

## Abstracts of presentations at the Congress of the South African Thoracic Society in Cape Town, 22 - 25 August 2017

### Childhood asthma: A clinical study in southern Nigeria

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**Introduction.** Childhood bronchial asthma is a major cause of chronic respiratory morbidity and mortality and its worldwide prevalence is notably on the rise.

**Objectives.** To determine the prevalence of asthmatic children in hospital, analyse the severity of their asthma, and identify associated disease risk factors.

**Methods.** A questionnaire-based, cross-sectional, hospital-based study carried out on paediatric patients attending the respiratory clinic of the University Teaching Hospital from 1 July to 31 December 2013.

**Results.** The hospital prevalence of asthmatic children was 1.2% ( $N=40$ ), with a male to female ratio of 3.4:1. The mean (standard deviation) age at onset of asthma symptoms, was 4.24 (3.36) years. Extreme cold was found to exacerbate asthma symptoms in 72.5% ( $n=29$ ) of patients, while a positive family history of asthma was the most commonly identified childhood risk factor for the development of asthma (52.5%,  $n=21$ ). Thirty-five of the subjects (87.5%) had mild, intermittent asthma. More males than females ( $p=0.689$ ), and more adolescents than children <10 years old ( $p=0.117$ ) had persistent asthma ( $p=0.117$ ). Males had a significantly higher frequency of asthma-related hospital admissions ( $p=0.023$ ).

**Conclusion.** The low prevalence of asthma (1.2%) seen in this study, may be attributed to the hospital-based nature of the study, which does not provide an accurate representation of the prevalence of childhood asthma in the community. The male preponderance and high frequency of hospital admissions among the males is similar to the findings in other studies.

### An audit of the common aeroallergens in children with asthma and allergic rhinitis in a regional hospital in KwaZulu-Natal Province, South Africa

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**Introduction.** Asthma is the most common chronic childhood disease. It affects 10 - 20% of South African children, with allergic rhinitis (AR) being comorbid in up to 80% of children. Researchers lack data regarding the role of allergens in low- and middle-income countries, particularly in tropical regions.

**Objectives.** To identify the common allergens in children with asthma and/or AR. To quantify the prevalence of atopy, and draw a correlation between disease severity and atopy.

**Methods.** A retrospective chart review of children with asthma and AR was compiled over a 1-year period. The GINA 2015 and ARIA guidelines were used for disease severity grading. Laboratory tests included Phadiatop and fx5, as well as RAST for the evaluation of the different allergens. The Fisher's exact tests and  $\chi^2$  tests were used to test for associations between disease severity and atopy. The Kruskal-Wallis rank test was further used to compare allergen load and disease severity.

**Results.** The study analysed 100 children, with a (standard deviation) age 5.5 (1.5) years; 60% of the children were male. The most common aeroallergens were *Dermatophagoides pteronyssinus* and *Dermatophagoides farinae*, with 66% of children being atopic. There was a significant correlation between AR severity and the presence of *D. pteronyssinus* ( $p=0.012$ ), and *D. farinae* ( $p=0.013$ ), respectively. There was also a significant correlation between the persistence of AR and the presence of *D. pteronyssinus* ( $p=0.007$ ) and *D. farinae* ( $p=0.009$ ). There was no association between the severity or persistence of asthma and the presence of allergens ( $p>0.05$ ).

**Conclusion.** House dust mites were the most common aeroallergens and resulted in more severe and persistent symptoms.

### Deep-vein thrombosis in a surgical intensive care unit: Prevalence and risk factors

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**Introduction.** Critically ill patients are at a high risk of developing venous thromboembolism.

**Objectives.** The objective of this study was to determine the prevalence of, and risk factors for, lower extremity deep-vein thrombosis (DVT) among critically ill intensive care unit (ICU) patients Thailand.

**Methods.** Patients >15 years, who were admitted to a surgical ICU of a tertiary care hospital, were enrolled. Bilateral lower extremity compression Doppler ultrasonographic examination was performed to detect DVT within 14 days of ICU admission. Demographic data, primary disease, operative intervention, comorbidities, acute physiology and Acute Physiology and Chronic Health Evaluation health evaluation (APACHE) II score, and the length of ICU stay were evaluated for association with the presence of DVT.

**Results.** Among the 190 first-time-admitted ICU patients with a mean (standard deviation) (interquartile range) APACHE II score of 9.2 (6.0) (0 - 29), 20 patients (10.5%) had DVT. Thromboprophylaxis was not administered to any patients. The only independent and significant risk factor for DVT, was a longer ICU stay. Age,

sex, APACHE II score, presence of comorbidities, and operative intervention were not associated with the presence of DVT.

**Conclusion.** The prevalence of DVT in critically-ill patients in a Thai surgical ICU, was ~10.5%. Further research is needed to evaluate the risks and benefits of venous thromboprophylaxis in Thai patients.

## **The evaluation and surgical management of tracheal strictures following intubation at a thoracic surgery referral centre in South Africa**

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**Introduction.** The Department of Cardiothoracic Surgery at Inkosi Albert Luthuli Central Hospital (IALCH) is the sole provider of cardiothoracic surgical care for the KwaZulu-Natal Province and the eastern seaboard of South Africa, encompassing ~14 million patients. Investigating the aetiology, prevalence, and most importantly the outcomes of surgical intervention, will assist us to identify risk factors for surgical complications and improve patient outcomes.

**Objectives.** The surgical treatment of tracheal stenosis following endotracheal intubation, or tracheostomy, is well-described in the developed world. We present our surgical experience, and highlight nuances in the diagnosis and management of tracheal stenosis, in sub-Saharan Africa.

**Methods.** We reviewed the clinical records and archived images of patients who had undergone tracheal resection and reconstruction, for post-intubation tracheal stenosis, between 1 July 2003 and 31 July 2014, in the Department of Cardiothoracic Surgery at IALCH.

**Results.** During the study period, 42 patients underwent tracheal resection. We evaluated the preoperative bronchoscopic characteristics of the tracheal stricture in all patients, and computed tomography (CT) was used as an adjunct in 28 (66%) patients. Most of the patients (85.7%,  $n=36$ ) underwent surgery via a cervical approach, and 14.3% ( $n=6$ ) of patients via a right thoracotomy. There was no early mortality, but surgery was complicated by vocal cord palsy in 4 cases, restenosis in 2 cases, infection in 1 case, and paraparesis in 1 case.

**Conclusion.** Tracheal resection for the treatment of post-intubation tracheal stenosis can be performed safely, with minimal complications, in the developing world. A preoperative evaluation of the stricture through a combination of bronchoscopy and CT scans remains the most accurate technique to plan tracheal resection and reconstruction, while most lesions are removed via a cervical approach.

## **The epidemiology of RSV bronchiolitis – a retrospective review from Steve Biko Academic Hospital: 2013 - 2016**

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**Introduction.** Respiratory syncytial virus (RSV) causes seasonal morbidity and is an enormous burden on health systems across the world. High-risk groups, including premature infants and infants with underlying medical conditions, present significantly higher morbidity and mortality rates.

**Objectives.** The aim of this study is to describe the incidence of RSV bronchiolitis amongst patients  $\leq 24$  months of age who presented to a tertiary institution with a diagnosed viral bronchiolitis over a 4-year period.

**Methods.** A retrospective, chart-based analysis of laboratory-confirmed RSV cases was conducted in children ( $\leq 24$  months) who presented to the Steve Biko Academic Hospital between January 2013 and December 2016.

**Results.** A total of 1 127 nasopharyngeal aspirates were collected, with RSV isolated from 162. The median age (interquartile range) was 3.7 (9 days - 2 years) months, with the majority (63.4%) being  $< 6$  months old. Of the patients with known HIV status, only two were HIV-positive. A total of 49 (30.2%) patients with RSV were admitted to the intensive care unit (ICU), of whom 34 (69.4%) were  $< 6$  months old. There were 8 (4.9%) confirmed deaths. Premature birth, followed by cardiac lesions, were the most common risk factors for RSV bronchiolitis, a condition occurring predominantly during autumn and winter.

**Conclusion.** RSV is commonly detected among infants who are admitted for bronchiolitis. Significant risk factors were premature birth, age  $< 6$  months, and congenital cardiac disease. Gender and HIV status did not appear to increase the risk of RSV bronchiolitis. Young babies, especially premature infants with RSV bronchiolitis, are at considerable risk and likely to be admitted to the ICU. The case fatality rate was 4.9% in children  $< 6$  months old, with premature birth being the main risk factors.

## **The use of airway clearance therapy in children hospitalised with acute lower respiratory tract infections in a South African tertiary hospital**

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**Introduction.** Airway clearance therapy (ACT) is often advocated for the clinical management of children with lower respiratory tract infection (LRTI). However, there is minimal documentation on the prescription, frequency, nature and adverse events of ACT, with no South African data.

**Objectives.** To describe the characteristics, management and outcomes of children with acute LRTI who were admitted to a tertiary paediatric hospital, and to describe subsequent ACT prescription and practice.

**Methods.** A retrospective descriptive study was conducted using routinely collected data over a 6-month period.

**Results.** A total of 1 357 folders were screened, of which 1 208 were eligible for inclusion, accounting for 1 440 hospitalisations.

