CAHS Staff Publications 2015

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This list is updated regularly.

Articles are listed alphabetically by first author.

*Performance of a predictive algorithm in sensor-augmented pump therapy in the prevention of hypoglycaemia.*

Abraham M, Dong L, Rath S, O’Connell S, McKenzie F, Hakonarson H, Choong C and Levine M.
*Autosomal dominant Kenny-Caffey syndrome with congenital hypoparathyroidism, short stature and normal intellect: a case report.*

*Sirolimus therapy following subtotal pancreatectomy in neonatal hyperinsulinemic hypoglycaemia: a case report.*

*Neonatal diabetes as an isolated manifestation of ipex: an expanding spectrum of disease phenotype with FOXP3 mutation.*

*Efficacy and safety of sirolimus in a neonate with persistent hypoglycaemia following near-total pancreatectomy for hyperinsulinaemic hypoglycaemia.*
Journal of Pediatric Endocrinology and Metabolism. 2015; 0(0).

Abraham MB, Charles A, Gera P and Sreenivasjois R.
*Surgically managed perinatal testicular torsion: a single centre experience.*

Acharya AN, Coates H, Tavora-Vieira D and Rajan GP.
*A pilot study investigating basic fibroblast growth factor for the repair of chronic tympanic membrane perforations in pediatric patients.*

OBJECTIVE: A pilot study to investigate the utility of basic Fibroblast Growth Factor (bFGF) in tympanic membrane perforation (TMP) closure in a small cohort of pediatric patients. METHODS: Prospective cohort study. Suitability for inclusion in the study was confirmed by the application of defined inclusion and exclusion criteria, and informed parental consent obtained. The technique used was a modification of the bFGF-technique by Kanemaru et al. Response to treatment was monitored with serial otoscopy and audiometric outcomes were determined. Statistical analysis of the outcomes was carried out. RESULTS: TMPs were successfully closed in 7/12 children at the first attempt (58%) and in 10/12 children overall (83%). Hearing improvement was observed in 8/10 successfully treated cases (80%). There were no complications or adverse outcomes. CONCLUSIONS: The topical bFGF regeneration technique offers a promising, minimally invasive alternative to conventional myringoplasty in pediatric patients with comparable success and reduced morbidity and cost, especially considering the option of performing repeat applications. Patients with an active infection or inflammation are not suitable for the bFGF-mediated technique.

Agrawal S, Rao S and Patole S.

Updated 8/12/15
Probiotic supplementation for preventing invasive fungal infections in preterm neonates - a systematic review and meta-analysis.


Invasive fungal infections (IFI) are associated with significant health burden in preterm neonates. The objective of this study was to systematically review effect of probiotic supplementation (PS) for preventing IFI in preterm neonates. We searched Cochrane Central Register of Controlled Trials, Medline, Embase, Cumulative Index of Nursing and Allied Health Literature, and proceedings of the Pediatric Academic Society meetings in August 2014. Study selection was performed on randomised controlled trials (RCT) of PS in neonates born <37 weeks. Primary outcome of this study was IFI (isolation of fungus in blood/body fluids) and secondary outcome was fungal gut colonisation. Information on IFI/colonisation was available in 8 of 27 RCT. Meta-analysis (fixed effects model) showed that PS reduced the risk of IFI (RR: 0.50, 95% CI: 0.34, 0.73, I(2) = 39%). Results were not significant with random effects model (RR: 0.64, 95%, CI: 0.30, 1.38, P = 0.25, I(2) = 39%). Analysis after excluding the study with a high baseline incidence (75%) of IFI showed that PS had no significant benefits (RR: 0.89; 95% CI: 0.44, 1.78). Of the five studies reporting on fungal gut colonisation, three reported benefits of probiotics; two did not. Current evidence is limited to derive firm conclusions on the effect of PS for preventing IFI/gut colonisation in preterm neonates.


A body mass index (BMI) >22kg/m2 is a risk factor for type 2 diabetes (T2D) in Aboriginal Australians. To identify loci associated with BMI and T2D we undertook a genome-wide association study using 1.075,436 quality-controlled single nucleotide polymorphisms (SNPs) genotyped (Illumina 2.5M Duo Beadchip) in 402 individuals in extended pedigrees from a Western Australian Aboriginal community. Imputation using the thousands genomes (1000G) reference panel extended the analysis to 6,724,284 post quality-control autosomal SNPs. No associations achieved genome-wide significance, commonly accepted as P<5x10-8. Nevertheless, genes/pathways in common with other ethnicities were identified despite the arrival of Aboriginal people in Australia >45,000 years ago. The top hit (rs10868204 Pgenotyped = 1.50x10-6; rs11140653 Pimputed_1000G = 2.90x10-7) for BMI lies 5′ of NTRK2, the type 2 neurotrophic tyrosine kinase receptor for brain-derived neurotrophic factor (BDNF) that regulates energy balance downstream of melanocortin-4 receptor (MC4R). PiK3c2G (rs12816270 Pgenotyped = 8.06x10-6; rs10841048 Pimputed_1000G = 6.28x10-7) was associated with BMI, but not with T2D as reported elsewhere. BMI also associated with CNTNAP2 (rs6960319 Pgenotyped = 4.65x10-5; rs13225016 Pimputed_1000G = 6.57x10-5), previously identified as the strongest gene-by-environment interaction for BMI in African-Americans. The top hit (rs111242074 Pgenotyped = 5.59x10-6, Pimputed_1000G = 5.73x10-6) for T2D lies 5′ of BCL9 that, along with TCF7L2, promotes beta-catenin's transcriptional activity in the WNT signaling pathway. Additional hits occurred in genes affecting pancreatic (KCNJ6, KCNA1) and/or GABA (GABBR1, KCNA1) functions. Notable associations observed for genes previously identified at genome-wide significance in other populations included MC4R (Pgenotyped = 4.49x10-4) for BMI and IGF2BP2 Pimputed_1000G = 2.55x10-6) for T2D. Our results may provide novel functional leads in understanding disease pathogenesis in this Australian Aboriginal population.

Androga GO, Hart J, Foster NF, Charles A, Forbes D and Riley TV.


Large clostridial toxin-negative, binary toxin-positive (A(-) B(-) CDT(+) strains of Clostridium difficile are almost never associated with clinically significant C. difficile infection (CDI), possibly because such strains are not detected by most diagnostic methods. We report the isolation of an A(-) B(-) CDT(+) ribotype 033 (RT033) strain of C. difficile from a young patient with ulcerative colitis and severe diarrhea.

Athalye-Jape G, Rao S and Patole S.

Lactobacillus reuteri DSM 17938 as a Probiotic for Preterm Neonates: A Strain-Specific Systematic Review. JPEN J Parenter Enteral Nutr. 2015.

INTRODUCTION: Prevention of necrotizing enterocolitis (NEC) while optimizing enteral nutrition (EN) is a priority in preterm neonates. Lactobacillus reuteri DSM 17938 (L reuteri) is known to improve gut motility. Previous systematic reviews have not adequately assessed the effects of L reuteri in improving feed tolerance in preterm neonates. OBJECTIVE: To assess the effects of L reuteri in preterm neonates. DESIGN: A systematic review of randomized controlled trials (RCTs) and non-RCTs of L reuteri was conducted. We searched the Cochrane Central Register of Controlled Trials, PubMed, EMBASE, and CINAHL databases and

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proceedings of Pediatric Academic Society meetings in December 2014. RESULTS: Six RCTs (n = 1778) and 2 non-RCTs (n = 665) were included. Meta-analysis of RCTs estimated that the time to full feeds (mean difference [MD], -1.34 days; 95% confidence interval [CI], -1.81 to -0.86; 2 RCTs), duration of hospitalization (-10.77 days; 95% CI, -13.67 to -7.86; 3 RCTs), and late-onset sepsis (LOS) (relative risk [RR], 0.66; 95% CI, 0.52 to 0.83; 4 RCTs) were reduced in the L reuteri group. Mortality (RR, 0.79; 95% CI, 0.57-1.09; 3 RCTs) and >~/= stage II NEC (RR, 0.69; 95% CI, 0.47-1.01; 3 RCTs) were reduced but statistically not significant. There were no adverse effects of supplementation. Both non-RCT studies showed significant improvement in the incidence of NEC with L reuteri supplementation. CONCLUSIONS: Evidence from a limited number of studies suggests that L reuteri supplementation has the potential to reduce the risk of NEC and LOS while facilitating EN in preterm infants. Larger definitive RCTs are needed to confirm these findings.


Retinopathy of prematurity (ROP) is one of the leading and preventable causes of blindness. The investigation of choice for diagnosing ROP is binocular indirect ophthalmoscope (BIO) done by ophthalmologists. Since the number of ophthalmologists available to do BIO examination is limited, especially in developing countries, there is a need for an alternate, cheap, reliable and feasible test. Telemedicine imaging with Digital Retinal Photography (DRP) is one such alternate diagnostic test which can be performed easily by non-ophthalmologists, with adequate training. Our objective was to conduct a systematic review to evaluate the accuracy of DRP performed by trained personnel (non-ophthalmologists) in diagnosing clinically significant ROP. Medline, EMBASE, CINAHL and Cochrane databases were searched independently by two authors. Eligible studies were assessed using the Quality Assessment of Diagnostic Accuracy Studies (QUADAS)-2, an evidence-based tool for the assessment of quality in systematic reviews of diagnostic accuracy studies. Six were included in the review (three prospective; N=120, three retrospective; N=579). Studies had methodological limitations on QUADAS-2. Because of the heterogeneity of studies, data could not be pooled to derive single-effect size estimates for sensitivity and specificity. The included studies reported sensitivity of 45.5-100% with the majority being more than 90%; specificity 61.7-99.8% with the majority being more than 90%, positive predictive value 61.5-96.6% and negative predictive value of 76.9-100% for diagnosing clinically significant ROP. We conclude that diagnostic accuracy of DRP must be established in prospective studies with adequate sample size where DRP is compared against the simultaneously performed BIO examination.


Objective & Design. We undertook a retrospective review of children diagnosed with acute lymphoblastic leukemia (ALL) and treated with modern COG protocols (n = 80) to determine longitudinal changes in body mass index (BMI) and the prevalence of obesity compared with a healthy reference population. Results. At diagnosis, the majority of patients (77.5%) were in the healthy weight category. During treatment, increases in BMI z-scores were greater for females than males; the prevalence of obesity increased from 10.3% to 44.8% (P < 0.004) for females but remained relatively unchanged for males (9.8% to 13.7%, P = 0.7). Longitudinal analysis using linear mixed-effects identified associations between BMI z-scores and time-dependent interactions with sex (P = 0.0005), disease risk (P < 0.0001), age (P = 0.0001), and BMI z-score (P < 0.0001) at diagnosis and total dose of steroid during maintenance (P = 0.01). Predicted mean BMI z-scores at the end of therapy were greater for females with standard risk ALL irrespective of age at diagnosis and for males younger than 4 years of age at diagnosis with standard risk ALL. Conclusion. Females treated on standard risk protocols and younger males may be at greatest risk of becoming obese during treatment for ALL. These subgroups may benefit from intervention strategies to manage BMI during treatment for ALL.


We describe two half-siblings with monocarboxylate transporter 1 (MCT1, SLC16A1) deficiency, a defect on ketone body utilization, that has only recently been identified (van Hasselt et al., N Engl J Med, 371:1900-1907, 2014) as a cause for recurrent ketoacidoses. Our index patient is a boy with non-consanguineous parents who had presented acutely with impaired consciousness and severe metabolic ketoacidosis following a 3-day history of gastroenteritis at age 5 years. A 12.5-year-old half-brother who shared the proband's mother also had a
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previous history of recurrent ketoacidoses. Results of mutation and enzyme activity analyses in proband samples advocated against methylcrotoacetyl-coenzyme A thiolase ("beta-ketothiolase") and succinyl-coenzyme A: 3-oxoacyl coenzyme A transferase (SCOT) deficiencies. A single heterozygous c.982C>T transition in the SLC16A1 gene resulting in a stop mutation (p.Arg328Ter) was detected in both boys. It was shared by their healthy mother and by the proband's half-sister, but was absent in the proband's father. MCT1 deficiency may be more prevalent than is apparent, as clinical manifestations can occur both in individuals with bi- and monoallelic mutations. It may be an important differential diagnosis in recurrent ketoacidosis with or without hypoglycaemia, particularly in the absence of any specific metabolic profiles in blood and urine. Early diagnosis may enable improved disease management. Careful identification of potential triggers of metabolic decompensations in individuals even with single heterozygous mutations in the SLC16A1 gene is indicated.

Balsubramanian H, Ananthan A, Rao S and Patole S.
Odds ratio vs risk ratio in randomized controlled trials.
Postgraduate Medicine. 2015; 0(0): 1-9.

Barker N and Everard ML.
Getting to grips with ‘dysfunctional breathing’.
Paediatric respiratory reviews. 2015; 16(1): 53-61.
Dysfunctional breathing (DB) is common, frequently unrecognised and responsible for a substantial burden of morbidity. Previously lack of clarity in the use of the term and the use of multiple terms to describe the same condition has hampered our understanding. DB can be defined as an alteration in the normal biomechanical patterns of breathing that result in intermittent or chronic symptoms. It can be subdivided into thoracic and extra thoracic forms. Thoracic DB is characterised by breathing patterns involving relatively inefficient, excessive upper chest wall activity with or without accessory muscle activity. This is frequently associated with increased residual volume, frequent sighing and an irregular pattern of respiratory effort. It may be accompanied by true hyperventilation in the minority of subjects. Extra thoracic forms include paradoxical vocal cord dysfunction and the increasingly recognised supra-glottic ‘laryngomalacia’ commonly seen in young sportsmen and women. While the two forms would appear to be two discreet entities they often share common factors in aetiology and respond to similar interventions. Hence both forms are considered in this review which aims to generate a more coherent approach to understanding, diagnosing and treating these conditions.

Phenotyping: Targeting genotype's rich cousin for diagnosis.
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.

Beaton A and Carapetis J.
The 2015 revision of the Jones criteria for the diagnosis of acute rheumatic fever: implications for practice in low-income and middle-income countries.
Heart Asia. 2015; 7(2): 7-11.
The Jones criteria has long served as the primary guideline for diagnosing acute rheumatic fever (ARF). However, since the first iteration in 1944, the global epidemiology of ARF and our knowledge regarding the variability of its presentation have changed. In 2015, the American Heart Association took on an ambitious and successful revision, which accounts for these changes. For the first time, the criteria consider the risk within a population and offer two separate diagnostic pathways that prioritise specificity among those at low risk and sensitivity among those at moderate/high risk. Echocardiography is now recommended in all patients with suspected or confirmed ARF, and subclinical carditis can fulfil a major criterion for ARF in all populations. Finally, new and specific criteria are provided for the diagnosis of ARF recurrences. These changes improve the diagnosis of ARF among moderate/high-risk populations and re-establish the Jones criteria as the international

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gold standard for ARF diagnosis. It is our hope that they will also serve as a catalyst in the global community to increase advocacy, improve case detection, and invest in new research techniques that could ultimately control global ARF in our lifetimes.


Hypothermia for Traumatic Brain Injury in Children-A Phase II Randomized Controlled Trial.


OBJECTIVES: To perform a pilot study to assess the feasibility of performing a phase III trial of therapeutic hypothermia started early and continued for at least 72 hours in children with severe traumatic brain injury. DESIGN: Multicenter prospective randomized controlled phase II trial. SETTING: All eight of the PICUs in Australia and New Zealand and one in Canada. PATIENTS: Children 1-15 years old with severe traumatic brain injury and who could be randomized within 6 hours of injury. INTERVENTIONS: The control group had strict normothermia to a temperature of 36-37 degrees C for 72 hours. The intervention group had therapeutic hypothermia to a temperature of 32-33 degrees C for 72 hours followed by slow rewarming at a rate compatible with maintaining intracranial pressure and cerebral perfusion pressure. MEASUREMENTS AND MAIN RESULTS: Of 764 children admitted to PICU with traumatic brain injury, 92 (12%) were eligible and 55 (7.2%) were recruited. There were five major protocol violations (9%): three related to recruitment and consent processes and two to incorrect temperature management. Rewarming took a median of 21.5 hours (16-35 hr) and was performed without compromise in the cerebral perfusion pressure. There was no increase in any complications, including infections, bleeding, and arrhythmias. There was no difference in outcomes 12 months after injury; in the therapeutic hypothermia group, four (17%) had a bad outcome (pediatric cerebral performance category, 4-6) and three (13%) died, whereas in the normothermia group, three (12%) had a bad outcome and one (4%) died. CONCLUSIONS: Early therapeutic hypothermia in children with severe traumatic brain injury does not improve outcome and should not be used outside a clinical trial. Recruitment rates were lower and outcomes were better than expected. Conventional randomized controlled trials in children with severe traumatic brain injury are unlikely to be feasible. A large international trials group and alternative approaches to trial design will be required to further inform practice.


X-linked acrogigantism (X-LAG) syndrome: clinical profile and therapeutic responses.

Endocrine-Related Cancer. 2015.

X-linked acro-gigantism (X-LAG) is a new syndrome of pituitary gigantism, caused by microduplications on chromosome Xq26.3, encompassing the gene GPR101, which is highly upregulated in pituitary tumors. We conducted this study to explore the clinical, radiological and hormonal phenotype and responses to therapy in patients with X-LAG syndrome. The study included 18 patients (13 sporadic) with X-LAG and a microduplication in chromosome Xq26.3. All sporadic cases had unique duplications and the inheritance pattern in 2 families was dominant with all Xq26.3 duplication carriers being affected. Patients began to grow rapidly as early as 2-3 months of age (median 12 months). At diagnosis (median delay 27 months), patients had a median height and weight SDS score of >+3.9 SDS. Apart from the increased overall body size, the children had acromegalic symptoms including acral enlargement and facial coarsening. More than a third of cases had increased appetite. Patients had marked hypersecretion of GH/IGF-1 and prolactin, usually due to a pituitary macroadenoma or hyperplasia. Primary neurosurgical control was achieved with extensive anterior pituitary resection but postoperative hypopituitarism was frequent. Control with somatostatin analogs was not readily achieved despite moderate to high somatostatin receptor subtype-2 expression in tumor tissue. Postoperative adjuvant pegvisomant achieved control of IGF-1 all 5 cases in which it was employed. X-LAG is a new infant-onset gigantism syndrome that has a severe clinical phenotype leading to challenging disease management.


Hospitalisations up to adulthood for children born with orofacial clefts.

Journal of paediatrics and child health. 2015.

AIM: The aim of this study was to compare hospital admissions from infancy to adulthood, between children born with orofacial clefts (OFC) and those without OFC. METHODS: The method used was a cohort study using record-linked administrative datasets. Participants included all children liveborn in Western Australia (WA) between 1980 and 2010 diagnosed with OFC, who were frequency matched by year of birth to randomly selected liveborn children without OFC. We calculated rate ratios (RR) of hospital admission, number and

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reason of admissions, cumulative length of stay, for each cleft type (cleft lip only (CLO), cleft lip and palate (CL+P), cleft palate only (CPO), no OFC) and by age period (infancy, pre-school, primary and high school ages, and early adulthood). RESULTS: Overall, 1396 children were diagnosed with an OFC and compared with 6566 children without OFC. Individuals born with OFC were up to three times more likely to be admitted to hospital, had more admissions and longer cumulative length of stay in all age periods. Children with OFC were also more likely to be admitted for ear and digestive system conditions (RR up to 30 and six times higher, respectively). Children with CL+P and CPO were more likely to be admitted for respiratory conditions (RR 1.3-2.0) and children with CPO were six times more likely to be admitted for care for other congenital anomalies. CONCLUSIONS: Throughout childhood, individuals born with OFC were more likely to be admitted, and had more hospitalisations than those without OFC. Children born with CL+P or CPO had a higher hospitalisation burden than children born with CLO.

Bennett RJ, Jayakody DM, Eikelboom RH, Taljaard DS and Atlas MD.
A prospective study evaluating cochlear implant management skills: development and validation of the Cochlear Implant Management Skills (CIMS) survey.
Clin Otolaryngol. 2015.
OBJECTIVE: To investigate the ability of cochlear implant recipients to physically handle and care for their hearing implant device(s) and to identify factors that may influence skills. In order to assess device management skills a clinical survey was developed and validated on a clinical cohort of cochlear implant recipients. DESIGN: Survey development and validation. A prospective convenience cohort design study. SETTING: Specialist hearing implant clinic. PARTICIPANTS: Forty-nine postlingually deafened, adult cochlear implant recipients, at least 12 months post-operative. MAIN OUTCOME MEASURES: Survey test-retest reliability, inter-observer reliability and responsiveness. Correlations between management skills and participant demographic, audiometric, clinical outcomes and device factors. RESULTS: The Cochlear Implant Management Skills survey was developed, demonstrating high test-retest reliability (0.878), inter-observer reliability (0.972) and responsiveness to intervention (skills training) $t(20) = -3.913, p=0.001$. Cochlear Implant Management Skills survey scores range from 54.69% to 100% (mean: 83.45%, SD: 12.47). No associations were found between handling skills and participant factors. CONCLUSIONS: This is the first study to demonstrate a range in processor handling skills in cochlear implant recipients and offers clinicians and researchers a tool to systematically and objectively identify shortcomings in cochlear implant recipients' device handling skills. This article is protected by copyright. All rights reserved.

Bennett RJ, Taljaard DS, Brennan-Jones CG, Tegg-Quinn S and Eikelboom RH.
Evaluating hearing aid handling skills: A systematic and descriptive review.
OBJECTIVE: To review and appraise the content and quality of surveys that evaluate hearing aid handling. DESIGN: A systematic and descriptive review. STUDY SAMPLE: Twelve surveys were identified as containing at least one item evaluating hearing aid handling. RESULTS: Fifteen aspects of hearing aid handling were evaluated. None of the surveys evaluated all aspects of handling skills identified. While the majority of studies reported some psychometric evaluation during survey development, the quality of the methodology used and extent of psychometric evaluation reported varied considerably. CONCLUSIONS: There is currently no single survey that evaluates handling skills comprehensively. In the absence of an ideal survey, the Practical Hearing aid Skills Test appears to be the most inclusive clinician-administered survey and the Hearing aid User's Questionnaire appears to be the most inclusive self-report survey evaluating hearing aid handling precision; however, there are limitations in the analysis of their psychometric properties. Nonetheless, use of these surveys in clinical practice could identify areas of handling that warrant additional training in order to improve hearing aid success. Research identifying the full range of hearing aid handling skills necessary for successful hearing aid use will further contribute knowledge to the complex construct of successful hearing aid-use.

Sudden death in childhood cardiomyopathy: results from a long-term national population-based study.
BACKGROUND: Children with cardiomyopathy (CM) are at risk of sudden cardiac death (SCD), but the incidence and risk factors for this outcome are not clear. OBJECTIVES: This study sought to determine the incidence and risk factors for SCD in children with varying CM phenotypes from a long-term population-based study of childhood CM. METHODS: The NACCS (National Australian Childhood Cardiomyopathy Study) is an ongoing longitudinal cohort study including all children in Australia with primary CM who were diagnosed between January 1, 1987, and December 31, 1996, and were <10 years of age. The cumulative incidence and risk factors for SCD within individual CM phenotypes were explored using survival analysis. RESULTS: Of 289 eligible patients, 16 (5.5%) experienced SCD over a median follow-up of 11.9 years (interquartile range: 1.7 to

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15.4). The risk of SCD varied according to CM phenotype (p=0.007). The cumulative incidence of SCD at 15 years was 5% for dilated cardiomyopathy (DCM), 6% for hypertrophic cardiomyopathy (HCM), 12% for restrictive cardiomyopathy, and 23% for left ventricular (LV) noncompaction. Older age at diagnosis, positive family history of CM, and severity of LV dysfunction were related to increased risk of SCD in patients with DCM, and a higher posterior wall thickness Z-score was the sole risk factor identified for patients with HCM. CONCLUSIONS: Predictors of SCD include CM phenotype, family history of CM (DCM), severity of systolic dysfunction (DCM), and extent of LV hypertrophy (HCM). Continuing follow-up of this cohort into adulthood is likely to reveal an ongoing risk of SCD.

Blyth CC, Cheng AC, Jacoby P, Effler PV, Smith DW, Kelly H, Macartney KK and Richmond PC.
The effectiveness of influenza vaccination in preventing hospitalisation in children in Western Australia. Vaccine. 2015.
BACKGROUND: There is increasing evidence demonstrating influenza vaccine effectiveness (VE) in the prevention of influenza in children, including the very young. Data demonstrating the effectiveness against severe disease, including hospitalisation, are limited. We aimed to determine the VE of the southern hemisphere trivalent inactivated influenza vaccine (TIV) in preventing laboratory-confirmed influenza-associated hospitalisation in children. PATIENTS AND METHODS: Laboratory records were used to identify children with confirmed influenza hospitalised (i.e., cases) during a 5 year period (2008, 2010-2013) at the only tertiary paediatric facility in Western Australia. Cases and time, age and ward matched controls were retrospectively reviewed to determine risk factors, vaccination status and outcome. Adjusted odds ratios and VE estimates were derived using conditional logistic regression models. RESULTS: Three hundred and eighty five cases were identified (Influenza A, 64.9%; Influenza B, 35.1%). Influenza-like illness and pneumonia were the most frequent presentation (74.5% and 23.9%, respectively). The median length of stay was 2 days (Interquartile range 1-4 days). Twenty children (5.2%) required admission to the intensive care unit. Vaccine uptake in cases and controls was low (4.9% and 8.5%, respectively). Three hundred and six case-control pairs were included in the VE analysis, of which 19 pairs were informative with discrepant vaccination status. VE (fully vaccinated vs. unvaccinated) was estimated to be 62.3% (95% CI: -6.6%, 86.7%). CONCLUSION: In this study, the point estimate for the effectiveness of TIV in preventing influenza-associated hospitalisation in children was similar to that reported for emergency or outpatient attended, laboratory-confirmed influenza, yet confidence intervals were wide. Vaccine uptake remains low. Studies, enrolling larger numbers of children, ideally with higher vaccine uptake, are needed to provide additional evidence on TIV protection against influenza hospitalisation in children.

Influenza Vaccine Effectiveness and Uptake in Children at Risk of Severe Disease.
The Pediatric infectious disease journal. 2015.
BACKGROUND: Data demonstrating the effectiveness of inactivated trivalent influenza vaccine (TIV) for children at increased risk of severe disease are limited. Our objective was to determine the effectiveness of TIV in children with risk factors for severe disease and to compare vaccine uptake, parental attitudes and prescriber recommendations in children with and without risk factors for severe disease. METHODS: Children aged 6-59 months presenting for emergency care (2008-2014) with an influenza-like illness were eligible. Influenza PCR/culture were performed on nasopharyngeal samples. Vaccination status was confirmed via the national register and/or vaccine providers. The test-negative design was used to estimate vaccine effectiveness (VE). Risk factors, parental attitudes and prescriber recommendations were assessed by parental questionnaire. RESULTS: 2723 children were recruited. Risk factors for severe disease included comorbid medical conditions (11.6%), preterm birth (13.0%) and indigeneity (5.0%). Influenza was identified in 546 (20.1%) participants. Overall VE (2008, 2010-2014) was 70.0% (95%CI: 47.7,82.9); VE for children with medical comorbidities, children born preterm, and children <2 years were 82.5% (14.6,96.4), 79.2% (10.9,95.1) and 84.7% (49.6,95.3) respectively. Following adverse events in 2010, the number of children fully vaccinated with TIV declined significantly. This included children with and without risk factors for severe disease. Attitudes were similar in parents of children with and without risk factors for severe disease. CONCLUSIONS: VE for TIV in young children with and without risk factors for severe disease was >/=70%. Despite this, participation in the preschool influenza vaccination program remains low with parents and prescribers unconvinced of the benefits and safety of TIV.

Blyth CC, Walls T, Cheng AC, Murray RJ, Fisher DA, Ingram PR and Davis JS.
A comparison of paediatric and adult infectious diseases consultations in Australia and New Zealand.

Five-Year Antibody Persistence And Safety Following a Single Dose of Combined Haemophilus Influenzae Type B-Neisseria Meninigitidis Serogroup C-Tetanus Toxoid Conjugate Vaccine in Hib-Primed Toddlers.
The Pediatric infectious disease journal. 2015; 34(12): 1379-1384.

BACKGROUND: Antibody persistence is evaluated in healthy Australian children four and five years post-vaccination with a single dose of combined Haemophilus influenzae type b - Neisseria meningitidis serogroup C tetanus toxoid conjugate vaccine (Hib-MenC-TT) compared to separately administered Hib-TT and MenC-CRM197 vaccines (Hib+MCC).

METHODS: This is another follow-up of a phase III, open, randomized, controlled study (NCT00326118), in which 433 Hib-primed but MenC naive toddlers aged 12 to 18 months were randomized 3:1 to receive Hib-MenC-TT or Hib+MCC vaccines. Protection against i) MenC was measured by serum bactericidal antibody assay using rabbit complement (rSBA) and ii) against Hib by enzyme-linked immunosorbent assay of antibodies to polyribosylribitol phosphate (anti-PRP).

Study children were assessed for any potentially vaccine-related serious adverse events (SAEs) at each persistence study visit. RESULTS: The according-to-protocol cohorts for persistence at Years 4 and 5 included 282 and 263 children, respectively. The percentages of children with rSBA-MenC titers >1:8 at Years 4 and 5 were 12.5% and 19.0%, respectively, in the Hib-MenC group; and 12.3% and 25.0%, in the Hib+MCC group. All children in each group had anti-PRP concentrations >0.15 mug/ml at Year 5. Exploratory analyses suggested no potential differences between groups in rSBA-MenC or anti-PRP antibody persistence. No vaccine-related SAEs were reported.

CONCLUSIONS: Antibody persistence was similar for Years 4 and 5 after Hib-MenC-TT or Hib+MCC vaccination, with the majority of children retaining anti-PRP antibody concentrations >0.15 mug/ml at both timepoints. The percentage of children retaining rSBA-MenC titers >1:8 was low (<25%), suggesting that a MenC booster dose may be warranted before adolescence.

Bowen AC, Mahe A, Hay RJ, Andrews RM, Steer AC, Tong SY and Carapetis JR


OBJECTIVE: We conducted a comprehensive, systematic review of the global childhood population prevalence of impetigo and the broader condition pyoderma. METHODS: PubMed was systematically searched for impetigo or pyoderma studies published between January 1 1970 and September 30 2014. Two independent reviewers extracted data from each relevant article on the prevalence of impetigo. FINDINGS: Sixty-six articles relating to 89 studies met our inclusion criteria. Based on population surveillance, 82 studies included data on 145,028 children assessed for pyoderma or impetigo. Median childhood prevalence was 12.3% (IQR 4.2-19.4%). Fifty-eight (65%) studies were from low or low-middle income countries, where median childhood prevalences were 8.4% (IQR 4.2-16.1%) and 14.5% (IQR 8.3-20.9%), respectively. However, the highest burden was seen in underprivileged children from marginalised communities of high-income countries; median prevalence 19.4% (IQR 3.9-43.3%). CONCLUSION: Based on data from studies published since 2000 from low and low-middle income countries, we estimate the global population of children suffering from impetigo at any one time to be in excess of 162 million, predominantly in tropical, resource-poor contexts. Impetigo is an under-recognised disease and in conjunction with scabies, comprises a major childhood dermatological condition with potential lifelong consequences if untreated.

