Department of Paediatrics & Child Health

UNIVERSITY OF CAPE TOWN

ANNUAL RESEARCH DAYS 2014

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Programme and Abstract Book

28th & 29th October
7th Floor Lecture Theatre, ICH Building
Red Cross War Memorial Children's Hospital

CPD Points

Tuesday, 28 October 2014	***4 points***
Wednesday, 29 October 2014	***7 points***

Please sign the attendance register on both days to claim your points.

PROGRAMME AND CONTENTS PAGE

15H30 – 15H45	Incidence of pertussis in children hospitalised with lower respiratory tract infection at Red Cross War Memorial Children's Hospital.	F. Dube	13
15H45 – 16H00	Detection of common bacterial and viral causes of meningitis using molecular diagnostics at Red Cross War Memorial Children's Hospital.	P. Mteshana	14
16H00 – 16H15	Home environmental exposures to indoor air pollution and tobacco smoke in an African birth cohort.	A. Vanker	15
16H15 – 16H30	Incidence and severity of childhood pneumonia in the first year of life in a South African birth cohort: The Drakenstein Child Health Study.	D. le Roux	16

Wednesday, 29 October 2014

Session 3: Chairperson: **P Hartley**

08H30 – 08H45	The prevalence of IgE-mediated food sensitisation and food allergy in unselected 12-36 month old urban South African children.	M. Botha	17
08H45 – 09H00	Aeroallergen sensitisation and prevalence of asthma, allergic rhinitis and eczema in children with vernal keratoconjunctivitis attending Red Cross War Memorial Children's Hospital.	S. Naidoo	18
09H00 – 09H15	Description and outcomes of oral food challenges in a tertiary paediatric allergy clinic in South Africa.	T. van der Watt	19
09H15 – 09H30	An assessment of the association between domestic hygiene, diarrhoea and nutritional status in children under two years in Khayelitsha.	M. Sambo	20
09H30 – 09H45	Prevalence and management of microcytic anaemia in children seen at Red Cross War Memorial Children's Hospital.	M. Wege	21
09H45 – 10H00	Clinical outcome of children with Hodgkin lymphoma after chemotherapy alone – The Red Cross Children's Hospital experience.	G. Chagaluka	22
10H00– 10H15	Low grade gliomas treated at the University of Cape Town's combined paediatric neuro-oncology service.	A. Davidson	23
10H15– 10H30	Rhabdomyosarcoma at Red Cross War Memorial Children's Hospital 1990-2010.	M. Hendricks	24
10H30 – 11H00	**T E A & POSTERS**		

			Page No.
Session 4: Chairperson:		**P Nourse**	
11H00 – 11H15	M72/AS01$_E$ candidate vaccine has an acceptable safety profile and is immunogenic in adolescents in a TB endemic setting.	A. Penn-Nicholson	25
11H15 – 11H30	Comparative evaluation of diagnostic performance of XPERT® MTB/RIF assay between induced sputum and gastric washing specimens in children below 5 years of age from the MVA85A TB vaccine trial in Cape Town, South Africa.	E. Bunyasi	26
11H30 – 11H45	Direct ex vivo characterisation of the CD4 T cell response induced by the novel subunit TB vaccine, H1.	M. Musvosvi	27
11H45 – 12H00	An audit of transfers into the PICU at the Red Cross War Memorial Children's Hospital (RCWMCH): Ten years later.	K. Dimitriades	28
12H00 – 12H15	Ligamentous integrity in spinal cord injury without radiographic abnormality (SCIWORA).	S. Dix-Peek (obo A. Horn)	29
12H15 – 12H30	Salvageability of renal function following renal revascularization in children with Takayasu arteritis-induced renal artery stenosis.	P. Nourse (obo P. Obiagwu)	30
12H30 – 12H45	Recurrence rate post renal transplant of childhood nephrotic syndrome, at Red Cross Children's Hospital.	J. Buckley	31
12H45 – 13H00	Screening for hypothalamic-pituitary-adrenal axis suppression in asthmatic children on corticosteroids is not possible when employing clinical and static biochemical parameters.	E. Zollner	32
13H00 – 14H00	**L U N C H (Venue: Tea Room, Johnson & Johnson Building, RXH)**		
Session 5: Chairperson:		**G Riordan**	
14H00 – 14H15	The use of gabapentin for the management of pain in Gullain-Barre syndrome in the paediatric setting.	H. Hutton	33
14H15 – 14H30	Benzodiazepines and excitatory GABAergic signalling during epileptic seizures	R. Burman	34
14H30 – 14H45	Prenatal alcohol use, intimate partner violence and other psychosocial stressors and symptoms as predictors of poor developmental outcomes in infancy in a South African birth cohort.	N. Koen	35

14H45 – 15H00	Exposure to methamphetamine prenatally modifies white matter integrity and neurocognitive function in children.	A. Roos	36
15H00 – 15H15	Children with autism and epilepsy: A descriptive clinical cohort study from Red Cross War Memorial Hospital.	N. Ramsundhar	37
15H15 – 15H45	**T E A & POSTERS**		
Session 6: Chairperson:		**J Lawrenson**	
15H45 – 16H00	Echocardiographic screening for rheumatic heart disease in 4720 asymptomatic schoolchildren from South Africa and Ethiopia: implications for school health services.	M. Engel	38
16H00 – 16H15	Baseline characteristics, complications, and gaps in evidence-based interventions in 3343 children and adults with rheumatic heart disease from 14 countries: the Global Rheumatic Heart Disease Registry (The REMEDY study).	L. Zuhlke	39
16H15 – 16H30	Anomalous left coronary artery to pulmonary artery (ALCAPA) in Red Cross War Memorial Children's Hospital (RCWMCH).	B. Rossouw	40
16H30 – 16H45	Counting encounters: A quantitative estimation of the clinical workload of the Western Cape Paediatric Cardiology Service (WCPCS).	R. De Decker	42
16H45 – 17H00	***Feedback on Research Day presentations, with Award & Poster Draw and Research Prizes by Profs. D. & S. Hall*** ***Closing remarks by C Hugo-Hamman***		

Poster Presentations **Page No.**

Title: **A RANDOMISED CONTROLLED TRIAL OF HIGH OR LOW VOLUME INITIATION AND RAPID OR SLOW ADVANCEMENT OF MILK FEEDS FOR INFANTS ≤ 1000 G**

Authors: M Shukri Raban[1], Shalini Santhakumaran[2], Quanitah Keraan[1], Yaseen Joolay[1], Sabita N Uthaya[2], Alan R Horn[1], Neena Modi[2], Michael C Harrison[1]

Affiliation: [1.]Division of Neonatal Medicine, Department of Paediatrics, University of Cape Town, South Africa; [2.]Department of Medicine, Section of Neonatal Medicine, Imperial College London, London, UK

Background:
The optimal feeding regimen for infants ≤1000g at birth is not established. Wide variation in enteral feeding practice exists, emphasising the need for evidence of efficacy and safety. Within our institute, Lango et al. demonstrated that early introduction of enteral breast milk feeding with minimal use of parenteral nutrition (PN) in extremely low birth weight (ELBW) infants, resulted in a mean growth velocity comparable with that achieved by infants who received substantial early PN with later establishment of enteral feeds. A more rapid advancement of enteral feeds may reduce the risk of early nutritional deficits and improve growth velocity in ELBW infants.

Objective:
To establish safety and efficacy of commencing feeds at 24ml/kg/day on the day of birth and advancing feeds at 36ml/kg/day, in infants ≤1000g.

Methods:
In this 2x2 factorial randomized controlled trial we assessed enteral volume initiation and advancement rates as separate components. Infants ≤1000g were randomized to one of four groups receiving exclusive feeds of human milk: low volume initiation (4ml/kg/day)/slow advancement (24ml/kg/day); low volume initiation (4ml/kg/day)/rapid advancement (36ml/kg/day); high volume initiation (24ml/kg/day)/slow advancement (24ml/kg/day); or high volume initiation (24ml/kg/day)/rapid advancement (36ml/kg/day). The primary outcome was time to attain a weight of 1500g. Cox regression was used for time-to-event outcomes and logistic regression for binary outcomes; treatment effects are presented as hazard ratios and odds ratios respectively.

Results:
Two hundred infants were recruited (51 low/slow, 47 low/rapid, 52 high/slow, 50 high/rapid). Infants on rapid advancement regimens were the quickest to reach a weight of 1500g, (HR 2.3, p= 0.003, 95%CI 1.3-4.0). Rapid advancement was associated with fewer days to regain birth weight, (HR 2.3, p= 0.001, 95%CI 1.4-3.6) and fewer days in hospital (HR 1.9, p= 0.006, 95%CI 1.2-3.1).There were no significant differences between the groups in the rates of NEC, feed intolerance, or late-onset sepsis.

Conclusion:
Preterm and low birth weight rates are rising worldwide and the optimum care of these infants in resource-limited settings is a matter of growing importance. The stratagem we have evaluated is an important potential advance in the care of these vulnerable infants. Our finding that higher initiation feed volumes and larger daily feed increments in infants ≤1000g, were well tolerated, increased early weight gain and reduced hospital stay. These data provide justification for larger studies powered to address the impact on NEC and other adverse outcomes.

HREC 283/2011

Title: **NEONATAL SEPSIS AND ANTIBIOTIC SENSITIVITY PATTERNS AT GROOTE SCHUUR HOSPITAL NURSERY – EVOLUTION OVER A 9 YEAR PERIOD**

Authors: N Naidoo, Q Keraan, MS Raban, MC Harrison

Affiliation: Division of Neonatal Medicine, Department of Paediatrics, University of Cape Town

Background:
Neonatal infection is an important cause of morbidity, prolonged hospital stay and mortality in babies. Early and accurate diagnosis of neonatal sepsis remains challenging, resulting in the ubiquitous and speculative use of empiric antibiotic therapy. However, pathogens causing neonatal infections and their antibiotic susceptibility patterns may change over time and it is therefore prudent to monitor the epidemiology of neonatal infections.

Objectives:
To determine and compare the incidence of culture positive neonatal sepsis, pathogens and antibiotic resistance profiles between two time intervals over a 9 year period in the neonatal nursery at Groote Schuur Hospital.

Methods:
We compared two time periods; 2004 to 2013. Retrospective blood culture data were extracted from the local microbiology laboratory database and the Groote Schuur Hospital neonatal infection database. Culture positive neonatal infection was defined as the presence of a positive blood culture including fungal organisms. Early onset sepsis (EOS) was defined as infection in the first 48 hours of life and late onset sepsis (LOS) as infection occurring thereafter. This age cut-off is universally applied as it best reflects the transition between infections caused by pathogens acquired by vertical transmission and those acquired by horizontal transmission.

Results:
During 2004 a total of 817 blood cultures were taken, 143 (17.5%) were culture positive. Twenty six organisms were identified. The most common organisms causing EOS were: 3(2%) Klebsiella pneumoniae, 2(1.4%) Group B streptococcus (GBS) and 2 (1.4%) Enterococcus coli (E. coli). The most common organisms causing LOS were: 19 (13.3%) Klebsiella pneumoniae, 14 (9.7%) Staphylococcal aureus and 5(3.5%) E. coli.
The contamination rate with coagulase negative staphylococcal aureus (CONS) was 20 (14%) in the EOS group and 38 (26.5%) in the LOS group.

In 2013 a total of 1070 blood cultures were taken, 106 (9.9%) were culture positive. Twenty three organisms were identified. The most common organisms causing EOS were: 5 (4.7%) Klebsiella pneumoniae, 3(2.8%) GBS 3 (2.8%), and 2 (1.9%) E. coli.
The most common organisms causing LOS were: 32(30.2%), Klebsiella pneumoniae, 8(7.5%) E. coli and 5 (4.7%) S. aureus. The contamination rate with CONS was 5(4.7%) in the EOS group and 14 (13.2%) in the LOS group.

Antibiotic sensitivities changed over the 9 year time period. The 2013 cohort of Gram negative organisms (Klebsiella pneumoniae and E. coli) showed an overall resistance to penicillin and ampicillin with developing resistance to amikacin and gentamycin.

Conclusion:
This study provides insight into the evolving pathogens and guides the appropriate antibiotics for empiric therapy in our nursery. The emergence of resistant Gram negative organisms is of concern and illustrates the need for strong antibiotic stewardship policies, strict adherence to infection control measures with continued monitoring and surveillance.

HREC: R045/2013

Title: **THE INFLUENCE OF BIRTH SITE ON SHORT-TERM OUTCOMES OF ENCEPHALOPATHIC NEWBORN INFANTS TREATED WITH THERAPEUTIC HYPOTHERMIA AT GROOTE SCHUUR HOSPITAL, CAPE TOWN, SOUTH AFRICA**

Authors: Victoria K Nakibuuka,[1,2] Natasha Rhoda[1], Alan R Horn[1]

Affiliation: [1.]Division of Neonatal Medicine, Department of Paediatrics, Groote Schuur Hospital , University of Cape Town, South Africa; [2.]Department of Paediatrics, Nsambya Hospital, Uganda

Objectives:
International consensus guidelines recommend that term or near-term newborns with moderate or severe hypoxic ischaemic encephalopathy (HIE) should be treated with hypothermia within six hours of birth, but many of the affected babies are born outside the treatment centers. There are few data describing the influence of birth site on outcome after HIE in South Africa.
Our objectives were: i) To describe the demographic differences between inborn and out-born babies with HIE who are treated with hypothermia in a tertiary neonatal intensive care unit in South Africa; and ii) to compare the frequency of abnormal short-term outcome by discharge; including mortality, abnormal amplitude-integrated electroencephalogram (aEEG) at 48 hours, or failure to establish normal breast- or cup-feeding.

Methods:
This was a retrospective, comparative and descriptive analysis of data extracted from a prospectively collated registry of babies with moderate or severe HIE, who were admitted to the neonatal intensive care unit and treated with hypothermia at Groote Schuur Hospital between 1 January 2011 and 31 December 2012.

Results:
A total of 57 babies were treated with hypothermia of which 23 (40%) were inborn and 34 (60%) out-born. Cooling was initiated significantly earlier among the inborn babies (age 2.3 hours vs 4.3 hours, P=0.002). A non-reassuring cardiotocograph (CTG) and the occurrence of pregnancy complications were significantly more common in inborn babies (P=0.001 and P=0.03 respectively). More outborn babies died or had an abnormal aEEG at 48 hours (22% vs 32%) and fewer outborn babies achieved normal feeding at discharge (22% vs 38%), but these differences were not significant.

Conclusion:
This retrospective review quantifies the significant burden of HIE in outborn babies at this centre; it also quantifies the significant delays in initiating cooling in this group. Although short-term outcomes were not significantly increased in outborn babies, the apparent paucity of pregnancy and CTG abnormalities in referred infants may suggest opportunities for improved pregnancy and intrapartum monitoring; these findings should be used to inform a larger cohort study to adequately inform policy.

HREC approval number: 612/2013

Title: **THERAPEUTIC HYPOTHERMIA FOR HYPOXIC ISCHAEMIC ENCEPHALOPATHY USING LOW-TECHNOLOGY METHODS: A SYSTEMATIC REVIEW AND META-ANALYSIS**

Authors: Rossouw G[1], Irlam J[2], Horn AR[1]

Affiliation: [1.]Division of Neonatal Medicine, Department of Paediatrics, Faculty of Health Sciences, University of Cape Town, South Africa
[2.]Primary Health Care Directorate, Faculty of Health Sciences, University of Cape Town, South Africa

Objective:
The evidence showing the benefit of therapeutic hypothermia for term/near term newborn infants has largely been derived from studies using high-technology cooling methods. We aimed to perform a systematic review and meta-analysis to determine the effect of therapeutic hypothermia on mortality and morbidity, in term/near-term infants with hypoxic-ischaemic encephalopathy, using low-technology methods in an intensive care setting with facilities for mechanical ventilation.

Methods:
We searched three databases in November 2013: MEDLINE, the Cochrane Central Register of Controlled Trials, and Scopus; for randomised controlled trials comparing low-technology therapeutic hypothermia to standard care in an intensive care setting, in term/near term newborn infants with hypoxic ischaemic encephalopathy. Hypoxic ischaemic encephalopathy was defined using criteria for both intrapartum hypoxia and encephalopathy; and low-technology methods were defined as the manual application of cooling packs or non-electrical cooling methods. The primary outcome was mortality during primary hospital admission; secondary outcomes included mortality at 6 – 24 months and morbidity at discharge and at 6 – 24 months.

Two authors independently selected studies, and assessed the quality of the data. Disagreements were resolved by discussion with a third author. Standard Cochrane methodology and RevMan 5.1 software was used for data extraction and meta-analysis. The quality of the evidence was graded with the GRADE approach.

