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Articles are listed alphabetically by first author.

Abraham MB, Charles A, Gera P and Srinivasjois R.
Surgically managed perinatal testicular torsion: a single centre experience.
OBJECTIVE: The objective of this series is to describe the clinical features and immediate outcomes of surgically managed perinatal testicular torsion (PTT). METHODS: A retrospective chart review of the cases of PTT diagnosed in neonates less than 1 month of age was conducted. The cases were identified from the hospital database maintained prospectively over 24 years at the sole tertiary referral centre for the state of Western Australia. RESULTS: Twenty eight cases of PTT were identified, being 23 unilateral and 5 bilateral. All the five bilateral cases were asynchronous and three were identified incidentally on surgical exploration of unilateral torsion. The testis was clinically salvaged in two newborns at the time of follow-up. CONCLUSION: Asynchronous bilateral PTT could be missed on physical examination and identified on surgical exploration of unilateral PTT. Emergency exploration may result in salvage of the contralateral torsed testis.

Akesson LS, Burnett JR, Mehta DK and Martin AC.
Lipoprotein lipase deficiency presenting with neonatal perianal abscesses.
Lipoprotein lipase (LPL), a member of the triglyceride lipase gene family, is synthesised by parenchymal cells of the heart, skeletal muscle and adipose tissues before being transported to luminal surfaces of vascular endothelial cells to exert its main physiological function to hydrolyse plasma lipoproteins. LPL deficiency is a rare autosomal recessive disorder, resulting in severe hypertriglyceridaemia from birth. The effect of marked hypertriglyceridaemia on the immune function in children has not been described. We present a case of a neonate with LPL deficiency and grossly elevated plasma triglyceride levels, presenting with recurrent and recalcitrant perianal abscesses suggestive of underlying immunodeficiency. With reduced levels of plasma triglycerides, the recurrent perianal infections resolved. This case report reviews evidence for potential deleterious effects of hypertriglyceridaemia on immune function, however, underlying mechanisms are poorly understood. Whether hypertriglyceridaemia contributes to immune dysfunction in this context is unknown. If there is a pathophysiological link, this may have implications for hypertriglyceridaemia management.

Baker M, Long N and Parker C.
The world of FOAM: A practical guide to free online paediatric education resources.

Airway epithelial cells secrete altered exosomal microRNAs in murine experimental and human paediatric asthma.

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 survey.
OBJECTIVE: To investigate the ability of cochlear implant (CI) recipients to physically handle and care for their hearing implant device(s) and to identify factors that may influence skills. To assess device management skills, a clinical survey was developed and validated on a clinical cohort of CI recipients. DESIGN: Survey development and validation. A prospective convenience cohort design study. SETTING: Specialist hearing implant clinic. PARTICIPANTS: Forty-nine post-lingually deafened, adult CI recipients, at least 12 months postoperative. MAIN OUTCOME MEASURES: Survey test-retest reliability, interobserver reliability and responsiveness. Correlations between management skills and participant demographic, audiometric, clinical

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outcomes and device factors. RESULTS: The Cochlear Implant Management Skills survey was developed, demonstrating high test-retest reliability (0.878), interobserver reliability (0.972) and responsiveness to intervention (skills training) \( \text{f[(20)] = -3.913, P = 0.001} \). 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 cochlear implant device handling skills in CI recipients and offers clinicians and researchers a tool to systematically and objectively identify shortcomings in CI recipients' device handling skills.

Blackmore AM, Bear N, Blair E, Gibson N, Jalla C, Langdon K, Moshovis L, Steer K and Wilson AC.
Factors Associated with Respiratory Illness in Children and Young Adults with Cerebral Palsy.

Objective To describe associations between respiratory illness and its potential predictors in children and young adults with cerebral palsy (CP). Study design Cross-sectional survey of self- and caregiver-reported respiratory symptoms for individuals aged up to 26 years with CP. Respiratory illness was indicated by 2 outcomes: (1) ≥1 respiratory hospitalizations in the past year; and (2) ≥2 courses of antibiotics for respiratory symptoms in the past year. ORs were calculated using univariate and multivariate logistic regression. Results There were 551 participants, aged 1-26 years, distributed across all gross motor function classification scale (GMFCS) levels. In univariate analyses, factors significantly associated with respiratory hospitalizations were weekly respiratory symptoms (OR 2.31, 95% CI 1.7-3.0), respiratory symptoms during meals (OR 3.23, 95% CI 1.5-5.8), gastroesophageal reflux (OR 3.01, 95% CI 1.7-5.3), coughing or choking on saliva (OR 4.36, 95% CI 2.3-8.0), current asthma (OR 3.56, 95% CI 1.9-6.4), age (0-3 years) (OR 3.24, 95% CI 1.1-8.8, compared with 13-17 years), seizures (OR 3.45, 95% CI 1.96-6.0), and scoliosis (OR 2.14, 95% CI 1.16-3.9). Nonambulatory individuals (GMFCS IV-V) were at significantly increased risk of hospitalizations only if they had food modifications and/or nasogastric or gastrostomy tube feeds (OR 5.36, 95% CI 2.89-9.9, compared with GMFCS I-III with no food modifications and no tube). All factors, except seizures and scoliosis, were significantly associated with multiple courses of antibiotics in univariate analyses. Conclusions Oromotor dysfunction is strongly associated with respiratory illness in patients with CP.

Influenza Vaccine Effectiveness and Uptake in Children at Risk of Severe Disease.

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 to 2014) with an influenza-like illness were eligible. Influenza polymerase chain reaction/culture was 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: Two thousand seven hundred twenty-three 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 and 2010 to 2014) was 70.0% (95% confidence interval: 47.7 to 82.9); VE for children with medical comorbidities, children born preterm and children <2 years were 82.5% (14.6 to 96.4), 79.2% (10.9 to 95.1) and 84.7% (49.6 to 95.3), respectively. After 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.

Borland ML and Shepherd M.
Quality in paediatric emergency medicine: Measurement and reporting.

There is a clear demand for quality in the delivery of health care around the world; paediatric emergency medicine is no exception to this movement. It has been identified that gaps exist in the quality of acute care provided to children. Regulatory bodies in Australia and New Zealand are moving to mandate the implementation of quality targets and measures. Within the paediatric emergency department (ED), there is a lack of research into paediatric specific indicators. The existing literature regarding paediatric acute care quality measures has been recently summarised, and expert consensus has now been reported. It is clear that there is much work to be performed to generalise this work to ED. We review suggestions from the current literature.
relating to feasible indicators within the paediatric acute care setting. We propose options to develop a quality ‘scorecard’ that could be used to assist Australian and New Zealand EDs with quality measurement and benchmarking for their paediatric patients.

**Bowen AC, Harris T, Holt DC, Giffard PM, Carapetis JR, Campbell PT, Mc VJ and Tong SY.**
Whole genome sequencing reveals extensive community-level transmission of group A Streptococcus in remote communities.
Impetigo is common in remote Indigenous children of northern Australia, with the primary driver in this context being Streptococcus pyogenes [or group A Streptococcus (GAS)]. To reduce the high burden of impetigo, the transmission dynamics of GAS must be more clearly elucidated. We performed whole genome sequencing on 31 GAS isolates collected in a single community from children in 11 households with 2 GAS-infected children. We aimed to determine whether transmission was occurring principally within households or across the community. The 31 isolates were represented by nine multilocus sequence types and isolates within each sequence type differed from one another by only 0-3 single nucleotide polymorphisms. There was evidence of extensive transmission both within households and across the community. Our findings suggest that strategies to reduce the burden of impetigo in this setting will need to extend beyond individual households, and incorporate multi-faceted, community-wide approaches.

**Brischetto A, Leung G, Marshall CS and Bowen AC.**
A Retrospective Case-Series of Children With Bone and Joint Infection From Northern Australia.
Our clinical workload as infectious diseases pediatricians in northern Australia is dominated by complicated bone and joint infections in indigenous children. We reviewed the clinical presentation, microbiology, management, and outcomes of children presenting to Royal Darwin Hospital with bone and joint infections between 2010 and 2013, and aimed to compare severity and incidence with other populations worldwide. A retrospective audit was performed on children aged 0 to 18 years who were admitted to Royal Darwin Hospital between 1 January 2010 and 31 December 2013 with a bone and joint infection. Seventy-nine patients were identified, of whom 57 (72%) had osteomyelitis +/- associated septic arthritis and 22 (28%) had septic arthritis alone. Sixty (76%) were indigenous Australians. The incidence rate of osteomyelitis for indigenous children was 82 per 100,000 children. Staphylococcus aureus was the confirmed pathogen in 43/79 (54%), of which 17/43 (40%) were methicillin resistant. Median length of stay was 17 days (interquartile range: 10-31 days) and median length of IV antibiotics was 15 days (interquartile range: 6-24 days). Fifty-six (71%) required at least 1 surgical procedure. Relapse within 12 months was documented in 12 (15%) patients. We report 3 key findings: osteomyelitis incidence in indigenous children of northern Australia is amongst the highest reported in the world; methicillin-resistant S aureus accounts for 36% of osteomyelitis with a positive microbiological diagnosis; and the severity of disease requires extended antibiotic therapy. Despite this, 15% of the cohort relapsed within 12 months and required readmission.

**Bucks RS, Dunlop PD, Taljaard DS, Brennan-Jones CG, Hunter M, Wesnes K and Eikelboom RH.**
Hearing loss and cognition in the Busselton Baby Boomer cohort: An epidemiological study.
Laryngoscope. 2016.
OBJECTIVES/HYPOTHESIS: To determine the relationship between peripheral hearing loss (HL) in baby boomers (better-ear measure) and cognitive function, taking into account the impact of depression or cognitive reserve on this relationship and exploring binaural hearing. STUDY DESIGN: A prospective, epidemiology study. METHODS: Data from 1,969 participants aged 45 to 66 years were collected in the Busselton Healthy Ageing Study. Participants were assessed using pure-tone air-conduction thresholds at octave frequencies (250; 500; 1,000; 2,000; 4,000; and 8,000 Hz). Hearing loss was grouped using 1) pure-tone averages across 4 frequencies (500 to 4000Hz) in the better ear (BE4FA) or 2) latent profile analysis (LPA) using all thresholds from both ears. Cognition was tested with the Cognitive Drug Research System, verbal fluency, and National Adult Reading Test (premorbid-IQ). Regression was used to determine the impact of HL relative to no HL on age and education-adjusted cognition, controlling for mood, sex, and premorbid-IQ. RESULTS: According to BE4FA, 4.7% had mild (26-40 dB) HL; 0.8% had moderate (41-60 dB) HL; and 0.3% had severe (61-80 dB) HL. Based on the LPA, 20.5% had high-frequency HL; 7.8% had mid- to high-frequency HL; and 1.9% had significant HL across all frequencies. The HL group was not a predictor of cognitive performance in any domain using BE4FA and explained just 0.5% and 0.4% of variance in continuity-of-attention and speed-of-memory retrieval using LPA. Critically, those with the worst hearing did not differ cognitively from those with the best. CONCLUSION: Hearing loss is not an important determinant of contemporaneous attention, memory, or executive function in middle-aged adults once age, education, depression, cognitive reserve, and sex are controlled. LEVEL OF EVIDENCE: 2a. Laryngoscope, 2016.
The relationship between Bordetella pertussis genotype and clinical severity in Australian children with pertussis.
OBJECTIVES: Changes in circulating Bordetella pertussis genotypes, including a novel pertussis toxin promoter ptxP3 allele and absence of pertactin (Prrn) 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 Prrn deficient increased markedly between 2008 and 2012. Of B. pertussis isolates, the proportion considered severe was similar for Prrn positive (27/128, 21%) and Prrn deficient (127/1, 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 Prrn status (RRA: 0.95, [0.57-1.56]; p = 0.83). CONCLUSIONS: In children, we found no relationship between Prrn status and markers of severe pertussis. An increased proportion of severe disease in isolates with the ptxP3 allele was observed.

