-mite-specific IgG1 and increased responsiveness/sensitivity to methacholine. There were limited effects of human-rhinovirus-1B infection alone, and the combination of the two insults resulted in additive increases in neutrophil levels and lung parenchymal responses to methacholine (tissue elastance). We conclude that acute rhinovirus infection exacerbates house-dust-mite-induced lung disease in adult mice. The similarity of our results using the naturally occurring allergen house-dust-mite, to previous studies using ovalbumin, suggests that the exacerbation of allergic airways disease by rhinovirus infection could act via multiple or conserved mechanisms.


BACKGROUND: Scoliosis is a frequent association in boys with Duchenne Muscular Dystrophy when the ability to walk is lost around nine to 12 years of age. This study assessed the contribution of physical factors including lumbar posture to scoliosis in non-ambulatory youth with DMD in Nepal. METHODS: Linear regression was used to assess effects of time since loss of ambulation, muscle strength, functional severity and lumbar angle as a binary variable on coronal Cobb angle; again logistic regression was used to assess effects of muscle strength and cross-legged sitting on the presence of a lordotic lumbar posture in 22 non-ambulant boys and young men. RESULTS: The boys and young men had a mean (SD) age of 15.1 (4.0) years, had been non-ambulant for 48.6 (33.8) months and used a median of 3.5 (range 2 to 7) postures a day. The mean Cobb angle was 15.1 (range 0 to 70) degrees. Optimal accuracy in predicting scoliosis was obtained with a lumbar angle of -6 degrees as measured by skin markers, and both a lumbar angle <=-6 degrees (P=0.112) and better functional ability (P=0.102) were associated with less scoliosis. Use of cross-legged sitting postures during the day was associated with a lumbar angle <=-6 degrees (OR 0.061; 95% CI 0.005 - 0.672; P=0.022). CONCLUSIONS: Use of cross-legged sitting posture was associated with increase in lumbar lordosis. Higher angle of lumbar lordosis and better functional ability are associated with lesser degree of scoliosis. KEYWORDS: Duchenne Muscular Dystrophy; lumbar lordosis; lumbar posture; Nepal; scoliosis.


PURPOSE: To determine the effects of functional electrical stimulation (FES) on the main impairments affecting gait in children with unilateral spastic cerebral palsy. METHODS: A 20-week, multiple single-subject A-B-A design included a 6-week pre-FES phase, an 8-week FES phase, and a 6-week post-FES phase. Twelve children, aged 5 to 16 years, wore an FES device (the Walk Aide) daily for 8 weeks. Weekly measures included ankle range of motion, selective motor control, dorsiflexion and plantar flexion strength, gastrocnemius spasticity, single-limb balance, Observational Gait Scale (OGS) score, and self-reported toe drag and falls in the
community. RESULTS: Compared with the pre-FES phase, the FES phase showed significant improvements in ankle range of motion, selective motor control and strength, and reductions in spasticity, toe drag, and falls, but no change in OGS score. These improvements were maintained during the post-FES phase.

CONCLUSIONS: Intermittent, short-term use of FES is potentially effective for reducing impairments affecting gait in children with unilateral spastic cerebral palsy.