The median (interquartile range (IQR)) age of children included in the study was 7.6 (2.8 - 19.0) months. The most common primary diagnoses were bronchiolitis (46.0%), pneumonia (36.5%), unspecified LRTI (10.0%), and other diseases (0.2%). Comorbid conditions were common and nosocomial LRTI was considered likely in 106 included patients (7.4%). The median (IQR) duration of hospitalisation was 2.3 (1.5 - 5.0) days. The mortality rate was 0.7% ( $n=10$ ). Children with presumed nosocomial infections ( $n=6$ ) or pneumonia ( $n=3$ ) were at higher risk of death. ACT was performed by physiotherapists during 83 hospitalisations (5.8%) - most commonly for children who acquired nosocomial LRTI in hospital, followed by those admitted with community-acquired pneumonia; and least commonly for children with bronchiolitis. Manual chest wall vibrations (83.1%), modified postural drainage (55.4%), and percussions/clapping (38.6%) were the most common ACTs applied. Treatments were performed daily or bi-daily for a median (IQR) period of 3.0 (1.0 - 6.0) days. Transient desaturation occurred in 6 children during treatment and lung collapse in 1 child an hour post treatment. No other adverse events were reported.

**Conclusion.** ACT appears to be safe in this population of children with LRTI. Standard practice conforms to national guidelines for bronchiolitis management, which do not support the use of ACT in this population. Research is warranted to determine the indications and contraindications of ACT, and to establish safe and effective ACT procedures.

## The impact of assisted autogenic drainage in children with cystic fibrosis – a pilot study

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**Introduction.** Airway clearance therapy (ACT) is standard physiotherapy practice to promote pulmonary mucus clearance in children with cystic fibrosis (CF). The relative utility and superiority of individual ACTs in children <8 years old is unknown.

**Objectives.** To evaluate the feasibility of conducting a home-based, randomised, controlled trial to determine the effects of assisted autogenic drainage (AAD) compared with standard ACT, including conventional chest physiotherapy and breathing exercises in children with CF.

**Methods.** Children with CF, aged 1 - 8 years, were randomly assigned into intervention (AAD), or control (standard ACT) groups. Parents were taught these techniques and instructed to perform them bi-daily for a year. An intention-to-treat analysis was conducted and outcome assessors were blinded to allocation. Primary outcome measures were number of hospitalisations and exacerbations during 1 year. Secondary outcome measures included spirometry, health-related quality of life, CF clinical score, preference, neurodevelopmental screening, body mass index, weight and height for age, adherence, and mortality.

**Results.** Of the 36 children screened for inclusion, 16 were enrolled in

the study. The median interquartile range age of the study participants was 5.75 (4.27 - 6.28) years. There were no significant inter-group differences for any of the outcome measures; however, the number of exacerbations and the number of days on antibiotic therapy during 1 year revealed medium (Cohen's  $d=0.55$ ) and small-to-medium effect sizes (Cohen's  $d=0.48$ ), respectively, in favour of the intervention group. Although no significant changes were found within either group, there were trends towards improvement in CF subjective and total clinical scores, as well as health-related quality of life (HRQOL) with large effect sizes (Cohen's  $d=1.07, 0.87, 0.86$ , respectively) in the intervention group. Adherence to ACT was poor and no participant in the intervention group performed AAD solely as per the pre-set methodology.

**Conclusion.** The results of this pilot study are promising in terms of the observed reductions in exacerbations and antibiotic usage, the lack of adverse events, as well as the improved CF and HRQOL scores in children receiving AAD. The lack of adherence to ACT identifies the need for research to optimise compliance with essential CF management strategies. Although research is warranted to determine the usefulness of AAD in this population, the current research model should be reconsidered prior to implementation, particularly the selection of appropriate outcome measures and methods to improve adherence to therapy.

## The aetiology of malignant pleural effusion in South Africa

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**Introduction.** Malignant pleural effusion (MPE) represents a very common cause of pleural exudates, and is one of the most challenging pleural disorders to manage. This could be attributed to the paucity of high-quality experimental evidence, and inconsistent practice worldwide. South Africa (SA) currently has no data regarding the aetiology of MPE.

**Objectives.** The primary aim of this study was to identify the most common malignancies that cause MPE in the demographic served by our hospital, and specifically, the relative contribution of mesothelioma. The secondary aim was to evaluate the efficacy of chemical pleurodesis in these patients.

**Methods.** This was a 3-year retrospective analytical study on records of patients with MPE, who were treated by the hospital's combined oncology and pulmonology services, from January 2013 to December 2015.

**Results.** A total of 194 patients with MPE were included in the analysis. The aetiology of the MPE was: lung cancer in 139 patients (71.6%); breast cancer in 26 patients (13.4%); mesothelioma in 21 patients (10.8%); and MPE with unknown primary in 5 patients (2.6%). Among patients with lung cancer, 63.3% had adenocarcinoma. Talc pleurodesis was performed in 81 patients, of which 25 were followed

up for up to 3 months. The success rate for talc pleurodesis among these patients was 88%.

**Conclusion.** In our hospital, the main cause of MPE was lung cancer, followed by breast cancer and mesothelioma. Unknown primary still represents a small proportion of MPE patients. Chemical pleurodesis is a viable palliative measure for MPE in this population.

### A new technique for repair of a dislocated sternoclavicular joint using a sternal tension cable system

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**Introduction.** An unstable anterior or posterior sternoclavicular joint (SCJ) dislocation can cause severe morbidity with poor shoulder movement and strength. These dislocations need to be repaired, which can be challenging. Many different procedures have been described to obtain a stable joint fixation, with varying results.

**Objectives.** To report on a new technique for repairing a SCJ dislocation, by using a figure-of-eight sternal cable system.

**Methods.** Description of the surgical technique and a review of 15 patients with SCJ dislocations treated with a figure-of-eight sternal tension cable.

**Results.** There were eight anterior and seven posterior dislocations. Ten dislocations were on the left, and five on the right. A stable reduction and fixation could be obtained on all patients. The patients were followed up for 1 year and had good function and stability of the SCJ. Four patients experienced minor episodic discomfort over the joint, but the discomfort did not impair their work or daily activities.

**Conclusion.** This procedure was relatively simple and reproducible, and resulted in stable and functional sternoclavicular joints.

### Epidermal growth factor receptor and anaplastic lymphoma kinase mutations detected by immunohistochemistry in lung adenocarcinoma in patients from Johannesburg

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**Introduction.** Lung cancer is the leading cause of cancer mortality. Tyrosine kinase inhibitors that target the epidermal growth factor receptor (*EGFR*) and anaplastic lymphoma kinase (*ALK*) mutations are effective in specific lung cancer subtypes. *EGFR* mutations are present in 18 - 25% of lung cancers and are commonly represented by the E746\_A750 deletion on exon 19 and the L858R point mutation on exon 21. The *ALK* translocation which is present in

2 - 7% of lung cancers involves the *EML4-ALK* fusion gene product. Immunohistochemistry (IHC) to detect these mutations has the potential of being used as an initial screening tool to facilitate shorter diagnostic time and fast track treatment options.

**Objectives.** To test *EGFR* and *ALK* mutational status in lung cancer using IHC.

**Methods.** Biopsies of patients from Charlotte Maxeke Johannesburg Academic Hospital and Helen Joseph Hospital were sent to the National Institute for Occupational Health. Biopsies taken between 1 January 2008 and 30 June 2014 were reviewed and IHC analysis performed on 111 of these samples. Mutation-specific antibodies, *EGFR* SP111 and *EGFR* SP125 and the high-affinity *ALK* D5F3 antibody were used.

**Results.** Most patients were black males (61%) and the median (standard deviation) age was 58 (11.5) years. *EGFR* IHC was positive in 10 (9%) patients. There was no statistically significant association between age, sex, smoking history, and *EGFR* IHC status. *ALK* IHC was positive in 8 (7%) patients. *ALK* IHC status was statistically significantly associated with race ( $p=0.03$ ), and age ( $p=0.081$ ).

**Conclusion.** The low *EGFR* IHC rate may be due to antigen degradation, intratumoural heterogeneity, and/or low *EGFR* IHC sensitivity. The percentage of *ALK* IHC-positive biopsies of 7% was at the upper limit of the 2 - 7% described in international literature, raising the possibility that the *ALK* mutation in South African black patients may be particularly high. We propose an evidence-based diagnostic algorithm, using both *EGFR* and *ALK* IHC as rapid initial screening tests to facilitate targeted therapy.

### Autologous pleural blood patch as a remedy for postoperative air leaks

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**Introduction.** Although relatively uncommon, prolonged postoperative air leaks after lung resection or complicated thoracic surgery can be challenging. Current methods include closed low-pressure suction systems, Heimlich valves, or to ultimately redo the surgery. The instillation of autologous blood into the pleural space to occlude air leaks in selected patients has been reported in literature, but is not generally acknowledged or practised. We report our experience with a small case series, successfully employing the use of the autologous blood patch to resolve postoperative air leaks.

**Objectives.** To assess the efficacy of autologous blood instillation into the pleural space to resolve postoperative air leaks.