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

Craig JM, Logan AC and Prescott SL.
Natural environments, nature relatedness and the ecological theater: connecting satellites and sequencing to shinrin-yoku.
Recent advances in research concerning the public health value of natural environments have been remarkable. The growing interest in this topic (often housed under terms such as green and/or blue space) has been occurring in parallel with the microbiome revolution and an increased use of remote sensing technology in public health. In the context of biodiversity loss, rapid urbanization, and alarming rates of global non-communicable diseases (many associated with chronic, low-grade inflammation), discussions of natural vis-a-vis built environments are not merely fodder for intellectual curiosity. Here, we argue for increased interdisciplinary collaboration with the aim of better understanding the mechanisms-including aerobiological and epigenetic-that might help explain some of the noted positive health outcomes. It is our contention that some of these mechanisms are related to ecodiversity (i.e., the sum of biodiversity and geodiversity, including biotic and abiotic constituents). We also encourage researchers to more closely examine individual nature relatedness and how it might influence many outcomes that are at the interface of lifestyle habits and contact with ecodiversity.


Updated 14/4/16

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


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 ACTRN12606000441516 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 composite cognitive 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 a difference 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 Health, Fonds NutsOhra, and UK Clinical Research Network (UKCRN).

de Bock M, Cooper M, Rutterath A, Nicholas J, Ly T, Jones T and Davis E.

Continuous Glucose Monitoring Adherence: Lessons From a Clinical Trial to Predict Outpatient Behavior.


AIMS: This study reports continuous glucose monitoring (CGM) adherence patterns and contributing factors in patients who were part of a 6-month clinical trial using sensor augmented pump therapy with low glucose insulin suspension. METHODS: CGM data from 38 patients using sensor augmented pump therapy for 6 months were analyzed. CGM adherence was defined by having a working sensor available and determined by the time it was switched on as a proportion of available time for the 6 month study period with allowance for practical CGM use. Age, gender, HbA1c, duration of diagnosis, capillary blood glucose testing frequency, sensor accuracy, and insulin pump alarm frequency were characterized and examined for an association with CGM adherence. RESULTS: Overall CGM adherence was 75% (range: 35% to 96%), CGM adherence was demonstrated to fall after 9 to 11 weeks before reaching a steady rate. CGM adherence patterns showed substantial variation. Mean adherence differed (P < .01) between age groups 72% (<12 years), 69% (12-18 years), and 88% (>18 years). Sensor accuracy predicted adherence, where every 1% decline in mean absolute difference in a given week was associated with a 0.5% decline in sensor adherence (P < .01). Gender, HbA1c, duration of diagnosis, capillary blood glucose testing frequency, and insulin pump alarm frequency were not associated with CGM adherence. CONCLUSIONS: CGM adherence and patterns of use are individualized. However, a predictable fall in adherence at 9 to 11 weeks may present an opportunity for timed interventions to increase CGM use. Adolescent age and sensor accuracy predict CGM adherence.

Drake-Brockman TF, Datta A and von Ungern-Sternberg BS.


Paediatr Anaes. 2016.

BACKGROUND: Head-mounted devices (HMDs) are of significant interest for applications within medicine, including in anesthesia for patient monitoring. Previous devices trialed in anesthesia for this purpose were often
bulky, involved cable tethers, or were otherwise ergonomically infeasible. Google Glass is a modern HMD that is lightweight and solves many of the issues identified with previous HMDs. AIM: To examine the acceptance of Google Glass as a patient monitoring device in a pediatric anesthesia context at Princess Margaret Hospital for Children, Perth, Australia. METHODS: We developed a custom-designed software solution for integrating Google Glass into the anesthesia environment, which enabled the device user to continuously view patient monitoring parameters transmitted wirelessly from the anesthesia workstation. RESULTS: A total of 40 anesthetists were included in the study. Each anesthetist used the device for the duration of a theater list. We found 90% of anesthetists trialing the device agreed that it was comfortable to wear, 86% agreed the device was easy to read, and 82.5% agreed the device was not distracting. In 75% of cases, anesthetists reported unprompted that they were comfortable using the device in theater. Anesthetists reported that they would use the device again in 76% of cases, and indicated that they would recommend the device to a colleague in 58% of cases. CONCLUSION: Given the pilot nature of this study, we consider these results highly favorable. Anesthetists readily accepted Google Glass in the anesthetic environment, with further enhancements to device software, rather than hardware, now being the barrier to adoption. There are a number of applications for HMDs in pediatric anesthesia.

Duke JM, Randall SM, Fear MW, Boyd JH, Rea S and Wood FM.
Understanding the long-term impacts of burn on the cardiovascular system.
BACKGROUND: Whilst the most obvious impact of burn is on the skin, systemic responses also occur after burn that lead to widespread changes to the body, including the heart. The aim of this study was to assess if burn in mid-aged and older adults is associated with increased long-term admissions and death due to diseases of the circulatory system. METHODS: A population-based longitudinal study using linked hospital morbidity and death data from Western Australia was undertaken of adults aged at least 45 years when hospitalized for a first burn (n=6004) in 1980-2012 and a frequency matched non-injury comparison cohort, randomly selected from Western Australia's electoral roll (n=22,673). Crude admission rates and cumulative length of stay for circulatory diseases were calculated. Negative binomial and Cox proportional hazards regression modelling were used to generate incidence rate ratios (IRR) and hazard ratios (HR), respectively. HR was used as a measure of the mortality rate ratio (MRR). RESULTS: After adjustment for demographic factors and pre-existing health status, the burn cohort had 1.46 times (95% confidence interval (CI): 1.36-1.56) as many admissions and almost three times the number of days in hospital with a circulatory system diagnosis (IRR, 95%CI: 2.90, 2.60-3.25) than the uninjured cohort for circulatory diseases. The burn cohort had higher admission rates for ischaemic heart disease (IRR, 95%CI: 1.21, 1.07-1.36), heart failure (IRR, 95%CI: 2.29, 1.85-2.82) and cerebrovascular disease (IRR, 95%CI: 1.57, 1.33-1.84). The burn cohort was found to have increased long-term mortality caused by circulatory system diseases (MRR, 95%CI: 1.11, 1.02-1.20). CONCLUSIONS: Findings of increased hospital admission rates, prolonged length of hospital stay and increased long-term mortality related to circulatory system diseases in the burn cohort provide evidence to support that burn has long-lasting systemic impacts on the heart and circulation.

Dunne B, Suthers E, Xiao P, Xiao J, Litton E and Andrews D.
Medium-term outcomes after pulmonary valve replacement with the Freestyle valve for congenital heart disease: a case series.
OBJECTIVES: The Freestyle valve may be used for pulmonary valve replacement (PVR). Whether its stentless design and anticalcification treatment improve durability relative to alternative bioprostheses, however, is unknown and long-term data are lacking. METHODS: We performed a retrospective review of all Freestyle PVRs performed by a single surgeon in two institutions. All patients were contacted for follow-up to establish survival, New York Heart Association class and reintervention. Up to date, echocardiography was obtained to assess valve function. Perioperative factors associated with structural valve dysfunction (SVD) were assessed using Cox regression. RESULTS: Between 2000 and 2014, PVR with a Freestyle valve was performed in 114 patients with congenital heart disease. There were 70 males and 44 females. The median age was 21 years (interquartile range 11-35 years). The median clinical and echocardiographic follow-up was 62 months (interquartile range 35-115 months, n = 110) and 58 months (interquartile range 30-93 months, n = 107), respectively. Follow-up was complete for 107 of 114 patients (94%). The survival rate was 95% at 5 years and 91% at 10 years. The rate of freedom from SVD at 5 years was 82%, and at 10 years was 61%. The reintervention-free survival rate was 85% at 5 years, and 71% at 10 years. CONCLUSION: The Freestyle valve in the pulmonary position in a congenital population is associated with low medium-term incidences of SVD and reintervention. It performs equally well to the homograft when a conduit is required and can be considered a valid alternative to stented bioprostheses when PVR alone is required.

Updated 14/4/16
Screening for rheumatic heart disease: quality and agreement of focused cardiac ultrasound by briefly trained health workers.


BACKGROUND: Echocardiographic screening for rheumatic heart disease (RHD) has the potential to detect subclinical cases for secondary prevention, but is constrained by inadequate human resources in most settings. Training non-expert health workers to perform focused cardiac ultrasound (FoCUS) may enable screening at a population-level. We aimed to evaluate the quality and agreement of FoCUS for valvular regurgitation by briefly trained health workers. METHODS: Seven nurses participated in an eight week training program in Fiji. Nurses performed FoCUS on 2018 children aged five to 15 years, and assessed any valvular regurgitation. An experienced pediatric cardiologist assessed the quality of ultrasound images and measured any recorded regurgitation. The assessment of the presence of regurgitation and measurement of the longest jet by the nurse and cardiologist was compared, using the Bland-Altman method. RESULTS: The quality of FoCUS overall was adequate for diagnosis in 96.6%. There was substantial agreement between the cardiologist and the nurses overall on the presence of mitral regurgitation (kappa = 0.75) and aortic regurgitation (kappa = 0.61) seen in two views. Measurements of mitral regurgitation by nurses and the cardiologist were similar (mean bias 0.01 cm; 95% limits of agreement -0.64 to 0.66 cm). CONCLUSIONS: After brief training, health workers with no prior experience in echocardiography can obtain adequate quality images and make a reliable assessment on the presence and extent of valvular regurgitation. Further evaluation of the imaging performance and accuracy of screening by non-expert operators is warranted, as a potential population-level screening strategy in high prevalence settings.

Fractional exhaled nitric oxide for the management of asthma in adults: a systematic review.


The aim of this review was to evaluate the clinical effectiveness of fractional exhaled nitric oxide (FeNO) measured in a clinical setting for the management of asthma in adults.13 electronic databases were searched and studies were selected against predefined inclusion criteria. Quality assessment was conducted using QUADAS-2. Class effect meta-analyses were performed. Six studies were included. Despite high levels of heterogeneity in multiple study characteristics, exploratory class effect meta-analyses were conducted. Four studies reported a wider definition of exacerbation rates (major or severe exacerbation) with a pooled rate ratio of 0.80 (95% CI 0.63-1.02). Two studies reported rates of severe exacerbations (requiring oral corticosteroid use) with a pooled rate ratio of 0.89 (95% CI 0.43-1.72). Inhaled corticosteroid use was reported by four studies, with a pooled standardised mean difference of -0.24 (95% CI -0.56-0.07). No statistically significant differences for health-related quality of life or asthma control were found. FeNO guided management showed no statistically significant benefit in terms of severe exacerbations or inhaled corticosteroid use, but showed a statistically significant reduction in exacerbations of any severity. However, further research is warranted to clearly define which management protocols (including cut-off points) offer best efficacy and which patient groups would benefit the most.