The 'Can't Intubate Can't Oxygenate' scenario in pediatric anesthesia: a comparison of the Melker cricothyroidotomy kit with a scalpel bougie technique.
Paediatr Anaesth. 2014.
BACKGROUND: While the majority of pediatric intubations are uncomplicated, the 'Can't intubate, Can't Oxygenate' scenario (CICO) does occur. With limited management guidelines available, CICO is still a challenge even to experienced pediatric anesthetists. OBJECTIVES: To compare the COOK Melker cricothyroidotomy kit (CM) with a scalpel bougie (SB) technique for success rate and complication rate in a tracheotomy on a cadaveric 'infant airway' animal model. METHODS: Two experienced proceduralists repeatedly attempted tracheotomy in eight rabbits, alternately using CM and SB (4 fr) technique. The first attempt was performed at the level of the first tracheal cartilage with subsequent experimental trials of insertion progressively more caudal. Success was defined as intratracheal placement of cannula as seen on bronchoscope. Complications were assessed both by bronchoscopic and macropathological appearance. RESULTS: 32 attempts were made at tracheotomy. CM had an overall success rate of 100% compared to a 75% success rate for SB. Success rate for the first attempt was dependent on the level of the tracheotomy (Level 1 100%, level 2 62.5% and level 3 & 4 25%). While CM was associated with lateral and/or posterior wall damage on bronchoscopy/macropathology in 6% of 19% and 25% of 50% respectively, the damage observed was greater and more frequent with SB (19%/44% and 31%/50%, respectively). CONCLUSIONS: At level 1, the first attempt success rate was 100% for both devices. Overall CM showed a better success rate than SB; however, both techniques were associated with significant complication rates, which were more pronounced following the scalpel bougie technique.


American journal of respiratory and critical care medicine. 2014; (ja).

The Journal of Clinical Endocrinology & Metabolism. 2014.

PURPOSE OF REVIEW: Asthma is a common disease in the pediatric population, and anesthetists are increasingly confronted with asthmatic children undergoing elective surgery. This first of this two-part review provides a brief overview of the current knowledge on the underlying physiology and pathophysiology of asthma and focuses on the preoperative assessment and management in children with asthma. This also includes preoperative strategies to optimize lung function of asthmatic children undergoing surgery. The second part of this review focuses on the immediate perioperative anesthetic management including ventilation strategies. RECENT FINDINGS: Multiple observational trials assessing perioperative respiratory adverse events in healthy and asthmatic children provide the basis for identifying risk factors in the patient's (family) history that aid the preoperative identification of at-risk children. Asthma treatment outside anesthesia is well founded on a large body of evidence. Optimization and to some extent intensifying asthma treatment can optimize lung function, reduce bronchial hyperreactivity, and minimize the risk of perioperative respiratory adverse events. SUMMARY: To minimize the considerable risk of perioperative respiratory adverse events in asthmatic children, a good understanding of the underlying physiology is vital. Furthermore, a thorough preoperative assessment to identify children who may benefit of an intensified medical treatment thereby minimizing airflow obstruction and bronchial hyperreactivity is the first pillar of a preventive perioperative management of asthmatic children. The second pillar, an individually adjusted anesthesia management aiming to reduce perioperative adverse events, is discussed in the second part of this review.
Regli A and von Ungern-Sternberg BS.

Anesthesia and ventilation strategies in children with asthma: part II - intraoperative management.

PURPOSE OF REVIEW: As asthma is a frequent disease especially in children, anesthetists are increasingly providing anesthesia for children requiring elective surgery with well controlled asthma but also for those requiring urgent surgery with poorly controlled or undiagnosed asthma. This second part of this two-part review details the medical and ventilatory management throughout the perioperative period in general but also includes the perioperative management of acute bronchospasm and asthma exacerbations in children with asthma.

RECENT FINDINGS: Multiple observational trials assessing perioperative respiratory adverse events in healthy and asthmatic children provide the basis for identifying risk reduction strategies. Mainly, animal experiments and to a small extent clinical data have advanced our understanding of how anesthetic agents effect bronchial smooth muscle tone and blunt reflex bronchoconstriction. Asthma treatment outside anesthesia is well founded on a large body of evidence. Perioperative prevention strategies have increasingly been studied. However, evidence on the perioperative management, including mechanical ventilation strategies of asthmatic children, is still only fair, and further research is required.

SUMMARY: To minimize the considerable risk of perioperative respiratory adverse events in asthmatic children, perioperative management should be based on two main pillars: the preoperative optimization of asthma treatment (please refer to the first part of this two-part review) and - the focus of this second part of this review - the optimization of anesthesia management in order to optimize lung function and minimize bronchial hyperreactivity in the perioperative period.

Reid SL, Pitcher CA, Williams SA, Licari MK, Valentine JP, Shipman PJ and Elliott CM.