**Methods.** A case series of 6 patients between 2013 and 2017, who underwent thoracic surgical procedures, which were complicated by prolonged air leaks postoperatively. Autologous blood was introduced into patients' affected pleural spaces 5 - 10 days postoperatively, and their chest drains were monitored for resolution.

**Results.** All 6 patients had resolution of their air leaks within 6 hours of autologous blood instillation. One patient required a second administration, with subsequent resolution.

**Conclusion.** Modern surgical techniques and adherence to good surgical principles have made postoperative air leaks very

uncommon. Even so, postoperative air leaks increase patient discomfort and morbidity, and pleural autologous blood patches appear to be a feasible method to eliminate air leaks.

## A case of catamenial dyspnoea

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**Introduction.** The true prevalence of endometriosis in African women is unknown due to lack of adequate diagnostic capacity. Historically it was thought to be a rare disease in African women, however more recent data now shows endometriosis may in fact be commoner in African indigenous women. Endometriosis typically involves the pelvis, particularly the ovaries, cul-de-sac, broad ligament, and uterosacral ligaments. However, it may occur remotely with unusual manifestations. Rare examples include thoracic endometrial syndrome, which includes catamenial pneumothorax, catamenial haemothorax, catamenial haemoptysis, and pulmonology nodules. These syndromes represent diagnostic and therapeutic dilemmas, particularly in areas where limited pleural biopsies are performed.

**Methods.** An unmarried, 27-year-old, nulligravida presented to our sister obstetrics and gynaecology hospital with a presumptive diagnosis of Meigs' syndrome. Her presenting complaint was that of primary infertility. On enquiry, she reported mild abdominal distension during menstrual periods and dyspnoea, worse in the supine position and with associated chest discomfort. She was examined on the third day of her menses and displayed features consistent with a large right-side pleural effusion. She had mild pelvic ascites and a bulky ovary. A chest X-ray (CXR) showed a white out of the right hemithorax. Serum CA-125 was elevated at a level of 124 units/mL (reference range 0 - 35 units/mL). Blood-stained fluid was aspirated during diagnostic thoracentesis. The patient presented to our clinic 6 weeks later with a CXR that showed a moderate, small-sized pleural effusion. A computed tomography scan revealed a simple large right pleural effusion, with no pleural nodules or thickening and normal lung parenchyma. An intercostal drain was inserted a week later to relieve tension which had subsequently developed. Shortly thereafter, a diagnostic video-assisted thoracoscopic surgery pleural biopsy was performed.

**Results.** The histology revealed benign endometrial tissue. Mechanical pleurodesis was unsuccessful with a residual hydro-pneumothorax. She was placed on hormonal replacement therapy (danazol). A repeat pleurodesis is planned for the future.

**Conclusion.** Our case emphasises the importance of considering a broad differential diagnosis for females presenting with pleural effusion and pelvic pathology. Of particular importance in our patient is the long-term preservation of fertility together with resolution of thoracic disease.

## Diagnosis and outcome of primary solid thoracic tumours in a high tuberculosis-prevalent setting

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**Introduction.** Primary solid thoracic tumours (PSTTs) are rare, with diverse pathological spectrums, varying prognoses and survival rates. Early recognition, diagnosis and treatment is key to good outcome.

**Objectives.** We described the incidence, diagnostic challenges and outcomes of PSTT, determined patient demographics, histological spectrums and treatment methods.

**Methods.** A 32-year retrospective review, including children <16 years old, treated for malignant thoracic masses at Tygerberg Children's Hospital (TCH), from 1983 to 2015. Pulmonary metastases, benign tumours and cystic lesions were excluded.

**Results.** We documented 59 patients (22 with PSST), presenting with thoracic masses in TCH – a high HIV and tuberculosis (TB)-prevalent tertiary hospital. The incidence of PSTT was 0.09 per 100 000 children per year, with a mean (standard deviation) age of 4.74 (4.22) years old and a 55% female predominance. Complaints and symptomatology were nonspecific, and in 36% of cases a diagnosis was delayed due to initial incorrect treatment for TB (23%) or pneumonia (13%). Chest X-rays (CXRs) suggested pulmonary abnormalities in all cases, but accurate diagnoses required invasive testing. The histological spectrum included 6 neuroblastomas (27%), 3 rhabdomyosarcomas (13%), 3 ganglioneuroblastomas (13%), 2 each of pleuropulmonary blastoma, Kaposi sarcoma and Ewing's sarcomas (9%), 1 each of infantile fibrosarcoma, myoepithelioma, undifferentiated and osteogenic sarcoma (5%). At diagnosis, 69% were at early stage, and 31% at advanced disease stage. Management included chemotherapy (82%), radiotherapy (23%), and surgery (64%), with an overall survival rate of 64%. The outcome was better with surgical (83%) compared with non-surgical management (57%).

**Conclusion.** In this first study reporting on PSTT from a middle-income country, we identified numerous diagnostic challenges. However, despite these, the outcomes of children with PSTT remains comparable between under-developed and highly-developed countries. As these patients present with nonspecific symptomatology, children with pneumonia and TB who are not responsive to treatment need further evaluation to exclude PSTT. All children with PSTT had abnormal, but not diagnostic CXRs and diagnoses were confirmed by invasive testing.

## Establishment and evaluation of a smoking cessation clinic in South Africa

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**Introduction.** There are an estimated 7 million smokers in South Africa (SA), with high smoking-related mortality. SA is ranked as the second most stressful country to live in globally. A dedicated smoking cessation clinic was established at Groote Schuur Hospital in 2014. This facility was the first in SA to provide a clinical service and training centre.

**Objectives.** To motivate the health authorities to fund psychological support services, counselling, and access to nicotine replacement therapy, we created profiles for all patients with the goal to quit smoking at this facility.

**Methods.** Data on all patients who visited the clinic between 2014 and 2016 were captured. These included demographics, smoking history, nicotine dependence, CO levels and depression scores. All patients provided consent for data collection and audit. The UCT Faculty of Health Sciences Research Ethics Committee and hospital administration approved the review.

**Results.** Over a 2.5-year-period, 97 patients were seen. The mean (standard deviation) age of patients was 51.1 (10.9) years, with 59.8% male patients. The median (interquartile range (IQR)) age of smoking onset was 16 (8 - 28) years, with a median (IQR) cigarette consumption of 18 (2 - 80) per day. Men smoked more than women at 21 v. 14 cigarettes per day ( $p=0.002$ ), resulting in total packyears smoked: 34 v. 22 ( $p=0.001$ ). The level of nicotine dependence was moderate: the mean Fagerström test score was 5.3: men 6 v. women 5 ( $p=0.06$ ). Half of the patients had a Fagerström score  $\geq 6$ , and 22%  $\geq 8$ . The median (IQR) PHQ-9 depression score was 8 (4 - 11), with 49% of patients displaying symptoms of at least minor depression (score  $\geq 10$ ), similar in both men and women. At baseline, >60% had high ( $\geq 2/4$ ) Wisconsin Smoking Withdrawal Scale anxiety and anger scores.

**Conclusion.** In this group seeking help to quit smoking, moderate levels of nicotine addiction were observed. Additionally, moderate depression and anxiety symptoms co-existed. These data support the need for pharmacotherapy in some patients, but additional intensive psychological support is urgently required.

## **Epidemiology, risk factors and outcome for fungal infection in a paediatric intensive care unit**

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**Introduction.** Fungal infections and colonisation are common in hospital paediatric intensive care units (PICUs). Systemic antifungal agents have, however, been used successfully for the prevention of invasive fungal infections such as candidiasis.

**Objectives.** The aim of the study was to determine the incidence and identify the predictors of fungal infections. Furthermore, we describe the in-hospital mortality rate and how it is affected by fungal infections.

**Methods.** A retrospective case-control study conducted at the Inkosi Albert Luthuli Central Hospital (IALCH) PICU, between January 2015 and December 2016. Cases included confirmed invasive fungal infection (positive fungal blood cultures), as well as probable infections (elevated (1,3)- $\beta$ -D-glucan) and/or urine/endotracheal aspirate). Controls comprised negative fungal cultures, negative bacterial cultures, and positive, combined bacterial and fungal cultures.

**Results.** Invasive fungal infections were found in 19 of 1 029 patients with an incidence rate of 1.85 per 100 admissions. Predisposing risk factors were present in the majority of patients with central venous catheters (84%), urinary catheters (100%), previous surgeries (63%), total parenteral nutrition (63%) and previous broad-spectrum antibiotics (vancomycin; 47%). The in-hospital mortality rate was 16.5% (170/1 029), in which 36.8% (7/19) in the cases v. 16.1% (163/1 010) in controls. The average length of stay for the 19 cases was 20.5 days, compared with 8.3 days for the 19 who were culture-negative.

**Conclusion.** Fungal infections contribute to increased mortality and morbidity in the PICU at IALCH. Risk factors identified include catheter placements, previous surgery and use of parenteral nutrition and broad spectrum antibiotics.

## **Is adrenal suppression in asthmatic children reversible?**

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**Introduction.** Six hypocortisolaemic asthmatic children on physiological-dose steroid therapy were identified during a previous study.