Everard ML.
Paediatric respiratory infections.


Pulmonary infections remain a major cause of infant and child mortality worldwide and are responsible for a substantial burden of morbidity. During the 2015 European Respiratory Society International Congress in Amsterdam, some of the main findings from peer-reviewed articles addressing this topic that were published in the preceding 12 months were reviewed in a Paediatric Clinical Year in Review session. The following article highlights some of the insights provided by these articles into the complex interactions of the human host with the extensive and dynamic populations of microorganisms that call an individual "home".

Francis JR, Wyber R, Remenyi B, Croser D and Carapetis J.
Myositis complicating benzathine penicillin-G injection in a case of rheumatic heart disease.

IDCases. 2016.

Fricke TA, Bulstra AE, Naimo PS, Bullock A, Robertson T, d’Udekem Y, Brizard CP and Konstantinov IE.
Excellent Long-Term Outcomes of the Arterial Switch Operation in Patients With Intramural Coronary Arteries.


BACKGROUND: Intramural coronary arteries may complicate coronary artery transfer during the arterial switch operation. We sought to determine the long-term outcomes of 28 patients with intramural coronary arteries who underwent an arterial switch operation at a single institution. METHODS: All patients who had intramural coronary arteries and underwent an arterial switch operation were identified from the hospital database and

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RESULTS: From 1983 to 2009, 720 patients underwent an arterial switch operation at our institution. Twenty-eight (3.9%, 28 of 720) had intramural coronary arteries. Patients with intramural coronary arteries had transposition of the great arteries (96%, n = 27) or Taussig-Bing anomaly (4%, n = 1). There were no deaths. Follow-up was 100% complete. Mean follow-up was 16.3 years (median, 15.5 years; range, 5.6 to 26.9 years). No patient required reoperation or catheter reintervention on the coronary arteries. Freedom from reoperation was 93% at 10 years. No patient had more than mild aortic regurgitation at last follow-up. Nine (32%, 9 of 28) patients had coronary angiograms at median 16 months (range, 14 months to 17 years) after arterial switch operation. All patients were asymptomatic at the time of angiogram. One patient had mild stenosis of the circumflex coronary artery demonstrated on a routine coronary angiogram 14 months postoperatively. All 28 patients were asymptomatic and in New York Heart Association functional class I at last follow-up. CONCLUSIONS: Patients with intramural coronary arteries are not at increased risk of death or coronary reinterventions and have excellent late outcomes after the arterial switch operation.

Alpha-1 Antitrypsin Mitigates the Inhibition of Airway Epithelial Cell Repair by Neutrophil Elastase.
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 exist 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 assessed in healthy non-CF and CF pediatric primary airway epithelial cells (pAECnon-CF and pAECCF, respectively) during exposure to physiologically relevant NE. 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 pAECnon-CF and pAECCF owing to rapid cellular detachment that was accompanied by inflammatory cytokine release. Furthermore, both phenotypes initiated an apoptotic response to 100 nM NE, whereas >/=50 nM NE activity significantly inhibited the proliferative capacity of cultures. Similar concentrations of NE also significantly inhibited wound repair of pAECCF, but this effect was reversed by the addition of alpha1AT. Collectively, our results demonstrate free NE activity is deleterious for epithelial homeostasis and support the hypothesis that proteases in the airway contribute directly to CF structural lung disease. Our results also highlight the need to investigate antiprotease therapies in early CF disease in more detail.

Ghia T, Kanhangad M, Alessandri AJ, Price G, Gera P and Nagarajan L.
Opsoclonus-Myoclonus Syndrome, Neuroblastoma, and Insulin-Dependent Diabetes Mellitus in a Child: A Unique Patient.
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.

A systematic review of fractional exhaled nitric oxide in the routine management of childhood asthma.
BACKGROUND: Fractional exhaled nitric oxide (FeNO) is a non-invasive biomarker of eosinophilic inflammation which may be used to guide the management of asthma in childhood. OBJECTIVES: To synthesise the available evidence on the efficacy of FeNO-guided management of childhood asthma. METHODS: Databases including MEDLINE and the Cochrane Library were searched, and randomised controlled trials (RCTs) comparing FeNO-guided management with any other monitoring strategy were included. Study quality was assessed using the Cochrane risk of bias tool for RCTs, and a number of outcomes were examined, including: exacerbations, medication use, quality of life, adverse events, and other markers of asthma control. Meta-analyses were planned if multiple studies with suitable heterogeneity were available. However, due to wide variations in study characteristics, meta-analysis was not possible. RESULTS: Seven RCTs were identified. There was some evidence that FeNO-guided monitoring results in improved asthma control during the first year of management, although few results attained statistical significance. The impact on severe exacerbations was unclear. Similarly, the impact on use of anti-asthmatic drugs was unclear, and

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appears to depend on the step up/down protocols, and the clinical characteristics of patients. CONCLUSIONS: The potential benefit of FeNO monitoring is equivocal. Trends toward reduced exacerbation and increased medication use were seen, but typically failed to reach statistical significance. There are a number of issues that complicate data interpretation, including differences in the likely severity of included cohorts and variations in treatment algorithms. Further work is needed to systematically explore the impact of these parameters. Pediatr Pulmonol. 2016;51:316-328. (c) 2016 Wiley Periodicals, Inc.

Grover Z, Burgess C, Muir R, Reilly C and Lewindon PJ.
Early mucosal healing with Exclusive Enteral Nutrition is associated with improved outcomes in newly diagnosed children with luminal Crohn's disease.

BACKGROUND: Exclusive Enteral Nutrition (EEN) induction in children with luminal Crohn's disease (CD) gives early mucosal healing (MH) but long term benefits of EEN induced MH are just emerging. AIMS & METHODS: We prospectively followed an Australian cohort of newly diagnosed children with predominantly luminal CD who completed at least six weeks EEN and with paired clinical (PCDAI), biochemical (CRP) and endoscopic assessment at diagnosis and post EEN. All commenced Immunomodulators (IM's) early (<3 months from diagnosis) and had minimum 1 year follow up. Complete MH was SES-CD 0 and SES-CD>=1 ascribed active endoscopic disease (aED) and further divided into near complete MH (SES 1-3), mild active disease (SES-CD 4-10) and moderate to severe (SES-CD>10). Primary outcome was long term supervised sustained remission (SR) on IM's alone without need for Corticosteroids, Infliximab (IFX) or Surgery. RESULTS: 54 eligible children (33 Males) completing EEN induction were analysed. Median duration between pre & post EEN assessments was 60.5 days (IGR, 56-69.5). Post EEN: CR (PCDAI<10) was observed in 45/54 (83%), BR (PCDAI<10 and CRP<5mg/dl) in 39/54 (72%). Complete MH was observed in 18/54 (33%), near complete in 10/54(19%). SR was superior in those with complete MH vs. aED: 13/18, (72%) vs. 10/36 (28%), p=0.003 at 1 year, 8/16, (50%) vs. 3/24, (8%), p=0.008 at 2 years and (8/16, (50%) vs. 1/19, (6%), p=0.005) at 3 years. Near complete MH did not lead to superior SR. CONCLUSIONS: Only complete MH post EEN induction predicts more favourable SR up to 3 years.

Health service provider education and/or training in infant male circumcision to improve short- and long-term morbidity outcomes: protocol for systematic review.

BACKGROUND: There has been an expansion of circumcision services in Africa as part of a long-term HIV prevention strategy. However, the effect of infant male circumcision on morbidity and mortality still remains unclear. Acute morbidities associated with circumcision include pain, bleeding, swelling, infection, tetanus or inadequate skin removal. Scale-up of circumcision services could lead to a rise in these associated morbidities that could have significant impact on health service delivery and the safety of infants. Multidisciplinary training programmes have been developed to improve skills of health service providers, but very little is known about the effectiveness of health service provider education and/or training for infant male circumcision on short- and long-term morbidity outcomes. This review aims to evaluate the effectiveness of health service provider education and/or training for infant male circumcision on short- and long-term morbidity outcomes. METHODS/DESIGN: The review will include studies comparing health service providers who have received education and/or training to improve their skills for infant male circumcision with those who have not received education and/or training. Randomised controlled trials (RCTs) and cluster RCTs will be included. The outcomes of interest are short-term morbidities of the male infant including pain, infection, tetanus, bleeding, excess skin removal, glans amputation and fistula. Long-term morbidities include urinary tract infection (UTI), HIV infection and abnormalities of urination. Databases such as MEDLINE (OVID), PsycINFO (OVID), EMBASE (OVID), Cochrane Library (including CENTRAL and DARE), WHO databases and reference list of papers will be searched for relevant articles. Study selection, data extraction and synthesis and risk of bias assessment using the Cochrane risk of bias assessment tool will be conducted. We will calculate the pooled estimates of the difference in means and risk ratios using random effects models. If insufficient data are available, we will present results descriptively. DISCUSSION: This review appears to be the first to be conducted in this area. The findings will have important implications for infant male circumcision programmes and policy. SYSTEMATIC REVIEW REGISTRATION: PROSPERO CRD42015029345.

Ha JF, Ong F, Wood B and Vijayasekaran S.
Radiologic and Audiologic Findings in the Temporal Bone of Patients with CHARGE Syndrome.

Halliday GC, O`Reilly J, Kelsey C, Cole CH and Kotecha RS.

Updated 14/4/16
Successful Treatment of Congenital Erythroleukemia With Low-Dose Cytosine Arabinoside.

Hemming IA, Forrest AR, Shipman P, Woodward KJ, Walsh P, Ravine DG and Heng JI.
Reinforcing the association between distal 1q CNVs and structural brain disorder: A case of a complex 1q43-q44 CNV and a review of the literature.
Copy Number Variations (CNVs) comprising the distal 1q region 1q43-q44 are associated with neurological impairments, structural brain disorder, and intellectual disability. Here, we report an extremely rare, de novo case of a 1q43-q44 deletion with an adjacent duplication, associated with severe seizures, microcephaly, agenesis of the corpus callosum, and pachygyria, a consequence of defective neuronal migration disorder. We conducted a literature survey to find that our patient is only the second case of such a 1q43-q44 CNV ever to be described. Our data support an association between 1q43-q44 deletions and microcephaly, as well as an association between 1q43-q44 duplications and macrocephaly. We compare and contrast our findings with previous studies reporting on critical 1q43-q44 regions and their constituent genes associated with seizures, microcephaly, and corpus callosum abnormalities [Ballif et al., 2012; Hum Genet 131:145-156; Nagamani et al., 2012; Eur J Hum Genet 20:176-179]. Taken together, our study reinforces the association between 1q43-q44 CNVs and brain disorder. (c) 2016 Wiley Periodicals, Inc.

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.