Disability & Rehabilitation. 2014; (0): 1-6.

Reynolds V, Meldrum S, Simmer K, Vijayasekaran S and French N.

SIG 3 Perspectives on Voice and Voice Disorders. 2014; 24(3): 124-129.

Reynolds V, Meldrum S, Simmer K, Vijayasekaran S and French NP.


BACKGROUND: Mild dysphonia in childhood is surprisingly common, yet moderate to severe dysphonia is rare. The latter has been associated with complex medical conditions and congenital abnormalities. Intubation injury has also been documented as a cause of childhood dysphonia. Children born very preterm may be intubated as part of the intensive care administered in the perinatal and neonatal periods, yet there are few studies investigating dysphonia in this population. This study will be the first to: use an objective acoustic voice assessment in a paediatric study, document the incidence of dysphonia in very preterm children at school age, and conduct a controlled trial of behaviour voice therapy in this population. DESIGN: This study will consist of three phases: assessment of voice quality and its impact on quality of life in up to 200 children born at less than 32 weeks’ gestation; assessment of the nature and extent of laryngeal pathology in children with moderate to severe dysphonia; and a non-blinded, randomised controlled trial of behavioural voice therapy in children with moderate to severe dysphonia. DISCUSSION: This study will be the first to use clinical assessment to examine the voice quality of very preterm children, and to use fibre optic endoscopic evaluation of laryngeal function to determine the nature and extent of any laryngeal pathology in such children. Those participants with significant voice difficulties will be randomised to receive treatment immediately or after the eight week assessment. TRIAL REGISTRATION: This study is registered on the Australian New Zealand Clinical Trials Registry (ACTRN12613001015730/ACTRN12613001012763).

Roberts G, Jones TW, Davis EA, Ly TT and Anderson M.

Building tasks from verbal instructions: An EEG study on practice trial exposure and task structure complexity during novel sequences of behavior.

Robertson JD, Higgins P, Price J, Dunkley S, Barrese G and Curtin J.

Immune tolerance induction using a factor VIII/von Willebrand factor concentrate (BIOSTATE(R)), with or without immunosuppression, in Australian paediatric severe haemophilia A patients with high titre inhibitors: A multicentre, retrospective study.
Thromb Res. 2014.

INTRODUCTION: It has been postulated that factor VIII (FVIII) products containing von Willebrand factor (VWF) may improve immune tolerance induction (ITI) success rate in patients with haemophilia A and poor prognostic
factors. MATERIALS AND METHODS: We conducted a retrospective cohort analysis of a FVIII/VWF concentrate (BIOSTATE(R)) for ITI in paediatric patients with severe haemophilia A (SHA) and inhibitors, from January 2003 to December 2011 at 3 paediatric-only Haemophilia Treatment Centres in Australia. Response to ITI was assessed at or before 33 months and at completion of ITI. Fifteen male patients with SHA were included in the analysis. RESULTS: BIOSTATE was used for primary ITI in 8 patients (2 years, range 1.1-11.5 years) and for salvage ITI in 7 patients (9.9 years, range 1.1-15.4). At the end of the observation period there were 11 patients who achieved a complete response with BIOSTATE after a median duration of 21 months (range 5-85 months); a partial response was achieved in 2 patients in whom ITI is ongoing. Therefore, the overall response rate was 86.6%. Two patients were deemed treatment failures: one due to non-compliance after 18 months of ITI and another in whom a partial response had not been achieved after 22 months of ITI. CONCLUSION: BIOSTATE was well-tolerated and effective when used for primary or salvage ITI in this cohort of paediatric patients with SHA and a high-level inhibitor.


