



School of Child & Adolescent Health

UNIVERSITY OF CAPE TOWN

ANNUAL RESEARCH DAYS 2010



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## **Programme and Abstract Book**

**19th & 20th October**

**Nursing Education Function Hall, Johnson & Johnson Building  
Red Cross Children's Hospital**

## CPD Points

Tuesday, 19 October 2010

4 points

Wednesday, 20 October 2010

7 points

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

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**Title:** PANDEMIC INFLUENZA A H1N1 (2009) IN CRITICALLY ILL CHILDREN ADMITTED TO A PAEDIATRIC INTENSIVE CARE UNIT, SOUTH AFRICA

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Division of Paediatric Critical Care and Children's Heart Diseases, School of Child and Adolescent Health, University of Cape Town, Cape Town, South Africa

**Objectives:**

To describe the clinical course of children with confirmed pandemic influenza A (H1N1) (nH1N1(2009)) infection admitted to the PICU at RCWMCH from 1 August to 30 September 2009; in comparison with those admitted to the PICU over the same period with other respiratory viral infections.

**Methods:**

A retrospective descriptive single centre study.

**Results:**

During the study period 19 children in 20 PICU admissions tested positive for nH1N1(2009) and 8 patients in 9 admissions had other positive respiratory viral isolates.

	Gender (M:F)	Age (months) Median (Range)	HIV Positive	ICU Stay (days)	Ventilator Days	PELOD Score (admission)	ICU Mortality
nH1N1(2009) pos (N=20)	10:10	12 (1-100)	3/19	8 (2-24)	5 (0-27)	11	5/20
nH1N1(2009) neg (N=9)	8:1	12 (7-25)	1/8	6 (1-16)	4 (0-16)	1	0/9

Of the nH1N1 (2009) positive patients, four (20%) tested positive for another respiratory virus, 14 (70%) had major co-morbidities, 6 (30%) were under-weight-for-age one (5%) was overweight-for-age, and mean PIM2 score on admission was 0.059. Four of the 5 fatalities (80%) had major co-morbidities.

Rhinovirus was most commonly isolated in the nH1N1(2009) negative patients (n=7; 77.8%), followed by seasonal influenza A virus (n=2; 22.2%), adenovirus (n=1; 11.1%) and RSV (n=1; 11.1%). Five (55.6%) had major co-morbidities, 5 were underweight-for-age, and the mean PIM2 score on admission was 0.055.

**Conclusions:**

Children admitted to the PICU with confirmed nH1N1(2009) tended to have a longer ICU stay, and higher mortality than those with other respiratory viruses.



**Title:** THE MOLECULAR DIAGNOSIS OF *PNEUMOCYSTIS* PNEUMONIA IN CHILDREN USING NASOPHARYNGEAL ASPIRATE SAMPLES

**Authors:** Catherine Mary Samuel<sup>a,b</sup>, Andrew Whitelaw<sup>a,b</sup>, Craig Corcoran<sup>b,c</sup>, Brenda Morrow<sup>d</sup>, Nei-Yuan Hsaio<sup>b,c</sup>, Marco Zampoli<sup>d</sup>, Heather J Zar<sup>d</sup>

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b: National Health Laboratory Service, Cape Town.  
c: Division of Medical Virology, University of Cape Town  
d: Department of Paediatrics and Child Health, Red Cross War Memorial Children's Hospital, University of Cape Town

### **Introduction.**

Pneumocystis pneumonia (PCP) is a major cause of hospitalization and mortality in HIV-infected children. Diagnosis relies predominantly on silver or immunofluorescent staining of a lower respiratory tract specimen, which may be difficult to obtain. The aims of this study were to compare the diagnostic yield of real-time PCR when performed on upper and lower respiratory tract respiratory samples and to compare PCR with immunofluorescence (IF) for diagnosing PCP in children.

### **Methods.**

Children hospitalised between November 2006 and August 2008 with presumed PCP were prospectively studied. An upper respiratory tract sample (nasopharyngeal aspirate, NPA) and a lower respiratory tract sample (induced sputum, IS or bronchoalveolar lavage, BAL) were analyzed by real-time quantitative PCR and direct IF for the detection of *Pneumocystis jirovecii*.

### **Results.**

*P.jirovecii* was detected by PCR in 180/349 (52%) respiratory specimens obtained from 202 children. This was significantly higher than the overall detection rate by IF of 26/349 (7%);  $p < 0.0001$ . Detection rates by PCR on upper (87/183; 48%) compared with lower respiratory tract samples (93/166; 56%) were similar (OR, 0.71; 95% CI, 0.46 - 1.11).

### **Conclusions.**

Real-time PCR is more sensitive than immunofluorescence for the diagnosis of PCP in children. NPA samples are easier to obtain than lower tract samples and may be used for diagnostic purposes when PCR is utilised. Wider implementation of PCR on NPA samples is warranted for diagnosing PCP in children.

**Title:** SPUTUM INDUCTION FOR THE DIAGNOSIS OF TUBERCULOSIS: A SYSTEMATIC REVIEW AND A META-ANALYSIS

**Authors:** Yulieth Gonzalez-Angulo<sup>1,2,4</sup>, Charles Shey Wiysonge<sup>2,3</sup>, Shingai Machingaidze<sup>1,2,4</sup>, Hennie Geldenhuys<sup>1,2</sup>, Francesca Little<sup>1,4,5</sup>, Willem Hanekom<sup>1,2,3</sup>, Hassan Mahomed<sup>1,2,3,4</sup>, Gregory Hussey<sup>1,2,3</sup>, Mark Hatherill<sup>1,2,3</sup>

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**Objective:**

To review systematically all studies that assessed diagnostic yield of sputum induction for diagnosis of pulmonary tuberculosis.

**Methods:**

We searched PubMed, combining terms for sputum induction and tuberculosis, as well as bibliographies, and personal reference collections. Papers were reviewed if nebulized saline was used for sputum induction in patients with suspected pulmonary tuberculosis. A random-effects meta-analysis was conducted, assuming each study differed in percentage (%) diagnostic yield, defined as *Mycobacterium tuberculosis* culture positive cases by sputum induction divided by all culture-positive cases. Diagnostic yield was calculated with 95% confidence intervals (CI) and displayed as Forest plots. Heterogeneity was evaluated using Chi-squared and I-squared tests. Heterogeneity was explored by stratifying studies into subgroups: age, saline concentration, HIV prevalence, and comparison method/s for TB diagnosis.

**Results:**

Ninety publications were identified and screened, from which 28 full-text articles were reviewed, and 17 included in the analysis. These studies reported 627 patients culture positive by sputum induction, of 975 confirmed pulmonary tuberculosis cases. Diagnostic yield ranged from 35% to 95%. Pooled diagnostic yield was 73% (95%CI 64-81), with significant heterogeneity among studies ( $p < 0.0001$ ,  $I^2 = 86\%$ ). Pooled yield in stratified subgroups was 71% (95%CI 60-80) in adults; 79% (95%CI 61-92) in children; 72% (95%CI 62-82) using <5% saline; 75% (95%CI 58-88) using  $\geq 5\%$  saline; 75% (95%CI 65-83) in high HIV prevalence areas; 71% (95%CI 55-85) in low HIV prevalence areas; and 64% (95%CI 68-89) using fibre-optic bronchoscopy with bronchoalveolar lavage (FOB) as the comparison method, compared to 79% (95%CI 54-73) without FOB. Meta-regression analysis showed that, independent of co-variables, absolute diagnostic yield decreased by 5% for each % increase in saline concentration; increased by 54% in adults compared to children; and decreased by 62% in studies using FOB as a diagnostic modality, compared to those studies in which FOB was not performed. HIV prevalence in the study population did not independently affect diagnostic yield of sputum induction.

**Conclusion:**

Pooled diagnostic yield of sputum induction was 73%, but yield may range from 35% to 95% in individual studies. Significant heterogeneity between studies can be explained by saline concentration, age group, and comparison methods for TB diagnosis. Diagnostic yield is greater in adults, but decreases as saline concentration increases and is lower in studies using FOB. Diagnostic yield is not affected by HIV prevalence. These causes of variability in diagnostic yield of sputum induction require validation in prospective studies.

**Title:** THE IMPACT OF ISONIAZID PROPHYLAXIS AND ANTIRETROVIRAL THERAPY ON TUBERCULOSIS (TB) INCIDENCE IN HIV –INFECTED CHILDREN IN A HIGH TB INCIDENCE SETTING.

**Authors:** LJ Frigati<sup>1</sup>, K Kranzer<sup>2</sup>, MF Cotton<sup>3</sup>, HS Schaaf<sup>3</sup>, CJ Lombard<sup>4</sup>, HJ Zar<sup>1</sup>

**Department:** <sup>1</sup>Department of Paediatrics and Child Health, Red Cross War Memorial Children's Hospital, South Africa, <sup>2</sup>Clinical Research Unit, Department of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, UK, <sup>3</sup>Department of Paediatrics and Child Health, Stellenbosch University, South Africa, <sup>4</sup>Biostatistics Unit, Medical Research Council, South Africa

**Background:**

Tuberculosis (TB) is a major cause of morbidity and mortality among HIV-infected children. Strategies to prevent TB in children include isoniazid (INH) prophylaxis and antiretroviral therapy (ART). INH prophylaxis and ART has been reported to reduce TB incidence in adults but there are few studies in children.

**Objective:**

To investigate the combined effect of INH prophylaxis and ART on TB incidence in HIV-infected children

**Methods:**

A cohort analysis was done within a prospective, double-blinded placebo-controlled trial of INH compared to placebo in HIV-infected children in Cape Town, South Africa, a high TB incidence setting. In May 2004 the placebo arm was terminated and all children were switched to INH. ART was not widely available at the start of the study, but children were started on ART following the establishment of the national ART program in 2004. Data were analysed using Cox proportional Hazard regression.

**Results:**

After adjusting for age, nutritional status and immunodeficiency at enrolment INH alone, ART alone and INH combined with ART reduced TB incidence by 0.22 (95% CI 0.09-0.53), 0.32 (95% CI 0.07-1.55) and 0.10 (95% CI 0.04-0.29) respectively.

**Conclusions:**

The finding that INH prophylaxis is protective in children on ART has significant public health implications, as this offers a possible strategy for reducing TB in HIV-infected children, particularly as BCG is no longer recommended in such infants. Widespread use of this strategy will however require screening of children for active TB disease.

**Title: HOME VENTILATION FOR CHILDREN WITH CHRONIC RESPIRATORY FAILURE IN A THIRD WORLD SETTING**

**Authors:** L. Reynolds<sup>1,2,3</sup>, J. Booth<sup>4,5</sup>

**Department:** <sup>1</sup>Red Cross War Memorial Children's Hospital, <sup>2</sup>People's Health Movement, <sup>3</sup>Paediatrics & Child Health, University of Cape Town, <sup>4</sup>Nursing, <sup>5</sup>Home Care Tracheostomy and Ventilation Programme, Red Cross War Memorial Children's Hospital, Cape Town, South Africa

**Aims:**

The most fundamental benefits of home-based care for technology-dependent children derive from demedicalisation of care and integration into the home and community. This study examines the diagnoses and outcome of a home-based mechanical ventilation (HMV) programme for children with chronic respiratory failure in a setting of social and economic underdevelopment, poverty and large income inequality.

**Methods:**

Retrospective review of a prospectively maintained clinical database on PDA of patients referred for possible home ventilation. We report diagnosis and outcome, and the influence of socioeconomic conditions.

**Results:**

Diagnosis	Number	Duration of HMV Median (range)	Died
Central hypoventilation	4	78 (4 - 158)	2
Spinal chord disorders	3	112 (0 - 135)	2
NMDs	16	39 (0 - 76)	6
Chest wall	2	46 (14 - 79)	0
Lung disease	6	0 (0 - 62)	3
Multifactorial	4	1 (0 - 81)	1

*[Diagnosis and outcome of HMV patients]*

There were 35 patients on the HMV programme. Five were weaned, and 14 died, leaving 16 on the programme. One child died unexpectedly. The ratio of mask to tracheotomy-assisted ventilation was 4/31. Mothers or other family members became competent to provide all aspects of care. Only one patient also had a professional home attendant. Poverty per se did not influence acceptance, but lack of family cohesion delayed discharge in some patients. Lack of electrification in the home delayed discharge in one patient.

**Conclusions:**

Successful HMV is possible in conditions of poverty and inequality if technology if mothers or other care-givers are empowered to provide care by a multidisciplinary team.

**Conflict of Interest:** None declared

**Acknowledgement:** Mothers, families & care givers of the children and their community social networks. Multidisciplinary Home Care Tracheostomy and Ventilation Programme Team: nursing staff, Ward E1; social workers; physiotherapists, occupational therapists, dietitians, volunteer workers. The Breathe Easy Fund. Friends of the Children's Hospital.

**Funding Source:** None declared

**Title:** COMMUNICATING FAMILY-FRIENDLY PRACTICE – STARTING BY SAYING WHAT WE DO

**Authors:** Angela Leonard, Minette Coetzee, Anchen Verster, and Brenda Yates

**Department:** Child Nurse Practice Development Initiative, UCT School of Child and Adolescent Health

A growing evidence base confirms that Family-centered approaches improve outcomes in paediatric health care facilities. Child-friendly services aim to provide ‘the best possible’ healthcare by health workers who work together to minimize the fear, anxiety and suffering of children and their families.<sup>1</sup>

At the Red Cross War Memorial Children's Hospital a shift to family friendly care became the focus of the Child Nurse Practice Development Initiative in 2007. Extensive upgrades in the last 15 years have ensured state of the art facilities and equipment. Shifts in practice and communication norms are an ongoing commitment. Accommodating children in more child and family friendly ways has been an journey navigated by the Practice Development Initiative with nurses, doctors, administrative and housekeeping personnel and the volunteer based organisation at the hospital.

