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POSTER PRESENTATIONS

The utility of Xpert MTB/RIF performed on bronchial washings obtained in patients with suspected pulmonary tuberculosis in a high-prevalence setting

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Background. Xpert MTB/RIF has been shown to have a superior sensitivity to microscopy for acid-fast bacilli (AFB) in sputum and has been recommended as a standard first-line investigation for pulmonary tuberculosis (PTB). Bronchoscopy is a valuable tool in diagnosing PTB in sputum-negative patients. There are limited data on the utility of Xpert MTB/RIF performed on bronchial lavage specimens.

Objective. To evaluate the diagnostic efficiency of Xpert MTB/RIF performed on bronchial washings in sputum-scarce/negative patients with suspected PTB.

Methods. All patients with a clinical and radiological suspicion of PTB who underwent bronchoscopy between January 2013 and April 2014 were included. The diagnostic efficiencies of Xpert MTB/RIF and microscopy for AFB were compared with culture for *Mycobacterium tuberculosis*.

Results. Thirty-nine of 112 patients were diagnosed with culture-positive PTB. Xpert MTB/RIF was positive in 36/39 with a sensitivity of 92.3% (95% confidence interval (CI) 78 - 98%) for PTB, which was superior to that of smear microscopy (41%, 95% CI 26.0 - 57.8%, p=0.005). The specificities of Xpert MTB/RIF and smear microscopy were 87.7% (95% CI 77.4 - 93.9%) and 98.6% (95% CI 91.6 - 99.9%) respectively. Xpert MTB/RIF had a positive predictive value of 80% (95% CI; 65 - 89.9%) and negative predictive value of 95.5% (95% CI 86.6 - 98.8%). 3/9 patients with Xpert MTB/RIF-positive culture negative results were treated for PTB based on clinical and radiological findings.

Conclusion. Xpert MTB/RIF has a higher sensitivity than smear microscopy and similar specificity for the immediate confirmation of PTB in specimens obtained by bronchial washing and should be utilised in patients with a high suspicion of PTB.

A rare cause of a solitary pulmonary nodule

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We present a case of a solitary pulmonary nodule owing to peribronchial granulomatous process in a young female adult, who was also asthmatic, of which the aetiology is that of cosmetic talc inhalation. She was a newly diagnosed asthmatic with a previous history of tuberculosis (TB) and her HIV status was negative. She also had 7 pack years of smoking. Her initial presentation led to her work-up for infective disorders, of which TB and hydatid cyst were the differential diagnosis. Her TB work-up was negative and echinococcus serology was negative. A chest X-ray showed a solitary pulmonary nodule in the right upper zone, not associated with lymphadenopathy. A computed tomography chest scan confirmed the findings. A wedge biopsy of the pulmonary mass confirmed peribronchial granulomatous inflammation with giant cells containing refractile material resembling talc under polarised light. Further history from the patient revealed a daily use of talc-based cosmetic powder as make-up for at least 5 years prior to presentation and she denied any use of illicit drugs in any form. Her repeat chest X-ray post surgery showed postsurgical scarring and the inflammatory markers remained low. Her symptoms vanished post surgery and she was discharged on asthma medications only.

To explore the diagnostic value of endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) in diagnosing mediastinal lesions in a high-burden TB setting – Cape Town experience

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Background. Undiagnosed mediastinal lesions are a common cause for referral to our clinic. While mediastinoscopy is considered the 'gold standard' for diagnosing such patients, recent advances suggest that endobronchial ultrasound combined with transbronchial needle aspiration (EBUS-TBNA) is at least as valuable in obtaining suitable tissue samples for diagnosis, while reducing cost and expediting treatment, especially in our setting – where mediastinoscopy has a long waiting period.

Methods. We prospectively studied 146 patients who underwent EBUS-TBNA as a diagnostic tool between March 2013 and June 2015 at Groote Schuur Hospital. The first 10 patients were excluded from the analysis as they were considered part of our learning curve. All patients

with undiagnosed mediastinal adenopathy despite conventional work-up, including fibreoptic bronchoscopy, were included.
Results. The indications for EBUS were undiagnosed mediastinal nodes, staging for already diagnosed lung cancer or undiagnosed mediastinal mass. The diagnostic accuracy of EBUS-TBNA, regardless of indication, was 79.1%, with a positive predictive value of 100% and negative predictive value of 60.9%. False negative results were obtained in 16 patients (11.8%) eight of whom had a malignant diagnosis (3 lymphoma, 1 leiomyoma, 2 non-small cell lung carcinoma, 1 metastatic cervical carcinoma, 1 malignant cells unable to type), 4 patients had TB, while another 4 of the false negative patients had sarcoidosis. The diagnostic accuracy was significantly higher for malignant diseases as compared to benign disease (77.8% v. 60%, $p<0.01$). EBUS made the diagnosis of TB in 13/17 patients (76.4%). The procedure was well tolerated in 97.8% of the patients with procedure-related complications occurring in only three patients: two patients had reversible hypoxia while the other had bleeding of more than 50 mL. Both complications resolved with symptomatic treatment.
Conclusion. EBUS-TBNA is a safe and useful diagnostic tool for both benign and malignant diseases. However, the diagnostic accuracy for malignant conditions is higher. This study also further highlights the fact that EBUS-TBNA potentially saved about 60% of the patients from having a mediastinoscopy, thereby reducing cost and expediting treatment.

Clinical and demographic predictors of pre-treatment loss to follow-up: A multicentre study

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Background. In southern Africa, tuberculosis (TB) eradication is a major stumbling block for the effective functioning of the healthcare system. Up to 40% of patients diagnosed with TB are not initiated on anti-TB treatment as they do not return to the healthcare facilities for their diagnostic results. These individuals, referred to as 'pre-treatment loss to follow-up', represent an important defeat on both the national TB programme and provision of care.
Objectives. To identify clinical and demographic predictors of pre-treatment loss to follow-up and to examine if these differ from cases that were initiated on TB treatment in five primary care healthcare facilities in South Africa, Zimbabwe, Zambia and Tanzania.
Methods. Sociodemographic (age, gender, smoking status, alcohol consumption, health literacy score, highest level of education, employment, personal and household income) and clinical information (HIV status, CD4 count, pre-TB status, culture time-to-positivity (TTP), clinic and laboratory Xpert MTB/RIF cycle threshold (C_T) values, TB score and Kessler Psychological Distress Scale (K-10) score) were collected from a randomised controlled trial involving patients assigned to either the Xpert MTB/RIF arm or sputum smear microscopy arm.
Results. A total of 367 culture-positive TB cases were identified from both smear and Xpert arms, out of which 89% were initiated on treatment and 11% were pre-treatment loss to follow-up. The predictors, namely sputum bacterial load as measured by TTP and Xpert C_T values and global psychological distress as determined by K-10 score, differed significantly in the pre-treatment loss to follow-up.
Conclusion. This study has identified that the patients with TB who appear well seem to not get initiated on treatment contributing to pre-treatment loss to follow-up.