INTRODUCTION: It has been postulated that factor VIII (FVIII) products containing von Willebrand factor (VWF) may improve immune tolerance induction (ITI) success rate in patients with haemophilia A and poor prognostic factors. MATERIALS AND METHODS: We conducted a retrospective cohort analysis of a FVIII/VWF concentrate (BIOSTATE) for ITI in paediatric patients with severe haemophilia A (SHA) and inhibitors, from January 2003 to December 2011 at 3 paediatric-only Haemophilia Treatment Centres in Australia. Response to ITI was assessed at or before 33 months and at completion of ITI. Fifteen male patients with SHA were included in the analysis. RESULTS: BIOSTATE was used for primary ITI in 8 patients (2 years, range 1.1-11.5 years) and for salvage ITI in 7 patients (9.9 years, range 1.1-15.4). At the end of the observation period there were 11 patients who achieved a complete response with BIOSTATE after a median duration of 21 months (range 5-85 months); a partial response was achieved in 2 patients in whom ITI is ongoing. Therefore, the overall response rate was 86.6%. Two patients were deemed treatment failures: one due to non-compliance after 18 months of ITI and another in whom a partial response had not been achieved after 22 months of ITI. CONCLUSION: BIOSTATE was well-tolerated and effective when used for primary or salvage ITI in this cohort of paediatric patients with SHA and a high-level inhibitor.


BACKGROUND: The epidemic of allergic disease is a major public health crisis. The greatest burden of allergies is in childhood, when rapidly rising rates of disease are also most evident. General practitioners (GP) have a key role in recognising and addressing allergy-related problems and identifying whether a child requires referral to a paediatric allergist. OBJECTIVE: This article focuses on IgE-mediated food allergies and allergic rhinitis, the most commonly seen conditions in paediatric immunology. We will discuss prevention, diagnosis, management and treatment strategies. DISCUSSION: Currently there is no cure for food allergy. Oral tolerance induction continues to be a significant focus of research. All children with a possible food allergy should be referred to an allergist for further testing and advice. Children who develop allergic rhinitis need a regular review by their GP. Immunotherapy should be discussed early in the disease process and needs to be commenced by an allergist.


OBJECTIVES: The current Australian epidemiology of Kawasaki disease (KD) is poorly defined. Previous enhanced surveillance (1993-1995) estimated an incidence of 3.7/100 000 <5 years. METHODS: We identified all patients hospitalized in Western Australia (current population approximately 2.4 million) 1979 through 200...
with a discharge diagnosis of KD. We reviewed demographic, clinical, laboratory, and echocardiographic data from individual patient files and derived age-specific population estimates. KD diagnosis was made using standard criteria. RESULTS: There were 353 KD cases, with incomplete KD in 34 (9.6%). Male to female ratio was 1.7:1 and median age was 3.8 years (interquartile range 12-60 months). Fifty (18.1%) patients were Asian. Mean annual incidence increased from 2.82 per 100 000 children aged <5 years (95% confidence interval, 1.93-3.99) in 1980 to 1989, to 7.96 (6.48-9.67) in 1990 to 1999, to 9.34 (7.72-11.20) in 2000 to 2009. The highest incidence was 15.7 in 2005. A total of 293 children (83%) received intravenous immunoglobulin and 331 (95.4%) aspirin. Of 282 children who completed echocardiographic studies, 47 (16.7%) had coronary artery (CA) ectasia/dilatation and 19 (6.8%) had CA aneurysms; male gender was significantly associated with CA abnormalities. CONCLUSIONS: KD epidemiology in Western Australia mirrors that of other industrialized, predominantly European-Caucasian populations. The rising incidence likely reflects both improved ascertainment and a real increase in disease burden. The current Australian incidence is threefold higher than previously reported and similar to the United Kingdom. The CA outcomes, which include the pre-intravenous immunoglobulin era, are comparable to those reported elsewhere.

Shah P, Thompson K and Rao S.
Fetal Anemia With Persistent Pulmonary Hypertension: A Report of 3 Cases.
Fetal anemia may cause tissue hypoxia and hence has the potential to predispose to persistent pulmonary hypertension of the newborn (PPHN). Review articles and textbooks do not include severe anemia as a cause of PPHN. We report 3 cases of fetal anemia complicated by severe PPHN.