A main theme in this journey has been the development of materials to communicate with children and their families from various cultural and social backgrounds. To date this has included a participative review of signage, information brochures about various clinical areas and materials to facilitate communication about conditions and procedures. The methodology used in the development of these materials has been intentionally participative and has included working with parents, children and practitioners in various settings. This presentation will present the processes of development and evaluation of these materials in the last two years, with a focus on communication about conditions and procedures.

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<sup>1</sup> Nichols on S & Clarke A (2001). How ‘child friendly’ are you? *Paediatric Nursing* 13 (5): 12-15

**Title:** ESTABLISHING A MINIMALLY INVASIVE PAEDIATRIC UROLOGY SERVICE – LESSONS LEARNED

**Author:** John Lazarus

**Department:** Division of Urology, Red Cross Children’s Hospital, University of Cape Town

### **Introduction**

The spectrum of minimally invasive surgery (MIS) performed in paediatric urology has undergone dramatic growth in the past decade. Changes in instrumentation, visualisation and an evolution in surgical skill have provided children requiring surgery for urological disease the possibility of MIS. Ablative and reconstructive procedures are now possible with reduced postoperative pain, improved cosmesis and equivalent outcomes when compared to the “gold standard” of open operations.

We sought to audit our experience, document the learning curve and consider where future efforts need to focus to attain a MIS only service.

### **Methods**

We retrospectively audited the records of children undergoing MIS at Red Cross Children’s Hospital from 2006 – 2010 (5 years) within the Urology division.

### **Results**

In total 68 children have undergone MIS with at a mean age of 5.5 years. Procedures include: Nephrectomy/nephroureterectomy 20, heminephrectomy 4, pyeloplasty 4, ureteric reimplant 3, intersex 6, orchidopexy 9, hydrocele 6, varicocele 3, PCNL 9, other 5.

Objective outcomes for reconstructive surgeries include: all pyeloplasties have documented stable or improved MAG 3 function, ureteric reimplant showed resolution of reflux on indirect MAG 3 cystography and following orchidopexy all testis were palpable in the scrotum.

Complications included: conversion to open surgery in 3 cases for failure to progress, 1 duodenal injury during the 2<sup>nd</sup> nephrectomy attempted (required open repair) and 1 omental herniation.

### **Conclusion**

MIS procedures on children with urological disease are technically challenging, and require surgical and entire team expertise with equipment tailored for use on children. Such procedures can be safely performed with excellent functional outcomes. It is our hope to locally expand the indications for MIS and promote its use regionally.

**Title:** **IMAGING THE REX RECESSUS VEIN PRE-OPERATIVELY USING WEDGED HEPATIC VENOUS PORTOGRAPHY AND THE ROLE OF POST-OPERATIVE DOPPLER ULTRASOUND IN REX SHUNT SURVEILLANCE**

**Authors:** Andrew Lawson (Radiology)<sup>1</sup>, Dr Paul Rischbieter (Medical officer)<sup>2</sup>, Prof Alp Nomanoglu (Paed Surgery)<sup>3</sup>, Nicky Wieselthaler (Radiology)<sup>4</sup>

**Department:** Groote Schuur Hospital<sup>1</sup>, Themba Hospital, White River<sup>2</sup>, School of Child and Adolescent Health<sup>3</sup>, Red Cross Children's Hospital<sup>4</sup>

## **Background**

In children with extrahepatic portal vein obstruction (EHPVO), formation of a mesentericoportal bypass (Rex shunt) restores hepatopedal flow, relieves portal hypertension and reduces variceal bleeding. The Rex shunt is created by inserting a vein graft between the superior mesenteric vein and the umbilical segment of the left portal vein (Rex vein).

We report our experience with wedged hepatic venous portography (WHVP) in the pre-operative evaluation of the Rex vein and the post operative ultrasound findings.

## **Methods**

A retrospective chart review was done in patients with EHPVO who had been considered for a mesoportal bypass between January 2001 and January 2010 at Red Cross War Memorial Children's Hospital.

## **Results**

Sixteen patients (13 boys, 3 girls, mean age 5, range 1-13 years) were considered for mesoportal bypass including four post reduced-size liver transplant patients. Ten patients (62%) underwent WHVP. The Rex vein was clearly identified in 8 (80%) patients. A poorly canalised Rex vein was reported in one of these cases yet found to be functionally viable at surgery. One Rex vein was seen at surgery despite not being demonstrated at WHVP. Six mesoportal bypasses were performed without WHVP of which three (50%) were successful. Two of the patients who underwent WHVP were post liver transplant patients. A patent Rex vein was demonstrated in both these patients.

The average shunt sizes on the first post operative day as documented using Doppler ultrasonography was 7.8mm with an average flow of 20.8 cm/s. The average flow rate increased to 27.1cm/s after one month. All shunt occlusions (n=1) or partial thromboses (n=2) were detected by post operative doppler ultrasound.

## **Conclusions**

Our series demonstrates the use of WHVP as an effective tool with a sensitivity of 80% and specificity of 100% in the preoperative patency assessment of the Rex vein. The sensitivity of WHVP in patients who had undergone liver transplantation remains above 90%.

Doppler ultrasonography is useful for evaluating the size and flow rates in the post operative shunt and is sensitive (100%) to the detection of early shunt thrombosis.

**Title:**            **NECROTISING ENTEROCOLITIS: EARLY CONVENTIONAL AND FLUORESCEIN LAPAROSCOPIC ASSESSMENT**

**Authors:**        Numanoglu A, Millar AJW

### **Aim**

Clinical and radiological diagnosis of Necrotising Enterocolitis can be difficult. When radiological diagnosis is present often severity and complications such as perforation and full thickness necrosis may not be obvious. This study aims to establish early diagnosis of full thickness necrosis by using Photodynamic Diagnosis (PDD) with fluorescein laparoscopy before perforation occurs. It also aims for assessment of perforation before it is evident on radiology by conventional laparoscopy. University ethics committee approval has been obtained for the study.

### **Patients and Methods**

13 patients with preoperative presumed clinical and/or radiological diagnosis of necrotising enterocolitis underwent laparoscopy. A 4.7 mm umbilical or left upper quadrant port was inserted for camera by using the open method. Abdominal cavity inspected for bowel ischemia, fibrin, adhesion formation and presence of free intestinal contents. If necessary, one or two 3mm working ports were inserted for manipulation of bowel. Seven of these cases had Photodynamic Diagnosis (PDD) following intravenous injection of fluorescein.

### **Results**

Average age of patients was 20 days (3-38days). Their average weight was 1427 grams (910- 2415 grams). First 5 patients had laparoscopy only and 8 subsequent patients had fluorescein aided assessment added to the laparoscopy. Conventional laparoscopy identified perforation and/or gangrenous bowel in 8. One patient found to have chyle ascites and one patient had no abnormal findings on laparoscopy. Fluorescein identified gangrenous bowel in 3 additional patients. Laparotomy and necessary surgical intervention performed in all 11 patients with positive laparoscopy findings.

### **Conclusion**

Laparoscopy helps to improve assessment of patients with presumed diagnosis of NEC. It allows early identification of perforation and necrosis. Where ischemia is suspected fluorescein laparoscopy have an added benefit of identifying necrotic segments.



**Title:** A REVIEW OF MANAGEMENT OF WILMS' TUMOR WITH INTRACARDIAC EXTENSION

**Authors:** Westgarth-Taylor C, Abdullah MY Millar AJW, Karpelowsky J, Davidson A, Thomas J, Brooks A, Numanoglu A

**Aim:**

To review the management of patients with Wilms' tumor and intracardiac tumor extension.

**Patients and methods:**

Data were collected from patient's notes regarding patient presentation, operative details and outcome.

**Results:**

From 1984 to 2009, 244 patients with Wilms' tumors were treated at the Red Cross War Memorial Children's Hospital. 7 patients (2.86%) had cavo-atrial extension of the tumor thrombus and 2 of these had extension into the right ventricle. Pre-operative chemotherapy was administered in 6/7 patients with complete regression of the intra-cardiac tumor thrombus in 2 patients. Four patients with intra-cardiac tumor were operated on under cardiopulmonary bypass (CPB) with deep hypothermia and circulatory arrest (DHCA). The mean ischemic time was 30 minutes. There were no intra-operative deaths and no major complications. All tumors were favorable histology. To date, 4 patients are still alive, 3 disease free. 2 patients died from relapsed pulmonary metastases. One patient with intra-ventricular extension of a left Wilms' tumor has developed a right metachronous Stage 2 tumor and a regional metastasis. Both have been surgically excised and the patient is currently under treatment.

**Conclusion:**

Intracardiac extension of Wilms' tumor is rare and the management is technically challenging. Pre-operative chemotherapy is effective. CPB and DHCA for excision of the cavo-atrial tumor thrombus is safe. Distant metastases determines long-term prognosis.

**Title: LAPAROSCOPIC REPAIR OF ANORECTAL MALFORMATIONS: THE RED CROSS EXPERIENCE**

*Getting to the bottom of the problem!*

**Authors:** Richard J England, Sara Warren, Lorraine Bezuidenhout, Alp Numanoglu

**Objective:**

Patients with anorectal malformations are repaired using a Posterior Saggital Anorectoplasty (PSARP). Recently a minimally invasive technique, Laparoscopic Assisted Anorectoplasty (LAARP) has been performed at Red Cross Hospital. This study was designed to assess the outcome of this procedure and address a perceived concern regarding increased complication rates.

**Methods:**

A detailed case note review was conducted, identifying patients from the database of surgical procedures held by the Department of Paediatric Surgery and the colorectal database of the Anorectal Clinic. Patients attending routine clinic appointments were interviewed by Colorectal Nurse Specialists using the Krickenbeck standardised questionnaire.

**Results:**

Between September 2005 and June 2009, 24 patients underwent LAARP. Three patients were under 3<sup>rd</sup> centile for weight. No patients were known to be HIV positive, 2 patients were exposed but negative and status was not recorded in 54%. Sixteen patients had associated anomalies including 8 patients with renal and 4 patients with cardiac abnormalities.

Median age at surgery was 7.5 months (2.6-15.0). Subtypes of anorectal malformation were as follows: Vestibular 2, Bulbar 9, Prostatic 7, Vesical 3 and 3 with no fistula. There was a 16% early complication rate. Dilatation difficulties occurred in 62.5%. Redo anoplasty for anal stenosis was required in 37.5%. Twenty three patients have had their stoma closed. Ten patients had difficulties with follow-up; 5 lived away from Cape Town and 5 were poor attenders.

Fourteen patients had regular follow up and were analysed further. Potty training had been completed or was nearly complete in 8 patients. Five patients had a good or satisfactory outcome, despite two requiring a redo anoplasty for stenosis due to non-compliance with dilatations. A poor outcome due to incontinence was noted in 3 patients with 'high' lesions.

Six patients are awaiting toilet training or are unable to train due to incontinence. Five are complex cases due to non-compliance, poor nutrition or tethered cord. All have required at least 1 redo anoplasty or dilatation under anaesthetic.

**Conclusions:**

Anal stenosis is the most common complication post LAARP. Aetiology appears to be multifactorial but poor compliance with dilatations is a leading cause.

Education and close supervision with post-operative dilatations is essential prior to closure of colostomy. Regular long term follow-up and support is also required.

**Title:** PESTICIDE POISONINGS AT RED CROSS WAR MEMORIAL CHILDREN'S HOSPITAL (RCWMCH)

**Authors:** Kate Bloch<sup>1</sup>, Clare Roberts<sup>1</sup>, Marion Glasstone<sup>1</sup>, Linda Curling<sup>1</sup>, Andrea Rother<sup>2</sup>, Leslie London<sup>2</sup>, Heather Zar<sup>1</sup> and Mike Mann<sup>1</sup>

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### Objective

To describe the profile of acute pesticide poisonings presenting to RCWMCH from 2003-2008 inclusive, identify those poisonings due to illicit pesticides sold on the streets ("street pesticides") and assess notification of cases

### Methods

Audit of case records reviewed and recorded shortly after patient discharge, and the notification records of RCWMCH and the local health department

### Results

There were 306 patients with 311 incidents of pesticide poisoning, which accounted for 11% of total poisonings over the 6-year period. 278 (91%) children were under 6 years old and 164 (54%) were male. 217 (70%) patients came from large socio-economically diverse areas in the Cape Town Metropole, which range from informal settlements with extreme poverty to formal housing with lower to middle class populations. There was a summer predominance of acute pesticide poisonings.

The commonest pesticides were 203 cholinergics (includes organophosphates and carbamates), 35 anticoagulants, 11 naphthalenes, 11 benzoates and 45 unknowns.

100 (32%) pesticide poisonings were asymptomatic, 90 (29%) were admitted to the general wards and 121 (39%) required High Care or ICU admission. The median length of stay in hospital was 3 days (range 0-52). There were 6 (2%) deaths.

The cholinergic pesticide poisonings had a similar demographic distribution to the total pesticide poisonings. 195 of the 203 incidents were admitted to hospital with 120 requiring High Care or ICU.

There were 44 pesticide poisonings due to "street pesticides". They had similar demographic findings to the total group and 33 were cholinergic poisonings. 35 "street pesticide" poisonings were admitted with 21 requiring High Care or ICU.

87 (41%) of the total group of pesticide poisonings were notified, all of which were instances of cholinergic pesticide poisoning.

### Conclusion

Childhood pesticide poisoning is an important problem in South Africa. The number of children with pesticide poisoning attending RCWMCH is increasing. There is significant morbidity associated with cholinergic and "street" pesticide poisonings in particular, requiring advanced medical care and use of limited resources. The magnitude of the problem is masked by inadequate notification rates leading to delayed implementation of appropriate actions.

