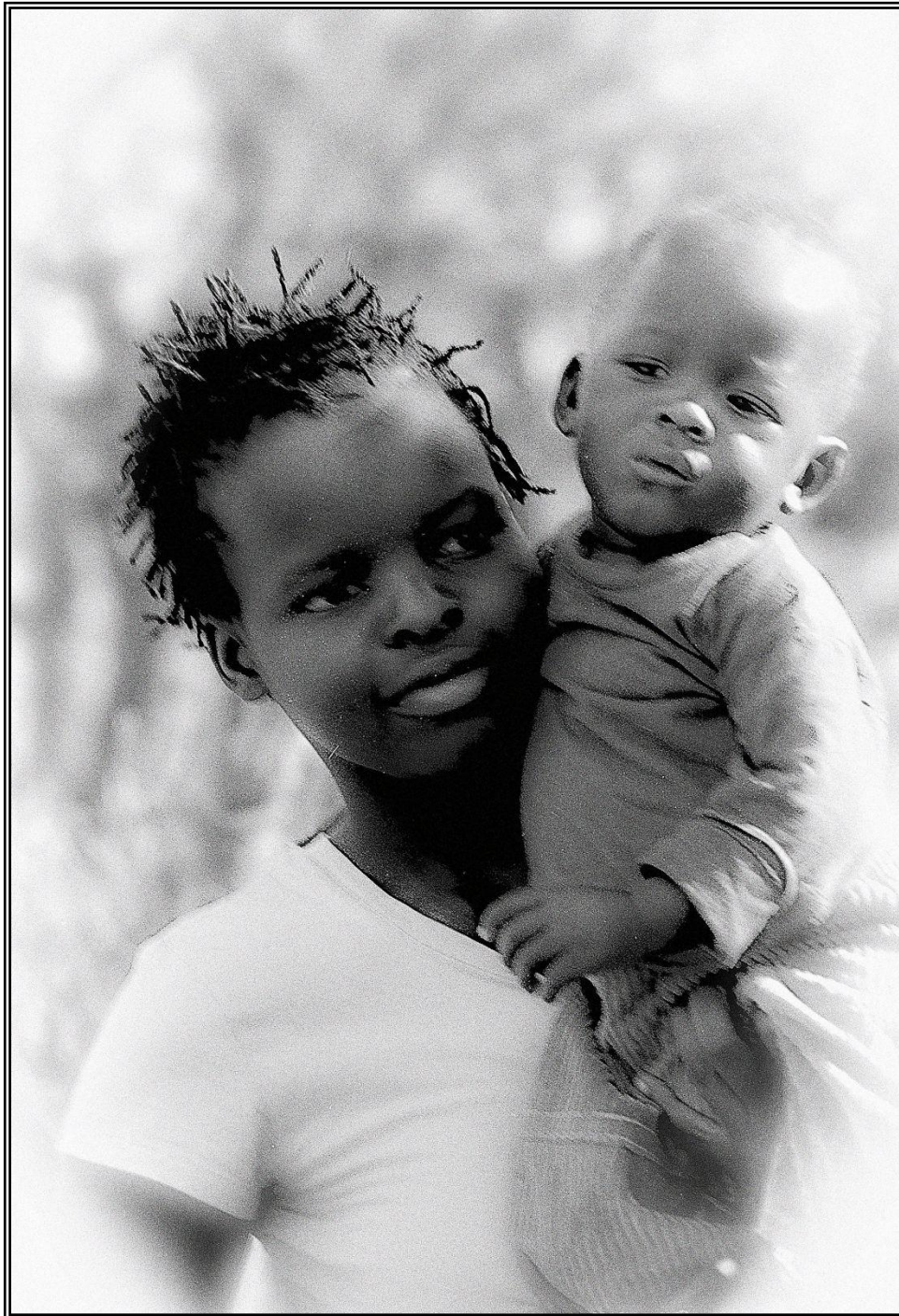




School of Child & Adolescent Health

UNIVERSITY OF CAPE TOWN

ANNUAL RESEARCH DAYS 2011



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## **Programme and Abstract Book**

**11th & 12th October  
D3 Lecture Theatre, D Floor  
Red Cross Children's Hospital**

## CPD Points

Tuesday, 11 October 2011

4 points

Wednesday, 12 October 2011

7 points

Wednesday, 12 October 2011

1 ethics pt

**Please sign the attendance register on both days to claim your points and also the separate register (before Session 6: Wed, 12 Oct) to claim your ethics point.**

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**Title: A PROSPECTIVE, DESCRIPTIVE STUDY TO DETERMINE THE PREVALENCE OF IgE-MEDIATED FOOD ALLERGY IN SOUTH AFRICAN CHILDREN WITH ATOPIC DERMATITIS: REVIEW OF THE FIRST 80 PATIENTS**

**Author:** Dr Claudia Gray

**Introduction and Objectives:**

There is increasing evidence of an association between IgE-mediated food allergy and atopic dermatitis (AD). Studies in Western populations reveal high rates of food sensitisation (50-60%) and allergy (30-40%) to common food allergens in children with AD. This association is strongest in children with early onset and severe eczema. There is great diversity in the ethnic makeup of children in the Western Cape; rates of sensitisation and allergies to foods in these populations are not well documented.

The *primary objective* of our study is to determine the prevalence of IgE-mediated food allergy to common allergenic foods in South African children (6 months-10 years) with AD, attending Red Cross Hospital (RXH) dermatology clinic.

**Method:**

In this prospective observational study, randomly selected children with AD are investigated for food allergies using a questionnaire, skin prick testing (SPT) and food- specific IgE (using immuno solid phase allergen chip-Phadia™). In all cases equivocal for food allergy, children undergo open oral food challenges.

*Sensitisation* is defined as positive SPT / specific IgE; *allergy* is sensitisation + convincing recent history of a reaction or positive food challenge.

The study is approved by the UCT ethics committee (REF 426/2009) and informed consent is obtained from parents.

**Results:**

To date, 80 children have completed the study, 31 of mixed race and 49 Xhosas. Overall **66% of patients showed sensitisation to at least one food**, most commonly egg (52% of patients), peanut (39%) and cow’s milk (25%). **41% of patients had at least one food allergy**, most commonly egg (26% of patients), and peanut (24%). Of the 33 cases of food allergies, 9 were diagnosed by sensitisation and convincing recent allergic symptoms, and 33 by food challenge.

The breakdown patterns for Mixed Race and Xhosa patients are provided in the table below:

	<i>Any sensitivities (%)</i>	<i>Any allergies (%)</i>	<i>Egg sensitised (%)</i>	<i>Egg Allergic (%)</i>	<i>Peanut sensitised (%)</i>	<i>Peanut allergic (%)</i>	<i>Cow’s milk sensitised (%)</i>	<i>Cow’s milk allergic (%)</i>
<i>Mixed race</i>	58%	48%	42%	29%	45%	35%	32%	3%
<i>Xhosa</i>	71%	37%	59%	24%	35%	16%	20%	0%
<i>Total</i>	66%	41%	52%	26%	39%	24%	25%	1%

**Conclusion:**

The prevalence of IgE-mediated food allergy in children with AD attending the RXH Dermatology clinic is high, and comparable with that in westernised countries. These preliminary results suggest that populations previously protected from the food allergy epidemic –such as the Xhosa population-now share equivalent rates of sensitisation and challenge-proven allergy to the westernised countries which led the allergy epidemic. It is of vital importance to differentiate sensitisation from allergy in eczema patients- as only half of sensitised patients are actually allergic.

**Title: SEVERE FOOD ALLERGY REQUIRING ADRENALINE AUTOINJECTORS AT RED CROSS CHILDRENS HOSPITAL**

**Presenter:** Tamara Kerbelker

**Background:**

Food allergy in children has a worldwide prevalence of 2-3%, which is even higher in the first year of life. It has been estimated at 6-8% in westernised countries. There are no studies on the incidence or characteristics of patients with food allergy in unselected populations in South Africa, but it has been reported as being very rare, especially in the Black African population.

Anaphylaxis is a severe life-threatening, generalised or systemic hypersensitivity reaction, which is typically mediated by IgE. There are known risk factors for severe reactions, namely previous severe reactions, poorly controlled asthma, past reactions to trace amounts of allergen and teenage years. Although all food allergens can potentially produce severe reactions, these are most commonly seen with peanut, tree nuts and shellfish. There are no studies on the characteristics of patients with anaphylaxis in South Africa.

**Aim:**

To describe the demographic, clinical manifestations and foods implicated in those patients prescribed adrenaline autoinjectors at Red Cross Food Allergy Clinic

**Method:**

A list of patients who had adrenaline autoinjectors dispensed from Red Cross pharmacy until 10 Sept 2011 was obtained. The folders were reviewed and information captured. Demographic data, type of reaction, food implicated, skin prick test and blood results were extracted.

The presence of comorbid allergic disorders and risk factors for severe reactions was recorded.

**Results:**

There are currently 41 patients at Red Cross who have had an adrenaline autoinjector prescribed. Of these, 2 are for bee venom allergy and therefore were excluded.

The mean age of the patients was 64.8 months (SD 32.49 min 23max 180). Thirty five (89%) were of mixed ancestry, 3 (7%) Black African and 1 white (2%).

Symptoms of anaphylaxis included angioedema and urticaria (n=31; 77%), respiratory arrest (n=2; 5%), airway signs (n=37; 95%) and cardiovascular collapse (n=5; 13%).

The most common food implicated was peanut in 25 patients (64%), followed by cow's milk and egg white in 7 patients each (18%). Tree nut allergy was present in 6 patients (13%), with only 1 patient (2%) allergic to soya. Severe food allergy to fish was seen in 3 patients (7%) and shellfish allergy in 2 (5%) patients.

Multiple food allergies were present in 23 (59%) of patients.

15 (38%) of patients had a history of a reaction to trace amounts of food, and 15 (38%) had previously received adrenaline for a severe food reaction.

None of the patients had mastocytosis or were on beta blockers. 22 (56%) patients were asthmatic.

Allergic comorbidity was present in 34 (89%) patients.

**Conclusion:**

The majority of patients with severe food allergy requiring adrenaline autoinjectors are of mixed ancestry. Peanut allergy is the most prevalent allergen, followed by cow's milk and hen's egg. Multiple foods are implicated in more than half of the patients. The only risk factor present for severe anaphylaxis in our patients is asthma. Almost 90% of patients have allergic comorbidity.



**Title:** DOSE RESPONSE RELATIONSHIP BETWEEN ASCARIS SENSITISATION AND ATOPY AND AIRWAY HYPERRESPONSIVENESS BUT NOT ALLERGIC DISEASES IN AN URBANISING ADOLESCENT AFRICAN POPULATION

**Authors:** Michael Levin<sup>1</sup>, MBChB, FCPaed, DipAllerg, MMed, PhD, Rudzani Muloiwa<sup>2</sup>, MBChB, DCH, FCPaed, MSc (LSHTM), Peter Le Souëf<sup>3</sup>, MBBS, FRACP, MD, Cassim Motala<sup>4</sup>, MBChB, FCPaed, FACAAl, FAAAAI

**Department:** <sup>1</sup>Division of Allergy, Department of Paediatrics, University of Cape Town, Cape Town, South Africa; <sup>2</sup>Division of Ambulatory Paediatrics, Department of Paediatrics, University of Cape Town, Cape Town, South Africa; <sup>3</sup>School of Paediatrics and Child Health, University of Western Australia, Perth, Australia; <sup>4</sup>Division of Allergy, Department of Paediatrics, University of Cape Town, Cape Town, South Africa

**Objective:**

The relationship between sensitisation to helminths and atopy, airway hyperresponsiveness and allergic diseases may differ depending on many factors, including the genes of the population studied. We sought to examine this relationship in an African cohort.

**Methods:**

Urban Xhosa children were tested for ascaris IgE levels, Airway hyperresponsiveness (AHR) by methacholine challenge, atopic sensitisation (skin tests to aeroallergens) and allergic disease (asthma, eczema and rhinitis) assessed by questionnaire.

**Results:**

Ascaris sensitisation was strongly associated with AHR but not with asthma, eczema or rhinitis. Higher levels of ascaris IgE were seen in those with AHR (Wilcoxon ranksum  $p=0.02$ ). There was a dose-response relationship between increasing class of ascaris IgE and increased AHR (Prevalence ratio (PR) 1.75; CI 1.09-2.82).

Ascaris IgE was associated with atopic sensitisation to aeroallergens. Higher levels of ascaris IgE were seen in those with HDM sensitisation (Wilcoxon ranksum  $p<0.001$ ) or grass sensitisation (Wilcoxon ranksum  $p<=0.01$ ). There was a dose-response relationship between increasing class of ascaris IgE and sensitisation to one or more allergen (PR 1.65; CI 1.27-2.13), sensitisation to house dust mites (HDM) (PR 1.79; CI 1.29-2.46) and grass (PR 2.66; CI 1.24-5.71) and number of positive skin prick tests (PR 1.78; CI 1.27-2.49).

Presence of any sensitisation to ascaris was associated with over double the number of positive skin prick tests (0.92 vs 0.42), more than doubling the prevalence of HDM sensitisation (41.5% vs 18.5%) and almost quadrupling the prevalence of grass sensitisation (10.8% vs 2.8%).

**Conclusions:**

Ascaris sensitisation was strongly associated with AHR and with atopy, but not with allergic diseases. Possible explanations might be that the type of ascaris infection that causes high levels of ascaris IgE in this genetic population may also favour the development of atopy or that atopics in Africa have upregulation of their defence system against parasitic infection. These hypotheses are not mutually exclusive.

**Title:** IS NON-THERAPEUTIC ASPIRIN USE IN CHILDREN A PROBLEM IN SOUTH AFRICA?

**Authors:** Kirsten Donald, Susan Hall, Cylene Seaton, Donald Tanyanyiwa

**Background:**

Aspirin should not be used in children except for specific therapeutic reasons. We report on a severely ill infant who had ingested aspirin contained in a traditional medicine and review 21 other patients with pre-admission non-therapeutic salicylate exposure.

**Objectives and methods:**

We reviewed laboratory, clinical and poisons unit records to determine how many children were admitted to our hospital over an 18-month period with evidence of salicylate ingestion not prescribed for therapeutic reasons. We determined the source of the salicylate, elapsed time between ingestion and laboratory assay, morbidity and mortality and final diagnosis.

**Results:**

Twenty-one children meeting our criteria, including 9 under 6 months of age, were admitted during this period. The most prevalent source of salicylate was over-the-counter (OTC) aspirin, but some had reportedly only been given traditional medicines. Nineteen were seriously ill, 4 died and 3 had severe brain injury. Two, initially diagnosed with Reye's syndrome, probably had inherited metabolic disorders. Only 2 patients had salicylate levels that at the time of measurement are normally considered toxic; however, the literature suggests that lower levels may exacerbate illness severity in young children.