Bradshaw S, Hellwig L, Peate D and Wilson A.

Promoting the uptake of preventative Aboriginal child health policy in Western Australia.


PROBLEM: Australian Aboriginal children are over-represented on all negative health indicators compared with non-Aboriginal children. Contributing factors to the disparity include the impact of historical events, racism and social determinants of health. Despite the benefits of child health checks, offered through the Medicare Benefit Schedule and community health services, uptake of these is low. DESIGN: In 2012, Western Australia Health implemented the Enhanced Aboriginal Child Health Schedule (EACHS) policy to address specific health needs of Aboriginal children. The Aboriginal Child Health Project (the Project), was a five-year initiative funded through the Council of Australian Governments. Project staff promoted the profile of preventative child health and the uptake of the EACHS policy across the state by agencies operating in the sector. SETTING: Western Australia. KEY MEASUREMENTS FOR IMPROVEMENT: Reach of the implementation workshop was measured by the number of staff attending policy implementation and the total number for agencies represented. One measure of impact was the number of agencies requesting the EACHS policy who adapted or adopted it to deliver evidence based comprehensive child health programs. STRATEGIES FOR CHANGE: The Project offered policy implementation workshops to health staff delivering services to young Aboriginal children. In addition to the evidence-based policy, a suite of resources were made available to support service delivery. EFFECTS OF CHANGE: The EACHS is a framework used by agencies to deliver consistent care and support governance

Updated 8/12/15
when providing child health services to Aboriginal families across Western Australia. LESSONS LEARNT: Providing a policy that was consistent with identified service strengths allowed agencies to individually build their capacity to deliver child health checks, using existing resources, at their own pace.

Brennan-Jones CG, Taljaard DS, Brennan-Jones SE, Bennett RJ, Swanepoel W and Eikelboom RH.
Self-reported hearing loss and manual audiometry: A rural versus urban comparison.
Aust J Rural Health. 2015.
OBJECTIVE: To examine whether self-reported hearing difficulty is an accurate measure of hearing loss compared with standard hearing screening with pure tone audiometry in rural and urban communities. DESIGN: Convenience sampling. SETTING: Urban and rural areas of Western Australia. PARTICIPANTS: A total of 2090 participants (923 men; 1165 women; 2 unknown) aged 20-100 years presenting for community-based hearing screening in urban (982) and rural (1090) areas. INTERVENTIONS: Self-reported hearing difficulty assessed with the Hearing Handicap Inventory for the Elderly - Screening questionnaire. Hearing loss defined as average hearing thresholds >25 dB in the better ear using screening audiometry conducted at 500, 1000, 2000 and 4000 Hz. MAIN OUTCOME MEASURES: Nil. RESULTS: The Hearing Handicap Inventory for the Elderly - Screening was sensitive (>/>=60 years = 76.69%; <60 years = 71.67%) but not specific (>/>=60 years = 45.15%; <60 years = 49.63%) for identifying hearing loss. The <60 age group had a hearing loss prevalence of 25.6%, and a false-positive rate of 67.12% compared with a prevalence of 69.12% and false-positive rate of 29.77% for the >=60 age group. For all ages, rural participants were more likely to have a disabling hearing loss (odds ratio 2.04 (95% confidence interval, 1.55-2.67); chi2 (1) = 27.28; P < 0.001), but there were no significant differences in hearing aid uptake. CONCLUSIONS: Patients in rural areas presenting for hearing screenings are more likely to suffer hearing loss than adults in urban areas. We suggest rural health practitioners incorporate a self-reported hearing loss questionnaire into health check-ups for adults, particularly patients aged >/>=60 years due to the high prevalence of hearing loss in this group.

Buratto E, McCrossan B, Galati JC, Bullock A, Kelly A, d’Udekem Y, Brizard CP and Konstantinov IE.
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 in adulthood.

Campbell DE, Boyle RJ, Thornton CA and Prescott SL.
Mechanisms of Allergic Disease - Environmental and genetic determinants for the development of allergy.
Clinical & Experimental Allergy. 2015: n/a-n/a.

Carapeti JD.
The stark reality of rheumatic heart disease.
Eur Heart J. 2015; 36(18): 1070-1073.

Influenza epidemiology in adults admitted to sentinel Australian hospitals in 2014: the Influenza Complications Alert Network (FluCAN).
The Influenza Complications Alert Network (FluCAN) is a sentinel hospital-based surveillance program that operates at sites in all states and territories in Australia. This report summarises the epidemiology of hospitalisations with laboratory-confirmed influenza during the 2014 influenza season. In this observational study.
study, cases were defined as patients admitted to one of the sentinel hospitals with an acute respiratory illness with influenza confirmed by nucleic acid detection. During the period 3 April to 31 October 2014 (the 2014 influenza season), 1,692 adult patients (>16 years) were admitted with confirmed influenza to one of 15 of 17 FluCAN sentinel hospitals (excluding 2 paediatric hospitals). Of these, 47% were over 65 years of age, 10% were Indigenous Australians, 3.3% were pregnant and 85% had chronic co-morbidities. The majority of cases were due to influenza A. Influenza B was detected in 7% of patients. There were a large number of hospital admissions detected with confirmed influenza in this national observational surveillance system in 2014. These are estimated to represent a national annual burden of around 15,000 admissions and almost 100,000 bed-days nationally. Commun Dis Intell 2015;39(3):E355-E360.

Chesshyre E, Goff Z, Bowen A and Carapetis J.
The prevention, diagnosis and management of central venous line infections in children.
With advancing paediatric healthcare, the use of central venous lines has become a fundamental part of management of neonates and children. Uses include haemodynamic monitoring and the delivery of lifesaving treatments such as intravenous fluids, blood products, antibiotics, chemotherapy, haemodialysis and total parenteral nutrition (TPN). Despite preventative measures, central venous catheter-related infections are common, with rates of 0.5-2.8/1000 catheter days in children and 0.6-2.5/1000 catheter days in neonates. Central line infections in children are associated with increased mortality, increased length of hospital and intensive care unit stay, treatment interruptions, and increased complications. Prevention is paramount, using a variety of measures including tunnelling of long-term devices, chlorhexidine antisepsis, maximum sterile barriers, aseptic non-touch technique, minimal line accessing, and evidence-based care bundles. Diagnosis of central line infections in children is challenging. Available samples are often limited to a single central line blood culture, as clinicians are reluctant to perform painful venepuncture on children with a central, pain-free, access device. With the advancing evidence basis for antibiotic lock therapy for treatment, paediatricians are pushing the boundaries of line retention if safe to do so, due to among other reasons, often limited venous access sites. This review evaluates the available paediatric studies on management of central venous line infections and refers to consensus guidelines such as those of the Infectious Diseases Society of America (IDSA).

Cho YH, Craig ME, Davis EA, Cotterill AM, Couper JJ, Cameron FJ, Benitez-Aguirre PZ, Dalton RN, Dunger DB, Jones TW and Donagheur KC.
Cardiac autonomic dysfunction is associated with high-risk albumin-to-creatinine ratio in young adolescents with type 1 diabetes in AdDiT (adolescent type 1 diabetes cardio-renal interventional trial).
OBJECTIVE: This study examined the association between cardiac autonomic dysfunction and high albumin-to-creatinine ratio (ACR) in adolescents with type 1 diabetes. RESEARCH DESIGN AND METHODS: Adolescents recruited as part of a multicenter screening study (n = 445, 49% female, aged 10-17 years, mean duration 6.9 years; mean HbA1c 8.4%, 68 mmol/mol) underwent a 10-min continuous electrocardiogram recording for heart rate variability analysis. Time-domain heart rate variability measures included baseline heart rate, SD of the R-R interval (SDNN), and root mean squared difference of successive R-R intervals (RMSSD). Spectral analysis included sympathetic (low-frequency) and parasympathetic (high-frequency) components. Standardized ACR were calculated from six early morning urine collections using an established algorithm, reflecting age, sex, and duration, and stratified into ACR tertiles, where the upper tertile reflects higher nephropathy risk. RESULTS: The upper tertile ACR group had a faster heart rate (76 vs. 73 bpm; P < 0.01) and less heart rate variability (SDNN 68 vs. 76 ms, P = 0.02; RMSSD 63 vs. 71 ms, P = 0.04). HbA1c was 8.5% (69 mmol/mmol) in the upper tertile vs. 8.3% (67 mmol/mmol) in the lower tertiles (P = 0.07). In multivariable analysis, upper-tertile ACR was associated with faster heart rate (beta = 2.5, 95% CI 0.2-4.8, P = 0.03) and lower RMSSD (beta = -9.5, 95% CI -18.2 to -0.8, P = 0.03), independent of age and HbA1c. CONCLUSIONS: Adolescents at potentially higher risk for nephropathy show an adverse cardiac autonomic profile, indicating sympathetic overdrive, compared with the lower-risk group. Longitudinal follow-up of this cohort will further characterize the relationship between autonomic and renal dysfunction and the effect of interventions in this population.

Criteria led discharge reduces length of hospital stay for children with acute asthma.
The Journal of asthma : official journal of the Association for the Care of Asthma. 2015: 1.

The relationship between Bordetella pertussis genotype and clinical severity in Australian children with pertussis.
J Infect. 2015.

Updated 8/12/15
OBJECTIVES: Changes in circulating Bordetella pertussis genotypes, including a novel pertussis toxin promoter ptxP3 allele and absence of pertactin (Prn) antigen, have been reported from several countries but limited data on relative severity are available. We compared markers of disease severity in children with B. pertussis infection due to strains of differing genotype. METHODS: Culture confirmed cases presenting to tertiary paediatric hospitals in three Australian states between 2008 and 2012 were classified as severe if they required a hospital stay greater than seven days, were admitted to intensive care, or if death occurred. Associations between age, vaccination, genotype and severity were assessed. RESULTS: Of 199 pertussis cases, 81 (41%) were <3 months, including 32/39 (82%) of severe cases. The proportion of isolates from these cases that were Prn deficient increased markedly between 2008 and 2012. Of B. pertussis isolates, the proportion considered severe was similar for Prn positive (27/128, 21%) and Prn deficient (12/71, 17%) cases but only 1/22 (4.5%) of non ptxP3 cases were severe versus 38/177 (21.4%) ptxP3 positive. Adjusting for ptxP type, vaccination status and age, disease severity was not significantly associated with Prn status (RRA: 0.95, [0.57-1.56]; p = 0.83). CONCLUSIONS: In children, we found no relationship between Prn status and markers of severe pertussis. An increased proportion of severe disease in isolates with the ptxP3 allele was observed.


One of the great success stories of modern medicine is undoubtedly the remarkable improvement in outcome for childhood cancer, achieved through the work of the co-operative groups enrolling patients in randomised controlled trials. In 1965, survival was almost zero; now 5-year survival rates exceed 80% in high-income countries. The lessons learned in the care of patients with the most common malignancy in childhood - acute lymphoblastic leukaemia - have been used in all other cancers of childhood and more recently in the management of adults. These lessons can be broadly applied in medical practice, because elements of laboratory science in all branches of pathology, as well as a deep understanding of biochemistry, physiology, pharmacology, genetics and molecular science, run through this story. Far from being a sad area of practice, paediatric haematology and oncology remains the champion of embedded clinical and translational research, diagnosis from bench to bedside and lifelong multidisciplinary management of the child and their family.


INTRODUCTION: Inflammatory myofibroblastic tumours of the bladder (IMTB) are rare, and feature a benign and reactive proliferation of myofibroblasts. 25% of the reported IMTB cases in the literature occur in children. The present study presents a review of IMTB in children. DISCUSSION: The data from 42 reported cases of paediatric IMTB in the world literature are summarised, including two recent cases from the present centre. Paediatric IMTB equally affects males and females. It mainly presents with haematuria, dysuria or abdominal pain. Lesions can vary in size, but mean size is 5.5 cm. Mean age is 7.5 years. The aetiology of IMTB is poorly understood, but includes infective or traumatic aetiologies, or a possible clonal lesion. IMTB may specifically show clonal gene rearrangements involving the anaplastic lymphoma kinase (ALK-1) gene. To differentiate IMTB from rhabdomyosarcoma, tissue diagnosis and careful histological analysis are essential. Tumour biopsy can be achieved by a transurethral approach or a transcutaneous approach with ultrasound guidance. Between 35 and 89% of cases of IMTB express ALK-1 by immunohistochemistry. ALK-1 expression is much less common in other bladder soft tissue tumours. ALK-1 is thus useful in the diagnosis of IMTB. The treatment of choice for IMTB is complete surgical resection of the lesion. In children, no proven recurrent or metastatic IMTB episodes are reported after excision. However IMTB recurrences are reported in adults, likely due to incomplete excision. Follow-up after excision is therefore recommended. CONCLUSIONS: Paediatric IMTB is uncommon. Tissue biopsy is essential for diagnosis. Careful histological assessment is required to differentiate IMTB from malignant paediatric bladder tumours such as rhabdomyosarcoma. ALK-1 expression is useful in confirming the diagnosis of IMTB. Treatment of choice is complete surgical resection of the lesion. Recurrence is reported in adult IMTB. Follow-up is therefore recommended.


OBJECTIVE: To determine if improvements in cognitive outcome detected at 18 months’ corrected age (CA) in infants born <33 weeks’ gestation receiving a high-docosahexaenoic acid (DHA) compared with standard-DHA diet were sustained in early childhood. DESIGN: Follow-up of a multicentre randomised controlled trial. Randomisation was stratified for sex, birth weight (<1250 vs >=1250 g) and hospital. SETTING: Five Australian...
tertiary hospitals from 2008 to 2013. PARTICIPANTS: 626 of the 657 participants randomised between 2001 and 2005 were eligible to participate. INTERVENTIONS: High-DHA (approximately 1% total fatty acids) enteral feeds compared with standard-DHA (approximately 0.3% total fatty acids) from age 2-4 days until term CA. PRIMARY OUTCOME: Full Scale IQ of the Wechsler Abbreviated Scale of Intelligence (WASI) at 7 years CA. Prespecified subgroup analyses based on the randomisation strata (sex, birth weight) were conducted. RESULTS: 604 (92% of the 657 originally randomised) consented to participate (291 high-DHA, 313 standard-DHA). To address missing data in the 604 consenting participants (22 for primary outcome), multiple imputation was performed. The Full Scale IQ was not significantly different between groups (high-DHA 98.3, SD 14.0, standard-DHA 98.5, SD 14.9; mean difference adjusted for sex, birthweight strata and hospital -0.3, 95% CI -2.9 to 2.2; p=0.79). There were no significant differences in any secondary outcomes. In prespecified subgroup analyses, there was a significant sex by treatment interaction on measures of parent-reported executive function and behaviour. Scores were within the normal range but girls receiving the high-DHA diet scored significantly higher (poorer outcome) compared with girls receiving the standard-DHA diet. CONCLUSIONS: Supplementing the diets of preterm infants with a DHA dose of approximately 1% total fatty acids from days 2-4 until term CA showed no evidence of benefit at 7 years’ CA. TRIAL REGISTRATION NUMBER: Australian New Zealand Clinical Trials Registry: ACTRN12606000327583.


Australia remains the only developed country to have endemic levels of trachoma (a prevalence of 5% or greater among children) in some regions. Endemic trachoma in Australia is found predominantly in remote and very remote Aboriginal communities. The Australian Government funds a National Trachoma Surveillance and Reporting Unit to collate, analyse and report trachoma prevalence data and document trachoma control strategies in Australia through an annual surveillance report. This report presents data collected in 2012. Data are collected from Aboriginal and Torres Strait communities designated as at-risk for endemic trachoma in the Northern Territory, Queensland, South Australia and Western Australia. The World Health Organization grading criteria were used to diagnose cases of trachoma in Aboriginal children with jurisdictions focusing screening activities on the 5-9 years age group; however, some children in the 1-4 and 10-14 years age groups were also screened. The prevalence of trachoma within a community was used to guide treatment strategies as a public health response. Aboriginal adults aged 40 years or older were screened for trichiasis. Community screening coverage of the designated at-risk communities was 96%. Screening coverage of the estimated population of children aged 5-9 years and adults aged 40 years or older in at-risk communities was 71% and 31%, respectively. Trachoma prevalence among children aged 5-9 years who were screened was 4%. Of communities screened, 63% were found to have no cases of active trachoma and 25% were found to have endemic levels of trachoma. Treatment was required in 87 at-risk communities screened. Treatment coverage of active cases and their contacts varied from 79%-97% between jurisdictions. Trichiasis prevalence was 2% within the screened communities.

Cox DW, Mullane D, Zhang GC, Turner SW, Hayden CM, Goldblatt J, Landau LI and Le Souef PN.
Longitudinal assessment of airway responsiveness from 1 month to 18 years in the PIAF birth cohort.
The European respiratory journal : official journal of the European Society for Clinical Respiratory Physiology. 2015.
The Perth Infant Asthma Follow-up (PIAF) study involves a birth cohort of unselected subjects who have undergone longitudinal assessments of airway responsiveness at 1, 6 and 12 months and 6, 11 and 18 years of age. The aim of this study was to determine the relationship between increased airway responsiveness throughout childhood and asthma in early adult life. Airway responsiveness to histamine, assessed as a dose-response slope (DRS), and a respiratory questionnaire were completed at 1, 6 and 12 months and 6, 11 and 18 years of age. 253 children were initially recruited and studied. Airway responsiveness was assessed in 203, 174, 147, 103, 176 and 137 children at the above-mentioned time points, respectively (39 participants being assessed on all test occasions). Asthma at 18 years was associated with increased airway responsiveness at 6, 12 and 18 years, but not during infancy (slope 0.24, 95% CI 0.06-0.42; p=0.01; slope 0.25, 95% CI 0.08-0.49; p=0.006; and slope 0.56, 95% CI 0.29-0.83; p<0.001, respectively). Increased airway responsiveness and its association with asthma at 18 years is established between infancy and 6 years. We propose that airway responsiveness in early life reflects the initial airway geometry and airway responsiveness later in childhood increasingly reflects immunological responses to environmental influences.

Electronic monitoring and reminding devices for improving adherence to inhaled therapy in patients with asthma. Cochrane Database of Systematic Reviews. DOI: 10.1002/14651858.CD011554

Updated 8/12/15
This is the protocol for a review and there is no abstract. The objectives are as follows: To assess the efficacy of electronic monitors, reminder devices or both, on adherence with regular inhaled medication regimes in people with asthma.

Czarniak P, Bint L, Favie L, Parsons R, Hughes J and Sunderland B.
Clinical setting influences off-label and unlicensed prescribing in a paediatric teaching hospital.

PURPOSE: To estimate the prevalence of off-label and unlicensed prescribing during 2008 at a major paediatric teaching hospital in Western Australia. METHODS: A 12-month retrospective study was conducted at Princess Margaret Hospital using medication chart records randomly selected from 145,550 patient encounters from the Emergency Department, Inpatient Wards and Outpatient Clinics. Patient and prescribing data were collected. Drugs were classified as off-label or unlicensed based on Australian registration data. A hierarchical system of age, indication, route of administration and dosage was used. Drugs were classified according to the Anatomical Therapeutic Chemical Code. RESULTS: A total of 1,037 paediatric patients were selected where 2,654 prescriptions for 330 different drugs were prescribed to 699 patients (67.4%). Most off-label drugs (n = 295; 43.3%) were from the nervous system; a majority of unlicensed drugs were systemic hormonal preparations excluding sex hormones (n = 22, 32.4%). Inpatients were prescribed more off-label drugs than outpatients or Emergency Department patients (p < 0.0001). Most off-label prescribing occurred in infants and children (31.7% and 35.9% respectively) and the highest percentage of unlicensed prescribing (7.2%) occurred in infants (p < 0.0001). There were 25.7% of off-label and 2.6% of unlicensed medications prescribed across all three settings. Common reasons for off-label prescribing were dosage (47.4%) and age (43.2%).

CONCLUSION: This study confirmed off-label and unlicensed use of drugs remains common. Further, that prevalence of both is influenced by the clinical setting, which has implications in regards to medication misadventure, and the need to have systems in place to minimise medication errors. Further, there remains a need for changes in the regulatory system in Australia to ensure that manufacturers incorporate, as it becomes available, evidence regarding efficacy and safety of their drugs in children in the official product information.

Neurodevelopmental outcome at 2 years of age after general anaesthesia and awake-regional anaesthesia in infancy (GAS): an international multicentre, randomised controlled trial.
Lancet. 2015.

BACKGROUND: Preclinical data suggest that general anaesthetics affect brain development. There is mixed evidence from cohort studies that young children exposed to anaesthesia can have an increased risk of poor neurodevelopmental outcome. We aimed to establish whether general anaesthesia in infancy has any effect on neurodevelopmental outcome. Here we report the secondary outcome of neurodevelopmental outcome at 2 years of age in the General Anaesthesia compared to Spinal anaesthesia (GAS) trial. METHODS: In this international assessor-masked randomised controlled equivalence trial, we recruited infants younger than 60 weeks postmenstrual age, born at greater than 26 weeks’ gestation, and who had inguinal herniorrhaphy, from 28 hospitals in Australia, Italy, the USA, the UK, Canada, the Netherlands, and New Zealand. Infants were randomly assigned (1:1) to receive either awake-regional anaesthesia or sevoflurane-based general anaesthesia. Web-based randomisation was done in blocks of two or four and stratified by site and gestational age at birth. Infants were excluded if they had existing risk factors for neurological injury. The primary outcome of the trial will be the Wechsler Preschool and Primary Scale of Intelligence Third Edition (WPPSI-III) Full Scale Intelligence Quotient score at age 5 years. The secondary outcome, reported here, is the composite cognitive score of the Bayley Scales of Infant and Toddler Development III, assessed at 2 years. The analysis was as per protocol adjusted for gestational age at birth. A difference in means of five points (1/3 SD) was predefined as the clinical equivalence margin. This trial is registered with ANZCTR, number ACTRN1260600441516 and ClinicalTrials.gov, number NCT00756600.

FINDINGS: Between Feb 9, 2007, and Jan 31, 2013, 363 infants were randomly assigned to receive awake-regional anaesthesia and 359 to general anaesthesia. Outcome data were available for 238 children in the awake-regional group and 294 in the general anaesthesia group. In the as-per-protocol analysis, the cognitive composite score (mean [SD]) was 98.6 (14.2) in the awake-regional group and 98.2 (14.7) in the general anaesthesia group. There was equivalence in mean between groups (awake-regional minus general anaesthesia 0.169, 95% CI -2.30 to 2.64). The median duration of anaesthesia in the general anaesthesia group was 54 min. INTERPRETATION: For this secondary outcome, we found no evidence that just less than 1 h of sevoflurane anaesthesia in infancy increases the risk of adverse neurodevelopmental outcome at 2 years of age compared with awake-regional anaesthesia.

FUNDING: Australia National Health and Medical Research Council (NHMRC), Health Technologies Assessment-National Institute for Health Research UK, National Institutes of Health, Food and Drug Administration, Australian and
New Zealand College of Anaesthetists, Murdoch Childrens Research Institute, Canadian Institute of Health Research, Canadian Anesthesiologists' Society, Pfizer Canada, Italian Ministry of Heath, Fonds NutsOhra, and UK Clinical Research Network (UKCRN).

Davies K, Bulsara MK, Ramelet AS and Monterosso L. 
Audit of Endotracheal Tube Suction in a Pediatric Intensive Care Unit. 
Clin Nurs Res. 2015. 
We report outcomes of a clinical audit examining criteria used in clinical practice to rationalize endotracheal tube (ETT) suction, and the extent these matched criteria in the Endotracheal Suction Assessment Tool (ESAT(c)). A retrospective audit of patient notes (N = 292) and analyses of criteria documented by pediatric intensive care nurses to rationalize ETT suction were undertaken. The median number of documented respiratory and ventilation status criteria per ETT suction event that matched the ESAT(c) criteria was 2 [Interquartile Range (IQR) 1-6]. All criteria listed within the ESAT(c) were documented within the reviewed notes. A direct link was established between criteria used for current clinical practice of ETT suction and the ESAT(c). The ESAT(c), therefore, reflects documented clinical decision making and could be used as both a clinical and educational guide for inexperienced pediatric critical care nurses. Modification to the ESAT(c) requires "preparation for extubation" to be added.

Davies K, Monterosso L, Bulsara M and Ramelet AS. 
Clinical indicators for the initiation of endotracheal suction in children: An integrative review. 
BACKGROUND: Critical decisions and interpretation of observations by the nurse caring for the paediatric intensive care (PIC) patient can have dramatic and potential adverse impact on the clinical stability of the patient. A common PIC procedure is endotracheal tube (ETT) suction, however there is inconsistent evidence regarding the clinical indicators to guide and support nursing action. Justification for performing this procedure is not clearly defined within the literature. Further, a review of the literature has failed to establish clear standards for determining if the procedure is warranted, especially for paediatric patients. OBJECTIVE: The objective of the review is to identify current clinical indicators used in practice to determine why ETT suction should be performed. METHOD: An integrative review using a systematic approach to summarise the empirical and theoretical evidence within the literature as it relates to clinical practice was used. RESULTS: Consensus of opinion indicates that ETT suctioning should only be performed when clinically indicated. There is no general consensus regarding which clinical indicators should be measured and used to guide the decision to perform ETT suctioning. CONCLUSION: Research is required to identify the clinical indicators that could be used to design a valid and clinically appropriate tool to use to assist in the decision making process to perform ETT suction.

de Bock M, Roy A, Dart J, Keenan B, Davis E and Jones T. 
Day and night glucose control using a hybrid closed loop system for the management of type 1 diabetes. 

de Bock MI, Roy A, Cooper MN, Dart JA, Berthold CL, Retterath AJ, Freeman KE, Grosman B, Kurtz N, Kaufman F, Jones TW and Davis EA. 
Feasibility of Outpatient 24-Hour Closed-Loop Insulin Delivery. 

de Dassel JL, Ralph AP and Carapetis JR. 
Controlling acute rheumatic fever and rheumatic heart disease in developing countries: are we getting closer? 
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

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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.

Deshmukh M, Balasubramanian H, Rao S and Patole S.
Effect of gastric lavage on feeding in neonates born through meconium-stained liquor: a systematic review.
Arch Dis Child Fetal Neonatal Ed. 2015; 100(5): F394-399.

OBJECTIVE: To evaluate the efficacy and safety of gastric lavage (GL) in neonates born through meconium-stained liquor (MSL). DESIGN: A systematic review of randomised controlled trials by searching databases MEDLINE (from 1966), EMBASE (from1980), CINAHL, Cochrane Central Register of Controlled Trials, Google Scholar and proceedings of Pediatric Academic Society meetings (2002-2014). SETTING: Delivery room/Neonatal ward. PATIENTS: Neonates with gestation >34 weeks and birth weight >/=1800 g born through MSL. INTERVENTIONS: Prophylactic GL versus no intervention before first feed. MAIN OUTCOME MEASURE: Feeding intolerance, defined as inability to initiate/upgrade feeds due to problems such as retching, vomiting, regurgitation and gastric residuals. RESULTS: A total of six studies (GL: 918, no GL: 966) were included in the review. Meta-analysis using fixed-effects model showed decreased incidence of feed intolerance following GL ((81/918 (8.8%) vs 114/966 (11.8%); risk ratio (RR): 0.71 (95% CI 0.55 to 0.93)). However, the results were not significant when random-effects model was used (RR: 0.78 (95% CI 0.55 to 1.09)). No significant adverse effects of GL were reported. CONCLUSIONS: Routine GL immediately after birth may improve feed tolerance in neonates born through MSL. However, the evidence is limited, with probable small-study bias and high risk of bias in a number of the included studies. Well-designed studies with adequate sample size are essential to confirm these findings.

Deshpande G, Rao S and Patole S.
Probiotics in neonatal intensive care - Back to the future.
Survival of extremely preterm and critically ill neonates has improved significantly over the last few decades following advances in neonatal intensive care. These include antenatal glucocorticoids, surfactant, continuous positive airway pressure support, advanced gentle modes of ventilation and inhaled nitric oxide. Probiotic supplementation is a recent significant milestone in the history of neonatal intensive care. Very few, if any, interventions match the ability of probiotics to significantly reduce the risk of death and definite necrotising enterocolitis while facilitating enteral feeds in high-risk preterm neonates. Probiotics also have a potential to benefit neonates with surgical conditions with significant gastrointestinal morbidity. Current evidence for the benefits of probiotic supplementation for neonates in an intensive care unit is reviewed. The mechanisms for the benefits of probiotics in this population are discussed, and guidelines for clinicians are provided in the context of the regulatory framework in Australia.

Dewar R, Love S and Johnston LM.
Exercise interventions improve postural control in children with cerebral palsy: a systematic review.
Aim: The aim of this study was to evaluate the efficacy and effectiveness of exercise interventions that may improve postural control in children with cerebral palsy (CP). Method: A systematic review was performed using American Academy of Cerebral Palsy and Developmental Medicine (AACPDM) and Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) methodology. Six databases were searched using the following keywords: (‘cerebral palsy’ OR ‘brain injury’); AND (‘postur’ OR ‘balance’ OR ‘postural balance’ [MeSH]); AND (‘intervention’ OR ‘therapy’ OR ‘exercise’ OR ‘treatment’). Articles were evaluated based on their level of evidence and conduct. Results: Searches yielded 45 studies reporting 13 exercise interventions with postural control outcomes for children with CP. Five interventions were supported by a moderate level of evidence: gross motor task training, hippotherapy, treadmill training with no body weight support (no-BWS), trunk-targeted training, and reactive balance training. Six of the interventions had weak or conflicting evidence: functional electrical stimulation (FES), hippotherapy simulators, neurodevelopmental therapy (NDT), treadmill training with body weight support, virtual reality, and visual biofeedback. Progressive resistance exercise was an ineffective intervention, and upper limb interventions lacked high-level evidence. Interpretation: The use of exercise-based treatments to improve postural control in children with CP has increased significantly in the last decade. Improved study design provides more clarity regarding broad treatment efficacy. Research is required to establish links between postural control impairments, treatment options, and outcome measures. Low-burden, low-cost, child-engaging, and mainstream interventions also need to be explored.

The Natural History of Scoliosis in Females with Rett Syndrome.