**Title:**           **WHAT HAPPENS WHEN A CHILD IS TRIAGED AS RED IN THE MEDICAL EMERGENCY ROOM AT THE RCWMCH? –DEVELOPING A TOOL FOR OBSERVATION**

**Authors:**        Candice Bonaconsa (RN), Assoc Prof Minette Coetzee & Prof Andrew Argent

**Objectives:**

Care of the critically ill child is complex in the medical emergency room. Appropriate early stabilisation, safety and best outcomes are dependent on the co-ordination, cooperation and functioning of a myriad of factors. A practice audit was conducted in the medical emergency unit to observe and describe what happens when a child is triaged as red with the aim of developing a reproducible tool for observation. The purpose of this tool was to bring a different understanding to this complex context by highlighting factors as they occur.

**Methods:**

This audit was a part of an ongoing practice development initiative at the hospital. The design of the study was fully participative with the medical emergency team and hospital leadership. Data was collected through direct observation of child pathways. Child pathways refer to all activities related to the child from entrance to the resuscitation room until transfer out to a ward. All activities, interventions, procedures and communications around a specific child were recorded as they occurred. The data collection tool was developed through a series of observations on 12 children.

**Results:**

From these observations the complexity of this environment became apparent. A child could not be observed in isolation, but the complex nature of “other activities” largely affected the care and outcome. These included factors like interruptions, the sporadic admission of children varying in acuity of illness who often required immediate attention, the number of staff versus the number of patients at any given time as well as communication norms and patterns. These became important elements which were built into the observation tool which later became known as the “15 minute data set”.

**Conclusions:**

This process highlighted the fact that care in the emergency context is extremely complex, and cannot be analyzed in isolation. The observation tool helped to display and highlights the factors which affect the care of the child under observation. The outcome of the practice audit and development of the observation tool challenges the processes required when reviewing at critical incidences, morbidity and mortality.

My contribution to this project was to carry out the observation and develop the tool. I was assisted and guided by my two supervisors.

**Title:** TRENDS IN INTENTIONAL AND UNINTENTIONAL INJURIES AT RED CROSS WAR MEMORIAL CHILDREN'S HOSPITAL, CAPE TOWN, FROM 1991 TO 2009

**Authors:** Audrey Sullivan, Jess Law, Pumla Mtambeke, Teri Kruger, Sebastian van As

**Department:** Childsafe South Africa  
Department of Paediatric Surgery, University of Cape Town

**Objective:**

To assess the trends of unintentional and intentional injuries seen at the Red Cross War Memorial Children's Hospital Trauma unit from 1991 to 2009.

**Methods:**

Records of paediatric patients presenting to the trauma unit of the Red Cross War Memorial Children's Hospital in Cape Town, South Africa, between 1991 and 2009 were reviewed. Data were obtained from the Child Accident Prevention Foundation of South Africa (CAPFSA) / Childsafe trauma registry. For intentional injuries, entries listing assault (blunt, sharp, rape/sexual assault, human bite, other) as the cause of injury were reviewed. Injuries caused by firearms were also included. Data were reviewed for number of cases, gender and admissions. For unintentional injuries a retrospective study from 1 January 1991 to 31 December 2009 (19 years) was performed for injuries due to falls, motor vehicle accidents and burns. The data was then split up into the different categories and analysed, cumulatively by month. These results were then depicted on graphs.

**Results:**

**Intentional injuries:**

We identified a total of 6415 (4.2%) children treated for injuries due to assault (blunt, sharp, rape/sexual assault, human bite, other) and firearms for the study period 1991 to 2009, from a total of 152 164 patient visits during this period. Of the 6415 children treated for injuries due to assault, 3491 were male children (54.4 %) and 2920 were female children (45.5 %). Sex was not recorded for 4 children (0.1%). There has been an increase in assault with a blunt object, other assaults, and rape and sexual assault. Assaults involving sharp instruments and firearms have decreased.

**Unintentional injuries:**

Apart from a dramatic decrease in total annual trauma cases between 1995 and 1998 (from 11944 to 6129, a 48,7% decrease in total annual trauma cases), the overall trend is increasing. The number of fall cases peak in December (3228) and drop to their lowest value in June (2206). The most common time of year for motor vehicle accident (MVA) trauma is December (2360). Injuries sustained by MVAs are high throughout the year (an average of 1937 injuries in each month). Burns cases increase steadily from February to July. Correlation can then be done between the average monthly temperature in Cape Town and the incidence of the different types of burns. All of the correlation coefficients are negative. The correlation coefficients varied from -0.83 to -0.95. Flame burns had the strongest correlation to temperature in Cape Town (-0.95).

**Conclusions:**

Peaks in childhood injuries can be explained by a decrease of supervision and child care during certain periods, most notably during the holidays. This information can be utilised to develop focussed injury prevention strategies at different times of year. Increased focus on the prevention of violence against children is necessary in order to curb the increasing trend of assaults on children. In order to ensure that prevention strategies are implemented, more funding is required for programmes aimed at violence and injury prevention. It is also important to address the underlying risk factors for violence in society, which include poor socio-economic status, unemployment, and gender inequality.

**Title:** EFFECTS OF AGE AND VACCINE DOSE ON THE T CELL RESPONSE TO THE TB VACCINE, MVA85A, IN CHILDREN.

**Authors:** TJ Scriba<sup>1</sup>, N Mansoor<sup>1</sup>, E Smit<sup>1</sup>, M Tameris<sup>1</sup>, L van der Merwe<sup>1</sup>, S Moyo<sup>1</sup>, N Brittain<sup>2</sup>, A Veldsman<sup>1</sup>, M Hatherill<sup>1</sup>, A Hawkrigde<sup>3</sup>, AVS Hill<sup>2</sup>, GD Hussey<sup>1</sup>, H Mahomed<sup>1</sup>, H McShane<sup>2</sup>, WA Hanekom<sup>1</sup>

**Department:** <sup>1</sup>South African Tuberculosis Vaccine Initiative, Institute of Infectious Diseases and Molecular Medicine, and School of Child and Adolescent Health, University of Cape Town, Observatory, South Africa  
<sup>2</sup>Centre for Clinical Vaccinology and Tropical Medicine & The Jenner Institute Laboratories, Nuffield Department of Medicine, Oxford University, Oxford, UK  
<sup>3</sup>Aeras Global Tuberculosis Vaccine Foundation, Rondebosch, South Africa

**Objectives:**

Tuberculosis (TB) kills more people than any other bacterial infection. The only licensed TB vaccine, BCG, affords poor protection against lung TB; a more effective vaccine is urgently needed. We characterized and compared the T cell responses induced by the novel TB vaccine, MVA85A, in adolescents, children and infants from a TB endemic setting. T cell responses induced by 3 different doses of MVA85A in infants were also compared.

**Methods:**

Cytokine expression by CD4 or CD8 T cells were measured by IFN- $\gamma$  ELISpot assay and intracellular cytokine staining and flow cytometry before and after vaccination.

**Results:**

MVA85A induced potent and durable CD4 T cell responses, comprising multiple CD4 T cell subsets, expressing IFN- $\gamma$ , TNF- $\alpha$ , IL-2, IL-17 and/or GM-CSF in all 3 age groups. Frequencies of specific CD4 T cells were significantly lower in infants and children, compared with adolescents. Vaccination of infants with 3 different doses,  $2.5 \times 10^7$ ,  $5 \times 10^7$  or  $1 \times 10^8$  pfu, had no marked effect on the magnitude or cytokine expression pattern of CD4 T cells.

**Discussion:**

The lower T cell response in younger children may be due to greater proportions of naïve T cells, compared with adolescents. Additional studies are necessary to elucidate this further. We conclude that MVA85A induces the type of immunity thought to be important in protection against TB in adolescents, children and infants.

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

**Title:**            **DEVELOPMENT OF AN INTRACELLULAR CYTOKINE STAINING ASSAY TO MEASURE INNATE IMMUNE RESPONSES IN INFANTS AND NEONATES.**

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

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

Dendritic cells (DCs) and monocytes constitute two major innate immunity cell populations. Upon pathogen recognition or infection, DCs and monocytes secrete cytokines. Development of DCs and monocyte responses over the first year of life is not yet well characterized in humans. Functional changes in these innate cells may affect T cell priming and thus efficacy of childhood vaccination. We aimed to develop an assay to monitor changes in innate immunity over the first year of life using very small volumes of whole blood.

We optimized whole blood stimulation conditions, fixation, red blood cell lysis and permeabilization methods using blood from healthy human adults. Whole blood was incubated with TLR ligands (CpG, R-848, LPS, PAM3), BCG or BCG-GFP for 6 hours to measure intracellular cytokine expression. We also optimized an antibody panel for analysis of monocytes and DCs by multiparameter flow cytometry.

We show that 200µl of blood was sufficient to reliably measure intracellular expression of IL-10, IL-6, IL-12, and/or TNF- $\alpha$  by monocytes and DCs after stimulation with TLR ligands or mycobacteria. Staining of permeabilized cells with a single antibody cocktail yielded better cytokine expression results than two-step staining. Cryopreservation of stimulated, fixed cells was also more optimal in 10% DMSO/FCS, compared with 10% DMSO/PBS. Further, treatment of cells with Brefeldin A was best for intracellular cytokine staining, compared with monensin, or both. We optimized our gating strategy to exclude granulocytes by using CD66a/c/e. Using optimal conditions, mDC and monocytes expressed high levels of IL-6, TNF- $\alpha$  and IL-12, and low levels of IL-10 upon stimulation. Up to 40% of monocytes and mDC were infected with BCG, as detected by GFP expression. pDC were not infected. Importantly, uninfected cells were also observed to express cytokines, presumed to be due to bystander activation.

We have optimized an intracellular cytokine staining assay for functional characterization of human DC and monocytes from pediatric samples.

**Funding:** This study is supported by TBRU grant NO1 AI 70022 to Willem Hanekom, and South African Tuberculosis and AIDS Training (SATBAT) grant D0711100-22.CM to Muki Shey

**Title:**           **COMPARISON OF THE DIRECT *EX VIVO* ELISPOT ASSAY WITH THE CULTURED ELISPOT ASSAY IN *MYCOBACTERIUM TUBERCULOSIS* ANTIGEN EPITOPE MAPPING**

**Authors:**       Munyaradzi Musvosvi, Brian Abel, Thomas Scriba, and Willem Hanekom

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

**Objectives:**

CD4 T cells are important for immunological protection against tuberculosis (TB). For this reason most TB vaccines under investigation are designed to induce T cell responses. However, very little is known about epitope recognition by mycobacteria-specific T cells. A more complete understanding of the factors that underlie epitope recognition and which epitopes are frequently targeted is important for the design of more efficacious vaccines and tools to study *Mycobacterium tuberculosis (M.tb)* T cell immunity. To determine the optimal assay for epitope mapping, we compared the sensitivity of T cell epitope recognition in a direct *ex vivo* ELISPOT assay with a cultured ELISPOT assay. We hypothesised that expansion of *M.tb*-specific T cells prior to detection by ELISPOT assay would result in a higher sensitivity compared with the direct *ex vivo* ELISPOT.

**Methods:**

Peripheral blood mononuclear cells (PBMC) were isolated from healthy adults infected with *M.tb*. Cells were cultured with an ESAT-6 peptide pool for 12 days in the presence of IL-2. After culture, cells were re-stimulated with single 15mer peptides and IFN- $\gamma$ -expressing cells detected by ELISPOT assay. For direct *ex vivo* analysis, PBMC were stimulated directly with single 15mer peptides and IFN- $\gamma$ -expressing cells detected as described above. The AID ELISPOT reader was used to count spots.

**Results:**

A greater number of ESAT-6 epitope-specific T cells were detected with the cultured ELISPOT assay compared with the direct *ex vivo* ELISPOT assay. With the exception of one epitope, all T cells detected with the direct *ex vivo* ELISPOT were also detected by the cultured ELISPOT. Generally, a higher frequency of IFN- $\gamma$ -expressing cells to single peptides was observed following 12 day culture compared with the direct *ex vivo* ELISPOT. Most epitopes detected with the cultured ELISPOT assay were recognised by CD4 T cells.

**Conclusion:**

We have shown that culturing PBMC with ESAT-6 peptides prior to epitope mapping resulted in more sensitive detection of peptide-specific responses. Furthermore, cultured ELISPOT requires fewer PBMC than the *ex vivo* ELISPOT due to the expansion of antigen-specific cells during the 12 day culture. We conclude that the cultured ELISPOT assay is optimal for epitope mapping of mycobacterial antigens.



**Title: RELATIVE FREQUENCY OF DIAGNOSTIC FEATURES COMPATIBLE WITH PULMONARY TUBERCULOSIS IN A VACCINE TRIAL SETTING**

**Authors:** Humphrey Mulenga<sup>1,2,3</sup>, Sizulu Moyo<sup>1,2,3</sup>, Lesley Workman<sup>2,3</sup>, Tony Hawkridge<sup>4</sup>, Willem Hanekom<sup>1,2,3</sup>, Hassan Mahomed<sup>1,2,3</sup>, Gregory Hussey<sup>1,2,3</sup>, Mark Hatherill<sup>1,2,3</sup>

**Department:** <sup>1</sup>South African Tuberculosis Vaccine Initiative (SATVI), <sup>2</sup>Institute of Infectious Diseases & Molecular Medicine, <sup>3</sup>School of Child & Adolescent Health, University of Cape Town, Cape Town, South Africa, <sup>4</sup>Aeras Global TB Vaccine Foundation, Rockville, USA

**Objective:**

To compare the frequency of clinical, radiological, and microbiological features of pulmonary tuberculosis (PTB) in an infant TB vaccine trial setting.