**Conclusions:**

We found inappropriate use of OTC aspirin in children that requires explanation. There may be policy implications for the content and presentation of patient information; the incorporation of pharmaceuticals in traditional medicines merits further study. Salicylate toxicity should be considered in children with unexplained metabolic acidosis out of keeping with the severity of their acute illness.

Ethics: HEC REC: 298/2009

**Title:** RETROSPECTIVE REVIEW: SUSPECTED CHILD ABUSE PRESENTING TO RED CROSS CHILDREN'S HOSPITAL'S TRAUMA UNIT IN 2010

**Presenter:** Davies, C.

**Aim:**

Sexual assault is the second most common crime committed against children in South Africa and includes rape, sodomy, indecent assault, child pornography, child prostitution and other sexual offences. The aim of this study was to investigate the number of children presenting to Red Cross Hospital with concerns of possible sexual assault from 2008 to 2010 and to gain a deeper understanding of the complex issues surrounding this problem by an in depth analysis of the data captured from the patients presenting in 2010 with special reference to the demographics, the presentations and types of injuries, the management and complications, the disclosures, the criminal documentation and identifying whether our current protocol is adequate in dealing with these problems.

**Method:**

The study was a descriptive retrospective folder review of all the patients presenting to the trauma unit at the Red Cross Children's Hospital with concerns of possible sexual assault in 2010. The patient folder numbers were obtained from the Child Safe Data Base, which has a record of the admissions to the trauma unit with concerns of sexual assault. The number of patients presenting to medical outpatient department was obtained from the NAI record book. Each folder was analysed and information on basic demographics ( home address, age, race, gender ), admission details ( history of presentation, duration of symptoms, injuries , disclosures and perpetrator information) management and follow up ( medical management, surgical management, pain management and adherence to current protocol) and legal documentation ( crime kit completion, J88 completion and referral to social services) were obtained, collated and evaluated.

**Results**

In 2010 there were a total of 197 children presenting to Red Cross Children's hospital with a primary concern of possible sexual assault. Of these, 129 presented to the trauma unit and 67 presented to MOPD. In 2009 there was a total of 193 and in 2008 there was a total of 164 with similar concerns.

The extensive review of the children presenting to the trauma unit in 2010 revealed the following.

Most of the children came from Mitchells Plain, Gugulethu and Khayelitsha. Of the 129 children, 92.2% (119/129) were girls and 11% (15/129) were boys. 70.5% (91/129) were under the age of 6. There were 28 different types of presenting complaints but the 5 most common included a disclosure of vaginal penetration in 30.2% (39/129), 11 of these 39 children had no other symptoms, PV bleeding in 19.3% (25/129), a primary parental concern of possible abuse in 16% (21/129), a description of fondling in 15.5% (20/129) and PV discharge in 8.5% (11/129). 67% (87/129) presented within 72 hours of the initial concern. In 39.5% (51/129) of the cases the assault was alleged to have occurred at home whilst in 25.5% (33/129) of cases it was alleged to have occurred in the neighbourhood. There were 44 different descriptions of the genital injury, but of importance was the fact that in 30% (39/129) the genital examination was recorded as being normal. 5.4% (7/129) of the children had genital injuries that were so extensive that they had to be repaired in theatre. Genital swabs were taken in 45% (58/129) of the children and only one was positive for NG. 35.6% (46/129) children were started on post exposure prophylaxis. 35.6% (46/129) patients were admitted to the trauma ward awaiting social assessment with no medical or surgical concerns, whilst 42% (54/129) were discharged with an outpatient social work review. 11.6% (15/129) required an anaesthetic either for an initial examination or for repair. On initial blood tests 3 children tested positive for HIV and no children tested positive for syphilis. On the children where data was available, no patient seroconverted for HIV. Crime kits were completed 43.4% (56/129) but there is only confirmation of 26.3% (34/129) J88's were completed in 72.8% (69/96) of cases. Only 6.9% (9/129) of patients were not referred to the social workers, however in 61% (33/54) of cases where the patients were supposed to return for social worker review, the patients appeared to default. In 68% (88/129) of the children there were positive disclosures of assault. In 75% of the disclosures the alleged perpetrator was known to the patient and in 33% of the disclosures the alleged perpetrator was under the age of 17 years, two as young as 5 where the history in both cases was of alleged vaginal penetration. In 50% (65/129) there was no follow up given; however in the remaining patients only 29.6% (19/64) were compliant with their appointments and the hospital protocol, whilst a 17% (11/64) showed partial compliance.

**Conclusion:**

This study highlights some of the complicated issues surrounding child sexual assault. The total hospital numbers reflect both an increasing trend but also a discipline that spans both the surgical and medical departments with respect to both resources and personal. The trauma study highlights a few important aspects, firstly, the fact that girls under the age of five living in our poorest communities are the most vulnerable to sexual assault. Secondly, that the majority of the cases presenting to the trauma unit are acute and that the most common sign is PV bleeding. Thirdly, contrary to international observation only 30% of the genital examinations were reported as being normal and alarmingly in more than 5% the injuries were extensive, something that is also not frequently described in the literature. Fourthly, that a disclosure, which is the most important aspect of the investigation, was positive in 68% of the cases, despite the young age of the victims. Fifthly, in keeping with the international literature the perpetrator is usually known to the victim. The study also highlighted the pressure of this problem on both the trauma unit and the social worker resources and despite many attempts to improve the follow up compliance, the majority of patients remain non compliant.

**Title:**           **RECOGNISING THE 22 DELETION SYNDROME AT RED CROSS HOSPITAL: TOWARDS A CLINICALLY USEFUL SCORING SYSTEM**

**Authors:**       Jason McMaster<sup>1</sup>, Theresa Ruppelt<sup>2</sup>, Rik De Decker<sup>3</sup>

**Department:**   2<sup>nd</sup> year UCT medical student<sup>1</sup>; NHLS Cytogenetics laboratory, Groote Schuur Hospital<sup>2</sup>; Paediatric cardiologist, SCAH<sup>3</sup>

**Objectives:**

1. A review of the phenotypic features of all patients with a FISH-confirmed 22q11.2 deletion at Red Cross War Memorial Hospital (RXH).
2. Previously presented work has shown that this syndrome is under-recognised by approximately 50% at RXH, resulting in potential mismanagement and lack of genetic counselling. The established and commonly used international scoring system (O-score) has been shown to have very poor sensitivity for recognising these patients in our patient population. An attempt is made, by using the above phenotypic features, to develop a more robust scoring system for the selection of patients for FISH (Fluorescent-in-situ-hybridisation) testing for the deletion. This scoring system will be presented and compared to the O-score system.

**Methods:**

A retrospective review of the clinical folders and other case notes of all patients with a positive FISH test for the 22q11.2 deletion, on the NHLS cytogenetics database of the Western Cape was undertaken. The database contained 121 patients. Of these the folders of 92 patients were available for data extraction.

**Results:**

Presenting complaints, clinical diagnoses, including specific congenital heart defects and common and uncommon diagnoses were enumerated. Seventeen diagnoses were found in more than 10% of patients. Congenital heart defects (classed as 1 diagnosis) included a spectrum of 10 distinct lesions. 45 different distinct diagnoses occurred in fewer than 10% of patients.

A two-tiered scoring system for children above and below 2 years old was then developed, based on these results. On review testing against the 92 patients, the system was found to detect 75 of 76 patients (98.6%) below 2 years old, and 13 of 16 (81.2%) children above 2 years old. This scoring system is compared to the O-scores for the same patients.

**Conclusions:**

This, the largest cohort of children with the 22q deletion syndrome described in South Africa, re-emphasises its dizzying phenotypic diversity. However, simple phenotype descriptions are of little utility in clinically identifying these children, and one needs to depend on a simple, yet reliable scoring system. The O-score system is of limited utility in our patient population due to the marked subtlety of the typical facial dysmorphism seen in South African children as opposed to the predominantly Caucasian children that the O-score is based on.

Ethics approval no: REC REF: 204/2002

**Title:** BLOOD GROUP INCOMPATIBLE PAEDIATRIC RENAL TRANSPLANTS – EXPANDING FRONTIERS

**Authors:** McCulloch MI, Mamode N.

**Department:** Evelina Children’s Hospital, Guy’s & St. Thomas’ NHS Foundation Trust, London

**Introduction:**

Patients with renal failure often have to spend many years on dialysis awaiting a renal transplant. This is especially detrimental for children in terms of growth as well as psychological development and schooling. Parents are often willing to donate but may not be the correct blood group

**Methods:**

Describe the progress of 2 paediatric renal transplant recipients from family members who were blood group incompatible

**Results:**

2 patients

	Patient 1	Patient 2
Age (yrs)	8.8	11.3
Gender	M	F
Donor	Mother	Aunt
Blood Group	O	B
Donor Group	A	A
Anti:A titres pre-op	1:64	1:16
Anti-Antibody Rx	Rituximab 1mth prior	Rituximab 1mth prior
Plasmafiltration pre Tx	4 sessions	1 session
Plasmafiltration post-Tx	Nil	Nil
Immunosuppression	Basiliximab, Tacrolimus, MMF, Prednisone	Basiliximab, Tacrolimus, MMF, Prednisone
Complications	Infections	Nil
Renal function post TX	Good @ 6mths	Good @ 1 mth
Current Titres post-Tx	1:4	1:4

**Conclusion:**

Following the successful use of ABO incompatible renal donors in over 60 Adult patients at Guy’s Adult Renal unit, we have now successfully performed the first 2 Paediatric renal transplants in the UK using blood group incompatible donors. This will expand the donor pool and hopefully reduce the transplant waiting times particularly in children.

**Title:** **ASSESSMENT FOR RENAL TRANSPLANT FEASIBILITY:  
Validity of a scoring system based on selection criteria devised for use at  
the Red Cross Childrens' Hospital**

**Authors:** Gajjar P, Collison N, Abdo T, Hoogersvorst L, Henley L, Beatty D, Nourse P

**Introduction:**

To improve our decision-making around selecting suitable transplant recipients, we have developed a list of selection criteria. Previously these were loosely applied with inconsistency and lack of objectivity. The criteria are: (1) medical factors, (2) caregivers, (3) family and social support, (4) financial resources, (5) housing, (6) recipients' cognition and development, (7) compliance record and (8) access to health care. A simple scoring system out of 16 is devised.

**Aim:**

To validate the listing criteria and the scoring system retrospectively against patients assessed for transplant between Jan 2009 and March 2011.

**Method:**

The case notes and social work reports of these patients were accessed. The criteria were applied systematically and the scores were correlated to whether the patient was listed for transplant; they were analysed to obtain a reasonable cut off score for listing, and the relevance of each category was evaluated.

**Results:**

Of the forty patients included, eight were previously transplanted. The mean age was 10.6 years. The mean score for those listed was 13.8, cf. 9, for not. This was statistically significant (p-value of <0.0001). A score of 11.5 showed a 95.45% sensitivity and 94.4% specificity for listing.

The criteria, caregiver (p-value <0.0001), compliance record (p-value <0.0001) and recipients cognition and development (p-value 0.0013) showed a significant association.

**Conclusion:**

The list of criteria used better defines the more implicit assessment process previously used. However, to ensure reliability, the criteria have to be applied consistently. Areas of vulnerability that might impact on outcome can easily be identified. The scoring system is valid, and can be improved by different weighting applied to some criteria. It will be interesting to prospectively correlate the scores to outcome.

**Title: BACTERAE MIC *KLEBSIELLA PNEUMONIAE* INFECTIONS IN HOSPITALISED CHILDREN AT RED CROSS WAR MEMORIAL CHILDREN'S HOSPITAL (RCWMCH) OVER A 4-YEAR PERIOD 2007-2010**

**Authors:** H Buys<sup>1</sup>, C Bamford<sup>2</sup>, K Kranzer<sup>3</sup>, E Madikane<sup>2</sup>, A Whitelaw<sup>2</sup>, K Reichmuth<sup>1</sup>  
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**Department:** <sup>1</sup>Red Cross War Memorial Children's Hospital and Department of Paediatrics, University of Cape Town. <sup>2</sup>Division of Clinical Microbiology, National Health Laboratory Services, and University of Cape Town. <sup>3</sup> London School of Hygiene and Tropical Medicine, London, UK

Extended spectrum beta lactamases (ESBLs) produced by *Klebsiella pneumoniae* (KP) and other gram negative bacilli cause multi-drug resistance. The aim of this study was to describe bloodstream KP infections in children hospitalised at RCWMCH between January 2007 and December 2010.

**Methods:**

A retrospective case notes review was conducted using conventional descriptive and comparative statistical methods.

**Results:**

Over the study period there were 290 hospitalised children with bacteraemic KP; 250 infections (86%) were ESBL-associated; 18 infections (6%) were community-acquired and 272 (94%) institution-associated. Infection rates per 10,000 hospital admissions are shown in the table. Baseline characteristics: median age (interquartile range): 5.0 (1.7, 15.0) months, 69% were below 12 months of age; gender: F: M: 146:144; HIV status: HIV uninfected: 142 (49%), HIV infected: 64 (22%), unknown status: 84 (29%); nutrition status: 84 (48%) were moderately or severely underweight. Possible risk factors: 135 (47%) of the children were hospitalised in the preceding month; 126 (44%) were treated with broad-spectrum antibiotics in the preceding 12 months, 61 (21%) acquired their infection in PICU, having been located in PICU for a median (IQR) of 6 (3-16) days prior to the diagnostic blood culture. Outcome: 204 children (70%) were discharged well and 86 (30%) died; septicaemia was the common cause of death accounting for 67 (78%) of all deaths. The median (IQR) time between KP diagnosis and death was 3 (1-12) days; the median age (IQR) of children who died was 4 (1.1-12.6) months; 27/86 (31%) of those who died were HIV-infected vs 37/204 (21.6%) survivors, p=0.01, RR=1.73 (95% CI: 1.13, 2.65); 53/86 (61.6%) who died were underweight vs 98/204 (48%) who survived, p=0.03, RR=1.28 (95% CI: 1.03, 1.60)

Year	Total number of hospital admissions	Number of KP bacteraemic episodes	KP infection rate	ESBL-associated KP infection: number (rate)	Non-ESBL-associated KP infection: number (rate)
2007	21 510	51	23.7	43 (20)	8 (3.7)
2008	21 600	73	33.8	64 (29.6)	9 (4.2)
2009	22 943	86	37.5	77 (33.6)	9 (3.9)
2010	22 731	80	35.2	66 (29)	14 (6.2)

All rates expressed as number of infections per 10,000 hospital admissions

**Conclusion:**

These provisional results suggest that ESBL- KP has become an important cause of nosocomial bacteraemic infection at our hospital and is associated with high morbidity and mortality.