**Objectives.** To establish whether hypothalamic-pituitary-adrenal axis suppression (HPAS) could be reversed in hypocortisolaemic asthmatic children treated with steroids, without jeopardising asthma control.

**Methods.** On diagnosis, six hypocortisolaemic asthmatic children were started on hydrocortisone (HC). Asthma treatment was modified by introducing steroid-sparing medications. Serum cortisol and repeat overnight metyrapone tests (ONMTPTs) were done until HPAS had recovered in all patients. A retrospective folder review was performed and the following extracted: body mass index (BMI) standard deviation score (SDS), asthma score, forced expiratory volume (FEV1), adherence, daily steroid type and dose, treatment modification, serum cortisol, final ONMTPT, and time taken for normalisation.

**Results.** Median serum cortisol recovered from 50 - 311 nmol after median (interquartile range (IQR)) period of 0.9 (0.4 - 2.2) years. The ONMTPT had normalised by median (IQR) 3.3. (7 - 7.1) years. Steroid load decreased from median 9.2 - 5.0 mg/m<sup>2</sup>/day (HC equivalent), while asthma score improved from median 1.42 to 0.85. The number of prednisone courses decreased from median (IQR) 5 (0 - 7) to 3. FEV1 before and after intervention were 79% and 82% (median values), respectively. The median BMI SDS decreased from -0.08 to -0.16. Poor adherence to therapy was noted in four children, subsequently affecting modification and recovery time of the HPAS. Inhaled corticosteroid dose could be reduced in all but one patient, who was not adhering to therapy. Nasal steroids were discontinued in one patient and reduced in another, but as a group, their dosage increased. Steroid-sparing medication included salmeterol, formoterol, montelukast and long-acting theophyllines.

**Conclusion.** Hypocortisolaemia developed while asthmatic children received physiological-dose steroid therapy. By reducing steroid load by 40%, and supplementing therapy with steroid-sparing medication, hypocortisolaemia and HPAS were reversed, while asthma control

improved. Poor adherence to therapy may have retarded axis recovery, while BMI increase did not affect it.

## Stool culture has limited diagnostic value in children with suspected pulmonary tuberculosis

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**Introduction.** Bacteriological confirmation of *Mycobacterium tuberculosis* is infrequently established in young children with tuberculosis (TB); specimen collection is resource-intensive and respiratory secretions are paucibacillary, limiting the sensitivity of available diagnostic tests. Although molecular tests are becoming increasingly available globally, mycobacterial culture remains the gold standard for diagnosis and determination of drug susceptibility, and is more sensitive than molecular methods for paucibacillary TB.

**Objectives.** We evaluated stool cultures as an alternative to respiratory specimens for the diagnosis of suspected intrathoracic TB.

**Methods.** Children <13 years of age who presented with suspected intrathoracic TB were enrolled from Tygerberg and Karl Bremer hospitals in Cape Town, South Africa. The culture of one stool specimen was compared with Xpert MTB/RIF results and cultures of up to four respiratory specimens. Stool specimens were homogenised with phosphate-buffered saline solution. Stool and respiratory specimens were digested and decontaminated with 1.25% N-acetyl-L-cysteine/NaOH, followed by concentrated fluorescent smear microscopy, Xpert MTB/RIF, and liquid culture. TB diagnoses were confirmed and classified using international consensus case definitions.

**Results.** A cohort of 188 children with a median (interquartile range) age of 14.4 (7.2 - 25.6) months; 15.4% were HIV-infected. Cultures were contaminated in 78/188 (41.5%) stool specimens. Of the 110 children with evaluable results, stool cultures detected 7/38 (18.4%) children with confirmed TB, and 7/90 (7.8%) children were initiated on TB treatment. The sensitivity and specificity of stool cultures, compared with culture and Xpert MTB/RIF of 4 respiratory specimens were 28.6% (95% confidence interval (CI) 11.3 - 52.2), and 98.9% (95% CI 93.9 - 100.0), respectively.

**Conclusion.** Stool culture should not be recommended for the diagnosis of intrathoracic TB in children, until laboratory protocols are developed to reduce contamination and validate its true diagnostic value.

## An approach to congenital lung disease

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**Introduction.** Congenital lung malformations are rare and vary widely in their clinical presentation. The incidence of congenital lung disease is between 1 in 25 000 and 1 in 35 000 live births. Despite

this low prevalence, the disorders lead to considerable morbidity and mortality when diagnosis is delayed. In addition, failure to recognise a malformation may lead to inappropriate intervention. There have also been controversies regarding the correct nomenclature regarding these anomalies. We describe our experience regarding these entities, in Durban.

**Objectives.** To describe our experience in Durban in order to provide a concise approach to congenital lung anomalies.

**Methods.** Case series literature review.

**Results.** Describe our Durban experience.

**Conclusion.** An approach for each lung anomaly is proposed. Management options, including surgery, are discussed.

## The detection of respiratory viruses in South African children with suspected pulmonary tuberculosis

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**Introduction.** Tuberculosis (TB) and acute pneumonia are major causes of morbidity and mortality in children globally. Although the importance of viral and bacterial infections in the aetiology of respiratory illness is well established, key questions regarding the prevalence of specific pathogens, and the association between viruses and TB, remain unanswered.

**Objectives.** To investigate the prevalence of respiratory viruses in children with suspected pulmonary TB (PTB).

**Methods.** Analyses were nested in a prospective hospital-based cohort study in children aged 0 - 14 years, routinely investigated for suspected PTB in Cape Town, South Africa (SA). At enrolment, investigations included collecting at least three respiratory samples for smear microscopy, Xpert MTB/RIF, and liquid culture. Nasopharyngeal aspirates were collected for viral respiratory investigation using a commercially available multiplex PCR (Anyplex II, RV16, Seegene, South Korea), including 16 viruses. Children started on TB treatment were classified as cases, while other children were classified as symptomatic controls.

**Results.** A total of 73 children with a median (interquartile range) age of 22 (10 - 48) months were enrolled; 41/73 (56.2%) were male and 13/73 (18.6%) were HIV-infected. TB treatment was initiated in 42/73 (57.5%), and 19/42 (45.2%) were bacteriologically confirmed (on Xpert or culture). In 70/73 (95.9%) children, one or more viruses were detected: 39/42 (92.9%) were cases and 31/31 (100%) controls. Human rhinovirus (HRV), the most prevalent virus, was detected in 53/73 (72.6%) children: 35/42 (83.3%) cases and in 18/31 (58.1%) of the controls; this difference was significant (odds ratio 3.61, 95% confidence interval (1.23 - 10.64;  $p=0.02$ ). Adenovirus was the second most prevalent virus, detected in 41/73 (56.2%) children: 24/42 (57.1%) cases and 17/31 (54.8%) controls.

**Conclusion.** Respiratory viruses were frequently detected in children with suspected PTB in SA. HRV and adenovirus were the

most common viruses, with HRV being detected more frequently in children diagnosed with TB, suggesting that HRV infections may unmask underlying airway diseases due to TB. More studies are needed to understand the role of respiratory viruses in children with suspected PTB.

## A clinical study report and evaluation of the ability of Strannik Virtual Scanning to screen the health of a randomly selected cohort of 50 patients

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**Introduction.** It is increasingly being recognised that political and financial factors limit the use of contemporary biomedicine – a challenge that affects the characterisation and treatment of serious medical conditions. The current diagnostic paradigm comprises numerous consultations, tests, pharmaceuticals, and other therapies, making it complex, time-consuming and expensive. Alternative technologies are clearly needed to simplify the healthcare process.

**Objectives.** To determine the efficacy of Strannik Virtual Scanning (SVS) compared with conventional diagnosis.

**Methods.** Fifty-eight patients were screened with SVS between March and September 2016. Patients reported ailments including cognitive, sleep, stress and neurological problems, as well as diabetes and cardiovascular issues.

**Results.** Of the 58 patients who participated in the study, 8 individuals did not confirm their known health status in a signed report, and their results were excluded from the study. Of the remaining 50 patients, SVS determined 271 medical conditions, of which 237 were known to the patients through previous relevant diagnostic procedures.

**Conclusion.** Strannik technology, particularly SVS, holds the potential to support doctors by making immediate and reasonably accurate assessments of patients' health statuses, thereby minimising the need for additional tests in secondary care environments. This information can be used to identify therapeutic interventions that could improve patients' quality of life.

## Adolescent use of electronic cigarette and tobacco products in Johannesburg – results from a survey

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**Introduction.** Individuals who start smoking during adolescence are more likely to continue smoking into adulthood. Electronic cigarettes (e-cigarettes) have been shown to encourage progression to conventional tobacco product smoking. Advertising e-cigarettes is currently permitted and the wide variety of flavours are attractive to adolescents.

**Objectives.** To investigate the use of e-cigarettes and other tobacco products among schooled adolescents.

**Methods.** A self-administered questionnaire to 14 - 18-year-old high school students in two different income schools.

**Results.** A total of 229 students were recruited, of whom 79% were female. In the group, 11% admitted to smoking cigarettes. The median (interquartile range) age at which students started smoking was 15 (12 - 17) years old; 23% had tried e-cigarettes, 9% of whom were using the device at the time of the study. In the lower-income school 25% of students had tried e-cigarettes, compared with 20% in the higher-income school ( $p=0.43$ ). In the grade 9 group (14 - 16-year-olds), 25% had tried e-cigarettes, compared with 20% in grade 11 (16 - 18-year-olds) ( $p=0.87$ ). In the lower-income school, 50% of students had tried hookah, while in the higher-income school, 17% had tried hookah ( $p=0.0001$ ).