Results:
Three trials (460 infants) met selection criteria for the meta-analysis. Low-technology therapeutic hypothermia resulted in a significant reduction in mortality at discharge (risk ratio (RR) 0.60 [95% confidence interval (CI)0.39, 0.92], risk difference (RD) -0.08 [95% CI -0.14, -0.02], number needed to treat for an additional beneficial outcome (NNTB) 13 [95% CI 6.9, 81.7]); and neurological morbidity at discharge (RR 0.46 [95% CI 0.33, 0.63], RD -0.24 [95% CI -0.33, -0.15], NNTB 4 [95% CI 2.9, 6.3]).

Conclusions:
There is evidence from three randomised controlled trials that in settings where there are resources to ventilate and intensively monitor infants, low-technology therapeutic hypothermia is beneficial in term/near term infants with hypoxic ischaemic encephalopathy. Further research should be directed towards determining the safety, feasibility and efficacy of low-technology hypothermia in settings where intensive care is not available.

Title: **NEONATAL HIV CASE SERIES: CHALLENGES IN DIAGNOSIS AND MANAGEMENT**

Authors: [1.] Dr Shakti Pillay; [2.] Dr Max Kroon; [3.] Dr Marvin Hsiao; [4.] Dr James Nuttall

Affiliation: [1.] Paediatric registrar, Red Cross Children's Hospital; [2.] Paediatrician, Mowbray Maternity Hospital; [3.] Virologist, Groote Schuur Hospital; [4.] Paediatric infectious disease consultant, Red Cross Children's Hospital

Introduction:
Early HIV diagnosis and treatment reduces infant mortality, slows disease progression and improves neurodevelopmental outcome. HIV disease is often already advanced when treatment is commenced at eight weeks of age. There is limited data on very early neonatal HIV diagnosis, treatment and outcome. Mowbray Maternity Hospital (MMH) identifies HIV-exposed neonates at increased risk of infection if PMTCT is suboptimal. These neonates receive dual prophylaxis (AZT, NVP) and have very early PCR testing. This study aims to evaluate the preliminary performance of the MMH High Risk PMTCT Protocol. Western Cape PMTCT guidelines recently included a risk-based approach.

Objectives:
The primary objectives were to determine the number and proportion of confirmed positive and negative HIV PCR tests in relation to the number of HIV exposed neonates both within 48 hours of birth and at 6 weeks of age and to describe the characteristics and management challenges of neonates diagnosed HIV-positive within 48 hours of birth.

Methods:
A six month retrospective descriptive folder review was performed at MMH from the 1st November 2013 to the 30th April 2014. All neonates who underwent HIV PCR testing within 48 hours of birth during the 6 month period were included. Patients were identified from the MMH HIV PCR register.

Results:
There were 117 neonates who had very early HIV PCR testing.
Nine babies (7.7%), including one set of twins, were confirmed positive. Five of the infected neonates' mothers were on ART: three for less than eight weeks; two for more than eight weeks but with unsuppressed viral loads (VL) (one on first-line ART, VL 2290 copies/ml; $\log_{10}$ 3.36; one on second-line ART, VL 49823 copies/ml; $\log_{10}$ 4.7). Three mothers were unbooked pregnancies, newly diagnosed with HIV and not yet on ART.
Median (IQR) birth weight was 1920g (1380-3260g). Mean gestational age was 34.9 weeks ±3.21 weeks, median (IQR) baseline CD4 percentage and $\log_{10}$ VL were 49.1% (39.1-50%) and 5.49 (3.92-5.8). All nine neonates received dual prophylaxis immediately after delivery. One had congenital syphilis and one congenital CMV infection.
Seven initiated ART at median 14 days (range 4-35 days). Three died, two before starting ART (one lethal congenital cardiac, one VLBW on day 13 with fulminant septicaemia), one at 11 weeks with fungal pneumonia and disseminated CMV following delayed ART initiation. Five remain on ART (1 lost to follow-up). One had an equivocal PCR result soon after birth but defaulted further testing and follow up. Results of HIV PCR testing at 6 weeks of age were available for 75 (69%) infants. Two (2.7%) of these infants were HIV PCR positive

Conclusion:
Implementation of a risk-based HIV transmission protocol incorporating HIV PCR testing within 48 hours of birth and provision of dual ARV infant prophylaxis may be a useful strategy to further reduce mother to child transmission rates and improve outcomes for HIV-infected neonates. In this study, intrauterine transmission of HIV infection was associated with significant morbidity and mortality and further research on this vulnerable population is needed.

UCT HREC REF 628/2014

Title: **EARLY DETERMINANTS OF LUNG FUNCTION IN AFRICAN INFANTS**

Authors: Dr. Diane Gray, diane.gray@uct.ac.za, MD[1], Ms. Lauren Willemse, lauren.willemse@uct.ac.za[1], Ms. Ane Alberts, ane.alberts@uct.ac.za[1], Prof. Graham Hall, grahamh@ichr.uwa.edu.au[2] and Prof. Heather Zar, heather.zar@uct.ac.za, MD[1].

Affiliation: [1]Department of Paediatrics and Child Health, University of Cape Town, Cape Town, South Africa and [2]Telethon Kids Institute, University of Western Australia, Perth, Australia.

Background:
There is limited data on lung function in African infants despite a high prevalence of respiratory disease.

Aim:
To assess antenatal and early life factors associated with early lung function in African infants.

Method:
Infants enrolled in the Drakenstein child health study, a South African birth cohort had lung function measured at 6-10 weeks of age. Measurements, made with the infant breathing via a facemask in natural sleep, included tidal breathing, exhaled nitric oxide and multiple breath washout measures. Information on antenatal and postnatal exposures was collected using questionnaires and, for tobacco smoke exposure, urine cotinine.

Results:
Successful tests were obtained in 512/552 (93%) infants with a med (IQR) age of 7.3 (6.6-8.1) weeks, weight 4.8 (4.3 – 5.4) kg, length 55 (53 - 57) cm and gestation 39 (38-10) weeks; 283 (51%) infants were male, 78 (14%) preterm (<37 weeks); 99 (18%) infants mothers were HIV infected and 185 (35%) mothers smoked. Two hundred and sixty (48%) infants were African race and 292 (52%) were mixed race. Prematurity and in utero exposure to HIV infection did not effect outcomes. Sex, smoking and ethnicity results below: Table 1

Male sex	Coefficient	95% CI	P	
FRC[1] ml mean (SD)		-0.6 to -0.3	0.03	
t_{PTEF}/t_E %		-4.3 t -0.01	0.05	
eNO [3]ppb		-1.5 to 0.8	0.5	
Maternal smoking				
FRC ml		-7.3 to 0.8	0.1	
t_{PTEF}/t_E %		-7.4 to -0.9	0.01	
eNO ppb		-0.25 to -0.02	0.02	
African ethnicity				
FRC ml		-2.6 to 4	0.7	
t_{PTEF}/t_E %		0.4 to 5.5	0.02	
eNO ppb		-1.5 to 0.8	0.5	

1: functional residual capacity, 2: ratio of time to peak tidal expiratory flow over total expiratory time, 3: exhaled nitric oxide

Conclusions:
Intrauterine and early life exposures have a significant impact on lung growth and function in early infancy, which may constitute a risk for subsequent respiratory illness.

HREC Ref: 423/2012

Title: **LUNG FUNCTION MEASURES IN UNSEDATED 1 YEAR SOUTH AFRICAN INFANTS**

Authors: Lauren Willemse[1], Diane Gray[1], Ane Visagie[1], GL Hall[2], HJ Zar[1]

Affiliation: [1]Department of Paediatrics and Child Health, University of Cape Town, South Africa [2]Telethon Kids Institute, University of Western Australia, Perth, Australia

Introduction:
Low lung function in early life is a risk factor for acute and chronic respiratory disease in later life. Measuring infant lung function (ILF) in older infants has been limited by the difficulty in obtaining quality measures in unsedated infants.

Aim:
To assess the feasibility of unsedated ILF measures in healthy 1 year South African infants.

Methodology:
Infants enrolled in the Drakenstein Child Health Study (DCHS) were tested at 1 year (11-13 months), during natural quiet sleep. Lung function measures included: tidal breathing (TBFVL), exhaled nitric oxide (eNO) and multiple breath washout (MBW).

Results:
Of the 219 infants tested, acceptable tests were obtained in 151/219 (69%) of TBFVL, 150/219 (69%) eNO and135/219 (62%) MBW test. Reasons for failed test were insufficient quiet sleep (32%), technical errors (1%) and failure to meet acceptable quality criteria (2%). Mean (SD) testing time for was 36 min (17min) min and total visit time, 2h56 (1h13).

Table 1: Lung function outcomes in unsedated 1 year infants

	Median (IQR)	CV Med (IQR)
Tidal Volume mL	93.2 (87 -101.5)	7.9 (6.2-9.7)
Respiratory Rate $n.min^{-1}$	27.6 (25-30.4)	6.4 (5.5-8)
$t_{PTEF}/t_{E\,\%}$	28.3 (22-35.7)	24.7 (20.8-28.8)
eNO ppb	8.5 (2.8-14.4)	9.3 (5-15.7)
NO output $mcL.s^{-1}$	12.4 (10.2-15.2)	4.8 (1.7-8)
Functional residual volume mL	200 (170-220)	4.6 (3.4-6.4)
Lung clearance index	6.7 (6.3-7)	4. (2.5-6)

CV: intra-subject coefficient of variation ,t_{PTEF}/t_E: time to peak tidal expiratory flow over total expiratory time

Conclusion:
ILF testing can be successfully undertaken in unsedated infants at 1 year. Success relies on dedicated skilled staff, adequate time and resources. This study supports the use of unsedated ILF measures in early life to improve our knowledge of early lung growth and risk for later lung disease.

Previous research presentation: South African Thoracic Society Congress, Durban, 2014; Ethics Approval Number: HREC Ref: 423/2012

Title: **INCIDENCE OF PERTUSSIS IN CHILDREN HOSPITALISED WITH LOWER RESPIRATORY TRACT INFECTION AT RED CROSS WAR MEMORIAL CHILDREN'S HOSPITAL**

Authors: Rudzani Muloiwa, Felix S. Dube, Mark P. Nicol, Heather J. Zar, Gregory D. Hussey

Background:
Despite the re-emergence of pertussis in high-income countries, little is known of the incidence of pertussis in children with lower respiratory tract infection (LRTI) on the African continent. We aimed to prospectively investigate the incidence of pertussis in South African children hospitalised with LRTI.

Methods:
Children less than 13 years old admitted to the acute short stay ward (S11), of the Red Cross War Memorial Children's Hospital, Cape Town, with LRTI were prospectively enrolled over one year. A nasopharyngeal swab (NP) and induced sputum (IS) specimen were taken and PCR specific for *Bordetella pertussis and Bordetella parapertussis* was performed

Results:
In total 460 children with a median age of 8 (IQR 4-18) months were enrolled. Infection was confirmed in 41 (8.9%; 95% CI 6.5 -11.9 %) of the children of whom 32 (7.0%) were due to *B. pertussis.* Of the 32 *B. pertussis* confirmed cases 7 were identified on NP only, 15 on IS only and the remaining 10 on both specimens. IS was able to identify 25/32 (78.1%) of all confirmed *B. pertussis* infections compared to 17/32(53.1%) on NP. Children whose diagnosis was confirmed on IS only had a much shorter duration of cough symptoms compared to children with a positive NP specimen [median 2 (IQR 2-3) days versus 5 (IQR 3-7) days; $p<0.001$].

The incidence of *B. pertussis* infection was higher in HIV exposed-uninfected (ARR 2.46 (95% CI 1.03-5.84) and HIV-infected [ARR 3.14 (95% CI 1.04-9.48)] children respectively while receipt of three [ARR 0.38 (95% CI 0.15-0.92)] or four [ARR 0.16 (95% CI 0.03-0.77)] doses of pertussis vaccine was protective.

Only four of the 41 (9.8%) laboratory confirmed cases were clinically diagnosed by the attending clinician as having pertussis.

Conclusion:
Pertussis is common in African children hospitalised with LRTI. IS provides a much higher yield than NP for diagnosis. Clinical diagnosis was rarely made; laboratory confirmation is needed for diagnosis.

Funding:
Sanofi Pasteur, Hamilton Naki Clinical Scholarship

Despite the re-emergence of pertussis in high-income countries

Title: **DETECTION OF COMMON BACTERIAL AND VIRAL CAUSES OF MENINGITIS USING MOLECULAR DIAGNOSTICS AT RED CROSS WAR MEMORIAL CHILDREN'S HOSPITAL**

Authors: Mteshana P, Muloiwa R, Kumalo J, Bamford C, Hardie D, Buys H.

Affiliation: [1.]Department of Paediatrics and Child Health, University of Cape Town, South Africa; [2.] Division of Medical Microbiology, Faculty of Health Science, University of Cape Town, South Africa; [3.]Department of Virology, University of Cape Town, South Africa

Background:
Viral meningitis is the commonest form of meningitis in children but the clinical picture may be confounded by the prior use of antibiotics. Following lumbar puncture many children with clinical meningitis may be hospitalised and treated unnecessarily for presumed bacterial meningitis.

Objectives:
To look at the additional number of cases of BM confirmed through the use of molecular methods(PCR) for each of *Neisseria meningitidis, Haemophilus influenzae* and *Streptococcus pneumoniae* in patients with abnormal CSF findings whether they received prior antibiotics or not. To also document the number of cases of VM due to *Herpes simplex (HSV), Mumps virus*, and *enterovirus* as well as to determine the association of abnormal CSF findings, PCR and culture with HIV infection.

Methods:
Data was collected retrospectively from 321 patients who presented to Red Cross War Memorial Children's Hospital (RCWMCH) emergency unit between 1 November 2012 and 30 October 2013 with clinical signs of meningitis and had abnormal CSF cell counts and chemistry at lumbar puncture. We evaluated their demographics, clinical presentation, prior use of antibiotics, HIV status and CSF microscopy and culture results; following which real-time multiplex PCR diagnostic assays were run on the CSF samples testing for common bacterial and viral pathogens.

Results:
There were 321 children with a mean age of 2.94 years. 53.5% were male**.** The HIV status was known in 202 patients: 9 (2.8%) were HIV infected and 193 (60 %) were uninfected. Routine CSF culture detected 3 cases of *Pneumococcal*, 1 Meningococcal and 1 Haemophilus influenzae meningitis. Real-time multiplex PCR assay detected 9, 3 and 1additional cases of *Streptococcus pneumoniae,Neisseria meningitides and Haemophilus influenza meningitis* respectively as well as 52 cases of viral meningitis:31 (10.3%) Herpes simplex,17 (5.7%) *enterovirus* and 4 (1.3%) *mumps*.

Overall 148 (46%) children were admitted and treated for suspected bacterial meningitis. Their median length of stay was 5 days. There was 1 death and 173 children (54%) were discharged home from the emergency unit following review with the CSF results.

Conclusion:
Real-time multiplex PCR offers value in accurately detecting common viral and bacterial pathogens thus allowing for appropriate patient management. Routine use of molecular diagnostics aid in the diagnosis of meningitis in children should be considered and a cost saving analysis should be conducted prior to its introduction.

Title: **HOME ENVIRONMENTAL EXPOSURES TO INDOOR AIR POLLUTION AND TOBACCO SMOKE IN AN AFRICAN BIRTH COHORT**

Authors: [1]Aneesa Vanker, [1]Whitney Barnett,[2] Robert P. Gie, [3]Polite Munyaradzi Nduru, [1]Heather J Zar

Affiliation: [1]Department of Paediatrics and Child Health, Red Cross War Memorial Children's Hospital, University of Cape Town; [2] Department of Paediatrics and Child Health, Tygerberg Children's Hospital, Stellenbosch University; [3]Centre for Infectious Disease Epidemiology and Research, University of Cape Town

Background:
Tobacco smoke and indoor air pollution is a risk factor for childhood disease. The contribution of indoor air pollution or tobacco smoke exposure to the incidence, severity and outcome of childhood respiratory illness has not been well studied in African children.

Objective:
To describe the home environment and exposures to indoor air pollution and tobacco smoke in a birth cohort in South Africa.

Methods:
Indoor air pollution(IAP) and tobacco smoke exposure were longitudinally measured in homes and mothers enrolled in the Drakenstein child health study, a birth cohort study in a peri-urban area outside Cape Town, South Africa. Mothers enrolled are from 2 distinct communities – Newman (predominantly mixed race population) and Mbekweni (black African population). Indoor air pollution and tobacco smoke exposure were measured at a home-visit conducted antenatally. Particulate matter 10µg/m3 (PM10), volatile organic compounds (VOC), nitrogen dioxide, sulphur dioxide and carbon monoxide were measured. The home environment was also assessed using questionnaires. Maternal urine cotinine was also measured.

Results:
Fossil fuels including gas, wood, paraffin or coal were used for cooking in 19% and heating in 15% of homes sampled, despite high electrification rates (93%). Levels of benzene (VOC) were higher than ambient standards in 61% of homes.
More than two thirds of women had urine cotinine levels that indicated either active smoking or passive exposure. Smoking prevalence differed significantly between the 2 communities studied ($p < 0.001$).