**Title:** SAFETY OF PROLONGED ISONIAZID PREVENTIVE THERAPY IN CHILDREN WITH HIV: A COMPARISON OF TWO DOSING SCHEDULES

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<sup>3</sup> Department of Paediatrics and Child Health, Stellenbosch University, Cape Town, South Africa;  
<sup>4</sup> Biostatistics Unit, Medical Research Council, South Africa

**Objective:**

To investigate the incidence of and risk factors for severe liver injury in HIV-infected children receiving prolonged isoniazid preventive therapy (IPT).

**Methods:**

HIV-infected children aged  $\geq 8$  weeks enrolled in a placebo-controlled, randomized trial of IPT (given with trimethoprim-sulphamethoxazole, daily or thrice weekly) in Cape Town, South Africa. Placebo was terminated early; IPT was given for up to 5 years. Alanine aminotransaminase (ALT) was measured at baseline, 6-monthly and during intercurrent illness; severe liver injury was defined as a  $\geq 10$ -fold increase from the upper limit of normal. Risk factors were assessed with incidence rate ratios (IRR) and hazard ratios from Cox proportional hazards regression.

**Results:**

Of 324 children enrolled, 159 (49%) received daily prophylaxis. At enrolment, median age was 23 months (IQR 9.5-48.6) and median CD4%, 20% (IQR 13.6-26.9). Placebo was given for 58.8 and IPT for 559.1 person-years; 207 (63.9%) children received combination antiretroviral therapy (cART). The median baseline ALT was 28 U/l (IQR 18-42). There were 19 episodes of severe liver injury: 16 occurred on IPT [incidence rate (IR) 2.86/100 person-years], versus 1 on placebo (IR 1.7/100 person-years; IRR 1.68, 95% CI 0.3-70.6); 2 occurred on anti-tuberculosis treatment. Children receiving IPT with cART had similar rates of severe liver injury compared to those receiving cART only (IRR 0.29, 95% CI 0.39– 12.88). Infants [adjusted hazard ratio (aHR) 3.20, 95% CI 1.27-9.47] and those with higher CD4% (aHR 1.06, 95% CI 1.01-1.12) were at increased risk. However, 14/19 (74%) events were unrelated to IPT. The incidence of IPT-related severe liver injury was 0.78/100 person-years. One child died of an unrelated cause. None had hepatic failure. All surviving children successfully restarted IPT.

**Conclusion:**

Prolonged IPT is safe in HIV-infected children.

*Ethics approval number: REC REF 057/2002*



**Title:** ACCURACY OF THE XPERT MTB/RIF TEST FOR THE DIAGNOSIS OF PULMONARY TUBERCULOSIS IN HOSPITALIZED CHILDREN IN A HIGH HIV-PREVALENCE AREA – A PROSPECTIVE STUDY

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**Department:** Division of Medical Microbiology and Institute for Infectious Diseases and Molecular Medicine, University of Cape Town, National Health Laboratory Service, Groote Schuur Hospital, Cape Town, South Africa (MP Nicol, W Zemanay,) Department of Paediatrics and Child Health, University of Cape Town and Red Cross War Memorial Children's Hospital, Cape Town, South Africa (HJ Zar, F Black, W Isaacs, J Munro, B Eley, L Workman) Foundation for Innovative New Diagnostics (FIND), Geneva, Switzerland (CC Boehme)

**Background:**

The World Health Organization recently recommended that the Xpert MTB/RIF test (Cepheid, Sunnyvale, CA, USA) replace smear microscopy for initial diagnosis of suspected HIV-associated TB or multidrug-resistant pulmonary TB (PTB). However, there are no published data in children.

**Aim:**

To investigate the accuracy of MTB/RIF for the diagnosis of PTB in hospitalized children.

**Methods:**

Children hospitalised with suspected PTB in Cape Town, South Africa, a high TB and HIV prevalence area were enrolled from Feb 2009 to Nov 2010. The diagnostic accuracy of MTB/RIF and concentrated, fluorescent acid fast smear was compared with a reference standard of liquid culture from two sequential induced sputum (IS) specimens.

**Results:**

452 children (median age 19.4 months) had at least one IS specimen; 108 children (23.9%) were HIV-infected. The number of children with a positive smear, culture or MTB/RIF was 27 (6%), 70 (16%) and 58 (13%) respectively. Using mycobacterial culture as the reference standard, two MTB/RIF tests detected twice as many cases (75.9%, 95% CI 64.5 – 87.2) as smear microscopy (37.9%, 95% CI 25.1 – 50.8) including all 22 smear-positive cases and 22 of 36 (61.1%, 95% CI 44.4 – 77.8) of smear-negative cases. For smear-negative cases, the incremental increase in sensitivity from testing a second specimen was 27.8% for MTB/RIF and 13.8% for culture. The specificity of MTB/RIF was 98.8% (95% CI 97.6 – 99.9). MTB/RIF provided more rapid results than culture (median time to positive MTB/RIF 1 day compared to 12 days for culture,  $p < 0.0001$ ).

**Conclusion:**

MTB/RIF testing of two IS specimens is warranted as the first-line diagnostic test for children with suspected PTB.

*Funding:* NIH RO1HD058971-03, USA, MRC South Africa

**Title:** THE USE OF PREMEDICATION FOR NEONATAL INTUBATION

**Authors:** L Boshoff, L Tooke and M C Harrison

**Department:** Neonatal Medicine, Department of Paediatrics, University of Cape Town

**Background:**

Endotracheal intubation is frequently performed in the Neonatal Unit (NICU). It is standard practice to use premedication for intubation in the older Paediatric population, however non sedated intubation of neonates is still accepted practice. This is despite mounting evidence that the procedure is painful, stressful and potentially has long term harmful effects. The adverse physiologic consequences of laryngoscopy and intubation can be attenuated with the appropriate use of premedication.

There has been a shift in clinical practice with regard to the use of premedication for neonatal intubation in many countries and the trend is towards its more frequent use.

Current international recommendations state, that for optimal intubating conditions, a vagolytic agent, followed by an analgesic and/or hypnotic agent and thereafter a muscle relaxant is required. There are no published data in the literature that reflect South African practice.

There is an existing protocol with regards to the use of premedication for intubation in our NICU which is in keeping with current international norms.

**Objective:**

To determine whether babies in the NICU at Groote Schuur Hospital are receiving adequate premedication prior to intubation for elective or semi- urgent intubation.

**Methods:**

Data was collected over a period of three months on all babies admitted to NICU for elective or semi-urgent ventilation. Excluded from the study were patients transferred from other hospitals, patients receiving in-out surfactant and emergency intubations in the labour ward. Data were obtained from nursing notes, medical notes, drug charts and collected in a structured proforma. Examples of data collected: gestational age, weight, reason for intubation, type of premedication used, dosage and dosage times, notes on intubation procedure. Data analysis was done on Excel.

**Results:**

A total of 40 patients were observed during the study period. Of these patients, 78% received some form of premedication. Of patients that were premedicated, only 23% received an analgesic, vagolytic and muscle relaxant as currently recommended. In many instances an inadequate dose of a drug was administered. There was documentation regarding the intubation procedure in the patient medical records in only 65% of cases.

**Conclusion:**

Despite existing guidelines in our NICU, we are using suboptimal regimes when performing elective intubations. Better awareness of existing guidelines is needed. The importance of adequate note keeping should be reinforced.

Ethical approval was obtained - HREC REF: 390/2011

**Title:** **GROWTH VELOCITY OF EXTREMELY LOW BIRTH WEIGHT (ELBW) PRETERM INFANTS AT GROOTE SCHUUR HOSPITAL NURSERY**

**Authors:** M O Lango, A R Horn and M C Harrison

**Department:** Neonatal Medicine, Department of Paediatrics, University of Cape Town

**Background:**

There is wide variation in the feeding practices of extreme low birth weight (ELBW) preterms often guided by tradition and resources. The feeding regimen at Groote Schuur Hospital (GSH) nursery follows a restricted use of parenteral nutrition and concentrates on early introduction of breast milk. There is a need to determine if this approach achieves acceptable growth velocity.

**Objective:**

This study aims to describe the growth velocity of ELBW babies at GSH nursery.

**Methods:**

Infant hospital records of all ELBW born at GSH from 1<sup>st</sup> March to 31<sup>st</sup> August 2010 were accessed from a previously collected database and relevant data extracted. Growth data was collected from birth to 8 weeks post natal age or discharge, whichever came first.

**Results:**

Ninety one ELBW babies were born during the study period. Forty were excluded from the study. Thirty died before discharge and 10 were excluded for other reasons. The mean (SD) gestation of the cohort was 28.5 (1.6) weeks and the median (range) birth weight was 875(640 to 995) g. The overall mean (SD) growth velocity was 14 (2.9) g/kg/day. There was no statistically significant association between the growth velocity and the type of feed given, days to establishing full enteral feeds, time to regaining birth weight, HIV exposure status, intra-uterine growth restriction or exposure to antenatal steroids.

**Conclusion:**

In our cohort of ELBW infants, growth velocity was within the range currently deemed acceptable by international consensus.

Ethical approval was obtained - HREC REF: 088/2010

**Title:** THE RISK OF MATERNAL HIV TRANSMISSION TO EXTREMELY LOW BIRTH WEIGHT (ELBW) INFANTS

**Authors:** L Tooke, Y Joolay, S Raban, N Rhoda, A R Horn and M C Harrison

**Department:** Neonatal Medicine, Department of Paediatrics, University of Cape Town

**Background:**

Mother to child HIV transmission occurs by three main routes: during pregnancy, peri-natally and through breastfeeding. Evidence shows that prematurity increases the peri-natal HIV transmission rate compared to term infants.

There is sparse literature documenting the transmission of HIV to the ELBW (<1000g) group of babies who are presumably at the greatest risk of acquiring peri-natal HIV. One of the reasons for the paucity of information may be that countries with high prevalence of HIV often also have high neonatal mortality rates and these babies usually do not survive.

The maternal HIV infection rate for all mothers delivering at Groote Schuur Hospital (GSH) is 16% and the survival rate for inborn ELBW infants cared for at GSH nursery is 68%. The unit is therefore uniquely placed to investigate mother to child HIV transmission in these infants.

**Objective:**

To determine the risk of transmission of HIV to ELBW infants born to HIV infected mothers at Groote Schuur Hospital nursery.

**Methods:**

A prospective database was maintained on all inborn ELBW infants over a 1 year period from March 2010 till February 2011. Data collected included variables such as birth weight, estimated gestational age, method of delivery, maternal and infant antiretroviral (ARVs) treatment. Outcomes in terms of survival and HIV PCR results were recorded.

DNA PCR was done on all exposed babies at 6 weeks of age.

**Results:**

There were a total of 180 ELBW infants included in the study. Fifty one (28%) of these babies were HIV exposed with a mean weight of 834g (range 485-1000g) and mean gestational age of 28.3 weeks (range 25-33 week). Of the 51 infants who were HIV exposed, 37 survived. PCR testing at 6 weeks of age revealed one positive HIV infant with 36(97.3%) babies testing negative. Twenty six (74%) of the mothers had received some PMTCT, but only 16/35 (46%) had been on HAART or prophylaxis for more than a month.

The infant who became HIV positive was the first born of a set of twins. The mother was not on ARVs and arrived in advanced preterm labour, delivering her babies vaginally.

**Conclusion:**

The rate of HIV transmission to this cohort of ELBW infants is low (2.7%) given their extreme prematurity and the fact that only 46% of the mothers had been on adequate ARVs. Transmission levels approach those quoted in developed countries (<2%) for term babies. We postulate that this is due to our high semi - elective (89%) Caesarian section rate, universal (100%) infant prophylactic ARVs and the exclusive use of pasteurized breast milk in this cohort of infants.

**Title:** THERAPEUTIC HYPOTHERMIA AND HYPOXIC ISCHAEMIC ENCEPHALOPATHY: OPINION AND PRACTICE OF SOUTH AFRICAN PAEDIATRICIANS

**Authors:** Y Joolay, M C Harrison and A R Horn

**Department:** Neonatal Medicine, Department of Paediatrics, University of Cape Town

**Background:**

Therapeutic hypothermia (TH) has recently been recommended as a treatment to reduce long-term neurological deficit in hypoxic ischaemic encephalopathy (HIE) survivors and is emerging as a standard of care in the developed world. International surveys in the last two years show that TH is emerging as a standard of care in the developed world and there is now consensus that TH should be used if neonatal intensive care facilities are available. The varied resources in South Africa may present difficulties in the implementation of this therapy.

**Objective:**

To determine South African Paediatricians' opinions and practice regarding therapeutic hypothermia and general practice with respect to the management of HIE.

**Methods:**

Two hundred and eighty eight South African Paediatricians and Neonatologists were invited by email to participate in a web-based survey. Practitioners were identified using the Medpages<sup>TM</sup> database.

**Results:**

Responses were received from 37.8% of the emails. Seventy-six percent of respondents stated that hypothermia was either effective or very effective while 4% stated TH was ineffective in the management of HIE. Forty-two percent of respondents offered TH, 9% transferred patients to other units for cooling, 24.5% did not offer TH but planned to institute the treatment and 24.5% did not use TH nor planned to introduce it into practice in the near future. Ninety-eight percent of respondents stated TH should be the standard of care in tertiary neonatal units. Total body cooling was the TH method of choice by 93% of respondents. Only 60% of respondents used electrical brain monitoring, but 93.5% used brain imaging. Phenobarbital was used by 90% of respondents as a first line anticonvulsant but 35% stated that they used it prophylactically.

**Conclusion:**

Most South African Paediatricians surveyed stated that TH is effective to reduce the neurological deficit in HIE, however less than half offered it as a treatment.

Ethical approval was obtained - HREC REF: 478/2010

**Title:**           **PROPORTIONS OF MYELOID AND LYMPHOID CELLS IN PERIPHERAL BLOOD ARE ASSOCIATED WITH PROSPECTIVE RISK OF TB DISEASE IN HEALTHY INFANTS**

**Authors:**       Elisa Nemes, Helen A Fletcher, Alana Keyser, Abdelali Filali-Mouhim, Jean-Philippe Goulet, Rachel Tanner, Thomas J Scriba, Cheong Kwet Choy Kwong Chung, Benjamin Kagina, Renaud Gaujoux, Anthony Hawkrige, Jane Hughes, Sebastian Gelderbloem, Cathal Seoighe, Hassan Mahomed, Helen McShane, Adrian VS Hill, Gilla Kaplan, Gregory D Hussey, Rafick-Pierre Sekaly, Willem A Hanekom.

**Background:**

We recently completed a study of correlates of risk of TB disease in healthy 10 week-old infants who were routinely vaccinated with BCG at birth. In an assessment of global gene expression profiles in PBMC, we observed that upregulation of genes associated with myeloid cells, at the expense of T cells, were associated with strong *in vitro* responsiveness to BCG and risk of developing TB disease.

**Objective:**

To assess whether peripheral blood proportions of myeloid and lymphoid cells in 10 week-old infants confirm our results of gene expression.