Updated 8/12/15
STUDY DESIGN: Population-based longitudinal observational study. OBJECTIVES: To describe the prevalence of scoliosis in Rett syndrome, structural characteristics and progression, taking into account the influences of age, genotype and ambulatory status. SUMMARY OF BACKGROUND DATA: Scoliosis is the most common orthopaedic comorbidity in Rett syndrome yet very little is known about its natural history and influencing factors such as age, genotype and ambulatory status. METHODS: The infrastructure of the Australian Rett Syndrome Database was used to identify all cases with confirmed Rett syndrome in Australia and collect data on genotype and walking status. We identified radiological records and described the Cobb angle of each curve. Time to event analysis was used to estimate the median age of onset of scoliosis and the log rank test to compare by mutation type. Latent class group analysis was used to identify groups for the trajectory of walking status over time and a multilevel linear model used to assess trajectories of scoliosis development by mutation type and walking status. We used a logistic regression model to estimate the probability of developing a scoliosis with a Cobb angle >60 degrees at 16 years in relation to Cobb angle and walking status at 10 years of age. RESULTS: The median age of scoliosis onset was 11 years with earliest onset in those with a p.Arg255 mutation or large deletion. Scoliosis was progressive for all mutation types except for those with the p.Arg306Cys mutation. Scoliosis progression was reduced when there was capacity to walk independently or with assistance. Cobb angle and walking ability at age 10 can be reliably used to identify those who will develop a very severe scoliosis by age 16. CONCLUSIONS: These data on prognosis of scoliosis inform clinical decision-making about the likelihood of progression to very severe scoliosis and the need for surgical management. LEVEL OF EVIDENCE: 4.

Drake-Brockman TF, Ledowski T, Hegarty M, Gessner M and von Ungern-Sternberg BS.
A comparison of the i-gel() and the PRO-Breathe((R)) laryngeal mask during pressure support ventilation in children.
Anesthesia. 2015; 70(12): 1412-1417.
Many studies comparing the i-gel() with laryngeal masks include patients in whom laryngeal mask cuff inflation pressures are higher than recommended, or involve the use of neuromuscular blocking drugs and positive pressure ventilation. We compared the i-gel with the PRO-Breathe((R)) laryngeal mask in anaesthetised, spontaneously breathing children. Two hundred patients aged up to 16 years were randomly allocated to either the i-gel or the PRO-Breathe laryngeal mask. The PRO-Breathe was inflated to an intracuff pressure of 40 cmH2O. All patients received pressure support of 10 cmH2O and positive end-expiratory pressure of 5 cmH2O. Successful insertion at the first attempt was 82% for the i-gel compared with 93% for the PRO-Breathe (p = 0.019). Leakage volume was significantly higher with i-gel sizes 1.5 (p = 0.015), 2 (p = 0.375), 2.5 (p = 0.021) and 3 (p = 0.003) compared with the equivalent-sized PRO-Breathe device. Device dislodgement following successful initial placement was more frequent with the i-gel (5%) compared with the PRO-Breathe laryngeal mask (0%). We conclude that the PRO-Breathe laryngeal mask is superior to the i-gel in terms of leakage volume and device dislodgement.

A mutation in MT-TW causes a tRNA processing defect and reduced mitochondrial function in a family with Leigh syndrome.
Leigh syndrome (LS) is a progressive mitochondrial neurodegenerative disorder, whose symptoms most commonly include psychomotor delay with regression, lactic acidosis and a failure to thrive. Here we describe three siblings with LS, but with additional manifestations including hypertrophic cardiomyopathy, hepatosplenomegaly, cholestatic hepatitis, and seizures. All three affected siblings were found to be homoplasmic for an m. 5559A>G mutation in the T stem of the mitochondrial DNA-encoded MT-TW by next generation sequencing. The m.5559A>G mutation causes a reduction in the steady state levels of tRNA(Trp) and this decrease likely affects the stability of other mitochondrial RNAs in the patient fibroblasts. We observe accumulation of an unprocessed transcript containing tRNA(Trp), decreased de novo protein synthesis and consequently lowered steady state levels of mitochondrial DNA-encoded proteins that compromise mitochondrial respiration. Our results show that the m.5559A>G mutation at homoplasmic levels causes LS in association with severe multi-organ disease (LS-plus) as a consequence of dysfunctional mitochondrial RNA metabolism.

Duke JM, Boyd JH, Randall SM and Wood FM.
Long term mortality in a population-based cohort of adolescents, and young and middle-aged adults with burn injury in Western Australia: A 33-year study.
BACKGROUND: Advances in the treatment and management of burn patients over the past decades have resulted in a decline of in-hospital mortality rates. Current estimates of burn-related mortality are usually in the

Updated 8/12/15
context of deaths occurring during the admission or within a short time period after the incident burn. Limited data are available that examine long term mortality after burn injury. This study aimed to assess the impact of burn injury on long-term mortality and quantify any increased risk of death attributable to burn injury. METHODS: A population-based cohort study of persons 15-44 years of age hospitalised for burn injury (n=14,559) in Western Australia (1980-2012) and a matched non-injured comparison group (n=56,822) using linked health administrative data was used. Hospital morbidity and death data were obtained from the Western Australian Hospital Morbidity Data System and Death Register. De-identified extraction of all linked hospital morbidity and death records for the period 1980-2012 were provided by the Western Australian Data Linkage System. Survival analysis was conducted using the Kaplan-Meier method and Cox proportional hazards modelling. RESULTS: The adjusted all-cause Mortality Rate Ratio (MRR) for burn injury was 1.8 (95%CI: 1.7-2.0); those with burn injury had a 1.8 times greater rate of mortality than those with no injury. The index burn injury was estimated to account for 44% of all recorded deaths in the burn injury cohort during the study period after discharge. Increased risk of mortality was observed for both severe (MRR, 95%CI: 1.9, 1.3-2.9) and minor (MRR, 95%CI: 2.5, 2.2-3.0) burns. CONCLUSIONS: An increased risk of long-term all-cause mortality is associated with both minor and severe burn injury. Estimates of total mortality burden based on the early inpatient period alone, significantly underestimates the true burden of burn injury in adolescents, and young and middle aged adults. These results have significant implications for burn injury prevention.

Duke JM, Boyd JH, Rea S, Randall SM and Wood FM. 
Long-term mortality among older adults with burn injury: a population-based study in Australia. 
Bull World Health Organ. 2015; 93(6): 400-406.

OBJECTIVE: To assess if burn injury in older adults is associated with changes in long term all-cause mortality and to estimate the increased risk of death attributable to burn injury. METHODS: We conducted a population-based matched longitudinal study - based on administrative data from Western Australia’s hospital morbidity data system and death register. A cohort of 6014 individuals who were aged at least 45 years when hospitalized for a first burn injury in 1980-2012 was identified. A non-injury comparison cohort, randomly selected from Western Australia’s electoral roll (n = 25,759), was matched to the patients. We used Kaplan-Meier plots and Cox proportional hazards regression to analyse the data and generated mortality rate ratios and attributable risk percentages. FINDINGS: For those hospitalized with burns, 180 (3%) died in hospital and 2498 (42%) died after discharge. Individuals with burn injury had a 1.4-fold greater mortality rate than those with no injury (95% confidence interval, Cl: 1.3-1.5). In this cohort, the long-term mortality attributable to burn injury was 29%. Mortality risk was increased by both severe and minor burns, with adjusted mortality rate ratios of 1.3 (95% CI: 1.1-1.9) and 2.1 (95% CI: 1.9-2.3), respectively. CONCLUSION: Burn injury is associated with increased long-term mortality. In our study population, sole reliance on data on in-hospital deaths would lead to an underestimate of the true mortality burden associated with burn injury.

Publisher: Abstract available from the publisher.

Duke JM, Randall SM, Fear MW, Boyd JH, Rea S and Wood FM. 
Increased admissions for musculoskeletal diseases after burns sustained during childhood and adolescence. 

BACKGROUND: Severe burn triggers systemic responses that result in reduced muscle mass and bone formation, with recent evidence also suggesting systemic effects on bone after minor burn. The aim of this study was to assess if children and adolescents who are hospitalised with a burn have increased long-term hospital service use for musculoskeletal conditions. METHODS: A population-based longitudinal study using linked hospital morbidity and death data from Western Australia was undertaken of those younger than 20 years when hospitalized for a first burn (n=13,244) during the period 1980-2012 and a frequency matched non-injury comparison cohort, randomly selected from Western Australia’s birth registrations and electoral roll (n=51,021). Crude admission rates and cumulative length of stay for musculoskeletal diseases were calculated. Negative binomial and Cox proportional hazards regression modelling were used to generate incidence rate ratios (IRR) and hazard ratios (HR), respectively. RESULTS: After adjusting for demographic characteristics and pre-existing health status, those who were hospitalised for a burn had 1.87 times as many hospital admissions for a musculoskeletal disease (95%CI: 1.69-2.08) and spent 2.61 times as long in hospital with musculoskeletal disease (95%CI: 2.09-3.27), than the unjureded comparison cohort. The burn cohort had significantly higher rates of first time admissions over the study period for arthropathies (HR, 95%CI: 1.14, 1.00-1.29, p=0.047), dorsopathies (HR, 95%CI: 1.64, 1.29-2.08) and for soft tissue disorders (HR, 95%CI: 1.33, 1.11-1.60); results were not statistically significant for incident admissions for osteopathies and chondropathies (HR, 95%CI: 1.07, 1.02-1.12).
0.71-1.59) or connective tissue disorders (HR, 95%CI: 0.54, 0.24-2.09). CONCLUSIONS: These results identified elevated post-discharge hospital service use for diseases of the musculoskeletal system for a prolonged period after discharge for those with both severe and minor burns.

Duke JM, Randall SM, Fear MW, Boyd JH, Rea S and Wood FM.
Long-term Effects of Pediatric Burns on the Circulatory System.

BACKGROUND: The systemic responses to burns (in particular, elevated levels of catecholamines and stress hormones) have been shown to have an impact on cardiac function for at least 3 years in children with burns. However, it is not clear if these changes lead to long-term effects on the heart. The aim of this study was to assess whether pediatric burn injury is associated with increased long-term hospital use for circulatory diseases. METHODS: A population-based longitudinal study was undertaken using linked hospital and death data from Western Australia for children younger than 15 years when hospitalized for a first burn injury (n = 10,436) in 1980-2012 and a frequency matched noninjury comparison cohort, randomly selected from Western Australia’s birth registrations (n = 40,819). Crude admission rates and cumulative length of stay for circulatory diseases were calculated. Negative binomial and Cox proportional hazards regression modeling were used to generate incidence rate ratios and hazard ratios, respectively. RESULTS: After adjustment for demographic factors and preexisting health status, the burn cohort had 1.33 (incidence rate ratio) times (95% confidence interval [CI]: 1.08-1.64) as many circulatory system hospitalizations, 2.26 times the number of days in hospital with a diagnosis of a circulatory disease (2.26, 95% CI: 1.06-4.61), and were at a higher risk of incident admissions (hazard ratio 1.22, 95% CI: 1.03-1.46), compared with the uninjured cohort. CONCLUSIONS: Children who sustain burn injury experience elevated hospital admission rates and increased length of hospital stay for diseases of the circulatory system for a prolonged period of time after burn discharge.

Duke JM, Rea S, Boyd JH, Randall SM and Wood FM.

OBJECTIVE: To assess the impact of burn injury sustained during childhood on long-term mortality and to quantify any increased risk of death attributable to burn injury. METHODS: A population-based cohort study of children younger than 15 years hospitalized for burn injury in Western Australia (1980-2012) and a matched noninjured comparison group. Deidentified extraction of linked hospital morbidity and death records for the period 1980-2012 were provided by the Western Australian Data Linkage System. An inception cohort (1980-2012) of burn cases younger than 15 years of age when hospitalized for a first burn injury (n = 10,426) and a frequency matched noninjured comparison cohort (n = 40,818) were identified. Survival analysis was conducted by using the Kaplan-Meier method and Cox proportional hazards regression. Mortality rate ratios and attributable risk percent adjusted for sociodemographic and preexisting health factors were generated. RESULTS: The median follow-up time for the pediatric burn cohort was 18.1 years after discharge. The adjusted all-cause mortality rate ratios for burn injury was 1.6 (95% confidence interval: 1.3-2.0); children with burn injury had a 1.6 times greater rate of mortality than those with no injury. The index burn injury was estimated to account for 38% (attributable risk percent) of all recorded deaths in the burn injury cohort during the study period. CONCLUSIONS: Burn injury sustained by children is associated with an increased risk of long-term all-cause mortality. Estimates of the total mortality burden based on in-hospital deaths alone underestimate the true burden from burn injury.

Eckersley LG and Shipton S.
Exercise-induced hypoxia secondary to an atrial septal defect and cor triatriatum dexter.
Cardiology in the young. 2015: 1-3.
A 14-year-old boy presented to us with a diagnosis of severe asthma and oxygen desaturation of 76% on a 6-minute-walk test. A contrast echocardiogram revealed echocontrast in the left and right atria simultaneously. A secundum atrial septal defect and partial cor triatriatum dexter were diagnosed, and the atrial defect was closed by cardiac catheterisation.

Everard ML, Wahn U, Dorsano S, Hossny E and Le Souef P.
Asthma education material for children and their families: a global survey of current resources.
World Allergy Organ J. 2015; 8: 35.
One of the keys to high quality paediatric asthma management is the provision of age appropriate information regarding the disease and its management. In order to determine whether the generation of a minimum dataset of information which can be translated into a wide range of languages might be used to assist children and their parents around the world, we undertook a survey of national Member Societies of the World Allergy Organization (WAO) to determine what educational material on asthma for children and their families already exists. A questionnaire was developed using Survey Monkey and distributed in 2014 to 263 representatives of

Updated 8/12/15
the WAO member Societies from 95 countries. Thirty-three replies were received from thirty-one countries. The survey highlighted a considerable disparity in availability of material among the responding countries, with some countries reporting that information was freely available in hard copy and online and others reporting a lack of suitable material locally. The results highlight the need to develop a core set of simple, clear and consistent age appropriate information that can be easily translated and delivered in a cultural and educationally effective format.

There is variability in the attainment of developmental milestones in the CDKL5 disorder.
BACKGROUND: Individuals with the CDKL5 disorder have been described as having severely impaired development. A few individuals have been reported having attained more milestones including walking and running. Our aim was to investigate variation in attainment of developmental milestones and associations with underlying genotype. METHODS: Data was sourced from the International CDKL5 Disorder Database, and individuals were included if they had a pathogenic or probably pathogenic CDKL5 mutation and information on early development. Kaplan-Meier time-to-event analyses investigated the occurrence of developmental milestones. Mutations were grouped by their structural/functional consequence, and Cox regression was used to investigate the relationship between genotype and milestone attainment. RESULTS: The study included 109 females and 18 males. By 5 years of age, only 75% of the females had attained independent sitting and 25% independent walking whilst a quarter of the males could sit independently by 1 year 3 months. Only one boy could walk independently. No clear relationship between mutation group and milestone attainment was present, although females with a late truncating mutation attained the most milestones. CONCLUSION: Attainment of developmental milestones is severely impaired in the CDKL5 disorder, with the majority who did attain skills attaining them at a late age. It appears as though males are more severely impaired than the females. Larger studies are needed to further investigate the role of genotype on clinical variability.

Forbes D and Grover Z.
Tube feeding: stopping more difficult than starting.

Friend J, Lindsey-Temple S, Gollow I, Whan E and Gera P.
Review of the radiation exposure during screening of surgically implanted central venous access devices.
PURPOSE: Ionizing radiation is used for the insertion of surgically implanted venous access devices (SIVADS) with children at the highest risk of cumulative radiation effects from these procedures. This study examines the radiation dose in a pediatric population during intraoperative radiological screening. METHODS: A retrospective study looked at all pediatric patients in a tertiary hospital between January 2008 and January 2014 who had a surgically implanted venous access device inserted using intraoperative fluoroscopy. Patient demographics, reason for SIVAD insertion, the type and method of insertion, fluoroscopy time and radiation dose area product were determined. RESULTS: A total of 605 patients had 682 SIVADS inserted, with 123 patients receiving multiple SIVAD over the six year period. There were two types of SIVAD inserted, 492 were totally implanted venous access devices (TIVAD) and 190 were tunneled central venous catheters (cuffed central line). Five hundred seven of the SIVAD inserted recorded the dose area product and fluoroscopy time. The median time for screening was 5 seconds (range 1 to 275 seconds) and the median dose area product was 0.00352 mGy m² (range 0.00001 mGy m² to 0.28 mGy m²). Of the 507 SIVAD that recorded the radiation data, 479 were open surgical cut-down insertion and 27 were percutaneous insertion. Percutaneously inserted surgically implanted venous access devices (mean 0.0060 mGy m²) had a longer dose area product than open insertion (mean 0.0034 mGy m²; p = 0.05). CONCLUSION: Screening of SIVAD involves low levels of radiation exposure and is comparable to a chest x-ray or a transatlantic flight. The excess lifetime cancer risk to patients is estimated to be very low and is considered to be outweighed by the benefits of insertion. Open surgical cut-down insertion has a significantly reduced radiation exposure compared to percutaneous techniques. Although radiation dose is higher with percutaneous procedures, the clinical effects are considered minimal, and the resultant radiation risk is estimated to be very low. Radiation dose should not determine technique of insertion of SIVAD.

Fuery A, Richmond PC and Currie AJ.
Human Infant Memory B Cell and CD4+ T Cell Responses to HibMenCY-TT Glyco-Conjugate Vaccine.
PloS one. 2015; 10(7): e0133126.
Carrier-specific T cell and polysaccharide-specific B cell memory responses are not well characterised in infants following glyco-conjugate vaccination. We aimed to determine if the number of Meningococcal (Men) C- and Y-specific memory B cells and; number and quality of Tetanus Toxoid (TT) carrier-specific memory CD4+ T cells are associated with polysaccharide-specific IgG post HibMenCY-TT vaccination. Healthy infants received

Updated 8/12/15
HibMenCY-TT vaccine at 2, 4 and 6 months with a booster at 12 months.Peripheral blood mononuclear cells were isolated and polysaccharide-specific memory B cells enumerated using ELISpot. TT-specific memory CD4+ T cells were detected and phenotyped based on CD154 expression and intracellular TNF-alpha, IL-2 and IFN-gamma expression following stimulation. Functional polysaccharide-specific IgG titres were measured using the serum bactericidal activity (SBA) assay. Polysaccharide-specific Men C- but not Men Y- specific memory B cell frequencies pre-boost (12 months) were significantly associated with post-boost (13 months) SBA titres. Regression analysis showed no association between memory B cell frequencies post-priming (at 6 or 7 months) and SBA at 12 months or 13 months. TT-specific CD4+ T cells were detected at frequencies between 0.001 and 0.112 as a percentage of CD3+ T cells, but their numbers were not associated with SBA titres. There were significant negative associations between SBA titres at M13 and cytokine expression at M7 and M12. CONCLUSION: Induction of persistent polysaccharide-specific memory B cells prior to boosting is an important determinant of secondary IgG responses in infants. However, polysaccharide-specific functional IgG responses appear to be independent of the number and quality of circulating carrier-specific CD4+ T cells after priming.

Gajjar A, Bowers DC, Karajannis MA, Leary S, Witt H and Gottardo NG.
Pediatric Brain Tumors: Innovative Genomic Information Is Transforming the Diagnostic and Clinical Landscape.
Pediatric neuro-oncology has undergone an exciting and dramatic transformation during the past 5 years. This article summarizes data from collaborative group and institutional trials that have advanced the science of pediatric brain tumors and survival of patients with these tumors. Advanced genomic analysis of the entire spectrum of pediatric brain tumors has heralded an era in which stakeholders in the pediatric neuro-oncology community are being challenged to reconsider their current research and diagnostic and treatment strategies. The incorporation of this new information into the next-generation treatment protocols will unleash new challenges. This review succinctly summarizes the key advances in our understanding of the common pediatric brain tumors (ie, medulloblastoma, low- and high-grade gliomas, diffuse intrinsic pontine glioma, and ependymoma) and some selected rare tumors (ie, atypical teratoid/rhabdoid tumor and CNS primitive neuroectodermal tumor). The potential impact of this new information on future clinical protocols also is discussed. Cutting-edge genomics technologies and the information gained from such studies are facilitating the identification of molecularly defined subgroups within patients with particular pediatric brain tumors. The number of evaluable patients in each subgroup is small, particularly in the subgroups of rare diseases. Therefore, international collaboration will be crucial to draw meaningful conclusions about novel approaches to treating pediatric brain tumors.

Congenital central hypventilation syndrome with hyperinsulinemia in an infant.

Matrix metalloproteinase activation by free neutrophil elastase contributes to bronchiectasis progression in early cystic fibrosis.
European Respiratory Journal. 2015.
Neutrophil elastase is the most significant predictor of bronchiectasis in early-life cystic fibrosis; however, the causal link between neutrophil elastase and airway damage is not well understood. Matrix metalloproteinases (MMPs) play a crucial role in extracellular matrix modelling and are activated by neutrophil elastase. The aim of this study was to assess if MMP activation positively correlates with neutrophil elastase activity, disease severity and bronchiectasis in young children with cystic fibrosis.Total MMP-1, MMP-2, MMP-7, MMP-9, tissue inhibitor of metalloproteinase (TIMP)-2 and TIMP-1 levels were measured in bronchoalveolar lavage fluid collected from young children with cystic fibrosis during annual clinical assessment. Active/pro-enzyme ratio of MMP-9 was determined by gelatin zymography. Annual chest computed tomography imaging was scored for bronchiectasis.A higher MMP-9/TIMP-1 ratio was associated with free neutrophil elastase activity. In contrast, MMP-2/TIMP-2 ratio decreased and MMP-1 and MMP-7 were not detected in the majority of samples. Ratio of active/pro-enzyme MMP-9 was also higher in the presence of free neutrophil elastase activity, but not infection. Across the study cohort, both MMP-9/TIMP-1 and active MMP-9 were associated with progression of bronchiectasis.Both MMP-9/TIMP-1 and active MMP-9 increased with free neutrophil elastase and were associated with bronchiectasis, further demonstrating that free neutrophil elastase activity should be considered an important precursor to cystic fibrosis structural disease.
Garratt LW, Sutanto EN, Ling KM, Looi K, Iosifidis T, Martinovich KM, Shaw NC, Buckley AG, Kicic-Starcevich E, Lannigan FJ, Knight DA, Stick SM and Kicic A

Alpha 1-antitrypsin Mitigates the Inhibition of Airway Epithelial Cell Repair by Neutrophil Elastase.

Am J Respir Cell Mol Biol. 2015.

Neutrophil elastase (NE) activity is associated with many destructive lung diseases and is a predictor for structural lung damage in early cystic fibrosis (CF), which suggests normal maintenance of airway epithelium is prevented by uninhibited NE. However, limited data exists on how the NE activity in airways of very young children with CF affects function of the epithelia. The aim of this study was to determine if NE activity could inhibit epithelial homeostasis and repair and whether any functional effect was reversible by antiprotease alpha 1-antitrypsin (alpha1AT) treatment. Viability, inflammation, apoptosis and proliferation were all assessed in healthy non-CF and CF pediatric primary airway epithelial cells (pAEChuman-CF and pAECCF respectively) during exposure to physiologically relevant NE. In addition, the effect of NE activity on pAECCF wound repair was also assessed. We report that viability after 48 hours was significantly decreased by 100 nM NE in both pAEChuman-CF and pAECCF, due to rapid cellular detachment that was also accompanied by inflammatory cytokine release. Furthermore, both phenotypes initiated an apoptotic response to 100 nM NE while >/=50 nM NE activity significantly inhibited proliferative capacity of cultures. Similar concentrations of NE also significantly inhibited wound repair of pAECCF but this was reversed by the addition of alpha1AT. Collectively, our results demonstrate free NE activity is deleterious for epithelial homeostasis and supports the hypothesis that proteases in the airways contribute directly to CF structural lung disease. It also highlights the need to investigate antiprotease therapies in early CF disease in more detail.

Garratt LW, Sutanto EN, Ling KM, Looi K, Iosifidis T, Martinovich KM, Shaw NC, Kicic-Starcevich E, Knight DA, Ranganathan S, Stick SM and Kicic A

Matrix metalloprotease activation by free neutrophil elastase contributes to bronchiectasis progression in early cystic fibrosis.


Neutrophil elastase is the most significant predictor of bronchiectasis in early-life cystic fibrosis; however, the causal link between neutrophil elastase and airway damage is not well understood. Matrix metalloproteases (MMPs) play a crucial role in extracellular matrix modelling and are activated by neutrophil elastase. The aim of this study was to assess if MMP activation positively correlates with neutrophil elastase activity, disease severity and bronchiectasis in young children with cystic fibrosis. Total MMP-1, MMP-2, MMP-7, MMP-9, tissue inhibitor of metalloproteinase (TIMP)-2 and TIMP-1 levels were measured in bronchoalveolar lavage fluid collected from young children with cystic fibrosis during annual clinical assessment. Active/pro-enzyme ratio of MMP-9 was determined by gelatin zymography. Annual chest computed tomography imaging was scored for bronchiectasis. A higher MMP-9/TIMP-1 ratio was associated with free neutrophil elastase activity. In contrast, MMP-2/TIMP-2 ratio decreased and MMP-1 and MMP-7 were not detected in the majority of samples. Ratio of active/pro-enzyme MMP-9 was also higher in the presence of free neutrophil elastase activity, but not infection. Across the study cohort, both MMP-9/TIMP-1 and active MMP-9 were associated with progression of bronchiectasis. Both MMP-9/TIMP-1 and active MMP-9 increased with free neutrophil elastase and were associated with bronchiectasis, further demonstrating that free neutrophil elastase activity should be considered an important precursor to cystic fibrosis structural disease.

Geraghty S, Bayes SJ and Hart A.

African immigrant parents' understanding of their teenager’s newly diagnosed diabetes status.


Ghia T, Kanhangad M, Alessandri AJ, Price G, Gera P and Nagarajan L.

Oposclonus-Myoclonus Syndrome, Neuroblastoma, and Insulin-Dependent Diabetes Mellitus in a Child: A Unique Case.

Pediatric neurology. Abstract/Aim We present a new and unique association of oposclonus-myoclonus-ataxia syndrome with neuroblastoma and type 1 diabetes mellitus. Patient description This 17-month-old child presented with oposclonus-myoclonus-ataxia syndrome. Investigations revealed a thoracic neuroblastoma. Eleven days later, she re-presented with diabetic ketoacidosis. The neuroblastoma was resected, and she was given immunotherapy. At 12 months' follow-up, her neurological signs and symptoms have significantly improved, but she continues to be insulin dependent. Discussion This child expands the clinical spectrum of autoimmune disorders associated with oposclonus-myoclonus-ataxia syndrome.

Ghia T, Kanhangad M, Alessandri AJ, Price G, Gera P and Nagarajan L.

Updated 8/12/15
Opsoclonus-Myoclonus Syndrome, Neuroblastoma, and Insulin-Dependent Diabetes Mellitus in a Child: A Unique Case.

Pediatric neurology. 2015.

Aim: We present a new and unique association of opsoclonus-myoclonus-ataxia syndrome with neuroblastoma and type 1 diabetes mellitus. Patient Description: This 17-month-old child presented with opsoclonus-myoclonus-ataxia syndrome. Investigations revealed a thoracic neuroblastoma. Eleven days later, she represented with diabetic ketoacidosis. The neuroblastoma was resected, and she was given immunotherapy. At 12 months' follow-up, her neurological signs and symptoms have significantly improved, but she continues to be insulin dependent. Discussion: This child expands the clinical spectrum of autoimmune disorders associated with opsoclonus-myoclonus-ataxia syndrome.

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)-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.

Streptococcus pneumoniae and Haemophilus influenzae in paediatric meningitis patients at Goroka General Hospital, Papua New Guinea: serotype distribution and antimicrobial susceptibility in the pre-vaccine era.

Background: Bacterial meningitis remains an important infection globally, with the greatest burden in children in low-income settings, including Papua New Guinea (PNG). We present serotype, antimicrobial susceptibility and outcome data from paediatric meningitis patients prior to introduction of Haemophilus influenzae type b (Hib) and pneumococcal conjugate vaccines (PCVs) in PNG, providing a baseline for evaluation of immunisation programs. Methods: Cerebrospinal fluid (CSF) was collected from children admitted to Goroka General Hospital with suspected meningitis between 1996 and 2005. Culture and sensitivity was conducted, and pneumococci and H. influenzae were serotyped. Laboratory findings were linked to clinical outcomes. Results: We enrolled 1884 children. A recognised pathogen was identified in 375 children (19.9%). Streptococcus pneumoniae (n = 180) and Hib (n = 153) accounted for 88.8% of pathogens isolated. 24 different pneumococcal serogroups were identified; non-PCV types 2, 24 and 46 accounted for 31.6% of pneumococcal meningitis. 10- and 13-valent PCVs would cover 44.1% and 45.4% of pneumococcal meningitis respectively. Pneumococcal isolates were commonly resistant to penicillin (21.5%) and 23% of Hib isolates were simultaneously resistant to ampicillin, co-trimoxazole and chloramphenicol. The case fatality rate in patients with a recognised bacterial pathogen was 13.4% compared to 8.5% in culture-negative patients. Conclusions: If implemented in routine expanded programme of immunisation (EPI) with high coverage, current PCVs could prevent almost half of pneumococcal meningitis cases. Given the diversity of circulating serotypes in PNG serotype replacement is of concern. Ongoing surveillance is imperative to monitor the impact of vaccines. In the longer term vaccines providing broader protection against pneumococcal meningitis will be needed.


Updated 8/12/15
Folate pathway gene polymorphisms and risk of childhood brain tumors: results from an Australian case-control study.


BACKGROUND: Recent research suggests that maternal folic acid supplementation is associated with a reduced risk of childhood brain tumors (CBT); polymorphisms in folate pathway genes could modify this association or directly influence CBT risk. METHODS: Associations between risk of CBT and folate pathway polymorphisms were investigated in a population-based case-control study in Australia (2005-2010). Cases were recruited through all Australian pediatric oncology centers and controls by national random digit dialing. Data were available from 321 cases and 552 controls. Six polymorphisms were genotyped in children and parents (MTHFR 677C>T, MTHFR 1298A>C, MTRR 66A>G, MTR 2756A>G, MTR 5049C>A, and CBS 2199 T>C). Maternal folic acid use was ascertained via questionnaire. ORs were estimated using unconditional logistic regression. Case-parent trio analyses were also undertaken.

RESULTS: There was weak evidence of a reduced risk of CBT for the MTRR 66GG genotype in the child or father: ORs 0.71 [95% confidence interval (CI), 0.48-1.07]; 0.54 (95% CI, 0.34-0.87), respectively. Maternal prepregnancy folic acid supplementation showed a stronger negative association with CBT risk where the child, mother, or father had the MTRR 66GG genotype (Pinteraction = 0.07, 0.10, and 0.18, respectively). CONCLUSIONS: Evidence for an association between folate pathway genotypes and CBT is limited in this study. There was possible protection by the MTRR 66GG genotype, particularly when combined with maternal prepregnancy folic acid supplementation; these results are novel and require replication. IMPACT: The possible interaction between folic acid supplementation and MTRR 66A>G, if confirmed, would strengthen evidence for prepregnancy folate protection against CBT. Cancer Epidemiol Biomarkers Prev; 24(6); 931-7. (c)2015 AACR.