Hogan B, Keating M, Chambers NA and von Ungern-Sternberg B.
Audit of anesthetic trainee's 'hands-on' operating room experience in an Australian tertiary children's hospital.
Paediatr Anaesth. 2016.
BACKGROUND: There are no internationally accepted guidelines about what constitutes adequate clinical exposure during pediatric anesthetic training. In Australia, no data have been published on the level of experience obtained by anesthetic trainees in pediatric anesthesia. There is, however, a new ANZCA (Australian and New Zealand College of Anaesthetists) curriculum that quantifies new training requirements. AIM: To quantify our trainees' exposure to clinical work in order to assess compliance with new curriculum and to provide other institutions with a benchmark for pediatric anesthetic training. METHODS: We performed a prospective audit to estimate and quantify our anesthetic registrars' exposure to pediatric anesthesia during their 6-month rotation at our institution, a tertiary pediatric hospital in Perth, Western Australia. RESULTS: Our data suggest that trainees at our institution will achieve the new ANZCA training standards comfortably, in terms of the required volume and breadth of exposure. Experience, however, of some advanced pediatric anesthetic procedures appears limited. CONCLUSIONS: Experience gained at our hospital easily meets the new College requirements. Experience of fiber-optic intubation and regional blocks would appear insufficient to develop sufficient skills or confidence. The study provides other institutions with information to benchmark against their own trainee experience.

Iosifidis T, Garratt LW, Coombe DR, Knight DA, Stick SM and Kicic A.
Airway epithelial repair in health and disease: Orchestrator or simply a player?
Epithelial cells represent the most important surface of contact in the body and form the first line of defence of the body to external environment. Consequently, epithelia have numerous roles in order to maintain a homeostatic defence barrier. Although the epithelium has been extensively studied over several decades, it

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remains the focus of new research, indicating a lack of understanding that continues to exist around these cells in specific disease settings. Importantly, evidence is emerging that airway epithelial cells in particular have varied complex functions rather than simple passive roles. One area of current interest is its role following injury. In particular, the epithelial-specific cellular mechanisms regulating their migration during wound repair remain poorly understood and remain an area that requires much needed investigation. A better understanding of the physiological, cellular and molecular wound repair mechanisms could assist in elucidating pathological processes that contribute to airway epithelial pathology. This review attempts to highlight migration-specific and cell-extracellular matrix (ECM) aspects of repair used by epithelial cells under normal and disease settings, in the context of human airways.

**Jagannathan N and von Ungern-Sternberg BS.**  

Mucormycosis in Australia: contemporary epidemiology and outcomes. Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases. 2016.

Mucormycosis is the second most common cause of invasive mould infection and causes disease in diverse hosts, including those who are immunocompetent. We conducted a multicentre retrospective study of proven and probable cases of mucormycosis diagnosed between 2004-2012 to determine the epidemiology and outcome determinants in Australia. Seventy-four cases were identified (63 proven, 11 probable). The majority (54.1%) were caused by Rhizopus spp. Patients who sustained trauma were more likely to have non-Rhizopus infections relative to patients without trauma (OR 9.0, p=0.001, CI (2.1-42.8)). Haematological malignancy (48.6%), chemotherapy (41.9%), corticosteroids (52.7%), diabetes mellitus (27%) and trauma (22.9%) were the most common co-morbidities or risk factors. Rheumatological/autoimmune disorders occurred in 9 (12.1%) instances. Eight (10.8%) patients had no underlying co-morbidity and were more likely to have associated trauma (7/8; 87.5% vs 10/66; 15.2%; p<0.001). Disseminated infection was common (39.2%). Apophysomyces spp. and Saksenaea spp. caused infection in immunocompetent hosts, most often associated with trauma and affected sites other than lung and sinuses. The 180-day mortality was 56.7%. The strongest predictors of mortality were rheumatological/autoimmune disorder (OR=24.0, p=0.038 CI (1.2-481.4)), haematological malignancy (OR=7.7, p=0.001, CI (2.3-25.2)) and ICU admission (OR=4.2, p=0.02, CI (1.3-13.8)). Most deaths occurred within one month. Thereafter we observed divergence in survival between the haematological and non-haematological populations (p=0.006). The mortality of mucormycosis remains particularly high in immunocompromised hosts. Underlying rheumatological/autoimmune disorders are a previously under-appreciated risk for infection and poor outcome.

**Kotecha RS, Wadia UD, Jacoby P, Ryan AL, Blyth CC, Keil AD, Gottardo NG, Cole CH, Barr IG and Richmond PC.**  

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 in 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.
Lim FJ, de Klerk N, Blyth CC, Fathima P and Moore HC.
Systematic review and meta-analysis of respiratory viral coinfections in children.
Respirology. 2016.
Respiratory infections are a common cause of paediatric morbidity. Clinical outcomes in children hospitalized with single respiratory virus infection are compared with those with two or more viral-viral coinfection. Studies were restricted to those reporting on children aged less than 5 years (PROSPERO CRD#42014009133). Published data to calculate risk ratios (RR) comparing children with single viral infections to coinfection using a random effects model were used. Similar analyses by pathogen pairs and by excluding children with comorbidities were performed. Of 4443 articles reviewed, 19 were included. Overall, no differences in the risk of fever, admission to an intensive care unit (ICU), oxygen use, mechanical ventilation and abnormal radiographs between children with single infection and those with coinfection were found. When analysing only children without comorbidities, the risk of fever (RR = 1.16 to RR = 1.24, 95% confidence intervals (CI) = 1.00-1.55) and ICU admission (RR = 1.08 to RR = 1.31, 95% CI = 0.93-1.83) increased but remained non-significant. Point estimates suggested an increased risk of ICU admission in those coinfected with either respiratory syncytial virus or human metapneumovirus compared with those with single infection but was non-significant. Our findings suggest that coinfection is not associated with increased clinical severity, but further investigations by pathogen pairs are warranted.

Love S, Gibson N, Smith N, Bear N and Blair E.
Interobserver reliability of the Australian Spasticity Assessment Scale (ASAS).
AIM: The aim of this paper is to present the Australian Spasticity Assessment Scale (ASAS) and to report studies of its intrarater reliability. The ASAS identifies the presence of spasticity by confirming a velocity-dependent increased response to rapid passive movement and quantifies it using an ordinal scale. METHOD: The rationale and procedure for the ASAS is described. Twenty-two participants with spastic CP (16 males; age range 1y 11mo-15y 3mo) who had not had botulinum neurotoxin-A within 4 months, or bony or soft tissue surgery within 12 months, were recruited from the spasticity management clinic of a tertiary paediatric teaching hospital. Fourteen muscles in each child were assessed by each of three experienced independent raters. ASAS was recorded for all muscles. Intrarater reliability was calculated using the weighted kappa statistic (quadratic weighting; kappaqw ) for individual muscles, for upper limbs, for lower limbs, and between raters. RESULTS: The weighted kappa ranged between 0.75 and 0.92 for individual muscle groups and was 0.87 between raters. INTERPRETATION: The ASAS complies with the definition of spasticity and is clinically feasible in paediatric settings. Our estimates of intrarater reliability for the ASAS exceed that of the most commonly used spasticity scoring systems.

Mariyappa B, Maruthayanan S, Samnakay N, Barker A and Khosa J.
Incidence of Post-Ureteric Reimplantation Urinary Tract Infection in Primary Vesicoureteral Reflux.

Martin AC, Anderson D, Lucey J, Guttinger R, Jacoby PA, Mok TJ, Whitmore TJ, Whitewood CN, Burgner DP and Blyth CC.
Predictors of Outcome in Pediatric Osteomyelitis: Five Years Experience in a Single Tertiary Center.
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 standardized 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, utilizing information available shortly after hospitalization, allows early identification of children at greatest risk of developing complicated osteomyelitis.

Maxwell S, James I, Dickinson JE and O'Leary P.
First trimester screening cut-offs for noninvasive prenatal testing as a contingent screen: Balancing detection and screen-positive rates for trisomy 21.

Updated 14/4/16
OBJECTIVE: To provide data on how screen-positive and detection rates of first trimester prenatal screening for fetal Down syndrome vary with changes in the risk cut-off and maternal age to inform contingency criteria for publicly funded noninvasive prenatal testing. MATERIALS AND METHODS: First trimester screening and diagnostic data were collected for all women attending for first trimester fetal aneuploidy screening in Western Australia between 2005 and 2009. Prenatal screening and diagnostic data were linked to pregnancy outcomes, including data from the Midwives’ Notification System and the Western Australian Registry of Developmental Anomalies. The prevalence of Down syndrome and performance of screening by risk cut-off and/or for women >35 years were analysed. RESULTS: The current screening risk cut-off of 1:300 has screen-positive and detection rates of 3.5% and 82%. The screen-positive rate increases by 0.7-0.8% for each 100 point change in risk, up to 19.2% at 1:2500 (96% detection rate). Including all women >35 years as screen positive would increase the screen-positive rate and detection rates to 30.2% and 97.2%. CONCLUSION: Variation in screening risk cut-off and the use of maternal age to assess eligibility for noninvasive testing could significantly impact the demand for, and cost of, the test. A contingent first trimester screening approach for risk assessment is superior to the use of a combination of screening and maternal age alone. These data will inform decisions regarding the criteria used to determine eligibility for publicly funded noninvasive prenatal testing.

Improving access to primary care for Aboriginal babies in Western Australia: study protocol for a randomized controlled trial.
Trials. 2016; 17(1): 82.

BACKGROUND: Despite a decade of substantial investments in programs to improve access to primary care for Aboriginal mothers and infants, more than 50% of Western Australian Aboriginal babies are still not receiving primary and preventative care in the early months of life. Western Australian hospitals now input birth data into the Western Australian electronic clinical management system within 48 hours of birth. However, difficulties have arisen in ensuring that the appropriate primary care providers receive birth notification and clinical information by the time babies are discharged from the hospital. No consistent process exists to ensure that choices about primary care are discussed with Aboriginal families. METHODS/DESIGN: We will undertake a population-based, stepped wedge, cluster randomized controlled trial of an enhanced model of early infant primary care. The intervention is targeted support and care coordination for Aboriginal families with new babies starting as soon as possible during the antenatal period or after birth. Dedicated health professionals and research staff will consult with families about the families’ healthcare needs, provide information about healthcare in the first 3 months of life, offer assistance with birth and Medicare forms, consult with families about their choice for primary care provider, offer to notify the chosen primary care provider about the baby’s health needs, and offer assistance with healthcare coordination at the time of discharge from the hospital. We will evaluate this model of care using a rigorous stepped wedge approach. Our primary outcome measure is a reduced hospitalization rate in infants younger than 3 months of age. Secondary outcome measures include completed Aboriginal and Torres Strait Islander child health screening assessments, immunization coverage, and satisfaction of the families about early infant primary care. We will also assess the cost effectiveness of the model of care. DISCUSSION: This study will be conducted over a 4-year period in partnership with birthing hospitals and primary care providers including Western Australian Aboriginal Community Controlled Health Services and the new Primary Health Networks. The results of our trial will be used to develop improved primary care models and to improve health outcomes for all Aboriginal infants. These are vital steps toward more equitable health service delivery for the Aboriginal and Torres Strait Islander children in Australia. TRIAL REGISTRATION: Australian New Zealand Clinical Trials Registry Registration number: ACTRN12615000976583 Date registered: 17 September 2015.