**Methods:**

Blood was obtained from 5,675 10 week-old healthy infants. During 2 years of follow-up, we identified children who developed culture-positive pulmonary TB (cases), and those who did not, despite exposure to adults with active TB (controls). We selected cases and controls whose gene expression profiles were predictive of clinical outcome. PBMC were thawed and immediately stained with fluorescent monoclonal antibodies to identify monocytes, dendritic cells, T and B cells. Samples were acquired on a LSRII flow cytometer and analyzed with FlowJo. Groups were compared using Mann-Whitney test.

**Results:**

We found that strong BCG responders, previously identified on the basis of gene expression profiles in response to BCG stimulation *in vitro*, had higher frequencies of CD14+ monocytes and higher myeloid to lymphoid cell ratios, compared with weak BCG responders. Within the strong BCG responder group, higher frequencies of CD14+ monocytes and higher myeloid to lymphoid cell ratios were associated with prospective risk of TB disease. The opposite was observed in infants who were weak BCG responders.

**Conclusions:**

As predicted by the global gene expression profiles, proportions of myeloid and lymphoid cells in peripheral blood are associated with *in vitro* differential responsiveness to BCG vaccine and prospective risk of TB disease in healthy infants.

Ethic approval number: University of Cape Town HREC 016/2001

Support: National Institutes of Health (grant RO1- AI065653), European and Developing Countries Clinical Trial Partnership, Aeras Global Tuberculosis Vaccine Foundation, and Bill & Melinda Gates Foundation.

**Title:** **FREQUENCIES OF SPECIFIC TH1 CELLS ARE SURROGATES OF DIFFERENTIAL RESPONSIVENESS TO BCG VACCINATION IN INFANTS**

**Authors:** Samuel Njikan, Elisa Nemes, Thomas Scriba, William Msemburi, Benjamin Kagina, Alana Keyser, Brian Abel, Elizabeth J Hughes, Andreia Soares, Hoyam Gamielien, Mzwandile Sidibana, Mark Hatherill, Sebastian Gelderbloem, Hassan Mahomed, Anthony Hawkrigde, Helen Fletcher, Gregory Hussey, Gilla Kaplan and Willem Hanekom.

**Background:**

We are studying correlates of risk of TB disease, which could guide future identification of correlates of protection. We collected and stored blood from 5,675 healthy infants at 10 weeks of age, following routine vaccination with BCG at birth. During 2 years of follow-up, infants who developed culture-positive pulmonary TB were considered at risk of TB disease (cases), while those who remained healthy despite exposure were considered not at risk of TB disease (controls). We measured a comprehensive array of T cell functions as potential correlates of risk of TB, including Th1 cytokine expression, cytotoxic capacity and lymphoproliferation. None of these outcomes were significantly different between cases and controls. However, when global gene expression profiles were analysed by microarray technology, we observed that some infants appeared to respond strongly to BCG (“BCG strong responders”), while others were weak responders to the vaccine (“BCG weak responders”).

**Objective:**

To determine whether frequencies of BCG-specific Th1 cytokine expressing CD4 T cells are different in BCG strong and weak responders and whether this differential responsiveness masks T cell correlates of risk of TB. We hypothesised that differential responsiveness to BCG masks T cell correlates of risk of TB disease.

**Method:**

We developed a logistic regression model to identify which T cell functions associated with strong or weak BCG responsiveness, as defined by gene expression profiles. We then applied the regression model classifier to a test set of new infants to identify strong and weak BCG responders, and subsequently assessed whether T cell outcomes within strong responders differed between cases and controls (Mann-Whitney test).

**Results:**

A model incorporating frequencies of CD4 T cells expressing IFN- $\gamma$ , TNF- $\alpha$  and IL-2, quantified by flow cytometry after BCG *in vitro* stimulation, allowed classification of strong and weak BCG responders with a specificity and sensitivity of 84.62% and 97.74%, respectively. 90.63% of infants were correctly classified using this model, when benchmarked against classification by gene expression profiles.

Amongst strong BCG responders, frequencies of total CD4 T cells expressing either IL-2, IL-17 or IFN- $\gamma$  were significantly different between cases and controls. Frequencies of CD4 T cells co-expressing the cytotoxic markers granulysin and granzyme B, CD8 T cells expressing only granulysin, and soluble levels of eotaxin and IL-12p40, were also different in cases and controls.

When we performed the same analyses in a test cohort of cases and controls for validation purposes, none of these markers could be validated as correlates of risk of TB disease.

**Conclusions:**

Classic Th-1 cytokines are surrogates of BCG responsiveness in 10 week old infants, but these outcomes are not correlates of risk of TB disease.

Ethic approval number: University of Cape Town HREC 016/2001.

Funding: National Institutes of Health (grant RO1- AI065653), European and Developing Countries Clinical Trial Partnership, Aeras Global Tuberculosis Vaccine Foundation, and Bill & Melinda Gates Foundation

**Title: DOSE-DEPENDENT IMMUNE RESPONSES TO NOVEL TUBERCULOSIS VACCINE, AERAS-402, ON MYCOBACTERIA-SPECIFIC CD4<sup>+</sup> AND CD8<sup>+</sup> T CELLS IN HEALTHY INFANTS PREVIOUSLY VACCINATED WITH BCG**

**Authors:** Benjamin M. N. Kagina<sup>1</sup>, Michele Tameris<sup>1</sup>, Brian Abel<sup>1</sup>, Nazma Mansoor<sup>1</sup>, Thomas J. Scriba<sup>1</sup>, Jane Hughes<sup>1</sup>, Marwou de Kock<sup>1</sup>, Wendy Whatney<sup>1</sup>, Hadn Africa<sup>1</sup>, Colleen Krohn<sup>1</sup>, Linda van der Merwe<sup>1</sup>, Hennie Geldenhuys<sup>1</sup>, Anthony Hawkrigde<sup>1</sup>, Ashley Veldsman<sup>1</sup>, Mark Hatherill<sup>1</sup>, Giulia Schirru<sup>2</sup>, Maria Grazia Pau<sup>2</sup>, Jenny Hendriks<sup>2</sup>, Gerrit JanWeverling<sup>2</sup>, Jaap Goudsmit<sup>2</sup>, Donata Sizemore<sup>3</sup>, J. Bruce McClain<sup>3</sup>, Margaret Goetz<sup>3</sup>, Jacqueline Gearhart<sup>3</sup>, Margaret A. Snowden<sup>3</sup> David A. Hokey<sup>3</sup> Tom Evans<sup>3</sup>, Hassan Mahomed<sup>1</sup>, Gregory D. Hussey<sup>1</sup>, Jerald C. Sadoff<sup>2</sup> and Willem A. Hanekom<sup>1</sup>  
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**Background:**

Infants and children have higher risk of developing TB disease than adults. Efforts to increase protection against TB in children include development of new and effective TB vaccines. Of the novel TB vaccines currently in clinical trials, only MVA85A has been tested in infant populations. A second TB vaccine, Aeras-402, is undergoing tests in the infant populations. We investigated whether administration of different doses of Aeras-402 is safe and immunogenic in infants in a heterologous prime-boost vaccination strategy.

**Methods:**

In a phase I, double-blinded, randomized controlled study, escalating doses of Aeras-402 were administered intramuscularly to 40 healthy infants who were at least six months old and previously vaccinated with BCG. Starting with the lowest Aeras-402 dose ( $1.5 \times 10^8$  viral particles), group 1 infants were randomized to receive the study vaccine or placebo at day 0. Upon satisfactory review of the safety experience in group 1 participants, enrollment progressed sequentially to the next higher doses for group 2 ( $1.5 \times 10^9$  viral particles), then group 3 ( $1.5 \times 10^{10}$  viral particles) and then group 4 ( $1.0 \times 10^{11}$  viral particles). Participants in groups 1, 2 and 3 received a single shot of the Aeras-402 or placebo on day 0 while group 4 received two doses at days 0 and 56. Bloods collected from the participants at days 0, 28, 84 (group 4 only) and 182 were used to characterise Aeras-402-induced CD4<sup>+</sup> and CD8<sup>+</sup> T cell immunity by a short-term whole blood intracellular cytokine staining assay. Comparisons of the specific T cell response were made either between the Aeras-402- and the placebo-vaccinated infants or at pre and post vaccination time points for all infants groups.

**Results:**

The Aeras-402-induced T cell response was highest at day 28 post-vaccination. Specific CD4<sup>+</sup> T cells dominated the vaccine-induced T cell response. Aeras-402-induced T cell response persisted up to day 182, but only after two vaccinations with the highest dose. Double vaccination with the highest dose induced a desirable mycobacteria-specific polyfunctional CD4<sup>+</sup> T cells whereas single low dose Aeras-402 vaccination induced a dominant monofunctional CD4<sup>+</sup> T cells. Regardless of the dose, Aeras-402 vaccination did not induce specific CD4<sup>+</sup> T cells co-expressing IL-17 with any of the type 1 cytokines. The magnitude of pre-existing mycobacteria-specific T cells was associated with the magnitude of vaccine-induced T cell responses. However, fold increases to Aeras-402-induced T cells were lower in presence of higher pre-existing mycobacteria-specific T cells.

**Conclusions:**

Aeras-402 is immunogenic when administered as a boost vaccine in healthy infants previously vaccinated with BCG at birth. Double vaccination with the highest dose induced polyfunctional CD4<sup>+</sup> T cells that were persistent. This is a promising finding as mycobacteria-specific polyfunctional CD4<sup>+</sup> T cell response is thought to be important for protection against intracellular pathogens, like *M.tuberculosis*, which causes TB.

-Ethics approval: Rec Ref: 289/2008



**TITLE:** **INCIDENCE OF TB IN ADOLESCENTS IN A HIGH TB BURDEN AREA**

**Authors:** H Mahomed, M Hatherill

**Department:** South African TB Vaccine Initiative, Institute of Infectious Disease and Molecular Medicine and School of Child and Adolescent Health, University of Cape Town, Cape Town, South Africa

**Background:**

TB incidence peaks in early childhood, drops during the school going years and starts increasing again in early adolescence. Little is known about the epidemiology of TB in adolescents who are a potential target for TB vaccines.

**Objective:**

To determine the incidence of TB in adolescents in a high TB burden area.

**Methods:**

A cohort of adolescents aged 12-18 were recruited from high schools in Worcester and surrounds. All subjects were screened at baseline for tuberculosis disease and infection and followed up for two to four years for incident cases. About half of participants were seen three monthly and the other half seen only at baseline and at a two year visit.

**Results:**

6,363 (58.2%) of 10,942 adolescents agreed to participate with 22 to 74% of school pupils participating per school. 55% of participants were TST positive ( $\geq 5$ mm) at baseline and 51% were QuantiFERON positive. 22 adolescents were on TB treatment at entry to the study and 21 were diagnosed through study screening procedures giving a prevalence of 676/100 000. 82% of participants were seen at two year follow up. There were 13 deaths giving a mortality rate of 0.2%. There were 67 TB incident cases which met the protocol definition (2 positive smears or at least one positive culture) during follow up giving an incidence rate of 453/100 000 person years of follow up. There was no significant difference in TB incidence detection between those followed up three monthly and those seen only for a baseline and two year visit.

**Conclusions:**

High TB infection rates and diseases rates are reported in adolescents in a high TB burden area. There was reasonably good cohort retention and a low mortality rate. Frequent visits did not significantly improve case detection.

Ethics approval number: 045/2005

**Title:** CHARACTERIZATION OF *MYCOBACTERIUM TUBERCULOSIS*-SPECIFIC CD8+ T-CELL RESPONSES IN INDIVIDUALS WITH LATENT AND ACTIVE TUBERCULOSIS

**Authors:** Noella Moshi, Deborah-Ann Abrahams, Michele van Rooyen, Terrence O'rie, Marwou de Kock, Willem A. Hanekom, Cheryl L. Day

**Department:** South African Tuberculosis Vaccine Initiative (SATVI), School of Child and Adolescent Health, Institute of Infectious Diseases and Molecular Medicine, Faculty of Health Sciences, University of Cape Town, Observatory 7925, South Africa.

**Objective:**

The aim of this study was to determine the phenotypes of *Mycobacterium tuberculosis* (MTB)-specific CD8 T cells in adults with latent MTB infection (LTBI) and active tuberculosis (TB) disease, in order to better understand the role of CD8 T cells in control of MTB infection. We hypothesized that activated MTB-specific CD8 T cells in individuals with TB would display an effector phenotype with a high rate of turnover, and be more prone to apoptosis, compared with LTBI.

**Methods:**

A multiparameter flow cytometry panel was designed and optimized to assess cell turnover, susceptibility to apoptosis and terminal differentiation/senescence in CD8 T cells from TB and LTBI donors. After short-term stimulation with immunodominant MTB peptide pools *ex vivo*, Bcl-2, Ki67, CD95, CD57, CD127 and IFN $\gamma$  expression was measured in each group, and the antigen-specific CD8 T cells were compared to the total CD8 T cell population.

**Results:**

Bcl-2 and CD57 expression were increased in the total CD8 T cell population in individuals with TB disease, compared with LTBI, which may be due to inflammatory-mediated alterations of the tissue microenvironment. CD127 expression was increased on MTB-specific CD8 T cells, compared with the total CD8 T cell population, in individuals with LTBI, but not TB, suggesting preservation of memory capacity in the context of successful immune control of MTB infection. Preliminary results suggest that initiation of anti-TB treatment may reverse the phenotype seen in TB disease, implying that MTB-specific CD8 T cell phenotype is associated with mycobacterial antigen load.

**Conclusion:** These data suggest that MTB-specific CD8 T cells from individuals with TB have a short-lived effector phenotype compared with MTB-specific CD8 T cells from individuals with LTBI. Overall these results provide further insight regarding the relationship between mycobacterial antigen load and the phenotype and functional capacity of MTB-specific CD8 T cell responses.

**Ethics approval number** 288/2008

Presenting author: Noella Moshi, MSc student (junior researcher). Completion of experiments and analysis of all data presented was performed by N. Moshi.

**Title:** THE NOVEL TB VACCINE, MVA85A, INDUCES LONG-LIVED MEMORY CD4 T CELLS WITH PROLIFERATIVE CAPACITY

**Authors:** <sup>1</sup>One Dintwe, <sup>1</sup>Cheryl Day, <sup>1</sup>Erica Smit, <sup>1</sup>Michele Tameris, <sup>2</sup>Helen McShane, <sup>1</sup>Gregory Hussey, <sup>1</sup>Hassan Mahomed, <sup>1</sup>Willem Hanekom and <sup>1</sup>Thomas J. Scriba

**Department:** <sup>1</sup>South African Tuberculosis Vaccine Initiative and School of Child and Adolescent Health, University of Cape Town, Cape Town, Republic of South Africa; <sup>2</sup>Centre for Clinical Vaccinology and Tropical Medicine & The Jenner Institute Laboratories, Nuffield Department of Medicine, Oxford University, Oxford, UK.