Ten years of experience with intravesical and intrasphincteric onabotulinumtoxinA in children.

OBJECTIVE: To review 10 years of experience with both intravesical and intrasphincteric onabotulinumtoxinA (Botox(R)) injections in children. PATIENTS AND METHODS: Fifty children aged between 1 and 18 years at first injection had a combined total of 134 injections (106 intravesical, 23 intrasphincteric and five combined) between January 2004 and December 2013 at Princess Margaret Hospital. Follow-up occurred 3 months post procedure, and then 3-6 monthly. Response to Botox was graded according to the International Children's Continence Society (ICCS) response to treatment scale. Response time was the time that the injection remained effective before symptoms relapsed to the ICCS 'no response' category Neveus et al., 2006.

RESULTS: Median response times to Botox by pathology are summarised in Table 1. For detrusor overactivity (DO), the response after each Botox injection was in the ICCS >90% symptom reduction' category Neveus et al., 2006. Two children had sustained responses to Botox for a tenth and eleventh injection, respectively. A total of 45% of children receiving intrasphincteric Botox for chronic dysfunctional voiding (DV) or detrusor sphincter dyssynergia (DSD) had no symptom recurrence. Intravesical Botox was effective for treating new-onset hydronephrosis secondary to neurogenic bladder in one child. Intravesical Botox had a sustained effect over five injections in eliminating trigonal hypersensitivity and pain with CIC in one child. Episodes of severe autonomic dysreflexia in one child with a high cord transection were effectively eliminated by intravesical Botox, and were sustained over three injections. Thirteen of the 134 Botox injections (9.7%) had a symptomatic culture-positive urinary tract infection (UTI) in the 2 weeks following injection. All had a history of previous UTI. Three children (2.8%) developed urinary retention after intravesical injection. DISCUSSION: Intravesical Botox remained effective after up to eleven injections. In children with DV or DSD, the response to Botox was more variable, but 45% experienced symptom resolution with no recurrence. Trigonal hypersensitivity with CIC improved in a child after Botox. Botox may confer long-term bladder and upper tract protection in the neurogenic patient group. Severe episodes of autonomic dysreflexia triggered by bladder fill in a child with high cord lesion were eliminated by intravesical Botox. CONCLUSION: This study demonstrated that intravesical Botox remained effective in response quality and response time in children up to an eleventh injection. This is one of the longer follow-up studies in children published to date. Botox was effective in numbing trigonal hypersensitivity, treating new-onset hydronephrosis secondary to neurogenic bladder, and eliminating episodes of autonomic dysreflexia in one patient each.

Grover Z and Lewindon P.
Two-Year Outcomes After Exclusive Enteral Nutrition Induction Are Superior to Corticosteroids in Pediatric Crohn's Disease Treated Early with Thiopurines.
Dig Dis Sci. 2015; 60(10): 3069-3074.

BACKGROUND: Impact of first-line induction therapy on medium-term outcomes in the setting of early thioupine (TP) use in children with Crohn's disease has not been evaluated, in particular whether choice of exclusive enteral nutrition (EEN) over corticosteroids (CS) for induction impacts clinical outcomes at 12 and 24 months. AIMS AND METHODS: In this retrospective study, 89 children from our database with new diagnosis
CD and follow-up of at least 2 years following induction with exclusive course of CS or EEN and early, dose-optimized TP (within 6 months from diagnosis) were evaluated. We compared steroid dependency (relapse <3 months of tapering first course CS or inability to wean <10 mg prednisolone), need for IFX, linear growth, and surgical resections over the first 2 years. RESULTS: Choice of EEN over CS induction was associated with reduced linear growth failure (7 vs. 26%, p = 0.02), CS dependency (7 vs. 43%, p = 0.002), and improved primary sustained response to IFX (86 vs. 68%, p = 0.02). Combined CS/IFX-free remission and surgical resection rates were similar. CONCLUSION: In the setting of early TP commencement, EEN induction is superior to CS induction for reducing growth failure, CS dependency, and loss of response to IFX over the first 2 years.


AIMS: Lacosamide (LCM) is a novel anti-epileptic drug (AED) that enhances the slow inactivation of voltage-gated sodium channels. Its efficacy as adjunctive therapy for focal seizures is confirmed in adult placebo controlled trials with >50% reduction in seizure frequency in up to 50% patients. There is paucity of data on its efficacy and tolerance in treatment-resistant epilepsy in childhood (TREC). This study aims to assess efficacy and tolerance of LCM as adjunct therapy in TREC. METHODS: Audit of medical records and seizure diaries in children with TREC on LCM. A response (RR) was defined as >/=50% reduction in seizure frequency. RESULTS: Forty children (age range: 2-19 years) with TREC received LCM as add-on therapy. All had abnormal electroencephalograms, and 36 had abnormal neuroimaging. All children failed >2 AED trials, nine had trialled the ketogenic diet, five had failed the vagal nerve stimulator and 11 had failed resective epilepsy surgery. Median dose and duration of LCM therapy were 5.7 mg/kg/day and 10.5 months, respectively. RR was seen in 20% with persistence of RR in 8/36, 8/30 and 8/26 children on LCM at 3-, 6- and 9-month follow-up. Two children became seizure free. Retention on LCM was 65% at 9 months. LCM was well tolerated with minor side effects in seven children; no child discontinued LCM because of side effects. CONCLUSION: LCM is a well-tolerated AED with RR in 20%; in 5%, it resulted in seizure freedom. LCM may be useful even in TREC when seizures have not responded to intervention with multiple modalities.


Most children will experience a small, clinically insignificant drop in oxygen saturation during air travel due to the effects of altitude. Clinically significant hypoxia may occur in individuals with an underlying cardio-respiratory condition, in particular young infants born prematurely or with chronic lung disease of prematurity and in children with neuromuscular disorders. To date there is very little in-flight data available in these clinical populations to allow the development of evidence based guidelines for pre-flight assessment of the risk of hypoxia in-flight. The hypoxia flight simulation test is considered the gold standard for assessing the risk of in-flight hypoxia in adults and existing clinical guidelines for pre-flight assessment are largely based on data extrapolated from adults. The hypoxia challenge test has not been validated in infants and children and there are data to suggest that the test may not be accurate in neonates. We recommend high risk paediatric patients are assessed on a case by case basis by a respiratory paediatrician, with consideration of a hypoxia flight simulation test in certain circumstances.


AbstractObjective To examine the prevalence and importance of psychological, behavioural, and situational correlates of impending psychiatric inpatient admissions in children and adolescents with eating disorders. Method The sample consisted of 285 patients (8–17 years, M = 14.4, SD = 1.49) with DSM-5 eating disorders assessed between 2006 and 2013 from the Helping to Outline Pediatric Eating Disorders (HOPE) Project. The sample was split into two groups, those with (n = 38) and without (n = 247) impending psychiatric admission; Discriminant function analysis was used to examine correlates. Results The prevalence of impending psychiatric admission was 13.3%. Suicidal ideation provided the greatest discriminating power, followed by eating pathology, depressive symptoms, anxiety, multiple methods of weight control, binge eating, and family

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functioning. Conclusions Earlier recognition of comorbid symptoms in eating disorders in the community may reduce the number of young people with eating disorders who present needing critical psychiatric care.


This is the first reported study to describe local bone mineral density, assess parameters of fracture risk and report history of fractures in adolescents with motor difficulties. Motor difficulties evidenced by poor coordination in adolescence should be considered a new risk factor for below-average bone strength and structure and fracture risk. INTRODUCTION: Adolescents with motor difficulties are characterised by poor coordination and low levels of physical activity and fitness. It is possible these deficits translate into below-average bone strength and structure. The objectives of this study were to describe local bone mineral density (BMD), assess parameters of fracture risk (stress-strain index, SSI) and report history of fractures in this group. METHODS: Thirty-three adolescents (13 females), mean age of 14.3 (SD = 1.5) years, with motor difficulties underwent peripheral quantitative computed tomography (pQCT) measurements at proximal (66 %) and distal (4 %) sites of the non-dominant radius (R4 and R66) and tibia (T4 and T66). One sample t test was used to compare Z-scores for total BMD, trabecular density, cortical density and stress strain index (SSI) against standardized norms. RESULTS: Significant differences were present at R4 total density mean Z-score = -0.85 (SD = 0.7, p < 0.001), R66 cortical density mean Z-score = -0.74 (SD = 1.97, p = 0.038), R66 SSI mean Z-score = -1.00 (SD = 1.08, p < 0.001) and T66 SSI mean Z-score = -0.70 (SD = 1.15, p < 0.001). There was a higher incidence of fractures (26.9 %) compared to the normal population (3-9 %). CONCLUSIONS: Motor difficulties in adolescence should be considered a risk factor for below-average bone strength and structure and fracture risk. Strategies are needed to improve bone health in this high-risk group.


BACKGROUND: High fractions of exhaled nitric oxide (FeNO) in the breath of patients with symptoms of asthma are correlated with high levels of eosinophils and indicate that a patient is likely to respond to inhaled corticosteroids. This may have a role in the diagnosis and management of asthma. OBJECTIVE: To assess the diagnostic accuracy, clinical effectiveness and cost-effectiveness of the hand-held electrochemical devices NIOX MINO(R) (Aerocrine, Solna, Sweden), NIOX VERO(R) (Aerocrine) and NObreath(R) (Bedfont Scientific, Maidstone, UK) for the diagnosis and management of asthma. DATA SOURCES: Systematic searches were carried out between March 2013 and April 2013 from database inception. Databases searched included MEDLINE, EMBASE, the Cochrane Database of Systematic Reviews, the Database of Abstracts of Reviews of Effects, Science Citation Index Expanded and Conference Proceedings Citation Index - Science. Trial registers such as ClinicalTrials.gov and the metaRegister of Controlled Trials were also searched in March 2013. All searches were updated in September 2013. REVIEW METHODS: A rapid review was conducted to assess the equivalence of hand-held and chemiluminescent FeNO monitors. Systematic reviews of diagnostic accuracy and management efficacy were conducted. A systematic review of economic analyses was also conducted and two de novo health economic models were developed. All three reviews were undertaken according to robust high-quality methodology. RESULTS: The rapid review (27 studies) found varying levels of agreement between monitors (Bland-Altman 95% limits of agreement up to +/-10 parts per billion), with better agreement at lower FeNO values. Correlation was good (generally r > 0.9). The diagnostic accuracy review identified 22 studies in adults (all ages) and four in children. No studies used NObreath or NIOX VERO and seven used NIOX MINO. Estimates of diagnostic accuracy varied widely. FeNO used in combination with another test altered diagnostic accuracy only slightly. High levels of heterogeneity precluded meta-analysis. Limited observations included that FeNO may be more reliable and useful as a rule-in than as a rule-out test; lower cut-off values in children and in smokers may be appropriate; and FeNO may be less reliable in the elderly. The management review identified five randomised controlled trials in adults, one in pregnant asthmatics and seven in children. Despite clinical heterogeneity, exacerbation rates were lower in all studies but not generally statistically significantly so. Effects on inhaled corticosteroid (ICS) use were inconsistent, possibly because of differences in management protocols, differential effectiveness in adults and children and differences in population severity. One UK diagnostic model and one management model were identified. Aerocrine also submitted diagnostic and management models. All had significant limitations including short time horizons and the selective use of efficacy evidence. The de novo diagnostic model suggested that the expected difference in quality-adjusted life-year (QALY) gains between diagnostic options is likely to be very small. Airway hyper-responsiveness by methacholine challenge test is expected to produce the greatest QALY gain but with an expected incremental cost-effectiveness ratio (ICER) compared with FeNO (NObreath) in combination with
bronchodilator reversibility of $1.125M per QALY gained. All remaining options are expected to be dominated. The de novo management model indicates that the IER of guidelines plus FeNO monitoring using NObreath compared with guidelines alone in children is expected to be approximately $45,200 per QALY gained. Within the adult subgroup, FeNO monitoring using NObreath compared with guidelines alone is expected to have an IER of approximately $2100 per QALY gained. The results are particularly sensitive to assumptions regarding changes in ICS use over time, the number of nurse visits for FeNO monitoring and duration of effect. CONCLUSIONS: Limitations of the evidence base impose considerable uncertainty on all analyses. Equivalence of devices was assumed but not assured. Evidence for diagnosis is difficult to interpret in the context of inserting FeNO monitoring into a diagnostic pathway. Evidence for management is also inconclusive, but largely consistent with FeNO monitoring resulting in fewer exacerbations, with a small or zero reduction in ICS use in adults and a possible increased ICS use in children or patients with more severe asthma. It is unclear which specific management protocol is likely to be most effective. The economic analysis indicates that FeNO monitoring could have value in diagnostic and management settings. The diagnostic model indicates that FeNO monitoring plus bronchodilator reversibility dominates many other diagnostic tests. FeNO-guided management has the potential to be cost-effective, although this is largely dependent on the duration of effect. The conclusions drawn from both models require strong technical value judgements with respect to several aspects of the decision problem in which little or no empirical evidence exists. There are many potential directions for further work, including investigations into which management protocol is best and long-term follow-up in both diagnosis and management studies. STUDY REGISTRATION: This study is registered as PROSPERO CRD42013004149. FUNDING: The National Institute for Health Research Health Technology Assessment programme.

Harris EL, Hart SJ, Minutillo C, Ravikumara M, Warner TM, Williams Y, Nathan EA and Dickinson JE.

The long-term neurodevelopmental and psychological outcomes of gastrochisis: A cohort study.

OBJECTIVES: Previous gastrochisis specific neurodevelopmental studies have focused on the first 3 years of life. The aim of this study was to assess the intellectual, behavioral and neurological outcomes of older children and adolescents born with gastrochisis. STUDY DESIGN: Of 99 gastrochisis survivors born in Western Australia, 1992 to 2005, and who were at least 5 years old, 42 agreed to take part in this study. The study assessed: intellectual ability, with age appropriate Wechsler intelligence scales; neurological status; hearing; vision; behavioral status with the Strengths and Difficulties Questionnaire (SDQ); and parenting style with the Parenting Relationship Questionnaire (PRQ). All results were compared to normative means. RESULTS: Median age at follow-up was 10 years (range 5-17). No child had evidence of cerebral palsy or hearing loss; 1 child had amblyopia. Psychometric tests were completed in 39 children: mean full scale IQ was 98.2 (standard deviation [SD] 10.7); the working memory index was the only subscale to show a significant decrease from the normative mean (mean 95.5, SD 12.4, p=0.038). The mean SDQ behavioral scores were significantly lower for 3 of 5 domains and the Total Difficulties score. PRQ scores were significantly abnormal for 4 of 7 domains: Communication, Discipline, Satisfaction with School and Relational Frustration. CONCLUSIONS: Overall intellectual abilities were within a normal range. The decrease in working memory index and the behavioral and parenting relationship impairments could be an effect of perinatal factors, gastrochisis management and complications or the complexity of the socio-economic environment.


Chronic orchalgia after surgical exploration for acute scrotal pain in children.
J Pediatr Urol.

SummaryObjectives The aim was to review the pediatric cohort undergoing surgical exploration for acute scrotal pain at our institution and assess the entity of chronic orchalgia post exploration in this cohort. Materials and methods A retrospective review of all pediatric patients who underwent surgery for acute scrotal pain at a single institution between 1 January 2001 and 1 January 2012 was conducted. Results A total of 1084 patients underwent scrotal exploration for acute scrotal pain where the underlying cause could not be clinically ascertained. Causes found at exploratory surgery are shown in the table. Forty-four children (4.1%) represented with another episode of acute scrotal pain and underwent re-exploration. A hundred of the 772 children with testicular appendage torsion at initial exploration had unilateral exploration only. Seven (7%) of these re-presented with contralateral appendage torsion. The complication rate of initial scrotal exploration was 5.6% and that of re-exploration was 6.8%. All complications were managed conservatively except for a painful reactive hydrocele that underwent the Jaboulay procedure. Fifteen (1.4%) children in this cohort developed chronic orchalgia. Thirteen (87%) of these had definite pathology found at initial exploration. One of 61 (2%) with postoperative complications (a reactive hydrocele) developed chronic orchalgia. Pediatric chronic pain specialists were consulted for all patients. In 10 of the 15 (67%), significant comorbidities included constipation, anxiety, somatization, hydrocele, dysfunctional voiding, and multiple joint pain. The Jaboulay procedure for reactive hydrocele and re-exploration to pex the testes due to suspected intermittent testicular torsion resolved

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chronic orchalgia in one patient each. Discussion Pediatric chronic orchalgia post exploration is uncommon. It has a multifactorial etiology. Comorbidities are common. It is possible that some unexplored patients labeled as chronic orchalgia in the literature may have underlying correctable pathology. Surgically correctable pathology such as intermittent testicular torsion, metachronous testicular appendage torsion, and symptomatic hydrocele or varicocele should be excluded in children with chronic orchalgia. Chronic pain specialists should be consulted and associated comorbidities managed. Prior surgical exploration and testicular fixation in children with chronic orchalgia helped reassure patients and families that there was no underlying surgical cause for the pain and facilitated compliance with chronic pain management. Conclusions Pediatric chronic orchalgia has a multifactorial etiology and is uncommon after scrotal exploration surgery. Comorbidities are common and must be managed. Surgical exploration helps reassure patients that there is no correctable cause for the pain and facilitates engagement with chronic pain management.


OBJECTIVES: The aim was to review the pediatric cohort undergoing surgical exploration for acute scrotal pain at our institution and assess the entity of chronic orchalgia post exploration in this cohort. MATERIALS AND METHODS: A retrospective review of all pediatric patients who underwent surgery for acute scrotal pain at a single institution between 1 January 2001 and 1 January 2012 was conducted. RESULTS: A total of 1084 patients underwent scrotal exploration for acute scrotal pain where the underlying cause could not be clinically ascertained. Causes found at exploratory surgery are shown in the table. Forty-four children (4.1%) represented with another episode of acute scrotal pain and underwent re-exploration. A hundred of the 772 children with testicular appendage torsion at initial exploration had unilateral exploration only. Seven (7%) of these re-presented with contralateral appendage torsion. The complication rate of initial scrotal exploration was 5.8% and that of re-exploration was 6.8%. All complications were managed conservatively except for a painful reactive hydrocele that underwent the Jaboulay procedure. Fifteen (1.4%) children in this cohort developed chronic orchalgia. Thirteen (87%) of these had definite pathology found at initial exploration. One of 61 (2%) with postoperative complications (a reactive hydrocele) developed chronic orchalgia. Pediatric chronic pain specialists were consulted for all patients. In 10 of the 15 (67%), significant comorbidities included constipation, anxiety, somatization, hydrocele, dysfunctional voiding, and multiple joint pain. The Jaboulay procedure for reactive hydrocele and re-exploration to pex the testes due to suspected intermittent testicular torsion resolved chronic orchalgia in one patient each. DISCUSSION: Pediatric chronic orchalgia post exploration is uncommon. It has a multifactorial etiology. Comorbidities are common. It is possible that some unexplored patients labeled as chronic orchalgia in the literature may have underlying correctable pathology. Surgically correctable pathology such as intermittent testicular torsion, metachronous testicular appendage torsion, and symptomatic hydrocele or varicocele should be excluded in children with chronic orchalgia. Chronic pain specialists should be consulted and associated comorbidities managed. Prior surgical exploration and testicular fixation in children with chronic orchalgia helped reassure patients and families that there was no underlying surgical cause for the pain and facilitated compliance with chronic pain management. CONCLUSIONS: Pediatric chronic orchalgia has a multifactorial etiology and is uncommon after scrotal exploration surgery. Comorbidities are common and must be managed. Surgical exploration helps reassure patients that there is no correctable cause for the pain and facilitates engagement with chronic pain management.


AIMS/HYPOTHESIS: The aim of this study was to determine the incidence and incidence rate trends for type 1 diabetes mellitus in children aged 0-14 years, Australia-wide, from 2000 to 2011. METHODS: Cases of type 1 diabetes mellitus diagnosed in 0- to 14-year-olds were identified from the National (insulin-treated) Diabetes Register, with a 97% ascertainment rate. Annual age-standardised, sex- and age-specific incidences were calculated and Poisson regression was used to analyse the incidence by calendar year, sex and age at diagnosis. Non-linear temporal trends were analysed using sine and cosine functions applied to Poisson regression models for 3, 4, 5, 6 and 7 year cycles, and the Akaike information criterion was used to assess goodness of fit. RESULTS: A total of 11,575 cases (6,049 boys and 5,526 girls) of childhood type 1 diabetes mellitus were registered between 2000 and 2011, giving a mean incidence of 23.6 per 100,000 person-years (95% CI 23.2, 24.0). The mean incidence was 4.9% (95% CI 1.1%, 8.8%) higher in boys than in girls. Compared with 0- to 4-year-olds, the mean incidence was 65% higher in 5- to 9-year-olds and 208% higher in
10- to 14-year-olds. A 5 year cyclical variation in incidence was observed overall, in both sexes and in all age groups. An average annual increase in incidence was observed only in the 10- to 14-year-old age group (increase of 1.2% per year [95% CI 0.4%, 2.1%]). CONCLUSIONS/INTERPRETATION: A sinusoidal pattern was observed in the incidence rate trend of childhood type 1 diabetes mellitus in Australia. The 5-yearly peaks and troughs in incidence rate trends observed Australia-wide corroborate findings previously reported for Western Australia and require further investigation.

A systematic review of the evidence that swimming pools improve health and wellbeing in remote Aboriginal communities in Australia.

OBJECTIVE: To provide an overview of the evidence for health and wellbeing benefits associated with swimming pools in remote Aboriginal* communities in Australia. METHODS: Peer-reviewed and grey literature from 1990 to 2014 was searched to identify studies set in remote Australia that evaluated health and wellbeing benefits that have been associated with swimming pools. Studies were categorised using an evidence classification scale. RESULTS: Twelve studies met our search criteria. All prospective studies that collected data on skin infections found access to swimming pools to be associated with a drop of skin sore prevalence and -where measured- severity. Studies documenting ear and eye infections showed mixed outcomes. Many wider community and wellbeing benefits were documented in various studies, although many of these were primarily anecdotal in nature. CONCLUSIONS: Although a case can be made regarding skin infections and the broader wellbeing benefits that swimming pools may bring to remote Aboriginal communities, the benefit to ear and eye health remains unresolved. IMPLICATIONS: The decision to provide swimming pools to remote Aboriginal communities should not hinge on the demonstration of direct health benefits alone. Equity considerations and the potential broader benefits such amenities may entail are equally important.

Herath VC and Carapetis J.
Sore throat: Is it such a big deal anymore?

Sore throat remains a common disease of childhood, and a major cost and cause for antibiotic prescriptions. The management of sore throat remains controversial in affluent countries with various guidelines available and overall poor adherence to those guidelines. Group A streptococcus is the commonest bacterial cause with important sequelae including acute rheumatic fever (ARF). The driver for diagnosis and treatment is still questionable. In most affluent populations it is difficult to justify antibiotic treatment on the basis of preventing ARF, whereas this remains the major driver for sore throat management in populations at higher risk of ARF. Reduction in severity and duration of symptoms may be a reasonable basis to consider antibiotic treatment, and thus accurate diagnosis of GAS pharyngitis, particularly in those with more severe symptoms. The potential role of rapid tests in diagnosis appears to be increasing.

Herath VCK and Carapetis J.
Sore throat: Is it such a big deal anymore?
Journal of Infection. 2015; (0).

Summary Sore throat remains a common disease of childhood, and a major cost and cause for antibiotic prescriptions. The management of sore throat remains controversial in affluent countries with various guidelines available and overall poor adherence to those guidelines. Group A streptococcus is the commonest bacterial cause with important sequelae including acute rheumatic fever (ARF). The driver for diagnosis and treatment is still questionable. In most affluent populations it is difficult to justify antibiotic treatment on the basis of preventing ARF, whereas this remains the major driver for sore throat management in populations at higher risk of ARF. Reduction in severity and duration of symptoms may be a reasonable basis to consider antibiotic treatment, and thus accurate diagnosis of GAS pharyngitis, particularly in those with more severe symptoms. The potential role of rapid tests in diagnosis appears to be increasing.

Herath VK and Carapetis J.
Rheumatic Fever: What is New?

Hirani K, Payne D, Mutch R and Cherian S.
Health of adolescent refugees resettling in high-income countries.
Arch Dis Child. 2015.

Adolescent refugees are a vulnerable population with complex healthcare needs that are distinct from younger and older age groups. Physical health problems are common in this cohort with communicable diseases being the focus of attention followed by an emphasis on nutritional deficiencies and other chronic disorders.

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Adolescent refugees have also often experienced multiple traumatic stressors and are at a heightened risk of developing mental health problems. Navigating these problems at the time of pubertal development adds further challenges and can exacerbate or lead to the emergence of health risk behaviours. Educational difficulties and acculturation issues further compound these issues. Adolescents who have had experiences in detention or are unaccompanied by parents are particularly at risk. Despite a constantly growing number of adolescent refugees resettling in high-income countries, knowledge regarding their specific healthcare needs is limited. Research data are largely extrapolated from studies conducted within paediatric and adult cohorts. Holistic management of the medical and psychological issues faced by this group is challenging and requires an awareness of the socioeconomic factors that can have an impact on effective healthcare delivery. Legal and ethical issues can further complicate their management and addressing these in a culturally appropriate manner is essential. Early identification and management of the healthcare issues faced by adolescent refugees resettling in high-income countries are key to improving long-term health outcomes and future healthcare burden. This review article aims to increase knowledge and awareness of these issues among paediatricians and other health professionals.

**Holobotovskyy V, Chong YS, Burchell J, He B, Phillips M, Leader L, Murphy TV, Sandow SL, McKitrick DJ, Charles AK, Tare M, Arnolda LF and Ganss R.**


Preeclampsia is a systemic vascular disorder of pregnancy and is associated with increased sensitivity to angiotensin II (AngII) and hypertension. The cause of preeclampsia remains unknown. We identified the role of regulator of G protein (heterotrimeric guanine nucleotide-binding protein) signaling 5 (RGSS) in blood pressure regulation during pregnancy and preeclampsia. RGSS expression in human myometrial vessels is markedly suppressed in gestational hypertension and/or preeclampsia. In pregnant RGSS-deficient mice, reduced vascular RGSS expression causes gestational hypertension by enhancing vascular sensitivity to AngII. Further challenge by increasing AngII results in preeclampsia-like symptoms, namely, more severe hypertension, proteinuria, placental pathology, and reduced birth weight. In pregnant heterozygote null mice, treatment with peroxisome proliferator-activated receptor (PPAR) agonists normalizes vascular function and blood pressure through effects on RGSS. These findings highlight a key role of RGSS at the interface between AngII and PPAR signaling. Because preeclampsia is refractory to current standard therapies, our study opens an unrecognized and urgently needed opportunity for treatment of gestational hypertension and preeclampsia.


Linked administrative population data were used to estimate the burden of childhood respiratory syncytial virus (RSV) hospitalization in an Australian cohort aged <5 years. RSV-coded hospitalizations data were extracted for all children aged <5 years born in New South Wales (NSW), Australia between 2001 and 2010. Incidence was calculated as the total number of new episodes of RSV hospitalization divided by the child-years at risk. Mean cost per episode of RSV hospitalization was estimated using public hospital cost weights. The cohort comprised of 870 314 children. The population-based incidence/1000 child-years of RSV hospitalization for children aged <5 years was 4.9 with a rate of 25.6 in children aged <3 months. The incidence of RSV hospitalization (per 1000 child-years) was 11.0 for Indigenous children, 81.5 for children with bronchopulmonary dysplasia (BPD), 10.2 for preterm children with gestational age (GA) 32-36 weeks, 27.0 for children with GA 28-31 weeks, 39.0 for children with GA <28 weeks and 6.7 for term children with low birthweight. RSV hospitalization was associated with an average annual cost of more than AUD 9 million in NSW. RSV was associated with a substantial burden of childhood hospitalization specifically in children aged <3 months and in Indigenous children and children born preterm or with BPD.

**Horstman AM, Barnett MK and Hensey CC.**


**Hoskin AK, Yardley A-ME, Hanman K, Lam G and Mackey DA.**

Sports-related eye and adnexal injuries in the Western Australian paediatric population. Acta Ophthalmologica. 2015: n/a-n/a.

**Hoskin AK, Yardley AE, Hanman K, Lam G and Mackey DA.**


Updated 8/12/15
PURPOSE: To identify the causes of sports-related eye and adnexal injuries in children in Perth, Western Australia, to determine which sporting activities pose the highest risk of eye and adnexal injury to children.

METHODS: We performed a 12-year retrospective review of children admitted to hospital from 2002 to 2013 with sports-related ocular and adnexal eye injuries. The main outcome measures were the cause and type of ocular and adnexal injuries, age and gender risk factors.

RESULTS: A total of 93 cases of sports-related ocular and adnexal injury were identified in the 12-year time period. A peak in injuries occurred for 12- to 14-year-olds with a second peak in 6- to 8-year-olds; the median age was 8.82 years (range = 1.5-16.47). Cycling, football (including soccer and Australian Rules Football), tennis, trampolining, fishing and swimming were the sports responsible for the greatest number of injuries, a total of 63%. More than one-third (35%) of injuries resulted from being struck by a blunt object, and more than a quarter (26%) were as a result of contact with a blunt projectile.

CONCLUSION: Serious ocular and adnexal injuries have occurred in children as a result of participating in sports, with cycling and football being the largest contributors in the 12-year period we assessed. As we continue to encourage children to spend more time participating in sports and recreational activities, identifying associated risk factors will help us develop injury prevention strategies to promote eye safety for children.


OBJECTIVES: To evaluate paediatric CT dosimetry in Australia and New Zealand and calculate size-specific dose estimates (SSDEs) for chest and abdominal examinations. METHODS: Eight hospitals provided data from 12 CT systems for 1462 CTs in children aged 0-15. Imaging data were recorded for eight examinations: head (trauma, shunt), temporal bone, paranasal sinuses, chest (mass) and chest HRCT (high-resolution CT), and abdomen/pelvis (mass/inflammation). Dose data for cranial examinations were categorised by age and SSDEs by lateral dimension. Diagnostic reference ranges (DRRs) were defined by the 25th and 75th percentiles. Centralised image quality assessment was not undertaken. RESULTS: DRRs for 201 abdominopelvic SSDEs were: 2.8-4.7, 3.6-11.5, 8.5-15.0, 7.6-15, and 10.6-16.2 for the <15 cm, 15-19 cm, 20-24 cm, 25-29 cm and >30 cm groups, respectively. For 147 chest examinations using these body width categories, SSDE DRRs were 2.0-4.4, 3.3-7.9, 4.0-9.4, 4.5-12, and 6.5-12. Kilovoltage peak (kVp), but not AEC or IR, was associated with SSDE (parameter estimate [standard error]: 0.12 (0.03); p < 0.0001). CONCLUSIONS: Australian and New Zealand paediatric CT DRRs and abdominal SSDEs are comparable to international data. SSDEs for chest examinations are proposed. Dose variations could be reduced by adjusting kVp. KEY POINTS: * SSDEs can be calculated for all patients, CT systems, and practices * Kilovoltage peak (kVp) has the greatest association with dose in similar-sized patients * Paediatric DRRs for CT are now available for use internationally.