Shah S, Keil A, Gara K and Nagarajan L.
Neurologic complications of influenza.
We report on a child with mild encephalopathy with reversible splenial lesion (MERS) associated with influenza infection and present a case series of neurologic complications associated with influenza infections in children who presented to a tertiary children's hospital in Australia over a period of one year.

Sheridan SL, Frith K, Snelling TL, Grimwood K, McIntyre PB and Lambert SB.
Waning vaccine immunity in teenagers primed with whole cell and acellular pertussis vaccine: recent epidemiology.

Shetty VB, Kiraly-Borri C, Lamont P, Bikker H and Choong CS.
NKX2-1 mutations in brain-lung-thyroid syndrome: a case series of four patients.
Brain-lung-thyroid syndrome (BLTS) characterized by congenital hypothyroidism, respiratory distress syndrome, and benign hereditary chorea is caused by thyroid transcription factor 1 (NKX2-1/TTF1) mutations. We report the clinical and molecular characteristics of four cases presenting with primary hypothyroidism, respiratory distress, and neurological disorder. Two of the four patients presenting with the triad of BLTS had NKX2-1 mutations, and one of these NKX2-1 [c.890_896del (p.Ala327Glyfs*52)] is a novel variant. The third patient without any identified NKX2-1 mutations was a carrier of mitochondrial mutation; this raises the possibility of mitochondrial mutations contributing to thyroid dysgenesis. Although rare, the triad of congenital hypothyroidism, neurological, and respiratory signs is highly suggestive of NKX2-1 anomalies. Screening for NKX2-1 mutations in patients with thyroid, lung, and neurological abnormalities will enable a unifying diagnosis and genetic counseling for the affected families. In addition, identification of an NKX2-1 defect would be helpful in allaying the concerns about inadequate thyroxine supplementation as the cause of neurological defects observed in some children with congenital hypothyroidism.

Siffleet J, Abbott T, Bourke A and Peter S.
Enhancing the quality and safety of the nursing model of care: planning for a new children's hospital in Western Australia.
International Practice Development Journal. 2014 May 1;4(1)

Sim G and Vijayasekaran S.
Novel use of Coblation technology in an unusual congenital tracheal stenosis.


BACKGROUND: Glycaemic control in infants undergoing therapeutic hypothermia (TH) for hypoxic ischaemic encephalopathy (HIE) may have a significant impact on long-term outcomes. Limited information is available on the optimal blood glucose levels in such infants. This study aims to explore (1) the glycaemic control in the first 72 h; and (2) the association between glycaemic control and neurodevelopmental outcomes at 2 years of these infants. METHOD: Medical charts of all infants with HIE treated with therapeutic hypothermia between 2008 and 2010 were reviewed. Clinical details including blood glucose levels (BGL), glucose delivery rate and fluid volume in the first 72 h of life and neurodevelopmental scores (BSID-II: Bayley scale of infant development 2(nd) edition) were recorded. RESULTS: 65 infants had a total of 918 glucose measurements within 72 h of life. Variation in BGLs was greatest in the 1(st)24 h and improved over time. Hypoglycaemia (BGL < 2.6 mmol/L) was present in 17/65 (26%) with most occurring during the 1(st)24 h. With increasing episodes of hypoglycaemia there was a trend to lower mean BSID-II scores (P > 0.05). Infants that had strict glycaemic control (BGLs between 4-8 mmol/L) showed a trend towards higher mean BSID-II scores than infants with BGLs outside that range (P > 0.05). CONCLUSIONS: Hypoglycaemia was common in our cohort. Hypoglycaemia and hyperglycaemia may have a negative influence on long-term neurodevelopment. Early and aggressive management of both hypo- and hyperglycaemia should be considered.