### **Background:**

The aim of vaccination is induction of long-lived memory cells that can respond rapidly to antigen re-encounter and proliferate to large numbers of effector cells. Memory cells should also have the capacity to home to the site of infection.

### **Objective:**

To characterise antigen-specific T cells induced by the novel TB vaccine, MVA85A, a modified vaccinia Ankara vector expressing the *M. tuberculosis* protein Ag85A, in humans. We hypothesised that (1) MVA85A-induced Ag85A-specific CD4 T cells express markers of skin homing; (2) Ag85A-specific CD4 T cells express a central memory phenotype, characteristic of long lived cells; (3) and these CD4 T cells have the potential to proliferate upon antigen reencounter.

### **Methods:**

We accessed blood samples from previously completed phase I/IIa clinical trials of the MVA85A vaccine. Healthy, *M.tb*-uninfected adults, adolescents and children were vaccinated with a single dose of  $5 \times 10^7$  pfu of MVA85A and blood collected up to 1 year after vaccination. Frozen peripheral blood mononuclear cells (PBMC) were thawed and stained with HLA-DRB1\*0301 class II tetramer bearing an Ag85A peptide. Cell surface markers of activation, homing marker expression and memory phenotype were measured on tetramer<sup>+</sup> CD4 T cells by flow cytometry. Ag85A or PPD-specific T cell proliferation was measured by Oregon Green dye dilution during 6 day *in vitro* culture of PBMC.

### **Results:**

*Ex vivo* frequencies of Ag85A-specific tetramer<sup>+</sup> CD4 T cells peaked 7 days after MVA85A vaccination and returned to baseline levels between 56 and 84 days after vaccination. Seven days post-vaccination, when Ag85A-specific CD4 T cells were highly activated, these cells predominantly expressed the skin homing marker, cutaneous lymphocyte antigen (CLA). CLA expression was short lived and returned to baseline levels by 14 days post-vaccination, when expression of the activation marker, CD38, had also returned to pre-vaccination levels. MVA85A-induced CD4 T cells predominantly displayed an effector (CD45RA<sup>-</sup>CCR7<sup>-</sup>CD27<sup>-</sup>) phenotype during the first month post-vaccination. As the effector response waned, the proportion of central memory cells (CD45RA<sup>-</sup>CCR7<sup>+</sup>CD27<sup>+</sup>) increased consistently, up to 168 days after vaccination. This emergence of central memory cells coincided with increasing Ag85A-specific CD4 T cell proliferation. Precursor frequencies of tetramer<sup>+</sup> CD4 T cells did not predict proliferative potential.

### **Conclusions:**

The expression of homing marker appeared to be dictated by the site of inflammation. Our data of T cell phenotype showing the emergence of a central memory phenotype and the cells capacity to proliferate suggest that MVA85A induces T cells with promising function. Since the aim of vaccination is to induce long-lived T cells that proliferate to large numbers upon secondary infection.

This work was supported by grants from the Wellcome Trust and EuropeAID.

**Title:** **EFFECT OF *MYCOBACTERIUM TUBERCULOSIS* INFECTION ON BREADTH OF T CELL RESPONSES**

**Authors:** Munyaradzi Musvosvi, Cheryl Day, Hassan Mahomed, Willem Hanekom and Thomas J. Scriba

**Department:** South African Tuberculosis Vaccine Initiative and School of Child and Adolescent Health, IIDMM, University of Cape Town, South Africa

**Objective:**

T cells are important for immunological protection against tuberculosis (TB). For this reason most novel TB vaccines are designed to induce T cell responses. However, clinical development of these novel TB vaccines is hampered by a lack of immune correlates of protection. A more complete understanding of the mycobacteria-specific immune response is needed. The role of breadth of epitope recognition by mycobacteria-specific T cells is not known. Further, identification of frequently targeted epitopes will allow design of new tools to study *Mycobacterium tuberculosis* (*M.tb*) T cell immunity. We investigated whether acquisition of *M.tb* infection resulted in changes to the number and/or pattern of epitopes recognised by mycobacteria-specific T cells.

**Methods:**

We compared epitope recognition before and after *M.tb* infection in 65 healthy adolescents, from a TB-endemic setting, who were followed up for 2 years. Acquisition of *M.tb*-infection during the follow-up period was defined as a conversion of the QuantiFERON® TB GOLD In-Tube assay and a tuberculin skin test. Cryopreserved peripheral blood mononuclear cells, collected at study enrolment and at the end of follow-up, were thawed and T cell recognition of Ag85A or Ag85B peptides was determined by cultured IFN- $\gamma$  ELISPOT assay. Recognition of each peptide by CD4 or CD8 T cells was confirmed with a second IFN- $\gamma$  ELISPOT assay and/or intracellular cytokine staining.

**Results:**

We did not observe a significant difference in the number of recognised T cell epitopes in the Ag85A ( $p=0.18$ ) and Ag85B ( $p=0.44$ ) proteins upon *M.tb* infection. Interestingly, CD4 T cells mediated all peptide responses. Although we did observe broad recognition of Ag85A and Ag85B overall, three immunodominant regions stood out in both proteins.

**Conclusions:**

Our results suggest that the breadth of T cell epitope recognition is similar before and after infection with *M.tb*. Our data suggest that the Ag85-specific T cell response induced by BCG vaccination and/or exposure to environmental mycobacteria is remarkably similar to the response induced by *M.tb*.

**Title:** GLYCOGENIC HEPATOPATHY: A SERIES OF FIVE CASES

**Authors:** Budree, S; Goddard, L; De Lacy, R; Pillay, K

**Introduction:**

Non-alcoholic fatty liver disease (NAFLD) has been well described in patients with diabetes, particularly type II diabetes. However, case studies have been published recently describing unique pathological changes on liver biopsies in patients with poorly controlled type I or insulin dependent diabetes mellitus. These biopsies have shown a pathologic overloading of hepatocytes with glycogen, a condition which has been termed Glycogenic Hepatopathy (GH).

**Aims:**

The aim of this study is to describe the histological findings of needle core liver biopsies in a case series of five patients with poorly controlled diabetes who presented with hepatomegaly and raised transaminases.

**Methods:**

A descriptive study reviewing the folders and histology obtained from liver biopsies of five patients with poorly controlled type I diabetes and hepatomegaly. Histology slides were reviewed by a senior pathologist based at Red Cross Children's Hospital. A review of the recent literature on Glycogenic Hepatopathy was conducted.

**Results:**

Patients with Type 1 diabetes mellitus with significant hepatomegaly and raised liver enzymes were identified. The case series comprised four males and one female with ages ranging between 15 and 18 years at time of presentation with hepatomegaly. All five patients had high HBA1C levels (range 11-14%) and recurrent admissions with diabetic ketoacidosis. All five patients underwent diagnostic needle core liver biopsies between 2003 and 2010.

Histological sections from needle core biopsies in four out of the five cases revealed GH with maintained hepatocyte architecture. Glycogen infiltration was demonstrated on Periodic Acid-Schiff (PAS) stain and confirmed in one case using electron microscopy. Only one case in the series demonstrated mild non-alcoholic steatosis.

Following implementation of a strict diabetic control plan in one patient, follow up examination revealed reversal of hepatomegaly and a return to normal hepatic function.

**Conclusion:**

Glycogenic hepatopathy is a rare and under-recognised condition occurring in poorly controlled type 1 diabetes. Clinically, GH cannot be distinguished from non-alcoholic fatty liver disease (NAFLD) by history, physical examination or ultrasound. Liver biopsy is essential to differentiate between the two conditions as it impacts management and long term outcome. In contrast to NAFLD, GH does not progress to fibrosis or liver cirrhosis and is completely reversible with good glycaemic control, as demonstrated in our case.

Conflicts of Interest: None

**Title:** DEVELOPING A “SYDENHAM”S CHOREA RATING SCALE” FOR USE IN AFRICA

**Authors:** K Walker, J Lawrenson, W Mathiassen, J Wilmshurst

**Department:** Neurology and Cardiology Red Cross Children’s Hospital. School of Child and Adolescent Health, University of Cape Town.

**Objective:**

To devise a rating scale for Sydenham’s chorea; suitable for use in South Africa— a scale that would assist junior doctors to assess progress and indicate when referral is indicated. Variation in the duration of chorea and a lack of methods to quantify the severity, together with the lack of a therapeutic index has made evaluation of therapy difficult.

**Methods:**

An open randomised study comparing the use of standard treatment to standard treatment plus intravenous immunoglobulins for Sydenham’s chorea was undertaken. Outcomes were measured using length of time on symptomatic therapies, changes on brain single photon emission computerized tomography (SPECT) and a clinical rating scale. The scale comprises 18 signs and symptoms and if present a score of one is allocated. A total score of 1-5 equates to mild chorea, 6-8 as moderate and 9-16 as severe .The scale assesses, behaviour, functionality of daily living and motor functioning. This rating scale was assessed by a blinded observer and the principal investigator. Twenty patients were assessed.

**Results:**

All three outcome tools showed improved outcomes in the group that received immunoglobulins. The differences of the baseline rating-scale scores of the 2 groups were not significant,  $p=0.246$ . The validity and reliability of the scale as an outcomes measurement tool was supported by the differences of the two groups rated with the scale showing a  $p$  value of 0.034. In addition the differences between the scores of the blinded observer and principal investigator were not significant  $p= 0.95$ .

**Conclusions:**

The W.W.W. (Walker, Wilmshurst, Wendy) Clinical Rating Scale for Sydenham’s chorea is a promising instrument for rating the clinical features of Sydenham’s chorea and their functional impact on the child. We believe it is practicable in Africa and may facilitate better management of Sydenham’s chorea at primary and secondary health care level.

Ethics approval: Ethics approval was obtained from the Research Ethics Committee of the University of Cape Town. (REC REF: 049/2002)

**Title:** EPIDEMIOLOGY OF CHILDREN WITH EPILEPSY AT A TERTIARY REFERRAL CENTRE IN SOUTH AFRICA

**Authors:** Sally Ackermann, Alvin Nondo, Hani Alkhaldi, Jo M Wilmshurst

**Department:** Paediatric Neurology, Red Cross War Memorial Children's Hospital, Cape Town

**Objectives:**

To describe a cohort of children with epilepsy in a tertiary referral centre in South Africa.

**Methods:**

Neurology departmental database records of all out patients managed over a 10 year period (Jan 2000 – 2010) were reviewed. The database was sorted to select the total number of children with epilepsy. Patient characteristics were reviewed using medical records. Comparison was made with results of equivalent studies.

**Results:**

From a cohort of 4823 patients, 53% had epilepsy (n=2544). Of these, 44% were female (n=1122) and 56% male (n=1422). 59% were of mixed ancestry, 38% African ancestry and 3% European ancestry. 60% of patients were below 1 year of age at first seizure presentation, 29% between the ages of 1 and 5 years and 11% between 5 and 12 years. 65% had structural/metabolic epilepsy, 20% genetic epilepsy and 15% epilepsy of unknown cause. Of the genetic group, 13% had a family history of epilepsy. 1293 (52%) had generalised epilepsy and 1154 (47%) partial epilepsy. 27% of these had identifiable epilepsy syndromes. 17% of patients had medication refractory epilepsy. Co-morbidities were evident in over 60% of patients (n=1559); motor disability was the most common co-morbidity identified.

**Conclusions:**

Epilepsy is a common childhood condition in South Africa. Over 60% of patients have symptomatic epilepsy, higher than quoted internationally; 50% of these have avoidable aetiologies. The presence of co-morbidities is significant for the large cohort of patients.

Ethics approval number HREC REF 275/2010

**Title:** A REVIEW OF THE UTILITY OF NEUROIMAGING IN CEREBRAL PALSY WITHIN A RESOURCE POOR SETTING

**Authors:** Andrew Redfern<sup>1</sup>, Kirsty Donald<sup>1</sup>

**Department:** <sup>1</sup>Dept of Paediatric Neurodevelopment, Red Cross Children's Hospital. University of Cape Town

Keywords: Neuroimaging, cerebral palsy (CP)

**Background:**

The American Academy of Neurology recommends that all children without a clear cause of CP be imaged, preferably with MRI. Our local experience of the utility of advanced neuroimaging techniques has lagged behind due to lack of availability, but MRI and multislice CT have become more accessible recently.

**Aim:**

To review the use of neuroimaging in a group of children with CP at a tertiary referral centre in Cape Town.

Objectives: 1. To analyse choice and frequency of imaging modality. 2. To analyse the neuroimaging findings.

**Method:**

182 consecutive folders of patients attending the CP clinic over a 3 month period were analysed. Demographic data, diagnoses, GMFCS score and neuroimaging findings were entered onto an excel spreadsheet. The neuroimaging findings were categorised into 7 groups, as described by Korzeniewski et al 2008. The results were then analysed.

**Results:**

171 patients had CP. 119 children had CT scans, 14 MRI's, and 7 both. Only 7 (5.3%) scans were normal, including 1 MRI. White matter damage was the most common finding (32%). Malformations comprised 6.8%. Hypoxic ischaemic encephalopathy was identified as the cause of CP in 40%, followed by prematurity (21%) and unknown (12%). 56% of patients were classified as GMFCS level 4 or 5.

**Conclusion:**

Birth asphyxia and acquired causes account for a large percentage of CP. Patients tend to be more disabled, which could account for the low percentage of normal scans. A significant number of children with no known cause of CP, or dyskinetic CP, were not imaged. MRI findings were frequently consistent with CT, and did not seem to be more sensitive at picking up abnormalities, but the low number of scans makes interpretation of the significance of this result difficult.

*We have no conflict of interest to declare.*

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**Title:** MATERNAL METHAMPHETAMINE USE DURING PREGNANCY AND SUBSEQUENT LONG-TERM NEURODEVELOPMENTAL AND BEHAVIOURAL SEQUELAE IN A COHORT OF CHILDREN IN CAPE TOWN

**Authors:** Jessie van Dyk<sup>1</sup>, Veruschka Ramanjam<sup>2</sup>, Kirsten Donald<sup>3</sup>

**Department:** <sup>1</sup>Division of Neonatal Medicine, Department of Paediatrics, Hospital for Sick Children and University of Toronto, Toronto, <sup>2</sup>Division of Developmental Paediatrics, School of Child and Adolescent Health, Red Cross Children's Hospital and University of Cape Town, Cape Town, <sup>3</sup> Division of Developmental Paediatrics, School of Child and Adolescent Health, Red Cross Children's Hospital and University of Cape Town, Cape Town

**Aim:**

To identify neurodevelopmental or behavioural deficits among children exposed to maternal methamphetamine (MA) use during pregnancy.