**Methods:**

- 11,680 South African newborns underwent 2-year community surveillance for TB contact or compatible symptoms during a Bacille-Calmette-Guerin vaccine trial.
- Infants were randomised by week of birth to receive Tokyo 172 BCG vaccine through the percutaneous or intradermal route within 24 hours.
- Evaluation involved clinical history and examination, tuberculin skin test, chest radiograph, 2 paired gastric lavages and induced sputa.
- Chest radiographs were reviewed by an expert panel of three radiologists blind to clinical information

**Results:**

- 1,445 (12.4%) children were admitted and investigated for PTB during this time and
- Median age at admission was 10.8 months
- Diagnostic combinations based on TB exposure and symptoms were several times more common than radiological and microbiological combinations as depicted in table 1

Table 1: Frequencies, percentages and 95% confidence intervals of diagnostic features in the 1,445 investigated children

Diagnostic Feature	Frequency	%	95% Ci
Culture positive for M. Tuberculosis	172	11.9	10.2-13.6
CXR suggestive of PTB	271	18.6	16.7-20.8
Symptom positive (LOW or FTT or Cough)	1,055	73	70.7-75.3
Exposure positive	851	59	56.4-61.5
Exposure and CXR suggestive of PTB	162	11.2	9.6-12.8
Exposure and Symptom positive	613	42.4	39.9-45
Symptom and CXR suggestive of PTB	217	15	13.2-16.9
Culture positive and CXR positive	49	3.4	2.4-4.3
Culture positive and Symptom positive	129	8.9	7.4-10.4
Culture positive and Exposure positive	124	8.6	7.1-10

**Conclusion:**

- Selection and combination of diagnostic features for the case definition in novel TB vaccine trials will have considerable effect on sample size.
- These data suggest that case definitions that incorporate TB exposure and symptoms would require a smaller sample size as compared to those incorporating radiological and/or microbiological features presumably at the expense of a loss in specificity.
- Based on these data, an end point defined by the classical triad of exposure, symptoms and radiological features occurs at a sufficiently high incidence to justify conducting a clinical trial in this study population.

**Funding:** Aeras Global TB Vaccine Foundation. The authors have no other conflict of interest to declare.

**Title:** T CELL RESPONSES INDUCED BY LATENCY-ASSOCIATED ANTIGENS IN BCG VACCINATED INFANTS.

**Authors:** William Kwong Chung<sup>1</sup>, David Miles<sup>1</sup>, Andreia Soares<sup>1</sup>, Hazel Dockrell<sup>2</sup>, Tom Ottenhoff<sup>3</sup> and Willem Hanekom<sup>1</sup>

**Department:** <sup>1</sup>South African Tuberculosis Vaccine Initiative (SATVI), Institute of Infectious Diseases and Molecular Medicine and School of Child and Adolescent Health, University of Cape Town, South Africa.

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Immune responses to latency-associated antigens may correlate with protection against tuberculosis (TB) disease, since immune recognition is higher in individuals with latent *M. tuberculosis* infection, compared with patients with TB disease. We aim to characterize T cell responses to these antigens following newborn vaccination with BCG, with the view of possible future inclusion in infant boost vaccines.

We are assessing immune responses to multiple latency associated antigens in 100 10-week old South African infants, routinely vaccinated with BCG at birth. This is done by measuring supernatant IFN- $\gamma$  following 5 days' incubation of PBMC with recombinant proteins of latency-associated antigens (ELISA). We are then characterizing epitope recognition of widely recognized antigens with a T cell proliferation assay (dilution of the dye Oregon Green). Ultimately, we will describe the character of the CD4 and CD8 T cell cytokine response to dominant epitopes.

We have shown that Rv0569 and Rv1733 were the most highly recognized in BCG vaccinated infants: 22.1% and 20.3% recognition, respectively. The median IFN- $\gamma$  production to Rv0569 and Rv1733 were 11.7 pg/ml (range: 4.7 - 65.1 pg/ml) and 28.2 pg/ml (range: 4.6 - 438.3 pg/ml), respectively. Preliminary results indicate dominance of certain epitopes of these 2 antigens in infants; these results, as well as the cytokine producing capacity of epitope-specific cells, will be presented. We propose that our results are important for the design of candidate vaccines that could induce both prophylactic and post-infection activity, allowing protection against all stages of TB. This work is funded by the South African Tuberculosis Vaccine Initiative and the Gates Global Challenge Consortium.

**Title:** T CELL CAPACITY TO PRODUCE CYTOTOXIC MOLECULES MAY BE A CORRELATE OF RISK OF TB DISEASE, FOLLOWING NEWBORN VACCINATION WITH BCG

**Authors:** Alana Keyser<sup>1</sup>, Jane Hughes<sup>1</sup>, David JC Miles<sup>1</sup>, Benjamin Kagina<sup>1</sup>, Brian Abel<sup>1</sup>, Thomas J. Scriba<sup>1</sup>, Gregory Hussey<sup>1</sup>, Gilla Kaplan<sup>2</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>Public Health Research Institute, Newark, NJ, USA.

Our aim was to identify biomarkers of protection against TB disease in infants, following routine vaccination with Bacille Calmette-Guerin (BCG) at birth.

5,675 infants were enrolled at 10 weeks of age, when blood was collected and stored. During 2 years of follow-up, 29 infants developed culture-positive pulmonary TB: they were regarded as not protected against TB. Two groups of healthy infants were regarded as protected against TB disease: 55 infants from households where adults had TB, and 55 infants randomly selected from the cohort.

PBMC from the unprotected and protected infants, stored at 10 weeks of age, were retrieved and mycobacteria-specific responses compared. We found no difference in proliferation of CD4 and CD8 T-cells following incubation of PBMC with BCG for 6 days, between the 3 groups. However, capacity of proliferating CD4 T-cells to express IFN $\gamma$  was greater in the unprotected group, compared to others. These infants' CD4 and CD8 T-cells also had greater capacity to produce granzyme B, perforin and granulysin, following incubation of PBMC with BCG for 3 days.

To validate findings, we repeated assays in another group of 29 unprotected and 55 protected infants, from the same cohort. The only finding that could be validated was a greater frequency of CD4 T-cells producing granzyme B among unprotected infants.

We conclude that a commonly used outcome of mycobacteria-specific immunity, the proliferative response, did not correlate with ultimate protection against disease. Rather, our results suggest that capacity to produce cytotoxic molecules might be a correlate of risk of TB disease, and should be studied further.

**Title:**           **IDENTIFICATION OF T CELL EPITOPES WITHIN MYCOBACTERIUM TUBERCULOSIS-SPECIFIC PROTEINS IN INDIVIDUALS WITH LATENT AND ACTIVE TUBERCULOSIS DISEASE.**

**Authors:**       Noella Moshi, Cheryl Day, Willem Hanekom

**Objective:**

The objective of this study is to identify sequences within *Mycobacterium tuberculosis* (MTB) proteins that elicit an immunodominant T cell response in individuals with controlled and uncontrolled MTB infection.

The underlying hypothesis is that successful immune control of MTB infection is associated with the maintenance of highly functional MTB-specific T cells which proliferate in response to antigenic stimulation.

**Methods:**

Peripheral blood was obtained from adults with asymptomatic latent MTB infection (LTBI) and no previous history of TB disease (controlled MTB infection), and adults with acid-fast bacilli (AFB) sputum smear-positive and/or culture-positive pulmonary TB disease (uncontrolled MTB infection). Peripheral blood samples were obtained from participants in these two groups and cryopreserved. MTB-specific CD8+ and CD4+ T-cell epitopes were identified using a six day dye-dilution proliferation assay in which cells were stimulated with individual peptides spanning highly immunogenic antigens found in MTB, namely ESAT-6 and CFP-10. Multiparameter flow cytometry was used to determine the proliferative capacity of MTB-specific CD8+ and CD4+ T-cells.

**Results:**

In latently infected individuals, proliferation was greater in magnitude in CD4 cells compared to CD8 cells, for both CFP-10 and ESAT-6. CD8 cells had high responses to peptides located near the C and N terminus of ESAT-6 (E2 and E12); however the CD4 cells response was restricted to the N terminus (E12). With respect to CFP-10, the responses of both CD4 and CD8 cells were localized to the N and C terminus (C4 and C17, C2 and C16, respectively). Preliminary data in TB diseased patients indicates responses to a broader range of peptides, however these studies are ongoing.

**Conclusions:**

There are specific N and C terminal regions that seem to be targeted more frequently by both CD4 and CD8 T cells in CFP-10. There is one region in ESAT-6 (E2) that elicits an immune response in CD8 cells, but not CD4 cells. Both cell types respond to stimulation by the C terminus of ESAT-6. The identification of key immunogenic regions of CFP-10 and ESAT-6 may allow for more targeted, rational design of novel TB vaccines.

**Title:** ARE RECENT QuantiFERON CONVERTERS AT HIGHER RISK OF PROGRESSION TO ACTIVE TB DISEASE WHEN COMPARED TO INDIVIDUALS WITH NO CONVERSIONS?

**Authors:** Shingai Machingaidze<sup>1,2,3</sup>, Fazlin Kafaar<sup>1,2</sup>, Humphrey Mulenga<sup>1,2</sup>, Mark Hatheril<sup>1,2</sup>, Sizulu Moyo<sup>1,2</sup>, Yulieth Angulo-Gonzalez<sup>1,2,3</sup> Willem Hanekom<sup>1,2</sup>, Hassan Mahomed<sup>1,2</sup>.

**Department:** <sup>1</sup>South African Tuberculosis Vaccine Initiative (SATVI), Institute of Infectious Diseases and Molecular Medicine (IIDMM), <sup>2</sup>School of Child & Adolescent Health, <sup>3</sup>School of Public Health & Family Medicine, University of Cape Town, Cape Town, South Africa

**Background:**

Tuberculosis (TB) remains a global health emergency as declared by the World Health Organization. The QuantiFERON Gold In-Tube test (QFT) is a whole blood IFN- $\gamma$  assay (IGRAs) that utilises *Mycobacterium tuberculosis* antigens to determine the presence of latent TB infection. Unlike the Tuberculin Skin Test where conversion from negative to positive has been shown to be a strong predictor for developing active TB disease within 2 years, the predictive value of an IGRA conversion remains unknown.

**Primary objective:**

To determine the risk of developing TB disease in adolescents who have converted their QFT status from negative at baseline (< 0.35 IU/ml) to positive ( $\geq$  0.35 IU/ml) at a subsequent timepoint during the study.

**Method:**

A prospective epidemiological cohort study of TB disease and infection was performed in 6363 adolescents 12-18 years old in the Worcester area of the Western Cape, SA (2005 –2009). 657 of these adolescents who converted their QFT status to positive are being observed for incident active TB disease over a period of a further two years and compared to a randomly sampled control group of adolescents whose QFTs remained negative throughout the original study.

**Results:**

After 11 months of observation, preliminary results show that 7/657(606 person-years of observation) of the QFT converter group have developed TB disease giving an incidence rate of 1155/100 000 person-years (95%CI 465-2361). In the QFT non-converter group 1/606 (557 person-years of observation) developed TB disease giving an incidence rate of 180/100 000 person-years (95%CI 5-996). QFT converters are 6.4 (95%CI 0.79-52.3) times more likely to develop active TB disease than QFT non-converters.

**Conclusions:**

The trend of a higher risk of TB disease in QFT converters which is not statistically significant at this stage may become clearer with continued observation.

**Title:** THE SIGNIFICANCE OF THE D8/17 MARKER (ON B LYMPHOCYTES) IN SOUTH AFRICAN CHILDREN WITH RHEUMATIC HEART DISEASE AND/OR POST STREPTOCOCCAL MOVEMENT DISORDERS

**Authors:** K Walker, M Cooper, K McCabe, J Hughes, W Mathiassen, J Lawrenson, J Wilmshurst

**Objective:**

Acute rheumatic fever and its chronic sequelae, rheumatic heart disease and neuropsychiatric movement disorders, remain major public health problems in South Africa. Early identification and treatment of streptococcal pharyngitis in susceptible individuals would prevent rheumatic heart disease. The B cell antigen D8/17 is a marker of susceptibility to rheumatic fever in some populations. Our aim was to determine its significance as a marker of susceptibility in South Africa.

**Methods:**

We assessed the significance of the D8/17 marker in a South African cohort. Blood was collected from 107 individuals; 40 patients had previous confirmed rheumatic fever and attended the Rheumatic Fever Clinic, 20 were first degree relatives who accompanied these patients to the clinic and 47 were controls. Controls were from the same population and age groups as the index cases and were recruited from Out Patients Clinics where they were having venesection for other indications. Informed consent was obtained and interpreters were used where indicated. The expression of D8/17 in each sample was analysed by flow cytometry. The mean and standard deviation of the percentage of B cells positive for D8/17 were calculated for each group. Analysis of variance was calculated and the differences between the means of each category and the 95% confidence interval of these differences were calculated. Ethical approval was obtained from the Research Ethics Committee of the University of Cape Town; Ethics approval number REC/REF 011/2006.

**Results:**

The mean proportion B cells that were D8/17 positive was 0.5% in the index cases, 0.47% in their relatives and 0.27% in the controls. There was a significant difference between the index cases and the controls,  $p=0.03$ . However the actual percentages in this cohort were markedly lower than in other populations, ranging from 0.14% - 1.53% compared to 11.6%-39.3%.

**Conclusions:**

D8/17 monoclonal antibody required to test for D8/17 marker is not commercially available and can only be sourced from the Rockefeller Institute. Flow cytometry requires sophisticated laboratories which are not available in areas where the prevalence of acute rheumatic fever is high. The D8/17 marker is not robust and is impractical as a screening tool in South Africa.

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

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

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

**Introduction:**

There is limited data available on the prevalence and characteristics of children with epilepsy in South Africa.

**Aim:**

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

**Methods:**

Departmental database records of all patients with neurological disorders managed over a 10 year period (Jan 2000 – 10) were reviewed. The database was sorted to select the total number of children with epilepsy and their characteristics reviewed. Comparison was made with equivalent studies.