AIM: The prevalence of vitamin D deficiency has risen in countries with a high ultraviolet index and sunny environment such as Australia. There is lack of information on vitamin D status and best possible therapy in Australian Aboriginal children. We aim to (i) describe the vitamin D status in an opportunistic sample of Aboriginal children in Western Australia and (ii) compare the efficacy of oral daily vitamin D with oral stoss vitamin D therapy in this sample. METHOD: Participants were recruited from a metropolitan area (31° S) and a rural area (17° S). Those with a 25(OH)D level less than 78 nmol/L were randomised to receive daily or stoss vitamin D therapy with follow-up at 4-6 months and 9-12 months. Biochemical and clinical parameters such as 25(OH)D, alkaline phosphatase, calcium and sun exposure were collected. RESULTS: Seventy-three participants were enrolled (61 from a metropolitan and 12 from a rural area). 25(OH)D levels were greater than 78 nmol/L in 9/12 (75%) participants in the rural group and 21/61 (34%) in the metropolitan group. 25(OH)D levels were less than 78 nmol/L in 43/73 (59%) participants. Of these, 34/43 (79%) were insufficient (50-78 nmol/L), 8/43 (19%) mildly deficient (27.5-50 nmol/L) and 1/43 (2%) deficient (<27.5 nmol/L). Daily vitamin D therapy had a higher average increase in 25(OH)D levels from baseline than stoss therapy; however, this was not significant. CONCLUSION: Vitamin D insufficiency is common in Aboriginal children of Western Australia and stoss therapy is a safe alternative to daily vitamin D therapy but requires further evaluation of timing and doses.
Thom GA and Cheah KC.
Perforating foreign body reaction to unheated liquid contents of lava lamp.
A 21-month-old girl developed a local skin reaction after the unheated liquid contents of a broken lava lamp were in contact with her skin overnight. Several weeks later, small umbilicated erythematous papules containing central keratotic spines developed within the affected areas. Biopsy showed a granulomatous foreign body reaction with focal transepidermal elimination. Electron microscopy and energy-dispersive X-ray spectroscopy analysis of the tissue revealed carbon-based material, consistent with substances reported to be present in lava lamp liquid.

Tiddens HA, Stick SM and Davis S.
Multi-modality monitoring of cystic fibrosis lung disease: The role of chest computed tomography.

Gigantism and Acromegaly Due to Xq26 Microduplications and GPR101 Mutation.
Background Increased secretion of growth hormone leads to gigantism in children and acromegaly in adults; the genetic causes of gigantism and acromegaly are poorly understood. Methods We performed clinical and genetic studies of samples obtained from 43 patients with gigantism and then sequenced an implicated gene in samples from 248 patients with acromegaly. Results We observed microduplication on chromosome Xq26.3 in samples from 13 patients with gigantism; of these samples, 4 were obtained from members of two unrelated kindreds, and 9 were from patients with sporadic cases. All the patients had disease onset during early childhood. Of the patients with gigantism who did not carry an Xq26.3 microduplication, none presented before the age of 5 years. Genomic characterization of the Xq26.3 region suggests that the microduplications are generated during chromosome replication and that they contain four protein-coding genes. Only one of these genes, GPR101, which encodes a G-protein-coupled receptor, was overexpressed in patients' pituitary lesions. We identified a recurrent GPR101 mutation (p.E308D) in 11 of 248 patients with acromegaly, with the mutation found mostly in tumors. When the mutation was transfected into rat GH3 cells, it led to increased release of growth hormone and proliferation of growth hormone-producing cells. Conclusions We describe a pediatric disorder (which we have termed X-linked acrogigantism [X-LAG]) that is caused by an Xq26.3 genomic duplication and is characterized by early-onset gigantism resulting from an excess of growth hormone. Duplication of GPR101 probably causes X-LAG. We also found a recurrent mutation in GPR101 in some adults with acromegaly. (Funded by the Eunice Kennedy Shriver National Institute of Child Health and Human Development and others.).