Updated 8/12/15

Productive Infection of Human Embryonic Stem Cell-Derived NKK2.1+ Respiratory Progenitors With Human Rhinovirus.

Stem Cells Transl Med. 2015.

Airway epithelial cells generated from pluripotent stem cells (PSCs) represent a resource for research into a variety of human respiratory conditions, including those resulting from infection with common human pathogens. Using an NKK2.1-GFP reporter human embryonic stem cell line, we developed a serum-free protocol for the generation of NKK2.1+ endoderm that, when transplanted into immunodeficient mice, matured into respiratory cell types identified by expression of CC10, MUC5AC, and surfactant proteins. Gene profiling experiments indicated that day 10 NKK2.1+ endoderm expressed markers indicative of early foregut but lacked genes associated with later stages of respiratory epithelial cell differentiation. Nevertheless, NKK2.1+ endoderm supported the infection and replication of the common respiratory pathogen human rhinovirus HRV1b. Moreover, NKK2.1+ endoderm upregulated expression of IL-6, IL-8, and IL-1B in response to infection, a characteristic of human airway epithelial cells. Our experiments provide proof of principle for the use of PSC-derived respiratory epithelial cells in the study of cell-virus interactions.


Follicular thyroid carcinoma in a child presenting as autonomously functioning thyroid nodule.


Justice TD, Hammer GL, Davey RJ, Paramalingam N, Guelfi KJ, Lewis L, Davis EA, Jones TW and Fournier PA.


Physiol Rep. 2015; 3(5).

This study investigated whether a prior bout of moderate-intensity exercise attenuates the glycemia-increasing effect of a maximal 30-sec sprint. A secondary aim was to determine whether the effect of antecedent exercise on the glucose regulatory response to sprinting is affected by sex. Participants (men n = 8; women n = 7) were tested on two occasions during which they either rested (CON) or cycled for 60-min at a moderate intensity of ~65% VO2 peak (EX) before performing a 30-sec maximal cycling effort 195 min later. In response to the sprint, blood glucose increased to a similar extent between EX and CON trials, peaking at 10 min of recovery, with no difference between sexes (P > 0.05). Blood glucose then declined at a faster rate in EX, and this was associated with a glucose rate of disappearance (R d) that exceeded the glucose rate of appearance (R a) earlier in EX compared with CON, although the overall glucose R a and R d profile was higher in men compared with women (P < 0.05). The response of growth hormone was attenuated during recovery from EX compared with CON (P < 0.05), with a lower absolute response in women compared with men (P < 0.05). The response of epinephrine and norepinephrine was also lower in women compared with men (P < 0.05) but similar between trials. In summary, a prior bout of moderate-intensity exercise does not affect the magnitude of the glycemia-increasing response to a 30-sec sprint; however, the subsequent decline in blood glucose is more rapid. This blood glucose response is similar between men and women, despite less pronounced changes in glucose R a and R d, and a lower response of plasma catecholamines and growth hormone to sprinting in women.


Impact of an Ivermectin Mass Drug Administration on Scabies Prevalence in a Remote Australian Aboriginal Community.


BACKGROUND: Scabies is endemic in many Aboriginal and Torres Strait Islander communities, with 69% of infants infected in the first year of life. We report the outcomes against scabies of two oral ivermectin mass drug administrations (MDAs) delivered 12 months apart in a remote Australian Aboriginal community. METHODS: Utilizing a before and after study design, we measured scabies prevalence through population census with sequential MDAs at baseline and month 12. Surveys at months 6 and 18 determined disease acquisition and treatment failures. Scabies infestations were diagnosed clinically with additional laboratory investigations for crusted scabies. Non-pregnant participants weighing >/=15 kg were administered a single 200 mug/kg ivermectin dose, repeated after 2-3 weeks if scabies was diagnosed, others followed a standard alternative algorithm. PRINCIPAL FINDINGS: We saw >1000 participants at each population census. Scabies prevalence fell from 4% at baseline to 1% at month 6. Prevalence rose to 9% at month 12 amongst the baseline cohort in association with an identified exposure to a presumptive crusted scabies case with a higher prevalence of 14%

Updated 8/12/15
amongst new entries to the cohort. At month 18, scabies prevalence fell to 2%. Scabies acquisitions six months after each MDA were 1% and 2% whilst treatment failures were 6% and 5% respectively. CONCLUSION: Scabies prevalence reduced in the six months after each MDA with a low risk of acquisition (1-2%). However, in a setting where living conditions are conducive to high scabies transmissibility, exposure to presumptive crusted scabies and population mobility, a sustained reduction in prevalence was not achieved. CLINICAL TRIAL REGISTRATION: Australian New Zealand Clinical Trial Register (ACTRN-12609000654257).

Khan TK, Palmer DJ and Prescott SL.
In-utero exposures and the evolving epidemiology of paediatric allergy.
Purpose of review: Emerging evidence suggests that the rising prevalence of early-onset ‘noncommunicable’ diseases, such as paediatric atopy, is related to modern environmental changes, the effects of which appear to commence in utero or even preconception. Here, we review how recent publications have contributed further to our understanding of the influence of in-utero exposures on the predisposition to immune dysregulation, with a particular focus on the evolving epidemiology of paediatric allergy. Recent findings: New evidence suggests that inter-individual variations in immune function development are principally driven by nonheritable factors, for example periconceptional environment. One of the most significant influences is maternal nutrition during pregnancy. New studies further support a healthy balanced maternal diet that contains immunomodulatory nutrients, prebiotics and probiotics, which benefit multiple aspects of fetal development, including immune development. In addition, declining maternal biodiversity, maternal stress and exposures to environmental pollutants further interact to have adverse influences on the developing immune system. Summary: The in-utero period appears to be a critical time point. Further investigations of gene–environmental interaction mechanisms are essential prior to further recommendations of early-life preventive strategies to reduce the growing global burden of allergic disease, as well as other ‘noncommunicable’ diseases.

Ko DWH, Zurynski Y, Gilbert GL and Group GBSS.
Group B streptococcal disease and genotypes in Australian infants.
Journal of paediatrics and child health. 2015: n/a-n/a.

Kotecha RS, Kees UR, Cole CH and Gottardo NG.
Rare childhood cancers—an increasing entity requiring the need for global consensus and collaboration.
Rare childhood cancers have not benefited to the same extent from the gains that have been made for their frequently occurring counterparts. In recent years, this gap has been recognized and a number of vehicles now exist to improve outcome, including rare tumor groups, disease-specific registries, and clinics. The multitude of approaches has allowed significant progress, however, this framework is limited by patient number and is not inclusive for every type of rare childhood cancer. These shortcomings can be overcome by a single global unified approach to the study of rare childhood tumors.

Kotecha RS, Wadia UD, Jacoby P, Ryan AL, Blyth CC, Keil AD, Gottardo NG, Cole CH, Barr IG and Richmond PC.
Immunogenicity and clinical effectiveness of the trivalent inactivated influenza vaccine in immunocompromised children undergoing treatment for cancer.
Cancer Med. 2015.
Influenza is associated with significant morbidity and mortality in children receiving therapy for cancer, yet recommendation for, and uptake of the seasonal vaccine remains poor. One hundred children undergoing treatment for cancer were vaccinated with the trivalent inactivated influenza vaccine according to national guidelines in 2010 and 2011. Influenza-specific hemagglutinin inhibition antibody titers were performed on blood samples taken prior to each vaccination and 4 weeks following the final vaccination. A nasopharyngeal aspirate for influenza was performed on all children who developed an influenza-like illness. Following vaccination, seroprotection and seroconversion rates were 55 and 43% for H3N2, 61 and 43% for H1N1, and 41 and 33% for B strain, respectively. Overall, there was a significant geometric mean fold increase to H3N2 (GMFI 4.56, 95% CI 3.19-6.52, P < 0.01) and H1N1 (GMFI 4.44, 95% CI 3.19-6.19, P < 0.01) strains. Seroconversion was significantly more likely in children with solid compared with hematological malignancies and in children <10 years of age who received a two-dose schedule compared to one. Influenza infection occurred in 2% of the vaccinated study population, compared with 6.8% in unvaccinated controls, providing an adjusted estimated vaccine effectiveness of 72% (95% CI -26-94%). There were no serious adverse events and a low reactogenicity rate of 3%. The trivalent inactivated influenza vaccine is safe, immunogenic, provides clinical protection and should be administered annually to immunosuppressed children receiving treatment for cancer. All children <10 years of age should receive a two-dose schedule.

Updated 8/12/15
Larcombe AN, Kicic A, Mullins BJ and Knothe G.
Biodiesel exhaust: the need for a systematic approach to health effects research.
Biodiesel is a generic term for fuel that can be made from virtually any plant or animal oil via transesterification of triglycerides with an alcohol (and usually a catalyst). Biodiesel has received considerable scientific attention in recent years, as it is a renewable resource that is directly able to replace mineral diesel in many engines. Additionally, some countries have mandated a minimum biodiesel content in all diesel fuel sold on environmental grounds. When combusted, biodiesel produces exhaust emissions containing particulate matter, adsorbed chemicals and a range of gases. In many cases, absolute amounts of these pollutants are lower in biodiesel exhaust compared with mineral diesel exhaust, leading to speculation that biodiesel exhaust may be less harmful to health. Additionally, engine performance studies show that the concentrations of these pollutants vary significantly depending on the renewable oil used to make the biodiesel and the ratio of biodiesel to mineral diesel in the fuel mix. Given the strategic and legislative push towards the use of biodiesel in many countries, a concerning possibility is that certain biodiesels may produce exhaust emissions that are more harmful to health than others. This variation suggests that a comprehensive, systematic and comparative approach to assessing the potential for a range of different biodiesel exhausts to affect health is urgently required. Such an assessment could inform biodiesel production priorities, drive research and development into new exhaust treatment technologies, and ultimately minimize the health impacts of biodiesel exhaust exposure.

Ledowski T, O'Dea B, Meyerkort L, Hegarty M and von Ungern-Sternberg BS.
Postoperative Residual Neuromuscular Paralysis at an Australian Tertiary Children's Hospital.
Purpose. Residual neuromuscular blockade (RNMB) is known to be a significant but frequently overlooked complication after the use of neuromuscular blocking agents (NMBA). Aim of this prospective audit was to investigate the incidence and severity of RNMB at our Australian tertiary pediatric center. Methods. All children receiving NMBA during anesthesia were included over a 5-week period at the end of 2011 (Mondays to Fridays; 8 a.m.-6 p.m.). At the end of surgery, directly prior to tracheal extubation, the train-of-four (TOF) ratio was assessed quantitatively. Data related to patient postoperative outcome was collected in the postoperative acute care unit. Results. Data of 64 patients were analyzed. Neostigmine was given in 34 cases and sugammadex in 1 patient. The incidence of RNMB was 28.1% overall (without reversal: 19.4%; after neostigmine: 37.5%; n.s.). Severe RNMB (TOF ratio < 0.7) was found in 6.5% after both no reversal and neostigmine, respectively. Complications in the postoperative acute care unit were infrequent, with no differences between reversal and no reversal groups. Conclusions. In this audit, RNMB was frequently observed, particularly in cases where patients were reversed with neostigmine. These findings underline the well-known problems associated with the use of NMBA that are not fully reversed.

Licari MK, Billington J, Reid SL, Wann JP, Elliott CM, Winsor AM, Robins E, Thornton AL, Jones R and Bynevelt M.
Cortical functioning in children with developmental coordination disorder: a motor overflow study.

Lim FJ, Blyth C, de Klerk N, Valenti B, Rouhiainen OJ, Wu DY-A, Jansz C and Moore HC.
Optimisation required when using linked hospital and laboratory data to investigate respiratory infections.
Journal of Clinical Epidemiology. 2015.
AbstractObjective Despite a recommendation for microbiological testing, only 45% of children hospitalised for respiratory infections in our previous data linkage study linked to a microbiological record. We conducted a chart review to validate linked microbiological data. Study Design and Setting The chart review consisted of children aged &lt;5 years admitted to 7 selected hospitals for respiratory infections in Western Australia, 2000-2011. We calculated the proportion of admissions where testing was performed and any pathogens detected. We compared these proportions between the chart review and our previous data linkage study. Poisson regression was used to identify factors predicting the likelihood of microbiological tests in the chart review cohort. Results From the chart review, 77% of 746 records had a microbiological test performed compared with 46% of 18,687 records from our previous data linkage study. Of those undergoing testing, 66% of the chart review and 64% of data linkage records had ≥1 respiratory pathogen(s) detected. In the chart review cohort, frequency of testing was highest in children admitted to metropolitan hospitals. Conclusion Validation studies are essential to ensure the quality of linked data. Our previous data linkage study failed to capture all relevant microbiological records. Findings will be used to optimise extraction protocols for future linkage studies.

Lovegrove MT.
Adolescent presentations with alcohol intoxication to the emergency department at Joondalup Health Campus in 2013.

Updated 8/12/15
Emergency Medicine Australasia. 2015: n/a-n/a.

Objective To document the number of adolescents aged 16 years and under presenting to the ED at Joondalup Health Campus (JHC) with problems related primarily to alcohol intoxication, and document information about these presentations. Method Presentations of adolescents were sourced from the Emergency Department Information System database at JHC. The patient's notes were interrogated for data on presentation and discharge times, means of arrival to the ED, age, gender, arrival Glasgow Coma Score (GCS), location from where the adolescent was brought and blood alcohol levels (BALs), if done. These were analysed, and descriptive statistics was reported. Results Fifty-six adolescents (61% girls) were brought in to JHC ED with alcohol intoxication in 2013. The majority (76.8%) arrived between 21.00 hours and 05.00 hours, most often by ambulance or police (58.9%). Most adolescents had BALs performed (80.4%) and of those, nearly seven in eight (86.7%) had a BAL > 0.1 g/L, with a mean of 0.161 g/L (SD 0.066). Girls had a lower mean BAL, but 26.5% presented with a GCS <14. Most 16 year olds were brought from organised parties, whereas other age groups were more likely drinking at a friend's house or with friends. Few (12.5%) were drinking at home. Conclusion Adolescents requiring review in an ED for alcohol intoxication are most often brought in by ambulance or police in the late evening or early morning. They are most likely to have high BALs and a significant proportion will have a GCS <14.


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.


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 10(5) 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.

MacMillan KK, Ohan J, Cherian S and Mutch RC. Refugee children's play: Before and after migration to Australia. Updated 8/12/15
AIM: Play is vital to children’s development, health and resilience. Play modulates cognitive, emotional and social well-being. Children constitute approximately half of all humanitarian refugee entrants resettled in Australia. Refugee children are commonly victims and witnesses of war and persecution, living across resource-poor environs during transit. Little is known about the effects of refugee migration on play. This study explores how refugee children engaged in play pre-migration (in their home country) and post-migration (Australia). METHODS: Refugee children attending the Refugee Health Clinic of a tertiary children’s hospital were invited to complete a qualitative descriptive study of play. The children were asked to draw how they played pre- and post-migration. Drawings were analysed for (i) the presence of play; (ii) location of play; and (iii) drawing detail. RESULTS: Nineteen refugee children were recruited (mean age 8.5 years +/- standard deviation 6.4 months). Significantly fewer children drew play pre- versus post-migration (11/19, 58% vs. 18/19, 95% P < 0.03). Girls had greater comparative changes in play with migration (pre: 2/8, 25% vs. post: 7/8, 87%. P = 0.06), trending to significance. Of those children who drew play, almost all drew playing outside (pre-migration: 10/11, 90.9%; post-migration: 17/18, 94.4%). Drawings showed equivalent detail pre- and post-migration. CONCLUSION: Resettled refugee children, especially girls, demonstrated limited play pre-migration, with higher levels of engagement post-resettlement. Facilitating opportunities for variety of play may strengthen positive resettlement outcomes for children and parents. Larger longitudinal studies examining play in refugee children and associations with physical, development and psychological well-being are warranted.

Atypical haemolytic uremic syndrome treated with the complement inhibitor eculizumab: the experience of the Australian compassionate access cohort.

BACKGROUND/AIM: This study aimed to report the clinical characteristics and outcomes of Australian patients treated with eculizumab for atypical haemolytic uremic syndrome (aHUS). METHODS: A retrospective cohort study was undertaken of all patients in Australia treated with eculizumab provided in a compassionate access programme for a clinical diagnosis of aHUS using prospectively collected clinical data. RESULTS: A total of 10 patients with a median age of 23.5 years (interquartile range (IQR) 24.83 years) received compassionate access eculizumab for aHUS in Australia. Eight patients were female, and three had a family history of aHUS. Three received eculizumab for an initial acute aHUS presentation, three for relapsing and refractory acute aHUS, two for de novo aHUS post-renal transplantation, and one each for aHUS recurrence post-transplantation and facilitation of transplantation with a history of aHUS. The median duration of eculizumab therapy has been 911.5 days (IQR 569 days) with a cumulative exposure of 9184 days. At baseline all patients had renal and extra-renal aHUS involvement, with up to three non-renal organs affected. All but one patient, who died from uncontrollable gastrointestinal aHUS manifestations, have continued. The nine continuing patients achieved remission of aHUS. Two of the four patients requiring renal replacement therapy (RRT) at eculizumab commencement subsequently ceased RRT. Clinical events occurring in this cohort while on eculizumab treatment included neutropenia (two), posterior reversible encephalopathy syndrome (one), cardiomyopathy (one), pulmonary embolus (one), antibody-mediated rejection resulting in renal graft failure (one), iron deficiency (one), gastrointestinal haemorrhage (one) and death (one). CONCLUSION: Eculizumab has been an effective therapy for aHUS in this cohort, including when other therapies have failed.

Joint Aspiration for Acute Hemarthrosis in Children Receiving Factor VIII Prophylaxis for Severe Hemophilia: 11-year Safety Data.
J Rheumatol. 2015; 42(5): 885-890.
OBJECTIVE: The aims of this study were (1) to document the prevalence of acute hemarthrosis in a cohort of 46 boys with severe hemophilia A receiving full primary prophylaxis in Western Australia (WA), and (2) to investigate the safety of the WA protocol over 11 years for management of hemarthrosis. METHODS: Case review. The WA protocol involves a pediatric rheumatologist washing out all acute hemarthrosis of large joints promptly and then instilling intraarticular (IA) corticosteroids. RESULTS: This study showed that joint bleeds occurred in 22 boys of 46 (47.8%). In over 11 years, 84 washouts were performed on 32 joints in 22 boys. No adverse events occurred. Fifteen of 22 boys had normal joints with a Hemophilic Joint Health Score = 0. Fifteen boys who had had all hemarthrosis washed out had clinically normal joints (100%). Seven boys had sustained joint damage prior to full instigation of the protocol, each having had documented hemarthrosis without aspiration. Parents needed to understand that joint bleeds constituted an emergency. CONCLUSION: Of our cohort, 47.8% of patients with severe hemophilia receiving prophylaxis developed joint bleeding. The WA protocol is safe. There is evidence suggesting joint outcomes of hemophilic patients having hemarthrosis despite factor VIII prophylaxis may be much improved if there is access to a center using a procedure similar to the WA protocol.

Updated 8/12/15
Predictors of disease severity in children hospitalized for pertussis during an epidemic.
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: One hundred twenty hospitalised children 0-17 years of age were enrolled with a median PSS of 5 (interquartile range 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 coinfection [odds ratio (OR): 4.82, CI: 1.66-14.00], <2 months old (OR: 4.76, CI: 1.48-15.32), fever >37.5 degrees C (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. A total of 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 coinfection, history of prematurity or fever on presentation need close monitoring.

Martin AC, Anderson D, Lacey J, Guttinger R, Jacoby PA, Mok TJ, Whitmore TJ, Whitewood CN, Burgner DP and Blyth CC.
Predictors of Outcome in Pediatric Osteomyelitis: 5 Year Experience in a Single Tertiary Center.
The Pediatric infectious disease journal. 2015.
BACKGROUND: Acute haematogenous osteomyelitis is a bacterial infection of bone, which occurs most frequently in children. Outcomes are excellent for the majority of children, but a minority develop complicated osteomyelitis. Predicting which children will develop complicated osteomyelitis remains a challenge, particularly in developed countries where most patients are discharged home after a relatively short period in hospital. METHODS: We conducted a 5 year retrospective case note review of all children aged 3 months to 16 years admitted with a diagnosis of acute haematogenous osteomyelitis. We compared standardised clinical and laboratory parameters in those who developed simple and complicated osteomyelitis. RESULTS: Of the 299 children who met inclusion, 241 (80.6%) had simple and 58 (19.4%) had complicated osteomyelitis. The major predictors of complicated disease were older age, a temperature greater than 38.5 degrees C and a higher C-reactive protein at admission. CONCLUSIONS: A risk prediction model, utilising information available shortly after hospitalisation, allows early identification of children at greatest risk of developing complicated osteomyelitis.

Martinez FE, Panwar R, Kelty E, Smalley N and Williams C.
Idiopathic interstitial pneumonia in the ICU: an observational cohort.
In the absence of a clearly identifiable cause, the prognosis of patients with interstitial lung disease is grim. This study describes our institutional experience in management of patients who are admitted to an ICU with respiratory insufficiency secondary to idiopathic interstitial pneumonia (IIP). This study was performed to obtain Australian data on patients admitted to an ICU with respiratory insufficiency secondary to IIP. This is a retrospective cohort study of patients with IIP who were admitted to the ICU between December 2007 and December 2013 at one of two university-affiliated academic hospitals in Newcastle, New South Wales. Thirty-six patients (69% male) were admitted to the ICU in respiratory insufficiency from IIP. The median age of the cohort was 71 (66 to 77) years. The median APACHE III score was 68 (56 to 97). Sixty-nine percent (25/36) of patients died in hospital. The median ICU and hospital lengths of stay were 6 (2 to 13.5) and 12 (4.8 to 18.3) days respectively. No significant difference was observed between admission characteristics and mortality. Patients admitted to ICU with respiratory failure secondary to IIP are aggressively investigated and treated, but still have a high mortality rate. Accurate predictors of mortality would be useful in offering aggressive treatment to patients who would benefit from it.

Maurel A, Gollow I and Gera P.
Click it: do not risk it: lap seat belt causing extensive abdominal injuries.
ANZ J Surg. 2015; n/a-n/a.

Updated 8/12/15
Maxwell S, Bower C and O’Leary P.  
Impact of prenatal screening and diagnostic testing on trends in Down syndrome births and terminations in Western Australia 1980 to 2013. 
Prenat Diagn. 2015.  
OBJECTIVE: To assess how prenatal screening and diagnostic testing have impacted the diagnosis, termination and birth prevalence of Down syndrome in Western Australia (1980-2013). METHOD: We analysed trends in termination rates and the birth prevalence of Down syndrome using aggregated data (1980-2013). We modelled the expected live-birth rate and prevalence of Down syndrome and compared different eras of screening and diagnosis with respect to the impact on live birth rate and prevalence of Down syndrome. RESULTS: Between 1980 and 2013, the rate of Down syndrome pregnancies increased, corresponding to a greater proportion of babies born to older women. Following the introduction of screening in 1994, the rate of liveborns with Down syndrome reduced significantly (p = 0.001). The rate of terminations of pregnancy for Down syndrome remained stable over this period. In the absence of termination, the Down syndrome live-birth rate would have risen from 1.1 to 2.17/1000 between 1980 and 2013. CONCLUSION: Prenatal testing in WA has reduced the birth prevalence of Down syndrome despite an increased rate of Down syndrome pregnancies. Most women for whom a prenatal diagnosis of fetal Down syndrome is made, choose to terminate the pregnancy (93%) and this proportion has not changed over the study period.

Maxwell S, Dickinson JE, Murch A and O’Leary P.  
The potential impact of NIPT as a second-tier screen on the outcomes of high-risk pregnancies with rare chromosomal abnormalities.  
AIM: To describe the potential impact of using noninvasive prenatal testing (NIPT) as a second-tier test, on the diagnosis and outcomes of pregnancies identified as high risk through first trimester screening (FTS) in a cohort of real pregnancies. MATERIALS AND METHODS: Western Australian FTS and diagnostic data (2007-2009) were linked to pregnancy outcomes. Karyotype results from invasive prenatal testing in high-risk women were analysed. The outcomes of abnormal results that would not be detected by NIPT, assuming a panel of trisomy 21/18/13 and sex chromosome aneuploidies, and the likelihood of diagnosis in a screening model using NIPT as a second-tier test are described. RESULTS: Abnormal karyotype results were reported in 224 of 1488 (15%) women with high-risk pregnancies having invasive diagnostic testing. NIPT potentially would have identified 85%. The 33 abnormalities unidentifiable by NIPT were triploidies (n = 7, 21%), balanced (n = 8, 24%) and unbalanced rearrangements (n = 10, 30%) and level III mosaicsisms (n = 8, 24%). For conditions not identifiable by NIPT, fetal sonographic appearance was likely to have led to invasive testing for 10 of 17 (59%) pathogenic abnormalities. If a policy was adopted recommending invasive testing for FTS risk >1:50 and/or ultrasound detected abnormality, the residual risk of an unidentified pathogenic chromosomal abnormality in those without a diagnosis would have been 0.33% (95% CI 0.01-0.65%). CONCLUSIONS: A screening model with NIPT as a second-tier for high-risk pregnancies would be unlikely to have changed the outcome for the majority of pregnancies. Optimising the diagnosis of rare pathogenic abnormalities requires clear indicators for invasive testing over NIPT.

Novel application of luciferase assay for the in vitro functional assessment of KAL1 variants in three females with septo-optic dysplasia (SOD).  
KAL1 is implicated in 5% of Kallmann syndrome cases, a disorder which genotypically overlaps with septo-optic dysplasia (SOD). To date, a reporter-based assay to assess the functional consequences of KAL1 mutations is lacking. We aimed to develop a luciferase assay for novel application to functional assessment of rare KAL1 mutations detected in a screen of 422 patients with SOD. Quantitative analysis was performed using L6-myoblasts stably expressing FGFR1, transfected with a luciferase-reporter vector containing elements of the FGF-responsive osteocalcin promoter. The two variants assayed [p.K185N, p.P291T], were detected in three females with SOD (presenting with optic nerve hypoplasia, midline and pituitary defects). Our novel assay revealed significant decreases in transcriptional activity [p.K185N: 21% (p < 0.01); p.P291T: 40% (p < 0.001)]. Our luciferase-reporter assay, developed for assessment of KAL1 mutations, determined that two variants in females with hypopituitarism/SOD are loss-of-function; demonstrating that this assay is suitable for quantitative assessment of mutations in this gene.

McCabe SM, Blackmore AM, Abbiss CR, Langdon K and Elliott C.  
Sleep concerns in children and young people with cerebral palsy in their home setting.  
Journal of paediatrics and child health. 2015.
AIMS: The aims were to identify in-home concerns about sleep in children and young people with cerebral palsy (CP) across age and Gross Motor Function Classification Scale (GMFCS) levels. METHODS: This was a retrospective review of clinical notes of 154 children and young people with CP, aged 1-18 years (M = 7.8; standard deviation = 5.4) who received a home-based sleep service. Reported concerns were synthesised, for analysis according to age groups (1-5, 6-13, 14-18) and GMFCS levels. RESULTS: Sixteen factors of concern were derived from the home-based assessment reports. Most children and young people had multiple factors of concern. These varied across age groups and GMFCS levels. Body position was of concern across all age groups, for over 90% at GMFCS levels IV and V, and for 10% at GMFCS level I. Settling routines were of concern for more than 90% at GMFCS levels I and II, but for less than 50% at GMFCS levels IV and V. Settling routines were of concern to over 65% of those under 6 years but less than 25% of those over 14 years. Conversely, pain and pressure care concerned less than 10% of children under 6, and more than 35% of those over 14 years. CONCLUSIONS: Concerns about sleep vary across ages and GMFCS levels of children and young people with CP. Concerns relate to impairment of body structure and function, activity, environment, and personal supports. Multi-disciplinary, home-based assessment and interventions are recommended to address these concerns.

McGarry S, Elliott C, McDonald A, Valentine J, Wood F and Girdler S.
“This is not just a little accident”: a qualitative understanding of paediatric burns from the perspective of parents. Disabil Rehabil. 2014.

Abstract Purpose: To describe the experiences of parents of children admitted to hospital for a burn. Methods: In-depth interviews were conducted with 21 parents (14 mothers and seven fathers) of children who had sustained a burn requiring hospitalisation. Face-to-face interviews were conducted six months post-burn, in rural, remote and metropolitan areas. The interview guide explored the overall experience of parents and included probing questions exploring the perceptions, thoughts and feelings of participants. Interviews were digitally recorded and transcribed verbatim. Transcripts were analysed according to the seven-step Coliazz method. Relationships between themes were explored to identify core concepts. Results: Analysis of interview transcripts revealed three phases that describe the parents’ journey: experiencing the accident, the in-patient phase and the return to community. Within these phases, themes were identified. Themes represented subthemes of stressors, behavioural and emotional responses and coping factors. Conclusion: Findings from this research will allow health professionals to optimise a holistic clinical service from a consumer’s perspective at all stages of the burn journey. These research conclusions could be used for the development of protocols to underpin a comprehensive information and social support management plan for families that would complement and support the surgical, medical and therapeutic treatment plan, providing direction for comprehensive service delivery. Implications for Rehabilitation Health professionals should optimise a holistic clinical service from a consumer’s perspective taking into consideration all stages of the burn journey. Therapeutic supports are required to target each phase of the burn journey and address changes in coping strategies and behavioural responses. There is a need for the development of protocols to underpin a comprehensive information and social support management plan for families that will complement and support the surgical and medical treatment plan.


AIMS: Improving glycaemic control in people with Type 1 diabetes is known to reduce complications. Our aim was to compare glycaemic control among people with Type 1 diabetes using data gathered in regional or national registries. METHODS: Data were obtained for children and/or adults with Type 1 diabetes from the following countries (or regions): Western Australia, Austria, Denmark, England, Champagne-Ardenne (France), Germany, Epirus, Thessaly and Thessaloniki (Greece), Galway (Ireland), several Italian regions, Latvia, Rotterdam (The Netherlands), Otago (New Zealand), Norway, Northern Ireland, Scotland, Sweden, Volyn (Ukraine), USA and Wales) from population or clinic-based registries. The sample size with available data varied from 355 to 173 880. Proportions with HbA1c < 58 mmol/mol (< 7.5%) and >= 75 mmol/mol (>= 9.0%) were compared by age and sex. RESULTS: Data were available for 324 501 people. The proportions with HbA1c 58 mmol/mol (< 7.5%) varied from 15.7% to 46.4% among 44 058 people aged < 15 years, from 8.9% to 49.5% among 50 766 people aged 15-24 years and from 20.5% to 53.6% among 229 677 people aged >= 25 years. Sex differences in glycaemic control were small. Proportions of people using insulin pumps varied between the 12 sources with data available. CONCLUSION: These results suggest that there are substantial
variations in glycaemic control among people with Type 1 diabetes between the data sources and that there is room for improvement in all populations, especially in young adults.