**Results:**

From a cohort of 4823 patients, 53% had epilepsy (n=2571). Of these, 44% were female (n=1105) and 56% male (n=1440). 40% were of mixed ancestry, 37% African ancestry and 16% European ancestry. 271 patients were excluded from further analysis due to insufficient information regarding their epilepsy semiology or aetiology. 50% of the remaining patients presented below 1 year of age, 35% between the ages of 1 and 5 years and 15% between 5 and 12 years. 65% had symptomatic- and 35% idiopathic epilepsy. Of the idiopathic group, 5.8% had a positive family history of epilepsy. Semiological categorization was possible in 1788 patients: 764 (43%) had generalized epilepsy, 1024 (57%) partial epilepsy. 20% of patients had medication refractory epilepsy. Co-morbidities were evident in 55% of patients (n=1412/2571) resulting in a high demand for special care needs in these patients.

**Conclusions:**

Epilepsy is a common condition in South Africa; many of these patients have avoidable aetiologies. The presence of co-morbidities is significant for the large cohort of patients.

**Title:** SKETCHING A PICTURE OF TUBERCULOUS MENINGITIS AT RED CROSS CHILDREN'S HOSPITAL

**Authors:** Ursula Rohlwink, Sharron Isralls, Meeka Tulleken, Saxony Moolman, Larissa Hemraj, Marara Radue, Geoffrey Modise, Anthony Figaji

**Department:** Paediatric Neurosurgery Unit, Institute of Child and Adolescent Health, Red Cross War Memorial Children's Hospital, 021 658 5340

**Introduction:**

Tuberculous meningitis (TBM) is one of the most lethal forms of tuberculosis (TB) and continues to be associated with high rates of mortality and severe neurological disability. TBM occurs with high frequency among children in the Western Cape. Although Red Cross War Memorial Children's Hospital (RCCH) is the largest children's hospital draining this region, there is a paucity of information about the prevalence of TBM, diagnostic work-up and results, as well as details about patient treatment and management at this hospital.

**Objective:**

This study aimed to collect some preliminary data on patients admitted to RCCH for TBM in terms of presenting features, diagnostic work-up, as well as treatment and management protocols.

**Methods:**

This retrospective cross sectional study analysed data from a selection of patients admitted to RCCH for definite or suspected TBM over a 3 year period from 2007 to 2009. Definite TBM was defined by CSF culture positivity for mycobacterium tuberculosis or the presence of acid fast bacilli, and suspected TBM was defined by the initiation and continuation of anti-TB treatment. Data was collected from patient folders, the hospital infectious diseases registry, the neurosurgical database as well as the computed tomography (CT) scan record book. Data was collected on admission signs and symptoms, clinical, radiological and biochemical investigations and findings, treatment and management, as well as mortality. Data was analysed using descriptive statistics, probabilities, chi square and odds ratios.

**Results:**

Data was collected from 70 patients. The average age was 3.3 ( $\pm 3.2$ ) years and 65.7% of patients were HIV positive. A definite diagnosis of TBM was made in only 22.8% of patients. No significant differences were found between definite or probable TBM patients on clinical, radiological or biochemical data. Hydrocephalus was documented in 60% of patients; of these cases 64% had communicating hydrocephalus, 16% had non-communicating and for 19% it was not noted. CT scans were performed in 87% of children, and lumbar punctures (LP) in 88%. Half of the LP's were performed before the CT scan, and half afterward. Hyponatraemia was present in 44% of patients and was significantly associated with seizures (OR 2.87, 1.06 -7.79) and infarction (OR 4.51, 1.61 -12.62). Diagnoses of both syndrome of inappropriate anti-diuretic hormone secretion and cerebral salt wasting were occasionally made, however these were largely not investigated or treated. The mortality rate was 11.4%

**Conclusion:**

RCCH admits a considerable number of children with TBM, however the diagnostic rate of definite TBM is low, and patient management appears to be unsystematic and sometimes inappropriate. Patient management and diagnostic yield could be improved by the development of a clear management protocol which is faithfully followed.

**Ethics:** This project was part of the 2<sup>nd</sup> year medical students' Special Studies Module which has received blanket ethics approval. Permission to access hospital records was obtained from hospital administration.



**Title:** INTERPRETING THE BABY'S CUES, UNDERSTANDING THE MOTHER'S STORY: CHARACTERIZING A MEDIATED INTERVIEW

**Authors:** Claire Penn<sup>1</sup>, Astrid Berg<sup>2</sup>

**Department:** University of the Witwatersrand<sup>1</sup>, University of Cape Town<sup>2</sup>

**Introduction:**

The majority of health care interactions in South Africa take place in the presence of a third party, particularly in a primary health care setting; the success of health care intervention depends on the effectiveness of this three party relationship in which the infant plays a crucial role. A collaborative partnership has been developed at the Mdzlezana Centre of the UCT Parent-Infant Mental Health Service in Kuyasa in Khayelitsha.

**Objective:**

This pilot study explores in more detail the active components of this every day practice relationship, more specifically it

- Explores components of a successful partnership in an intercultural health setting
- Identifies the organizational routines in the setting
- Examines verbal and non verbal strategies for achieving mutual understanding

**Methods:**

- Ethnography of clinic
- Video-recording of clinical interactions
- Transcription, translation, review
- Interviews with all participants

**Findings:**

- Strategies of brokerage were observed on multiple levels of verbal and non-verbal communication, elucidating some of the mechanisms that underlie the collaborative relationship which is a prerequisite for a mediated interview.
- Organizational features contributed to providing a stable frame within which the collaborative relationship could take place

**Conclusions:**

This study highlights strategies which contribute towards a successful mediated interview. "Cultural safety" should be aimed for; the role of the cultural broker should be recognized and should be made an integral part of South African health care policy.

**Title:** PRIMARY IMMUNODEFICIENCIES: A 27 YEAR REVIEW AT A TERTIARY PAEDIATRIC HOSPITAL IN CAPE TOWN, SOUTH AFRICA

**Authors:** Naidoo R, Ungerer L, Cooper, M, Pienaar S, Eley BS

**Objectives:**

The epidemiology of primary immunodeficiencies (PID) is not well documented in Africa. The objective of this study was to identify the spectrum of PID at a tertiary paediatric centre in South Africa, and to describe clinical presentation, management and outcome.

**Methods:**

A retrospective descriptive analysis was conducted on patients diagnosed with PID at Red Cross Children's Hospital from 1983-2009.

**Results:**

Over the study period, 168 patients were diagnosed with PID. Antibody deficiencies predominated (51%) followed by well defined syndromes (24%) and combined B and T cell deficiencies (11%). Common variable immunodeficiency was the commonest antibody deficiency. The mean age of diagnosis was 51 months overall but decreased significantly to 35 months over the last 9 years. Recurrent infections rather than atypical infections were the most frequent presenting complaint (74%). A high incidence of regional or disseminated *Mycobacterium bovis* BCG disease was noted in combined immunodeficiencies. The overall mortality rate was 25% while combined immunodeficiencies accounted for 40% of the deaths.

**Conclusions:**

The spectrum of PID in South Africa was similar to international trends in Europe, Asia and Latin America. The declining mean age of diagnosis indicated improved recognition of PID. Future research should focus on identifying children with PID more effectively.

**Title:** A FAST SIMPLE GC-MS METHOD FOR URINARY HOMOVANILLIC ACID

**Authors:** Baldwin Foster, David Haarburger, Ryan Benjamin, George van der Watt

**Relevance:**

Homovanillic acid (HVA), the primary metabolite of dopamine is measured as a tumour marker for neuroblastoma, the most common extra-cranial tumour in children. Patients with neuroblastoma excrete large amounts of HVA in urine. Due to the low specificity of our current colorimetric method, a fast and accurate Gas Chromatography – Mass Spectrometry (GC-MS) based method was developed to overcome this issue.

**Materials and Methods:**

Extraction and derivatisation: An aliquot of acidified urine spiked with vanillic acid (VA) internal standard was double extracted into ethyl acetate and diethyl ether using a rapid low volume micro-extraction technique and the supernatant dried down with nitrogen prior to bis(trimethylsilyl)trifluoroacetamide and pyridine derivatisation at 80°C for 30 minutes. Analysis: A Single Ion Monitoring method was used for HVA quantitation using ions m/z 326 for HVA and m/z 297 to identify the VA internal standard on an Agilent 7890A5975C GC-MS system using a 30m, ID 0.25µm, HP-1 MS column.

**Method Evaluation:**

The method was found to be linear across the range 0.78 – 100µmol/L with a slope coefficient and coefficient of determination ( $r^2$ ) of 1.180 and 0.98 respectively. Within run and total imprecision (n=20), determined by analysis of variance was 3.0 and 3.3% at 50µmol/L respectively. The accuracy of the method was evaluated by recovery experiments and yielded recoveries of 96, 97 and 83% at 25, 50 and 200µmol/L respectively. In addition 4 Bio-Rad urine external quality scheme controls resulted within 2 standard deviations of the scheme median. Total method run time approximated 70 minutes

**Conclusion:**

The use of a low volume micro-extraction method together with a low cost non-isotopic internal standard allows rapid efficient screening for urine HVA by GC-MS with acceptable method performance parameters. Specificity will be evaluated but should be high as GCMS ion profiles are specific to each analyte. Clinical evaluation will follow.

**Title:** POSTSTREPTOCOCCAL SYNDROME UVEITIS IN CHILDREN

**Authors:** L.van Zyl, C.Tinley, R.Grötte

**Department:** (Red Cross Children's Hospital Ophthalmology Department)

**Objective:**

To describe the demographics, clinical features and management of the largest case series to date on poststreptococcal syndrome uveitis (PSU), a newly recognised immune-mediated response to group A beta-haemolytic streptococcus infection.

**Methods:**

Case notes of all patients presenting to the Red Cross Children's Hospital Eye Unit with serologically confirmed PSU between 2004 and 2010 were retrospectively reviewed. Epidemiological data, clinical findings, initial anti-streptolysin O (ASO) and anti-deoxyribonuclease B (anti-DNase B) titres, treatment strategies and outcomes were recorded.

**Results:**

A total of 22 cases were identified. Ages ranged from 4 to 12 years. 64% were black and 64% were male. Presenting visual acuities ranged from 6/6 to hand movements (median 6/24). 68% had bilateral uveitis. All had anterior uveitis (27% with posterior synechiae and 27% with hypopyon). 36% had vitritis and 23% a more severe panuveitis. None had systemic features of other poststreptococcal syndromes, such as rheumatic fever, glomerulonephritis, or reactive arthritis. ASO titres were 0.4 to 7.4 (mean 2.1) times greater than the age-specific upper limits of normal. Where these were not raised, the complementary anti-DNase B titres were significantly increased (0.5 to 40 times, mean 10.2). 91% had raised erythrocyte sedimentation rates (range 1-77mm/h, mean 40mm/h). In all cases, treatment comprised topical steroids and cycloplaegic agents. Those with more severe disease (41%) required systemic corticosteroid therapy. 82% had a single episode of uveitis. Four had recurrent attacks, one of which, with chronic relapsing disease (8 episodes), was treated with systemic methotrexate. 55% received a course of oral penicillin. Final visual acuities ranged from 6/6 to 6/30 (median 6/6).

**Conclusions:**

This case series effectively doubles the evidence of PSU currently available in the world literature. Heightened awareness of the condition and prompt serological screening will ensure good visual outcomes in this readily treatable, albeit uncommon cause of uveitis in children.

**Title:** A RETROSPECTIVE REVIEW OF GASTROSTOMY PLACEMENT FOR FEEDING AND SWALLOWING DIFFICULTIES IN THE PAEDIATRIC POPULATION AT RED CROSS WAR MEMORIAL CHILDREN'S HOSPITAL

**Authors:** Tessa Hittler, Nicole Jones, Nicoll Kenny, Robyn Mann, Samantha McFarlane, Anitah Moeng  
Supervisor: Vivienne Norman

**Background:**

Feeding and swallowing difficulties in the paediatric population frequently result in aspiration and inadequate oral intake. Respiratory health and growth may therefore be affected and may indicate the need for gastrostomy placement. A multidisciplinary team is required to optimally manage children receiving a gastrostomy. Benefits of gastrostomy placement have been discussed in the literature and include respiratory health and weight gain, there is however limited South African data.

**Aim:**

To describe the paediatric population requiring gastrostomies for feeding and swallowing difficulties and their service delivery needs.

**Objectives:**

In the paediatric population with feeding and swallowing difficulties who received gastrostomies at Red Cross War Memorial Children's Hospital (RCWMCH) between 2005 – 2009, the following were described: a) the underlying medical conditions; b) the indications for gastrostomy placement c) the health services required specifically related to feeding and swallowing difficulties and gastrostomy placement; d) the outcomes of gastrostomy placement in the study population with regard to feeding outcomes, respiratory health, weight gain and gastrostomy removal.

**Method:**

A retrospective descriptive survey of 114 participant folders of infants and children who underwent gastrostomy placement for feeding and swallowing difficulties from 2005 - 2009 was conducted. Descriptive (e.g. frequency) and inferential (paired *t*-tests) statistics were used to analyse data.

**Results:**

GIT (84.21%) and neurological disorders (82.46%) were the predominant medical diagnoses in the study population, and dysphagia (70.8%), aspiration (61.9%) and nutritional support (46%) the main indications for placement. A multidisciplinary team conducted various assessments and provided ongoing intervention for the study population. The majority of the study population (85%) was assessed by a speech-language therapist before gastrostomy placement, while 97% of the sample required follow up services from both the dietician and stoma sister. The mean duration of services from speech-language therapists was 17.93 months.

A significant decrease in admissions for failure to thrive ( $p < .016$ ) and significant weight gain ( $p < .004$ ) was documented after gastrostomy placement in the study sample. Feeding and respiratory health outcomes were also documented.