McLean J, Gill FJ and Shields L.
Family presence during resuscitation in a paediatric hospital: health professionals’ confidence and perceptions.

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. 2016; 46(2): 308-316.

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, IFNgamma 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 randomization to receive 'early egg' or a placebo as part of a randomized 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.

Mullins BJ, Kicic A, Ling KM, Mead-Hunter R and Larcombe AN.
Biodiesel exhaust-induced cytotoxicity and proinflammatory mediator production in human airway epithelial cells.
Increasing use of biodiesel has prompted research into the potential health effects of biodiesel exhaust exposure. Few studies directly compare the health consequences of mineral diesel, biodiesel, or blend exhaust exposures. Here, we exposed human epithelial cell cultures to diluted exhaust generated by the combustion of Australian ultralow-sulfur-diesel (ULSD), unprocessed canola oil, 100% canola biodiesel (B100), and a blend of 20% canola biodiesel mixed with 80% ULSD. The physicochemical characteristics of the exhaust were assessed and we compared cellular viability, apoptosis, and levels of interleukin (IL)-6, IL-8, and Regulated on Activation, Normal T cell Expressed and Secreted (RANTES) in exposed cultured cells. Different fuel types produced significantly different amounts of exhaust gases and different particle characteristics. All exposures resulted in significant apoptosis and loss of viability when compared with control, with an increasing proportion of biodiesel being correlated with a decrease in viability. In most cases, exposure to exhaust resulted in an increase in mediator production, with the greatest increases most often in response to B100. Exposure to pure canola oil (PCO) exhaust did not increase mediator production, but resulted in a significant decrease in IL-8 and RANTES in some cases. Our results show that canola biodiesel exhaust exposure elicits inflammation and reduces viability of human epithelial cell cultures in vitro when compared with ULSD exhaust exposure. This may be related to an increase in particle surface area and number in B100 exhaust when compared with ULSD exhaust. Exposure to PCO exhaust elicited the greatest loss of cellular viability, but virtually no inflammatory response, likely due to an overall increase in average particle size.

Naimo PS, Fricke TA, d’Udekem Y, Cochrane AD, Bullock A, Robertson T, Brizard CP and Konstantinov IE.
Surgical Intervention for Anomalous Origin of Left Coronary Artery From the Pulmonary Artery in Children: A Long-Term Follow-Up.
BACKGROUND: Anomalous left coronary artery from the pulmonary artery (ALCAPA) is a rare congenital heart defect with limited data on long-term outcomes after surgical intervention. METHODS: We conducted a retrospective review of all children (N = 42) who underwent surgical repair of ALCAPA between 1980 and 2014 at the Royal Children's Hospital, Melbourne. RESULTS: Twenty-nine (69% [29 of 42]) patients underwent coronary reimplantation, 12 (29% [12 of 42]) had intrapulmonary baffle (Takeuchi) repair, and 1 (2% [1 of 42]) patient had ligation of the anomalous coronary artery. Nine (21%, 9 of 42) patients had concomitant mitral valve (MV) repair at the time of ALCAPA repair. A left ventricular assist device (LVAD) was used in 36% (15 of 42) of patients. Early mortality was 2.4% (1 of 42 patients). Median follow-up was 14 years (mean, 13 years; range, 4 months-31 years). There were no late deaths. Survival was 98% at 20 years. Freedom from reoperation was 81%, 81%, and 76% at 5, 10, and 20 years after operation, respectively. Eight patients underwent late MV repair or replacement at a median of 3 years (mean, 8 years; range, 2 months-25 years) after operation. Freedom from late MV repair or replacement was 86% at 5 and 10 years and 81% at 20 years after operation. Eleven (26% [11 of 42]) patients had severe mitral regurgitation (MR) preoperatively. Of those 11 patients, 5 (45% [5 of 11]) had concomitant MV repair at the time of ALCAPA repair, 3 (27% [3 of 11]) had late MV repair or replacement, and the remaining 3 (27% [3 of 11]) patients had mild MR at last follow-up. Thirty-six (90% [36 of 41]) patients had normal left ventricular function and 4 (10% [4 of 41]) patients had mildly reduced left ventricular (LV) function at last follow-up. CONCLUSIONS: ALCAPA can be operated on with good outcomes. Persistent MR and a moderate rate of late MV repair warrants close follow-up.

Updated 14/4/16
Naylor LH, Davis EA, Kalic RJ, Paramalingam N, Abraham MB, Jones TW and Green DJ.
Exercise training improves vascular function in adolescents with type 2 diabetes.
The impact of exercise training on vascular health in adolescents with type 2 diabetes has not been previously studied. We hypothesized that exercise training would improve micro- and macrovascular health in adolescents with type 2 diabetes. Thirteen adolescents (13-21 years, 10F) with type 2 diabetes were recruited from Princess Margaret Hospital. Participants were randomized to receive either an exercise program along with standard clinical care (n = 8) or standard care alone (n = 5). Those in the intervention group received 12 weeks of gym-based, personalized, and supervised exercise training. Those in the control group were instructed to maintain usual activity levels. Assessments were conducted at baseline and following week 12. The exercise group was also studied 12 weeks following the conclusion of their program. Assessments consisted of conduit artery endothelial function (flow-mediated dilation, FMD) and microvascular function (cutaneous laser Doppler). Secondary outcomes included body composition (dual-energy X-ray absorptiometry, DXA), glycemic control (whole body insulin sensitivity, M) assessed using the euglycemic-hyperinsulinemic clamp protocol, cardiorespiratory fitness (V O2peak), and muscular strength (1RM). Exercise training increased FMD (P < 0.05), microvascular function (P < 0.05), total lean mass (P < 0.05), and muscle strength (P < 0.001). There were no changes in cardiorespiratory fitness, body weight, BMI, or M. In the control group, body weight (P < 0.01), BMI (P < 0.01), and total fat mass (P < 0.05) increased. At week 24, improvements in vascular function were reversed. This study indicates that exercise training can improve both conduit and microvascular endothelial function and health, independent of changes in insulin sensitivity in adolescents with type 2 diabetes.

Pang J, Martin AC, Mori TA, Beilin LJ and Watts GF.
Prevalence of Familial Hypercholesterolemia in Adolescents: Potential Value of Universal Screening?
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.
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.

Patole SK, Rao SC, Keil AD, Nathan EA, Doherty DA and Simmer KN.
BACKGROUND: Systematic reviews of randomised controlled trials report that probiotics reduce the risk of necrotising enterocolitis (NEC) in preterm neonates. AIM: To determine whether routine probiotic supplementation (RPS) to preterm neonates would reduce the incidence of NEC. METHODS: The incidence of NEC >/= Stage II and all-cause mortality was compared for an equal period of 24 months 'before' (Epoch 1) and 'after' (Epoch 2) RPS with Bifidobacterium breve M-16V in neonates <34 weeks. Multivariate logistic regression analysis was conducted to adjust for relevant confounders. RESULTS: A total of 1755 neonates (Epoch I vs. II: 835 vs. 920) with comparable gestation and birth weights were admitted. There was a significant reduction in NEC >/= Stage II: 3% vs. 1%, adjusted odds ratio (aOR) = 0.43 (95%CI: 0.21-0.87); 'NEC >/= Stage II or all-cause mortality': 9% vs. 5%, aOR = 0.53 (95%CI: 0.32-0.88); but not all-cause mortality alone: 7% vs. 4%, aOR = 0.58 (95% CI: 0.31-1.06) in Epoch II. The benefits in neonates <28 weeks did not reach statistical significance: NEC >/= Stage II: 6% vs. 3%, aOR 0.51 (95CI: 0.20-1.27), 'NEC >/= Stage II or all-cause mortality', 21% vs. 14%, aOR = 0.59 (95%CI: 0.29-1.18); all-cause mortality: 17% vs. 11%, aOR = 0.63 (95%CI: 0.28-1.41). There was no probiotic sepsis. CONCLUSION: RPS with Bifidobacterium breve M-16V was
associated with decreased NEC≥ Stage II and ‘NEC≥ Stage II or all-cause mortality’ in neonates <34 weeks. Large sample size is required to assess the potential benefits of RPS in neonates <28 weeks.

Peirce D, Brown J, Corkish V, Lane M and Wilson S.
Instrument validation process: a case study using the Paediatric Pain Knowledge and Attitudes Questionnaire. Journal of clinical nursing. 2016: n/a-n/a.

Phan JA, Kicic A, Berry LJ, Sly PD and Larcombe AN.

PURPOSE: Recent studies have employed animal models to investigate links between rhinovirus infection and allergic airways disease, however, most do not involve early life infection, and none consider the effects of sex on responses. MATERIALS AND METHODS: Here, we infected male and female mice with human rhinovirus 1B (or control) on day 7 of life. Mice were then subjected to 7 weeks of exposure to house-dust-mite prior to assessment of bronchoalveolar inflammation, serum antibodies, lung function, and responsiveness to methacholine. RESULTS: There were significant differences in responses between males and females in most outcomes. In males, chronic house-dust-mite exposure increased bronchoalveolar inflammation, house-dust-mite specific IgG1 and responsiveness of the lung parenchyma, however, there was no additional impact of rhinovirus infection. Conversely, in females, there were additive and synergistic effects of rhinovirus infection and house-dust-mite exposure on neutrophilia, airway resistance, and responsiveness of the lung parenchyma. CONCLUSIONS: We conclude that early life rhinovirus infection influences the development of house-dust-mite induced lung disease in female, but not male mice.

Ten-year outcomes of Fontan conversion in Australia and New Zealand demonstrate the superiority of a strategy of early conversion dagger.
OBJECTIVE: To investigate the benefits of a strategy of early Fontan conversion. METHODS: Using the Australia and New Zealand Fontan Registry, retrospective analysis of their long-term follow-up data was performed. RESULTS: Between 1990 and 2014, a total of 39 patients underwent surgical conversion in 6 centres at a median age of 23.8 years (IQR: 19.3-28.2), 18.7 +/- 5.0 years post-Fontan. One centre tended to perform conversion earlier: interval since first documented arrhythmia 2.9 +/- 4.0 vs 4.0 +/- 4.2 years, average NYHA Class 2 +/- 0.4 vs 3 +/- 0.9 (P = 0.008), mean number of preop anti-arrhythmics 1 +/- 0.4 vs 2 +/- 0.6 (P = 0.05). Two patients underwent conversion to an extracardiac conduit only, while 36 had concomitant right atrial cryoablation, of which 16 also had pacemaker implantation. Nine patients suffered major cardiac-related complications (7 low output syndrome, 3 ECMO, 3 acute renal failure, one stroke) (2/17 from the early conversion centre and 7/22 of the others; P = 0.14). Four patients died in hospital (10.3%) and 4 later after a median of 0.9 years [95% confidence interval (CI): 0.5-1] after conversion. An additional 2 patients needed transplantation at 1 and 8.8 years after conversion, respectively. The 10-year freedom from heart transplantation was 86% (95% CI: 51-97%). Outcomes from the centre with an early conversion strategy were significantly better: 8-year freedom from death or heart transplantation was 86% (95% CI: 53-96) vs 51% (95% CI: 22-74; log-rank P = 0.007). Eight additional patients required pacemaker implantation and 5 had arrhythmia recurrence. CONCLUSIONS: Fontan conversion is associated with lasting survival outcomes up to 10 years after conversion. A strategy of surgical conversion at earlier stage of failure may be associated with better survival free from transplantation.