McWilliams T, Hendricks J, Twigg D and Wood F.
Burns education for non-burn specialist clinicians in Western Australia.
BACKGROUND: Burn patients often receive their initial care by non-burn specialist clinicians, with increasingly collaborative burn models of care. The provision of relevant and accessible education for these clinicians is therefore vital for optimal patient care. DESIGN/METHODS: A state-wide survey of multidisciplinary non-burn specialist clinicians throughout Western Australia identified learning needs related to paediatric burn care. A targeted education programme was developed and delivered live via videoconference. Pre-post-test analysis evaluated changes in knowledge as a result of attendance at each education session. RESULTS: Non-burn specialist clinicians identified numerous areas of burn care relevant to their practice. Statistically significant differences between perceived relevance of care and confidence in care provision were reported for aspects of acute burn care. Following attendance at the education sessions, statistically significant increases in knowledge were noted for most areas of acute burn care. CONCLUSIONS: Identification of learning needs facilitated the development of a targeted education programme for non-burn specialist clinicians. Increased non-burn specialist clinician knowledge following attendance at most education sessions supports the use of videoconferencing as an acceptable and effective method of delivering burns education in Western Australia.

Elevated IL-5 and IL-13 responses to egg proteins predate the introduction of egg in solid foods in infants with eczema.
Clinical and experimental allergy : journal of the British Society for Allergy and Clinical Immunology. 2015.
BACKGROUND: Egg allergy is a leading cause of food allergy in young infants, however little is known about early allergen specific T cell responses which predate the presentation of egg allergy, and if these are altered by early egg exposure. OBJECTIVE: To investigate the early T cell responses to multiple egg proteins in relation to patterns of egg exposure and subsequent IgE-mediated egg allergy. METHODS: Egg-specific T cell cytokine responses (IL-5, IL-13, IL-10, IFN-gamma and TNFalpha) to ovomucoid (OM), ovalbumin (OVA), conalbumin (CON) and lysozyme (LYS) were measured in infants with eczema at 4 months of age (n=40), before randomisation to receive ‘early egg’ or a placebo as part of a randomised controlled trial (Australian New Zealand Clinical Trials Registry number 12609000415202), and at 12 months of age (n=58), when IgE-mediated egg allergy was assessed by skin prick test and food challenge. RESULTS: In 4 month old infants, who had not directly ingested egg, those who subsequently developed egg allergy already had significantly higher Th2 cytokine responses to multiple egg allergens, particularly elevated IL-13 responses to OVA (P=0.004), OM (P=0.012) and LYS (P=0.003), and elevated IL-5 to the same antigens (P=0.031, 0.04 and 0.003 respectively). IL-13 responses (to OVA and LYS) and IL-5 responses (to LYS) at 4 months significantly predicted egg allergy at 12 months. All responses significantly declined with age in the egg allergic infants, and this did not appear to be modified by ‘early’ introduction of egg. CONCLUSIONS & CLINICAL RELEVANCE: Elevated egg-specific Th2 cytokine responses were established prior to egg ingestion at 4 months and were not significantly altered by introduction of egg. Th2 responses at 4 months of age predicted egg allergy at 12 months, suggesting that this could be used as a biomarker to select infants for early prevention and management strategies. This article is protected by copyright. All rights reserved.

Disruption of beta-catenin/CBP signaling inhibits human airway epithelial-mesenchymal transition and repair.
The epithelium of asthma is characterized by reduced expression of E-cadherin and increased expression of the basal cell markers ck-5 and p63 that is indicative of a relatively undifferentiated repairing epithelium. This phenotype correlates with increased proliferation, compromised wound healing and an enhanced capacity to undergo epithelial-mesenchymal transition (EMT). The transcription factor beta-catenin plays a vital role in epithelial cell differentiation and regeneration, depending on the co-factor recruited. Transcriptional programs driven by the beta-catenin/CBP axis are critical for maintaining an undifferentiated and proliferative state, whereas the beta-catenin/p300 axis is associated with cell differentiation. We hypothesized that disrupting the beta-catenin/CBP signaling axis would promote epithelial differentiation and inhibit EMT. We treated monolayer cultures of human airway epithelial cells with TGFbeta1 in the presence or absence of the selective small molecule ICG-001 to inhibit beta-catenin/CBP signaling. We used western blots to assess expression of an EMT signature, CBP, p300, beta-catenin, fibronectin and ITGbeta1 and scratch wound assays to assess epithelial cell migration. Snai-1 and -2 expressions were determined using q-PCR. Exposure to TGFbeta1

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induced EMT, characterized by reduced E-cadherin expression with increased expression of alpha-smooth muscle actin and EDA-fibronectin. Either co-treatment or therapeutic administration of ICG-001 completely inhibited TGFbeta1-induced EMT. ICG-001 also reduced the expression of ck-5 and -19 independent of TGFbeta1. Exposure to ICG-001 significantly inhibited epithelial cell proliferation and migration, coincident with a down regulation of ITGbeta1 and fibronectin expression. These data support our hypothesis that modulating the beta-catenin/CBP signaling axis plays a key role in epithelial plasticity and function.

Montini G and Hewitt IK.
The challenges of implementing the 2007 UK guidelines for paediatric urinary tract infection.

Adverse effects of topical corticosteroids in paediatric eczema: Australasian consensus statement.
Australasian Journal of Dermatology. 2015: n/a-n/a.

Mordaunt DA, Jolley A, Balasubramaniam S, Thorburn DR, Mountford HS, Compton AG, Nicholl J, Manton N, Clark D, Bratkovic D, Friend K and Yu S.
Phenotypic variation of TTC19-deficient mitochondrial complex III deficiency: A case report and literature review.
American Journal of Medical Genetics Part A. 2015: n/a-n/a.

Mullins RJ and Loh RK.
Childhood food allergy and anaphylaxis: an educational priority.

Munns A, Forde KA, Krouzecky M and Shields L.
Rainbows: A primary health care initiative for primary schools.
Collegian. 2015; (0).
Summary Within the current Australian health system is the understanding of a need to change from the predominate biomedical model to incorporate a comprehensive primary health care centred approach, embracing the social contexts of health and wellbeing. Recent research investigated the benefits of the primary health care philosophy and strategies in relation to the Rainbows programme which addresses grief and loss in primary school aged students in Western Australia. A multidisciplinary collaboration between the Western Australian Departments of Health and Education enabled community school health nurse coordinators to train teacher facilitators in the implementation of Rainbows, enabling support for students and their parents. The results of this qualitative study indicate that all participants regard Rainbows as effective, with many perceived benefits to students and their families.

Mutch RC, Watkins R and Bower C.
Fetal alcohol spectrum disorders: Notifications to the Western Australian Register of Developmental Anomalies.
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.

Seizure outcomes in children with epilepsy after resective brain surgery.

Updated 8/12/15
PURPOSE: To assess the role of resective brain surgery in childhood epilepsy. METHODOLOGY: We retrospectively analysed the seizure outcomes in 55 children with epilepsy who had resective brain surgery between 1997 and 2012, at our centre. The children were 1.5-18 years at the time of surgery; their seizure onset was between 0.2 and 15 years of age. 48 had refractory epilepsy. One child died of tumour progression. Follow-up duration in the survivors ranged from 2 to 16 years (mean: 9). Presurgical evaluation included clinical profiles, non-invasive V-EEG monitoring, neuroimaging with MRIs in all; SPECT and PET in selected patients. 54 had intraoperative ECoG. RESULTS: An Engel Class 1 outcome was seen in 78% of the cohort, with 67% being off all AEDs at the most recent follow-up. Children with tumours constituted the majority (56%), with 87% of this group showing a Class 1 outcome and 84% being off AEDs. Children with cortical dysplasia had a Class 1 outcome in 56%. CONCLUSION: Resective brain surgery is an efficacious option in some children with epilepsy. We found ECoG useful to tailor the cortical resection and in our opinion ECoG contributed to the good seizure outcomes.

Child with a heterozygous deletion of 2 megabases that includes the DAG1 gene, presenting as developmental delay.

Naimo PS, Fricke TA, Yong MS, d’Udekem Y, Kelly A, Radford DJ, Bullock A, Weintraub RG, Brizard CP and Konstantinov IE.
Outcomes of truncus arteriosus repair in children: 35 years of experience from a single institution.
Seminars in Thoracic and Cardiovascular Surgery. 2015.
Abstract Objective To evaluate long-term outcomes following repair of truncus arteriosus (TA) from a single-institution. Methods A retrospective review of children (n=171) who underwent TA repair between 1979 and 2014 in a single institution. Results Early mortality was 11.7% (20/171). There were 19 late deaths. Most deaths (74%, 29/39) occurred within the first year following surgery. One-year mortality in 1979–2004 was 18% (25/136) and decreased to 11% (4/35) in 2005–2014. Overall survival was 73.6% at 30 years. Multivariate analysis identified post-operative extra-corporeal membrane oxygenation (ECMO) (p=0.003), operative weight ≤2.5 kg (p=0.012), prior surgical intervention (p=0.018), and coronary artery anomaly (CAA) (p=0.037) as risk factors for early mortality. Cox-regression identified DiGeorge syndrome (p=0.008) as a risk factor for late mortality. Freedom from right ventricular outflow tract reoperation was 4.6% at 20 years. Concomitant truncal valve (TV) repair/replacement was undertaken in 20 patients. Fourteen additional patients underwent late TV repair/replacement. Overall survival in patients who had TV operation was 76.9% at 20 years. Nineteen patients had concomitant interrupted aortic arch (IAA) with survival of 89.5% at 20 years. Median follow-up was 19 years (mean 17 years, range 1–34 years). All patients were in New York Heart Association Class I/II at last follow-up. Conclusions Following repair of TA, patients had good long-term functional status, but high reoperation rate. Repair of IAA and TV were not risk factors for mortality. Postoperative ECMO, operative weight ≤2.5 kg, prior surgical intervention and CAA were risk factors for early death. DiGeorge syndrome was associated with late death. Ultra-mini abstract Repair of 171 patients with TA had early mortality was 11.7% and 19 late deaths. Surgery has good long-term functional outcomes, but high reoperation rate. Postoperative ECMO, operative weight ≤2.5 kg, prior surgical intervention and CAA were risk factor for early death. DiGeorge syndrome was associated with late death.

Nicholls W, Jennings R, Yeung Y, Walters M, Hewitt B and Gillett D.
Antenatal Ultrasound Detection of Cleft in Western Australia from 2003 to 2012: A Follow-Up Study.
The Cleft Palate-Craniofacial Journal. 2015; 0(0): null.

Nicol P, Anthonappa R, King N, Slack-Smith L, Cirillo G and Cherian S.
Caries burden and efficacy of a referral pathway in a cohort of preschool refugee children.
Australian dental journal. 2015; 60(1): 73-79.

Noonan K, Prunty S, Ha JF and Vijayasekaran S.
Surgical management of chronic salivary aspiration.
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 Updated 8/12/15
(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.

Novoselova TV, Rath SR, Carpenter K, Pachter N, Dickinson JE, Price G, Chan LF, Choong CS and Metherell LA.
NNT pseudoexon activation as a novel mechanism for disease in two siblings with familial glucocorticoid deficiency.
J Clin Endocrinol Metab. 2015; 100(2): E350-354.
CONTEXT: Intronic DNA frequently encodes potential exonic sequences called pseudoexons. In recent years, mutations resulting in aberrant pseudoexon inclusion have been increasingly recognized 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 nonconsanguineous 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 genomic DNA (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 4-bp duplication responsible for its activation. The variants segregated with the disease: p.Arg71* was inherited from the mother, the pseudoexon change was inherited 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; one causing pseudoexon inclusion in combination with another leading to 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 lifesaving therapy, and the possibility of preventative or curative intervention.

Eating disorder examination: Factor structure and norms in a clinical female pediatric eating disorder sample.
International Journal of Eating Disorders. 2015: n/a-n/a.
Objective The factor structure of the eating disorder examination (EDE) has never been tested in a clinical pediatric sample, and no normative data exist. Method The factor structure of an adapted EDE was examined in a clinical sample of 665 females aged 9–17 years with anorexia nervosa spectrum (70%), bulimia nervosa spectrum (12%), purging disorder (3%), and unspecified feeding and eating disorders (15%). Results The original four-factor model was a good fit in a confirmatory factor analysis as well a higher order model with three dimensions of restraint, eating concern, and combined weight concern/shape concern. Normative data are reported for clinicians to identify the percentiles in which their patients' score. Discussion The findings support dimensions of restraint, eating concern, weight concern, and shape concern in a clinical pediatric sample. This supports the factorial validity of the EDE, and the norms may assist clinicians to evaluate symptoms in females under 18 years. © 2015 Wiley Periodicals, Inc. (Int J Eat Disord 2015)

Oo S and Le Souef P.
The wheezing child: an algorithm.
BACKGROUND: Wheezing is a common presentation in young children. Diagnosis and treatment of these children can be challenging, as arriving at a final diagnosis often requires a process of elimination. OBJECTIVE: This article aims to provide an algorithm for managing a young child with wheeze in the primary care setting. We will aim to address key questions of some controversy that relate to this algorithm: 1. Does the child actually have wheeze - how accurate is the parents' description? 2. Do antibiotics have a role? The emergence of protracted bacterial bronchitis (PBB) 3. Is it asthma or viral wheeze, and which children outgrow this phenomenon? DISCUSSION: The exact cause of wheezing can be unclear in children, particularly those under pre-school age .

Updated 8/12/15
Osowicki J, Blyth CC, Britton PN, Clark J, Cooper CM, Haeusler GM, McMullan B and Bryant PA.

The study design of any new intervention trials should measure vitamin D levels at multiple time points during

Multicentre single-day hospital-wide point prevalence survey in 2012, in conjunction with the Antimicrobial

status and eczema outcomes, including lower serum vitamin D levels associated with increased incidence and

few prescriptions (4%) were deemed inappropriate. CONCLUSION: This is the first Australia-wide PPS of

Resistance and Prescribing in European Children study. The appropriateness of antimicrobial prescriptions was

tertiary children's hospitals. The findings highlight positive practices and potential targets for quality

There are limited data on antimicrobial prescribing practices for hospitalised neonates. We aimed to describe

and skin barrier function, both critical in the pathogenesis of eczema. However heterogeneous results have

across 5 states. SETTING: 6 neonatal units in tertiary children's hospitals across 5 states. PARTICIPANTS: All patients admitted at 8 am on the survey day to dedicated neonatal wards. MAIN OUTCOME MEASURES: An analysis of the quantity and quality of antimicrobial prescribing. RESULTS: The PPS included 6 neonatal units and 236 patients. Of 109 (46%) patients receiving at least one antimicrobial, 66 (61%) were being treated for infection, with sepsis the most common indication. There were 216 antimicrobial prescriptions, 134 (62%) for treatment of infection and 82 (38%) for prophylaxis, mostly oral nystatin. Only 15 prescriptions were for targeted as opposed to empirical treatment. Penicillin and gentamicin were the most commonly prescribed antibiotics, with vancomycin third most common. Half of all treated patients were receiving combination antimicrobial therapy. There was marked variation in vancomycin and gentamicin dosing. Overall, few prescriptions (4%) were deemed inappropriate. CONCLUSION: This is the first Australia-wide PPS of neonatal antimicrobial prescribing in tertiary children's hospitals. The findings highlight positive practices and potential targets for quality improvement.


Australia-wide point prevalence survey of antimicrobial prescribing in neonatal units: how much and how good?


BACKGROUND: There is increasing recognition of the threat to neonatal patients from antibiotic resistance.

There are limited data on antimicrobial prescribing practices for hospitalized neonates. We aimed to describe

antimicrobial use in hospitalised Australian neonatal patients, and to determine its appropriateness. METHODS: Multicentre single-day hospital-wide point prevalence survey in 2012, in conjunction with the Antimicrobial Resistance and Prescribing in European Children study. The appropriateness of antimicrobial prescriptions was also assessed. All patients admitted at 8 am on the survey day, in 6 neonatal units in tertiary children's hospitals across 5 states, were included in an analysis of the quantity and quality of all antimicrobial prescriptions. RESULTS: The point prevalence survey included 6 neonatal units and 236 patients. Of 109 patients (46%) receiving at least 1 antimicrobial, 66 (61%) were being treated for infection, with sepsis the most common indication. There were 216 antimicrobial prescriptions, 134 (62%) for treatment of infection and 82 (38%) for prophylaxis, mostly oral nystatin. Only 15 prescriptions were for targeted as opposed to empirical treatment. Penicillin and gentamicin were the most commonly prescribed antibiotics, with vancomycin third most common. Half of all treated patients were receiving combination antimicrobial therapy. There was marked variation in vancomycin and gentamicin dosing. Overall, few prescriptions (4%) were deemed inappropriate. CONCLUSION: This is the first Australia-wide point prevalence survey of neonatal antimicrobial prescribing in tertiary children's hospitals. The findings highlight positive practices and potential targets for quality improvement.


Australia-wide Point Prevalence Survey of Antimicrobial Prescribing in Neonatal Units: How Much and How Good?


BACKGROUND: There is increasing recognition of the threat to neonatal patients from antibiotic resistance.

There are limited data on antimicrobial prescribing practices for hospitalized neonates. We aimed to describe

antimicrobial use in hospitalised Australian neonatal patients, and to determine its appropriateness. METHODS: Multicentre single-day hospital-wide point prevalence survey in 2012, in conjunction with the Antimicrobial Resistance and Prescribing in European Children study. The appropriateness of antimicrobial prescriptions was also assessed. All patients admitted at 8 am on the survey day, in 6 neonatal units in tertiary children's hospitals across 5 states, were included in an analysis of the quantity and quality of all antimicrobial prescriptions. RESULTS: The point prevalence survey included 6 neonatal units and 236 patients. Of 109 patients (46%) receiving at least 1 antimicrobial, 66 (61%) were being treated for infection, with sepsis the most common indication. There were 216 antimicrobial prescriptions, 134 (62%) for treatment of infection and 82 (38%) for prophylaxis, mostly oral nystatin. Only 15 prescriptions were for targeted as opposed to empirical treatment. Penicillin and gentamicin were the most commonly prescribed antibiotics, with vancomycin third most common. Half of all treated patients were receiving combination antimicrobial therapy. There was marked variation in vancomycin and gentamicin dosing. Overall, few prescriptions (4%) were deemed inappropriate. CONCLUSION: This is the first Australia-wide point prevalence survey of neonatal antimicrobial prescribing in tertiary children's hospitals. The findings highlight positive practices and potential targets for quality improvement.

Palmer DJ.

Vitamin D and the Development of Atopic Eczema.


A “vitamin D hypothesis” has been proposed to explain the increased prevalence of eczema in regions with

higher latitude. This review focuses on the current available evidence with regard to the possible effect of

vitamin D on the development of atopic eczema. Observational studies have indicated a link between vitamin D

status and eczema outcomes, including lower serum vitamin D levels associated with increased incidence and

severity of eczema symptoms. Vitamin D is known to have a regulatory influence on both the immune system

and skin barrier function, both critical in the pathogenesis of eczema. However heterogeneous results have

been found in studies to date investigating the effect of vitamin D status during pregnancy and infancy on the

prevention of eczema outcomes. Well-designed, adequately powered, randomised controlled trials are needed.

The study design of any new intervention trials should measure vitamin D levels at multiple time points during

Updated 8/12/15
the intervention, ultraviolet (UV) radiation exposure via the use of individual UV dosimeters, and investigate the role of individual genetic polymorphisms. In conclusion, the current available evidence does not allow firm conclusions to be made on whether vitamin D status affects the development of atopic eczema.

Pang J, Martin AC, Mori TA, Bellin LJ and Watts GF.
Prevalence of Familial Hypercholesterolemia in Adolescents: Potential Value of Universal Screening?
The Journal of pediatrics. 2015.
Familial hypercholesterolemia (FH) significantly increases the risk of coronary heart disease. Most individuals are unaware they have the condition. In the Western Australian Pregnancy Cohort (Raine) Study, 1 in 267 adolescents were found to have FH. Universal cholesterol screening in childhood may offer the best strategy for diagnosing FH.

Pasterkamp H, Brand PL, Everard M, Garcia-Marcos L, Melbye H and Priftis KN.
Towards the standardisation of lung sound nomenclature.
The European respiratory journal : official journal of the European Society for Clinical Respiratory Physiology. 2015.
Auscultation of the lung remains an essential part of physical examination even though its limitations, particularly with regard to communicating subjective findings, are well recognised. The European Respiratory Society (ERS) Task Force on Respiratory Sounds was established to build a reference collection of audiovisual recordings of lung sounds that should aid in the standardisation of nomenclature. Five centres contributed recordings from paediatric and adult subjects. Based on pre-defined quality criteria, 20 of these recordings were selected to form the initial reference collection. All recordings were assessed by six observers and their agreement on classification, using currently recommended nomenclature, was noted for each case. Acoustical analysis was added as supplementary information. The audiovisual recordings and related data can be accessed online in the ERS e-learning resources. The Task Force also investigated the current nomenclature to describe lung sounds in 29 languages in 33 European countries. Recommendations for terminology in this report take into account the results from this survey.

Paul S, Resnick S, Gardiner K and Ramsay JM.
Long-distance transport of neonates with transposition of the great arteries for the arterial switch operation: A 26-year Western Australian experience.
Aim: There is evidence that outcomes of complex paediatric cardiac procedures including the arterial switch operation (ASO) for transposition of the great arteries (TGA) are improved when performed at higher volume centres. While in utero transport for surgery is considered ideal, antenatal detection rates of TGA are low. Long-distance transport of post-natally diagnosed neonates has the potential to destabilise the patient's clinical condition. Since 1986, many neonates with TGA have been transported interstate from Perth to Melbourne or Brisbane for ASO surgery. The aim of this study was to review the Western Australian experience of interstate transport of newborns with TGA for ASO, noting transport complications and comparing the early mortality of these patients with published outcomes of the ASO from Royal Children's Hospital (RCH), Melbourne. METHOD: In this retrospective cohort study, we reviewed the neonatal and cardiology databases and medical records to identify infants with TGA born between 1986 and 2011 and requiring ASO surgery during the 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.


Paxton GA, Cherian S and Zwi KJ.
The Royal Australasian College of Physicians position statement on refugee and asylum seeker health.

Immune responses to a recombinant, four-component, meningococcal serogroup B vaccine (4CMenB) in adolescents: A phase III, randomized, multicentre, lot-to-lot consistency study.

Vaccine. 2015; 33(39): 5217-5224.

BACKGROUND: For decades, a broadly effective vaccine against serogroup B Neisseria meningitidis (MenB) has remained elusive. Recently, a four-component recombinant vaccine (4CMenB) has been developed and is now approved in Europe, Canada, Australia and some Latin American countries. This phase III, randomized study evaluated the lot consistency, early immune responses and the safety profile of 4CMenB in 11 to 17-year-old adolescents in Australia and Canada (NCT01423084). METHODS: In total, 344 adolescents received two doses of one of 2 lots of 4CMenB, 1-month apart. Immunogenicity was assessed before, 2-weeks and 1-month following the second vaccination. Serum bactericidal activity using human complement (hSBA) was measured against three reference strains 44/76-SL, 5/99 and NZ98/254, selected to express one of the vaccine antigens; Neisseria adhesin A (NadA), factor H binding protein (fHbp) and porin A (PorA) containing outer membrane vesicle (OMV), respectively. Responses to the Neisseria heparin binding antigen (NHBA) were assessed with enzyme linked immunosorbent assay (ELISA). Local and systemic reactions were recorded for 7 days following each vaccination; unsolicited adverse events were monitored throughout the study. RESULTS: Immunological equivalence of the two lots of 4CMenB was established at 1-month. At baseline, </i>&lt;7% of participants had hSBA titers &gt;=5 to all three reference strains. Two weeks following the second dose of 4CMenB, all participants had hSBA titers &gt;=5 against fHbp and NadA compared with 84-96% against the PorA reference strains. At 1-month, corresponding proportions were 99%, 100% and 70-79%, respectively. Both lots were generally well tolerated and had similar adverse event profiles. CONCLUSIONS: Two doses of 4CMenB had an acceptable safety profile and induced a robust immune response in adolescents. Peak antibody responses were observed at 14 days following vaccination. While a substantial non-uniform antigen-dependent early decline in antibody titers was seen thereafter, a significant percentage of participants continued to maintain protective hSBA titers at 1-month.

Perrett KP, Richmond PC, Borrow R, Nolan T and McVernon J.

Antibody persistence in Australian adolescents following meningococcal C conjugate vaccination.

BACKGROUND: In Australia, following the introduction of serogroup C meningococcal (MenC) conjugate vaccine for toddlers and catch-up immunization through adolescence, MenC disease incidence plummeted and remains low. However, individual protection following MenC conjugate vaccination, particularly in young children, may be short-lived. We investigated the persistence of MenC serum bactericidal antibody (SBA) titers in adolescents, more than 7 years after a single “catch-up” dose of MenC conjugate vaccine. We also investigated their exposure and susceptibility to meningococcal serogroups A, W and Y. METHODS: MenC SBA titers and Men A, C, W and Y IgG geometric mean concentration were measured in 240 healthy 11- to 16-year-old adolescents. The correlate of protection was an rSBA titer of &gt;=8. RESULTS: An rSBA &gt;=8 was observed in 105 [44% (95% confidence interval [CI], 37–50%)] of 240 adolescents (mean age, 13.2 years, mean interval since MenC immunization, 8.2 years). The proportion with an rSBA &gt;=8, geometric mean rSBA titer and geometric mean IgG concentration increased with age, from 22% to 75%, 3.7 to 33.4 and 0.13 to 0.52 μg/mL, in participants who received MenC vaccine at mean age 2.8 to 7.5 years, respectively. Natural acquired antibody to Men A, W and Y was low with IgG geometric mean concentrations of 1.26, 0.38 and 0.47 μg/mL, respectively. CONCLUSIONS: More than half of Australian adolescents have inadequate serological protection against MenC disease and low natural immunity to MenA, W and Y.

Phelan H, Donaghe K, Cameron F, Clapin H, Cotterill A, Couper J, Craig M, Davis E, Jefferies C, Tham E and Jones T.
The Australasian diabetes data network (ADDN): first steps towards a national database resource.

Pool D, Elliott C, Bear N, Donnelly CJ, Davis C, Stannage K and Valentine J.

Neuromuscular electrical stimulation-assisted gait increases muscle strength and volume in children with unilateral spastic cerebral palsy.
Dev Med Child Neurol. 2015.
AIM: To determine if neuromuscular electrical stimulation (NMES) applied to the ankle dorsiflexors during gait improves muscle volume and strength in children with unilateral spastic cerebral palsy (CP). METHOD: Thirty-two children (15 females, 17 males; mean age 10y 8mo, age range 5y 5mo-18y 1mo) with unilateral spastic CP and a Gross Motor Function Classification System of level I or level II were randomly assigned to either the 8-week daily NMES treatment group or control group (usual or conventional treatments). Outcomes at week 8 (post-NMES) and week 14 (carryover) included magnetic resonance imaging for muscle volumes (tibialis
anterior, anterior compartment, and gastrocnemius), strength (hand-held dynamometry for isometric dorsiflexion strength and heel raises for functional strength), and clinical measures for lower limb selective motor control.

RESULTS: At week 8, the treatment group demonstrated significantly (p<0.05) increased muscle volumes for tibialis anterior, anterior compartment, medial and lateral gastrocnemius, and dorsiflexion strength not only when compared to their baseline values but also when compared to the control group at week 8. At week 14, both tibialis anterior and lateral gastrocnemius volumes in the treatment group remained significantly increased when compared to their baseline values. However, only lateral gastrocnemius volumes had significantly greater values when compared to the control group at week 14. There were no between group differences in the clinical measures for lower limb selective motor control at week 8 and 14. INTERPRETATION: Eight weeks of daily NMES-assisted gait increases muscle volume and strength of the stimulated ankle dorsiflexors in children with unilateral spastic CP. These changes are use-dependent and do not carry over after the 8-week treatment period. Gastrocnemius volume also increased post-treatment with carryover at week 14.

Pool D, Valentine J, A. Marie Blackmore AM, Colegate J, Bear N and Stannage K.
Daily functional electrical stimulation during everyday walking activities improves performance and satisfaction in children with unilateral spastic cerebral palsy: a randomized controlled trial.

Pool D, Valentine J, Bear N, Donnelly CJ, Elliott C and Stannage K.
The orthotic and therapeutic effects following daily community applied functional electrical stimulation in children with unilateral spastic cerebral palsy: a randomised controlled trial.

BACKGROUND: The purpose of this study was to determine the orthotic and therapeutic effects of daily community applied FES to the ankle dorsiflexors in a randomized controlled trial. We hypothesized that children receiving the eight-week FES treatment would demonstrate orthotic and therapeutic effects in gait and spasticity as well as better community mobility and balance skills compared to controls not receiving FES. METHODS: This randomized controlled trial involved 32 children (mean age 10 yrs 3 mo, SD 3 yrs 3 mo; 15 females, 17 males) with unilateral spastic cerebral palsy and a Gross Motor Function Classification System of I or II randomly assigned to a FES treatment group (n = 16) or control group (n = 16). The treatment group received eight weeks of daily FES (four hours per day, six days per week) and the control group received usual orthotic and therapy treatment. Children were assessed at baseline, post FES treatment (eight weeks) and follow-up (six weeks after post FES treatment). Outcome measures included lower limb gait mechanics, clinical measures of gastrocnemius spasticity and community mobility balance skills. RESULTS: Participants used the FES for a mean daily use of 6.2 (SD 3.2) hours over the eight-week intervention period. With FES, the treatment group demonstrated a significant (p < 0.05) increase in initial contact ankle angle (mean difference 11.9 degrees 95% CI 6.8 degrees to 17.1 degrees), maximum dorsiflexion ankle angle in swing (mean difference 8.1 degrees 95% CI 1.8 degrees to 14.4 degrees) normalized time in stance (mean difference 0.27 95% CI 0.05 to 0.49) and normalized step length (mean difference 0.06 95% CI 0.03 to 0.126) post treatment compared to the control group. Without FES, the treatment group significantly increased community mobility balance scores at post treatment (mean difference 8.3 units 95% CI 3.2 to 13.4 units) and at follow-up (mean difference 8.9 units 95% CI 3.8 to13.9 units) compared to the control group. The treatment group also had significantly reduced gastrocnemius spasticity at post treatment (p = 0.038) and at follow-up (dynamic range of motion mean difference 6.9 degrees, 95% CI 0.4 degrees to 13.6 degrees; p = 0.035) compared to the control group. CONCLUSION: This study documents an orthotic effect with improvement in lower limb mechanics during gait. Therapeutic effects i.e. without FES were observed in clinical measures of gastrocnemius spasticity, community mobility and balance skills in the treatment group at post treatment and follow-up. This study supports the use of FES applied during daily walking activities to improve gait mechanics as well as to address community mobility issues among children with unilateral spastic cerebral palsy. TRIAL REGISTRATION: Australian New Zealand Clinical Trials Register ACTRN1261400949684 . Registered 4 September 2014.