**Conclusion:**

The profile and outcomes of the South African paediatric population with gastrostomies is similar to published literature.

**Title:** FACING THE CHALLENGES OF CARING FOR THE PAEDIATRIC ONCOLOGY PATIENT WITH A CENTRAL VENOUS ACCESS DEVICE

**Authors:** Dorothy Moodie, Claudine Jefthas, Barbara Olsen, Angela Leonard, Minette Coetzee, Alan Davidson

**Department:** Red Cross Children's Hospital, Cape Town, South Africa

### **Objective**

Children in our unit receive chemotherapy either peripherally or by means of central venous access devices (CVADs); portacaths and indwelling double lumen lines. These CVADs may be complicated by infection or blockage, often necessitating removal, or the accidental removal of an indwelling line by the patient. The purpose of the study was to measure the complication rates of CVADs, to compare the advantages and disadvantages of different forms of access, and to consider what measures we can take to treat or prevent complications.

### **Methods**

A retrospective chart review was done on oncology/haematology patients being treated in our unit between 2006 – 2008. We calculated the proportions managed with peripheral access, portacaths and indwelling double lumen lines. We then examined these groups to see how many lines became infected or blocked, and how many required removal as a result, or were removed accidentally.

### **Results**

Of the 342 patients reviewed 68 (20%) had CVADS, and 274 (80%) were treated through peripheral lines. Among the patients with CVADs 33 (48.5%) had portacaths and 35 (51.5%) had indwelling double lumen lines. Infection rates were 21% for portacaths, of which 71% had to be removed, and 29% for indwelling double lumen lines, of which 80% had to be removed. Three (8.6%) of the indwelling double lumen lines were removed accidentally.

By comparison, none of those patients treated with peripheral access suffered significant line sepsis.

### **Conclusions**

The advantages to patients and staff of CVAD have to be weighed against the potential for infection. A high standard of care needs to be maintained to decrease the likelihood of the device being removed due to infection, blockage or accident. Untimely removal of an expensive device is neither cost-effective nor helpful in decreasing the pain and trauma experienced by paediatric oncology patients.

**Title: PERITONITIS IN CHILDREN ON PERITONEAL DIALYSIS (PD) IN SOUTH-AFRICA: EPIDEMIOLOGY AND RISK FACTORS**

**Authors:** Renske Raaijmakers, Priya Gajjar, Cornelis Schröder, Peter Nourse

**Objectives:**

To evaluate the peritonitis epidemiology in pediatric patients in Cape Town South Africa and to identify risk factors for peritonitis

**Methods:**

A retrospective cohort study was performed. All patients younger than 18 years enrolled in the peritoneal dialysis program between 2000 and 2008 were analyzed. Baseline characteristics and potential risk factors were recorded, including: housing, socio-economic circumstances, distance to PD centre, type of PD, mode of catheter placement, weight and height. Outcome indices for peritonitis were peritonitis rate, time to first peritonitis and peritonitis free patients. All peritonitis episodes were analyzed concerning causative organism, severity of peritonitis (fungal or gram negative), catheter policy, occurrence of technique failure and survival.

**Results:**

67 patients were included, who were on PD for a total of 544 months. The total number of peritonitis episodes was 129. Median peritonitis rate was 0.23/patient month (range 0-1.76). Median time to first infection was 2.03 months (range 0-21.5 months), while 28.4% of patients remained free from peritonitis. Patients with good housing and good socio-economic circumstances had a significantly lower peritonitis rate and a longer time to first peritonitis episode. The other risk factors were not associated with a higher risk of peritonitis outcome.

**Conclusions:**

Peritonitis rate is high in this cohort, compared to numbers in the developed world, the characteristics of causative organisms are comparable. Most important risk factors for development of peritonitis are poor housing and poor socio-economic circumstances.

**Title:** REVIEW OF 10 YEARS OF ACUTE PERITONEAL DIALYSIS IN PICU SETTING

**Authors:** McCulloch MI, Gajjar PJ, Nourse P, Du Buisson C, Sinclair PJ, Argent A.

**Department:** Red Cross Children's Hospital (RXH), University of Cape Town.

### **Introduction**

Acute kidney injury carries a high mortality in paediatric multi-organ dysfunction syndrome (MODS). Advances in technology have seen a shift in management from peritoneal dialysis (PD) to continuous renal replacement therapy (CRRT) in many countries. Yet PD remains the mainstay of therapy in many PICU's especially in poorly resourced countries

### **Aim**

Retrospective case-review of all patients receiving acute PD from 2000 to 2009 at RXH including overall mortality and specific mortality rates, indications for dialysis, types of PD and complications.

### **Results**

Total of 406 cases in 10 years with a weight range from 900g to 70kg and age range 1 day to 16 years. Indications included predominantly hyperkalaemia, anuria, acidosis, oliguria and fluid overload.

Specific groups were reviewed and included Neonates (< 1month) 85/406(21%); Infants (<1 year) 221/406(54%) and Cardiac patients 95/406(23%).

Types of PD catheters used (Cook, Peel away Tenckhoff and Surgical Tenckhoff) and type of PD (Manual, Cycling machines and CRRT) were analysed per year.

Overall complications of 15.6% overall was recorded; mainly being due to poor drainage or catheter blockage. No deaths due to catheter insertion seen.

A wide range of disease processes was seen ranging from Diphtheria to Liver Transplants. Kwashiorkor in particular had a poor outcome with 7/7(100%) mortality.

Mortality rates overall 42%; Neonates 53%, Infants 53% and Cardiac 41%.

### **Conclusion**

Acute PD is available and appropriate in resource poor environments but is also appropriate in well-resourced countries in certain patient groups such as post-operative cardiac patients and haemodynamic instability. This modality can be commenced rapidly and does not require high levels of training.

The overall mortality rate of 42% compares favourably with other forms of renal replacement therapy. No deaths were seen as direct result of PD catheter insertion.



**Title:** IS IT AN EFFECTIVE USE OF RESOURCES FOR PAEDIATRICIANS TO ATTEND ALL ELECTIVE CAESARIAN SECTIONS?

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

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

**Background:**

It is currently a requirement for a paediatrician to attend all non-complicated elective Caesarean sections (C/S) at Groote Schuur Hospital (GSH). This has significant implications for the effective utilisation of scarce medical personnel.

A number of studies have been conducted in the developed world to determine which deliveries require medical attendance in the form of a paediatrician. They all found that the attendance of a paediatrician at uncomplicated elective C/S conducted under regional anaesthesia was unnecessary. This requirement has fallen away in many other countries but continues in most parts of South Africa. There have been no local studies investigating the appropriateness of this practice.

**Aim:**

To determine the need for resuscitation at the birth of babies delivered by elective C/S at GSH.

**Methods:**

Data was collected prospectively on all elective C/S performed at GSH over a 3 month period. The attending paediatricians were trained to complete a structured proforma. Data collected included: total time involved for paediatrician from call to leaving theatre, management of infant (requiring any form of resuscitation), Apgars and neonatal outcome (e.g. admission to nursery).

**Results:**

Data were recorded for 138 deliveries. 15 were excluded as they did not meet the criteria for non-complicated elective C/S (emergency C/S, multiple births, prematurity and VLBW). There remained a total of 123 deliveries. The primary reasons for elective C/S were: Previous C/S (85), previous C/S and infant of diabetic mother (IDM) (15), big baby (10), IDM (6), other (7).

The data recorded that 7 infants required moderate resuscitation at birth (bag and mask). On reviewing the medical records of these 7 infants, 6 of them did not meet the criteria of non complicated elective C/S. 3 were delivered under general anaesthetic, 1 was in a breech position and 2 were preterm deliveries.

1 low risk infant out of a total of 116 deliveries required moderate resuscitation with bag and mask for a short period of time and did not require admission to the nursery

The average time spent at each elective caesarean section by the paediatrician was 37 minutes.

**Conclusions:**

Non complicated elective C/Ss performed under regional anaesthesia at GSH are low risk deliveries. These deliveries do not require the routine attendance of a paediatrician. This conclusion would allow more effective use of scarce manpower resources.

**Title:** **WHAT IS THE CURRENT RATE OF CATHETER RELATED BLOODSTREAM INFECTION IN THE PAEDIATRIC INTENSIVE CARE UNIT AT THE RCWMCH?**

**Authors:** Susan Carolus, Angela Leonard, Charmaine Rinquist, Bernie Francis, Candice Bonaconsa, Minette Coetzee & Andrew Argent (in Collaboration with the Lucille Packard Children's Hospital and Heartlink)

**Objective:**

Central venous catheters are frequently used to provide secure vascular access for monitoring and also for therapy (TPN and infusion of vasoactive drugs) in critically ill children. This results in a significant number of children being at risk for developing catheter related bloodstream infections (CRBSI). These infections are associated with significant mortality, morbidity, prolonged hospital admission and obvious healthcare costs. With this in mind, a team was established in the RCWMCH Paediatric Intensive Care Unit (PICU) as a part of a practice improvement project to address CRBSI in the unit.

**Methods:**

Daily information on the number of central lines in use was collected from the PICU. Blood stream infections were identified from laboratory results. All children with positive blood cultures were reviewed to assess whether the infection was related to a central venous line (using definitions from the CDC).

**Results:**

Over the 3 months period (1st May to 31st July 2010), four children (median age 6, range 2-42 months) were identified with CRBSI and a total of 546 line days. Reasons for admission were: metabolic acidosis, flame burns, measles and pneumonia and emergency admission for head trauma. Duration of PICU stay was 6(2-42) days, and risk of mortality on admission was 15.3 % ( 6.5-33%). Over the 3 month period the rate of CR-BSI was 7.3 per 1000 catheter day (range per month 3.7 to 16.2).

**Conclusions:**

Current rates of CR-BSI are unacceptably high (by international standards). This study has provided baseline data for further interventions in an effort to reduce this infection rate.

**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>Linda van der Merwe, <sup>1</sup>Ashley Veldsman, <sup>1</sup>Mark Hatherill, <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.

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. Our objective was to characterise 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) the proliferative capacity of Ag85A-specific CD4 T cells would increase over time following MVA85A vaccination; (2) and this will be associated with the emergence of Ag85A-specific CD4 T cells expressing a central memory phenotype.

Participants were vaccinated with a single dose of  $5 \times 10^7$  pfu of MVA85A; all received BCG at birth and were not infected with *M. tuberculosis*. Ag85A peptide pool or PPD-specific T cell proliferation was measured in PBMC by Oregon Green dye dilution. PBMC were stained with an Ag85A peptide loaded HLA-DRB1\*0301 class II tetramer, and activation and memory phenotype assessed.

Ag85A-specific CD4 T cell proliferation pre-vaccination was low, but increased to peak 56 days post-vaccination, and remained above pre-vaccination levels during the 6-month follow-up period. *Ex vivo* frequencies of tetramer<sup>+</sup> CD4 T cells peaked 7 days after vaccination and returned to baseline levels between 56 and 84 days after vaccination. Precursor frequencies of tetramer<sup>+</sup> cells did not predict proliferative potential. Expression of the activation marker CD38 on tetramer<sup>+</sup> cells peaked at 7 days and returned to pre-vaccination levels by 28 days. These cells predominantly displayed an effector (CD45RA<sup>-</sup>CCR7<sup>-</sup>CD27<sup>-</sup>) phenotype during the first month post-vaccination; the proportion of central memory cells (CD45RA<sup>-</sup>CCR7<sup>+</sup>CD27<sup>+</sup>) increased consistently up to 168 days after vaccination. A central memory phenotype correlated with proliferative potential.

We concluded that MVA85A induces long-lived, central memory CD4 T cells with potential proliferative capacity upon antigen re-encounter.

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

**Title:** CHILDHOOD ANTI-NEUTROPHIL CYTOPLASMIC ANTI-BODIES (ANCA) POSITIVE VASCULITIS: A Case Series of Four Patients

**Authors:** P Gajjar<sup>1</sup>, P Nourse<sup>1</sup>, K Pillay<sup>2</sup>

**Department:** <sup>1</sup>Renal Unit, Red Cross Children's Hospital  
<sup>2</sup>Histopathology services, Red Cross Children's Hospital

**Introduction:**

ANCA positive vasculitis is rare in childhood with few case reports in the literature. ANCA constitutes a marker of a group of systemic vasculitis including Wegeners granulomatosis, microscopic polyangiitis (MPA), Churg-Strauss angiitis and necrotising, crescentic glomerulonephritis without extra-renal involvement.

**Aim:**

(1) to document the clinical, histological and serological characteristics of children with ANCA positive vasculitis presenting to Red Cross Children's, and Tygerberg Hospital; and  
(2) to review their management and outcome.

**Method:**

A retrospective folder review of patients with the following criteria:

- 1) clinical manifestations of small vessel inflammation
- 2) histological features of necrotising glomerulonephritis, predominantly pauci-immune, and
- 3) serological finding of ANCA positivity, either cytoplasmic (cANCA), or perinuclear (pANCA)

**Results:**

Four patients met the criteria. They were all girls, ranging from 5 yrs to 12 yrs; mean age of 7.5 yrs. The main clinical findings were: influenza-like symptoms (75%), haematuria/proteinuria (100%), pulmonary-renal syndrome with haemoptysis in 50%, and acute renal failure in 50%. One patient presented to the ophthalmologist with bilateral lacrimal gland swelling. All were hypertensive. One patient presented initially with rapidly progressive nephritis, and six years later had a pulmonary haemorrhage. In the rest, the diagnosis was confirmed within two months of presentation.

All had an elevated ESR, with normal complement and antinuclear antibody levels.

Three of the four patients had an elevated pANCA; the patient with lacrimal gland swelling was cANCA positive.

All underwent a renal biopsy, showing necrotising lesions with fibrous and fibrocellular crescents. One biopsy showed positive immunofluorescence, the rest were pauci-immune.