Tu J, Foster RS, Bint LJ and Halbert AR.
Topical rapamycin for angiofibromas in paediatric patients with tuberous sclerosis: follow up of a pilot study and promising future directions.
One of the most visible and potentially disfiguring cutaneous manifestations of tuberous sclerosis complex is the development of multiple facial angiofibromas, present in over 80% of patients. Topical rapamycin has been shown in many reports to be a safe and effective treatment for facial angiofibromas. In February 2012 we reported the results of a pilot study of four patients undertaken at a paediatric tertiary hospital in Australia. Since then, we have continued to refine the optimal formulation and concentration of topical rapamycin and expanded our selection of patients. We present an update on our current cohort of treated patients, discuss the optimal formulation of topical rapamycin and include a literature review on all published cases to date. Although topical rapamycin is not a curative treatment, we have demonstrated that its early institution significantly reduces both the vascularity and palpability of angiofibromas and prevents their progression with age. It is well tolerated and now a cost effective option.

A multicentre, randomised, double-blind, placebo-controlled trial of aminophylline for bronchiolitis in infants admitted to intensive care.


OBJECTIVE: To determine whether aminophylline reduced the duration of respiratory support in children admitted to intensive care with bronchiolitis. DESIGN: A multicentre, randomised, double-blind, placebo-controlled trial. SETTING: Paediatric intensive care units in teaching hospitals. PARTICIPANTS: Forty-five children with severe bronchiolitis. INTERVENTION: Patients were randomly assigned to receive an infusion of aminophylline (23) or placebo (22). The primary outcome measure was the number of hours of respiratory support required in the 120 hours after randomisation; respiratory support was defined as either nasal continuous positive airways pressure or mechanical ventilation. RESULTS: The trial was stopped early due to poor recruitment. Respiratory support was required for a median of only 1.5 days (interquartile range [IQR], 0.4-3.5 days) in the aminophylline group compared with 1.9 days (IQR, 0.3-3.5) days in the placebo group. However, more patients in the placebo group were receiving respiratory support at the time of randomisation and, after adjustment for this, there was no suggestion of a beneficial effect of aminophylline among the small number of patients studied (P=0.54, exact log-rank test stratified by respiratory support at the time of randomisation and censored at the time of death in one child in the aminophylline group). CONCLUSION: Not enough children were recruited for the study to test the hypothesis that aminophylline reduces the need for respiratory support in severe bronchiolitis. Consequently, the role of aminophylline in the management of severe bronchiolitis remains unknown.

Ugonna K, Bingle CD, Plant K, Wilson K and Everard ML.

Macrophages are required for dendritic cell uptake of respiratory syncytial virus from an infected epithelium.


We have previously shown that the respiratory syncytial virus [RSV] can productively infect monocyte derived dendritic cells [MoDC] and remain dormant within the same cells for prolonged periods. It is therefore possible that infected dendritic cells act as a reservoir within the airways of individuals between annual epidemics. In the present study we explored the possibility that sub-epithelial DCs can be infected with RSV from differentiated bronchial epithelium and that in turn RSV from DCs can infect the epithelium. A dual co-culture model was established in which a differentiated primary airway epithelium on an Air Liquid Interface (ALI) was cultured on a transwell insert and MoDCs were subsequently added to the basolateral membrane of the insert. Further experiments were undertaken using a triple co-culture model in which in which macrophages were added to the apical surface of the differentiated epithelium. A modified RSV [rr-RSV] expressing a red fluorescent protein marker of replication was used to infect either the MoDCs or the differentiated epithelium and infection of the reciprocal cell type was assessed using confocal microscopy. Our data shows that primary epithelium became infected when rr-RSV infected MoDCs were introduced onto the basal surface of the transwell insert. MoDCs located beneath the epithium did not become infected with virus from infected epithelial cells in the dual co-culture model. However when macrophages were present on the apical surface of the primary epithelium infection of the basal MoDCs occurred. Our data suggests that RSV infected dendritic cells readily transmit infection to epithelial cells even when they are located beneath the basal layer. However macrophages appear to be necessary for the transmission of infection from epithelial cells to basal dendritic cells.

von Ungern-Sternberg BS, Escajeda M and Johnson C.

New soft clinical indicators of neonatal illness severity.


von Ungern-Sternberg BS.

Respiratory Complications in the Pediatric Postanesthesia Care Unit.