Table 1 Prevalence of maternal smoking and exposure in 2 communities

	Site		
Smoke category	**Mbekweni (n, %)**	**TC Newman (n,%)**	**Total (n,%)**
Non smoker (cotinine <10)	106 (35.8)	36 (11.3)*	142 (23.1)
Passive Smoker (cotinine 11-499)	152 (51.4)	114 (35.9)*	266 (43.3)
Active Smoker (cotinine >500)	38 (12.8)	168 (52.8)*	206 (33.6)
Total	296 (100)	318 (100)	614 (100)

*p <0.001

Conclusion:
There are high rates of exposure to prenatal tobacco smoke and VOC from indoor fossil fuel usage that may impact negatively on maternal and child health.

Funding Bill & Melinda Gates Foundation (OPP1017641), Discovery Foundation, AstraZeneca Respiratory Fellowship, CIDRI Clinical Fellowship, MRC clinician scholarship.

Ethics UCT Health Sciences Faculty Ethics HREC REF: 149/2013

Title: **INCIDENCE AND SEVERITY OF CHILDHOOD PNEUMONIA IN THE FIRST YEAR OF LIFE IN A SOUTH AFRICAN BIRTH COHORT: THE DRAKENSTEIN CHILD HEALTH STUDY**

Authors: David M le Roux[1], Landon Myer[2], Mark P Nicol[3], Heather J Zar[1]

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Background:
Childhood pneumonia produces substantial mortality and morbidity. Accurate measurements of pneumonia incidence are lacking in low and middle income countries (LMIC), particularly after pneumococcal conjugate vaccine (PCV) implementation. This study aimed to describe incidence, severity and risk factors for pneumonia in the first year of life in children enrolled in a South African birth cohort.

Methods:
Pregnant women living in a peri-urban area of South Africa were enrolled in a birth cohort, the Drakenstein Child Health Study. Mother-infant pairs were followed till 1 year of age; data on risk factors and respiratory symptoms were collected. Children received 13-valent PCV according to national immunisation schedule. Pneumonia surveillance systems were established. Ambulatory and hospitalised pneumonia episodes were documented. Pneumonia incidence rate ratios were calculated using mixed-effect Poisson regression.

Results:
From May 2012 till May 2014, 697 children accrued 513 child-years of follow-up. Maternal smoking (24%) and HIV infection (19%) were common; no infant was HIV-infected. There were 141 pneumonia episodes, incidence 0.27 e/cy, (95% CI 0.23 –0.32); 32 cases were severe pneumonia, incidence 0.06 e/cy, (95% CI 0.04 – 0.08). There were 2 pneumonia deaths (1.4%). Maternal HIV, maternal smoking, male sex and malnutrition were associated with an increased incidence of pneumonia.

Conclusion:
Pneumonia incidence was high in the first year of life, despite a strong immunisation program including PCV13. Risk factors for pneumonia amenable to interventions were identified.

Funding: Bill and Melinda Gates Foundation, grant number OPP1017641; South African Thoracic Society; Federation of Infectious Diseases Societies of South Africa; UCT PhD research associateship

UCT HREC 401/2009 and REF 651/2013

Title: **THE PREVALENCE OF IGE MEDIATED FOOD SENSITISATION AND FOOD ALLERGY IN UNSELECTED 12-36 MONTH OLD URBAN SOUTH AFRICAN CHILDREN**

Authors: Maresa Botha, Wisdom Basera, Claudia Gray, Heidi Facey-Thomas, Mike Levin

Objectives:
To determine the prevalence of IgE mediated Food sensitisation and Food Allergy in unselected 12-36 month old children in Cape Town.

Methods:
This cross-sectional study recruited 12-36 month old toddlers from randomly selected registered crèches in Cape Town. Parents completed a questionnaire and their children had skin prick tests (SPT) for cow's milk, egg, soya, wheat, peanut, hazelnut and fish (cod) performed. Participants with SPT test >1mm than the negative control and who were not tolerant to that food had an OFC to assess for IgE-mediated food allergy. Parents choosing not to participate completed a non-participant questionnaire to control for bias.

Results:
Participants were black African (47%), Mixed Race (42%) Caucasian (12%), which is similar to Cape Town Census 2011 data on the ethnic distribution of 0-4 year olds in Cape Town. The mean age was 27 months.
The prevalence for SPT≥1mm to any food was 11.6 % (95% CI: 8.1-15.9%), SPT ≥ 3mm 9.9% (95% CI: 6.7-13.9%), ≥7mm 4.2% (95% CI: 2.2-7.3%) and OFC confirmed food allergy 1.8% (95%CI: 0.6-4.1%).The most common sensitisation was to egg (≥1mm 7.4%, 7.7% ≥3mm, 3.9% ≥7mm with 4 (1.4%) positive OFC's) and then peanuts (3.9%≥1mm, 3.2 % ≥3mm and 1.1%≥7mm with 3 (1.1%) positive OFC's).

Sensitisation ≥1mm for soya was 2.0%, wheat 1.6% and for cow's milk, fish and hazelnut 1.2% each. 4.7% of participants were poly sensitised.

The prevalence of any sensitisation (SPT≥1mm) and SPT ≥3mm was significantly higher in Black African children than in the other ethnic groups (15.8% vs 7.9% with p=0.04 and 14.3%vs 6.0% with p=0.02). This difference did not reach statistically significant levels for SPT≥7mm (6.0%vs2.6% with p=0.16).

Conclusions:
This is the first food challenge proven prevalence of FA determined in unselected children in Africa and provides a basis for further monitoring of a population possibly only at the beginning of the food allergy epidemic. The higher sensitisation rates in Black African children are similar to the high rates of aeroallergen sensitisation seen in unselected and allergic populations which supports the hypothesis that food allergies are on the increase in this population.

Further expansion in the next phase will compare the prevalence of sensitisation and food allergy between urban Caucasian, Mixed race and black African children and between rural and urban Black African Xhosa children and generate population-specific cut-off levels for SPT and Immunocaps with 95% positive predictive values.

HREC REF: 497/2013

Title: **AEROALLERGEN SENSITISATION AND PREVALENCE OF ASTHMA, ALLERGIC RHINITIS AND ECZEMA IN CHILDREN WITH VERNAL KERATOCONJUNCTIVITIS ATTENDING RED CROSS WAR MEMORIAL CHILDREN'S HOSPITAL**

Authors: S. Naidoo, C. Tinley, T. Pollock, M. Levin

Background:
Vernal Keratoconjunctivitis (VKC) is a severe inflammatory disease of the conjunctiva, with complex inflammatory pathways involving IgE and non IgE mechanisms. Studies have suggested that there are marked differences in the clinical expression of VKC in Africa with less atopy than in European and Asian cohorts.

Aim:
Describe the prevalence of allergic sensitisation to common aeroallergens as well as the prevalence of asthma, allergic rhinitis, and eczema in a cohort of children attending Red Cross Children's Hospital, Cape Town, South Africa.

Methods:
A cross sectional descriptive study where patients under 13 years had a diagnosis of VKC confirmed by an ophthalmologist , completed a questionnaire regarding atopic diseases and symptoms , underwent a physical examination (both general and ophthalmological) and had sensitisation evaluated by skin prick testing (SPT) to common aeroallergens.

Results:
214 patients were enrolled, mainly male (74.7%), black African (71%) and ranging from 14 months to 12 years, 10 months. Co-morbid atopic disease were as follows:

	No	%
Active eczema	17	7.9
Chronic eczema	27	12.6
Non-specific wheeze	79	36
Previous asthma diagnosis	38	17
Previous diagnosis of allergic rhinitis	47	21
Allergic Rhinitis	**122**	**57%**

The rates of atopic disease in this cohort were concordant with other SA studies, with the exception of allergic rhinitis which has a national prevalence, in an unselected population, of 38.5%. (ISAAC Study Phase II, 2003)

Aeroallergen spread	>3mm wheal (no)	>3mm wheal (%)
HDM	123	57.7%
Grass	74	34.7%
Cockroach	40	18.77%
Cat	24	11.26%
Dog	30	14%
Tree pollens	17	7.98%
Mould	8	3.75 %

Conclusion:
A higher incidence of allergic sensitisation and atopic disease was seen in our cohort of 214 children than in previous African studies. Our cohort more closely resembles the quoted VKC data from Europe and Asia than the earlier African studies.
The prevalence of asthma and eczema found in this study is similar to non-selected South African subjects in other studies. However, the prevalence of allergic rhinitis is strikingly higher than in a non-selected SA population. Major aeroallergens are HDM, grass and cockroach with very high levels of sensitisation noted, which are the highest sensitivities currently reported out of Africa.

Title: **DESCRIPTION AND OUTCOMES OF ORAL FOOD CHALLENGES IN A TERTIARY PAEDIATRIC ALLERGY CLINIC IN SOUTH AFRICA**

Authors: Talita A Ferreira-van der Watt (MBChB, FCPaeds, MMED Paeds, DCH), Wisdom Basera (HBMLS), Michael E Levin (MBChB, FCPaeds, PhD, DipAllergy)

Affiliation: Division of Allergy, Red Cross War Memorial Children's Hospital, University of Cape Town.

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Objective:
To describe the prevalence of true food allergies in a selected population as confirmed by oral food challenges and to determine significance of specific IgE levels compared to challenge outcome.

Methods:
Retrospective, descriptive study of children who presented to Red Cross Children's Hospital's tertiary Allergy clinic with food allergies and subsequently had oral food challenges (OFC) during the 39 month period from February 2011 to April 2014.

Results:
Two hundred and two OFC were performed on 142 children (age 9 months to 14 years). Challenges were done to 18 different foods. Egg, peanut, baked egg and cow's milk made up the largest number at 64, 37, 29 and 25 respectively.
Thirty eight (18.8%) challenges were positive with reactions varying from mild rash to wheeze. The rate of positive reactions increased significantly over the study period from 11.6% (n=5/43) in 2011 to 14.5% (n=10/69) in 2012, 21.5% (n=14/65) in 2013 and 36% (n=9/25) in 2014 (p=0.01). The most common reaction was urticaria in 23 (60.5%) and angioedema in 11 (28.9%). Three (7.9%) had wheezing. Fourteen percent of egg challenges (n=9/64), 35.1% of peanut challenges (n=13/37), 17.2% of baked egg challenges (n=5/29) and 20% of cow's milk challenges (n=5/25) had a positive outcome.
Co-morbidities were common in our population; atopic dermatitis was present in 73.9% (n=105/202), asthma in 37.3% (n=53/202), allergic rhinitis in 45.8% (n=65/202) and allergy to multiple foods in 62.7% (n=89/202). Co-morbidity prevalence was significantly different between groups with positive and negative OFC outcomes (p<0.01).
IgE levels for each food and each challenge outcome were compared to the published 95% positive predictive values (PPV)[1]. In challenges to egg, 36.1% (17/47) mixed race and 42.9% (3/7) black African had negative OFC's with IgE above the 95% PPV. In cow's milk challenges, 40.0% (6/15) mixed race and 80.0% (4/5) black African children had negative OFC's with IgE above the 95% PPV. For peanut challenges, 21.7% (5/23) mixed race children had negative OFC outcomes with IgE above the 95% PPV.

Conclusion:
The diagnosis and confirmation of food allergies can be challenging. The gold standard for diagnosing food allergy is the double-blind, placebo-controlled oral food challenge, however open food challenges (OFC) are useful to exclude food allergies.[2] In this setting, increased utilization of OFC's increased numbers of diagnoses of true food allergy. The prevalence and age of food allergy varies with different foods tested. Peanut allergy was the most common food allergy diagnosed. The presence of other atopic diseases had a significant impact on the outcome of food challenges. Large numbers of patients have negative challenges despite IgE levels above the internationally derived 95% PPVs. A higher proportion of Black African children have negative egg and milk challenges despite IgE levels above the internationally derived 95% PPV's.

References:

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2. Leung DYM, Sampson HA, Geha R, Szefler SJ. Pediatric allergy. Principles and practise. 2nd edition. Saunders Elsevier: 2010.

Title: **AN ASSESSMENT OF THE ASSOCIATION BETWEEN DOMESTIC HYGIENE, DIARRHOEA AND NUTRITIONAL STATUS IN CHILDREN UNDER TWO YEARS IN KHAYELITSHA**

Authors: Sambo MG, MPhil, LT Bourne, (RD) SA, PhD, M Hendricks, MBChB; MMed (Paed); MTropPaed (UK); DCH MBChB, Laubscher R, B.Com, Jordaan E, MSc. (Stat)

Background:
Diarrhoeal disease continues to be the most important cause of morbidity and mortality in children under five years globally and in South Africa. Diarrhoea is part of a vicious cycle of malnutrition, poverty, poor hygiene, poor access to water and sanitation, inappropriate feeding practices and early weaning (De Lange, 2010). The home has been implicated as an important source of the spread of diarrhoeal disease. Research has shown that provision of water and sanitation alone cannot prevent diarrhoea. Proper hygiene can prevent diarrhoea in the household with minimum access to water and sanitation. The aim of the study was to assess the association between domestic hygiene, socio-demographic factors and malnutrition with diarrhoea in children under-two years, in selected households in Khayelitsha

Methodology:
A case-control study was conducted in Khayelitsha clinics involving infants less than two years of age. The sample size of 100 cases and 100 controls was calculated to detect an odds ratio of at least 2.25, with 80% power with a 5% level of significance. A structured, pre-tested questionnaire was used consisting of anthropometric, child care and demographic factors, socio-demographic factors, hygiene and environmental factors. An observational checklist was also used to collect information on domestic hygiene and municipal services at the homes of cases and controls. Multiple logistic regression analyses were performed to identify the factors associated with diarrhoea. A backward stepwise regression method was used to arrive at the final model. All variables that were significant at $P \leq 0.1$ remained in the model. Results were expressed as odds ratios and 95% confidence intervals, as well as the p-values. Statistical significance was indicated by $p<0.05$.

Results:
With respect to the anthropometric status of the children, the results showed that children with and without diarrhoea had similar profiles in weight-for-age, weight-for-length, and length-for-age z-scores. Regarding the observed hygienic practices of mothers/caregivers in the home environment, there was no association between any of the household variables and diarrhoea using univariate and multivariate analyses. The self-reported hygiene behaviours that showed significant association with diarrhoea were mothers/caregivers washing dishes in a container (OR=0.39; 95% CI=0.19-0.84; p=0.015) and grandmothers preparing food at home for the child (OR=0.38; 95% CI=0.91-0.98; p= 0.046). With respect to the socio-demographic factors and domestic hygiene and diarrhoea, the variables that were significantly associated with diarrhoea in children < 2 years were day care attendance or the child being cared for by a family member/relative during the day (OR=2.79; 95% CI=1.25-6.21; p=0.012). The socio-demographic factors which were marginally associated with diarrhoea were rats in the house, toilet problems, the location of the kitchen and maternal/caregiver age.

Conclusion and recommendations:
In conclusion the study shows that contrary to previous studies nutritional status was not associated with diarrhoea. Practices relating to child care during the day, the person preparing food for the child and the designated place where dishes were washed were significant predictors of diarrhoea in children < 2 years. It further shows that access to a kitchen sink and having the mother preparing food does not necessarily protect the child from diarrhoea. Based on the findings of the study, recommendations are made relating to domestic hygiene and safe food handling, health promotion in communities relating to adequate sanitation and safe water and environmental control.

Title: **PREVALENCE AND MANAGEMENT OF MICROCYTIC ANAEMIA IN CHILDREN SEEN AT RED CROSS WAR MEMORIAL CHILDREN'S HOSPITAL**

Authors: Martie Wege, Patricia Harley, Rudzani Muloiwa

Introduction:
Anaemia is a common problem in early childhood and usually discovered as an incidental finding in children presenting to hospital for other reasons. Although a Full Blood Count (FBC) is a frequently performed test on this group of children as part of an evaluation for infection or other disease processes, little is known of the epidemiology of Iron deficiency anaemia (IDA) - a problem that manifests as microcytic hypochromic anaemia - in this population of children.

Our study aimed to describe the prevalence of anaemia in children aged between 6 and 36 months presenting to the Medical Emergency Unit (MEU), Short stay ward (SSW) and medical outpatient department (MOPD) at Red Cross War Memorial Children's Hospital (RCWMCH) as well as the management of children with suspected IDA.

Methods:
A retrospective quantitative cross-sectional study was carried out between September 2013 and April 2014. Data from the National Health Laboratory Services at RCWMCH were used to determine the proportion of all children aged 6 - 36 months seen in the MEU, MOPD or SSW between the 1st of January 2012 and the 31st of December 2012 with anaemia. A random sample of half of the children with anaemia was taken for a detailed folder review. Data including clinical presentation, investigations performed and subsequent management of the children were extracted.