Pope N, Tallon M, McConigley R and Wilson S.
The experiences of acute non-surgical pain of children who present to a healthcare facility for treatment: a systematic review protocol.
JBI Database of Systematic reviews. 2015; 13(10).

Porter M, Charles AK, Nathan EA, French NP, Dickinson JE, Darragh H and Keil AD.
Haemophilus influenzae: a potent perinatal pathogen disproportionately isolated from Indigenous women and their neonates.
BACKGROUND: Nontypeable Haemophilus influenzae (NTHi) bacteraemia in pregnant women is strongly associated with pregnancy loss and preterm delivery. However, the clinical significance of isolation of NTHi from
nonsterile sites is unknown. AIMS: To examine the hypothesis that isolation of NTHi from any specimen is associated with adverse perinatal outcomes and to investigate the impression that NTHi is disproportionately isolated from indigenous women and their neonates. MATERIALS AND METHODS: Cases where NTHi was isolated from maternal, fetal or neonatal specimens during the period from 1 July 1997 to 1 July 2009 were identified. Demographic and clinical data were extracted from case notes. Histopathological material was re-reviewed by a perinatal pathologist. Demographic and clinical features of the affected group were compared with the hospital obstetric population. RESULTS: NTHi was isolated from maternal, fetal or neonatal specimens in 97 pregnancies. Two women had NTHi isolated during different pregnancies. Two mothers and 10 neonates were bacteraemic. Indigenous women comprised 28% of pregnancies where NTHi was isolated, compared with 6% of the hospital obstetric population (P < 0.001). Pregnancy loss occurred in six cases (6%). Median gestation at delivery was 33 weeks. Of 96 liveborn neonates, 88 (92%) required admission to a neonatal special care unit. Four liveborn neonates died (4%). Chorioamnionitis was confirmed by histology in 31/33 (93.9%) of placents examined. CONCLUSIONS: Isolation of NTHi occurred more commonly in indigenous women and neonates. Isolation of NTHi from any obstetric or neonatal specimen is associated with chorioamnionitis, preterm birth, pregnancy loss, early-onset neonatal sepsis and neonatal death.

Haemophilus influenzae: using comparative genomics to accurately identify a highly recombinogenic human pathogen.
BACKGROUND: Haemophilus influenzae is an opportunistic bacterial pathogen that exclusively colonises humans and is associated with both acute and chronic disease. Despite its clinical significance, accurate identification of H. influenzae is a non-trivial endeavour. H. haemolyticus can be misidentified as H. influenzae from clinical specimens using selective culturing methods, reflecting both the shared environmental niche and phenotypic similarities of these species. On the molecular level, frequent genetic exchange amongst Haemophilus spp. has confounded accurate identification of H. influenzae, leading to both false-positive and false-negative results with existing speciation assays. RESULTS: Whole-genome single-nucleotide polymorphism data from 246 closely related global Haemophilus isolates, including 107 Australian isolate genomes generated in this study, were used to construct a whole-genome phylogeny. Based on this phylogeny, H. influenzae could be differentiated from closely related species. Next, a H. influenzae-specific locus, fucP, was identified, and a novel TaqMan real-time PCR assay targeting fucP was designed. PCR specificity screening across a panel of clinically relevant species, coupled with in silico analysis of all species within the order Pasteurellales, demonstrated that the fucP assay was 100 % specific for H. influenzae; all other examined species failed to amplify. CONCLUSIONS: This study is the first of its kind to use large-scale comparative genomic analysis of Haemophilus spp. to accurately delineate H. influenzae and to identify a species-specific molecular signature for this species. The fucP assay outperforms existing H. influenzae targets, most of which were identified prior to the next-generation genomics era and thus lack validation across a large number of Haemophilus spp. We recommend use of the fucP assay in clinical and research laboratories for the most accurate detection and diagnosis of H. influenzae infection and colonisation.

Relapse and outcome patterns of patients with central nervous system mixed malignant germ cell tumors treated without irradiation: Findings from the third international central nervous system (CNS) germ cell tumor (GCT) study.
OBJECTIVES: To evaluate patterns of relapse and outcome in patients newly diagnosed with CNS Mixed Malignant GCT (MMGCT) treated initially with chemotherapy alone. METHODS: A retrospective chart review was conducted using all 25 patients enrolled on the International CNS GCT Study III, with at least 7 years follow-up for all surviving patients. RESULTS: Thirteen patients at diagnosis had CNS MMGCT by pathology and tumor markers (n = 11), or tumor markers alone (n = 2). Twelve received chemotherapy alone, one additionally receiving foci irradiation prior to relapse. Six patients (46%) relapsed (mean of 30.5 months; range 6-59 months), two beyond and four within the primary site alone. Three patients relapsed early (6-23 months from diagnosis), two with alpha-fetoprotein elevations and one without tumor markers assessed; all three expired of progressive disease at 2-10 months following initial relapse. Three patients relapsed late (37-59 months) without AFP elevations, one with pathologically pure germinoma, two with mild beta-human chorionic gonadotropin elevations; these patients survive disease-free at 86+, 94+, and 126+ months following additional treatment. CONCLUSIONS: Patients with CNS MMGCT relapsing following chemotherapy alone display two distinct patterns of recurrence and outcome; patients relapsing early possess MMGCT elements and have a dismal prognosis, while patients relapsing late do so with pure germinomatous elements and have an excellent

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outcome. Current cooperative group studies utilizing more localized fields of irradiation should monitor closely the patterns of relapse and outcome; late recurrences with germinomatous elements might be avoided by initial use of low-dose larger field irradiation in select patients.

The 'Can't Intubate, Can't Oxygenate' scenario in pediatric anesthesia: a comparison of the Melker cricothyroidotomy kit with a scalpel bougie technique.

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 caudad. 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.

Prunty SL, Spilsbury K, Kadhim AL, Semmens JB, Coates HL and Lannigan FJ.
Long-term Outcomes for Children with Middle Ear Disease in Western Australia.

Rakshasbhuvankar A, Paul S, Nagarajan L, Ghosh S and Rao S.
Amplitude-integrated EEG for detection of neonatal seizures: a systematic review.
Seizure. 2015.

PURPOSE: Amplitude-integrated electroencephalogram (aEEG) is being used increasingly for monitoring seizures in neonatal units. Its accuracy, compared with "the gold-standard" conventional electroencephalogram (cEEG) is still not well established. We aimed to conduct a systematic review to evaluate the diagnostic accuracy of aEEG when compared with cEEG, for detection of neonatal seizures. METHOD: A systematic review was conducted using the Cochrane methodology. EMBASE, CINAHL and PubMed databases were searched in September 2014. Studies comparing simultaneous recordings of cEEG and aEEG for detection of seizures in neonatal population were included. QUADAS 2 tool was used to examine "risk of bias" and "applicability". RESULTS: Ten studies (patient sample 433) were included. Risk of bias was high in five studies, unclear in one and low in four. For the detection of individual seizures, when "aEEG with raw trace" was used, median sensitivity was 76% (range: 71-85), and specificity 85% (range: 39-96). When "aEEG without raw trace" was used, median sensitivity was 39% (range: 25-80) and specificity 95% (range: 50-100). Detailed meta-analysis could not be done because of significant clinical/methodological heterogeneity. Seizure detection was better when interpreted by experienced clinicians. Seizures with low amplitude/brief duration and those occurring away from aEEG leads were less likely to be detected. CONCLUSION: Studies included in the systematic review showed aEEG to have relatively low and variable sensitivity and specificity. Based on the available evidence, aEEG cannot be recommended as the mainstay for diagnosis and management of neonatal seizures. There is an urgent need of well-designed studies to address this issue definitively.

Anaesthesia. 2015; 70(10): 1160-1164.

Increased levels of exhaled nitric oxide (eNO) may be a more objective predictor in identifying children at higher risk of peri-operative adverse respiratory events than the presence of risk factors such as recent cold or wheeze. Children with either none or >/= 2 risk factors had eNO measured before surgery and any peri-operative adverse respiratory events were recorded. We found that an elevated eNO level was only predictive of adverse respiratory events in children with >/= 2 risk factors (OR 2.96 (95% CI 1.48-5.93), p = 0.002). The presence of risk factors had a better predictive capability than a raised eNO level (OR 3.83 (95% CI 1.85-7.95),

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p < 0.001). The combination of both predictors did not improve the predictive capability for adverse respiratory events (OR 1.93 (95% CI 1.44-2.59), p < 0.001). We conclude that measuring eNO levels does not lead to improved prediction of adverse respiratory events and that, in routine clinical practice, an accurate history of risk factors remains the most appropriate tool for successfully identifying children at risk of peri-operative adverse respiratory events.


This study aimed to evaluate the ability of the forced oscillation technique (FOT) to detect underlying lung disease in preschool children with cystic fibrosis (CF) diagnosed following newborn screening. 184 children (aged 3-6 years) with CF underwent lung function testing on 422 occasions using the FOT to assess respiratory resistance and reactance at the time of their annual bronchoalveolar lavage collection and chest computed tomography scan. We examined associations between FOT outcomes and the presence and progression of respiratory inflammation, infection and structural lung disease. Children with CF who had pronounced respiratory disease, including free neutrophil elastase activity, infection with pro-inflammatory pathogens and structural lung abnormalities had similar FOT outcomes to those children without detectable lung disease. In addition, the progression of lung disease over 1 year was not associated with worsening FOT outcomes. We conclude that the forced oscillation technique is relatively insensitive to detect underlying lung disease in preschool children with CF. However, FOT may still be of value in improving our understanding of the physiological changes associated with early CF lung disease.

Ramsey KA, Schultz A and Stick SM. Biomarkers in Paediatric Cystic Fibrosis Lung Disease. Paediatric respiratory reviews. 2015.

Biomarkers in cystic fibrosis are used i. for the measurement of cystic fibrosis transmembrane regulator function in order to diagnose cystic fibrosis, and ii. to assess aspects of lung disease severity (e.g. inflammation, infection). Effective biomarkers can aid disease monitoring and contribute to the development of new therapies. The tests of cystic fibrosis transmembrane regulator function each have unique strengths and weaknesses, and biomarkers of inflammation, infection and tissue destruction have the potential to enhance the management of cystic fibrosis through the early detection of disease processes. The development of biomarkers of cystic fibrosis lung disease, in particular airway inflammation and infection, is influenced by the challenges of obtaining relevant samples from infants and children for whom early detection and treatment of disease might have the greatest long term benefits.


OBJECTIVE: To investigate if adults who are hospitalised for a burn injury have increased long-term hospital use for musculoskeletal diseases. DESIGN: A population-based retrospective cohort study using linked administrative health data from the Western Australian Data Linkage System. SUBJECTS: Records of 17,753 persons aged at least 20 years when hospitalised for a first burn injury in Western Australia during the period 1980-2012, and 70,758 persons who were age and gender-frequency matched with no injury admissions randomly selected from Western Australia's electoral roll. MAIN OUTCOME MEASURES: Admission rates and cumulative length of stay for musculoskeletal diseases. Negative binomial and Cox proportional hazards regression modelling were used to generate incidence rate ratios (IRR) and HRs with 95% CIs, respectively. RESULTS: After adjustment for pre-existing health status and demographic characteristics, the burn cohort had almost twice the hospitalisation rate for a musculoskeletal condition (IRR, 95% CI 1.98, 1.86 to 2.10), and spent 3.70 times as long in hospital with a musculoskeletal diagnosis (95% CI 3.10 to 4.42) over the 33-year period, than the uninjured comparison cohort. Adjusted survival analyses of incident post-burn musculoskeletal disease admissions found significant increases for the 15-year post burn discharge period (0-6 months: HR, 95% CI 2.51, 2.04 to 3.11; 6 months-2 years: HR, 95% CI 1.77, 1.53 to 2.05; 2-15 years: HR, 95% CI 1.32, 1.23 to 1.42). Incident admission rates were significantly elevated for 20 years post-burn for minor and severe burn injury for a range of musculoskeletal diseases that included arthropathies, dorsopathies, osteopathies and soft tissue disorders. CONCLUSIONS: Minor and severe burn injuries were associated with significantly increased post-burn incident admission rates, long-term hospital use and prolonged length of stay for a range of musculoskeletal diseases. Further research is required that facilitates identification of at-risk patients and appropriate treatment pathways, to reduce the long-term morbidity associated with burns.

Regli A and von Ungern-Sternberg B.

Updated 8/12/15
Diagnosis and Management of Respiratory Adverse Events in the Operating Room.
Current Anesthesiology Reports. 2015: 1-12.

Reynolds JE, Licari MK, Billington J, Chen Y, Aziz-Zadeh L, Werner J, Winsor AM and Bynevelt M.
The aim of this study was to reveal cortical areas that may contribute to the movement difficulties seen in children with Developmental Coordination Disorder (DCD). Specifically, we hypothesized that there may be a deficit in the mirror neuron system (MNS), a neural system that responds to both performed and observed actions. Using functional MRI, 14 boys with DCD (x =10.08 years +/-1.31, range=7.83-11.58 years) and 12 typically developing controls (x =10.10 years +/-1.15, range=8.33-12.00 years) were scanned observing, executing and imitating a finger sequencing task using their right hand. Cortical activations of mirror neuron regions, including posterior inferior frontal gyrus (IFG), ventral premotor cortex, anterior inferior parietal lobule and superior temporal sulcus were examined. Children with DCD had decreased cortical activation mirror neuron related regions, including the precentral gyrus and IFG, as well as in the posterior cingulate and precuneus complex when observing the sequencing task. Region of interest analysis revealed lower activation in the pars opercularis, a primary MNS region, during imitation in the DCD group compared to controls. These findings provide some preliminary evidence to support a possible MNS dysfunction in children with DCD.

Reynolds V, Meldrum S, Simmer K, Vijayasekaran S and French N.
Laryngeal pathology at school age following very preterm birth.
INTRODUCTION: Intubation injury resulting in laryngeal pathology is recognised as a possible complication of preterm birth, yet few published studies have examined such pathology and its relation to voice outcomes. This study reports on the results of prospective laryngeal function examinations of a cohort of very preterm children, all of whom presented with significant dysphonia at school age. MATERIALS AND METHODS: The laryngeal pathology of 20 very preterm children, born between 23 and 29 weeks gestation, was examined under halogen and stroboscopic conditions. Laryngeal structure and function were assessed using a rigid laryngoscope or a flexible nasendoscope. The approach was selected based on the age and/or likely compliance of the child. RESULTS: Nineteen children were found to have structural laryngeal pathology. Fourteen children presented with a chink to the posterior glottis and all demonstrated at least a mild degree of supraglottic hyperfunction. Other common findings were arytenoid prolapse and vocal fold immobility. More isolated findings included posterior scar band, vocal fold atrophy, arytenoid oedema and growth on the vocal folds. One child who presented with structural laryngeal pathology was never intubated. DISCUSSION: Supraglottic hyperfunction was common to all participants, regardless of the nature and extent of underlying structural laryngeal pathology. Posterior glottic chink was the most common pattern of incomplete vocal fold closure. These data support the hypothesis that very preterm children adopt supraglottic tightening to compensate for underlying laryngeal pathology. The mechanism underlying laryngeal damage in the child who was not intubated is unclear. CONCLUSIONS: Voice quality of very preterm children is affected by both laryngeal structure and function. A trial of behavioural voice treatment is recommended to evaluate any therapeutic response in this population.

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 33months 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 (2years, range 1.1-11.5years) and for salvage ITI in 7 patients (9.9years, 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 21months (range 5-85months); 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 18months of ITI and another in whom a partial response had not been achieved after 22months 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.
Rosenow T, Oudraad MCJ, Murray CP, Turkovic L, Kuo W, de Bruijne M, Ranganathan SC, Tiddens HAWM and Stick SM.
PRAGMA-CF: a Quantitative Structural Lung Disease CT Outcome in Young Children with Cystic Fibrosis.
American journal of respiratory and critical care medicine. 2015.

Rothenbury A.
A new paradigm for assessment of infant feeding deviation.
Normal child development is slow from birth to 25 years. Since Neolithic times, humans have relied on common sense, learned by trial and error, and mourned infants lost to infection and malnutrition. In recent times, knowledge of the process accelerated with increasing interest in child survival and health improvement. Historically, infant survival relied on breastfeeding until pathogens were identified, food technology developed, and infant/child surveillance commenced within the ethos of public health. Today, universal screening of infants from birth aims to identify deviation from the norm in all areas of development, allowing early intervention and correction. The personal experience of health professionals can be a positive factor in reflective practice, questioning orthodoxy and generating new perspectives and corrective strategies. Clinical settings generate practice-based evidence, a prerequisite for research. This concept of the infant as a primary cause of feeding problems demands consideration of a new paradigm and prompts research.

Rueter K, Haynes A and Prescott S.
Developing Primary Intervention Strategies to Prevent Allergic Disease.

Rueter K, Prescott SL and Palmer DJ.
Nutritional approaches for the primary prevention of allergic disease: An update.
The dramatic rise in early childhood allergic diseases indicates the specific vulnerability of the immune system to early life environmental changes. Dietary changes are at the centre of lifestyle changes that underpin many modern inflammatory and metabolic diseases, and therefore are an essential element of prevention strategies. Although modern dietary changes are complex and involve changing patterns of many nutrients, there is also an interest in the early life effects of specific nutrients including polyunsaturated fatty acids, oligosaccharides (soluble fibre), antioxidants, folate and other vitamins that have documented effects on immune function as well as metabolism. A better understanding of nutritional programming of immune health, nutritional epigenetics and the biological processes sensitive to nutritional exposures in early life may lead to dietary strategies that provide more tolerogenic conditions during early immune programming and reduce the burden of many inflammatory diseases, not just allergy.

Salamon ER, Gain KR and Hall GL.
Defining the appropriate waiting time between multiple-breath nitrogen washout measurements.

Adolescent and young adult medicine in Australia and New Zealand: towards specialist accreditation.

Schaefer N, Chong J, Griffin A, Little A, Gochee P and Dixon N.
Schneiderian-Type Papilloma of the Middle Ear: A Review of the Literature.
Schneiderian-type papilloma of the middle ear is a rare finding. We present a 46-year-old Aboriginal man with a large tympanic membrane perforation and a Schneiderian-type papilloma filling the middle ear. The aim of this study is to familiarize clinicians with this uncommon disease through discussion of its clinical presentation, diagnostic considerations and management. A search of English-language peer-reviewed literature was undertaken using the key words "Schneiderian-type papilloma,” “inverted papilloma,” and “middle ear.” A total of 29 cases (including the present case) of Schneiderian-type papilloma involving the middle ear were reviewed. Common presenting symptoms include hearing loss, otalgia, and otorrhea. Middle ear disease is associated with higher rates of recurrence and malignant transformation than its sinonasal counterpart. Radical surgical resection is the only curative treatment. Schneiderian-type papilloma is a benign, but locally aggressive, epithelial neoplasm most commonly arising in the sinonasal tract. Whilst involvement of the middle ear is
extremely rare, knowledge of this condition is important due to its propensity to recur and the high rate of malignant transformation.

Response to low dose growth hormone treatment in infants and toddlers with Prader-Willi Syndrome.

Schultz A and Stick S.
Early pulmonary inflammation and lung damage in children with cystic fibrosis.
Individuals with cystic fibrosis (CF) suffer progressive airway inflammation, infection and lung damage. Airway inflammation and infection are present from early in life, often before children are symptomatic. CF gene mutations cause changes in the CF transmembrane regulator protein that result in an aberrant airway microenvironment including airway surface liquid (ASL) dehydration, reduced ASL acidity, altered airway mucin and a dysregulated inflammatory response. This review discusses how an altered microenvironment drives CF lung disease before overt airway infection, the response of the CF airway to early infection, and methods to prevent inflammation and early lung disease.

Outcomes of infants with Apgar score of zero at 10 min: the West Australian experience.
Arch Dis Child Fetal Neonatal Ed. 2015; 100(6): F492-494.
BACKGROUND: Infants who have an Apgar score of zero at 10 min of age are known to have poor long-term prognosis. Expert committee guidelines suggest that it is reasonable to cease resuscitation efforts if the asphyxiated infant does not demonstrate a heart beat by 10 min of life. These guidelines are based on data from the era when therapeutic hypothermia was not the standard of care for hypoxic ischaemic encephalopathy (HIE). Hence, we aimed to review our unit data from the era of therapeutic hypothermia to evaluate the outcomes of infants who had an Apgar score of zero at 10 min and had survived to reach the neonatal intensive care unit. METHODS: Retrospective chart review. STUDY PERIOD: 2007-2013. RESULTS: 13 infants (gestational age >=35 weeks) with Apgar scores of zero at 10 min were admitted to the neonatal intensive care unit. All were born outside the tertiary perinatal centre. Of them, eight died before discharge. The type and duration of follow-up varied. Of the five survivors, three had normal cognitive scores (100, 100 and 110) on Bayley III assessment at 2 years of age and one had normal Griffiths score (general quotient (GQ) 103) at 1 year. Only one infant developed severe spastic quadriplegia. CONCLUSIONS: 4 out of 13 (30.7%) infants with 10 min Apgar scores of zero who survived to reach the neonatal intensive care unit had normal scores on formal developmental assessments. Information from large databases (preferably population based) is necessary to review recommendations regarding stopping delivery room resuscitation in term infants.

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.

Sheel M, Moreland NJ, Fraser JD and Carapetis J.
Development of Group A streptococcal vaccines: an unmet global health need.
Group A Streptococcus (GAS) infections are a significant global cause of morbidity and mortality. GAS diseases disproportionately affect those living in conditions characterized by poverty and social injustice, in both developing countries and in marginalized populations of industrialized nations. In Australia and New Zealand, GAS-associated Acute Rheumatic Fever (ARF) is a major cause of health inequality disproportionally affecting indigenous children. Recognition of these inequalities by the governments of Australia and New Zealand has resulted in the formation of a Trans-Tasman Coalition to Advance New Vaccines for group A Streptococcus (CANVAS). This review provides an update on the current status of GAS vaccine development, and describes global efforts by CANVAS and others to accelerate the development of GAS vaccines.

Clinical presentation of eating disorders in young males at a tertiary setting.

Updated 8/12/15
BACKGROUND: Young males with eating disorders are a neglected study population in eating disorders. The aim of this study was to provide knowledge about the clinical presentation of eating disorders in young males.

METHODS: The data source was the Helping to Outline Paediatric Eating Disorders (HOPE) Project (N ~ 1000), a prospective, ongoing registry comprising consecutive paediatric (<18 years) tertiary eating disorder referrals. Young males with DSM-5 eating disorders (n = 53) were compared with young females with eating disorders (n = 704).

RESULTS: There was no significant difference in the prevalence of diagnosis of bulimia nervosa (2 % vs 11 %, p = 0.26) among sexes. Males had comparable duration of illness (9 months; p = 0.28) and a significantly earlier age of onset (M = 12 years; p <0.001). Shape concern (2.39 vs 3.57, p <0.001) and weight concern (1.97 vs 3.09, p <0.001) were lower in males, and body mass index z score (-1.61 vs -1.42, p = 0.29) and medical compromise (odds ratio [OR] = 0.64, 95 % CI: 0.36, 1.12) were comparable. Males had a two-fold higher odds of being diagnosed with unspecified feeding or eating disorders (40 % vs 22 % for females, p = 0.004). Driven exercise to control weight and shape was common and comparable in prevalence among males and females (51 % vs 47 %, p = 0.79) and males were less likely to present with self-induced vomiting (OR = 0.23, 95 % CI: 0.09, 0.59).

CONCLUSION: Boys with eating disorders are an understudied group with similarities and differences in clinical presentation from girls with eating disorders. Parents and physicians are encouraged to consider changes in weight, disturbed vital signs, and driven, frequent exercise for the purposes of controlling weight or shape, as possible signs of eating disorders among male children. Diagnostic classification, assessment instruments, conceptualisation, and treatment methods need to be refined to improve application to young males.

Siffleet J, Williams AM, Rapley P and Slatyer S.
Delivering Best Care and Maintaining Emotional Wellbeing in the Intensive Care Unit: the Perspective of Experienced Nurses.
Applied Nursing Research. 2015.

Simpson SJ, Hall GL and Wilson AC.
Lung function following very preterm birth in the era of 'new' bronchopulmonary dysplasia.
Respirology. 2015: n/a-n/a.

Progressive ventilation inhomogeneity in infants with cystic fibrosis after pulmonary infection.
The European respiratory journal : official journal of the European Society for Clinical Respiratory Physiology. 2015.

Measures of ventilation distribution are promising for monitoring early lung disease in cystic fibrosis (CF). This study describes the cross-sectional and longitudinal impacts of pulmonary inflammation and infection on ventilation homogeneity in infants with CF. Infants diagnosed with CF underwent multiple breath washout (MBW) testing and bronchoalveolar lavage at three time points during the first 2 years of life. Measures were obtained for 108 infants on 156 occasions. Infants with a significant pulmonary infection at the time of MBW showed increases in lung clearance index (LCI) of 0.400 units (95% CI 0.150-0.648; p=0.002). The impact was long lasting, with previous pulmonary infection leading to increased ventilation inhomogeneity over time compared to those who remained free of infection (p<0.05). Infection with Haemophilus influenzae was particularly detrimental to the longitudinal lung function in young children with CF where LCI was increased by 1.069 units for each year of life (95% CI 0.484-1.612; p<0.001). Pulmonary infection during the first year of life is detrimental to later lung function. Therefore, strategies aimed at prevention, surveillance and eradication of pulmonary pathogens are paramount to preserve lung function in infants with CF.

Invasive infections due to filamentous fungi other than Aspergillus: epidemiology and determinants of mortality.
Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases. 2015; 21(5): 490.e491-410.

The epidemiology of invasive fungal disease (IFD) due to filamentous fungi other than Aspergillus may be changing. We analysed clinical, microbiological and outcome data in Australian patients to determine the predisposing factors and identify determinants of mortality. Proven and probable non-Aspergillus mould infections (defined according to modified European Organization for Research and Treatment of Cancer/Mycoses Study Group criteria) from 2004 to 2012 were evaluated in a multicentre study. Variables associated with infection and mortality were determined. Of 162 episodes of non-Aspergillus IFD, 145 (89.5%) were proven infections and 17 (10.5%) were probable infections. The pathogens included 29 fungal species/species complexes; mucormycetes (45.7%) and Scedosporium species (33.3%) were most common.
The commonest comorbidities were haematological malignancies (HMs) (46.3%) diabetes mellitus (23.5%), and chronic pulmonary disease (16%); antecedent trauma was present in 21% of cases. Twenty-five (15.4%) patients had no immunocompromised status or comorbidity, and were more likely to have acquired infection following major trauma (p < 0.01); 61 (37.7%) of cases affected patients without HMs or transplantation. Antifungal therapy was administered to 93.2% of patients (median 68 days, interquartile range 19-275), and adjunctive surgery was performed in 58.6%. The all-cause 90-day mortality was 44.4%; HMs and intensive-care admission were the strongest predictors of death (both p < 0.001). Survival varied by fungal group, with the risk of death being significantly lower in patients with dematiaceous mould infections than in patients with other non-Aspergillus mould infections. Non-Aspergillus IFD affected diverse patient groups, including non-immunocompromised hosts and those outside traditional risk groups; therefore, definitions of IFD in these patients are required. Given the high mortality, increased recognition of infections and accurate identification of the causative agent are required.

Smith Z, Leslie G and Wynaden D.
Australian perioperative nurses' experiences of assisting in multi-organ procurement surgery: a grounded theory study.
INTRODUCTION/BACKGROUND: Multi-organ procurement surgical procedures through the generosity of deceased organ donors, have made an enormous impact on extending the lives of recipients. There is a dearth of in-depth knowledge relating to the experiences of perioperative nurses working closely with organ donors undergoing multi-organ procurement surgical procedures. AIM: The aim of this study was to address this gap by describing the perioperative nurses experiences of participating in multi-organ procurement surgical procedures and interpreting these findings as a substantive theory. DESIGN: This qualitative study used grounded theory methodology to generate a substantive theory of the experiences of perioperative nurses participating in multi-organ procurement surgery. SETTING: Recruitment of participants took place after the study was advertised via a professional newsletter and journal. The study was conducted with participants from metropolitan, rural and regional areas of two Australian states; New South Wales and Western Australia. PARTICIPANTS: Thirty five perioperative nurse participants with three to 39 years of professional nursing experience informed the study. METHODS: Semi structured in-depth interviews were undertaken from July 2009 to April 2010 with a mean interview time of 60 min. Interview data was transcribed verbatim and analysed using the constant comparative method. RESULTS: The study results draw attention to the complexities that exist for perioperative nurses when participating in multi-organ procurement surgical procedures reporting a basic social psychological problem articulated as hiding behind a mask and how they resolved this problem by the basic social psychological process of finding meaning. CONCLUSION: This study provides a greater understanding of how these surgical procedures impact on perioperative nurses by providing a substantive theory of this experience. The findings have the potential to guide further research into this challenging area of nursing practice with implications for clinical initiatives, management practices and education.

Smith Z, Leslie G and Wynaden D.
Hiding behind a mask: Australian perioperative nurses' experiences of participating in multi-organ procurement surgery.
International Journal of Nursing Studies. 2015; (0).
AbstractIntroduction/Background Multi-organ procurement surgical procedures through the generosity of deceased organ donors, have made an enormous impact on extending the lives of recipients. There is a dearth of in-depth knowledge relating to the experiences of perioperative nurses working closely with organ donors undergoing multi-organ procurement surgical procedures. Aim The aim of this study was to address this gap by describing the perioperative nurses experiences of participating in multi-organ procurement surgical procedures and interpreting these findings as a substantive theory. Design This qualitative study used grounded theory methodology to generate a substantive theory of the experiences of perioperative nurses participating in multi-organ procurement surgery. Setting Recruitment of participants took place after the study was advertised via a professional newsletter and journal. The study was conducted with participants from metropolitan, rural and regional areas of two Australian states; New South Wales and Western Australia. Participants Thirty five perioperative nurse participants with three to 39 years of professional nursing experience informed the study. Methods Semi structured in-depth interviews were undertaken from July 2009-April 2010 with a mean interview time of 60 minutes. Interview data was transcribed verbatim and analysed using the constant comparative method. Results The study results draw attention to the complexities that exist for perioperative nurses when participating in multi-organ procurement surgical procedures reporting a basic social psychological problem articulated as hiding behind a mask and how they resolved this problem by the basic social psychological process of finding meaning. Conclusion This study provides a greater understanding of how these surgical procedures impact on perioperative nurses by providing a substantive theory of this experience. The findings
have the potential to guide further research into this challenging area of nursing practice with implications for clinical initiatives, management practices and education.