**Conclusion.** Secondary school adolescents, especially from lower-income schools, commonly experiment with tobacco products. E-cigarette use is as common as conventional tobacco use. The prevalent use of hookahs is a major concern regarding lung damage and the spread of communicable diseases such as tuberculosis. The small sample size is, however, an important limitation. Another important consideration is the predominant female population, which occurred due to schools sampled. This has likely resulted in a biased view, as males generally engage in riskier behaviour, leading to an underestimation of the use of tobacco and e-cigarettes.

## The outcome of thoracic surgery in HIV-positive and HIV-negative children: A comparative retrospective study

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**Introduction.** South Africa has a high burden of complicated chronic lung disease in children, who often requiring thoracic surgery. Outcomes are rarely reported in the literature, especially in HIV-positive children.

**Objectives.** The aim of this study was to describe the indications, surgical outcomes and mortality of children undergoing thoracic surgery in a middle-income country, and to compare the outcomes of HIV-positive and -negative children.

**Methods.** We conducted a retrospective cohort study of children admitted to Tygerberg Children's Hospital between 2010 and 2013, who underwent thoracic surgery. The study included all children from 29 days to 13 years of age with pulmonary disease who required thoracic surgery.

**Results.** A total of 107 children were included, 21% were HIV-exposed and -positive, 71% were HIV-negative. The mean age was 19 months. In total, 45 (42%) children were <12 months and 62 (58%) were >12 months old. Indications for surgery in both groups were lymph gland compression caused by *Mycobacterium tuberculosis* (29%), thoracic empyema (16%), and diagnostic lung biopsies for undiagnosed diffuse lung disease (17%). There were 28 (26%) complications: most frequent were prolonged ventilation (>24 hours), persistent air leak (>24 hours), and anaemia requiring a blood transfusion post operatively. The only statistically significant difference in the complication rate was that the HIV-positive and HIV-exposed children received more blood transfusions than the HIV-negative



children ( $p=0.04$ ). Of the HIV-positive children ( $n=14$ ), 50% were receiving highly active antiretroviral therapy (HAART). There was no statistically significant difference between children receiving HAART and those who were not receiving HAART regarding indications for surgery, or complication rates.

**Conclusion.** There was no difference in thoracic surgery outcomes in HIV-positive and HIV-negative children. Further studies, with larger numbers of HIV-exposed and HIV-positive children, are required for statistically verifiable results.

## An unusual presentation of angiosarcoma

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**Introduction.** Angiosarcoma is a rare, malignant tumour of the vascular endothelium, accounting for 2% of all sarcomas. Pulmonary involvement is usually metastatic. Affected patients typically present at the late stage of the disease, and the clinical presentation is usually related to the amount of normal tissue replaced by tumour. Angiosarcomas are known to constitutively produce active vascular endothelial growth factor (VEGF), a molecule that has been implicated in the pathogenesis of hypertrophic osteoarthropathy (HOA). To date, there is a paucity of data in the literature describing a clinical association between angiosarcoma and HOA. This is a case report of a 50-year-old female who presented with HOA, weight loss, and lung nodules.

**Objectives.** To describe an unusual presentation of angiosarcoma.

**Methods.** A 50-year-old female was sent for a thoracoscopic lung biopsy, technetium-labelled bone scan, wrist X-rays, and a positron emission tomography (PET) scan. An echocardiogram was finally used to confirm the absence of an intracardiac tumour.

**Results.** The lung biopsy revealed angiosarcoma to be the cause of her symptoms. A technetium-labelled bone scan was consistent with HOA, as was an X-ray of her wrist. A PET scan showed areas of increased 2-deoxy-2-(18F)fluoro-D-glucose uptake in her liver, suggesting a possible hepatic primary. Echocardiography was negative for an intracardiac tumour.

**Conclusion.** We describe an unusual presentation of metastatic angiosarcoma, that of HOA. We postulate that the HOA is caused by increased levels of VEGF, a molecule that is constitutively produced and active in angiosarcomas. At the time of submission of this manuscript, attempts were being made to measure VEGF levels in the patient's serum.

## Rare cause of negative pressure pulmonary oedema – Presenting as “canon-ball” like lesions on imaging a case presentation

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**Introduction.** Negative pressure pulmonary oedema (NPPE) is a form of non-cardiogenic pulmonary oedema, that results from the

generation of high negative intrathoracic pressure in an attempt to overcome upper airway obstruction. Causes include post-extubation laryngospasm, hanging, choking, strangulation, and laryngeal tumours. We report a case of a previously well patient who developed NPPE due to strangulation.

**Objectives.** To describe an interesting case of NPPE.

**Methods.** Case report.

**Results.** A 28-year-old male, presented with an incidence of strangulation, which occurred during a robbery. His presenting complaints included neck pain, dyspnoea and haemoptysis. He was initially seen at the trauma department, who performed an examination, neck X-rays, and cleared any injuries. The patient was transferred to respiratory medicine after a chest X-ray (CXR) revealed a bilateral alveolar filling pattern. He was hypoxic on room air with an oxygen saturation of 87%, and diffuse bilateral crackles. A full work-up for infectious causes and possible non-benign lesions, which included HIV-testing, procalcitonin (PCT), lung function tests,  $\beta$ -hCG, alpha-fetoprotein, thyroglobulin and anti-thyroglobulin were negative. A non-urgent computed tomography CT scan was booked; however, symptoms started to improve on the second day following admission, with a decrease in respiratory symptoms and normal saturation on room air. A repeat CXR was performed on the third day, which confirmed complete resolution of alveolar infiltrates and a subsequent diagnosis of NPPE was made.

**Conclusion.** NPPE is a fair diagnosis to consider in a previously healthy, young and fit patient, who experiences acute airway obstruction, as in our case. It is characterised by rapid onset and resolution of pulmonary oedema, within 12 - 48 hours. NPPE carries a good prognosis if promptly diagnosed and appropriately treated, with or without mechanical ventilation

## Childhood necrotising pneumonia in a region with high burden of tuberculosis and HIV

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**Introduction.** Necrotising pneumonia (NP) is a rare complication of community-acquired pneumonia (CAP). The most common cause of NP remains *Streptococcus pneumoniae*.

**Objectives.** To describe the clinico-radiological features and outcomes of children with NP, who were admitted to Tygerberg Children's Hospital (TCH), a children's hospital in South Africa, a middle-income country with a high prevalence of tuberculosis and HIV.

**Methods.** A retrospective descriptive study performed at TCH between 2004 and 2007. NP was defined as a complicated pneumonia with typical radiological findings, which was unresponsive to standard antibiotics.

**Results.** Thirty-eight children were identified with NP and 32 were included in the study. The median (interquartile range) age was 16.5 (10 - 33) months and 32% were HIV-positive. All cases had complicated CAP. Blood cultures were performed in 27 samples, and 8 cultures were positive, with *Streptococcus* spp. isolated in 7 cultures. Seven pleural aspirates ( $n=18$ ) were culture-positive of which 6 cultured *Staphylococcus aureus*, and 1 yielded *S. pneumoniae*.

A bacteriological cause was identified in 41% of the study population. Tuberculosis (TB) specimens were collected and 24 (25%) tested positive for *Mycobacterium tuberculosis* (*M.tb*). Two pleural aspirates were Ziehl-Neelsen stain positive, and in the TB group ( $n=8$ ), 75% were HIV-positive ( $p=0.007$ ). Chest X-rays were performed on 27 children and parenchymal disease was observed in 96%, with the presence of both effusion and necrosis observed in 67%. Computed tomography (CT) scan results showed pleural effusions in 91%, necrosis in 88%, and parenchymal disease in all children. Mediastinal lymphadenopathy was observed in both the TB and non-TB groups ( $p=0.5$ ), and 47% of cases had surgery.

**Conclusion.** A bacterial cause was identified in 66% of cases. *Streptococcus* spp. and *S. aureus* made up 41% of organisms and *M.tb* the rest. To date, *M.tb* has not been described as a cause for NP. Chest CT scans were not diagnostic of TB. Any child with NP should therefore be actively screened. A prospective study is needed in an age with new molecular techniques (GeneXpert), the availability of pneumococcal conjugate vaccine and antiretroviral therapy.

### Massive haemoptysis due to Rasmussen aneurysms: Report of two cases

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**Introduction.** Life-threatening haemoptysis due to tuberculosis (TB) most commonly originates from the bronchial arteries. However, haemorrhage may occur less frequently in the pulmonary arterial circulation.

**Objectives.** Case reports of two patients presenting with massive haemoptysis.

**Methods.** We describe two patients who presented with massive haemoptysis due to ruptured Rasmussen aneurysms.

**Results.** Active pulmonary TB was the most likely underlying aetiology of the Rasmussen aneurysms in our patients. Coil embolisation was successfully performed, resulting in immediate cessation of haemoptysis. Follow-ups of both patients confirmed good outcomes.