Superior mediastinal masses: Two cases of lymphoma

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Background. The exact incidence of superior mediastinal masses in children is largely unknown. They present as a spectrum of disease ranging from an incidental finding on a chest X-ray to markedly symptomatic with superior vena cava syndrome or obstruction of the upper airways. Certainly, tumours are the most common causes in children.
Objective. To describe the of outcome of two patients with superior mediastinal masses.
Methods. A 4-year-old male presented with a 1-week history of cough and shortness of breath with respiratory distress. Chest X-ray of this child revealed a left-sided pleural effusion with shift of the mediastinum; a widened superior mediastinum was also noted which became more apparent on drainage of the effusion. The effusion was exudative in nature with a very high adenosine deaminase of 184 U/L. Cytology of the effusion revealed atypical lymphocytes suggestive of a malignancy. Another patient, a 2-year-old male, presented with an acute history with cough and shortness of breath following a choking episode. This was a clinically well child with no respiratory symptomatology that had an incidental finding of a widened superior mediastinum. There were no peripheral lymph nodes to biopsy and haematological work-up was noncontributory. On awaiting theatre for a histological specimen of the mass, the patient had an unexpected cardiorespiratory arrest and failed resuscitation.
Results. The definitive diagnosis of a T-cell lymphoma was made on biopsy of the mass of the first patient. Portmortem samples of the second patient revealed a T-cell lymphoma.
Conclusion. T-cell lymphomas are one of the most common causes of superior mediastinal masses in the paediatric population. A mass in the superior mediastinum requires a histological diagnosis. These patients, despite appearing clinically stable, can be challenging to manage and caution should be employed, with intensive care unit facilities being readily available.

A descriptive analysis of thymic tumours at Chris Hani Baragwanath Academic Hospital

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Background. Thymic tumours are rare and may present to the pulmonologist for investigation of an abnormal chest radiograph. Other medical conditions, such as myasthenia gravis, may occur in association.
Objective. To undertake a descriptive analysis of the demographics, thymic tumour type and HIV status of patients.
Methods. A retrospective analysis from 1992 to 2015 was undertaken, utilising records of the Division of Pulmonology at Chris Hani Baragwanath Academic Hospital.

Results. Thymic tumours were diagnosed in 25 patients. Seventeen patients (68%) were female, of whom 6 (35.3%) had malignant tumours. Four out of the eight male patients (50.0%) had a malignant tumour. The median age was 39 (range 18 - 87) years. Myasthenia gravis was the presenting feature in 9 patients (36.0%), of whom 2 (22.2%) had malignant tumours. In the remaining 16 patients without myasthenia, 50.0% had malignant thymic tumours. Seven patients were HIV-seropositive, 7 were HIV-seronegative and the remainder were either not tested or the HIV status not recorded. There was no significant difference in the proportion of malignant tumours when stratified by HIV status, although the number of patients in each group was too small for useful statistical analysis.
Conclusion. In this select population, most patients with thymic tumours were female. Forty per cent had malignant thymic tumours. Approximately one-third had associated myasthenia gravis. Fifty per cent of those whose HIV status was determined or recorded were seropositive.

Case report: Hypereosinophilia as a paraneoplastic phenomenon in non-small cell lung carcinoma

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Hypereosinophilia is a very rare paraneoplastic finding in malignant disease, particularly lung cancer. When it occurs, it usually is indicative of metastatic disease and poor prognosis. We report a case of a 52-year-old male patient with paraneoplastic hypereosinophilia associated with primary adenocarcinoma of the right lower lobe and extensive metastatic disease. Presenting features were cough and significant weight loss for 2 months on a background of chronic obstructive pulmonary disease and well-controlled long-standing epilepsy. Examination revealed a wasted patient, cognitive slowing without focal neurological signs, percussion dullness with diminished breath sounds over the right lower zone and hepatomegaly extending 8 cm below the costal margin. His full blood count showed a markedly elevated white cell count (peak level 114.18 $\times 10^9$/L) with an absolute eosinophilia ranging from 29.81 to 82.33 $\times 10^9$/L during the course of his admission. The bone marrow trephine showed marked eosinophilia with no malignant infiltrate or evidence of clonal eosinophilic proliferation. Radiological investigations revealed a right lower lobe mass measuring 9.1 × 6.0 × 6.7 cm, bilateral pulmonary nodules, multiple liver lesions and a left adrenal mass. No endoluminal lesion was visible on fibreoptic bronchoscopy. A core biopsy of the mass was consistent with poorly differentiated primary lung adenocarcinoma.

Surgery for bronchiectasis in HIV-positive children: Indications, complications and outcome

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Background. Bronchiectasis in HIV-infected children remains a significant cause of morbidity and mortality, especially in areas that are endemic to tuberculosis. Currently, the treatment modalities for bronchiectasis in HIV-positive children focus mainly on prevention of subsequent infections and management of symptoms. The surgical management in non-CF bronchiectasis is well established. Surgery for bronchiectasis in HIV-positive children is often not even mentioned as a management strategy. This study aims to describe the indications and complications of surgical resection for bronchiectasis in HIV-positive children and investigate variables influencing outcome.
Methods. Between January 2007 and September 2014, a retrospective medical records review was conducted in all HIV-infected children 14 years and younger who underwent surgical resection for bronchiectasis. This analysis specifically considered the following variables: the immune status, antiretroviral treatment, *Mycobacterium tuberculosis* treatment, operative complications and symptom relief.
Results. Twelve HIV-positive children on antiretroviral treatment underwent surgical resection. The mean age was 7 years (range 22 - 159 months). Indications for surgery were recurrent infections, chronic cough and persistent lobar collapse. The most common procedures were left lower lobe lobectomy (42%), left pneumonectomy (16%) and right bi-lobectomy (16%). Complications were limited to a persistent pneumothorax in one child. There were no deaths. Ten children (83%) showed significant improvement of symptoms at follow-up.
Conclusion. Surgical resection for bronchiectasis in HIV-positive children can be safely performed with low complication rates and leads to significant improvement of symptoms and quality of life.