Results:
Anaemia was found in 1088 (40.8%) of 2661 children. Five hundred and forty four (50%) folders of children with anaemia were sampled, of which 502 could be located for a detailed review. Mild anaemia (Hb 10 – 10.5) was found in 181 (36%) of the 502 while 264(53%) had a moderate anaemia (Hb 8 – 10) and 57 (11%) had severe anaemia (Hb < 8).

There was poor correlation between finding of pallor and laboratory confirmed anaemia with only 91/502(18%) noted to be pale on clinical examination. A microcytic pattern was found in 328/502(65.5%) of the children, 172 (34%) had a normocytic anaemia and only two (<1%) patients had macrocytic anaemia.

Of the 328 children with a microcytic anaemia, 180 (55%) were discharged without any iron therapy while 75(23%) received one month or less of treatment. Only 73(22%) of the patients had more than one month of iron therapy.

Conclusions:
The prevalence of anaemia in children aged 6-36 months at RCWMCH is almost double the predictable prevalence for children in South Africa. Microcytic anaemia is the most common type of anaemia in this group. More than 75% of children with suspected iron deficiency anaemia receive no iron therapy or less than one month of treatment.

Acknowledgement
NHLS Haematology Laboratory at RCWMCH

Title: **CLINICAL OUTCOME OF CHILDREN WITH HODGKIN LYMPHOMA AFTER CHEMOTHERAPY ALONE- THE RED CROSS CHILDREN HOSPITAL EXPERIENCE**

Authors: George Chagaluka[1], Marc Hendricks[1], Wendy Mathiassen[1], Ann Van Eyssen[1], Karl Thomas[1], Alan Davidson[1]

Affiliation: [1]Haematology and Oncology Service, Department of Paediatrics and Child Health, Red Cross Children's Hospital, University of Cape Town.

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Objective:
To assess the efficacy of hybrid chemotherapy protocol for Hodgkin lymphoma.

Methodology:
The 35 accessible documents of patients treated for Hodgkin lymphoma between 2005 and 2012 at Red Cross Children's Hospital, were reviewed to evaluate overall survival (OS), Event free survival (EFS) and cause of death. The protocol used included chlorambucil, vinblastine, prednisolone, procarbazine (ChlVbPP) alternating with adriamycin, bleomycin, vincristine, dacarbazine (ABVD). Relapsed or refractory patients received six courses of etoposide, prednisolone, ifosfamide and cisplatin (EPIC) with involved field radiotherapy (IFRT). Autologous stem cell transplant (ASCT) was treatment of choice for patients who had poor response to the first four courses of EPIC.

Results:
Of the 35 patients treated, median age was 9.5 at diagnosis and 25 (71%) were male. Two (6%) patients were HIV infected. The cervical region was the commonest site of primary disease and 14 (40%) had bulk disease. Seven (20%) had bone marrow involvement and Stage IV disease was recorded in 11 (31%) patients. Twenty two (63%) had Nodular Sclerosing histology. Thirty one were alive, including two lost to follow up in remission, including two patients with Stage III disease who relapsed off treatment and were salvaged. One Stage IV patient died soon after admission, and four Stage IV patients had refractory disease, one of whom was salvaged with EPIC, ASCT and IFRT. OS and EFS were 87% and 79% respectively for the whole study group. OS for stage I, II and III was 100% declining to 59% in Stage IV (p=0.02). EFS was 100% for stage I and II, 68% for stage III, 55% for stage IV (p=0.02). All patients who died, and all but one of those who relapsed had Nodular Sclerosing histology.

Conclusion:
Hybrid chemotherapy is associated with good outcome in stage I, II and III Hodgkin disease. Refractory Stage IV disease remains a problem and earlier evaluation with a view to adopting alternative strategies is warranted.

Title: **LOW GRADE GLIOMAS TREATED AT THE UNIVERSITY OF CAPE TOWN'S COMBINED PAEDIATRIC NEURO-ONCOLOGY SERVICE**

Authors: Alan Davidson[1], Anthony Figaji[2], Komala Pillay[3], Tracy Kilborn[4], Llewellyn Padayachy[2], Marc Hendricks[1], Ann van Eyssen[1], Jeannette Parkes[5]

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Objective:
To review the management of low grade gliomas (WHO I and II) by the combined neuro-oncology services of the University of Cape Town.

Methods:
A retrospective analysis was performed on all patients diagnosed at the Red Cross Children's Hospital (RCCH) and Groote Schuur Hospital (GSH) between 2001 and 2013. Data was collected from RCCH folders, as well as from RCCH paediatric oncology and GSH radiotherapy records.

Results:
There were 60 children, aged 0.41 to 13.75 years [median 5.38]. Forty six tumours (77%) were WHO grade I, and 14 were WHO grade II, including 7 fibrillary astrocytomas, 4 pilomyxoid astrocytomas and one pleomorphic xanthoastrocytoma. The commonest sites were cerebellum (30%), hypothalamus (20%), cerebrum (15%) and optic tract (12%). Fourteen patients were managed expectantly at diagnosis, including 5 of the 8 with neurocutaneous syndromes. Thirty two patients underwent definitive surgery in the form of debulking or gross total resection, and 11 patients required surgery for recurrence or progression. Fifteen patients (25%) received radiotherapy; 5 at diagnosis, 4 as second line treatment and 6 after surgery for recurrence. Thirteen patients (median age 2.67) were treated with chemotherapy; 11 of them with vincristine and carboplatin as the first line regimen. Ten of these patients had juvenile pilocytic astrocytomas and 3 had pilomyxoid astrocytomas. One progressed, three showed stable disease and nine responded, reducing in volume by 40-93% (median 68%).
Estimated 5-year Overall Survival (OS) was 89.2% for the whole group; 92.3% for WHO I tumours and 74.2% for WHO II tumours. Estimated 5-year Progression Free survival (PFS) for the whole group was 53.5%. The patients treated with chemotherapy had an OS of 100% and a PFS of 33%.

Conclusions:
Multidisciplinary team management is an effective strategy for the management of low grade gliomas, and is eminently viable in middle income settings.

Ethics: HREC 389/2014

New research.

Title: **RHABDOMYOSARCOMA AT RED CROSS WAR MEMORIAL CHILDREN'S HOSPITAL 1990-2010**

Authors: M Hendricks[1], A Davidson[1], A van Eyssen[1], W Matthiasen[1], F Desai[1], P Hartley[1] K Pillay[3], A Numanoglu[2], C Sinclair-Smith[3]

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Aim:
To evaluate the outcomes of children with biopsy proven rhabdomyosarcoma through a period of protocol transition from 1990 - 2010.

Methods:
All data was collected retrospectively by folder review. All patients included in the study were diagnosed between 1 January 1990 and 31 December 2010.

Results:
One hundred and fifteen patients with rhabdomyosarcoma appeared on our institutional registry between 1990 and 2010. Forty patients were excluded: 3 absconded, 5 patients had records missing or unavailable and 32 were treated primarily at another centre. Of the remaining 75 patients, 34 were female and 41 male. Thirty seven patients had embryonal histology and 18 were alveolar. Patients by stage and group were: Stage 1 (20); Stage 2 (5); Stage 3 (37) and 13 stage 4. Sites of metastases for S4G4 included 3 pulmonary, 6 bone marrow and 4 other. Primary disease sites included 17 para-meningeal tumours, 15 head and neck (non-orbital / non-para-meningeal), 11 pelvic (non-bladder, non-prostate), 9 extremity, 6 bladder, 6 vagina, 5 abdominal, 5 orbital and 1 in which no primary was found. By protocol division, 28 patients were treated on the current protocols introduced after 2005, 5 were treated with new protocols introduced in 2003 and 42 on protocols used prior to 2003. With respect to treatment toxicity the main complication was febrile neutropaenia. Twenty eight patients relapsed and only 2 patients were salvaged. Two patients died of infection during chemotherapy, 2 died of refractory / progressive disease, 1 was lost to follow up and 4 died of late secondary malignancies. Thirty eight patients are alive and disease free (5 year OS 61%: stage 1-80%; Stage 2-80%; Stage 3-51%; Stage 4-42%).

Conclusion:
The unit treats proportionally larger numbers of patients with rhabdomyosarcomas with adverse anatomical primaries. Toxicity has been acceptable with very few deaths from infection (2/75). The salvage rate post relapse was dismal (2/28). There is a trend to suggest that protocol revision has impacted positively on survival (OS: pre-2003: 54.1%; 2003-2005: 59.4%; post 2005: 64.2%).

Title: **M72/AS01$_E$ CANDIDATE VACCINE HAS AN ACCEPTABLE SAFETY PROFILE AND IS IMMUNOGENIC IN ADOLESCENTS IN A TB ENDEMIC SETTING**

Authors: Adam Penn-Nicholson[1], Hennie Geldenhuys[1], Wivine Burny[2], Erik Jongert[2], Philippe Moris[2], Cheryl L. Day[1,3,4], Anne Bollaerts[2], Mark Hatherill[1], Marie-Ange Demoitie[2], Angelique Kany Kany Luabeya[1], Evi De Ruymaeker[2], Michele Tameris[1], Thomas J. Scriba[1], Didier Lapierre[2], Robbert van der Most[2], Opokua Ofori-Anyinam[2], Willem Hanekom[1]

Affiliation: [1.] South African Tuberculosis Vaccine Initiative, Institute of Infectious Disease and Molecular Medicine and School of Child and Adolescent Health, University of Cape Town, Cape Town, South Africa; [2.] GlaxoSmithKline Vaccines, Rixensart, Belgium; [3.] Department of Global Health, Rollins School of Public Health and [4.] Emory Vaccine Center, Emory University, Atlanta, Georgia, USA

Objectives:
Vaccination that prevents spread of tuberculosis (TB) disease would have the greatest impact on the global TB epidemic. M72/AS01$_E$, a novel TB vaccine candidate, has a clinically acceptable safety profile and is immunogenic in adults, but has not been evaluated in adolescents, who also spread the pathogen when diseased. We aimed to evaluate the safety, reactogenicity and immunogenicity of M72/AS01$_E$ in healthy adolescents, regardless of *Mycobacterium tuberculosis (M.tb)* infection, living in a TB endemic region.

Methods:
In a phase II, double-blind randomised, controlled study (ClinicalTrials.gov, number NCT00950612), two doses of M72/AS01$_E$ or placebo were administered intramuscularly, one month apart. Participants were followed-up for seven months to assess endpoints. Antigen-specific immunogenicity was evaluated by intracellular cytokine staining analysis of T cells and NK cells by flow cytometry.

Results:
M72/AS01$_E$ had an acceptable safety profile; no serious adverse events were recorded. The vaccine induced a durable specific T cell and antibody response 6 months after vaccination. Induced CD4 T cells expressed multiple combinations of Th1 cytokines and IL-17, and drove expression of IFN-γ by NK cells. The peak measured specific T cell response occurred earlier, and the magnitude and breadth were higher, in *M.tb*-infected participants, compared with uninfected participants. Induced M72-specific immune responses were sustained above baseline at 6 months post last vaccination.

Conclusions:
M72/AS01$_E$ vaccination had a clinically acceptable safety profile and induced a sustained immune response in adolescents living in a TB endemic area. These encouraging results support the move to efficacy trials.

Title: **COMPARATIVE EVALUATION OF DIAGNOSTIC PERFORMANCE OF XPERT® MTB/RIF ASSAY BETWEEN INDUCED SPUTUM AND GASTRIC WASHING SPECIMENS IN CHILDREN BELOW 5 YEARS OF AGE FROM THE MVA85A TB VACCINE TRIAL IN CAPE TOWN, SOUTH AFRICA**

Authors: E. Bunyasi, M. Tameris, H. Geldenhuys, A. Luabeya, H. Mulenga, M. Hatherill.

Objective:
Timely and accurate diagnosis of childhood tuberculosis [TB] is hindered by difficulty in obtaining quality specimens and its paucibacillary nature. We compared performance of *Xpert® MTB/RIF assay* [Xpert] between paired induced sputum [IS] and gastric washing [GW] samples from children in a TB vaccine trial setting.

Methods:
We retrospectively analysed diagnostic data of 1020 children aged below 3.5 years evaluated for TB disease in the MVA85A Phase IIB infant TB vaccine trial conducted between July 2009 and October 2012 near Cape Town, South Africa. Specimens underwent standard *auramine* smear-microscopy, mycobacterial liquid culture, drug-susceptibility testing and Xpert assay. We calculated sensitivity and specificity using Wilson's score method with culture as the gold standard, compared median Time-To-Positive culture by specimen type using Wilcoxon's sign rank test and semi-quantitative median cycle threshold data across sample types using Kruskal Wallis' test. The trial from which this data are derived was approved by UCT HREC, ethics number 291/2008.

Results:
1214 admission events to a dedicated trial case verification ward to rule out TB disease were reported. 52 of 4463 [<1%] and 26 of 4606 [<1%] samples were positive on culture and Xpert assay for *Mycobacterium tuberculosis* respectively. Using 1st or 2nd IS, sensitivity of Xpert test against culture as the gold standard was 8/30 [27% 95% CI: 14-44]; whereas this was 7/31 [23% CI: 11-40] for 1st or 2nd GW. Corresponding specificity was 893/893 [100% CI: 99-100] and 885/890 [99% CI: 99-100] respectively. The *McNemar's $\chi 2$* test showed no significant difference in diagnostic performance of Xpert assay between paired IS and GW samples [P-value=0.4669]: a result also observed when analysis was limited to children with either a positive Xpert or culture on any specimen [p=0.6291].

Conclusions:
We observed no significant difference in diagnostic performance of Xpert assay between paired IS and GW specimens in children aged below 5 years.

Title: **DIRECT EX VIVO CHARACTERISATION OF THE CD4 T CELL RESPONSE INDUCED BY THE NOVEL SUBUNIT TB VACCINE, H1.**

Authors: M. Musvosvi[1], A. Penn-Nicholson[1], R. Dreyer[2], O. Dintwe[1], H. Geldenhuys[1], A. Sette[3], D. Baker[3], P. Andersen[4], ST. Hoff[4], M. Hatherill[1], and T. Scriba[1].

Affiliation: [1.]South African Tuberculosis Vaccine Initiative and School of Child and Adolescent Health, University of Cape Town, Cape Town, South Africa; [2.]Department Of Immunology, Institute of Infectious Disease and Molecular Medicine, University of Cape Town, Cape Town, South Africa; [3.]La Jolla Institute for Allergy and Immunology, La Jolla, United States; [4.]Statens Serum Institut, Copenhagen, Denmark

Objective:
Understanding the role of CD4 T cells in controlling *Mycobacterium tuberculosis* (*M.tb*) infection is critical for the development and evaluation of novel vaccination strategies against tuberculosis (TB). Recent results suggest that frequencies of mycobacteria-specific Th1 cytokine expressing CD4 T cells, a common measure of TB vaccine immunogenicity, do not correlate with risk of TB. Characterisation of T cell functions beyond those historically thought to be critical for protection is needed to develop a comprehensive understanding of the role of mycobacteria-specific CD4 T cells. To this end, we performed an in-depth characterisation of the transcriptomic profiles of mycobacteria-specific CD4 T cells induced by natural *M.tb* infection and vaccination with H1, a novel TB vaccine.

Methods:
We studies CD4 T cell responses in *M.tb*-infected and uninfected adolescents that participated in a phase II clinical trial for the novel TB vaccine, H1. Adolescents received 2 doses of H1 and where followed up for 7 months. We measured the memory phenotypes and expression levels of 96 genes within mycobacteria-specific CD4 T cells sorted from peripheral blood mononuclear cells.

Results:
H1 vaccination significantly boosted frequencies of Ag85B-specific CD4 T cells in infected and uninfected adolescents. Ag85B-specific tetramer-positive CD4 T cells predominantly displayed an effector memory phenotype. Preliminary transcriptomic analyses suggest that underlying M.tb infection markedly affects mRNA expression patterns in Ag85B-specific CD4 T cells.

Conclusions:
We have successfully combined two novel methodologies to perform *ex vivo* transcriptomic profiling of low frequencies of antigen-specific CD4 T cells induced by H1 vaccination. Transcriptome analysis of chemokine receptors, cytokines, transcription factors and effector molecules is currently ongoing.

Acknowledgement
We acknowledge the NIH Tetramer Core Facility (contract HHSN272201300006C) for provision of HLA class II tetramers.

Title: **AN AUDIT OF TRANSFERS INTO THE PICU AT THE RED CROSS WAR MEMORIAL CHILDREN'S HOSPITAL (RCWMCH): TEN YEARS LATER**

Authors: K Dimitriades[ab], BM Morrow[ab], AC Argent[ab]

Affiliation: Paediatric Intensive Care Unit, Red Cross War Memorial Children's Hospital[a]; and School of Child and Adolescent Health[b], University of Cape Town Rondebosch, Cape Town, South Africa

Background:
Children are transferred from various facilities into PICU for critical care, without a specialised paediatric transfer service. A previous audit in 2003 reported a high incidence of technical, clinical and critical adverse events during transfers.