Initial treatment included pulsed intravenous methylprednisone, steroids, and minimum of 6 doses of monthly intravenous Cyclophosphamide; followed by maintenance treatment with steroids plus a purine antagonist.

One patient had frequent relapses, progressed to end stage renal failure, and subsequently died. The rest are well, in remission.

**Conclusion:**

Small vessel vasculitis should be considered early in the differential diagnosis of patients presenting with constitutional symptoms or unusual presentation involving the upper or lower respiratory tract, with abnormal urinalysis. An autoimmune screen should include ANCA serology. The goal is prompt accurate diagnosis and early initiation of appropriate therapy. Steroids and Cyclophosphamide are effective as induction therapy.

**Title: INDUCED HYPOTHERMIA FOR INFANTS WITH HYPOXIC ISCHEMIC ENCEPHALOPATHY USING A SERVO-CONTROLLED FAN: PROTOTYPE DEVELOPMENT AND SHORT-TERM OUTCOMES.**

**Authors:** AR Horn, MC Harrison, Y Joolay, M Richards, G Moller, N Rhoda, C Pieper, L Tooke, MS Raban, C Thompson.

**Objective**

Therapeutic hypothermia is beneficial in selected newborn infants with hypoxic-ischemic encephalopathy (HIE). However, the established cooling methods are labour-intensive, expensive or technically difficult to use. The objective of this study was to describe the use, efficacy and physiological impact of an inexpensive servo-controlled cooling fan blowing room-temperature air and to develop a prototype for potential distribution.

**Patients and methods**

A servo-controlled fan was manufactured and used to cool 31 infants with HIE, to a rectal temperature of 33–34 °C. The first 10 infants were cooled using a computer-driven fan with a separate heat shield over the head. Data from these 10 infants was used to inform the programming and manufacture of a separate microprocessor-controlled fan with an incorporated heat shield. 21 further infants with HIE were cooled using this prototype. The infants were sedated with phenobarbital, and morphine was given if shivering or restlessness occurred. A servo-controlled radiant warmer was used simultaneously with the fan to prevent overcooling and the temperature data from this warmer that was transmitted to the fan, informed the subsequent fan speed. Re-warming was achieved by turning off the fan and then increasing target temperature in 0.2°C increments until a rectal temperature of 36.5 °C was attained. Physiological data was recorded hourly. Adverse events and short-term outcomes were recorded.

**Results**

Data is presented for all 31 cooled infants as single group. A rectal temperature of 34 °C or less was achieved in less than an hour in 77% of infants. Overcooling did not occur and the mean temperature during cooling was 33.7 ± 0.1 °C. Adverse events including seizures, hypoglycaemia, ventilation requirement, coagulopathy and inotrope requirement progressively decreased every day during the three days of cooling, and base excess and creatinine levels similarly improved with time over the same period. Mean Thompson HIE scores decreased progressively from 12 at presentation to 2 by the 10<sup>th</sup> day. 45% of infants were either discharged or had a Thompson score less than 2 by the 7<sup>th</sup> day. Of the 16 infants with a severely abnormal aEEG at presentation, 44% had normalized aEEG voltage by 24 hours. Long term neurological outcomes are awaited.

**Conclusions**

Servo-controlled fan cooling with room-temperature air, combined with servo-controlled radiant warming was an effective, simple and safe method of inducing and maintaining rectal temperatures of 33–34 °C in sedated infants with HIE. Warmer-controlled re-warming at 0.2 °C increments every 30 – 60 minutes resulted in a well-controlled temperature rise. Adverse events typically associated with HIE progressively improved during the 3 days of cooling and more infants showed aEEG recovery at 24 hours than is described in similar non-cooled infants with HIE.

**Title:** BACTERAEMIA IN A COHORT OF HIV-INFECTED CHILDREN FROM CAPE TOWN, SOUTH AFRICA.

**Authors:** David M le Roux, \*Mark F Cotton, Stanzi M le Roux, \*\*Carl J Lombard, Heather J Zar

**Department:** School of Child and Adolescent Health, Red Cross War Memorial Children's Hospital, University of Cape Town, \*Department of Paediatrics and Child Health, Tygerberg Children's Hospital, Stellenbosch University, \*\* Biostatistics Unit, Medical Research Council, South Africa

**Aims:**

Bacteraemia is an important cause of morbidity and mortality in HIV-infected children. In sub-Saharan Africa, many children do not yet have access to anti-retroviral therapy. We describe the incidence of bacteraemia in a cohort of HIV-infected children from South Africa.

**Methods:**

HIV-infected children enrolled in a randomised controlled trial evaluating 2 regimens of co-trimoxazole preventative therapy (CPT) were followed for 5 years from January 2003. Blood cultures were taken during acute admissions, when clinically indicated.

**Results:**

324 children were followed for 672 person-years; 361 blood cultures were taken from 125 children. 47 bacteraemias occurred in 30 children; there were 22 (47%) Gram positive and 25 (53%) Gram negative bacteria. *S. pneumoniae* was the commonest isolate, 32% of the total.

53 children died during the study (16.4%); children with documented bacteraemia had higher risk of death than those without bacteraemia (risk ratio 3.18, 95% CI 1.93 to 5.05). Children receiving intermittent CPT had higher incidence of bacteraemia than those receiving daily CPT (9.63 vs. 4.08 per 100 person-years, incidence rate ratio (IRR) 2.36, (95% CI 1.21 to 4.86). Children established on highly active antiretroviral therapy (HAART) had lower incidence than children not on HAART (2.2 vs. 8.5 per 100 person years, IRR 0.26, 95% CI 0.09 to 0.61).

**Conclusion:**

Bacteraemia in HIV-infected children is common and associated with high mortality; we observed lower rates of bacteraemia in children established on HAART. Measures such as pneumococcal vaccines, cotrimoxazole preventative therapy and HAART should be scaled up for HIV-infected children in Africa.

**Title:** IPNA FELLOWSHIP PROGRAM FEED-BACK IN AN AFRICAN CENTRE

**Authors:** McCulloch MI, Gajjar PJ, Nourse P, Sinclair PJ.

**Department:** Red Cross Children's Hospital, University of Cape Town, South Africa.

**Introduction:**

IPNA assisted in establishing a Fellowship Program in 2003 to allow paediatricians from various parts of Africa to train within Africa in the field of paediatric nephrology.

**Objectives/Methods:**

Review feedback by questionnaire of IPNA Fellows who have trained at a single centre, Red Cross Children's Hospital (RXH), Cape Town, South Africa from September 2003 to March 2010.

**Results:**

Ten fellows were accepted onto the program of which 2 are still completing their training. All 8 trainees who completed their fellowship have returned to work in their country of origin and 7/8 completed the questionnaire. Countries of origin of trainees included Nigeria (3 fellows), Kenya (3), Benin (1), Ghana (1) and Uganda (1). Time spent in training ranged from 6 months to 2 years (mean 15months, median 18 months). On return to countries of origin; 4/7 are based in state practice only, 1/7 in private practice only and 2/7 both state and private. Their nephrology work-load is judged as 4/7(50-75% of total work), 2/7(25 – 50%) and 1/7(10-25%).

Training useful	Yes 7/7(100%)
Specific areas useful	Clinical approach and hands-on skills 7/7 (100%) Biopsies 5/7(71%) Dialysis 7/7(100%)
Areas to improve in training	More Haemodialysis 2/7(29%) More Histology 2/7(29%) More on-calls 1/7(14%) More structured program 1/7(14%) No improvement needed 1/7(14%)
SA Paeds Nephrol Certificate(need 18mths training to qualify- not required by IPNA)	Successful 4/7(57%)
On-return to home Institution	Support by Institution 5/7(71%)
Challenges	Poor Staffing 7/7(100%) Lack of facilities and equipment 6/7(86%) Radiology – Ultrasound only 6/7(86%) Histology support poor in 4/7(57%)
Fellows presenting papers at Congresses	7/7 presented papers at RXH and Local African meeting (100%) 5/7 International Congress (71%)

**Conclusion:**

IPNA sponsored fellows feel that this is a successful program in an African setting, with appropriate clinical teaching and 'hands-on' learning of biopsy and basic acute peritoneal dialysis skills. They also developed oral presentation skills at academic meetings.

All the fellows in this program returned to their countries of origin, often facing difficult circumstances requiring personal motivation and imagination to adapt skills to their environment. They felt that further support was needed on return, in terms of institutional support, staff and resources in particular.

**Title:**           **INCREASING LEARNING OPPORTUNITIES IN PAEDIATRIC ONCOLOGY SETTINGS**

**Authors:**       Dorothy Moodie, Angela Leonard and Minette Coetzee

Ward G1 at Red Cross War Memorial Children's War Memorial Hospital is the specialist Haematology/Oncology Unit, involving technological dependent care. We deal with life threatening illness with potentially dangerous treatment. Among the many children treated each year, a group of these children are referrals from as far a field as Ghana. While most treatments are done at this unit, an increasing number of children are referred to regional centres for less complicated chemotherapy regimens. However nurses lack the required specialization to train and treat paediatric oncology.

Following last year's child nurse practice development initiative project which improved patient safety by increasing awareness and decreasing the number of extravasations that occur, in 2010 we shifted our focus to increasing learning opportunities.

We tracked all teaching sessions, including bedside teaching in the ward. We encouraged participation of nursing staff, medical staff and other. We looked for opportunities linked to practice issues as these arose in the ward. We used opportunities to expand beyond the ward, hospital and our region. We increased teaching in ward from 3 documented in 2009 to 23 in 2010; in addition we gave 9 teaching sessions to regional nurses and at an international conference presented a poster and presentation.

This poster serves to track the increasing number of learning opportunities, for bedside, hospital, regional and international learning opportunities. As well as how this pertains to nurses' perceptions in the G1 oncology ward. It will also explain the challenges of maintaining oncology training of nurses in this type of specialist oncology unit.



**Title:** AN INVESTIGATION INTO THE EFFECT OF CLOSED SYSTEM SUCTIONING ON THE INCIDENCE OF PAEDIATRIC VENTILATOR-ASSOCIATED PNEUMONIA IN A DEVELOPING COUNTRY.

**Authors:** Morrow BM; Mowzer R; Pitcher R; Argent AC

**Objective:**

To investigate the effect of closed system (CSS) vs. open endotracheal suctioning (OES) on the incidence of ventilator-associated pneumonia (VAP) and outcome in a Paediatric Intensive Care Unit in a developing country.

**Methods:**

A prospective observational and nonrandomized controlled clinical study was conducted in infants and children mechanically ventilated for >24 hours. Suctioning systems were alternated monthly. Demographic, clinical and laboratory data were prospectively recorded. An 8-month interim analysis was planned with *a priori* efficacy and futility study termination boundaries set at  $p < 0.006$  and  $p > 0.52$  respectively.

**Results:**

250 patients aged 3.8 (1.2 – 15.0) months (median (IQR)) in 263 PICU admissions were included. 78 (29.7%) admissions developed VAP, with a calculated rate of 63.8 infections per 1000 ventilated days. There was no difference in characteristics or outcome between patients on CSS (n = 83) vs. OES (n = 180). The VAP incidence for patients on CSS and OES was 31.3% and 28.9% respectively ( $p = 0.69$ ), reaching the *a priori* set limit of futility. The study was therefore terminated at the point of interim analysis. Patients who developed VAP spent 11(8 – 16) and 22 (13 – 33) days in PICU and hospital respectively compared to 5 (4 – 8) and 14 (10 – 22.5) days in those without VAP ( $p < 0.0001$ ). Mortality was not affected. Identified risk factors for VAP were duration of mechanical ventilation, reintubation, carbapenem therapy and blood transfusion.

**Conclusion:**

CSS did not affect the incidence of VAP or patient outcome in this setting.

**Title:** SPECTRUM OF PEDIATRIC CYTOMEGALOVIRAL INFECTION IN SURGICAL AND AUTOPSY SPECIMENS

**Authors:** Maxine Naicker, Komala Pillay

**Department:** Department of Histopathology, National Health Laboratory Services and University of Cape Town

**Objective:**

A study was conducted at Red Cross Children's hospital in the histopathology department to determine the spectrum of sites of infection in paediatric cytomegalovirus (CMV), to determine whether there were any unusual sites of infection and to assess the virus as an opportunistic pathogen.

**Methods:**

A computer database search was conducted to identify cases where CMV was diagnosed at Red Cross between June 2002 and June 2010. Information such as age and gender of the patient, HIV status, site of CMV infection and other relevant pathologies were recorded. All the histology slides were reviewed to note the stains used for diagnosis, number of CMV inclusions present and the type of cells affected by the CMV.

**Results:**

There were 73 children diagnosed with CMV at Red Cross between June 2002 and June 2010, 50 surgical specimens and 23 specimens collected at autopsy. In the surgical cases the GIT had the most involvement with 3 stoma sites found to be infected even though previous bowel resections were not infected with CMV, autopsy results showed that CMV mostly caused a systemic infection.

**Conclusions:**

The results showed that most cases of CMV were associated with secondary causes of immune suppression and that CMV is often accompanied by other opportunistic pathogens.

**Title:** DNA SEQUENCE ANALYSIS OF THE IL12P40 PROMOTER, ONE OF THE CANDIDATE GENES FOR SUSCEPTIBILITY OR RESISTANCE TO TB

**Authors:** Sandy Pienaar<sup>1</sup>, Brian Eley<sup>1</sup>, Mike Levin<sup>2</sup>, Howard Henderson<sup>3</sup>

**Department:** 1 Department of Paediatrics and Child Health, Red Cross Children's Hospital  
2 Faculty of Medicine, Imperial College of Science, Technology and Medicine, London  
3 Department of Chemical Pathology, Red Cross Children's Hospital/GSH

**Objective:**

DNA sequence analysis of the promoter of the IL12p40 gene, one of the critical components of the IFN $\gamma$  pathway and a strong candidate gene for susceptibility or resistance to TB in children.