Aspergilloma complicated by fungal empyema and mycotic aneurysm

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Background. Patients with healed pulmonary tuberculosis may develop aspergillomas in residual pulmonary cavities. The most common complication is haemoptysis. Rarely, an aspergilloma may rupture into the pleural space, causing a fungal empyema. Aneurysm formation from pleuropulmonary sepsis is another rare complication.
Case presentation. A 30-year-old woman who previously had tuberculosis presented with a left-sided empyema from which *Aspergillus fumigatus* was cultured. She was wasted, not immunocompromised and tested HIV-negative. Radiologically, aspergillomas were evident in cavities in her right upper lobe and left lower lobe. A pigtail catheter was introduced for drainage of the left empyema. The patient subsequently suffered significant episodes of haemorrhage into the pleural space, requiring multiple blood transfusions. An angiogram demonstrated an aneurysm near the left hilum. A repeat angiogram 3 months later showed resolution of the aneurysm. An open pleural biopsy showed chronic inflammation but no invasion by *Aspergillus* hyphae. The Grocott stain of the necrotic material showed positive staining of fungal hyphae with acute angle branching. Ziehl Neelsen staining was negative. The morphological features favoured pleural aspergillosis from a fungal pneumonia or an aspergilloma with rupture into the pleural space. The patient was treated with voriconazole for 2 months and also underwent an open drainage procedure. On follow-up she had gained 8 kg. She remained

well for 8 months following discharge, but unfortunately demised from an upper gastrointestinal bleed.
Conclusion. Rupture of apergillomas into the pleural space is rare. Consequent fungal empyemas require drainage and lengthy treatment with systemic anti-fungal treatment such as voriconazole for cure. This patient also developed a haemothorax probably due to rupture of a mycotic aneurysm. However, iatrogenic vascular injury related to the insertion of a pigtail catheter cannot be excluded.

Mono- and multidrug-resistant tuberculosis

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Background. Drug-resistant tuberculosis (TB) is a rapidly emerging health problem in the Republic of South Africa, and there is a paucity of data on mono- and poly-resistant TB.
Methods. This study is a retrospective analysis of a database for the period 1 March 2009 to 31 December 2011, of drug-resistant TB cases treated at TB Focal Point, Helen Joseph Hospital, a public hospital in Gauteng Province, South Africa.
Results. Rifampicin mono-resistant TB was the largest group in this study (34%), highlighting the presence of rifampicin mono-resistant TB as an entity separate to multidrug-resistant TB. Our study showed no clear patient characteristics in terms of risk factors for acquisition of mono- or poly-resistant TB, nor any clear predictors of outcome. The majority (86.6%) of the patients were HIV-positive, with a median CD4 of 67 cells/mm^3.
Conclusion. Rifampicin mono-resistant TB was the most prevalent drug-resistant TB type and treatment outcomes are poor. This study was unable to identify predictors for drug-resistant TB type and drug-resistant TB treatment outcome, but research in this area should continue to enable the treating clinician to anticipate and aggressively manage patients with predicted poorer outcomes.

Factors affecting compliance and control of asthma at Chris Hani Baragwanath Academic Hospital, Department of Pulmonology

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Background. There is a sense among the respiratory physicians that asthma is not well controlled in the public sector hospitals. This may be due to lack of education in patients, poor compliance or lack of knowledge regarding inhaler technique.
Objective. To describe the status of control in patients attending the adult asthmatic outpatient department at Chris Hani Baragwanath Academic Hospital.
Methods. A retrospective record review was done on outpatient files of asthmatics known to the respiratory clinic. Data obtained included demographics, level of control and number of admissions and exacerbations.
Results. A total of 525 patient files were obtained of which 86% were female. The mean (SD) age was 46 (16.5) years. 47.2% of patients were controlled, 30.5% partly controlled and 22.3% uncontrolled. Most patients (88%) had no admissions in the previous year and 60% had no exacerbations. Most patients were only on short-acting beta agonists and inhaled steroids.
Conclusion. In this population of mostly middle-aged female asthmatics, less than half the patients were well-controlled despite very few admissions or exacerbations in the previous year. In a number of significant areas, such as FEV_1 predicted and knowledge of inhaler technique, the majority (>60%) of the data had not been recorded in the files.

The effect of therapeutic pleural drainage on the short- and long-term sequelae of tuberculous pleural effusions

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Background. Tuberculosis remains a common cause of pleural exudates in many parts of the globe. Pleural fibrosis with restriction is a well-known complication of tuberculous pleuritis. Current evidence suggests that pleural drainage offers little benefit over and above anti-tuberculous treatment in improving pulmonary function testing.
Methods. We enrolled 20 patients with proven tuberculosis pleural effusions (mean age 32.7 years, 10 males, 12 HIV-positive), and performed therapeutic pleural drainage in 10 randomly selected cases. Pulmonary function testing, chest radiography and transthoracic ultrasound were performed on all patients prior to treatment, at 7 - 10 days, 3 months and 6 months.
Results. Complete therapeutic drainage was achieved in only 4/10 patients randomised to undergo drainage. No significant immediate benefit was achieved in the 10 patients assigned to intervention. However, the intervention group showed significant changes compared with the non-intervention group in several functional parameters at 6 months, including change in forced vital capacity from baseline (FVC 1.40 L v. 0.65 L, $p<0.001$), change in forced expiratory volume in 1 sec (FEV_1 1.37 L v. 0.60 L, $p=0.002$), change in total lung capacity (TLC 1.76 L v. 0.88 L, $p=0.034$) and change in the diffusion capacity for carbon monoxide (DL_{co} 7.42 v. 2.19, $p=0.013$). No difference was observed in the change in the 6-minutes walking distance (6MWD 113.4 m v. 126 m, $p=0.798$) compared with the control group at 6 months.
Conclusion. Therapeutic drainage may offer additional medium- and long-term functional benefits to patients with pleural tuberculosis, as evident in the improvement of pulmonary function testing.

ORAL PRESENTATIONS

Do specialist pulmonologists adhere to current treatment guidelines for thoracic surgery for drug-resistant pulmonary tuberculosis?