Objective:
To conduct a follow-up audit on interfacility transfers into PICU to determine practice and outcome changes.

Methodology:
Prospective observational study of all patients transferred into PICU between 1 December 2013 and 30 November 2014. Ethical approval was obtained (HREC 702/13).

Results:
Interim analysis at six months was performed on 104 transfers (median (IQR) age 1.7 (0.3 – 10.5) months and compared to results reported by Hatherill et al (2003).

There was a decrease in the proportion of medical transfers (49% to 36.5% p=0.04) and of referrals from metropolitan hospitals (34.7% to 18.3%, p = 0.003); whilst the number of referrals from academic hospitals increased from 35.1% to 50% (p = 0.01).
Staff categories accompanying transfers and transfer times remained unchanged.
The proportion of fixed wing transfers increased from 14.4% to 24% (p=0.035), with helicopter use decreasing from 9.9% to 0% (p<0.0001). 58.4% of patients were intubated for transfer in 2003 compared to 70.2% in 2014 (p = 0.04).
The rate of total technical (35.6% to 45.2%, p = 0.1), clinical (26.7% to 26.9%, p = 0.9), and critical (8.9% to 4.8%, p = 0.3) adverse events remained unchanged.
PICU Mortality decreased from 16.8% to 8.6% (p=0.07), which may relate to improved PICU care.

Conclusion:
The rate and staffing structure of interfacility transfers into PICU have remained unchanged over a decade, and associated adverse event rates remain high. Research is needed to identify ways of improving PICU retrieval services.

Title: **LIGAMENTOUS INTEGRITY IN SPINAL CORD INJURY WITHOUT RADIOGRAPHIC ABNORMALITY (SCIWORA)**

Authors: Dr Anria Horn, Dr Stewart Dix-Peek

Purpose of study:
The question of prolonged bracing following injury in patients diagnosed with SCIWORA remains controversial. Proponents of the 'Segmental Spinal Instability' hypothesis claims that there is occult ligamentous injury leading to instability and a risk of recurrent injury. The contradicting 'differential stretch hypothesis' is based on the premise that the spinal column will deform elastically, exceeding the elastic deforming potential of the more fragile spinal cord, but will return to its baseline stability. The purpose of this study is to evaluate the need for bracing in patients with SCIWORA based on MRI evidence of instability.

Methods:
A retrospective chart review was performed for a series of eleven patients with documented SCIWORA that presented to Red Cross Children's Hospital over the past 8 years. Details regarding mode of injury, age at presentation, neurological deficit at presentation, MRI findings and long term prognosis were documented. MRI's were reviewed by the authors as well as a consultant radiologist.

Results:
There were 8 males and 3 females. The average age was 3.5 years. All patients were victims of motor vehicle accidents and had multiple injuries. Six patients had high cervical injuries, 4 had injuries at the cervico-thoracic junction or thoracic spine. One patient had both a cervical and a thoracic lesion. There were five complete lesions and 6 incomplete lesions. One patient's MRI showed isolated disruption of the ligamentum flavum at the affected level. Patients with only T2 changes demonstrated progressive neurological recovery within a few months following injury. There were no recurrences and none of the patients were braced following the diagnosis of SCIWORA.

Conclusion:
Our results from this small series support the 'differential stretch hypothesis' and we maintain that patients with SCIWORA do not demonstrate spinal instability and therefore do not require bracing following injury.

Title: **SALVAGEABILITY OF RENAL FUNCTION FOLLOWING RENAL REVASCULARIZATION IN CHILDREN WITH TAKAYASU ARTERITIS-INDUCED RENAL ARTERY STENOSIS**

Authors: Obiagwu PN, Priya Gajjar, Mignon McCulloch, Christian Scott, Angus Alexander, Alp Numanoglu, Peter Nourse

Objective:
Renal revascularization procedures are usually carried out on children with renal artery stenosis from varied causes. The salvageability of renal function in children who had renal revascularization for Takayasu arteritis-induced renal artery stenosis is studied.

Methods:
A retrospective analysis of children ≤ 16 years of age with angiographically-confirmed renal artery stenosis who underwent renal revascularization procedures at Red Cross Children's Hospital between 1990 and 2010 was conducted. Outcomes of renal function were studied over a period of two years and defined as (i) Improvement: greater than 20% increase in estimated glomerular filtration rate (e-GFR) from pre-surgery value (ii) Stabilization: e-GFR within 20% of pre-surgery value (iii) Failure: Greater than 20% deterioration in e-GFR from pre-surgery value.

Results:
Twenty children, 9 males and 11 females, had 27 renal revascularization procedures. Their ages ranged between 2 and 14 years. Thirteen of the patients (65%) had bilateral renal artery stenosis. Baseline mean e-GFR was 88.6 (±25.4) ml/min/1.73m^2 and the mean duration of follow up was 34.1 months. All patients had stable or improved renal functions up until the two-year follow up when the proportion decreased to 92% (12/13, $p < 0.05$) as failure was recorded in one child. Bilateral revascularization was found to be significantly associated with an improvement in renal function in the early post-operative period (OR 0.03; 95% CI 0.001 – 0.851; $p = 0.04$) but not in the further follow up periods ($p > 0.05$).

Conclusion:
Renal revascularization procedures are successful in salvaging the renal functions of children with Takayasu arteritis-induced renal artery stenosis.

Title: **RECURRENCE RATE POST RENAL TRANSPLANT OF CHILDHOOD NEPHROTIC SYNDROME, AT RED CROSS CHILDREN'S HOSPITAL**

Authors: Jonathan Buckley, Priya Gajjar, Peter Nourse

Affiliation: Paediatric Nephrology, Red Cross War Memorial Children's Hospital; School of Child and Adolescent Health, University of Cape Town

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Introduction:
Nephrotic syndrome (NS) is a recognized cause of ESRD in children, which requires therapy including renal transplantation. Many forms of NS are known to recur in the graft kidney, especially Focal Segmental Glomerulosclerosis (FSGS), with a recurrence rate of 20-30%. Little has been published on the characteristics as well as the recurrence rate in children, in an African setting.

Methods:
This was a retrospective descriptive study. The medical records of all patients with nephrotic syndrome, who received a renal transplant at Red Cross Children's Hospital from 1996 to 2012, were reviewed.

Results:
149 children were transplanted between 1996-2012. Twenty eight (18.7%) had nephrotic syndrome. Complete records could only be obtained for 19 patients.
Mean age at presentation was 5yrs (range 1-14yrs); mean age at transplant was 10yrs (range 3-15yrs). Male: female ratio: 11:8.
Histological diagnosis at presentation: Focal segmental glomerulosclerosis 16 (57%), Mesangiocapillary Glomerulonephritis 7 (25%), Mesangioprolierative GN 2 (7.1%), Congenital NS 3 (9.6%).
Nine (47%) were black African, 9 (47%) were of mixed race and one (5%) was Caucasian. Fourteen (77.7%) were steroid resistant at presentation.
The one and five year graft survival was 89% and 50% percent.
Two patients, both with FSGS, had recurrence of disease (12,5% of the FSGS group). Both presented between 6-15yrs of age. Both had induction therapy at transplant. Neither was Caucasian, and neither developed ESRD within 3yrs of presentation. In both, the donors were young (18 and 32yrs), and the kidneys were from deceased donors. Only one patient had nephrectomies. One patient had a biopsy showing no mesangial proliferation. Mean duration of follow up was 4yrs.

Conclusion:
FSGS was the most common histological type of NS, leading to renal transplantation. Our recurrence rate of 12,5%, in our small group of FSGS patients, is low. A possible explanation is that this is a single center study, and that the spectrum of the NS, we see is different (rather secondary than primary FSGS).

Title: **SCREENING FOR HYPOTHALAMIC-PITUITARY-ADRENAL AXIS SUPPRESSION IN ASTHMATIC CHILDREN ON CORTICOSTEROIDS IS NOT POSSIBLE WHEN EMPLOYING CLINICAL AND STATIC BIOCHEMICAL PARAMETERS**

Authors: Ekkehard W Zöllner, PhD[1], Carl J Lombard, PhD[2], Ushma Galal, MSc[2], Stephen F Hough[3] FCP MMed MD, Elvis M Irusen, PhD[4], Eugene Weinberg, FCP (SA)[5]

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Background:
It is impractical to test all asthmatic children for hypothalamic-pituitary-adrenal axis suppression (HPAS) with dynamic adrenal function tests.

Objective:
To determine which parameter is the most useful screening test for HPAS in asthmatic children.

Methods:
143 asthmatic children, 5-18 years old, treated with corticosteroids were recruited. Height velocity (HV), weight velocity (WV), height standard deviation score (SDS), weight SDS, change in systolic blood pressure from supine to standing (ΔSBP) were recorded. Early morning urinary free cortisol (UFC), morning serum cortisol (C), adrenocorticotropin hormone (ACTH) and dehydroepiandrosterone sulphate (DHEAS) were collected. UFC was expressed as a ratio of creatinine (Cr) excretion and as a ratio of body surface area. A metyrapone (MTP) test was performed if the 08:00 hr C was >83nmol/l. Spearman correlation coefficients (r) were calculated between the post-MTP ACTH, 11-deoxycortisol (11DOC), 11DOC+C, and each variable. Diagnostic statistics were calculated for the most promising test.

Results:

Screening Variable	**ACTH**		**11DOC**		**11DOC+C**	
	r	**p**	**r**	**p**	**r**	**p**
Height SDS	0.12	0.186	-0.13	0.120	-0.05	0.542
Weight SDS	0.10	0.262	-0.01	0.195	-0.10	0.279
HV SDS	0	0.999	0.07	0.420	0.07	0.452
WV SDS	-0.04	0.638	0.07	0.421	0.09	0.302
ΔSBP	0	0.992	0.05	0.538	-0.04	0.616
cortisol	0.05	0.538	0.08	0.374	0.12	0.176
ACTH	0.10	0.248	0.04	0.640	0.10	0.263
DHEAS	**0.20**	**0.025**	**0.21**	**0.017**	0	0.995
UFC (nmol/m2)	0.08	0.379	**0.19**	**0.033**	**0.20**	**0.022**
UFC (nmol/mmolCr)	0.08	0.397	0.14	0.111	0.16	0.064

The area under the receiver operating characteristics (ROC) curve for DHEAS in boys at 10-14 yrs (n=37) is the highest with 76 %. The screening performance at 2.0 µmol/l: sensitivity 100 (95%CI 63.1-100.0) %, specificity 38 (95%CI 17.9-54.3) %, accuracy 51 (95%CI 31.9-65.6) %, positive likelihood ratio (LR) 1.6 (95%CI 1.4-2.4), negative LR 0.0 (95%CI 0.0-4.5).

Conclusions:
No useful screening test for utilization at all ages could be identified.

Title: **THE USE OF GABAPENTIN FOR THE MANAGEMENT OF PAIN IN GUILLAIN-BARRE SYNDROME IN THE PAEDIATRIC SETTING**

Authors: [1.] Dr Hayley Hutton (MB CH, DCH SA) and [2.] Jo M Wilmshurst (MD)

Affiliation: [1.] Paediatric Fellow, Red Cross War Memorial Children's Hospital, University of Cape Town, South Africa; [2.] Head of Paediatric Neurology, Red Cross War Memorial Children's Hospital, University of Cape Town, South Africa

Introduction:
Pain is a common presenting problem in children admitted with Guillain-Barré Syndrome. The management is suboptimal, compounded by inappropriate tools to assess pain and the lack of clinical practice guidelines for children.

Methods:
In a retrospective observational study, all patients admitted with Guillain-Barré Syndrome between 2002 and 2012, to the Red Cross War Memorial Children's Hospital, were reviewed for their level of pain and treatment modalities used to manage this complication. Comparison was made between the outcomes for patients prescribed carbamazepine versus gabapentin, which are the two standard agents administered for chronic pain control in our centre.

Results:
Eighty six patients were identified with Guillain-Barré Syndrome. The prevalence of pain in this population was 76%. Pain rating tools were used in 3% of the patients. Twenty-nine patients received carbamazepine and twenty-two gabapentin. The use of Gabapentin increased from 2009-2012 (average 73% per annum) with a marked reduction in carbamazepine use. There were no significant differences in outcomes measured based on length of hospital stay, duration and severity of pain, long-term disability and use of adjuvant therapy.

Discussion:
The study highlighted the inadequate assessment of pain and the lack of evidence based clinical guidelines for pain management in patients with Guillain-Barré Syndrome. In reality the absence of effective pain scales for paralysed children demonstrates the challenges in adequately assessing these patients.
Although there were no crude differences between the two treatment groups of Gabapentin and Carbamazepine; the subtleties of pain control and quality of life cannot be compared based on the data available for this retrospective, observational study. There was an observable change in clinical practice with a dramatic increase in the use of Gabapentin for the treatment of pain in Guillain-Barré Syndrome.

This highlights the need for further research into this area of clinical practice.

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HREC 231/2013

Title: **BENZODIAZEPINES AND EXCITATORY GABAERGIC SIGNALLING DURING EPILEPTIC SEIZURES**

Authors: RJ Burman[1], HS Tomes[1], & JV Raimondo[2]

Acknowledgements: JM Wilmshurst[3]

Affiliation: [1]Department of Human Biology, Faculty of Health Sciences, University of Cape Town; [2]MRC Receptor Biology Unit, Division of Medical Biochemistry, Department of Clinical Laboratory Sciences, University of Cape Town; [3]Department of Paediatric Neurology, Red Cross war Memorial Children's Hospital

Background:
Status epilepticus (SE) describes a state of persistent seizures which are unrelenting, and is considered as a medical emergency. Treatment for SE uses a group of drugs benzodiazepines) that promote the action of the major inhibitory neurotransmitter within the brain, GABA.
Previous data from in vitro animal models has demonstrated that during SE, instead of being inhibitory, GABA can in fact become excitatory or 'proepileptic'. It is believed that this may be due to a disruption in the chloride gradient which follows periods of neuron hyperexcitability. Furthermore, this could explain why benzodiazepines often fail to halt SE.

Objective:
The aim of this research is to investigate the effect of diazepam (DZP) on GABAergic signaling and seizure dynamics using in vitro models of epileptic seizures.

Methods:
Using both rat organotypic and acute brain slices, whole cell recordings were made from hippocampal pyramidal neurons using patch-clamp technology, which allowed for inhibitory postsynaptic potentials (IPSPs) and seizure-like events (SLEs) to be recorded. Pressurized-puffs of muscimol, a GABAA selective GABA agonist, were applied in the presence and absence of DZP.

Results:
It can be confirmed that DZP enhances inhibitory GABA signaling under physiological conditions in both organotypic ($p=0.005$) and acute brain slices ($p=0.02$). Preliminary data utilizing *in vitro* seizure models suggests that DZP may not be effective in arresting seizure-like events.

Conclusions:
From the results obtained, it can be confirmed that DZP acts on the GABAA receptor to enhance inhibitory signalling under physiological conditions. However, our data suggests that during in vitro seizure activity DZP is ineffective in controlling neuronal hyperexcitability. These results serve as a basis for further investigation into the mechanisms underlying benzodiazepine resistance in patients suffering from uncontrolled epileptic seizures.

Ethics Number: AEC REF NO: 013/025 & HREC REF: 533/2013

Title: **PRENATAL ALCOHOL USE, INTIMATE PARTNER VIOLENCE AND OTHER PSYCHOSOCIAL STRESSORS AND SYMPTOMS AS PREDICTORS OF POOR DEVELOPMENTAL OUTCOMES IN INFANCY IN A SOUTH AFRICAN BIRTH COHORT**

Authors: Nastassja Koen, Kirsten A. Donald, Gail E. Wyatt, Muyu Zhang, Landon Myer, Whitney Barnett, Adele Marais, Colleen M. Adnams, Heather J. Zar, Dan J. Stein

Background and Objective:
Maternal exposure to psychosocial stressors and symptoms - such as intimate partner violence (IPV) and other stressors, and substance use and other mental disorders - during pregnancy is an important public health concern. Such exposure may be associated with a range of adverse sequelae, including poor developmental outcomes in early childhood. Despite the high burden of maternal stressors and symptoms and of poor childhood development in the low-middle income (LMIC) setting, there remains a paucity of data from developing countries such as South Africa. We examined the association between antenatal exposure to such psychosocial stressors and symptoms, and subsequent infant developmental outcomes in a South African birth cohort.

Methods:
This study reports data from the Drakenstein Child Lung Health Study (DCLHS), a multidisciplinary birth cohort investigation of the influence of antecedent risk factors on maternal and infant health outcomes over time. Pregnant women seeking antenatal care were recruited from two primary care clinics in a low income, semi-rural area outside Cape Town. Antenatal stressors and symptoms were assessed using a battery of validated and reliable questionnaires. Predictor variables were those pertaining to maternal sociodemographic variables (age, marital status, income); general medical health (composite biomedical and reproductive health); psychosocial stressors and symptoms (pregnancy intention, degree of partner support, childhood/adult trauma exposure, substance misuse, maternal mental health disorders); and newborn/infant anthropometry. Infant developmental outcomes at age 6 months were assessed using the Bayley Scales of Infant and Toddler Development, Third Edition (Bayley-III). Bivariate and multiple regression analyses were performed to determine the association between psychosocial stressors and symptoms during pregnancy and poor developmental outcomes in the infant.