**Methods:**

Griffiths Mental Developmental Scales assessments were completed on 15 toddlers aged 2-4 years with a known history of maternal methamphetamine use during pregnancy. These were compared to 21 controls without a history of maternal methamphetamine use. Each child also had a hearing test, vision screen and Child Behaviour Checklist completed by a parent or caregiver. Cases and controls were matched for age, gestational age at birth, socio-economic status and geographic distribution.

**Results:**

Fifteen toddlers were assessed and compared to twenty-one controls. Baseline comparison revealed no significant difference between age at testing, gestational age, socio-economic status or geographic distribution. Methamphetamine-exposed children obtained lower scores on General Quotients ( $p=0.0220$ ), but significantly poorer performance was noted specifically on the Personal-Social Ability Subscale ( $p<0.0001$ ) and on the Hand and Eye Co-ordination Subscale ( $p=0.0002$ ). There were also concerns regarding aggressive behaviour and attention deficit/hyperactivity on the CBCL for the exposed group, although this did not reach statistical significance.

**Conclusion:**

Among children exposed to maternal methamphetamine use during pregnancy, specific developmental and behavioural deficits were increased when compared to controls.

**Title:** WILMS TUMOR OUTCOMES AT RED CROSS CHILDREN'S HOSPITAL 1979-2008

**Authors:** Joyce Balagadde-Kambugu<sup>1</sup>, Alan Davidson<sup>1</sup>, Marc Hendricks<sup>1</sup>, Farieda Desai<sup>1</sup>, Alp Numanoglu<sup>2</sup>, Alastair Millar<sup>2</sup>.

**Department:** <sup>1</sup>Haematology-Oncology Service, Red Cross Children's Hospital, Department of Paediatrics and Child Health, University of Cape Town, Cape Town  
<sup>2</sup>Department of Paediatric Surgery, Red Cross Children's Hospital, Department of Paediatrics and Child Health, University of Cape Town, Cape Town

**Objective:**

To review a series of patients presenting to the Red Cross Children's Hospital Oncology Unit with unilateral Wilms tumor (UWT).

**Methods:**

A retrospective analysis was performed on all patients diagnosed with UWT from January 1979 to December 2008.

**Results:**

There were 221 children who presented with UWT; 133 were female (60%) and 88 were male (40%). Age at diagnosis ranged from 0.24 to 12.83 years with a median of 3.21 years. Sixty-nine of the children were stage I (31.2%), 34 were stage II (15.4%), 70 were stage III (31.7%) and 48 were stage IV (21.7%). Thirty-one patients (14%) had unfavorable histology; 15 with diffuse anaplasia and 13 with focal anaplasia. The patients were treated on NWTS-based protocols (NWTS-5 since 1979).

The estimated overall 5-year survival (OS) for the whole group is 77.1%. Patients with diffuse anaplasia (35.9%) and focal anaplasia (59.4%) fared worse than those with FH (81.6%). OS among the FH tumours according to stage was as follows: 93.9% for stage I, 96.3% for stage II, 79% for stage III and 51.1% for stage IV. The OS for FH patients treated between 1979 and 1998 (n=128) was 84.7%, while the OS for patients treated on NWTS-5 between 1999 and 2008 (n=65) was 72.5% (Log Rank p value 0.11). Comparing these groups by stage, the stage III patients fared better in the modern era (87.9% vs 75.4%) while the stage IV patients fared less well (23.2% vs 54.4%).

**Conclusions:**

Where surgical expertise allows, NWTSG protocols continue to produce excellent results for stages I, II and III tumors. Survival rates for stage IV tumors have shown no improvement on NWTS-5 and we will have to consider the routine use of alkylators, etoposide and carboplatin (as per SIOP 2001) for metastatic as well as anaplastic tumours.

**Title:** CASE REPORT SERIES OF PATIENTS RECEIVING SOY, MCT, OLIVE OIL, FISH OIL LIPID EMULSION (SMOF)

**Authors:** Cader, S, Saayman, BD, Millar, AJW.

**Department:** Departments of Dietetics and Pediatric Surgery, Red Cross War Memorial Children's Hospital and University of Cape Town

**Introduction:**

Parenteral nutrition [PN] is a vital component in the management of intestinal failure. However, long term PN is associated with many complications, particularly, parenteral nutrition associated cholestasis [PNAC]. The cause of PNAC is multifactorial with recent evidence identifying the type of lipid emulsion provided parenterally as a causal link. The use of soya based lipid emulsion has been the standard choice in PN. A novel lipid emulsion, consisting of soya [30%], medium chain triglycerides [30%], olive oil [25%] and fish oil [15%] has shown positive outcomes in PNAC in infants and children. The safety and tolerance when using this lipid emulsion has been tested in both adults and preterm infants.

**Objective:**

To evaluate the effect of a novel lipid emulsion, containing a mixture of soybean oil, MCT, olive oil and fish oil, on cholestasis in patients receiving long-term PN.

**Methods:**

We reviewed all patients receiving this lipid emulsion after developing PNAC. All other causative factors were considered before changing the type of lipid emulsion from soya based to the novel lipid emulsion. Serum total and conjugated bilirubin were monitored weekly until resolution and thereafter 2 consecutive weekly serum levels to ensure complete resolution. The time period to resolution of PNAC was assessed.

**Results:**

Five patients (3 females, 2 males) were started on the new lipid emulsion after an average of 53 days (15-116 days) of receiving PN. All patients were initially managed on a soy based lipid emulsion. Three patients had short bowel syndrome secondary to jejunal atresia with 2 having bowel lengths of 14cm and 11cm with intact ileocaecal valves, 1 had gastroschisis and 1 had abdominal tuberculosis. The average total bilirubin count at start of the novel lipid emulsion was 113µg/l. Cholestasis reversal (total bilirubin  $\leq$ 21µg/l, conjugated bilirubin  $\leq$  6µg/l) was seen in 3 patients. Average time to reversal of cholestasis was 2.7 months (1month-5months) since starting the new lipid emulsion. Reversal of cholestasis was maintained up to 3 months after initiation. Two patients did not show reversal but displayed a downward trend in bilirubin levels when compared to baseline. Both these patients had ongoing severe infections (recurrent line sepsis, ongoing TB, fistulae).

**Conclusion:**

The use of soya, MCT, olive oil, fish oil lipid emulsion has reversed PNAC in 3 patients with no recurrence and 2 patients have shown a reduction in levels of bilirubin when compared to baseline. Therefore replacing the standard emulsion with this novel lipid emulsion has beneficial effects for long term patients at risk of developing PNAC.

**Title:** CHILD SAFETY IN TWO INFORMAL SETTLEMENTS: ZIMBABWE AND SOUTH AFRICA

**Authors:** Chiedza Mavengere, Pumla Mtambeka, Dorothy Schulman, Ailsa Holloway, Sebastian van As

**Department:** -Disaster Mitigation for Sustainable Livelihoods Programme at the University of Cape Town  
-Childsafe South Africa

**Objective:**

This study sought to explore and examine the role of human behaviour in reducing and managing everyday risks in two African informal settlements through the lens of child injury prevention.

**Methods:**

The methodology used for data collection and data analysis comprised both qualitative and quantitative research methods. A total of 100 household questionnaires were administered in the two study sites. In addition, field observations, two focus group discussions in each study site were facilitated and key informants interviews were conducted. Descriptive statistics were used to analyse quantitative data, which was complemented by qualitative data.

**Results:**

The findings in this study suggest that informal settlements can vary substantially and each particular settlement is likely to have its unique characteristics. In this study, both mothers and caregivers from the two sites differed significantly in their socio-demographic profile and this subsequently led to major differences in the levels of prevention strategies adopted. Also, this research has highlighted the important role of community mobilisation and vigilance as an active strategy in child injury prevention. Furthermore, a need for preserving traditional practices such as back-carrying was seen as an essential factor in reducing child vulnerability and thereby reducing child injuries.

**Conclusions:**

This study demonstrated that child protection and injury prevention can only be successfully achieved by incorporating both active and passive strategies. This will not be achieved without responsibility being taken at both household and community scales.

Ethics approval: SFREC 024\_2010

**Title:** PAEDIATRIC SURGERY MORTALITY AT RED CROSS CHILDREN'S HOSPITAL 2006 -2010

**Author:** Matthew Dold

**Aims:**

To investigate the trends and causes of surgical mortality of children at Red Cross Children's Hospital between 2006 and 2010.

**Rationale:**

Although child mortality at Red Cross Children's Hospital was covered comprehensively in *Death at the Red Cross Children's Hospital 1999-2003* (Grandin W et al, 2005), there is need for more understanding of surgical mortality in South Africa from 2003 till present day.

**Methods:**

Data from death notification forms was collected for all surgical deaths at Red Cross Children's Hospital between 2006 and 2010. All surgical admissions were collected from hospital registers and databases.

**Results:**

Overall surgical mortality has decreased by 8.7% since 2006. The male: female surgical mortality ratio was 1.09:1 and patients 1 year or younger had the highest surgical mortality rates. The leading causes of death were motor vehicle accidents (MVA), necrotizing enterocolitis (NEC) and burns while the leading group of causes was trauma. There were periods of increased surgical mortality in July and October.

**Main Conclusions:**

Although there were 275 recorded mortalities in surgery at Red Cross Children's Hospital between 2006 and 2010, there was a decreasing trend in the case fatality rate per year. Other observations included a significant drop in MVA, NEC and burn mortality since 2007 as well as age-specific distribution for these causes of death.

**Title:** INCIDENCE AND CHARACTERISTICS OF PAEDIATRIC TRAUMA IN THE SUBURBS OF CAPE-TOWN

**Authors:** G.J. Haaring, P. Mtambeka P, D. Schulman, A.B. van As.

**Purpose:**

To describe and compare the incidence and characteristics of paediatric traumatic injury between the different suburbs of Cape-Town, South-Africa.

**Study design:**

Retrospective data analysis.

**Methodology:**

Patient, accident, and injury characteristics were obtained by retrospective data analysis of the Red Cross Hospital's trauma registry. Twenty-seven suburbs from different districts of Cape-Town were selected randomly for sub-analysis. Population demographics of the individual suburbs were obtained from StatsSA's Census 1996 and 2001 data. Population numbers were extrapolated for the year 2007. Subsequently incidences of the various injury types and their proportions compared to all injuries were calculated per suburb and compared to the total group for the years 1996, 2001 and 2007.

**Statistical analysis:**

Categorical variables were analyzed using the one-sample chi-square test. Bonferonni correction was applied where appropriate. For continuous variables the Wilcoxon signed-rank test was used. Spearman's correlation coefficient was used to assess the correlation between the incidence and the logarithm of the distance of the accident to the hospital.

**Results:**

Median ages in 1996, 2001, and 2007 were 4, 5 and 5 years old respectively. Total injury incidences were higher in Garden Village (1996, 2001, 2007), Bonteheuwel (1996, 2001), Mowbray (1996, 2001, 2007), Langa (1996, 2001), Maitland (1996, 2001, 2007), Gugulethu (1996, 2007), Woodstock (1996, 2001, 2007), Grassy Park (2007), Observatory (2001, 2007) ( $p < 0.05$ ). A negative correlation was found between injury incidence and distance from place of occurrence to the hospital for 1996, 2001 and 2007 ( $Rho = -0.609$ ,  $p = 0.000$ ;  $Rho = -0.511$ ,  $p = 0.003$ ;  $Rho = -0.526$ ,  $p = 0.002$  respectively).

The following injuries formed a bigger proportion of the total injuries occurring in the particular suburb ( $p < 0.005$ ). Transport injuries: Khayelitsha Site C (1996). Assaults: Uitsig (1996), Khayelitsha (2001), Langa (2001). Burns: Langa (1996), Gugulethu (1996), Bishop Lavis (2001, 2007), Ravensmead (2001, 2007), Uitsig (2001), Belhar (2007), Ruyterwacht (2007). Falls: Beacon Valley (1996). Miscellaneous: Bonteheuwel (1996, 2007).

**Conclusion:**

The calculated incidence is dependent on the distance to the hospital. To be able to make an accurate estimation of the true incidence it is necessary to register all injuries. This can only be done for an area when all hospitals in that area implement trauma registration. The proportions of injuries show what injury type most frequently occurs in an area; however it does not show the magnitude. This information helps targeting specific problems in suburbs by adjusting preventive strategies to the specific demands of the area.

Contribution of junior researcher:

Involved in all parts of the research. The study consists of retrospective analysis of the Red Cross Hospital's trauma database. The retrieval and optimisation of the data, data selection, statistical analysis and the reporting of the data was done by the junior researcher.

HREC Ref: 401/2011

Federal Wide Assurance Number: FWA00001637

Institutional Review Board (IRB) number: IRB00001938

**Title:** CHARACTERISTICS OF CHILDHOOD SYSTEMIC LUPUS ERYTHEMATOSUS IN CAPE TOWN, SOUTH AFRICA

**Presenter:** Graeme Spittal

**Introduction:**

Systemic Lupus Erythematosus is a multi-system autoimmune disease characterised by the formation of antinuclear antibodies. The prevalence of SLE in adult black South Africans is 12.2/100 000 and there are no accurate figures available for children. Faller et al reported on a cohort of 36 patients from the Gauteng region in South Africa and suggested that this disease is increasingly recognised in black South African children as the socioeconomic and political landscape has shifted.<sup>1</sup> There is a perception that SLE is more common in the western cape than in other parts of the country and that the disease is more aggressive in this population<sup>2</sup> The patient profile, disease characteristics, morbidity and complications have not been described in the Western Cape, which has a different genetic profile to other parts of South Africa.

Aim: We aim to document the disease characteristics, disease activity, morbidity and treatment practices in our cohort of patients with childhood onset SLE from Cape Town, South Africa.

**Methods:**

A retrospective folder review of all patients with Paediatric SLE seen at the Red Cross Children's Hospital, Groote Schuur Hospital was undertaken and clinical and demographic data collected.

Results: Twenty six patients were included. Mean age at presentation: 9.1(2-15) years. male/female ratio was 1:13. Average follow up: 5.9 years. The most common clinical/laboratory features presentation are represented in table 1. Renal disease was present in 18/26. Renal Biopsy (17/18) results showed that 7/18 (39%) had Class IV nephritis. End stage renal failure requiring dialysis/transplant occurred in 33%.

Table 1.

Manifestation	(%)
Renal disease	62
Arthritis, Malar rash	57
Fever	35
Lymphadenopathy, photosensitivity	27
Pericarditis,Thrombocytopenia	23
Leukopenia,Oral Ulcers, Hemolytic Anemia	19
Raynauds Phenomenon Hypertension	15
Seizures	7

**Conclusion:**

South African patients from the Western Cape region appear to have similar features at presentation to those described in other studies, though there appears to be a higher incidence of Class IV nephritis.

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<sup>1</sup> Faller G et al, Demographics and presenting clinical features of childhood systemic lupus erythematosus. *S Afr Med J* 2005; 95: 424-427.