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Background. Adjuvant lung resection in patients with drug-resistant tuberculosis (DR-TB) is cheaper than a 2-month course of drug therapy and, more importantly, has a higher cure rate than medical therapy alone. Cure rates for selected patients with multiple DR-TB, treated with adjuvant lung resection, is about 90% as compared with about 60% in patients treated with medical therapy alone. With the more severe forms of DR-TB, surgical cure rates remain equivocal while cure rates with medical therapy alone drastically diminish. Despite this compelling evidence, it appears that the number of adjuvant lung resections undertaken for DR-TB is incongruent with the high incidence of DR-TB. Moreover, adjuvant lung resection in selected patients with DR-TB/HIV co-infection does not have a higher surgical complication rate despite an alarmingly high mortality with medical therapy alone. In South Africa, directly observed treatment, short-course has a 67% success rate. Repeated hospital admissions, inadequate laboratory facilities, lengthy treatment duration, discomfort from daily injectables, inadequate drug penetration into lung cavities/nodules and problems of malabsorption in HIV co-infected patients serve as a catalyst for this epidemic.
Objective. To determine whether specialist pulmonologists in South Africa adhere to the recommended guidelines for thoracic surgical intervention for DR-TB.
Methods. A questionnaire (18 questions) was forwarded to all specialist adult pulmonologists who are members of the South African Thoracic Society to determine whether these doctors adhere to surgical guidelines for DR-TB. The questionnaire predominantly focused on how these doctors utilise thoracic surgery in their management of DR-TB.
Results. There were 24 respondents. From a surgical perspective, 8/24 (33.3%) respondents did not know the indications for lung resection for DR-TB. 21/24 (87.5%) of respondents stated that if they knew these indications, it would influence referral for surgery.
Conclusion. The necessity of a multidisciplinary team will improve treatment outcomes in patients with DR-TB.

The utility of intensified case finding combined with a package of novel TB diagnostics using a mobile clinic in Cape Town – A randomised controlled trial

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Background. Intensified case finding (ICF) is identified by the World Health Organization (WHO) as one of the core prevention strategies necessary to reduce the prevalence of tuberculosis (TB) in high-burden settings. Novel TB diagnostic tools have not been studied as part of a screening strategy for ICF, and their operational feasibility as a point-of-treatment diagnostic technology based in a mobile van has not been assessed.
Objective. To compare the impact of a package of novel intensive-case finding diagnostic tools with a standard intensive-case finding strategy on the proportions of patients initiating TB treatment, using a mobile van.
Methods. We prospectively recruited individuals with suspected TB from several community-based sites in Langa, Cape Town, using a mobile van and randomised them to either standard diagnostic tools (sputum smear performed at the lab and liquid culture) or a package of novel diagnostic tools (urine LAM strip testing if HIV-infected and sputum Xpert MTB/RIF performed in the van and liquid culture). The proportion of culture-positive patients initiating treatment by 2 months was the primary endpoint.
Results. 37/375 (14.51%) of patients with suspected TB had culture-positive TB. The sensitivity of Xpert at point of care was 71.4%, (47.8 - 88.7) v. 25.0% (7.3 - 52.4) for smear microscopy at the lab. No patients tested positive for LAM. Time-to-treatment initiation among culture-positives was 31 days in the standard arm and 4 days in the novel diagnostics arm (p=0.02). However, the proportion of patients initiated on TB treatment was the same (63% v. 81%, p=0.21).
Conclusion. A novel ICF strategy using Xpert dramatically decreases time-to-treatment initiation compared with smear microscopy, but does not improve on treatment initiation rates at 2 months if the conventional strategy has culture as a backup. Reduced diagnostic lead-time may have important effects on TB transmission and clinical outcome in this setting and requires further study.

Bronchial thermoplasty at Groote Schuur Hospital: A preliminary report

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Background. Bronchial thermoplasty (BT) is recommended for uncontrolled severe asthma despite optimised medical therapy, and has been endorsed by several guidelines including NICE, BTS and GINA. However, there are no data from Africa and patients with more severe forms of asthma (FEV_1<60% predicted, on maintenance oral corticosteroid (OCS) and with previous intensive care unit (ICU) admission) are poorly represented in published studies.
Objective. To review the preliminary safety and efficacy of BT in patients treated at Groote Schuur Hospital.
Methods. Patients with severe asthma undergoing BT (three procedures, 1 month apart for each patient) were prospectively enrolled into a registry. Data in the 12 months prior to BT were compared with those 12 months after the procedure (ACT scores, exacerbation rates, OCS dose and spirometric data). Adverse events were recorded.
Results. Of 7 patients who underwent BT (21 procedures; 2 patients have insufficient post-BT data) the baseline median FEV_1 was 62% predicted, 71% were on OCS >10 mg/day, 67% had previous ICU admissions and 83% had an exacerbation rate of >6 per annum. BT was in general well tolerated, but 4 out of the 21 (19%) procedures were complicated by post-procedural bronchospasm necessitating overnight admission. A total of 83 months follow-up in the 5 patients (median 18 months) showed increased mean ACT scores (11/25 to 15/ 25 (p=0.03)); 64% reduction in exacerbations per year (8 v. 2.5; p=0.01) and 38% reduction in OCS dose (p=0.01). Mean FEV_1 and FVC increased marginally by 4% (p=0.3) and 10% (p=0.02), respectively.
Conclusion. In this preliminary report of 21 BT procedures, although post-treatment exacerbations occurred, BT was overall well tolerated in patients with severe asthma not previously included in published clinical trials. All of the patients had improved ACT scores, significantly lower exacerbation rates, and significant reduction in OCS usage post BT.

Rapid point-of-care urine-based testing for tuberculosis and its impact on mortality: A multi-centre, randomised controlled trial

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Background. HIV-associated tuberculosis (TB) in hospitalised patients has high mortality but is difficult to diagnose. Frequent extra-pulmonary presentation, inability to obtain sputum, and the paucibaciliary nature of samples obtained often negate the usefulness of newer polymerase chain reaction-based diagnostic tests. We evaluated the impact of lateral flow-based point-of-care (POC) urine lipoarabinomannan (LAM) testing on the mortality of TB patients.

Method. In this pragmatic, randomised, parallel-group, multicentre trial, we randomly allocated 2 659 adult HIV-infected patients admitted to hospitals with possible TB in South Africa, Zimbabwe, Zambia and Tanzania. Eligible patients received urine LAM strip testing plus available routine diagnostics (smear microscopy, Xpert-MTB/RIF and culture) or routine diagnostics alone. The primary endpoint was all-cause mortality at 8 weeks.

Results. Urine LAM testing resulted in more patients starting TB treatment (52% v. 47%, p=0.024), a decrease in the median (inter-quartile range (IQR)) days to treatment initiation (0 (0 - 2) v. 1 (0 - 3), p<0.001) and decreased empiric treatment (47% v. 71%, p<0.001). There was a 16% (95% confidence interval (CI) 3 - 27%) relative risk reduction in all-cause mortality in the LAM group at 8 weeks (22.4% v. 26.7%; hazards ratio 0.82 (95% CI 0.70 - 0.96); p=0.016). Patients who received LAM testing had a similar length of hospitalisation (4 (2- 7) v. 4 (2 - 7) days, p=0.244) and in 8-week TB-related morbidity (median (IQR) change in TB score: 5 (3 - 6) v. 5 (3 - 6), p=0.637; and Karnofsky performance status: 30 (10 - 40) v. 30 (10 - 40), p=0.811).