Srinivasjois R, Rao S and Patole S.  
Probiotic supplementation in children with autism spectrum disorder.  
Arch Dis Child. 2015; 100(5): 505-506.

Stirweiss A, McCarthy K, Oommen J, Crook ML, Hardy K, Kees UR, Wilton SD, Anazodo A and Beesley AH.  
A novel BRD4-NUT fusion in an undifferentiated sinonasal tumor highlights alternative splicing as a contributing oncogenic factor in NUT midline carcinoma.  
Oncogenesis. 2015; 4: e1174.

NUT midline carcinoma (NMC) is a fatal cancer that arises in various tissues along the upper midline of the body. The defining molecular feature of NMC is a chromosomal translocation that joins (in the majority of cases) the nuclear testis gene NUT (NUTM1) to the bromodomain protein family member 4 (BRD4) and thereby creating a fusion oncogene that disrupts cellular differentiation and drives the disease. In this study, we report the case of an adolescent NMC patient presenting with severe facial pain, proptosis and visual impairment due to a mass arising from the ethmoid sinus that invaded the right orbit and frontal lobe. Treatment involved radical resection, including exenteration of the affected eye with the view to consolidate treatment with radiation therapy; however, the patient experienced rapid tumor progression and passed away 79 days post resection. Molecular analysis of the tumor tissue identified a novel in-frame BRD4-NUT transcript, with BRD4 exon 15 fused to the last 124 nucleotides of NUT exon 2 (BRD4-NUT ex15:ex2Deltant1-585). The partial deletion of NUT exon 2 was attributed to a mid-exonic genomic breakpoint and the subsequent activation of a cryptic splice site further downstream within the exon. Inhibition of the canonical 3' acceptor splice site of NUT intron 1 in cell lines expressing the most common NMC fusion transcripts (PER-403, BRD4-NUT ex11:ex2; PER-624, BRD4-NUT ex15:ex2) induced alternative splicing from the same cryptic splice site as identified in the patient. Detection of low levels of an in-frame BRD4-NUT ex11:ex2Deltant1-585 transcript in PER-403 confirmed endogenous splicing from this alternative exon 2 splice site. Although further studies are necessary to assess the clinical relevance of the increasing number of variant fusions described in NMC, the findings presented in this case identify alternative splicing as a mechanism that contributes to this pathogenic complexity.

Tan JK, Kearns P, Martin AC and Siafarikas A.  
Randomised controlled trial of daily versus stoss vitamin D therapy in Aboriginal children.  

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.

Tasani M, Tong SY, Andrews RM, Holt DC, Currie BJ, Carapetis JR and Bowen AC.  
The Importance of Scabies Co-Infection in the Treatment Considerations for Impetigo.  
The Pediatric infectious disease journal. 2015.

BACKGROUND: Skin infections account for a high disease burden in Indigenous children living in northern Australia. Although the relationship between impetigo and scabies is recognised, the prevalence of scabies in children with impetigo is not well reported. We report the prevalence, demographics and treatment success outcomes of impetigo and scabies co-infection in Indigenous children who were participants in a randomized controlled trial of impetigo treatment conducted in remote communities of the Northern Territory, Australia. METHODS: Of 1715 screening episodes for impetigo, 508 children were randomized to receive intramuscular benzathinepenicillin (BPG), twice daily co-trimoxazole (SXT) for 3 days (4mg/kg trimethoprim plus
20mg/kg sulphamethoxazole per dose) or once daily co-trimoxazole (SXT) for 5 days (8mg/kg trimethoprim plus 40 mg/kg sulphamethoxazole per dose). A clinical diagnosis of scabies, tinea of the skin, scalp or nail, and head lice was made on all children. Scabies presence was not confirmed using diagnostic scrapings. In a post-hoc analysis, we determined whether co-infection with scabies had an impact on treatment success for impetigo.

**FINDINGS:** Of children randomized to receive treatment for impetigo, 84/508 (16.5%) had scabies. The presence of scabies ranged from 14.3% to 20.0% in the three treatment groups. Treatment success for impetigo with and without scabes co-infection was 75.9% and 86.6% respectively, absolute difference 10.7% (95% CI +1% to +21%). Treatment success for impetigo with and without scabies co-infection in the BPG group was 69.6% and 88.0% respectively, absolute difference 18.4% (95%CI -1 to +38%). In the pooled SXT groups the treatment success for impetigo with and without scabies co-infection was 78.6% and 86.0% with absolute difference 7.4% (95%CI -4 to +18%). Treatment success in the pooled SXT group with scabies (78.6%) was higher than in the BPG group (69.6%) with scabies, absolute difference 9.0% (95% CI +0.1 to +18%). Prediction of treatment success for impetigo is dependent on the presence or absence of scabies and for scabies co-infected impetigo it was higher in the group treated with SXT.

**CONCLUSIONS:** The burden of scabies in an impetigo trial for Indigenous children was high. Treatment success for scabies co-infection was lower than for impetigo overall, with a higher success seen in the co-trimoxazole group than the benzylpenicillin group.

**Taylor LJ, Maybery MT, Wray J, Ravine D, Hunt A and Whitehouse AJO.**

Are there differences in the behavioural phenotypes of Autism Spectrum Disorder probands from simplex and multiplex families?


Recent research suggests that different genetic pathways may operate for families with one child affected with Autism Spectrum Disorder (simplex ASD), compared to families that have multiple affected children (multiplex ASD). In this study, we investigated possible differences in the behavioural phenotypes of probands from simplex and multiplex ASD families using parent-report and standardised behavioural measures. Participants were 59 probands from multiplex ASD families (28 families), who were each matched on chronological age and sex with two probands from simplex families. Probands from multiplex families had greater social impairment (measured using the Social Responsiveness Scale) and worse pragmatic language (on the Children's Communication Checklist-2) than probands from simplex families. However, the multiplex children had less severe symptoms than the simplex children on the ADOS-G, and a significantly higher proportion of multiplex children did not meet autism spectrum cut-offs on this measure. These findings indicate that there are behavioural differences in children with ASD from simplex and multiplex families. In addition, the results reveal an important discrepancy between parent-report and clinician observation of autistic-like characteristics in siblings of an affected child, which may have implications for the assessment and diagnosis of ASD.

**Thalayasingam M, Noble V, Franzmann A and O'Sullivan M.**

Outcome of mixed nut biscuit challenges in low-risk patients who are on tree nut exclusion diet.

Pediatric allergy and immunology : official publication of the European Society of Pediatric Allergy and Immunology. 2015; 26(7): 682-684.

**Thomas R, Rao S and Minutillo C.**

Cuffed endotracheal tubes for neonates and young infants: a comprehensive review.

Archives of Disease in Childhood - Fetal and Neonatal Edition. 2015.

Traditionally, uncuffed endotracheal tubes (ETTs) have been used for artificial ventilation of infants and children. More recently, newer designed high-volume low-pressure (HVLP) cuffed ETTs are being used with increasing frequency in infants from birth. Considering that many paediatric anaesthetists and intensivists are already using cuffed ETTs in infants >3 kg from birth, should neonatologists be doing the same? This review examines the reasons behind the traditional use of uncuffed ETTs and the problems associated with their use; newer HVLP cuffed ETTs and what they can potentially offer neonates; and reviews evidence from studies comparing the use of cuffed and uncuffed ETTs in neonates and small infants.

**Thornton A, Licari M, Reid S, Armstrong J, Fallows R and Elliott C.**

Cognitive Orientation to (Daily) Occupational Performance intervention leads to improvements in impairments, activity and participation in children with Developmental Coordination Disorder.

Disabil Rehabil. 2015; 0(0): 1-8.


Updated 8/12/15
Next generation sequencing in a large cohort of patients presenting with neuromuscular disease before or at birth.

Orphanet J Rare Dis. 2015; 10: 148.

BACKGROUND: Fetal akinesia/hypokinesia, arthrogriposis and severe congenital myopathies are heterogeneous conditions usually presenting before or at birth. Although numerous causative genes have been identified for each of these disease groups, in many cases a specific genetic diagnosis remains elusive. Due to the emergence of next generation sequencing, virtually the entire coding region of an individual's DNA can now be analysed through "whole" exome sequencing, enabling almost all known and novel disease genes to be investigated for disorders such as these. METHODS: Genomic DNA samples from 45 patients with fetal akinesia/hypokinesia, arthrogriposis or severe congenital myopathy from 38 unrelated families were subjected to next generation sequencing. Clinical features and diagnoses for each patient were supplied by referring clinicians. Genomic DNA was used for either whole exome sequencing or a custom-designed neuromuscular sub-exonic supercapture array containing 277 genes responsible for various neuromuscular diseases. Candidate disease-causing variants were investigated and confirmed using Sanger sequencing.

Some of the cases within this cohort study have been published previously as separate studies. RESULTS: A conclusive genetic diagnosis was achieved for 18 of the 38 families. Within this cohort, mutations were found in eight previously known neuromuscular disease genes (CHRND, CHNMG, ECEL1, GBE1, MTM1, MYH3, NEB and RYR1) and four novel neuromuscular disease genes were identified and have been published as separate reports (GPR126, KLHL40, KLHL41 and SPEG). In addition, novel mutations were identified in CHRND, KLHL40, NEB and RYR1. Autosomal dominant, autosomal recessive, X-linked, and de novo modes of inheritance were observed. CONCLUSIONS: By using next generation sequencing on a cohort of 38 unrelated families with fetal akinesia/hypokinesia, arthrogriposis, or severe congenital myopathy we therefore obtained a genetic diagnosis for 47% of families. This study highlights the power and capacity of next generation sequencing (i) to determine the aetiology of genetically heterogeneous neuromuscular diseases, (ii) to identify novel disease genes in small pedigrees or isolated cases and (iii) to refine the interplay between genetic diagnosis and clinical evaluation and management.


Leukocyte Populations in Human Preterm and Term Breast Milk Identified by Multicolour Flow Cytometry.


<sec id="sec001" title="Background">Extremely preterm infants are highly susceptible to bacterial infections but breast milk provides some protection. It is unknown if leukocyte numbers and subsets in milk differ between term and preterm breast milk. This study serially characterised leukocyte populations in breast milk of mothers of preterm and term infants using multicolour flow cytometry methods for extended differential leukocyte counts in blood.</sec>

<sec id="sec002" title="Methods">Sixty mothers of extremely preterm (≤28 weeks gestational age), very preterm (28–31 wk), and moderately preterm (32–36 wk), as well as term (37–41 wk) infants were recruited. Colostrum (d2–5), transitional (d8–12) and mature milk (d26–30) samples were collected, cells isolated, and leukocyte subsets analysed using flow cytometry.</sec>

<sec id="sec003" title="Results">The major CD45+ leukocyte populations circulating in blood were also detectable in breast milk but at different frequencies. Progression of lactation was associated with decreasing CD45+ leukocyte concentration, as well as increases in the relative frequencies of neutrophils and immature granulocytes, and decreases in the relative frequencies of eosinophils, myeloid and B cell precursors, and CD16- monocytes. No differences were observed between preterm and term breast milk in leukocyte concentration, though minor differences between preterm groups in some leukocyte frequencies were observed.</sec>

<sec id="sec004" title="Conclusions">Flow cytometry is a useful tool to identify and quantify leukocyte subsets in breast milk. The stage of lactation is associated with major changes in milk leukocyte composition in this population. Fresh preterm breast milk is not deficient in leukocytes, but shorter gestation may be associated with minor differences in leukocyte subset frequencies in preterm compared to term breast milk.</sec>


Antimicrobial Protein and Peptide Concentrations and Activity in Human Breast Milk Consumed by Preterm Infants at Risk of Late-Onset Neonatal Sepsis.


<sec title="Objective">We investigated the levels and antimicrobial activity of antimicrobial proteins and peptides (AMPs) in breast milk consumed by preterm infants, and whether deficiencies of these factors were associated with late-onset neonatal sepsis (LOS), a bacterial infection that frequently occurs in preterm infants in the neonatal period.</sec>

<sec title="Study design">Breast milk from mothers of preterm infants (≤32 weeks gestation) was collected on days 7 (n = 88) and 21 (n = 77) postpartum.

Updated 8/12/15
Concentrations of lactoferrin, LL-37, beta-defensins 1 and 2, and alpha-defensin 5 were measured by enzyme-linked immunosorbent assay. The antimicrobial activity of breast milk samples against *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Escherichia coli*, and *Streptococcus agalactiae* was compared to the activity of infant formula, alone or supplemented with physiological levels of AMPs. Samples of breast milk fed to infants with and without subsequent LOS were compared for levels of AMPs and inhibition of bacterial growth.

Levels of most AMPs and antibacterial activity in preterm breast milk were higher at day 7 than at day 21. Lactoferrin was the only AMP that limited pathogen growth &gt;50% when added to formula at a concentration equivalent to that present in breast milk. Levels of AMPs were similar in the breast milk fed to infants with and without LOS, however, infants who developed LOS consumed significantly less breast milk and lower doses of milk AMPs than those who were free from LOS.

The concentrations of lactoferrin and defensins in preterm breast milk have antimicrobial activity against common neonatal pathogens.

Vale S, Smith J, Said M, Mullins RJ and Loh R.
ASCIA guidelines for prevention of anaphylaxis in schools, pre-schools and childcare: 2015 update.
The aim of these guidelines is to assist staff in school and childcare settings to plan and implement appropriate risk minimisation strategies, taking into consideration the needs of the allergic child, the likely effectiveness of measures and the practicality of implementation. Although these guidelines include risk minimisation strategies for allergic reactions to insect stings or bites, latex and medication, the major focus relates to food allergy. This is due to the higher relative prevalence of food allergy in childhood (compared with other allergic triggers) and the higher likelihood of accidental exposure in these settings. Care of the allergic child in the school, pre-school or childcare settings requires accurate information obtained from parents and carers, staff training in the recognition and management of acute allergic reactions, planning for unexpected reactions (including in those not previously identified as being at risk), age appropriate education of children with severe allergies and their peers, and implementation of practical strategies to reduce the risk of accidental exposure to known allergic triggers. Strategy development also needs to take into account local or regional established legislative or procedural guidelines and the possibility that the first episode of anaphylaxis may occur outside the home. Food bans are not recommended as the primary risk minimisation strategy due to difficulties in implementation and lack of proven effectiveness.

Valentine J, Stannage K, Fabian V, Ellis K, Reid S, Pitcher C and Elliott C.
Muscle Histopathology in Children with Spastic Cerebral Palsy Receiving Botulinum toxin Type A.
Muscle Nerve. 2015.
INTRODUCTION: Botulinum toxin A (BoNTA) is routine treatment for hypertonicity in children with cerebral palsy (CP). METHOD: Single blind prospective cross sectional study of 10 participants (mean age 11 years, 7 months) was done to determine the relationship between muscle histopathology and BoNTA in treated medial gastrocnemius muscle of children with CP. Open muscle biopsies were taken from medial gastrocnemius muscle and vastus lateralis (control) during orthopedic surgery. RESULTS: Neurogenic atrophy in the medial gastrocnemius was seen in 6 participants between 4 months to 3 years post BoNTA. Type 1 fiber loss with type 2 fiber predominance was significantly related to the number of BoNTA injections (r = 0.89, P < 0.001). DISCUSSION: The impact of these changes in muscle morphology on muscle function in CP is not clear. It is important to consider rotating muscle selection or injection sites within the muscle or allowing longer time between injections. This article is protected by copyright. All rights reserved.

Vandevelde A and Gera P.
Carcinoid tumours of the appendix in children having appendicectomies at Princess Margaret Hospital since 1995.
AIM: The diagnosis of carcinoid tumour is a relatively rare one. Our surgical approach has changed over the last two decades from predominantly open to predominately laparoscopic with a tendency to leave the mesoappendix in situ. The aim of this audit was to identify how many cases we had at PMH and to see whether the shift in surgical approach allowed us to make prognostic decisions in keeping with current best practice and whether this made any difference in further surgery requirements or outcome for patients. METHODS: A retrospective review of all cases of carcinoid identified in our search of all appendicectomy histopathology results was conducted. Results were compared to those found in other studies. Duration of follow up and further investigations was reviewed, as was whether or not there was any recurrence. RESULTS: Our incidence of carcinoid tumours in patients undergoing appendicectomy since 1995 was 0.35%, similar to that in other centres. None of our patients had surgery beyond an appendicectomy and our active follow up varied from none to 6 months. There were no recurrences in this time. CONCLUSIONS: The literature review carried out suggests
further meta-analysis is needed including data on long term follow up before definitive guidelines regarding extent of surgical treatment and follow up based on histopathology are created. The condition is rare and the studies small, resulting in no clear consensus on the best practice for tumours measuring between 1 and 1.5cm in diameter. Our surgical approach to appendicectomies has changed; it is unclear whether this has resulted in a change in outcome.

Effect of exercise intensity and blood glucose level on glucose requirements to maintain stable glycaemia during exercise in individuals with type 1 diabetes.

von Ungern-Sternberg BS.
Rare events can be fatal and must not be ignored; how much needs to happen before we act?

von Ungern-Sternberg BS, Ramgolam A, Hall GL, Sly PD and Habre W.
Peri-operative adverse respiratory events in children.
Anaesthesia. 2015; 70(4): 440-444.
Three quarters of all critical incidents and a third of all peri-operative cardiac arrests in paediatric anaesthesia are caused by adverse respiratory events. We screened for risk factors from children's and their families' histories, and assessed the usefulness of common markers of allergic sensitisation of the airway as surrogates for airway inflammation and increased risk for adverse respiratory events. One hundred children aged up to 16 years with two or more risk factors undergoing elective surgery were included in the study. Eosinophil counts, IgE level, specific IgE for D. pteronyssinus, cat epithelia and Gx2 (grass pollen) were measured for each child and adverse respiratory events (bronchospasm, laryngospasm, oxygen desaturation < 95%, severe persistent coughing, airway obstruction and postoperative stridor) were recorded. Twenty-one patients had an adverse respiratory event but allergic markers were poor predictors. Binary logistic regression showed a lack of predictive value of the eosinophil range and adverse respiratory events (p = 0.249). Receiver operating characteristic (ROC) curves for the presence of adverse respiratory events vs level of specific IgE antibody (to Gx2 (AUC 0.614), cat epithelia (0.564) and D. pteronyssinus (0.520)) demonstrated poor predictive values. However, the presence of risk factors was strongly associated with adverse respiratory events (p < 0.001) and a ROC-curve analysis indicated a fair capacity to predict adverse respiratory events (AUC 0.788). There was a significant difference (p = 0.001) between the presence of adverse respiratory events in patients with more than four (p = 0.006), compared with less than four (p = 0.001), risk factors. We conclude that while risk factors taken from the child's (or family) history proved good predictors of adverse respiratory events, immunological markers of allergic sensitisation demonstrated low predictive values. Pre-operative identification of children at high risk for an adverse respiratory event should rely on clinical, rather than immunological, assessment.

Online parent-targeted cognitive-behavioural therapy intervention to improve quality of life in families of young cancer survivors: study protocol for a randomised controlled trial.
Trials. 2015; 16(1): 153.

BACKGROUND: Due to advances in multimodal therapies, most children survive cancer. In addition to the stresses of diagnosis and treatment, many families are now navigating the challenges of survivorship. Without sufficient support, the ongoing distress that parents experience after their child's cancer treatment can negatively impact the quality of life and psychological wellbeing of all family members. METHODS/DESIGN: The 'Cascade' (Cope, Adapt, Survive: Life after C AncEr) study is a three-arm randomised controlled trial to evaluate the feasibility and efficacy of a new intervention to improve the quality of life of parents of young cancer survivors. Cascade will be compared to a peer-support group control and a 6-month waitlist control. Parents (n = 120) whose child (under 16 years of age) has completed cancer treatment in the past 1 to 12 months will be recruited from hospitals across Australia. Those randomised to receive Cascade will participate in four, weekly, 90-minute online group sessions led live by a psychologist. Cascade involves peer discussion on cognitive-behavioural coping skills, including behavioural activation, thought challenging, mindfulness and acceptance, communication and assertiveness skills training, problem-solving and goal-setting. Participants randomised to peer support will receive four, weekly, 90-minute, live, sessions of non-directive peer support. Participants will complete measures at baseline, directly post-intervention, one month post-intervention, and 6 months post-intervention. The primary outcome will be parents' quality of life. Secondary outcomes include parent depression, anxiety, parenting self-agency, and the quality of life of children in the family. The child cancer survivor and all siblings aged 7 to 15 years will be invited to complete self-report quality of life measures covering physical, emotional, social and school-related domains. DISCUSSION: This article reviews the
empirical rationale for group-based, online cognitive-behavioural therapy in parents of children who have recently finished cancer treatment. The potential challenges of delivering skills-based programs online are highlighted. Cascade's videoconferencing technology has the potential to address the geographic and psychological isolation of families after cancer treatment. Teaching parents coping skills as they resume their normal lives after their child's cancer may see long-term benefits for the quality of life of the family as a whole.

TRIAL REGISTRATION: ACTRN1261300270718 (registered 6 March 2013).

Walsh P, Manners PJ, Vercoe J, Burgner D and Murray KJ.
Chronic recurrent multifocal osteomyelitis in children: nine years' experience at a statewide tertiary paediatric rheumatology referral centre.
Rheumatology (Oxford), 2015; 54(9): 1688-1691.

OBJECTIVE: To describe the clinical features, management and outcome of 34 children with chronic recurrent multifocal osteomyelitis (CRMO) diagnosed at a single centre over 9 years. METHODS: All children identified with CRMO for the period 2005-13 were identified from a prospectively collected database, with additional data from hospital records. RESULTS: Thirty-four patients, 21 female and 13 male, were identified. The average age at symptom onset was 9.8 years (range 3.8-17.9) and at diagnosis was 10.9 years (range 5.2-18.2), with an average delay in diagnosis of 12 months. Follow-up was 0.3-7.9 years (average 2.1), with 104 individual bony lesions identified, with a median of 3 (range 1-9) per patient. Six patients had unifocal disease. The sites involved included the tibia (n = 19), femur (n = 14), clavicle (n = 12), vertebrae (n = 10) and fibula (n = 8). Approximately half of patients had an inflammatory arthritis at diagnosis, and two-thirds in total eventually developed an arthritis. Pustulosis occurred in eight patients (24%), severe acne in four (12%) and psoriasis in three (9%). NSAIDs were used in 91%, CSs in 82% and MTX in 38%. Two patients were treated with anti-TNF agents. Episodic disease was most common (79%), while 21% had a monophasic pattern. Clinical remission occurred in 94% of children, with prolonged remission in 17%. Seven patients did not require medications for >12 months. CONCLUSION: CRMO is more common than previously recognized, but diagnosis may be delayed. Episodic multifocal disease was most common, but some had unifocal and/or monophasic disease. Most patients responded to NSAIDs and/or intermittent CSs, but many required DMARDs.

Global Epidemiology of Pediatric Severe Sepsis; the Sepsis PRevalence, OUcomes, and Therapies Study. American journal of respiratory and critical care medicine. 2015.

Safe integration of nelarabine into intensive chemotherapy in newly diagnosed T-cell acute lymphoblastic leukemia: Children's Oncology Group Study AALL0434.

BACKGROUND: Nelarabine has shown impressive single agent clinical activity in T-cell acute lymphoblastic leukemia (T-ALL), but has been associated with significant neurotoxicities in heavily pre-treated patients. We showed previously that it was safe to add nelarabine to a BFM-86 chemotherapy backbone (AALL00P2). Children's Oncology Group (COG) AALL0434 is a Phase III study designed to test the safety and efficacy of nelarabine when incorporated into a COG augmented BFM-based regimen, which increases exposure to agents with potential neurotoxicity compared to the historical AALL00P2 regimen. PROCEDURE: AALL0434 included a safety phase to assess nelarabine toxicity. Patients with high-risk (HR) T-ALL were randomized to receive Capizzi-style escalating methotrexate (MTX) plus pegaspargase or high dose (HD) MTX with/without five 10-day courses of nelarabine. We report results from 94 patients who participated in the initial safety phase of the study. RESULTS: There were no differences in the incidence of peripheral motor neuropathies, sensory neuropathies or central neurotoxicities among those randomized to the nelarabine (n = 47) and non-nelarabine arms (n = 47). CONCLUSIONS: The addition of nelarabine to COG-augmented BFM chemotherapy regimen is safe and feasible. The ongoing AALL0434 Efficacy Phase will determine whether the addition of nelarabine treatment improves outcome for patients with T-ALL.

Wormald R, Hinton-Bayre A, Bumbak P and Vijayasekaran S.
Congenital nasal pyriform aperture stenosis 5.7mm or less is associated with surgical intervention: A pooled case series.

OBJECTIVES: Congenital nasal pyriform aperture stenosis (CNPAS) is a rare cause of upper airway obstruction in the newborn. CNPAS is diagnosed clinically and confirmed with CT scanning. Early diagnosis and management is essential for this potentially life-threatening condition. Patients can be managed conservatively or surgically. Surgical treatment is usually reserved for those patients that fail conservative treatment. Our

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objective was to provide a radiologically-measured pyriform aperture (PA) width that predicts the need for surgical intervention. METHODS: This study was a retrospective chart review of patients treated in a tertiary paediatric hospital as well as a review of the literature. Outcome measures were defined as surgical or conservative intervention for the management of congenital pyriform aperture stenosis. RESULTS: Data from 26 individual patients (7 patients from our own case series and 19 patients from previously published reports) was analysed to calculate those patients requiring surgical intervention. CONCLUSIONS: A PA width of less than 5.7mm in a neonate is 88% sensitive and specific in predicting that a patient will require surgical intervention.

Wynter M, Gibson N, Willoughby KL, Love S, Kentish M, Thomason P and Graham HK.
Australian hip surveillance guidelines for children with cerebral palsy: 5-year review.
Dev Med Child Neurol. 2015; 57(9): 808-820.

Aim: To ensure hip surveillance guidelines reflect current evidence of factors influencing hip displacement in children with cerebral palsy (CP). METHOD: A three-step review process was undertaken: (1) systematic literature review, (2) analysis of hip surveillance databases, and (3) national survey of orthopaedic surgeons managing hip displacement in children with CP. RESULTS: Fifteen articles were included in the systematic review. Quantitative analysis was not possible. Qualitative review indicated hip surveillance programmes have decreased the incidence of hip dislocation in populations with CP. The Gross Motor Function Classification System was confirmed as the best indicator of risk for displacement, and evidence was found of hip displacement occurring at younger ages and in young adulthood. Femoral geometry, pelvic obliquity, and scoliosis were linked to progression of hip displacement. A combined data pool of 3366 children from Australian hip surveillance databases supported the effectiveness of the 2008 Consensus Statement to identify hip displacement early. The survey of orthopaedic surgeons supported findings of the systematic review and database analyses. INTERPRETATION: This review rationalized changes to the revised and renamed Australian Hip Surveillance Guidelines for Children with Cerebral Palsy 2014, informing frequency of radiographic examination in lower risk groups and continuation of surveillance into adulthood for adolescents with identified risk factors.

Yardley AM, Hoskin AK, Hanman K, Wan SL and Mackey DA.
Animal-inflicted ocular and adnexal injuries in children: A systematic review.

Eye injury remains the leading cause of monocular blindness in children despite 90% of injuries being potentially preventable. Children interact with animals in a variety of situations, and the associated dangers may be underestimated. Animals are capable of causing ocular and adnexal injuries that are cosmetically and visually devastating. We examine the current literature regarding the nature and severity of animal-inflicted ocular and adnexal injuries in children.

Yardley AM, Mackey DA and Tandon A.
Running with scissors.

Yazar S, Hewitt AW, Forward H, Jacques A, Ing C, von Ungern-Sternberg BS and Mackey DA.
Early Anesthesia Exposure and the Effect on Visual Acuity, Refractive Error, and Retinal Nerve Fiber Layer Thickness of Young Adults.
The Journal of pediatrics. 2015.

OBJECTIVE: To investigate whether being anesthesia administered at least once in early life influenced 3 main proxies of visual function: visual acuity, refractive error, and optic nerve health in young adulthood. STUDY DESIGN: At age 20 years, participants of the Western Australian Pregnancy Cohort Study had comprehensive ocular examinations including visual acuity, postcycloplegic refraction, and multiple scans of the optic disc. We identified individuals who had at least 1 procedure requiring anesthesia during the first 3 years of life (between 1990 and 1994) and compared their visual outcomes with nonexposed individuals. We excluded 40 participants with strabismus or other ophthalmic disease or surgery and 136 with non-European background. RESULTS: Of 834 participants, 15.2% (n = 127) were exposed to anesthesia at least once before age 3 years. In both exposed and nonexposed groups, median visual acuity (measured using the logarithm of the minimum angle of resolution [LogMAR] chart) was -0.06 LogMAR in the right eye and -0.08 LogMAR in the left eye (P > .05). Median spherical equivalent refractive error was +0.44 diopters (IQR -0.25, +0.63) and +0.31 diopters (IQR -0.38, +0.63) in the exposed and nonexposed group, respectively (P = .126). No difference was detected in mean global retinal nerve fiber layer thickness of the 2 groups (100.7 vs 101.1 mum, P = .830). CONCLUSIONS: We were unable to demonstrate an association of exposure to anesthesia as a child with reduced visual acuity or increased myopia or thinning of retinal nerve fiber layer. These findings support the

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view that anesthesia is unlikely to impair visual development, but further work is needed to establish whether more subtle defects are present and repeated exposures have any effects.

Yeoh DK, Ryan AL and Blyth CC.
Infectious Prophylaxis in Paediatric Oncology and Stem Cell Transplantation.

Western environment/lifestyle is associated with increased genome methylation and decreased gene expression in Chinese immigrants living in Australia.
Environmental and Molecular Mutagenesis. 2015: n/a-n/a.

Zyrianova Y, Alexander L and Faruqui R.
Neuropsychiatric presentations and outcomes in children and adolescents with primary brain tumours: Systematic review.
OBJECTIVE: The purpose of this study was to systematically review the literature relating to the neuropsychiatric symptoms at presentation and outcome of childhood brain tumours. METHODS: Seven online databases pertaining to the neuropsychiatric presentation and outcomes of childhood CNS tumours were searched and PRISMA guidelines were followed. Temporal limits were not applied to the searches. RESULTS: There were 1879 relevant search results in total. After discovering the large body of both primary and secondary research in the field of cognitive and neuropsychological outcomes of brain tumours in children, these studies were excluded. Quality-of-life studies were excluded for the same reason. Thirty-one papers were chosen for discussion in this review. CONCLUSION: This timely systematic review concluded that neuropsychiatric presentations are common in children with CNS tumours-with the presence of behavioural and psychological symptoms in up to 57% of cases, their frequency varies according to age of onset and is strongly associated with time since diagnosis. The findings highlight the necessity for routine psychological and psychiatric screenings of children with suspected brain tumours and at follow-up and a number of clinical recommendations to this effect are listed.