**Conclusion.** Massive haemoptysis owing to Rasmussen aneurysms, is a relatively rare occurrence despite the high prevalence of TB in our population. Coil embolisation of these aneurysms, is an effective and life-saving modality of emergency management.

### A case report on AIHA as a paraneoplastic phenomenon in lung cancer

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**Introduction.** Autoimmune haemolytic anaemia (AIHA) is a well-described paraneoplastic phenomenon in lymphoproliferative disorders. However, its occurrence in solid tumours has not been well described. In a critical analysis of AIHA as a paraneoplastic phenomenon in solid tumours, it was found to occur most commonly

in tumours originating from the kidney, ovary, thymus gland and Kaposi sarcoma. Nine out of the 52 cases analysed, were lung cancers, all of which were non-small-cell lung cancers (NSCLC). In solid cancers, two thirds of paraneoplastic AIHA are warm-type, while one third is cold-type.

**Objectives.** To describe a case report of a 58-year-old male patient who presented to Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) with AIHA as paraneoplastic phenomenon of lung cancer.

**Methods.** This case report describes a 58-year-old male patient who presented to CMJAH in December 2016 with severe anaemia, the aetiology of which was determined to be warm anti-body AIHA. Routine chest radiography revealed left upper lobe atelectasis and a Luftsichel sign. A staging computed tomography scan showed metastatic disease. A left upper lobe endobronchial mass was discovered at bronchoscopy. An endobronchial biopsy of the mass showed NSCLC on histopathology. Further immunohistochemical staining was inconclusive; the final diagnosis was NSCLC, not otherwise specified.

**Results.** After exclusion of connective tissue disease and mycoplasma infection, a diagnosis of paraneoplastic AIHA was made. The patient responded poorly to systemic corticosteroid therapy, as well as chemotherapy and passed away shortly after diagnosis.

**Conclusion.** AIHA is a rare paraneoplastic phenomenon associated with lung cancer.

### Isolated unilateral absence of left pulmonary artery: A case report and literature review

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**Introduction.** Isolated agenesis of the pulmonary artery is a very rare condition that was first described by Frentzel in 1868. It has an estimated prevalence ranging from 1 in 200 000 to 1 in 300 000 adults, with a female predominance of 2:1. It frequently occurs as an isolated unilateral absence of the pulmonary artery (UAPA), but can be associated with other cardiovascular abnormalities, such as atrial or ventricular septal defect and tetralogy of Fallot. Isolated UAPA may be asymptomatic in childhood and present in adulthood, with dyspnoea as the most common symptom. It may also present with chest pain, minor or massive haemoptysis, recurrent chest infections, and symptoms of right heart failure in advanced cases.

**Objectives.** To present the case of a 51-year-old South African female, with UAPA.

**Methods.** Our patient had received a ventilation perfusion scan, showing a large mismatched defect and pulmonary hypertension, presumed to be secondary to chronic thromboembolic disease. She was therefore referred to us for further analysis. She received a chest computed tomography (CT) scan and was later treated with pulmonary arterial vasodilators and diuretics.

**Results.** The pulmonary angiogram from the CT scan showed typical UAPA features, confirming the diagnosis. Our patient had also developed pulmonary hypertension, which was treated with pulmonary arterial vasodilators and diuretics.

**Conclusion.** Diagnosing UAPA can be challenging because the presentation is nonspecific and the condition is rare. No treatment is required if patients are asymptomatic. Surgical revascularisation can be attempted in selected cases if they present in childhood. We took this opportunity to present the case because, although it has been reported in literature, no cases have been reported in South Africa.

## Generational avian-induced hypersensitivity pneumonitis

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**Introduction.** Hypersensitivity pneumonitis (HP), is an immunologically-mediated lung disease, resulting from continued exposure of an inhaled antigen (<5 µm). It provokes a hypersensitivity reaction characterised by non-necrotising granulomatous inflammation in the distal bronchioles, lung interstitium, and alveoli of susceptible individuals. Generational cases have reported hypersensitivity pneumonitis caused by exposure to birds.

**Objectives.** To describe a case of avian-induced HP in a mother and daughter pair.

**Methods.** A 41-year-old mother and her 10-year-old daughter were diagnosed with avian-induced HP. Their diagnoses were based on their history of bird contact, presentation of dyspnoea on exertion, crepitations on auscultation, and hypoxemia on room air with saturations of 84% and 86%, respectively. Clinical processes included: pulmonary function tests, radiological imaging, bronchoalveolar lavage, lung biopsies, avian Ag-Ab tests to birds, and provocation tests.

**Results.** Diffuse ground glass infiltrates was observed on imaging of both subjects. The pulmonary function tests on both mother and daughter showed severe restrictive lung disease. Measurements were made for mother and daughter, respectively: forced vital capacity (FVC; 41% and 40%); forced expiratory volume (FEV1; 46% and 44%); diffusing capacity (DLCO; 67% and 15%); and total lung capacity (TLC; 60% and 36%). After removal from exposure and being on steroids, clinical improvements included: FVC (70% and 80%); FEV1 (71% and 79%); DLCO (95% and 59%); and TLC (77% and 84%), respectively. Specific avian Ag-Ab test results were negative in the daughter (4.20 mgA/L < 30 mg/L regarded as negative), whereas the mother's test was positive (54.7 mgA/L > 30 mg/L regarded as positive). Bronchoalveolar lavage of the daughter showed 39% lymphocytes, whereas the mother's showed scattered lymphocytes. The mother's histology report illustrated acellular chronic interstitial pneumonia with accentuated peribronchiolar parenchyma, ill-defined non-necrotising granulomata, and multinucleate giant cells.

**Conclusion.** HP can present across generations in the same family and with varying chronicity.

## Sardine run

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**Introduction.** Amoebic disease usually manifests as dysentery and is often asymptomatic. Occasionally amoebiasis, caused primarily

by *Entamoeba histolytica*, can have extra-intestinal presentations involving the pulmonary, cardiac, central nervous or hepatic systems. The protozoan gains access to the human body through the gastrointestinal system following the foecal-oral route of infection. Thus, infection is typically higher in areas with poor sanitation or poor socioeconomic conditions, with prevalence rates of up to 50%. It is thought that, from the initial intestinal infection, amoeba ascend the portal vein to infect the liver, which is the most common extra-intestinal site.

**Objectives.** Case report.

**Methods.** A 46-year-old man with no significant medical history presented to Helen Joseph Hospital, Johannesburg, South Africa, complaining of massive haemoptysis and a two-week history of weight loss and fever. An initial chest X-ray (CXR) revealed a mass in the left lower zone followed by a preliminary urgent computed tomography (CT) scan of the chest. This scan was inconclusive due to incessant coughing, but indicated a fluid-filled mass. The patient was initiated on antibiotics and antitussives, and was transferred to Chris Hani Baragwanath Academic Hospital to gain access to bronchial artery embolisation (BAE) facilities.

**Results.** CT scan planning for BAE showed a fluid-filled mass in the left lower lobe of the lung, which was inseparable from the diaphragm, and associated with oedema of the left lobe of the liver. Blood tests showed raised inflammatory markers with a preserved haemoglobin level. The patient was monitored in a high-care setting. No haemoptysis was noted; however, an anchovy paste-like fluid was subsequently drained from the mass.

**Conclusion.** With drainage and antibiotics, the patient's condition improved. Serology for amoeba was positive and the patient continued on metronidazole for 2 weeks. He was well on discharge with resolution on CXR.

## The combination of ABCA3 and pulmonary interstitial glycogenosis as a cause of neonatal interstitial lung disease

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**Introduction.** Interstitial lung diseases are diffuse pulmonary disorders, with altered interstitial structure, resulting in abnormal gas exchange. ATP-binding cassette A3 (*ABCA3*) genetic mutations form part of the surfactant dysfunction mutations seen in interstitial lung disease. Most case reports of *ABCA3* genetic mutations document very severe disease, while pulmonary interstitial glycogenosis (PIG) has a favourable outcome.

**Objectives.** We report two cases diagnosed in a middle-income setting with mutated *ABCA3* and PIG.

**Methods.** Case report.

**Results.** Patient A presented at 26 days old, with increased work of breathing and requiring ventilatory support. He required very high pressures on the ventilator and had multiple desaturations. Chest X-rays showed generalised alveolar disease. He also had severe pulmonary hypertension, which responded to vasodilators. Lung biopsy showed

glycogen in the interstitial cells – a spectrum of surfactant bodies with dense concentric lamellations, which also contain a dense body. The latter bodies bare some resemblance to *ABCA3* surfactant deficiency. The patient was pulsed with methylprednisolone with minimal response. Despite the support, the patient died.