Conclusion. In hospitalised patients from TB endemic settings with advanced HIV-related immunosuppression and possible TB, bedside urine LAM testing resulted in decreased all-cause mortality.

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The role of IL4 and Th2-like cytokines in pulmonary tuberculosis

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Background. What constitutes an effective protective immune response to tuberculosis (TB) remains a matter of contention. Despite high IFN-γ levels, the Th1 cytokine associated with protection at the site of disease, many individuals still progress to active disease. Whether a Th2-like mechanism plays a role in TB pathogenesis remains unclear.

Objective. To determine (1) the levels of Th1/Th2/Th2-like cytokines in the lungs and blood of TB patients and latent TB infection (LTBI) controls and (2) if Th2 cytokines (IL-4) are detrimental to *Mycobacterium tuberculosis*-specific host immunity *in vitro.*

Methods. Blood and/or bronchoalveolar lavage (BAL) were obtained from individuals with pulmonary TB n=25) and LTBI (n=25). Th1 and Th2 cytokine mRNA and protein levels were determined by qPCR and Luminex, respectively. Human recombinant IL-4 (hrIL-4) was cloned and functionally assessed using ^{3}H thymidine proliferation and B-cell flow cytometric assays. The effect of IL-4 on mycobacterial survival was determined using a mycobacterial containment assay. Mycobacterial survival was assessed by counting *M. tuberculosis* colony-forming units. The IL-4-modulating effects on cytokine and cell sub-type expression in this model were evaluated by flow cytometry.

Results. TB patients expressed higher IL-4 mRNA levels (p=0.02) and a lower IFN-γ/IL-4 ratio (p=0.01) compared with LTBI controls in whole blood. Similarly, IL-9 protein levels were increased in TB v. LTBI BAL (p=0.02). Functionally active hrIL-4 increased T-cell proliferation and B-cell CD23 expression. Addition of hrIL-4 reduced mycobacterial containment in an IL-4 dose-dependent manner. Flow cytometric analysis revealed that addition of IL-4 increased Treg levels (CD4+CD25+FoxP3+; p<0.01), decreased CD4+IFNg and TNFα expression (p<0.01) and increased macrophage DC-SIGN expression (p=0.02). These effects were abrogated with the addition of anti-IL-4 antibody.

Conclusion. TB patients exhibit a highly compartmentalised Th2-skewed cytokine profile. *In vitro*, IL-4 subverts mycobacterial containment in human macrophages, possibly through a Treg effect and a subsequent down-regulated Th1 response. These finding have implications in TB vaccine design.

Integrated positron emission tomography/computed tomography for evaluation of mediastinal lymph node staging of non-small cell lung cancer in a tuberculosis-endemic area: A 5-year prospective observational study

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Background. Integrated positron emission tomography/computed tomography (PET-CT) is a well-validated modality for assessing mediastinal lymph node metastasis in non-small cell lung cancer (NSCLC), which determines management and predicts survival. Tuberculosis (TB) is known to lead to false positive PET-CT findings.
Objective. To assess the diagnostic accuracy of PET-CT in identifying mediastinal lymph node involvement of NSCLC in a high TB-endemic area.
Methods. Patients who underwent both PET-CT and lymph node tissue sampling for the investigation of suspected NSCLC were prospectively included in this observational study. Results were analysed per patient and per lymph node stage. A *post hoc* analysis was performed to test the validity of a maximum standardised uptake value (SUVmax) cut-off for lymph node positivity.
Results. PET-CT had a sensitivity of 92.6%, specificity of 48.6%, positive predictive value of 56.8% and negative predictive value (NPV) of 90.0% in the per-patient analysis. Diagnostic accuracy was 67.2%. Similar values were obtained in the per-lymph node stage analysis. TB was responsible for 21.1% of false positive results. A SUVmax cut-off of 4.5 yielded an improvement in diagnostic accuracy from 64.0% to 84.7% compared with a cut-off of 2.5, but at the cost of decreasing the NPV from 90.6% to 83.5%.
Conclusion. In a high TB-endemic area, PET-CT remains a valuable method for excluding mediastinal lymph node involvement in NSCLC. Patients with a negative PET-CT may proceed to definitive management without further invasive procedures. However, PET-CT-positive lymph nodes require pathological confirmation and the possibility of TB must be considered.

Long-term follow-up of symptomatic and silent myocardial scar in sarcoidosis patients – LGE predicts adverse events

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Background. Sarcoidosis is an inflammatory disorder that results in granulomatous myocardial infiltration and focal scar in at least 13 - 32% of patients. Cardiac involvement is the main determinant of poor outcomes. Recently, the presence of late gadolinium enhancement (LGE) in non-ischaemic cardiomyopathies was reported to be predictive of adverse outcome.
Objectives. To determine whether the presence and extent of LGE with contrast-enhanced cardiac magnetic resonance (CECMR) can predict adverse events during long-term follow-up of sarcoidosis patients.
Methods. We followed 84 consecutive biopsy-proven pulmonary sarcoidosis patients, who had baseline CECMR performed, which included inversion-recovery gradient-echo sequences. During a median follow-up of 59 (range 47 - 67) months, patients underwent regular outpatient follow-up and had additional diagnostic tests performed at the discretion of the managing physicians. Endpoints consisted of admission for congestive heart failure, cardiac death, appropriate implantable cardioverter defibrillator therapy, or pacemaker implantation for high-degree atrioventricular block.
Results. LGE was demonstrated in 27 patients (32%), and amounted to a median of 20% (range 8 - 45) of left ventricular (LV) mass. Patients with LGE had more cardiac symptoms ($p<0.001$), systolic LV impairment and dilation (both $p<0.001$). During follow-up, 8/10 endpoints occurred in the patient group with LGE. Presentation with ventricular tachycardia, LV or biventricular LGE yielded Cox hazard ratios of 8.452 (95% confidence interval (CI) 2.428 - 29.427), 9.22 (95% CI 1.96 - 43.45), and 12.093 (95% CI 3.427 - 42.677) for an endpoint, respectively. In a multivariate model, the predictive value of sustained ventricular tachyarrhythmias (VT) and LGE, particularly biventricular LGE, for adverse events was superior to symptoms of congestive heart failure, systolic LV dysfunction or ventricular dilation. Kaplan Meier event-free survival curves were most significant for LGE (log rank with $p=0.001$).
Conclusion. LGE in sarcoidosis patients strongly correlates with cardiac symptoms, ventricular volumes, function and ventricular arrhythmias at presentation. Sustained VT and LGE are the strongest, independent predictors of adverse events. Patients with small, asymptomatic myocardial scar have a favourable long-term outcome.