Results:
The final study sample comprised 105 mother-infant dyads. The regression model predicting fine motor development in the infant reached significance [$r2$ = 0.20 (adjusted $r2$ = 0.13, F(8,88) = 2.75, p = 0.009], with maternal alcohol use during pregnancy [t = -2.29, p = 0.02) and exposure to past-year sexual IPV [t = -2.86 p = 0.005] each found to be significant for predicting poor outcome in infant fine motor development at age 6 months, when controlling for study site (clinic), maternal marital status, socioeconomic status, depression, posttraumatic stress disorder, and tobacco use.

Conclusions:
Alcohol use and exposure to sexual IPV during pregnancy may each have clinically significant effects on infant development. These effects may be identified even in early infancy using sensitive developmental measures. There is an ongoing need for further research in this field to elucidate the underlying neurobiology of these associations, to develop effective preventive strategies, and to assist in health policy decision-making in the LMIC context.

Ethics Approval Number: HREC REF: 401/2009
New Research: These findings have not yet been presented at previous research days

Contribution to Research Presented: As a junior researcher in the Department of Psychiatry and Mental Health, I also serve as Project Manager for the psychosocial component of the Drakenstein Child Lung Health Study. In this role, I assist in the co-ordination of all aspects of project planning, procedural development, HR development management and protocol amendment; I serve as a principle liaison with the site co-ordinators; and I oversee and assist with short-term surveillance of study participants and monitoring of research activities

Title: **EXPOSURE TO METHAMPHETAMINE PRENATALLY MODIFIES WHITE MATTER INTEGRITY AND NEUROCOGNITIVE FUNCTION IN CHILDREN**

Authors: [1]Roos A, [2]Kwiatkowski MA, [3]Narr KL, [2]Thomas KGF, [1,4]Stein DJ, [5]Donald KA

Affiliation: [1]MRC Unit on Anxiety & Stress Disorders, Department of Psychiatry, Stellenbosch University; [2]Department of Psychology, University of Cape Town; [3]Department of Neurology, University of California, Los Angeles; [4]Department of Psychiatry and Mental Health, University of Cape Town; [5]Division of Developmental Paediatrics, University of Cape Town

Objective:
There has been a marked increase in methamphetamine (MA) use. Yet, its effect on brain structure including white matter tracts and neurocognitive function in prenatally exposed children is largely unknown. This study aimed to investigate white matter integrity and associations with neurocognitive performance in children with prenatal MA exposure, compared to healthy controls.

Methods:
Six to seven year old children with known MA exposure during pregnancy (n=17) and matched controls (n=15) were included in the study. Children underwent diffusion tensor imaging using a 3T MRI scanner to investigate white matter structure; and neurocognitive assessment of motor function, executive function and memory using validated, age-appropriate tests. Whole brain analyses of white matter structure were performed using FSL's tract-based spatial statistics comparing fractional anisotropy (FA), mean diffusivity (MD), radial diffusivity (RD) and axial diffusivity (AD). Mean diffusion values were extracted from white matter regions shown to differ across groups to determine whether variations in FA predicted neurocognitive performance. Analyses were controlled for gender and nicotine use.

Results:
MA-exposed children showed significantly lower FA as well as higher MD, RD and AD in tracts that traverse striatal, limbic and frontal regions. Abnormal FA levels were significantly associated with poorer motor coordination and executive function.

Conclusions:
Our findings suggest that, consistent with previous studies in older children, there are disruptions of white matter integrity in striatal, limbic and frontal regions of young MA-exposed children, with prominent neurocognitive implications. Future longitudinal studies may clarify how prenatal MA exposure affects white matter structural connectivity at different stages of brain development. The information gained from both brain imaging and neurocognitive assessments may assist in understanding the underlying mechanisms of prenatal MA exposure.

Ethics approval number: HREC 235/2009

This research has been presented (in part) at a previous symposium (28 June - 2 July, 2014; New York).

Title: **CHILDREN WITH AUTISM AND EPILEPSY: A DESCRIPTIVE CLINICAL COHORT STUDY FROM RED CROSS WAR MEMORIAL HOSPITAL**

Authors: Ramsundhar.N[1]; Wilmshurst J[2]; Donald. KA[1]

Affiliation: [1]Division of Developmental Paediatrics, Red Cross War Memorial Hospital and University of Cape Town; [2]Division of Paediatric Neurology and Neurophysiology, Red Cross War Memorial Hospital and University of Cape Town

Introduction:
Seventy percent of children with autism spectrum disorder (ASD) have a co-morbid disorder. A common comorbidity of ASD is epilepsy. The prevalence of ASD in epilepsy ranges from 5%-38.4%. Both ASD and epilepsy are chronic disorders with significant impact on the lives of the children and their families. Reported risk factors for epilepsy in autism include intellectual disability; poor expressive language ability and female gender. In resource poor settings such as South Africa, little is known about the status of ASDs the morphological profile of children with ASD and the prevalence of co-morbidities of ASD. Identifying children with both epilepsy and ASD may improve health delivery and better collaboration between multidisciplinary teams. This will be the first South African review of the profile of the co-morbidities, primarily epilepsy, in autism.

Objectives:
1. To determine the prevalence of epilepsy in children with a clinical diagnosis of ASD in a tertiary developmental service.
2. To determine if autistic children with moderate to severe Developmental Quotient (DQ) and female gender have a greater prevalence of epilepsy than those without, in this group.
3. To describe the seizure semiology in patients with autism and epilepsy in this cohort.

Methods:
A retrospective folder review of children younger than 13 years diagnosed with ASD hat attended the Red Cross War Memorial Hospital(RCWMH) developmental clinic from 1January 2009 to 31November 2013.This data was derived from using Clinicom which is a hospital based information management system on ICD10 diagnostic codes. The data obtained was cross referenced with the paediatric epilepsy database at RCWMH. This data was entered on an electronic database with restricted access to ensure patient confidentiality. Analysis of the data is by various methods. Ethical approval was obtained from the University of Cape Town Human Research Ethics Committee.

Results:
Three hundred children with ASD were identified .In this cohort 41 children 16.5% had epilepsy and autism. Children with ASD who had moderate to severe DQ, poor expressive language and a preceding neurological insult were more predisposed to the development of epilepsy. Female gender was not identified as an association for epilepsy in ASD. Generalised seizures were the predominant seizure type in the autism and epilepsy cohort.

Conclusion:
The prevalence of epilepsy in autism in this cohort is within the range of that described in the literature. This study is in accordance with previous studies in showing an association of poor expressive language and low DQ with the development of epilepsy. These can been used to flag children with autism ensuring earlier detection and improved management.

HREC REF 164/2014

Title: **ECHOCARDIOGRAPHIC SCREENING FOR RHEUMATIC HEART DISEASE IN 4720 ASYMPTOMATIC SCHOOLCHILDREN FROM SOUTH AFRICA AND ETHIOPIA: IMPLICATIONS FOR SCHOOL HEALTH SERVICES**

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Background:
In sub-Saharan Africa the screening for asymptomatic rheumatic heart disease (RHD) has been conducted in single communities using non-standardised echocardiographic criteria. We used a standardised echocardiographic approach in South Africa and Ethiopia to screen for asymptomatic RHD in schoolchildren.

Methods:
Randomly selected schoolchildren from 4 through 24 years of age in Bonteheuwel and Langa communities of Cape Town, South Africa and Jimma, Ethiopia were screened for RHD according to the standardised echocardiographic diagnostic criteria of the World Heart Federation.

Results:
We screened 4720 schoolchildren. In South Africa (n=2720), 1604 (58.9%) were female, and the mean age was 12.2±4.2 years. In Ethiopia (n=2000), 1012 (50.6%) were female and the mean age was 10.7±2.5 years. Echocardiographic screening revealed 60 cases of RHD in Ethiopia and 55 cases in South Africa, corresponding to a prevalence of 30 cases per 1000 (95% confidence interval (CI), 22.9-38.4) and 20.2 cases per 1000 (95% CI, 15.3-26.2), respectively. The odds of detecting a child with RHD in Ethiopia was 1.5 times that in South Africa (OR 1.5; 95% CI, 1.01-2.2, P=0.03). The prevalence of RHD was 27 cases per 1000 (95% CI, 19.3 to 36.8) in Langa, and 12.5 cases per 1000 (95% CI, 7.1-20.2) in Bonteheuwel. The odds of detecting a schoolchild with RHD in Langa compared to Bonteheuwel were 2.2 (OR 2.2; 95% CI, 1.2 to 4.2, P=0.0071)

Interpretation:
There were significant differences in the detecting asymptomatic RHD in schoolchildren of different countries and different communities in the same country in sub-Saharan Africa.

Title: **BASELINE CHARACTERISTICS, COMPLICATIONS, AND GAPS IN EVIDENCE-BASED INTERVENTIONS IN 3343 CHILDREN AND ADULTS WITH RHEUMATIC HEART DISEASE FROM 14 COUNTRIES: THE GLOBAL RHEUMATIC HEART DISEASE REGISTRY (THE REMEDY STUDY)**

Authors: Dr Liesl Zuhlke for the REMEDY investigators

Aims:
Rheumatic heart disease (RHD) is responsible for up to 1.4 million deaths annually worldwide. Despite the heavy global burden, there are no contemporary data documenting the presentation, complications, and treatment of RHD. The Global Rheumatic Heart Disease registry (the REMEDY study) was designed to assemble a contemporary cohort of RHD patients from LMICs to comprehensively evaluate disease and treatment patterns with particular reference to valvular involvement, the prevalence of adverse cardiac events and pharmacological treatments used, and adherence to particularly secondary antibiotic prophylaxis and oral anticoagulation therapy.

Methods and Results:
The Global Rheumatic Heart Disease Registry (REMEDY study) is a prospective, international, multicenter, hospital-based study of characteristics, management and outcome of RHD. This paper reports the clinical features, complications and adherence to management guidelines at the time of enrolment. We enrolled 3343 participants (median age 28 years, interquartile range (IQR) 18 to 40; 28% < 19 years; female: male ratio, 2:1) from 25 centres in 14 countries low and middle income countries. 33% had congestive heart failure (CHF), while 25% were in NYHA III or IV. 13% had a history of stroke, major bleeding, pulmonary embolus or infective endocarditis. 53% had multi-valvular disease with decreased systolic function in 21% adults and 5% children; 23% of adults and 14% of children had a dilated left ventricle. A quarter were in atrial fibrillation (AF), of these 21% were not on anticoagulation. 61% had had no or less than three International Normalised Ratio (INR) tests in the previous six months, 70% of INRs were not in therapeutic range. 45% of participants and 69% of post-surgical patients were not on secondary prophylaxis for rheumatic fever. There was high use of additional medication: 40% of patients were on beta-blockers, 35% on digoxin, 5% on antiarrhythmic drugs, and 68% on diuretics. In women of child-bearing age, only 5% of those with prosthetic heart valves and 2% of those with severe mitral stenosis were on contraception. A total of 73 women (3•6%) were pregnant at the time of enrolment, the youngest 14 years, and the oldest 51 years of age. In total, 15 (20•6%) pregnant women were on warfarin. Utilisation of valvuloplasty and valve surgery was higher in upper-middle income compared to lower-middle and low income countries (P<0•01).

Conclusion:
To the best of our knowledge, REMEDY is the first large multi-centre and multi-national prospective study of the clinical features, use of evidence-based interventions and outcome in children and adults with RHD from lower and middle income countries (LMICs).RHD patients from developing countries are young, predominantly female with high functional disability, CHF, stroke, AF and multi-valvular disease. There is poor utilization of secondary prophylaxis, poor quality of oral anticoagulation and low use of valve surgery or valvuloplasty. The REMEDY baseline study has demonstrated the feasibility and capacity of the investigators to assemble a large number of well-characterised children and adults with RHD from LMICs. This study provides unequivocal evidence of that RHD is a disease of children and young adults from lower social strata who have limited access to health care interventions of proven effectiveness. There is a need for the implementation of known interventions and research into new modalities in order to ensure that the mortality from this disease by 25% by the year 2025.

Title: **ANOMALOUS LEFT CORONARY ARTERY TO PULMONARY ARTERY (ALCAPA) IN RED CROSS WAR MEMORIAL CHILDREN'S HOSPITAL (RCWMCH)**

Authors: B Rossouw [1,2] , L Zuhlke [1,2] , J Lawrenson [1,2,3]

Affiliation: [1] Red Cross War Memorial Children's Hospital (RCWMCH), Cape Town; [2]School of Child and Adolescent Health, University of Cape Town, Cape Town; [3]Tygerberg Children's Hospital, University of Stellenbosch, Cape Town

Aim:
To audit patients admitted to RCWMCH with a new diagnosis of ALCAPA.

Method:
Retrospective descriptive folder review of ALCAPA patients admitted between July 2004 and August 2011.

Results:
25 patients newly diagnosed with ALCAPA. Median age at presentation was 5.3 (range 0.5- 30) months. Male: female ratio 11:14.
22 patients were from the Western Cape Province where 10% of the children in South Africa live. Three patients came from the Eastern Cape that house 15% of the childhood population.
The common presenting symptoms were recession and tachypnea in 96%, cardiomegaly 92%, coughing 88%, failure to thrive 60%, feeding difficulty 52%, desaturation and gallop in 44%. Median length of symptoms before presenting to RCWMCH was 23 days (range: 1-300). The median time from RCWMCH admission to diagnosis and surgery was 1.5 (range: 0-16) and 5 (range: 1-20) days respectively.
The diagnosis was made on echocardiography in 68% and remainder via cardiac catheterization. Most common findings on echocardiography were pathological MR and dilated left ventricle in 79%, bright papillary muscles in 78%. The median ejection fraction on admission was 26%.
All the patients underwent coronary reinplantation, 4 needed PDA ligation and 2 needed mitral valve annuloplasty in addition. Median cross clamp and bypass time was 71 and 140 minutes. 24% had delayed sternal closure. Median length of hospital stay, ICU stay, ventilation and inotropic support was 21, 10.8, 7.4 and 9.3 days respectively. Median Wernovsky inotrope score was 32 (5-85) during ICU stay.
Perioperative complications included sepsis 68%, pleural effusion 24%, arrhythmias needing pacing 20%, bleeding 16%, renal replacement therapy 12.5%, cardiac arrest post-operative 8% and pericardial effusion needing drainage in 8%.
92% (23/25) survived to hospital discharge, 1 patient died pre surgery and 1 during surgery. 3 patients died of intercurrent chest infections during subsequent, more than 30 days after surgery.

	Short ICU stay (≤10 days) N=12	Long ICU stay (≥ 11 days) N=13	p
Age of presentation	2.6 months	7.7 months	0.008
Days ventilated	4.3	10.3	0.001
Days on inotropes	5.4	13	0.001
Adrenaline dose (mcg/kg/min)	0.14	0.23	0.036
CBP time	138 min	142 min	0.003
ICU sepsis	N=10	N=7	0.06
Outcome	1 late death	2 late deaths	0.476
LV EF	33.5%	28.2%	0.95

	RCWMCH N=25 7yr	Johannesburg N=27 17yrs	Paris N=62 21yr	Toronto N=67 48yr	Berlin N=27 14 yr	Beijing N=19 17 yr
Hospital survival	92%	96%	90%	92%	100%	73.3%
Age at time of surgery (months)	5	4.6	16	7.7	9.6	-
Median LVEF	30.7%	34.7%	32%	40%	45%	56%
ECMO/LVAD	0	7	4	5	7	0
		Journal of Thoracic Cardio vascular Surgery 2012	*European Journal Cardio Thoracic Surgery 2009*	*Annals Thoracic Surgery 2003*	*Journal of Thoracic Cardio vascular Surgery 2011*	*Pediatric Cardiology 2011*

Conclusion:

- RCWMCH can expect 3 new ALCAPA cases per year presenting in congestive cardiac failure.

  ALCAPA may be under diagnosed in the Eastern Cape Province.
- Treatment is successful without the use of mechanical cardiac support devices, with mortality rates comparable to the developed world. Older age at presentation, higher inotrope requirements, longer bypass time and sepsis, predicts longer PICU stay.

- The major complication for ALCAPA patients at RCWMCH is PICU related sepsis.