<sup>2</sup> Tikly M et al. Lupus in the developing world--is it any different? *Best Pract Res Clin Rheumatol.* 2008 Aug; 22(4):643-55.

**Title:** FOP IN SOUTH AFRICA: AWARENESS LEADS TO DIAGNOSIS

**Presenter:** Chris Scott

**Introduction:**

Fibrodysplasia Ossificans Progressiva (FOP) is a genetic disorder (autosomal dominant) in which there is progressive ossification of skeletal muscle. The majority of affected persons represent new mutations for the determinant gene, ACVR1 the protein product of which acts to regulate Bone Morphogenic Protein expression. {{ 9 Kaplan,F.S. 2008;}}

FOP presents in early childhood, with painful, hard areas of ossification in the muscles of the back/neck and progressive limitation leading to immobilisation of all joints by adulthood.

Previously there were few reports of FOP from Africa. We recently reported on 3 patients from South Africa {{ 331 Scott,C. 2011;}} and have in the last 18months diagnosed a further 6 patients.

**Methods:**

We document 9 affected individuals in the Xhosa, Afrikaner and mixed ancestry community.

**Results:**

Two were reported in childhood almost three decades ago, five are young children, and two presented in their teens. All have the typical features of heterotopic ossification as well as the characteristic hallux valgus. Two patients underwent unnecessary and harmful biopsies and one patient sustained a fracture of one of the areas of heterotopic bone during positioning for diagnostic x-rays. In these three cases the tissue trauma exacerbated and stimulated heterotopic bone formation.

**Conclusion:**

FOP is a devastating condition with no known cure, but early diagnosis is essential to prevent unnecessary and directly harmful special investigations. In our experience an increased awareness has led to a flurry of new diagnoses, leading to early referral and appropriate counselling and management. Paediatric rheumatologists should be aware of this condition, in order to facilitate patient diagnosis and avoid harmful procedures.



**Title:** JUVENILE IDIOPATHIC ARTHRITIS (JIA) IN TWO TERTIARY CENTRES IN THE WESTERN CAPE SOUTH AFRICA

**Authors:** K.Weakley, C Rainier-Pope, M. Esser, C.Scott

**Background:**

JIA is a disease that shows wide variations between differing populations. Due to recent international consensus on classification criteria, JIA has been widely described in many countries and population groups. There has been almost no data that describes JIA in an African, specifically Sub-Saharan African setting.

**Objective:**

To describe disease characteristics and functional disability in two tertiary centres in the Western Cape, South Africa.

**Methods:**

87 children were recruited during random clinic visits to rheumatology clinics at Tygerberg and Groote Schuur Hospital between April 2010 and April 2011. Children had to have a diagnosis of JIA according to 2001 International League of Associations for Rheumatology (ILAR) 2001 classification criteria. Consent was obtained, all children's medical records were examined, all had Childhood Health Assessment Questionnaires (CHAQ) completed by themselves or their parents and all children were examined by a researcher in conjunction with a paediatric rheumatologist. A visual analogue scale (VAS) for pain and general wellbeing was completed for each patient. HIV status as well as tuberculosis disease and previous treatment were investigated.

**Results:**

Out of 87 children, 78 matched inclusion criteria. There were 39 boys (50%) and 39 girls (50%). There were 6 Systemic JIA patients (7.69%), 17 Oligoarthritis patients (21.79%), 11 Polyarthritis rheumatoid factor (RF) positive (14.10%), 21 Polyarthritis RF negative (26.9%), 1 psoriatic arthritis (1.28%), 18 enthesitis related arthritis (23%), 4 Oligoextended JIA (5.12%). The mean CHAQ for the group was 0.73 (CI 0.18), the mean VAS for pain was 2.50cm (CI 0.55) and mean VAS for general wellbeing was 2.8cm (CI 0.61). Kruskal-Wallis equality-of-populations rank test showed significant differences ( $p < 0.05$ ) between CRP, ESR, number of active joints and limited joints between subtypes.

**Conclusion:**

JIA has a unique epidemiology in the Western Cape of South Africa, with equal male:female predominance and increased rates of Polyarticular RF positive and Enthesitis related Arthritis. Functional disability and pain/general wellbeing scores are relatively similar to other developing countries. Confounding factors such as HIV and TB make the issue of JIA more complicated in a Sub-Saharan context.

**Title:** ACID PHOSPHATASE STAIN FOR ASSESSMENT OF ADEQUACY OF INDUCED SPUTUM SAMPLES

**Authors:** S Ford, K Pillay, M Zampoli, B Morrow, H Zar

**Objective:**

To report our early experience in assessing the adequacy of induced sputum specimens in young children using two different cytological techniques.

**Methods:**

Induced sputums collected prospectively in children less than 5 years of age with cystic fibrosis were examined using 2 different techniques: the haematoxylin and eosin (H&E), Papanicolaou stain and acid phosphatase stain. A sample with at least 10 macrophages per slide was regarded as adequate.

**Results:**

28 samples were received thus far: 13 of the initial samples were stained with H&E/ Papanicolaou only: all samples were subsequently stained with acid phosphatase. Using acid phosphatase stain: 19 were classified as adequate, 2 were of borderline adequacy and 7 were classified as inadequate. The acid phosphatase stain highlights the macrophages as bright red. This feature together with the morphology is helpful to distinguish these cells from the lighter staining respiratory epithelial cells. After reviewing the samples stained with H&E/ Papanicolaou: 5 were revised from inadequate to adequate after acid phosphatase staining. Subsequently only acid phosphatase stains were performed..

**Conclusions:**

The acid phosphatase stain is superior to H&E and Papanicolaou stains in assessing adequacy of induced sputum specimens.

Ethics: HREC REF 294/2010 (part of Dr Marco Zampoli's cystic fibrosis study)

**TITLE:** A FLOW CYTOMETRY ASSAY OF MYCOBACTERIA-SPECIFIC KILLING

**Authors;** Alana Keyser<sup>1</sup>, Nancy Marin<sup>2</sup>, Thomas J. Scriba<sup>1</sup>, Jane Hughes<sup>1</sup>, Willem Hanekom<sup>1</sup>

**Department:** <sup>1</sup>The South African Tuberculosis Vaccine Initiative, Institute of Infectious Diseases and Molecular Medicine and School of Child and Adolescent Health, University of Cape Town, Cape Town, South Africa. <sup>2</sup>Grupo de Inmunología Celular e Inmunogenética, Centro de Investigaciones Médicas, Universidad de Antioquia, Medellín, Colombia

*Mycobacterium tuberculosis* (Mtb), the causative pathogen of tuberculosis, still remains responsible for 1.8 million deaths per year. Cytotoxic T cells play an important role in the control of Mtb through the expression and release of cytolytic molecules such as granzyme B and perforin. We have previously assessed expression of these molecules in T cells following incubation of PBMC with mycobacterial antigens for 3 days. Both CD4 and CD8 T cells showed the capacity to produce cytotoxic molecules in response to mycobacterial antigen.

Our aim was to develop a flow cytometric-based assay to assess killing of target cells by cytotoxic T cells, and to determine whether the production of cytotoxic molecules by mycobacteria-specific T cells correlates with killing of target cells pulsed with mycobacterial antigens.

Mycobacteria-specific effector T cells were generated through a 6-day culture in the presence of BCG or PPD. Target cells were prepared by incubating fresh autologous monocytes either pulsed with BCG or PPD or incubated without antigen (control) for 18 hours. Pulsed and control monocytes were then stained with the fluorescent dyes, Oregon Green and Cell Tracker Orange, respectively. Equal numbers of control and pulsed monocytes were co-cultured with effector T cells for 18 hours at different effector:target ratios. Cells were then acquired and killing assessed by flow cytometry. Effector T cells were also assessed for the production of the cytotoxic molecules granzyme B, perforin and granzyme B by flow cytometry.

Results showed a reduction in the number of antigen-pulsed targets, compared with control targets, with increasing effector:target ratios. T cells expanded with either BCG or PPD showed the ability to kill PPD-pulsed monocytes. Assessment of cytotoxic marker expression showed a good correlation between granzyme B<sup>+</sup>perforin<sup>+</sup>granzyme B<sup>+</sup> CD4 T cells and killing of target cells.

In summary, we have optimized a flow cytometric-based assay that can detect the killing of mycobacteria-infected monocytes by specific cytotoxic T cells. Killing by BCG- and PPD-expanded T cells is specific and co-expression of cytotoxic molecules by mycobacteria-specific T cells correlates with killing of infected monocytes.

Local IRB reference: # 016/2001

**Title:** IS FNA NECESSARY PRIOR TO NEOADJUVANT CHEMOTHERAPY IN CHILDREN WITH SUSPECTED WILMS TUMOUR?

**Authors:** P Kyei, E Dollie, K Pillay, A Alexander, A Davidson

**Objective:**

To correlate the fine needle aspiration (FNA) cytology results with the diagnosis at the time of definitive excision of the tumour in order to determine whether FNA is necessary prior to neoadjuvant chemotherapy in children with suspected Wilms tumour.

**Methods:**

Fine needle aspiration is currently performed prior to neoadjuvant chemotherapy in children with suspected Wilms tumour. All fine needle aspiration reports of kidney tumours from the last 10 years were retrieved from the archives of the Histopathology department at Red Cross Hospital. Reports were retrieved manually (by searching through patient folders) or electronically (with the use of computers). Folders from the Oncology department were also retrieved. The correlating reports of the surgical excision specimen were also retrieved and the diagnoses were compared. The cytology of the FNA and the histological findings from the surgical excision were compared.

**Results:**

36 patients suspected of having Wilms tumour or neuroblastoma (in some cases) had undergone the FNA procedure roughly in the last 10 years. Out of the 36 patients who were suspected of having Wilms tumour on FNA, 34 of them actually had Wilms tumour on definitive excision specimen, one FNA specimen was not representative as the patient had a large cystic mass on excision (and is excluded), and one patient had a malignant Pheochromocytoma on excision. Therefore the procedure is 97% correct in diagnosing Wilms tumour. 5 out of the 35 cases had a clinical differential diagnosis on the form that included neuroblastoma, however on FNA the diagnosis of Wilms tumour was made in those cases. On FNA the tumours had a varying combination of epithelial, stromal and blastemal elements. In this study, the excision specimens correlating with the fine needle aspirations showed mainly mixed tumours (30). Out of the 34 cases with Wilms tumour there were 2 cases with focal anaplasia and 2 cases with diffuse anaplasia on the excision specimen. Anaplastic cells were seen on the FNA in both cases of diffuse anaplasia. There were 9 cases of rhabdomyomatous differentiation on the excision specimen. Rhabdomyoblasts were identified on FNA in the two cases with extensive rhabdomyomatous differentiation. The rest of the cases showed either focal or less rhabdomyomatous differentiation compared to these cases. 23/35 cases had cell blocks performed as part of the FNA assessment, all of which correlated with the excision specimens. The rest of the cases were mainly referred slides from other provinces. The cell blocks made diagnosis easier as more architectural detail was present and immunohistochemistry is easier to perform. Cell blocks were performed in all the cases where anaplasia and rhabdomyomatous elements were identified. Both have these features have clinical implications.

**Conclusion:**

The FNA procedure, which is 97% accurate, is necessary prior to neoadjuvant chemotherapy as the clinical differential diagnosis may include neuroblastoma. The use of cell blocks improves diagnostic accuracy and features that have clinical implications such as anaplasia and rhabdomyomatous elements may also be more easily identified especially if they are diffusely present in the tumour.

Ethics: HREC REF 381/2001

**Title:** THE SOUTH AFRICAN MEASLES OUTBREAK 2009-2010:  
EXPERIENCE OF A SINGLE PAEDIATRIC HOSPITAL IN CAPE TOWN

**Authors:** David M le Roux; Stanzi M le Roux; James J Nuttall; Brian S Eley

**Department:** Department of Paediatrics and Child Health, Red Cross War Memorial Children's Hospital and University of Cape Town, South Africa

**Introduction:**

South Africa experienced a measles outbreak in 2009-2010 with more than 18 000 confirmed cases reported by the National Institute of Communicable Diseases. We studied the impact of the outbreak on a paediatric hospital in Cape Town.

**Methods:**

Children with measles at Red Cross Children's Hospital from 1 November 2009 to 31 July 2010 were retrospectively identified from hospital admissions data and notification records. Basic demographic information was obtained for outpatients; inpatient data was captured in detail.

**Results:**

In total, 1859 children with measles were seen; 1309 (70%) were seen as outpatients and 550 (30%) were admitted. The most common reason for admission was pneumonia (376, 68%) and/or diarrhoea (262, 48%). The median age of those admitted was 7.43 months (IQR 5.0 to 10.8). Vaccine status was known in 92/195 (47%) of children older than 9 months; 41/92 (45%) had had at least one dose of measles vaccine. 508/550 (92%) received at least one dose of Vitamin A. The median duration of admission was 4 days (IQR 2-6); total hospital admission time was 4257 days (11.7 years). Only 272/550 (49%) children had known HIV status; 39/272 (14%) of children with known HIV status were HIV-infected; 20 (59%) of these children were on anti-retroviral therapy (ART) at the time of measles diagnosis. 19 children died (3.4% of all admissions); 16 of these (84%) were less than 1 year old. 7/39 (18%) of HIV-infected children died, versus 10/233 (4%) of known HIV-uninfected children; risk ratio for death 4.18 [95% confidence interval (CI) 1.69 – 10.33, p=0.001]. There was a higher case fatality among girls than boys: 14/260 girls died versus 5/290 boys, risk ratio 3.12 (95% CI 1.14 – 8.55, p=0.02).

**Conclusions:**

The measles outbreak of 2009-2010 added a large burden of outpatient visits and hospital inpatient time. The improvement of measles vaccination coverage should be a national public health priority

UCT Human Ethics Committee HREC REF: 511/2010

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**Title:** WILMS TUMOR OUTCOMES AT RED CROSS CHILDREN'S HOSPITAL 1979-2008

**Authors:** Joyce Balagadde-Kambugu<sup>1</sup>, Alan Davidson<sup>1</sup>, Marc Hendricks<sup>1</sup>, Farieda Desai<sup>1</sup>, Alp Numanoglu<sup>2</sup>, Alastair Millar<sup>2</sup>.

**Department:** <sup>1</sup>Haematology-Oncology Service, Red Cross Children's Hospital, Department of Paediatrics and Child Health, University of Cape Town, Cape Town  
<sup>2</sup>Department of Paediatric Surgery, Red Cross Children's Hospital, Department of Paediatrics and Child Health, University of Cape Town, Cape Town

**Objective:**

To review a series of patients presenting to the Red Cross Children's Hospital Oncology Unit with unilateral Wilms tumor (UWT).

**Methods:**

A retrospective analysis was performed on all patients diagnosed with UWT from January 1979 to December 2008.