Interpreting Xpert MTB/RIF results in TB patients: Distinguishing true from false positive results

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We prospectively evaluated the relationship between Xpert-MTB/RIF and culture status in 2 889 suspects (837 culture-positive). In retreatment cases, the false positive Xpert-MTB/RIF rate was 5% and was associated with a chest radiograph incompatible with active tuberculosis (TB), a high cycle threshold and shorter proximity to previous TB treatment. However, these factors were unable to confidently distinguish false positive from true positive results. These data inform clinical practice.

Determinants of short-term serial changes in fractional exhaled nitric oxide (FeNO) in spice mill workers

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Background. This study evaluated the determinants of high fractional exhaled nitric oxide (FeNO) (>50 ppb) and serial changes in FeNO over a 24-hour period in spice mill workers at risk of work-related allergic respiratory disease and asthma.
Methods. A cross-sectional study of 150 workers used ECRHS questionnaires, Phadiatop, serum specific IgE (garlic, chilli pepper, wheat) (Phadia, ImmunoCAP), spirometry and FeNO. A hand-held portable nitric oxide sampling device (NIOX MINO, Aerocrine AB, Sweden) measured FeNO before and after the 8-hour shift and after 24 hours from baseline.
Results. The mean age of workers was 33 years, 71% were male, 46% current smokers and 45% atopic. Among workers with garlic sensitisation, 13% were monosensitised and 6% were cosensitised to chilli pepper. Baseline preshift FeNO geometric mean (GM=14.9 ppb) was similar to mean change across shift (GM=15.4 ppb) and across 24-hour period (GM=15.8 ppb). In multivariate linear models, chilli pepper (β=0.47) and smoking (β=–0.47) were more strongly associated with FeNO, than atopy (β=0.41) and recent green vegetable consumption (β=0.28). Cosensitisation to chilli pepper was more strongly correlated with FeNO (r=0.32) and FeNO >50 ppb (odds ratio=17.04, p=0.005) than garlic monosensitisation. FeNO increase (>12%) across 24 hours demonstrated a strong association with elevated exposures to general spice dust particulate (odds ratio = 3.77, confidence interval 1.01 - 14.24).
Conclusion. Cosensitisation to chilli pepper in garlic-sensitised individuals is a major determinant of high FeNO (>50 ppb) in spice mill workers. Elevated inhalant spice dust particulate is associated with a delayed elevation of FeNO across the 24-hour period.

Electronic cigarettes, nicotine and tobacco smoke impair human immune responses to tuberculosis infection

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Background. Electronic cigarettes (E-cigs) are gaining widespread popularity as a 'safer alternative' to tobacco. There is a paucity of data evaluating their short-term impact on respiratory infections. Tobacco cigarettes impair human immune responses to mycobacterial infection and double the risk of developing tuberculosis.
Methods. Human monocytes from healthy individuals were infected with BCG or virulent mycobacterium: H37Rv (laboratory strain) or CDC1551(clinical strain). Monocytes were cocultured with: E-cig liquid, E-cig vapour, cigarette smoke extract (CSE) or nicotine. E-cig liquid and vapour were obtained from nicotine containing Twisp brand E-cigs. E-cig vapour was collected through RPMI during a 3- and 5-minute 'vape' in a similar method to previously published data. Cell viability and tumour necrosis factor (TNF) responses were measured at 218 hours by ELISA.
Results. Toxicity experiments demonstrated a dose-dependent toxicity of CSE, nicotine and E-cig liquid. Using low concentrations of exposures, we demonstrated a consistent reduction in TNF-α production for all exposures: Nicotine 100 ug/mL reduced TNF-α production by mean (SD) 43% (24) (p<0.001), 10% CSE by 67%(23) (p<0.001), 1% E-cig liquid by 78% (23) (p<0.001) and 50% E-cig vapour 3 min 38% (26) (p<0.001) and 5 min 78% (20) (p<0.001).
Conclusion. Although E-cigs are reported to be less harmful than tobacco, these data demonstrate impairment to a key mycobacterial immune response. Caution should be advocated, especially in tuberculosis-endemic regions, about using E-cigs until the full effect on mycobacterial immunity is clarified.

Cytokine levels associated with acute lower respiratory infections and HIV in young South African children

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Background. It is widely accepted that altered host immune responses, such as cytokine responses, play a key role in the pathogenesis of acute lower respiratory infections (ALRI). The existing literature on cytokine responses in ALRI is largely limited to a select few cytokines, mainly in adults. The aim of this study was to determine that there are cytokine responses unique to ALRI, HIV-infection and specific viral infections.
Methods. Children admitted to the Steve Biko Academic Hospital or Tshwane District Hospital and diagnosed with ALRI (pneumonia or bronchiolitis) were enrolled as cases. Nasopharyngeal aspirates for viral identification and plasma concentrations of 19 cytokines (G-CSF, GM-CSF, IFN-α, IFN-γ, IL-1β, IL-1RA, IL-2, IL-2R, IL-4, IL-5, IL-6, IL-7, IL-8, IL-10, IL-12, IL-13, IL-15, IL-17 and TNF-α), 7 chemokines (Eotaxin, IP-10, MCP-1, MIG, MIP-1α, MIP-1β and RANTES) and 4 growth factors (EGF, FGF-basic, HGF and VEGF) were measured using the Human Cytokine 30-Plex Panel.
Results. A total of 106 ALRI cases and 54 controls were enrolled. Seventeen children were HIV-infected. At least one respiratory virus was identified in 72 (84.7%) ALRI cases and 33 (70.2%) non-respiratory controls. Mean cytokine concentrations for G-CSF, IFN-γ, IL-5 and MCP-1 were significantly higher in ALRI cases than in non-respiratory controls. Mean cytokine concentrations for IFN-α, IFN-γ, IL-4, IL-5, IL-13, TNF-α and MIP-1α were significantly lower in HIV-infected cases than in HIV-uninfected cases while IP-10 and MIG were significantly higher in HIV-infected cases than in HIV-uninfected cases. For human rhinovirus (HRV), mean cytokine concentrations for IL-5, TNF-α, IL-2, G-CSF, IL-7 and IL-17 were significantly higher in HRV-positive ALRI cases than in HRV-negative ALRI cases.
Conclusion. Of the 7 cytokines that were significantly lower in HIV-infected children, TNF-α is a known pro-inflammatory cytokine while IL-4 and IL-13 are known anti-inflammatory cytokines. Hence, these findings challenge the pro-inflammatory v. anti-inflammatory hypothesis put forth by Tudela and colleagues. HRV has been shown to generate strong Th2 and Th17 cytokine responses, which are known to regulate airway inflammation during respiratory viral infections.