This article focuses on common respiratory complications in the postanesthesia care unit (PACU). Approximately 1 in 10 children present with respiratory complications in the PACU. The article highlights risk factors and at-risk populations. The physiologic and pathophysiologic background and causes for respiratory complications in the PACU are explained and suggestions given for an optimization of the anesthesia management in the perioperative period. Furthermore, the recognition, prevention, and treatment of these complications in the PACU are discussed.

Waddington CS, Snelling TL and Carapetis JR.

Management of invasive group A streptococcal infections.


Invasive group A streptococcal (GAS) disease in children includes deep soft tissue infection, bacteremia, bacteraemic pneumonia, meningitis and osteomyelitis. The expression of toxins and super antigens by GAS
can complicate infection by triggering an overwhelming systemic inflammatory response, referred to as streptococcal toxic shock syndrome (STSS). The onset and progression of GAS disease can be rapid, and the associated mortality high. Prompt antibiotics therapy and early surgical debridement of infected tissue are essential. Adjunctive therapy with intravenous immunoglobulin and hyperbaric therapy may improve outcome in severe disease. Nosocomial outbreaks and secondary cases in close personal contacts are not uncommon; infection control measures and consideration of prophylactic antibiotics to those at high risk are important aspects of disease control. To reduce a substantial part of the global burden of GAS disease, an affordable GAS vaccine with efficacy against a broad number of strains is needed.


Wood JM, Athanasiadis T and Allen J. Laryngitis. BMJ. 2014; 349: g5827.

BACKGROUND: Absent pulmonary valve syndrome is associated with aneurysmal dilatation of the pulmonary arteries and compression of the tracheobronchial tree and may lead to significant respiratory compromise. We describe the outcomes of surgical correction of absent pulmonary valve syndrome and risk factors for mortality and reoperation. METHODS: A review of 52 patients with absent pulmonary valve syndrome who underwent surgical correction between 1975 and 2013 was conducted. The median age and weight at repair were 9 months (range, 4 days to 24.2 years) and 6.9 kg (range, 1.8 to 56 kg). Preoperative intubation was required in 15 patients (29%), and 21 patients (40%) underwent urgent repair. The pulmonary valve was replaced with a valved conduit in 16 patients (31%) or monocusp valve in 16 patients (31%). Valveless repair was performed in 20 patients (38%). Pulmonary artery reduction was performed in 39 patients (75%), and 2 patients (4%) underwent a Lecompte maneuver. RESULTS: The median follow-up time was 13 years (range, 1 month to 35 years). Early mortality was 18.8% (3 of 16) during 1975 through 1989, 19% (4 of 21) during 1990 through 2000, and 0% (0 of 15) during 2001 through 2013. Late mortality was 6.7% (3 of 45). Overall survival at 5, 10, and 20 years was 81.4% +/- 5.6%. On multivariate analysis, preoperative ventilation (p = 0.009) was the only risk factor for overall mortality. Freedom from late reoperation at 5, 10, and 20 years was 79.7% +/- 6.9%, 69.4% +/- 8.2%, and 52.1% +/- 9.8%, respectively. No difference in reoperation rates was found between valved conduit, monocusp, or valveless techniques. Risk factors for late reoperation on multivariate analysis were prematurity (p = 0.001) and neonatal primary repair (p = 0.007). Longer postoperative ventilation periods were predicted by preoperative ventilation (p < 0.001) and surgery during infancy (p = 0.01). CONCLUSIONS: Long-term survival for absent pulmonary valve syndrome has improved during the last decade. Preoperative ventilation predicted longer postoperative ventilation and mortality.

Zerwas S, Holle AV, Watson H, Gottfredson N and Bulik CM.
Childhood anxiety trajectories and adolescent disordered eating: Findings from the NICHD study of early child care and youth development.

Following Hospital Presentation With A Wheezing Exacerbation, Children With A Parental History Of Asthma Or Allergies Have Increased Recurrence Of Human Rhinovirus (hrv).