**Results:**

There were 221 children who presented with UWT; 133 were female (60%) and 88 were male (40%). Age at diagnosis ranged from 0.24 to 12.83 years with a median of 3.21 years. Sixty-nine of the children were stage I (31.2%), 34 were stage II (15.4%), 70 were stage III (31.7%) and 48 were stage IV (21.7%). Thirty-one patients (14%) had unfavorable histology; 15 with diffuse anaplasia and 13 with focal anaplasia. The patients were treated on NWTS-based protocols (NWTS-5 since 1979).

The estimated overall 5-year survival (OS) for the whole group is 77.1%. Patients with diffuse anaplasia (35.9%) and focal anaplasia (59.4%) fared worse than those with FH (81.6%). OS among the FH tumours according to stage was as follows: 93.9% for stage I, 96.3% for stage II, 79% for stage III and 51.1% for stage IV. The OS for FH patients treated between 1979 and 1998 (n=128) was 84.7%, while the OS for patients treated on NWTS-5 between 1999 and 2008 (n=65) was 72.5% (Log Rank p value 0.11). Comparing these groups by stage, the stage III patients fared better in the modern era (87.9% vs 75.4%) while the stage IV patients fared less well (23.2% vs 54.4%).

**Conclusions:**

Where surgical expertise allows, NWTSG protocols continue to produce excellent results for stages I, II and III tumors. Survival rates for stage IV tumors have shown no improvement on NWTS-5 and we will have to consider the routine use of alkylators, etoposide and carboplatin (as per SIOP 2001) for metastatic as well as anaplastic tumours.

**Title:** **CYSTIC FIBROSIS: 6 YEARS OF MUTATION DETECTION IN THE WESTERN CAPE.**

**Authors:** Meldau S, Leisegang F, Owen EP.

**Department:** National Health Laboratory Services, Groote Schuur, Division Chemical Pathology, UCT, Cape Town.

**Objective:**

Cystic fibrosis (CF), caused by mutations in the CFTR gene, occurs with high frequency in the South African caucasian and mixed ancestry populations, with delta F508(dF508) being the predominant mutation (frequency of 76% and 50% in caucasian and mixed ancestry CF patients respectively).

CF is rare in the SA black population, and the mutation spectrum is largely unknown. However one mutation (3120+1G>A) occurs with a frequency of 46% and 17% in black and mixed ancestry CF patients respectively.

To date more than 1500 additional mutations have been described worldwide, with the mutation frequency being race dependent. Many of the known mutations in the SA population can be detected using the Tepnel Elucigene CF 30 kit, a commercial allele-specific multiplex PCR kit. This kit screens for a total of 30 of the most common European mutations and includes the African mutation 3120+1G>A.

**Methods:**

Up until April 2008 we used in-house, inexpensive methods to screen for dF508 and 3120+1G>A. After 4/2008 we introduced the CF30 kit to improve the service, especially for caucasian and mixed ancestry patients. In addition, sequencing of all 27 exons of the CFTR gene was introduced for sweat test positive African black patients.

**Results:**

We present results from the 3 population groups obtained during a 6 year period, 3 years before and 3 years after the introduction of the CF30 kit, together with the full sequencing of 5 sweat test positive black CF patients.

Caucasian and mixed ancestry patient results for 3 yrs prior to April 2008:

- 75 tested for dF508 and 3120+1G>A (mixed ancestry patients only) - 13% of alleles carried dF508 (none were positive for 3120+1G>A).
- 6 individuals (8%) were genetically confirmed as CF positive (homozygous for dF508)

Caucasian and mixed ancestry patient results for 3 yrs post April 2008:

- 77 tested using the CF30 kit - 30% of alleles carried mutations.
- 23 individuals (30%) genetically confirmed as CF positive (homozygous or compound heterozygotes).

Results for black patients during the 6 year period:

- 38 screened for 3120+1G>A – 10.5% of alleles carried 3120+1G>A.
- 3 individuals genetically confirmed as CF positive (homozygous for 3120+1G>A).

4/5 black sweat test positive CF patients who were heterozygous for the 3120+1G>A mutation were positive for additional CF mutations detected through sequencing, none of which are included in the CF30 kit. 1 patient also carried the 5T allele in the IVS8 polyT tract.

**Conclusions:**

From our experience, use of the Elucigene CF 30 kit enhanced confirmation of CF in caucasian and mixed ancestry patients from 8 to 30%.

Mutation detection of 3120+1G>A in black patients only confirmed CF in 7.9% of patients. Sequencing of the gene in confirmed black CF patients could greatly improve this to 80%. However this method is expensive and should only be used in sweat test confirmed patients.

Since primers for the entire gene are available, we can now determine homo-/heterozygosity of single mutations identified with the CF30 kit.

It is not known what percentage of the undiagnosed patients were sweat test positive or clinically confirmed CF in the patient groups studied above.

**TITLE: THE RELATIONSHIP BETWEEN THE INTRARENAL LOCATION OF A WILMS TUMOUR AND ADRENAL GLAND INVOLVEMENT**

**Authors:** D Naicker, T Swiel, K Pillay, A Alexander, A Davidson

**Objective:**

Wilms tumour is the most common malignant primary renal neoplasm in children. The mean age at diagnosis is about 3 years and is slightly more prevalent in females. It is treated with a variable combination of chemotherapy, surgical excision and radiotherapy. Most commonly a radical nephrectomy is performed but if it is bilateral or the individual is at risk of bilateral Wilms tumour, then nephron sparing surgery can be performed. A low incidence of adrenal involvement has led to questioning the common practice of adrenalectomies in Wilms tumour. The primary objective of the study is to determine whether the intrarenal location of the tumour (upper, middle or lower pole) can reliably predict whether or not the adrenal gland will be involved.

**Methods:**

A retrospective study of all the cases of Wilms Tumour at the Red Cross Children's Hospital (RCCH) since the year 2000 was conducted. Cases referred to RCCH Histopathology laboratory were included in the study. All of the histological reports for Wilms tumours were retrieved and reviewed. Only the cases in which the patient was treated with a nephrectomy (either partial or radical) were used. Relevant information about the cases were recorded including: The stage at excision, histology (type, presence of anaplasia, degree of necrosis), bilateral/unilateral, location of tumour (upper, middle, lower third), capsular breach, renal/adrenal vein involvement and involvement of adrenal gland. Where relevant data was not found in the histological reports, the patient folders were located and where necessary, the histology was reviewed. This data was then correlated to determine the relationship between the location of the tumour and involvement of the adrenal gland.

**Results:**

There were 128 cases of Wilms tumour from the year 2000 to date including 11 (8.66%) cases of bilateral Wilms tumour. In total there were 137 nephrectomies reviewed. According to SIOP histological typing there was 1 low risk tumour (cystic partially differentiated nephroblastoma), 103 intermediate risk tumours (epithelial, stromal, mixed and regressive type nephroblastoma) and 33 high risk tumours (blastema and diffuse anaplasia type nephroblastoma).

In 79 of the 137 nephrectomies the adrenal gland was not excised or not mentioned in the histological report. Of the 58 cases where adrenalectomy was performed the adrenal gland was found to be involved histologically in 9 cases (15.5%). In more than a third of the cases (48, 35.04%) the entire kidney was involved with tumour. A component of the tumour was located in the upper pole in 79 cases (57.66%), the middle pole in 75 cases (54.74%), and the lower pole in 79 cases (57.66%). In all the cases with adrenal involvement there was a component of the tumour in the upper pole. In 30 of the cases with no adrenal involvement (62.50%) there was a component of the tumour in the upper pole of the kidney.

**Conclusions:**

There is a relationship between the intrarenal location of the tumour and involvement of the adrenal gland with all of the cases found with adrenal involvement having a component of tumour in the upper pole. Tumours with a component in the upper pole of the kidney were significantly more likely to have adrenal gland involvement than those without an upper pole component ( $p = 0.045$ ). Adrenal involvement in Wilms tumour without tumour present in the upper pole of the kidney seems extremely rare. Therefore the adrenal gland may be spared in surgery for Wilms tumours without upper lobe involvement.

Ethics No: HREC REF 380/2011



**Title:** AUDIT OF CHILDREN WITH SEIZURES ATTENDING A NEURO-HIV CLINIC AT RED CROSS WAR MEMORIAL CHILDREN'S HOSPITAL

**Authors:** Reneva Petersen, Kathy Walker, Kirsty Donald, Jo Wilmshurst

**Department:** Division Developmental Paediatrics, School of Child and Adolescent health, Red Cross War Memorial Children's Hospital, Cape Town.

**Introduction:**

Neurological involvement has been reported in 50 -60% of children with HIV and in 18 % of children as a presenting symptom of AIDS. Internationally the prevalence of epilepsy in children with HIV is reported as between 2-20 %.

**Aim:**

To describe the prevalence of seizures amongst a selected population of children with HIV-1 referred for neurological problems.

**Method:**

Data was collected prospectively over a 2 year period from all children attending a subspecialist paediatric HIV Neurology clinic. All children who had a history of seizures were selected and clinical information gathered for analysis.

**Provisional Results:**

From a total of 89 patients 26% ( n=24) had seizures as part of their clinical picture.. The age range was 12-145 months (mean age 80.56 months). 91% (22/24) were on antiretroviral medication at the time of their clinic visit. In 20.8 % ( n=5) a secondary cause for the seizures could be identified: 8% (n=2) stroke, 8%(n=2) bacterial meningitis and 4.1%(n=1) tuberculous meningitis. In addition 79.1% (n=19) were found to have developmental delay and 41.6% (n=10) presented also with behaviour problems.

**Conclusion:**

The prevalence of seizures in our cohort was higher than suggested by previous reports of the general HIV infected paediatric population (local and international) These results however, do indicate that seizures (primary or secondary) represent a significant burden of disease in this subgroup. These children are frequently on multiple agents and are often difficult to manage. Defining this population and their co-morbidities is important in understanding both aetiology and management issues.

**Title: MYCOBACTERIA-INDUCED PRO-INFLAMMATORY CYTOKINE PRODUCTION INCREASES OVER THE FIRST 9 MONTHS OF LIFE**

**Authors:** <sup>1</sup>Muki Shey, <sup>1</sup>Thomas Scriba, <sup>1</sup>Marwou de Kock, <sup>1</sup>Hadn Africa, <sup>1</sup>Charlene Barnard, <sup>2</sup>Thomas Hawn, <sup>3</sup>Tobias Kollmann, <sup>1</sup>Willem Hanekom.

**Department:** <sup>1</sup>South African TB Vaccine Initiative and School of Child and Adolescent Health, University of Cape Town, Cape Town, South Africa; <sup>2</sup>University of Washington School of Medicine, Seattle, USA; <sup>3</sup>University of British Columbia, Vancouver, Canada.

Newborns and infants are particularly susceptible to infectious diseases and typically do not respond to vaccination as well as older children and adults. We hypothesised that this susceptibility may be due to sub-optimal function of immature innate cells in newborns, compared with more mature innate cells in infants. We aimed to characterise maturational changes in innate immunity over the first 9 months of life.

Whole cord blood from newborns (n=25) or whole blood from infants at 10 (n=25) and 36 (n=25) weeks of age, was incubated with viable BCG, LPS, or left unstimulated, for 6 hours. Intracellular cytokine expression was measured in monocytes, DCs and granulocytes by multiparameter flow cytometry. We also determined the soluble levels of cytokines by luminex bead array.

In newborns and infants, high numbers of DCs and monocytes expressed IL-6 and TNF- $\alpha$ , while low numbers of these cells expressed IL-12 and IL-10, upon stimulation with BCG. Expression of pro-inflammatory cytokines, IL-6, TNF- $\alpha$  and IL-12 by monocytes was lower in newborns compared with infants. The levels expressed by DCs were similar in newborns and adults. Soluble levels of these cytokines in plasma were also lower in newborns, compared with infants. By contrast, expression of the anti-inflammatory cytokine, IL-10 by monocytes and DCs and soluble levels of IL-10 were not different in newborns and infants.

Our data suggest that increasing mycobacteria-induced expression of pro-inflammatory cytokines may be associated with the decreasing susceptibility to infections during the first 9 months of life. These results may also explain previous observations of sub-optimal priming of Th1 responses by BCG vaccination at birth, compared with vaccination at a later time.

Ethics approval numbers: UCTREC Ref: 126/2006 (for healthy infants); UCTREC Ref: 479/2009 (for cord blood).

**Title:** IMPLEMENTATION LESSONS LEARNT FROM THE FIRST INFANT EFFICACY TRIAL OF A NEW TB VACCINE SINCE BCG

**Authors:** M Tameris [1], H McShane[2], B McClain[3], S Lockhart[2], B Landry[3], M Hatherill[1], W Hanekom[1], H Mahomed[1]

**Department:** [1]South African TB Vaccine Initiative, UCT  
[2]Oxford-Emergent Tuberculosis Consortium Ltd  
[3]Aeras Global Tuberculosis Vaccine Foundation

**Background:**

The epidemiology of TB in the developing world shows a peak in TB disease in early childhood. While BCG is effective in reducing the risk of disseminated TB, it has not been able to control pulmonary TB making infants a prime candidate for a new TB vaccine. MVA85A/ Aeras 485 developed by the University of Oxford is a leading new TB vaccine candidate designed as a booster vaccine to BCG. A phase IIb trial in infants with MVA85A/ Aeras 485 was initiated in June 2009 at the South African TB Vaccine Initiative (SATVI) site in Worcester, South Africa under the sponsorship of the Aeras Global TB Vaccine Foundation and support of the Oxford-Emergent Consortium Ltd. The trial aims to enrol 2784 infants and to follow them up for clinical endpoints for up to two years after vaccine administration. Enrolment was completed by end April 2011 with 2797 enrolled.

**Lessons learnt:**

Enrolment started off at a slower pace than expected but through examination of recruitment procedures and exclusion/inclusion criteria and practices, refinement of procedures took place which had an important impact on recruitment.

- Recruitment: the initial plan to recruit via public sector clinics was not as effective as anticipated and this was changed to recruit subjects using birth registers and home visits.
- Household TB contact was an exclusion criterion and it was found necessary to define this clearly to minimise exclusions due to this factor.
- High platelet counts were found to be such a common occurrence that the normal laboratory ranges being applied were not appropriate for this community. After consultation with the relevant specialists, a more discretionary approach was used to interpret these results.
- Haemolysis of blood specimens requiring repeat blood draws was addressed through centrifugation of specimens soon after blood draw and prior to being sent for laboratory processing
- Withdrawal of participants after consenting but prior to vaccination became a significant screening failure factor, and it was found that caregiver discomfort with phlebotomy procedures was an important reason for this withdrawal.

**Conclusion:**

Important lessons have been learnt through this trial in an environment that is significantly different from when the first BCG trials were conducted. Some lessons may be of site specific relevance whereas others may be of broader value to other sites planning to conduct such trials.