Factors that predict for positive GeneXpert MTB/RIF on bronchoalveolar lavage samples in children with suspected tuberculosis

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Background. Pilot studies have reported that GeneXpert MTB/RIF (Xpert) testing of bronchoalveolar lavage (BAL) samples improves diagnostic yield and the rapid detection of drug resistance in children undergoing bronchoscopy for complicated intrathoracic tuberculosis (TB).
Objective. To determine factors predictive of positive Xpert on BAL in children with suspected TB.
Methods. Children <13 years undergoing fibre-optic bronchoscopy for suspected complicated intrathoracic TB between October 2012 to January 2014 were studied. Clinical data, including duration of TB treatment prior to bronchoscopy and chest X-ray changes, were collected. During bronchoscopy under general anaesthesia, airways were evaluated for compression, severity of obstruction and lymph gland ulceration into the airways. BAL samples obtained were analysed by fluorescent smear microscopy, automated liquid culture and Xpert.
Results. Forty children (3 HIV-positive, median age 18 months) were studied. The median duration of TB treatment prior to bronchoscopy was 8 (range 0 - 85) days. TB was confirmed in 31 (78%) by either BAL Xpert or culture. Xpert and culture were positive in 29 (73%) (8 were also Ziehl Neelsen stain-positive) and 23 (58%) cases respectively. In 21 (53%) both Xpert and culture were positive. Incremental value of Xpert was 8 cases (35%); only 2 cases were culture positive but Xpert negative. The median time to culture positivity was 14 (range 7 - 44 days). Positive Xpert was associated with lymph nodes ulcerating into the airway (p=0.03) but not with airway obstruction (p=0.5), chest X-ray changes (p=0.6) or duration of treatment ≤14 days (p=0.8).
Conclusion. In children with complicated pulmonary TB, Xpert on BAL increases the diagnostic yield by >35% and is associated with lymph-node ulceration into the airways.

Lung function in the first year of life in African infants: Effect of early-life pneumonia

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Background. Early-life lung function is associated with increased risk of respiratory disease in later life. Identifying factors that impact lung function in the first years of life is important if we are to develop strategies to strengthen paediatric respiratory health.
Objective. To investigate the impact of early-life exposures, including pneumonia, on lung function during the first year.
Methods. Infants enrolled in the Drakenstein Child Health birth cohort had lung function tested at 6 weeks and 1 year of age. Testing, done during quiet natural sleep, included tidal breathing (TBFVL), exhaled nitric oxide (eNO) and SF6 multiple breath washout (MBW) measures. Early-life information was collected by questionnaire at scheduled study visits. Study staff examined infants at the time and 4 - 6 weeks after a pneumonia episode.
Results. Of 389 eligible infants, 304 were tested both at 6 weeks and 1 year; 279 (70%) TBFVL, 266 (68%) eNO and 262 (66%) MBW tests were successful with good-quality results. Lung function tracked strongly from 6 weeks through to 1 year. Pneumonia during the first year of life was independently associated with decreased tidal volume (average −3.6 mL lower, 95% confidence interval (CI) −6.6 - −0.5, p=0.02) and increased respiratory rate at 1 year (6% higher, 95% CI 1.01 - 1.10, p=0.01). This effect was stronger if the infant required hospitalisation. Repeat episodes of pneumonia further increased respiratory rate (5% higher, 95% CI 1.02 - 1.08; p=0.001), decreased tidal volume (−2.5 mL lower, 95% CI −4.7 - −0.3; p=0.02) and were associated with increased lung clearance index (0.2 turnovers, 95% CI 0.00 - 0.26, p=0.05).
Conclusion. Early-life pneumonia lowers lung function achieved at 1 year, an effect independent of baseline lung function. These data provide evidence that preventing early-life pneumonia is an important factor in optimising early lung growth and function and strengthening respiratory health in later childhood.

The effect of body position on regional distribution of ventilation and respiratory muscle activity in infants and children – An EIT study

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Background. The adult pattern of ventilation distribution towards the dependent lung is well established, recent studies contradict the common belief that ventilation preferentially distributes to the nondependent lung in paediatrics. Recent studies in older infants and children are limited. In addition, there are no studies reporting whether body position affects respiratory muscle activity.
Objective. To determine the effect of body positions on regional distribution of ventilation and respiratory muscle activity in healthy children.
Methods. Thoracic electrical impedance tomography (EIT) measurements and surface electromyography (sEMG) readings were taken in the supine position and right- and left-side lying in spontaneously breathing, healthy children. Functional EIT images were produced offline and total regional relative tidal impedance (ΔZ) in the left and right lung (proportional to tidal volume) was calculated for each patient in each position. Muscle activity of the diaphragm and intercostal muscles was determined offline.
Results. Data on the 24 participants (13 male) aged 2 - 5 years are presented. The previous paediatric pattern was consistently demonstrated in two (9%) of participants. Forty-eight per cent of

participants demonstrated a varied pattern of ventilation distribution in side-lying positions. Diaphragm (p=0.068) and intercostal (p=0.36) activity was not significantly affected by body position.

Conclusion. Distribution of ventilation in children is not as straightforward as previously described. This study provides normative data with which future studies in respiratory disease and mechanical ventilation can be compared.

Adenoviral-associated pneumonia at Red Cross War Memorial Children's Hospital in 2011: Presentation, clinical course and outcomes

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Background. Pneumonia is an important cause of morbidity and mortality in children. Viruses have emerged as important aetiological agents in childhood pneumonia. The aim of this study was to document the clinical presentation, severity and outcome of adenoviral-associated pneumonia (AVP) at Red Cross War Memorial Children's Hospital in children below 5 years of age and identify risk factors associated with poor outcome.

Methods. A retrospective study of laboratory-confirmed AVP cases was conducted between 1 January and 31 December 2011. The medical records of adenovirus polymerase chain reaction positive respiratory tract samples identified through the National Health Laboratory Service (NHLS) database were retrieved. Demographic, clinical and outcomes data of children with AVP were extracted and analysed. Outcome measures were death and development of chronic lung disease (CLD).