Patient B, who presented on day 2 of life, had increased work of breathing. Multiple doses of surfactant were administered, but the patient's condition deteriorated and he required mechanical ventilation. A chest computed tomography scan, which showed the “crazy paving” picture and lung biopsy, confirmed PIG. Genetic studies showed compounds heterozygous for the NM\_001089.2(*ABCA3*): c.128G>A and c.316C>T variants. The patient received pulsed steroids and hydroxychloroquine in addition to sildenafil for pulmonary hypertension. He still had very high oxygen requirements post extubation, with continuous positive airway pressure, resulting in a tracheostomy. At the time of submission of this manuscript, the patients were still on ventilators. **Conclusion.** The combination of mutated *ABCA3* and PIG can cause severe lung disease in neonates. When neonates do not respond to surfactant replacement therapy, surfactant deficiency must be considered. We describe a previously unknown *ABCA3* mutation. In children with PIG, who do not respond to treatment, surfactant deficiency must be considered.

## The assessment of lung function abnormalities and functional outcomes in adult patients with first-time pulmonary tuberculosis in a high HIV prevalent setting

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**Introduction.** Research in the last decade has confirmed that the end of tuberculosis (TB) treatment does not in fact equate to a clean bill of health; on the contrary, it is the commencement of chronic lung function abnormalities. It is reported, that up to 60% of TB patients suffer from abnormal lung function in the form of obstructive, restrictive or mixed patterns. There is limited research on the prevalence of the pulmonary disease caused by TB in South Africa in an urban setting.

**Objectives.** To establish the prevalence of lung function abnormalities in adult patients being treated for pulmonary TB near completion of treatment (4 - 6 months), with or without HIV co-infection.

**Methods.** A cross-sectional, observational study design using a sample of convenience, was carried out among 315 patients with first-time TB, who had completed at least 4 months of treatment. Demographic data were recorded, and the following lung function parameters measured: forced expiratory volume (FEV1), forced vital capacity (FVC), the Tiffeneau-Pinelli index (FEV1/FVC), functional capacity using the six-minute-walk test, physical activity levels using the global physical activity questionnaire (GPAQ), and quality of life questionnaires using the EQ-5D and SGRQ. These measurements were used to obtain on-off data to ascertain the prevalence of lung function abnormalities and functional outcomes. Lung functions were classified as either normal or abnormal (obstructive, restrictive or mixed).

**Results.** The sample had 173 (55%) males and 141 (45%) females. The mean age was 37 years and 162 (52%) patients were HIV-positive. Abnormal lung functions were observed in 84 of 236 participants (35.6%) with acceptable spirometry reports. Further in-depth analyses are progressing to determine predictors of abnormal lung function.

**Conclusion.** The preliminary conclusion is that the prevalence of abnormal lung function, although not as high as in previous studies, is clinically significant in first-time TB patients.

## Xpert MTB/RIF Ultra for diagnosis of pulmonary tuberculosis in children using induced sputum samples

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**Introduction.** Rapid microbiological confirmation of paediatric pulmonary tuberculosis (PTB) is necessary for diagnosis and therapy. Xpert MTB/Rif Ultra (Ultra) can detect disease with fewer bacilli than Xpert and so may offer an improved rapid diagnostic.

**Objectives.** To investigate the diagnostic yield of Ultra compared to cultures from induced sputum (IS) samples in children.

**Methods.** Children hospitalised for suspected PTB were enrolled from 2011 to 2016. One to three IS samples were collected: the first was split for culture and Xpert the second was split for culture and Xpert or storage, and the third sample was stored. Ultra was performed in December 2016, on a single IS sample from stored second or third IS samples. The accuracy of Ultra was compared to culture as the reference standard.

**Results.** Culture results were available for 380 samples. The median (interquartile range) age of children was 34.0 (15.5 - 73.4) months and 71 children (18.7%) were HIV-positive. On per sample analysis, cultures were positive in 73 (19.2%) and Ultra in 65 (17.1%). Xpert results were available for 114 samples were positive in 17 (14.9%). The sensitivity and specificity of Ultra on per sample analysis (culture and Ultra on the same sample) were 75.3% and 96.7%, respectively, with similar results in HIV-positive (sensitivity 70.6%; specificity 98.1%) and HIV-negative (sensitivity 76.8%; specificity 96.4%) children. Ultra was positive in ten children with negative cultures, of whom seven were treated as ‘unconfirmed TB’ according to the National Institutes of Health (NIH) classification. Sensitivity and specificity of Ultra on per patient analysis (Ultra from one IS sample v. culture from multiple IS samples) were 67.5% and 96.6%, respectively. If the seven clinically-diagnosed TB cases that were positive on Ultra were regarded as true positives, the sensitivity and specificity of Ultra on per sample analysis, were 77.5% and 99%, respectively.

**Conclusion.** Ultra provides rapid detection of *Mycobacterium tuberculosis* from a single IS sample in most children with culture-confirmed TB. Ultra may detect an additional group of children who are not detected by culture.

## Experiences of non-invasive ventilation in older people with hypercapnic respiratory failure

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**Introduction.** Non-invasive ventilation (NIV) is proven to be an effective way of treating hypercapnic respiratory failure (HRF) in older people, in whom endotracheal intubation may not provide long-term benefits.

**Objectives.** The aim of this study was to examine the experiences of older people with HRF and on NIV treatment, to understand treatment tolerance and treatment preferences.

**Methods.** A qualitative approach, using a semi-structured interview, was conducted with 11 individuals (5 males and 6 females), who were receiving NIV treatment for the first time. The mean (interquartile range) age of the participants was 72 (67 - 76) years. Participants were recruited from a hospital in Wales, UK. Twelve participants were interviewed and 11 were chosen to analyse the richness of the data in terms of the participants' lived experiences, while receiving NIV treatment. One interview was excluded due to insufficient data.

**Results.** Five superordinate themes were identified: (i) significant moment in life, (ii) the impact of the NIV machine, (iii) understanding the benefits of the NIV machine, (iv) decision-making in a life-threatening experience, (v) conflict managing the NIV machine. These analyses indicated that starting NIV caused bewilderment and confusion because participants were not aware that their respiratory conditions required such intense therapy. Health benefits, such as improved breathing, ostensibly motivated the continued use of NIV. Decision-making in patients suffering from life-threatening conditions, such as HRF, was influenced by issues like health benefits, the spouse's voice, the desire to improve, and most importantly, the burden of treatment v. the quality of life.

**Conclusion.** In this study, opinions of NIV treatment, as experienced by older people with HRF, were explored. Furthermore, factors influencing the refusal or acceptance at the initiation stage of NIV treatment in older people have been identified.

## Impact of tobacco smoke exposure or indoor air pollution on nasopharyngeal bacteria in African infants in a birth cohort study

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**Introduction.** Bacterial nasopharyngeal (NP) carriage precedes the development of lower respiratory tract infection (LRTI), a leading cause of childhood illness globally. Exposure to indoor air pollution (IAP) or environmental tobacco smoke (ETS) may influence NP bacterial carriage.

**Objectives.** To investigate the impact of antenatal or postnatal IAP and ETS exposure on NP bacterial carriage in infants.

**Methods.** Mother-infant pairs enrolled in a South African birth cohort study and were followed from birth for 1 year. Immunisation, including conjugate 13-valent pneumococcal vaccine and *Haemophilus influenzae* b were given. IAP exposures (particulate matter, nitrogen dioxide and volatile organic compounds) were measured at an antenatal and postnatal home visit. Maternal and infant urine cotinine levels were used to measure ETS exposure. NP swabs were taken at birth, 6 and 12 months for bacterial culture. Associations between NP organisms and environmental exposures were investigated using multivariate logistic regression.

**Results.** A total of 2 596 NP swabs were collected from 986 infants. The predominant NP bacteria were *Streptococcus pneumoniae* ( $n=1\,136$ , 44%), *Moraxella* ( $n=893$ , 34%), *H. influenzae* ( $n=709$ , 27%) and *Staphylococcus aureus* ( $n=239$ , 9%). Antenatal ETS exposure was associated with *S. pneumoniae* at 6 months, (odds ratio (OR) 1.62 95%; CI 1.10 - 2.37). Antenatal toluene exposure was also associated with *S. pneumoniae* at 6 months, (OR2.51; 95% CI 1.23 - 5.13) and with *H. influenzae* at 12 months, (OR2.27; 95% CI 1.24 - 4.16). Postnatal ETS exposure was associated with *S. pneumoniae* at 6 months, (OR1.46; 95% CI 1.01 - 2.12) and *H. influenzae* at 12 months (OR2.56; 95% CI 1.21 - 5.41).

**Conclusion.** Early-life environmental exposures increase the prevalence of specific NP bacteria during infancy, which may predispose to the development of LRTI.

## Pectus carinatum: An external custom-made carinatum brace

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**Introduction.** The Ravitch procedure for correction of a pectus carinatum has been the standard repair procedure for many years. Following the Nuss repair for pectus excavatum introduced by Nuss in 1997, Abramson adjusted this operation for pectus carinatum with great success. Various external braces were subsequently developed for a non-surgical attempt to repair the deformity.

**Objectives.** To introduce the custom-made, adjustable brace, and to describe the preliminary results.

**Methods.** This is a review of the first 12 cases performed in South Africa. All have shown improvements, some within 2 months of wearing the brace. The important point is that the patients need to wear the brace for an adequate number of hours. The brace is also worn at night. It is only removed when partaking in sports and for showering. The brace is custom-made for each patient, the size is adjustable, as is the pressure required to correct the deformity. Pressure sores develop when excessively high pressure is applied – this may be avoided by adjusting the pressure as the deformity corrects. I will compare the brace with the Abramson procedure.