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 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

Updated 14/4/16
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 placentaes 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.

Improving delivery of secondary prophylaxis for rheumatic heart disease in remote Indigenous communities: study protocol for a stepped-wedge randomised trial.

BACKGROUND: Rheumatic heart disease (RHD), caused by acute rheumatic fever (ARF), is a major health problem in Australian Aboriginal communities. Progress in controlling RHD requires improvements in the delivery of secondary prophylaxis, which comprises regular, long-term injections of penicillin for people with ARF/RHD. METHODS/DESIGN: This trial aims to improve uptake of secondary prophylaxis among Aboriginal people with ARF/RHD to reduce progression or worsening of RHD. This is a stepped-wedge, randomised trial in consenting communities in Australia's Northern Territory. Pairs of randomly-chosen clinics from among those consenting enter the study at 3-monthly steps. The intervention to which clinics are randomised comprises a multi-faceted systems-based package, in which clinics are supported to develop and implement strategies to improve penicillin delivery, aligned with elements of the Chronic Care Model. Continuous quality improvement processes will be used, including 3-monthly feedback to clinic staff of adherence rates of their ARF/RHD clients. The primary outcome is the proportion of people with ARF/RHD receiving >/=80 % of scheduled penicillin injections over a minimum 12-month period. The sample size of 300 ARF/RHD clients across five community clusters will power the study to detect a 20 % increase in the proportion of individuals achieving this target, from a worrying low baseline of 20 %, to 40 %. Secondary outcomes pertaining to other measures of adherence will be assessed. Within the randomised trial design, a mixed-methods evaluation will be embedded to evaluate the efficiency, effectiveness, impact and relevance, sustainability, process and fidelity, and performance of the intervention. The evaluation will establish any causal link between outcomes and the intervention. The planned study duration is from 2013 to 2016. DISCUSSION: Continuous quality improvement has a strong track record in Australia's Northern Territory, and its use has resulted in modest benefits in a pilot, non-randomised ARF/RHD study. If successful, this new intervention using the Chronic Care Model as a scaffold and evaluated using a well-developed theory-based framework, will provide a practical and transferable approach to ARF/RHD control. TRIAL REGISTRATION: Australian New Zealand Clinical Trials Registry: ACTRN12613000223730 . Date registered: 25 February 2013.

Lung Clearance Index and Structural Lung Disease on Computed Tomography in Early Cystic Fibrosis.

RATIONALE: The lung clearance index is a measure of ventilation distribution from the multiple breath washout technique. Lung clearance index has been suggested as a surrogate for chest computed tomography to detect structural lung abnormalities in individuals with cystic fibrosis, however the associations between lung clearance index and early structural lung disease are unclear. OBJECTIVE: We assessed the ability of lung clearance index to reflect structural lung disease on chest computed tomography across the entire paediatric age range. METHODS: Lung clearance index was assessed in 42 infants (0-2y), 39 preschool (3-6y), and 38 school-aged (7-16y) children with cystic fibrosis prior to chest computed tomography, and 72 healthy controls. Scans were evaluated for CF-related structural lung disease using the PRAGMA quantitative outcome measure. MEASUREMENTS AND MAIN RESULTS: In infants with cystic fibrosis, lung clearance index is insensitive to structural disease (Kappa -0.03 (-0.05, 0.16)). In preschool children with cystic fibrosis, lung clearance index correlates with total disease extent. In school-aged children lung clearance index correlates with extent of total disease, bronchiectasis, and air trapping. In preschool and school aged children, lung clearance index has a good positive (83-86%), but poor negative (50-55%), predictive value to detect the presence of bronchiectasis. CONCLUSIONS: These data suggest lung clearance index may be a useful surveillance tool to monitor structural lung disease in preschool and school age children with cystic fibrosis. However, lung clearance index cannot replace chest imaging using computed tomography to screen for bronchiectasis in this population.

Rao SC, Athalye-Jape GK, Deshpande GC, Simmer KN and Patole SK.
Probiotic Supplementation and Late-Onset Sepsis in Preterm Infants: A Meta-analysis.

Updated 14/4/16
CONTEXT: Late-onset sepsis (LOS) is a major cause of mortality and morbidity in preterm infants. Despite various preventive measures, its incidence continues to remain high, hence the urgent need for additional approaches. One such potential strategy is supplementation with probiotics. The updated Cochrane Review (2014) did not find benefits of probiotics in reducing the risk of LOS in preterm infants (19 studies, N = 5338). Currently there are >30 randomized controlled trials (RCTs) of probiotics in preterm infants that have reported on LOS. OBJECTIVES: To conduct a systematic review including all relevant RCTs. DATA SOURCES: PubMed, Embase, Cochrane Central Register of Controlled Trials, Cumulative Index of Nursing and Allied Health Literature, and E-abstracts from the Pediatric Academic Society meetings and other pediatric and neonatal conference proceedings were searched in June and August 2015. STUDY SELECTION: RCTs comparing probiotics versus placebo/no probiotic were included. DATA EXTRACTION: Relevant data were extracted independently by 3 reviewers. RESULTS: Pooled results from 37 RCTs (N = 9416) using fixed effects model meta-analysis showed that probiotics significantly decreased the risk of LOS (675/4852 [13.9%] vs 744/4564 [16.3%]; relative risk, 0.86; 95% confidence interval, 0.78-0.94; P = .0007; I(2) = 35%; number needed to treat, 44). The results were significant even after excluding studies with high risk of bias. CONCLUSIONS: Probiotic supplementation reduces the risk of LOS in preterm infants.

Parental pre-pregnancy BMI is a dominant early-life risk factor influencing BMI of offspring in adulthood.
Obesity Science & Practice. 2016; n/a-n/a.
Objective We examined parental and early-life variables in order to identify risk factors for adulthood overweight and obesity in offspring. We report here on the longitudinal prevalence of overweight and obesity in Australian children born between 1989 and 1991 and followed from birth to age 22. Methods Data were analysed on 1355 participants from the Western Australian Pregnancy Cohort (Raine) Study, with anthropometry collected during pregnancy, at birth, one year and at three yearly intervals thereafter. Multivariate analyses and cross-sectional logistic regression quantified the timing and contribution of early-life risk factors for overweight and obesity in young-adulthood. Results At five years of age 12.6% of children were overweight and 5.2% were obese. By early adulthood, the prevalence of obesity had increased to 12.8%, whilst overweight remained relatively stable at 14.2% (range from early childhood to adulthood 11–16%). Parental pre-pregnancy body mass index (BMI) was the strongest determinant of adult offspring BMI. Although rapid first year weight gain was associated with increased offspring BMI, the impact of first year weight-gain diminished over childhood, whilst the impact of parental BMI increased over time. Conclusions Parental pre-pregnancy BMI and rapid early-life weight gain predispose offspring to obesity in adulthood.

Regan AK, Tracey LE, Blyth CC, Richmond PC and Efler PV.
A prospective cohort study assessing the reactogenicity of pertussis and influenza vaccines administered during pregnancy.
Vaccine. 2016.
BACKGROUND: Pertussis vaccination during pregnancy can prevent 91% of infant infections. In 2015, antenatal pertussis vaccination programs were introduced across Australia. METHODS: To monitor the safety of this program, pregnant women who received trivalent influenza vaccine (TIV) and/or diphtheria-tetanus-acellular pertussis vaccine (dTpa) were surveyed by text message seven days post-vaccination about possible adverse events following immunization (AEFI). Univariate logistic regression models were used to calculate the odds of reporting an AEFI following dTpa compared to TIV. Similar analyses were used to compare AEFI reported by women who received a previous dose of dTpa in 2011/2012 as part of a state-wide cocooning program. RESULTS: Of 5155 women, 4347 (84.3%) replied; 10.8% indicated they experienced an AEFI. There was no difference in the proportion of women who reported any reaction by vaccine; however, women who received dTpa were more likely to report a local reaction than women who received TIV (7.1% and 3.2%, respectively; OR: 2.29; 95% CI: 1.61-3.26). There was evidence suggesting local reactions were more common among women with a previous dose of dTpa (11.4%) compared to women with no previous dose (6.0%; OR: 2.00; 95% CI: 0.95-4.25); 11 (0.3%) women reported attending a hospital emergency department. Subsequent follow-up indicated symptoms resolved and mother and infant were healthy. There was no difference in the proportion of women attending hospital by vaccine (p=0.05). DISCUSSION: Data on systemic and local reactions following receipt of TIV and dTpa during pregnancy support the safety of antenatal vaccination.

Reynolds V, Meldrum S, Simmer K, Vijayasekaran S and French N.
Voice problems in school-aged children following very preterm birth.
Arch Dis Child. 2016.
BACKGROUND AND OBJECTIVE: Very preterm children may be at risk of voice abnormalities (dysphonia). Risk factors previously identified in extremely preterm children include female gender, multiple intubations, complicated intubation and very low birth weight. This study sought to identify the prevalence of dysphonia in...
very preterm children, at school age. METHODS: Children born between 23 and 32 weeks’ gestation were included in this prospective observational study. Participants were randomly selected from a sample stratified by gestational age and number of intubations, and were aged between 5 and 12 years at the time of assessment. Clinical voice assessments were conducted by a speech pathologist, and a diagnosis of dysphonia was made based on the presence and severity of disturbance to the voice. RESULTS: 178 participants were assessed. The prevalence of dysphonia in this cohort was 61%. 31% presenting with significant dysphonia, that is, voice disturbance of greater than mild in severity. Female gender (p=0.009), gestational age (p=0.031) and duration of intubation (p=0.021) were significantly associated with dysphonia although some preterm children with dysphonia were never intubated. CONCLUSIONS: Significant voice abnormalities were observed in children born at up to 32 weeks’ gestation, with intubation a major contributing factor. TRIAL REGISTRATION NUMBER: ACTRN12613001015730.

Rincon J, Tan A, Firth M and Saleh A. 
Comparison of adjunctive azithromycin and amoxicillin/metronidazole for patients with chronic periodontitis: preliminary randomized control trial. 
Australian dental journal. 2016. 

BACKGROUND: There are insufficient guidelines for the use of adjunctive systemic antibiotics for patients with periodontal disease. AIM: To compare clinical outcomes for patients with moderate-advanced chronic periodontitis treated with: scaling and root planing (SRP), SRP with amoxicillin and metronidazole (A+M), SRP with Azithromycin (Az). MATERIALS AND METHODS: Thirty seven non-smokers with generalized moderate to advanced chronic periodontitis were divided into three treatment groups: SRP, A+M and Az. Patients received the medications after the last SRP session and were reviewed three months later. Changes in clinical parameters were compared between the groups. Separate analyses were executed for: "all sites", "molar sites", "sites with different PPD severities" and "number of sites with shallow, moderate and deep PPD". RESULTS: The three groups exhibited improvements in most clinical parameters. At three months, A+M showed a higher reduction in PPD compared to Az in the "all sites analysis". Molars exhibited better reduction in BOP and PPD with A+M than SRP. Pocket depth of the 4-6mm category reduced more in the A+M than SRP. A+M experienced a higher increase in the number of sites with PPD 1-3mm than Az. CONCLUSION: Adjunctive systemic antibiotics in the initial phase of treatment may result in improved clinical outcomes. This article is protected by copyright. All rights reserved.