Results. 1910 respiratory samples were submitted to the NHLS from which 206/1910 (11%) AVP cases were identified. The median age was 12 months (inter-quartile range 6 - 24), 70 (34%) children were malnourished and 14 (7%) HIV-infected. Fever was the most common presenting symptom, occurring in 159 (77%) of cases. Seventy-six (37%) required intensive care unit (ICU) admission. There was a high prevalence of comorbid conditions, with 98 (47%) having at least one; cardiac disease was the most common, with 48 (23%), of which 35 (17%) had congenital heart disease. Twenty-nine (14%) developed CLD that was associated with hypoxia at presentation (26/29, 90%, p=0.01) and admission to ICU (18/29, 62%, p<0.01). Eighteen (9%) children died. Mortality was associated with hypoxia at presentation (17/18, 94%, p=0.02), admission to ICU (14/18, 78%, p<0.01), blood stream infection (4/18, 22%, p=0.01) and underlying cardiac disease (8/18, 44%, p=0.02).

Conclusion. Adenoviral-associated pneumonia is an important cause of pneumonia and CLD in children less than 5 years of age. Underlying cardiac disease, hypoxia, blood stream infection and ICU admission were associated with poor outcome.

Tobacco smoke exposure and birth outcomes in a South African birth cohort

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Background. Tobacco smoke exposure is a major risk factor for childhood respiratory disease, with exposures often beginning in early life. However, this has not been well described in an African setting.

Objective. To investigate the prevelance of antenatal and early-life tobacco smoke exposure and the association with birth outcomes in a South African birth cohort.

Methods. Tobacco smoking and exposure was assessed in pregnant women enrolled to the Drakenstein Child Health Study using self-report questionnaires administered at the first antenatal care visit. This was validated using urine cotinine measures in the mother and infant antenatally, at birth and at 6 - 10 weeks of life; classifying exposure as active smoker, passive exposure or non-smoker. Multivariate regression models were used to explore the association between tobacco smoke exposure and birth outcomes.

Results. Of the 789 pregnant women included, 250 (32%) were active smokers on cotinine testing. The sensitivity of self-reported smoking compared with urine cotinine tests was 72%. At birth, 135/241 (56%) of neonates had passive exposure and 44(18%) were classified as active smokers on cotinine results. At 6 - 10 weeks, 154/291 (53%) of infants had cotinine tests indicative of passive exposure. Household smoking was reported in two-thirds of homes and was significantly associated with positive infant urine cotinine tests. There were marked differences in smoke exposure between black and mixed race participants. Antenatal maternal smoking was associated with decreased infant birth weight-for-age z-score (0.3, 95% confidence interval 0.1 - 0.5).

Conclusion. The high prevalence of antenatal and early-life smoke exposure may impact on birth and subsequent child health outcomes. Smoking cessation and public health interventions are urgently needed to reduce maternal and household smoking in poor African communities.

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The indications and role of paediatric bronchoscopy in a developing country with high incidence of pulmonary tuberculosis and HIV

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Background. Bronchoscopy is an important method of investigation and tool in the management of childhood respiratory pathology. A number of comprehensive studies have been carried out in First-World and developed countries. There are limited studies carried out in developing countries such as South Africa.

Objectives. To describe our clinical experience in paediatric bronchoscopy over a period of 3 years 6 months, describing the indications, study population, clinical findings and complications.

Methods. A retrospective analysis of participants' medical records, indications and outcomes of children who underwent a bronchoscopy. Participants included in this study were traced from the bronchoscopy registry of the Paediatric Pulmonology Department at Tygerberg Academic Hospital, Cape Town, South Afrca.

Results. From January 2010 to June 2013, a total of 509 bronchoscopies were performed. There were 294 boys (57.8%) and 215 girls (42.2%). The mean age was 18 months. The youngest child was 1 day of age and the

oldest was 14.6 years old. Twelve children (2.3%) were under 1 month of age and the largest group (43.0%) being 13 - 36 months of age. The HIV status was positive for 26 patients (5.1%). The procedure has precise indications: the most common are severe lower airway obstruction by nodal compression of the lower airways due to tuberculosis infection (93.3%), the aetiology of complicated pneumonia (14.1%), subglottic stenosis (4.4%) and removal of foreign bodies (6.9%).

Conclusion. Bronchoscopy is a safe and useful procedure and the results are very similar to those published from developed countries. Except for tuberculosis nodal compression, the indications did not differ from those publish in the developed world. The yield is high as in this study with 72% having confirmed abnormalities. The value of interventional bronchoscopy is increasing, with nearly 25% of bronchoscopies done in this study for intervention purposes. It also highlights the importance that congenital vascular anomalies and interstitial lung disease need to be considered in the developing world.

Aetiology and incidence of empyema in South African children

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Background. South Africa introduced the 7-valent pneumococcal conjugate vaccine (PCV7) in 2009 and PCV13 in 2011. The aetiology and incidence of childhood empyema in an 8-year period overlapping the introduction of PCV were investigated.

Methods. Children less than 12 years of age admitted with empyema at a tertiary paediatric hospital in Cape Town, South Africa, from December 2006 to December 2011 (cohort A) and January 2012 to December 2014 (cohort B) were investigated. Pathogens were identified by culture of pleural fluid and blood. In addition, polymerase chain reaction (PCR) targeting bacterial pathogens and *Streptococcus pneumoniae* serotypes was conducted on pleural fluid in a subset of patients enrolled 2009 - 2011.

Results. *Cohort A*: 142 children were prospectively enrolled, with a median age of 17 months (inter-quartile range 8 - 43). Most (92%) children were unimmunised with PCV. *S. pneumoniae* and *Staphylococcus aureus* were the most common culture-identified pathogens (each 25/142; 18%); PCR of pleural fluid increased yield of *S. pneumoniae* detection by 31% (26/54 (48%) v. 9/54 (17%), $p<0.001$). Serotypes were identified for 24/26 (92%) patients with *S. pneumoniae*, of which 22/24 (92%) were included in PCV13. *Cohort B*: 22 patients were retrospectively identified. No pathogen was found in 12/22 (54.5%) patients and *S. pneumoniae* in one patient (4.5%). Empyema incidence declined by 50% in cohort B compared with cohort A (4.2 v. 10.4 cases/1 000 pneumonia admissions; risk ratio 0.5; 95% confidence interval 0.3 - 0.7).

Conclusion. *S. pneumoniae* is the most common cause of childhood empyema in South Africa. PCV has been highly effective at reducing empyema incidence in South African children.