HREC/Ref: 340/2014

Title: **COUNTING ENCOUNTERS: A QUANTITATIVE ESTIMATION OF THE CLINICAL WORKLOAD OF THE WESTERN CAPE PAEDIATRIC CARDIOLOGY SERVICE (WCPCS)**

Authors: Rik De Decker, Rachel Chater, Oliver Barry, John Lawrenson

Objective:
The Red Cross War Memorial Children's Hospital (RXH) is the hospital in the Western Cape Paediatric Cardiology Service (WCPCS) that delivers a full paediatric cardiac service to children of the Western Cape. Resource limitations constrain service delivery severely, leading to long waiting lists with significant risks of serious morbidity and mortality. By elucidating the current imbalance between service demand and supply and showing its impact on child health, we hope to be able to implement changes that may redress this imbalance. An apparent bottleneck in service provision is the limitation of clinical staffing in relation to clinical load. The objective of the project was therefore to document the activities of the clinical staff of the WCPCS to accurately determine both numbers and intensity of all cardiac patient encounters.

Methods:
A patient encounter is defined as any activity that may directly influence the clinical outcome of a patient of the WCPCS, including direct interactions with, as well as clinical activities remote from but related to a specific, identifiable patient. Over a continuous period of 2 weeks, four full-time cardiology staff members (3 consultants, 1 senior registrar) were "tailed" by 9 medical students observing all their daily duties. As far as possible, the names and folder numbers of each patient, the time and duration of each encounter and its nature (clinical, analytical, procedural, or discussion with other clinical staff) were recorded for each separate encounter. Interruptions of ongoing encounters (e.g. by telephone calls) were documented as such. The encounters were recorded on pre-designed time sheets, transferred to Excel spread sheets and analysed using simple summary statistics.

Results:
A total of 2014 encounters were recorded over 10 working days. On average, each clinician was involved in 45.3 (45.2-58.5) encounters per day, involving 30.9 (17.7-56.2) patients (implying that many patients are encountered more than once per day). All encounters were timed from onset to completion; this number of encounters required an average of 6.6 hours of dedicated clinical time per day. For the purposes of comparison, a novel *patient encounter index (PEI)* was conceived. This serves to index the total daily encounter time as a ratio of a contractual 8-hour day. The four clinicians' PEIs ranged from 0.74 to 0.96. The context and implications of these and other data (such as encounter intensity) will be presented in detail.

Conclusions:
1. In addition to this excessive clinical load, joint service contract doctors are expected to perform academic (30% time) and administrative (20% time) duties during their contractual 8-hour working day. With a full complement of 4 clinicians, "uninterrupted" clinical duties consume 74-96% of their day, leaving little time for other essential duties.
2. For at least 4 months per year, one clinician will be away on leave, resulting in an 8% increase of each remaining clinician's clinical workload (resulting in PEIs of 0.82-1.04).
3. Elective surgical output can potentially reach 322 cases p.a. if *all* elective theatre slots are used. However, the output in 2013 totalled only 261 cases – this is a ratio of approximately 27 clinical patients seen per surgical case output. To reach a total of 322 cases, this ratio would need to increase by 23.4%, obviously not sustainable by the current cardiology full-time staffing (resulting in PEIs of 0.91-1.18).

This operational study has clearly shown that the cardiology service of the WCPCS is severely understaffed. The implications of this conclusion will be discussed.

Ethics approval number: HREC/REF 471/2014

Title: **VIRUSES IN CHILDREN WITH BURNS INJURY IN THE PICU AT THE RED CROSS WAR MEMORIAL CHILDREN'S HOSPITAL (RCWMCH)**

Authors: K Dimitriades[ab], BM Morrow[ab], D Hardie[c], AC Argent[ab]

Affiliation: [a]Paediatric Intensive Care Unit, Red Cross War Memorial Children's Hospital; [b]School of Child and Adolescent Health, University of Cape Town Rondebosch, Cape Town, South Africa; [c]National Health Laboratory Service; South Africa; Department of Virology

Background:
Children with burn injuries are commonly admitted to the PICU at RCWMCH, especially during winter when respiratory viruses are prevalent.

Objective:
To investigate the prevalence, spectrum and seasonality of respiratory viral infections in children admitted to PICU with burn injuries, and to describe the clinical outcomes of these children.

Methodology:
A retrospective review of all children admitted to PICU with burn injuries over 55 months. The institutional human research ethics committee approved this study with waived consent.

Results:
Two hundred admissions were recorded in 174 children (63.5% male) with burn injury. Fifty-one viruses were isolated in 45 admissions of 43 patients (24.7%) Sixteen viruses (31.3%) were isolated after 48 hours of admission in the PICU. The most commonly identified viruses were Rhinovirus A (n=20 isolates), Adenovirus (n=15) and respiratory syncytial virus (n=5). A seasonal peak in burn injury and viral observations was noted over the winter months.
Children with viral infections were younger (median (interquartile range, IQR,) age 18.7 (12.2 – 40.4) versus 33.3 (14.3 – 70.4) months, p=0.02) and had a longer PICU admission (median (IQR) 7 (4 – 11) vs. 3 (1 – 7) days, p<0.0001). There was no association between inhalational thermal injury and viral identification.
Overall mortality was 12%, with no significant difference between those with and without positive viral isolates.

Conclusion:
Respiratory viruses are common in children admitted to the PICU with burn injury and are associated with increased PICU length of stay. Further studies are required to examine the role of specific viruses in these children.

Title: **A REVIEW OF NECTROSING ENTEROCOLITIS AT GROOTE SCHUUR HOSPITAL**

Authors: Mbalenhle Gumede (Junior Registrar), Michael Harrison, Lloyd Tooke

Background:
Despite many advances in neonatology, necrotising enterocolits (NEC) remains a common (7%) and serious medical emergency amongst very low birth weight (VLBW) infants with significant morbidity and mortality. There is a paucity of local data on the profile of those babies who develop this condition, and their outcomes.

Objectives:
1) To determine prevalence of NEC at Groote Schuur Hospital (GSH)
2) To describe the epidemiology, clinical, laboratory and radiological presentation of these infants
3) To determine the short and medium term outcome of these infants

Methods:
A retrospective folder review of all cases of NEC in VLBW infants was performed for the years 2012-2013. Patients were identified from the Vermont Oxford Network and folders reviews were done. X-rays were assessed with a consultant and all data entered onto an Excel Spreadsheet.

Results:
A total of 58 out of 1032 VLBW infants were diagnosed with NEC (5.6%). Half the babies were <1000g. Nearly a third of them presented within the first ten days of life and the overall trend was for the smaller babies to present later. 41% of all babies were HIV exposed. Four babies developed NEC within 48 hours of a blood transfusion. A CRP was the most useful laboratory investigation at presentation and the most common findings on AXR were a bubbly appearance in the bowel lumen (84%) and thickened bowel wall (64%). Mortality was 60% but of the babies who received laparotomies only 1 died and short term neuro-developmental outcome was satisfactory.

Conclusions:
NEC is a significant concern with a high mortality rate. Babies who are appropriate for surgical intervention did better than expected. The role of HIV exposure needs further study.

HREC: R038/2014

Title: **TUBERCULIN SKIN TEST REACTIONS AND INCIDENCE OF TUBERCULOSIS DISEASE IN THE FIRST YEAR OF LIFE IN A SOUTH AFRICAN BIRTH COHORT: THE DRAKENSTEIN CHILD HEALTH STUDY**

Authors: David M le Roux[1], Shrish Budree[1], Landon Myer[2], Mark P Nicol[3], Heather J Zar[1]

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Background:
South Africa has a high burden of tuberculosis (TB) disease. Childhood TB infection can be asymptomatic before progressing to severe disease. Incidence of asymptomatic infection is difficult to measure and may be confounded by non-tuberculous mycobacteria or BCG vaccination.. This study aimed to describe tuberculin skin test (TST) reactivity in the first year of life in children enrolled in a South African birth cohort.

Methods:
Pregnant women living in a peri-urban area of South Africa were enrolled in an observational birth cohort, the Drakenstein Child Health Study. Mother-infant pairs were followed till 1 year of age. Tuberculin skin testing using intradermal injection of 0.1ml of purified protein derivative was routinely performed at 6 and 12 months of age, or if children were diagnosed with pneumonia, and was performed by study staff. Transverse diameter of induration of $\geq$ 10mm was considered evidence of TB infection. Diagnosis of asymptomatic infection or active TB disease was made by doctors and nurses in local community clinics based on symptoms (chronic cough, weight loss), known household TB contacts, and chest x-ray findings.

Results:
From May 2012 till August 2013, 494 children were born into the birth cohort; by 1 September 2014, 420 had completed 12 months of follow up, 440 child years of follow-up had accrued, and 74 children had been disenrolled. By 6 months of age, 55 children (11.1%) had reactive TST; by 1 year, 86 children (17.4%) had reactive TST. The incidence of tuberculosis infection was 19.5 per 100 child years, 95% confidence interval 15.6 to 24.1. Thirty-nine children (7.9%) were given treatment for TB disease, and 37/494 (7.5%) were given isoniazid chemoprophylaxis. Of the 86 children with reactive TST, 26 (30%) were not provided with any form of anti-tuberculous chemotherapy.

Conclusion:
Many children had large-induration TST reactions, suggesting high incidence of mycobacterial infection; some skin reactions may have been due to non-tuberculous mycobacteria or BCG vaccination. Incidence of clinically-diagnosed tuberculosis disease very high in the first year of life in this cohort; review of clinical criteria for diagnosis of tuberculous disease is needed.

Funding: Bill and Melinda Gates Foundation, grant number OPP1017641; South African Thoracic Society; Federation of Infectious Diseases Societies of South Africa; UCT PhD research associateship

UCT HREC 401/2009 and REF 651/2013

Title: **PULSE: PEDIATRIC UPDATE ON LUPUS IN SOUTH AFRICA: EPIDEMIOLOGY AND MANAGEMENT**

Authors: Laura B. Lewandowski MD, MSc[1,2], Laura E Schanberg MD[2], Nathan Thielman MD[1], Christiaan Scott, MD[3]

Affiliation: [1]Hubert-Yeagan Center / Duke Global Health Institute, Durham, NC 27710, [2]Duke University Medical Center Pediatric Rheumatology Durham, NC 27710, [3]Paediatric Rheumatology Red Cross War Memorial Children's Hospital, Cape Town, South Africa

Objective:
Systemic Lupus Erythematosus (SLE) is a life-threatening multisystem autoimmune disease. In developed nations, SLE is more common and severe in people of African extraction than in Caucasians. The epidemiology of SLE in Africa is largely undetermined. Historically, the incidence of SLE in Africa was presumed to be low. Recent studies have challenged this theory. In general, children present with higher disease activity, require more therapy, and accrue more organ damage than adult-onset patients. Although African children with SLE may be at high risk for poor outcomes, little research has investigated this population. A pediatric SLE (pSLE) registry could provide information about epidemiology of pediatric SLE in Africa, and yield important information to aid diagnosis and management.

Methods:
We conducted a retrospective chart review of pediatric and adult rheumatology and nephrology patients seen at 2 centers in Cape Town, South Africa from 1988-2014 meeting American College of Rheumatology criteria for SLE. Patient age, gender, race, and presenting features were recorded and compared to previously described pediatric SLE cohorts in South Africa and worldwide.

Results:
Initial review of patients yielded 68 patients (age 12.2; 83% female). The racial distribution was 68% colored, 26% black, 3% white, and 3% Asian/Indian. A much larger proportion of patients in our cohort are of colored or black race compared to a previously published South African cohort, reflecting changes in post-apartheid access to care and population differences between the Western Cape and Gauteng provinces. The majority of our patients presented with severe renal disease. Renal biopsy was performed in 49%; all biopsied had lupus nephritis (LN). Of the patients with LN, 84% presented with ISN class IV or higher. PSLE nephritis cohorts from developed nations report 6-7% of LN patients progressing to end stage renal disease (ESRD), and reports from developed nations report 8-12%. Within the cohort, 13% went on to develop ESRD requiring transplant, strikingly higher than previously reported cohorts. Our cohort had active disease evidenced by mean SLEDAI score of 20.4 at diagnosis, compared to scores of 4-13 in previously reported pSLE cohorts. Also, the PULSE cohort had evidence of end organ damage, with an average SLICC score of 1.9. 63% of the cohort had a SLICC score >0, compared to only 23% in a previously reported US cohort of 221 pSLE patients.

Conclusions:
This cohort represents the largest registry of pSLE patients in Africa to date. Preliminary findings show these children to present with high disease activity, and progress to end organ damage at higher rates than pSLE cohorts in developed nations. These children have a greater chance of progression to ESRD compared to their peers in developed countries. We will continue to expand this review to other centers and follow this cohort prospectively to further delineate pSLE epidemiology in South African patients. Further work may help determine barriers to diagnosis and treatment of pSLE and identify modifiable risk factors for poor outcomes in this population.

Approved by UCT Ethics, IRB00001938

Title: **A RETROSPECTIVE STUDY OF THE AGE AT PRESENTATION, CLINICAL COURSE AND OUTCOME OF PATIENTS WITH INFLAMMATORY BOWEL DISEASE SEEN AT RED CROSS WAR MEMORIAL HOSPITAL BETWEEN 2004 AND 2014.**

Authors: Dr. Waceke Nganga (PI); Dr. Liz Goddard; Dr. Ronalda de Lacy; Prof. Brenda Morrow (Supervisors)

Objective:
The incidence of ulcerative colitis and Crohn's disease has been on the rise globally. The most common time of onset of IBD is during the preadolescence /adolescence era and young adulthood. Paediatric IBD is characterised by both extensive intestinal involvement at the onset and rapid progression of the disease. This study aims to elucidate the profile of paediatric inflammatory bowel disease in an African setting. The objectives of the study were thus:-

- To describe the demographics of patients diagnosed with Inflammatory Bowel disease.
- To describe the presenting complaints of the patients.
- To describe use of laboratory and radiological markers associated with inflammatory bowel disease.
- To describe treatment, course and clinical outcome of children diagnosed with inflammatory bowel disease

Methods:
This is a retrospective descriptive folder review. All patients whose disease were classified under the International Statistical Classification of Diseases and Related Health Problems (ICD 10) codes for Crohn's disease- K50 or Ulcerative colitis –K51 will be included. Other databases such as the record of gastroenterology clinic patients and list of histology biopsies with diagnosis of IBD will be sought to ensure any data that may have been erroneously missed out by the clinicom is captured. The analysis will take the form of a descriptive study discussing the frequency of the various events studied. Continuous variables will be expressed as means.

Results:
Preliminary results show age at presented ranged between 9 years and 13 years with more males than females. There were more cases of Crohn's disease than ulcerative colitis. Abdominal pain, bloody diarrhea, and growth faltering were the most common presenting complaints. Iron deficiency anemia was the most common extraintestinal manifestation. Platelets and ESR were invariable elevated. Fecal calprotectin was also elevated in those patients who had the test performed. The diagnoses were confirmed on histology with typical features seen. Medical treatment was effective in all but one patient who went on to have a total colectomy.

Conclusion:
The study is still ongoing and as such conclusions cannot be made now. This is postulated to have been finished by the time of the presentation.

Title: **HIGH DP RATIOS IN CHILDREN ON ACUTE PERITONEAL DIALYSIS**

Authors: Nourse P1, Gajjar P1

Affiliation: Red Cross War Memorial Children's Hospital, University of Cape Town, South Africa

Objectives:
To establish the peritoneal transport characteristics and Kt/V's of children on acute peritoneal dialysis.

Methods:
This study was approved by our university ethics committee and consent was signed by each child's parent or guardian. The dialysate to plasma (D:P) creatinine ratios and Kt/v of children undergoing acute PD in paediatric ICU for acute kidney injury (AKI) secondary to a variety of illnesses was calculated. Manual peritoneal dialysis was performed with a prescription as follows: Fill volume = 20ml/kg; dwell time = one hour; fill time = 1-10 min; drainage = 20min. The dialysate was collected and urea creatinine and sodium levels were analysed. The D:P creatinine ratios were calculated in 7 patients using the formula dialysate creatinine / two hour serum creatinine. Some patients had more than one test performed on separate cycles. An estimate of the weekly Kt/V 's were done in 9 children by calculating the clearance using the six hour pooled dialysate and then multiplying this by 4 to calculate the clearance for a day and then by 7 to calculate the clearance for a week . The clearance was then divided by the total body water (according to the mellits cheek formula) to calculate the Kt/V.

Results:
The average age of the patients was 7.04 months (STD=6.4; range=0.4-20). The average weight of the patients was 6.4Kg (STD =3.2; range=2.2-8.4). The average DP ratio was 0.7 (SD=0.16) with a range of 0.49-0.94. The average Kt/V was 2.96(SD=0.59) with a range of 1.87-3.45

Conclusions:
Our patients had high DP ratios after a one hour dwell. Kt/V were also high in all patients except one .Our results support the recent guidelines pertaining to the short dwell times required in acute peritoneal dialysis in children, however more data is needed.