**Methods:**

DNA was sourced from a cohort of children with TB and healthy controls. A 2022bp section of the IL12 p40 promoter was amplified by PCR in eight overlapping sections. These individual fragments were screened for mutations by the WAVE method. DNA fragments with mutations were sequenced for description of the sequence changes and unique Multiplex PCR assays designed for detection of the alterations.

**Results:**

Two single nucleotide polymorphisms (SNPs) were detected in this promoter region, an A $\rightarrow$ G substitution at nucleotide -1515 and a C $\rightarrow$ T substitution at nucleotide -1564. Both SNPs were only found in the heterozygous state.

In a subcohort of children analyzed, comparisons of the frequencies of these SNPs between patients and controls revealed the A $\rightarrow$ G SNP to be significantly less prevalent in the patients compared to controls [1.67% vs 7.04%; ( $p = 0.015$  Fischer's Exact);  $n=180$  and  $142$ , respectively]. The A $\rightarrow$ G SNP was found to lie within a GTATA pentanucleotide sequence, reported to bind nuclear proteins. No significant difference was found between the subject groupings for the C $\rightarrow$ T SNP. Further screening was done for the A $\rightarrow$ G and C $\rightarrow$ T SNPs in additional paediatric and adult samples.

Total paediatric samples screened ( $n=437$ ), TB cases ( $n=291$ ), controls ( $n=146$ ).

Total adults samples screened ( $n=776$ ), TB cases ( $n=20$ ), controls ( $n=756$ ).

Analysis of the SNPs in the larger group showed no significance between TB cases and controls, although a trend of more A $\rightarrow$ G SNPs in the control group was seen.

**Conclusions:**

Two novel SNPs have been found in the promoter of the IL12 p40 gene. They have been submitted to the SNP database and submitter numbers allocated. The possible biological importance of these SNPs in the regulation of gene expression is currently being investigated through reporter assays using the Dual Luciferase Reporter Assay. Clinical descriptions and cytokine levels (TNF $\alpha$ , IFN $\gamma$  and IL12) have been recorded for these children.

**Title:** EXPRESSION OF DC-SIGN AND DC-SIGN-R IN PLACENTAS OF HIV (HUMAN IMMUNODEFICIENCY VIRUS) POSITIVE PATIENTS

**Authors:** K Pillay<sup>1</sup>, M Cloete<sup>2</sup>, H McCleod<sup>1</sup>, L Myer<sup>3</sup>

**Department:** Department of Anatomical Pathology, NHLS Red Cross Children's Hospital/GSH<sup>1</sup>, Department of Obstetrics and Gynaecology, GSH<sup>2</sup>, Department of Public Health<sup>3</sup>, University of Cape Town

**Objective:**

To compare the expression of DC-SIGN and DC-SIGNR (candidate molecules for mediating intrauterine transmission of HIV) in placentas of HIV positive and negative patients, to correlate the expression of DC-SIGN and DC-SIGNR with viral loads, history of antiretroviral therapy and evidence of in-utero HIV transmission (if possible) and to assess the placentas from HIV positive patients for pathology, including chorioamnionitis and the presence of specific infective agents.

**Materials and methods:**

40 term placentas from HIV+ mothers and 21 term placentas from HIV- mothers were processed routinely. DCSIGN and DCSIGN-R immunohistochemistry was performed. 5 random sets of 10 villi were assessed and an average number of positive cells were counted in each case. In addition, where possible, maternal and cord blood viral loads and maternal CD4 counts were performed.

**Results:**

The median maternal CD4 count was 324.5 and 27% of participants had undetectable viral loads; the median detectable viral load was 3.59 log.

97% of the cord bloods tested had lower than detectable viral loads. HIV+ cases had significantly greater expression of both DCSIGN-R (median values in HIV+ cases, 14.5 positive cells/10villi (pc/10villi), compared to 11 pc/10villi in HIV- cases,  $p=0.020$ ) and DCSIGN (median values in HIV+ cases, 26.5, compared to 23 in HIV- cases,  $p=0.037$ ). There was no significant difference between the incidence of placental membrane inflammation (PMI) between HIV positive and HIV negative patients ( $p=0.173$ ). There was also no difference in expression of DCSIGN and DCSIGN-R in patients with and without PMI. In addition, the expression of DC-SIGN and DC-SIGN-R was inversely associated with CD4 count in HIV positive cases ( $p<0.05$  for both) and positively associated with maternal viral load (but not statistically significant).

**Conclusions:**

Both DCSIGN and DCSIGN-R expression were higher in placentas from HIV positive mothers compared to HIV negative cases and this was statistically significant. There was possible in-utero transmission of HIV in one case. There was no association of DCSIGN or DCSIGN-R expression with the presence of chorioamnionitis, but there was a statistically significant inverse relationship between DC-SIGN and DC-SIGNR expression and maternal CD4 counts in HIV positive cases.

**Title:**           **IMPLEMENTING THE 2- 4- 6 RULE OF NIL PER MOUTH DURING THE PRE OPERATIVE PERIOD AT RED CROSS WAR MEMORIAL CHILDRENS' HOSPITAL**

**Authors:**       Angeline Schrikker, Angela Leonard and Minette Coetzee

In 2009, a rapid survey in the surgical wards at Red Cross War Memorial Children's Hospital revealed different prescriptions and practices around the pre-operative care of children. A collaborative practice improvement project across the surgical wards with the Child Nurse Practice Development Initiative was initiated in 2009 to standardise nursing practice during the pre-operative period, which continued during 2010.

The objective of this project was to assess current practice, by exploring the fasting pre-operative period for children and then to facilitate transition in the fasting regime to the 2-4-6 rule to improve outcomes of care.

Despite a 2009 circular instructing fasting periods of 2-4-6 hours practice is slow to change, the results show that the 'nil-by-mouth-from-midnight' fasting policy is still evident as staff believe that it is safer for the patients and allows greater flexibility of the theatre slate. In 2010 the aim was to promote the 2-4-6 rule of fasting through the introduction of a ward poster, a journal club presentation and in-service training.

The method used to track the process was a series of surveys of fasting times, incorporating children from the surgical in-patient and day surgery units. This process revealed the complexities of varying departments responsible for a child's visit to theatre and highlighted the importance of collaboration and communication among the nursing staff caring for the child, theatre staff and the surgical team who are juggling theatre slates.

While the project encountered a variety of hurdles, there have been measurable practical improvements, including an understanding of the risks of prolonged fasting in children. This poster presentation will present the process as well as the lessons learnt in the quest to establish a sustainable pre-operative fasting model.

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Submitted from the Child Nurse Practice Development Initiative,

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**Title:** THE USE OF RECOMBINANT FVIIA (NOVOSEVEN) IN DAMAGE CONTROL SURGERY FOR ABDOMINAL TRAUMA IN PAEDIATRIC PATIENTS

**Authors:** Westgarth-Taylor C, Hodges O, Thomas J, Millar AJW

## **Introduction**

Recombinant FVIIa (NovoSeven) was developed for use in haemophilia complicated by inhibitors to FVIII/FIX (1). Since its introduction, it has been successfully used “off-label” in treating massive haemorrhage. Few studies have looked at the use of rFVIIa in paediatric trauma patients. We present 2 cases in which it has been used for treatment of severe haemorrhage, following blunt and penetrating abdominal trauma.

## **Case A**

Patient A, a 20kg seven year old male sustained blunt abdominal trauma and a fractured right femur following a Road traffic accident. Findings at laparotomy were of a grade IV right liver lobe fracture. Surgery included performing the Pringle manoeuvre and packing the liver with abdominal swabs. rFVIIa was administered intra-operatively after resuscitation with 3 adult units packed red cells. Adequate haemostasis was achieved and the patient made a successful recovery.

## **Case B**

Patient B, a 40kg nine year old female sustaining 2 abdominal gunshot wounds.. Findings at laparotomy were extensive injuries of the inferior vena cava and left iliac vein. Both vessels were ligated and rFVIIa was administered intra-operatively after extensive resuscitation with 13 adult units packed red cells, 2 units fresh frozen plasma and 2 units of pooled platelets. Haemostasis was satisfactory and the patient made a successful recovery.

## **Discussion**

Few reports are available on the use of rFVIIa in the paediatric patients. Reports indicate that rFVIIa could significantly decrease blood-product administration. Although extremely expensive, the cost must be balanced against the potential risk of transmission of blood-borne pathogens and the cost of surgery and blood products. Acidosis and hypothermia further aggravates coagulopathy and it is important to reverse the above causes before administering rFVIIa. Recommended target blood levels before administration are: hematocrit >24%, fibrinogen >0.5 to 1 g/L, platelets >50 to 100,000 × 10<sup>9</sup>/L, and pH ≥7.2. The role of rFVIIa in resuscitation protocols need to be clarified and large trials are needed to elucidate this.

**Title:** A CITY RESPONDS TO CHILDHOOD DIARRHOEA: LESSONS FROM CAPE TOWN, SOUTH AFRICA

**Author:** ATR Westwood

**Department:** School of Child and Adolescent Health, University of Cape Town

Acute gastroenteritis (AGE) is one of the leading causes of childhood death in Cape Town, South Africa. Since 2005, city-wide attempts have been made to address this, from prevention to critical care.

**Aims & Methods:**

This paper critically reviews the processes, interventions and outcomes since then by examining leadership, and vertical and horizontal service responses.

**Results:**

On the negative side, responses were almost all within the health system with limited prioritisation of water and sanitation provision. Only in the fourth year was leadership provided at local level for community-based and primary health care responses. The potential of community-based workers in promotion and prevention has not been realised. Monitoring has not been systematic, limiting the role of information in effective service planning.

On the positive side, initiatives within the District health System are now bearing fruit. Vertical integration of all child health services has been strengthened. The profile of AGE has risen, accelerating the implementation of newer strategies such as Rotavirus immunisation and zinc therapy. Mortality has dropped.

**Conclusion:**

Lessons learnt from these responses to AGE have the potential to inform further child health and other programmatic interventions.

(Presented as a poster at the IPA 2010.)

**Title:** A REVIEW OF AN ADOLESCENT HIV SERVICE IN SOUTH AFRICA: IMPLICATIONS FOR PUBLIC HEALTH SERVICES IN RESOURCE POOR COUNTRIES.

**Author:** Dr Claire Wright

**Objective.**

To compare the current health and clinical outcomes of a cohort of HIV (vertically-acquired) infected adolescents attending the Groote Schuur Hospital/Kidzpositive Adolescent Clinic, with similar cohorts in the developed world.

**Methods.**

Retrospective data collection from the clinical notes of patients attending the Adolescent Clinic between January and August 2010. Data collected included anthropometry, mode of presentation, results of initial and post HARRT blood tests, exposure to antiretroviral medications, incidence of mycobacterium tuberculosis infection and current health.

**Results.**

Children in our cohort, had first presented to hospital with HIV-associated disease either as young children or as adolescents. The mean period of treatment with HAART was fifty-three months, with over sixty-five percent still on their original regimen. One third of the cohort had been treated for Mycobacterium Tuberculosis infection. Over three-quarters of the children are currently virologically suppressed and clinically well, with low non-TB related morbidity across the cohort.

**Conclusions.**

The majority of the patients in the Adolescent Clinic, are currently well maintained on HAART, with low morbidity and mortality rates. The current clinical outcomes of our adolescents, many of whom were started on HAART in the early 2000's, is comparable to similar cohorts in the developed world. For resource-poor countries, where HAART is increasing available and commenced much earlier in life, it is expected that, as in the developed world, more HIV infected children will live into their adolescence. The subsequent cost of long-term HAART and the need for adolescent friendly health care services, will have widespread financial and logistical implications for already resource-poor countries.



**Title:** *M.Tuberculosis* (TB) INFECTION IN SOUTH AFRICAN CHILDREN WITH PLEURAL EMPYEMA

**Author:** Dr M Zampoli

**Department:** Red Cross War Memorial Children's Hospital; Division of Paediatric Pulmonology and Department of Paediatrics and Child Health; University of Cape Town

**Aim:**

To describe the aetiology, clinical course and outcome of empyema in South African children and investigate the incidence of M tuberculosis infection in children presenting with empyema.

**Methods:**

A retrospective review of clinical details and routine microbiological investigations in children admitted to Red Cross Children's Hospital with empyema from July 2006 to January 2009.

**Results:**

Fifty-nine children (61% male; 25% HIV-infected) with a median age of 16.1 months (IQR 6.8-52.4) were identified. Symptom duration was < 1 week in 36 (61%) patients; 25/44 (57%) received antibiotics prior to hospitalisation. Fifteen (25%) children presented with pyopneumothorax. Microbiological aetiology was established in 29 (49%) children by positive blood and/or pleural fluid cultures; pleural fluid was cultured for TB in 37 (63%) subjects. *S.aureus* and *S.pneumoniae* were the most common isolates (n=11, 19% each), followed by culture-confirmed TB in 6 (10%), *H. influenzae* (n=2, 3%) and anaerobes (n=1, 1.5%). Fifty-six (95%) children had an intercostal drain inserted and 21 (36%) required surgery. *M tuberculosis* was cultured from induced sputum or gastric washings in 5/6 children with TB empyema. Children with TB empyema were older (median age 70 vs. 7 months, p=0.002) and required longer hospitalisation (median 30 vs. 16 days, p=0.05) than children without TB. HIV co-prevalence was similar in children with and without TB (2/6 vs. 11/45; p=0.6).

**Conclusion:**

TB is an important co-infection in children presenting with empyema. Pleural fluid should routinely be cultured for *M. tuberculosis* in older children with empyema in high TB prevalence settings.

**Disclaimer:** No conflicts of interest declared

**Funding:** None