Genomic dissection of Australian Bordetella pertussis isolates from the 2008-2012 epidemic. 
OBJECTIVES: Despite high pertussis vaccination coverage, Australia experienced a prolonged epidemic in 2008-2012. The predominant Bordetella pertussis genotype harboured pertussis toxin promoter allele, ptxP3, and pertactin gene allele, pmr2. The emergence and expansion of prn non-expressing isolates (Prn negative), were also observed. We aimed to investigate the microevolution and genomic diversity of epidemic B. pertussis isolates. METHODS: We sequenced 22 B. pertussis isolates collected in 2008-2012 from two states of Australia which are geographically widely separated. Ten of the 22 were Prn negative isolates with three different modes of silencing of prn (prn::IS481F, prn::IS481R and prn::IS1002). Five pre-epidemic isolates were also sequenced for comparison. RESULTS: Five single nucleotide polymorphisms were common in the epidemic isolates and differentiated them from pre-epidemic isolates. The Australian epidemic isolates can be divided into five lineages (EL1-EL5) with EL1 containing only Prn negative isolates. Comparison with global isolates showed that three lineages remained geographically and temporally distinct whereas two lineages mixed with isolates from 2012 UK outbreak. CONCLUSION: Our results suggest significant diversification and the microevolution of B. pertussis within the 2008-2012 Australian epidemic.

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 disproportionally 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.

Updated 14/4/16
**Shetty VB, Fournier PA, Davey RJ, Retterath AJ, Paramalingam N, Roby HC, Cooper MN, Davis EA and Jones TW.**


**CONTEXT:** No recommendations exist to inform the carbohydrate amount required to prevent hypoglycemia associated with exercise of different intensities in individuals with type 1 diabetes (T1D). **OBJECTIVE:** The relationship between exercise intensity and carbohydrate requirements to maintain stable euglycemia in individuals with T1D remains to be determined. It was predicted that an “inverted-U” relationship exists between exercise intensity and the amount of glucose required to prevent hypoglycemia during exercise at basal insulinemia. Our objective was to investigate this relationship and elucidate the underlying glucoregulatory mechanisms. **DESIGN, PARTICIPANTS, AND INTERVENTION:** We subjected nine individuals (mean +/- SD age, 21.5 +/- 4.0 years; duration of disease, 11.4 +/- 6.4 years; glycated hemoglobin, 7.9 +/- 0.8% [60 mmol/mol]; body mass index, 25.4 +/- 5.5 kg/m(2); VO2peak, 34.8 +/- 5.1 mL.kg(-1).min(-1); and lactate threshold, 59.9 +/- 5.9% VO2peak) with T1D to a euglycemic clamp, whereby euglycemia was maintained by infusing basal insulin doses with concomitant infusion of [6,6-(2)H2]glucose for determining glucose kinetics. Glucose was infused to maintain euglycemia during and for 2 hours after exercise of different intensities (35, 50, 65, and 80% VO2peak). **MAIN OUTCOME MEASURES:** The glucose infusion rate (GIR), levels of glucoregulatory hormones, and rates of endogenous glucose appearance and disappearance were compared between conditions. **RESULTS:** The mean GIR to maintain euglycemia during exercise increased with intensity up to 50% (4.0 +/- 1.6 g/h; P < .05) and 65% (4.1 +/- 1.7 g/h), but no glucose was required at 80% VO2peak. Glucose rate of appearance and disappearance increased with intensity and, together with plasma catecholamines, reached higher levels at 80% VO2peak. **CONCLUSION:** Our findings support the predicted inverted-U relationship between exercise intensity and glucose requirement. However, the relationship between iv and oral glucose requirements needs to be investigated to translate these GIR data to clinical practice.

**Sommerfield D, Ramgolam A, Barker A, Bergesio R and von Ungern-Sternberg BS.**


Background Surgical correction of vesicoureteric reflux through ureteric reimplantation is a common, highly successful treatment. Postoperative pain can be severe and may relate to somatic wound pain from the lower abdominal incision or from visceral bladder spasm pain. Aim To conduct a prospective quality improvement audit to compare four perioperative analgesic techniques. Methods Observational data were collected on 217 patients following open ureteroneocystostomy over 5 days. The patients were split into four groups: (i) ‘morphine’ infusion; (ii) ‘caudal’—single-shot caudal; (iii) ‘epidural’—epidural catheter inserted at T10-L2 given a bolus, followed by an infusion of 0.125% bupivacaine with fentanyl 2 μg.ml(-1); (iv) ‘caudal catheter’—caudal placed epidural catheter was treated similar to the epidural catheter. Data regarding postoperative analgesic interventions were recorded. Intravesical pethidine was used for bladder spasm pain and i.v. morphine for wound pain. Results Over the study period, the caudal catheter technique (mean interventions/patient = 1.8 ± 2.6) and the single-shot caudal (6.1 ± 4) needed significantly less bladder spasm interventions than morphine (9.2 ± 4) and epidural (8.0 ± 4.4) patients. For wound pain, the caudal catheter (8.8 ± 3.3) and epidural groups (11.4 ± 3.2) needed significantly less interventions than morphine (16.1 ± 3) and caudal (15.3 ± 3.3) patients. Overall, caudal catheter patients on average required about half the number of pain interventions and were associated with less high nursing workload. Conclusions Despite some limitations in data collection and study design, the caudal catheter technique was superior at reducing pain interventions, particularly bladder spasm interventions. Overall epidural analgesia was not superior to a single-shot caudal followed by opioid infusion. The issue of bladder spasm may be similar to the phenomenon of sacral sparing in obstetric epidural anesthesia. Thus, regional techniques, such as caudal epidural, targeting a better balance between sacral and lumbar nerves are required.

**Strathie Page S and Foster R.**


Acrodermatitis dysmetabólica is an umbrella term encompassing the other metabolic causes of an erosive periorificial and acral dermatitis that mimics acrodermatitis enteropathica. Causes include acquired zinc, amino acid, biotin, and fatty acid deficiencies. We present the case of an exclusively breastfed, 2-month-old boy with known cystic fibrosis admitted with failure to thrive and erosive dermatitis. A diagnosis of acrodermatitis dysmetabólica was made when investigations revealed a normal zinc level but low amino acid levels.

**Tan JK, Murray C and Schultz A.**

Updated 14/4/16
ABCA3 lung disease in an ex 27 week preterm infant responsive to systemic glucocorticosteroids.

We present a case of an infant born at almost 28 weeks gestation, found to be homozygous for a missense mutation of ABCA3, with diffuse lung disease that has continued throughout infancy. The patient's clinical course and chest imaging was highly suggestive of diffuse lung disease of infancy, and not of chronic lung disease of prematurity. The lung disease proved to be highly responsive to systemic corticosteroids. This is a case of ABCA3 lung disease that demonstrated improvement after systemic glucocorticosteroid administration. 
Pediart Pulmonol. 2016;51:E1-E3. (c) 2015 Wiley Periodicals, Inc.

Thacker K, Jevon G and Whan E.
Unusual presentation of duodenal Web in an infant.
Journal of Gastroenterology and Hepatology. 2016: n/a-n/a.

Thomas R, Rao S and Minutillo C.
Cuffed endotracheal tubes for neonates and young infants: a comprehensive review.

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.

INTRODUCTION: Children diagnosed with Developmental Coordination Disorder (DCD) present with a variety of impairments in fine and gross motor function, which impact on their activity and participation in a variety of settings. This research aimed to determine if a 10-week group-based Cognitive Orientation to Daily Occupational Performance (CO-OP) intervention improved outcome measures across the impairment, activity and participation levels of the International Classification of Functioning, Disability and Health (ICF) framework.

METHODS: In this quasi-experimental, pre-post-test, 20 male children aged 8-10 years (Formula: see text)9y1m +/- 9 m) with a confirmed diagnosis of DCD participated in either the 10 week group intervention based on the CO-OP framework (n = 10) or in a control period of regular activity for 10 weeks (n = 10). Outcome measures relating to impairment (MABC-2, motor overflow assessment), activity (Handwriting Speed Test) and participation [Canadian Occupational Performance Measure, (COPM) and Goal Attainment Scale) were measured at weeks 0 and 10 in the intervention group. RESULTS: Children who participated in the CO-OP intervention displayed improvements in outcome measures for impairment, activity and participation, particularly a reduction in severity of motor overflow. Parent and child performance and satisfaction ratings on the COPM improved from baseline to week 10 and all goals were achieved at or above the expected outcome.

No significant changes were reported for the control group in impairment and activity (participation was not measured for this group). CONCLUSION: The strategies implemented by children in the CO-OP treatment group, targeted towards individualised goal attainment, show that CO-OP, when run in a group environment, can lead to improvements across all levels of the ICF. Implications for Rehabilitation Development Coordination Disorder is a condition which has significant physical, academic and social impacts on a child and can lead to activity limitations and participation restrictions. Cognitive Orientation to Daily Occupational Performance is an approach which uses cognitive-based strategies to improve performance of specific tasks based on child chosen goals. The intervention program had a positive effect on self-perceived levels of performance which may lead to changes in quality of life. Parents felt the intervention enhanced socialisation, peer modelling and encouragement and felt that this increased confidence and independence.


An acquired brain injury in children disrupts brain development and neural pathways, which may have serious implications on occupational role performance. Assessment and management of children with neurological disorders is complex and treatment requires the engagement of a multidisciplinary team. Increasing evidence indicates that both occupational therapists and music therapists work effectively towards similar goals with children with acquired brain injury. This evaluation investigated the effectiveness of a joint music therapy and occupational therapy group in promoting the development of self-regulation skills in children with an acquired
brain injury or neurological condition, as part of a pilot project at a regional paediatric hospital in Australia. Six participants, aged five and half to ten years, were recruited through the acquired brain injury and neurology outpatient service at a regional paediatric hospital. Children underwent occupational therapy assessment and were identified to have sensory processing difficulties that negatively impacted on the child’s occupational roles of “friend” and “student.” The intervention group, In the Groove, received seven, weekly, one-hour sessions, held for one hour on a weekly basis. Each session involved a variety of joint music therapy and occupational therapy activities, specifically planned to achieve intervention goals. A range of standardised occupational therapy and music therapy outcome measures were used, as well as non-standardised measures. All children received positive outcomes following intervention for at least one outcome measure. The findings indicate that joint music therapy and occupational therapy intervention may provide children with acquired brain injury and neurological impairment opportunities to develop self-regulation skills.

Ugonna K, Douros K, Bingle CD and Everard ML.