Title: **THE QUALITY OF LIFE OF CHILDREN WITH SEVERE CEREBRAL PALSY IN A TERTIARY PAEDIATRIC CLINIC IN CAPE TOWN**

Authors: Reneva Petersen[1] Jo Wilmshurst[1] Kirsty Donald[1]

Cerebral Palsy (CP) is the most common cause of physical disability in children across the world. The diagnosis of cerebral palsy has a significant impact on all areas of an individual's life. Comprehensive evaluation of patient well-being is important to ensure that medical, educational and social interventions are not only effective but appropriate to patient needs and expectations.

Aim:
The aim of the study was to document the health status and quality of life of children with severe cerebral palsy attending a tertiary service in Cape Town using the Child Health Questionnaire. (CHQ)
Methods: Children with severe CP between the ages of 4 and 18 years were recruited from the specialist cerebral palsy clinic at the Red Cross War Memorial Hospital in Cape Town. The CHQ PF 28 caregiver questionnaire was completed by parents or caregiver and used to measure the parent's perception of their child's physical (PHY) and psychosocial (PSY) health. Demographic information was collected from folder review and clinical assessment done by clinician in clinic.
Ethics approval was obtained from the UCT health sciences research ethics committee.

Results:
Participants:
Children with cerebral palsy: N=99 Male=66 Female=33 Mean age +/- standard deviation (SD) =7.75 +/- 3.05 years
Healthy controls: N=100 Male= 55 Female= 45 Mean age +/- SD= 8 +/- 2.6 years)The median physical summary score for children with severe cerebral palsy was 12.3 (IQR= 5.57-31.03) with a significant difference compared to physical summary score of the control group.(median= 43.10, IQR=39.31-53.33) The median psychosocial summary score for children with cerebral palsy was 40.15 (IQR=32.52-47.59) compared to the summary score for control group(47.81 IQR= 37.77- 54.69) The scores were also lower compared to reference samples (US normed population) as well as other international reports. No correlation was found between sex, socioeconomic background and presence of comorbidities and summary scores.

Conclusion:
The quality of life of children with severe CP in Cape Town as reported by the CHQ PF 28 is lower compared to children with severe cerebral palsy in other countries. There could be related to a lack of access to services and education services of children in the cohort. Further exploration of these factors are indicated.

HREC REF: 661/2012

Title: **ARE NEWBORNS RECEIVING PREMEDICATION BEFORE ELECTIVE INTUBATION IN SOUTH AFRICA?**

Authors: MS Raban, Y Joolay, AR Horn, MC Harrison

Affiliation: Division of Neonatal Medicine, Department of Paediatrics, University of Cape Town, Cape Town, South Africa

Background:
Intubation is a common neonatal procedure. Premedication is accepted as a standard of care, but its use is not universal and wide variations exist in practice.
Intubation induces noxious stimuli often associated with adverse physiological events such as raised intracranial pressure, hypoxaemia and cardiovascular instability. Recent studies have shown that premedication for elective and semi-urgent intubation of infants significantly improves intubation conditions; decreases the time and number of attempts needed to complete the intubation procedure, and minimizes the potential for intubation-related airway trauma.
Premedication practices have been surveyed in Europe, North America and Australia. The European surveys had a profound effect on current practice; Whyte et al. in 1998 demonstrated that 63% of UK neonatal units did not use premedication prior to intubation. This study prompted much discussion, and a decade later when the survey was repeated, ≥ 90% of neonatal units have adopted premedication as a standard of care.

Objective:
To evaluate current practices for premedication use prior to elective neonatal intubation in South Africa (SA).

Methods:
We invited 481 clinicians to participate in a cross-sectional web-based survey.

Results:
We received responses from 28.3% of the clinicians surveyed; 54.1% were from the private sector and 45.9% from the state sector. Most respondents worked in medium-sized neonatal units with 6-10 beds. Most paediatricians (76%) worked in the private sector, 78.6% of neonatologists worked in the state sector. Premedication was practiced by 71.9% of the respondents, only 38.5% of neonatal units had a written policy. Sedatives were used for premedication by 63.2% of the respondents. Midazolam (41.5%), morphine (34%) and ketamine (20.8%) were most commonly used. Muscle relaxants and atropine were not routinely administered. Suxamethonium was the muscle relaxant of choice. Varied combinations of agents or single agents were used for premedication. Midazolam used alone was the preferred option.

Conclusion:
This is the first survey of the use of premedication for neonatal intubation in SA. It illustrates that almost 30% of the SA clinicians surveyed were *not* administering premedication to infants prior to elective or semi-elective intubation. The survey demonstrates clinician's reluctance to participate in surveys, suggesting a need for a national collaborative network to obtain representative data. There were variations in practice and a minority of clinicians had a written policy. The findings can be used to benchmark practice and also inform the design of local collaborative trials determining optimal premedication prior to neonatal intubation.

HREC 548/2013

Title: **A CASE SERIES OF PLEXIFORM NEUROFIBROMAS IN A COHORT OF SOUTH AFRICAN CHILDREN WITH NEUROFIBROMATOSIS 1**

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Introduction:
Plexiform Neurofibromas are serious complications of Neurofibromatosis 1 and remain a major management dilemma globally. These tumors are both chemo and radiotherapy resisitant and are often difficult to excise. A viable therapeutic agent is yet to be found. 25% of children attending the multidisciplinary Neurofibromatosis Clinic at Red Cross War Memorial Hospital presented with Plexiform Neurofibromas, with 16% having life threatening Head and Neck lesions. This series is aimed at establishing a specific management plan taking into account the unique socio-demographic challenges of this cohort, as well as the resource limitations of this centre.

Method:
All children with Plexiform Neurofibromas who presented to the multidisciplinary service at Red Cross War Memorial Hospital, since January 2001 are summarised in detail.

Results:
23 children presented with Plexiform Neurofibromas, 9 girls and 14 boys. A family history of NF1 was present in 9 of the 23, with 14 having a new mutation. Children presented between 6weeks and 10years of age with a median age of 3years. MRI scans of suspected lesions were done in all children. 12 children presented with Plexiform Neurofibromas involving the Neck and Chest. (52% n=23) 3 had Periorbital lesions with extensive spread into the Occipital soft tissues, proptosis, and distortion of the orbit. 2 were located in the face, and 1 involved the soft tissues of the occiput. The remaining 5 children had lesions involving the lower limbs (n=2), upper limb (n=1) buttock and pelvis(n=1) and lumbar paraspinal tissue (n=1). Only 6 children underwent surgery. 2 of the 3 children with Periorbital lesions underwent repeated surgical debulking after enucleation and ball implants. In both cases growth continued postoperatively. Only 3 (n=12)with lesions of the head, neck and chest underwent surgery. 1 child had an emergency tracheostomy due to acute airway compromise. The second child underwent a Spinal Laminectomy and tumor debulking due to spinal cord compression. The 3rd child required a spinal rod insertion and debulking. Only 1 child had a complete excision of his Occipital lesion. Both children with lower limb involvement had associated hemihypertrophy and have orthopaedic surgery planned. Malignant transformation was suspected in 1 patient WHO had a rapid growth of her head, neck and chest lesion at age 16yrs with symptoms of pain, weakness and airway compromise. She demised 1 month after exacerbation of her symptoms.

Conclusion:
The management of children with Plexiform neurofibromas remains a dilemma globally. This is the first series describing children from an African setting many of whom are from poor socio-economic environments with limited access to services. .

Title: **INTRODUCING THE STRUCTURED COMMUNICATION TOOL SBAR (SITUATION, BACKGROUND, ASSESSMENT AND RECOMMENDATION) TO THE NEONATOLOGY DEPARTMENT OF A TERTIARY SOUTH AFRICAN HOSPITAL**

Authors: M Raymond[1] and M C Harrison[2]

Affiliation: [1]NHS Improving Global Health Fellow, Thames Valley and Wessex Leadership Academy; [2]Division of Neonatal Medicine, Groote Schuur Hospital and Department of Paediatric and Child Health, University of Cape Town

Background:
Effective communication, cooperation and teamwork have been identified as key determinates of patient safety. SBAR (Situation, Background, Assessment and Recommendation) is a structured communication tool recommended by the WHO (World Health Organization) [1] and the NHS (National Health Service). [2]
SBAR is a structured method for communicating critical information that requires immediate attention and action contributing to effective escalation and increased patient safety. To our knowledge, this is the first study showing use of SBAR in South Africa.

Objective:
To determine the effectiveness of adopting the SBAR communication tool in an acute clinical setting in South African.

Methods:
In the first phase of this study, neonatal nurses and doctors at Groote Schuur Hospital were gathered in a focus group and given a questionnaire asking about communication in the neonatal department.
Neonatal nurses and doctors were then trained to use SBAR.

Results:
A telephone audit demonstrated an increase in SBAR use by registrars when calling consultants for help from 29% to 70% post training. Post-training, the majority of staff agreed that SBAR had helped with communication, confidence, training, and quality of patient care.

Conclusions:
Adopting SBAR in our practice was associated with improvement in perception of communication between professionals and their perception of the quality and safety of patient care. It is hoped that this simple tool can be introduced to multiple hospitals in South Africa.

HREC Ref: 568/2013

Title: **HAEMATOLOGY AND BIOCHEMISTRY VALUES OF INFANT POPULATION IN WORCESTER**

Authors: Bey-Marrié Schmidt*, Mark Hatherill[1] and Michele Tameris[1]

Affiliation: *Junior researcher, SATVI Masters in Public Health (Epidemiology) Research Fellowship; [1]SATVI

Background:
Reference ranges for paediatric haematology and biochemistry values currently used in Africa are derived from white Western children. Studies performed in Africa have questioned the applicability of these values to local African children.
The South African Tuberculosis Vaccine Initiative (SATVI) operating from a field site in Worcester, Western Cape, has been enrolling healthy non-HIV-exposed volunteers into phase I and II TB vaccine trials since 2005. There are strict participant inclusion and exclusion criteria, including chemical and haematological measures that must fall within the laboratory provided reference ranges for phase I trials or within limits clinically acceptable to investigators for phase II trials. Relevant reference ranges are used for screening, safety follow-up and routine clinical management of trial participants.
Currently recommended reference ranges for the Worcester population are derived from white populations of developed countries. Age, gender, ethnicity and environment may affect reference values of various populations.

Objective:
To determine whether reference ranges provided by the National Health Laboratory Services (NHLS) reflect the haematology and chemistry results of Worcester infants.

Methods:
Between 2008 and 2012 SATVI conducted clinical trials of three novel TB vaccines in infants from the Worcester area. The inclusion and exclusion criteria of all three trials were the same. Healthy infants between 12-52 weeks were recruited from the general population using vaccination clinic records, birth registers and word of mouth. General good health was determined by a study clinician on medical history and examination at the time of both the screening and dosing visit. The screening blood chemistry, full blood count and differential results of infants between 3 and 6 months were assessed and compared to age-categorised reference ranges supplied by National Health Laboratory Services (NHLS), who processed the samples.

Results:
639 full blood counts were obtained during screening visits and compared to NHLS reference ranges to determine 'normality'. 90% (577/639) of the total sample had platelet counts above the NHLS upper limit of normal (350 x 10^9/L). The NHLS range for mean corpuscular hemoglobin (MCH) for this age group is 26.0-34.0pg. 57% of the sample had MCH values below the NHLS lower limit. The mean cell/corpuscular volume (MCV) reference range is 77.0-105.0fl and 55% of the samples were below the NHLS lower limit. The chemistry values of the Worcester infants are generally within the NHLS ranges.

Conclusion:
Deviations of platelet counts, MCH and MCV values from the NHLS supplied reference ranges in an otherwise healthy infant population suggest secondary or reactive thrombocytosis, possibly due to iron depletion. These findings suggest that haematology and chemistry values of African infants be interpreted with caution against Western-derived reference ranges.

The ethics approval numbers: C020-485: 291/2008; C029- 402: 403/2009; TB 014: 150/2007

Title: **HOW DECREASING MATERNAL SEPARATION PRIOR TO SURGERY AFFECTS PHYSIOLOGICAL STABILITY IN INFANTS AND SMALL CHILDREN. A RANDOMISED CONTROL TRIAL**

Authors: Lydia Ssenyonga[1]; Nils Bergman[2]; Minette Coetzee[1]

Affiliation: Child Nurse Practice Development Initiative[1], Paediatrics and Child Health[2]; University of Cape Town, South Africa.

Introduction:
Intensive care of critically ill infants conventionally involves extended maternal–infant separation. The widely held belief that separation anxiety is a developmental phase which occurs in 7-9 month old infants, supports numerous practices of separation in hospital settings Extensive research in preterm and term infants has demonstrated the adverse effects of separation. A clear evidence-base now exists for maternal–infant skin-to-skin contact as an alternative place of care to the incubator in neonates. Better physiological outcomes and stability have been measured in skin to skin contact than the same care provided in closed servo-controlled incubators. The presence of the mother is linked to stress modulation and homeostatic control, and supportive of infant's immature autonomic system which orchestrates the physiological stress-response. Heart rate variability (HRV) is a means of quantifying autonomic nervous system activity. Effects of the mother's presence or absence during stressful medical interventions have not been established for infants below 6 months. The practice norm in the research setting of such infants not being accompanied to theatre by their mother, but by a nurse and a porter, presented the opportunity to investigate the physiological effect of possible separation stress in infants before and after anaesthesia and an invasive procedure.

Methods:
A prospective, single blinded, randomized controlled clinical trial was done to investigate the effects of maternal separation on a sample of 8 infants younger than 6 months of age and undergoing surgery. Subjects were recruited prior to surgery and randomized by opaque sealed envelopes. Continuous monitoring of the HRV and impedance cardiograph was added to standardised care, observation and postoperative pain data validated with the mother. Data were analysed without knowledge of the groups.

Results:
There was an increase in autonomic activity with sympathetic activation in infants without their mothers. This research will present the full results of this study and the implications for care of infants in critical care settings.

Title: **IMPACT OF *M. TUBERCULOSIS P*RE-CLEARANCE WITH ISONIAZID (INH) ON T-CELL RESPONSES TO BCG REVACCINATION IN LATENTLY INFECTED ADULTS**

Authors: Sara Suliman[1], Mark Hatherill[1], Hendrik Geldenhuys[1], John L. Johnson[2], Jane E. Hughes[1], Erica Smit[1], Asma Toefy[1], Bernadette Pienaar[1], Phalkun Chheng[2], Thomas Scriba[1], W. Henry Boom[2], Willem Hanekom[1]

Affiliation: [1]South African Tuberculosis Vaccine Initiative (SATVI), Institute of Infectious Disease & Molecular Medicine, and School of Child & Adolescent Health, University of Cape Town, Cape Town, South Africa; [2]Tuberculosis Research Unit, Department of Medicine, Case Western Reserve University and University Hospitals Case Medical Center, Cleveland, OH, U.S.A.

Objective:
Bacille Calmette-Guerin (BCG) is the only effective vaccine against TB, a leading cause of mortality, and is given once at birth in most countries. It is thought that immunity to BCG at older ages may be masked by mycobacterial sensitization due to BCG or exposure to environmental mycobacteria or *Mycobacterium tuberculosis* (*M.tb*). We hypothesized that mycobacterial pre-clearance with isoniazid (INH) would promote T-cell memory responses for optimal boosting by BCG revaccination. This strategy may provide a novel approach to enhance immunity to *M. tb* in latently infected adults.

Methods:
Tuberculin skin test (TST) positive, HIV-seronegative healthy South African adults, who received BCG at birth, were randomized in a phase I clinical trial to either receive 6 months of INH, followed by revaccination with BCG SSI (Statens Serum Institut, Copenhagen) (INH-BCG-Observation: IBO); or to be observed for 7 months, vaccinated with BCG, then treated with INH 6 months later (Observation-BCG-INH: OBI). Whole blood collected at multiple time-points was stimulated with BCG, *M.tb* peptide pools, positive control, or left unstimulated, for analysis of mycobacteria-specific T cell responses by intracellular cytokine staining (ICS). Protocol was approved by the Medicines Control Council (MCC) and University of Cape Town (387/2008).

Results:
Seventy-two participants were enrolled (IBO: n=33, OBI: n=39). We measured intracellular expression of several Th1 and Th17 cytokines in innate (CD56+CD3+ NKT and □□-TCR+ gamma delta) and adaptive (CD4+ and CD8+) T-cells. BCG boosted both Th1 and Th17 cytokine-expressing CD4 T-cells, and IFN-□-expressing CD8, gamma-delta, and NKT cells. Isoniazid treatment did not change frequency of T cells specific to BCG or *M.tb* peptides. Importantly, memory T-cell responses were boosted in both groups following BCG vaccination.

Conclusions:
The study provides a novel opportunity to demonstrate feasibility of boosting immune responses to mycobacterial antigens in TB-endemic areas with whole mycobacterium vaccines. Furthermore, it demonstrates that pre-clearance of latent *M.tb.* infection with isoniazid is dispensable for boosting underlying immunity to mycobacteria. The findings will enhance knowledge of how different interventions modulate the immune response to *M.tb.*, as well as aid in designing optimal intervention approaches in ongoing clinical trials of novel TB vaccines.