BACKGROUND: Primary respiratory syncytial virus (RSV) infections are characterized by high levels of IL-8 and an intense neutrophilia. Little is known about the cytokine responses in secondary infections. Preschool children experiencing RSV secondary infections were recruited from the siblings of infants admitted to hospital with RSV acute bronchiolitis. METHODS: Fifty-one infants with acute bronchiolitis (39 RSV positive, 12 RSV negative) and 20 age-matched control infants were recruited. In addition, seven older siblings of infants from the RSV-positive cohort and confirmed RSV infection were recruited. Samples of nasal secretions were obtained using a flocked swab, and secretions extracted using centrifugation. Cytokine bead array was used to obtain levels of interleukin (IL)-17A, IL-8, IL-6, IL-21, and tumor necrosis factor-alpha. RESULTS: Levels of IL-8 and IL-6 were significantly lower in the RSV-positive siblings compared with the RSV-positive infants. There were no significant differences between levels of the other cytokines in the primary and secondary infections. CONCLUSION: The very high levels of IL-8 and IL-6 response characteristic of the primary RSV infection was not observed in secondary RSV-positive infections and this did not appear to be due to a global reduction in cytokine production. Pediatric Research (2016); doi:10.1038/pr.2016.29.

Valentine J, Stannage K, Fabian V, Ellis K, Reid S, Pitcher C and Elliott C.


INTRODUCTION: Botulinum toxin A (BoNTA) is routine treatment for hypertonicity in children with cerebral palsy (CP). METHODS: This 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 and 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). CONCLUSIONS: 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. Muscle Nerve 53: 407-414, 2016.

Viswanathan V and Murray KJ.


Juvenile idiopathic arthritis (JIA) comprises a group of heterogeneous disorders of chronic arthritis in childhood and remains the commonest pediatric rheumatic disease associated with significant long-term morbidity. Advances in understanding of the pathogenesis, better definition of disease control/remission measures, and the arrival of biological agents have improved the outcomes remarkably. Methotrexate (Mtx) remains the first-line disease modifying (DMARD) therapy for most children with JIA due to its proven efficacy and safety. Sulphasalazine (SSz) (especially for enthesitis) and leflunomide may also have a secondary role. Tumor necrosis factor inhibitors (TNF-I), alone or in combination with Mtx have shown tremendous benefit in children with polyarticular JIA, enthesitis related arthritis (ERA) and psoriatic arthritis. Tocilizumab appears very efficacious in systemic arthritis and abatacept and tocilizumab also appear to benefit polyarticular JIA; the role of rituximab remains unclear, though clearly beneficial in adult RA. TNF-I with Mtx is also effective in uveitis associated with JIA. Biologicals have demonstrated an impressive safety record in children with JIA, although close monitoring for rare but potentially dangerous adverse events, such as tuberculosis and other infections; paradoxical development of additional autoimmune diseases; and possibly an increased risk of cancers is warranted.

Updated 14/4/16
von Ungern-Sternberg BS and Regli A.  
Big problem, small incidence, and large registry datasets.  

Ward R, Reynolds JE, Bear N, Elliott C and Valentine J.  
What is the evidence for managing tone in young children with, or at risk of developing, cerebral palsy: a systematic review.  

BACKGROUND AND OBJECTIVES: To conduct a systematic review of the evidence for the management of tone in infants 0-24 months of age, with or at risk of developing cerebral palsy.  
METHOD: This review was conducted and reported following the Preferred Reporting Items for Systematic Reviews and Meta-analyses Statement. The Cochrane Central Register of Controlled Trials, Embase, MEDLINE, CINAHL Plus and PsycINFO databases were systematically searched for relevant articles. Inclusion criteria were: children aged 0-24 months, identified as at risk of, or having cerebral palsy; >25% of participants <24 months, and included a standardized assessment of tone. Only peer reviewed journal articles were considered. Eligible studies were coded using the Oxford Levels of Evidence. Methodological quality was assessed using the PEDro scale for randomized controlled trials and the checklist for assessing the quality of quantitative studies of Kmet, Cook and Lee for non-randomized control trials.  
RESULTS: A total of 4838 studies were identified. After removing duplicates and unrelated studies, a total of 56 full text studies were reviewed. A total of five studies met inclusion criteria, two of which were RCTs, two pre-/post-test designs and one retrospective case audit. Interventions included BoNT-A, Oral Baclofen, Neurofacilitation of Developmental Reaction and Neurodevelopmental Therapy. The quality of evidence ranged from limited to moderate.  
CONCLUSION: The management of tone in infants and young children is not well described, with a dearth of high-level evidence to support intervention in the 0-24 month age-range. This is in contrast to a recent review completed by Novak et al. (2013) who report high levels of evidence of interventions for children with cerebral palsy, over 2 years of age. Implications for Rehabilitation  
High level of evidence to support clinical decision making for the management of tone in young children 0-24 months is not available. The lack of available evidence in the management of tone of young children underpins service delivery and intervention and impacts on patient outcomes. In the absence of clear research evidence, the systematic application of sensitive outcome measures is required to confirm treatment effects and generate new evidence. Hypertonia should not be managed in isolation. Consideration needs to be given to all components of the ICF-CY.

High expression of connective tissue growth factor accelerates dissemination of leukaemia.  
Oncogene. 2016.

To improve treatment of acute lymphoblastic leukaemia (ALL), a better understanding of disease development is needed to tailor new therapies. Connective tissue growth factor (CTGF/CCN2) is highly expressed in leukaemia cells from the majority of paediatric patients with B-lineage ALL (pre-B ALL). CTGF is a matricellular protein and plays a role in aggressive cancers. Here we have genetically engineered leukaemia cells to modulate CTGF expression levels. Elevated CTGF levels accelerated disease dissemination and reduced survival in NOD/SCID mice. In vitro studies showed that CTGF protein induces stromal cell proliferation, promotes adhesion of leukaemia cells to stromal cells and leads to overexpression of genes associated with cell cycle and synthesis of extracellular matrix (ECM). Corresponding data from our leukaemia xenograft models demonstrated that CTGF leads to increased proliferation of non-leukaemia cells and deposition of ECM in the bone marrow. We document for the first time a functional role of CTGF in altering disease progression in a lymphoid malignancy. The findings provide support for targeting the bone marrow microenvironment in aggressive forms of leukaemia.

West CE, Jenalm MC, Kozyrskýj AL and Prescott SL.  
Probiotics for treatment and primary prevention of allergic diseases and asthma: looking back and moving forward.  

Microbial ecosystems cover the surface of the human body and it is becoming increasingly clear that our modern environment has profound effects on microbial composition and diversity. A dysbiotic gut microbiota has been associated with allergic diseases and asthma in cross-sectional and observational studies. In an attempt to restore this dysbiosis, probiotics have been evaluated in randomized controlled trials. Here, we review treatment and primary prevention studies, recent meta-analyses, and discuss the current understanding of the role of probiotics in this context. Many meta-analyses have shown a moderate benefit of probiotics for eczema prevention, whereas there is less evidence of a benefit for other allergic manifestations. Because of very low quality evidence and heterogeneity between studies, specific advice on the most effective regimens cannot yet
be given - not even for eczema prevention. To be able to adopt results into specific recommendations, international expert organizations stress the need for well-designed studies.

White ME, Hunt J, Connell C and Langdon K.
Paediatric neurological melioidosis: a rehabilitation case report.

CONTEXT: Melioidosis is a rare condition, endemic to northern Australia and south-east Asia, caused by an infection from the bacteria <i>Burkholderia pseudomallei</i>. The largest epidemiological review to date describes 540 cases of melioidosis seen at Darwin Hospital, in northern Australia, over a 20-year period. Of these, 14 (less than 3%) presented with neurological manifestation, with three deaths. Reports of paediatric cases of melioidosis are rarer. In a review of paediatric cases in northern Australia only eight cases were identified in 10 years. Three of these patients presented with neurological melioidosis, of whom two died in hospital.

ISSUES: Whilst the literature refers to prolonged periods of hospitalisation for survivors, the trajectory of functional recovery and process of rehabilitation has not been described. This is a case report describing a 14-year-old boy who presented to a remote medical post with acute neurological symptoms (vomiting, severe headache, ataxia, cranial nerve VI and VII palsy) and was referred to the tertiary paediatric hospital in Perth, Western Australia. Cranial magnetic resonance imaging showed an extensive infiltrative lesion in the posterior fossa and hydrocephalus. Diagnosis of neurological melioidosis required isolation of the pathogen by brain biopsy through sub-occipital craniotomy. Medical treatment included surgical management of hydrocephalus, parenteral antibiotic treatment with meropenem and then a prolonged course of oral co-trimoxazole, enteral feeding and tonal management with levodopa-carbidopa and botulinum toxin A injections. Associated neurological signs and symptoms (bradykinesia, tremor, dysphagia, aphasia, hypertonia, exotropia) required intensive rehabilitation to address functional deficits and to promote independence. The purpose of this case report is to document the functional recovery and rehabilitation process of a paediatric case of neurological melioidosis. Knowledge of the recovery pathway is important to add to the understanding of natural history and treatment of this rare disease. LESSONS LEARNED: Occasions of service and functional assessments were recorded prospectively. Inpatient therapy (932 hours, with 934 occasions of service) was delivered across physiotherapy, occupational therapy and speech pathology over 9 months of an inpatient admission. Initial paediatric functional independence measure (WeeFIM) was 18/126, indicating complete dependence in all physical and cognitive domains. Following 9 months of intensive rehabilitation the WeeFIM was 53/126, indicating significant residual disability. This proved to be a challenge for discharge planning back to a remote region of Western Australia. Paediatric neurological melioidosis can lead to significant disability and long-term dependence, despite the provision of lengthy intensive rehabilitation. This case report highlights the challenges and complexity of the rehabilitation services required to optimise outcomes for this patient and achieve a safe discharge to a remote community where limited support services are available.

Use of ACE inhibitors in Fontan: Rational or irrational?

BACKGROUND: Despite a lack of evidence supporting the use of angiotensin-converting enzyme (ACE) inhibitors in patients with a Fontan circulation, their use is frequent. We decided to identify the rationale for ACE inhibitor therapy in patients within the Australia and New Zealand Fontan Registry. METHODS: All patients in the Registry taking an ACE inhibitor at last follow up were identified, and a review of medical records was undertaken to determine the rationale for treatment initiation and reasons for treatment continuation or dose increase. RESULTS: In 2015, 36% of the surviving patients in the Registry (462/1268) were taking an ACE inhibitor. Indications for initiation of therapy were ventricular systolic or diastolic dysfunction (29%), atrioventricular valve regurgitation (19%), preservation of normal ventricular function (7%), prolonged effusions at Fontan (6%), hypertension (6%), other (6%) and unknown (2%). No indication was stated in the remaining patients (25%). Those with hypoplastic left heart syndrome were more likely to be on an ACE inhibitor than those with an alternative primary morphology (70% vs 32%; p<0.001). Only 36% of the patients treated with an ACE inhibitor at last follow up (166/462) had an indication that would generally justify treatment in a two-ventricle circulation. CONCLUSION: It is likely that the use of ACE inhibitors in patients with a Fontan circulation is excessive within our region. The coordination of prospective, multicentre studies and initiatives such as the Australia and New Zealand Fontan Registry will facilitate further investigations to guide treatment decisions in the growing Fontan population.

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.

Updated 14/4/16
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 100.1 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 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.

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.