**Results.** Preliminary results have shown improvements in all cases. Two patients discontinued the use of the brace within 6 months as the deformity had been corrected. One patient did not wear the brace as he felt self-conscious at school. He had not experienced any improvement.

**Conclusion.** The brace has been shown to be an efficient non-surgical method for the correction of Pectus carinatum.

## Removal of Pectus Bars: How I do it!

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**Introduction.** The removal of pectus bars can present life-threatening complications, as described in the literature. This minor procedure is potentially fatal when performed incorrectly.

**Objectives.** I will describe my personal approach to this procedure, which aims to avoid complications.

**Methods.** An incision is made on the side of the thorax containing the pectus bar stabiliser. The stabiliser is removed, and the bar is straightened and rotated to loosen it along its entire length. The bar is then removed without excessive pressure. Occasionally, one requires a hammer and chisel to remove bony ingrowth into the bar. Exposing both ends of the bar is rarely required.

**Results.** Using the abovementioned method, 60 patients have had their pectus bars removed without complications.

**Discussion.** During pectus bar removal, the most critical complications are bleeding from the right ventricle (massive and life threatening) or the internal thoracic (mammary) artery, erosion of the sternum, lung trauma, and very rarely, damage to the aorta.

**Conclusion.** The most effective way to avoid complications during pectus bar removal is to insert it correctly. The bar must be inserted under direct vision to ensure that it is extra-pericardial. Multiple bars are often required to avoid excessive pressure on both the sternum and the internal thoracic artery. Finally, it is imperative to loosen bars with lateral rotation before withdrawing them.

## The injectable contraceptive medroxyprogesterone acetate decreases peripheral effector cell-mediated *Mycobacterium tuberculosis* containment through immunosuppression at multiple levels involving the glucocorticoid receptor

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**Introduction.** The potential effects of the widely used injectable contraceptives, medroxyprogesterone acetate (MPA) and norethisterone (NET) enanthate, on *Mycobacterium tuberculosis* pathogenesis has not been fully investigated. **Objectives.** To determine if MPA or NET reduces *M. tuberculosis* containment

in monocyte-derived macrophages through immunosuppression involving the glucocorticoid receptor.

**Methods.** We recruited HIV-negative females, who were not on a contraceptive, in Cape Town, South Africa, to determine if MPA or NET affects the ability of effector T-cells to contain *M. tuberculosis* within monocyte-derived macrophages through a mechanism involving the glucocorticoid receptor. We further investigated whether MPA or NET regulated key immune function genes known to be protective against TB using flow cytometry.

**Results.** MPA ( $p < 0.005$ ), but not NET, attenuated *M. tuberculosis* containment through a mechanism involving the glucocorticoid receptor. Addition of MPA, but not NET, to purified protein-derivative-stimulated effector T-cells resulted in regulatory T-cell upregulation (1.8-fold;  $p < 0.05$ ), reduced CD4+ T-cell interferon- $\gamma$  (IFN- $\gamma$ ) production (60%;  $p < 0.05$ ), and decreased CD8+ perforin (50%,  $p < 0.0001$ ) and CD4+ granzyme B production (50%;  $p < 0.005$ ). We provide further evidence that MPA regulates these immune responses by a mechanism involving the glucocorticoid receptor.

**Conclusion.** Our results suggest that MPA downregulates protective host immune responses against *M. tuberculosis* via the glucocorticoid receptor, whereas NET does not have the same effect. The data presented have potential implications for the use of MPA in high TB-burden countries.

## Evaluation and characterisation of interleukin-9-producing T-cell subsets in tuberculosis

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**Introduction.** Interleukin-9 (IL-9) has traditionally been considered a Th2 cytokine, but recent evidence suggests that the majority of IL-9 is produced by a distinct Th9 T-cell lineage. However, the involvement of IL-9 and Th9 cells in tuberculosis (TB) remains unclear.

**Objectives.** To determine IL-9 levels in blood and site of disease in TB patients and latent tuberculosis infection (LTBI) controls, and to further clarify the existence of the novel Th9 lineage.

**Methods.** Bronchoalveolar lavage (BAL) and peripheral blood mononuclear cells (PBMCs) were obtained from individuals with confirmed pulmonary TB ( $n=15$ ) and presumed LTBI ( $n=13$ ). IL-9 and Th1 protein levels were determined in mycobacterial-antigen-driven cell culture supernatants by Luminex. Flow cytometry was used to determine the frequency of IL-9-producing CD4 T-helper (Th) and CD8 T-cytotoxic (Tc) subsets, the coexpression levels of cytokines specific to other IL-9 producing T-cell lineages, and PU.1 coexpression, a proposed lineage defining transcription factors of Th9 cells.

**Results.** IL-9 protein levels (BAL,  $p=0.02$ ) and IL-9:Th1 ratio (BAL,  $p=0.001$ ; blood,  $p=0.049$ ) were increased in TB patients v. LTBI controls. CD4+IL-9+ (blood,  $p=0.02$ ; BAL,  $p=0.03$ ) and CD8+IL-9+ (blood,  $p=0.047$ ) cells were significant higher in TB patients vs. LTBI controls. In the CD4+IL-9+ population, few cells coexpressed IL-13 (Th2) or IL-17 (Th17) and most (94.0% in blood v. 80.4% in BAL) exhibited

a Th9 phenotype (CD4+IL-9+IL-13-IL-17-). Similarly, most CD8+IL-9+ cells exhibited a Tc9 phenotype (CD8+IL-9+L-13-IL-17-; 93.7% in blood v. 84.2% in BAL). However, expression levels of PU.1 in Th9 and Tc9 cells were very low.

**Conclusion.** In TB patients, IL-9 producing T-cells exhibit a Th9/Tc9 phenotype and are increased both at the site of disease and the periphery. These preliminary data suggest that a Th9 response may be involved in TB pathogenesis. Further investigations are required to elucidate the specific role of Th9 and Tc9 cells in TB.

## What is the role of Th2 cytokines in the host immune response to tuberculosis?

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**Introduction.** Tuberculosis (TB) vaccine candidates have been mostly ineffective and it remains unclear as to what constitutes protective host immunity. Despite high levels of IFN- $\gamma$ , the Th1 cytokine associated with protection at the site of disease, many individuals still have progressive active TB. Whether a Th2-like immune response can subvert protective host immunity requires clarification.

**Objectives.** To determine Th1 and Th2 cytokine levels in the lungs and blood of TB patients and LTBI controls, and how Th2 cytokines (IL-4) affect *Mycobacterium tuberculosis*-specific host immunity in vitro.

**Methods.** Blood and/or bronchoalveolar lavage fluid (BAL) were obtained from individuals with confirmed pulmonary TB ( $n=25$ ) and presumed latent TB infection (LTBI;  $n=25$ ). Th1 and Th2 cytokine mRNA levels were determined by qPCR. Human recombinant interleukin-4 (hrIL-4) was expressed in a baculovirus system and functionally validated using 3H-thymidine proliferation and B-cell flow cytometry. The effect of IL-4 on mycobacterial containment (colony-forming units (CFU)/mL) and on cellular and cytokine expression (flow cytometry) were evaluated in an in vitro mycobacterial containment assay.

**Results.** In whole blood, TB patients expressed higher IL-4 mRNA levels ( $p=0.02$ ) and had lower IFN- $\gamma$ /IL-4 ratios ( $p=0.01$ ) compared with LTBI controls. Functionally active hrIL-4 increased T-cell proliferation and B-cell CD23 expression in a dose-dependent manner. In the mycobacterial containment model, addition of hrIL-4 was associated with a reduction in mycobacterial containment ( $p=0.008$ ), increased levels of regulatory T-cells (CD4+CD25+FoxP3+;  $p<0.001$ ), decreased CD4+ Th1 cytokines (CD4+IFN- $\gamma$ ,  $p<0.001$ ; CD4+TNF $\alpha$ ,  $p=0.01$ ), and increased macrophage DC-SIGN expression ( $p=0.02$ ) in a dose-dependent manner. Anti-IL-4 antibodies abrogated the effect of IL-4 on mycobacterial containment ( $p=0.03$ ), as well as the expression of CD4+IFN $\gamma$  ( $p=0.03$ ) and regulatory T-cells ( $p=0.03$ ).

**Conclusion.** TB patients have a compartmentalised and Th2-skewed host immune response. IL-4 is associated with subversion

of mycobacterial containment in human macrophages through a regulatory T-cell-mediated Th1 downregulation. These data have implications for the selection of effective vaccine candidates and the design of appropriate TB-specific immunotherapeutic interventions.

## *Mycobacterium avium* complex immune reconstitution inflammatory syndrome presenting as endobronchial disease

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**Introduction.** *Mycobacterium avium* complex (MAC) infection is a common opportunistic infection in patients with AIDS. It is the most common disseminated bacterial infection in patients with AIDS in industrialised countries. Despite this, endobronchial disease in MAC infection has very rarely been reported, with no reported cases in South Africa. MAC is also frequently associated with the immune reconstitution inflammatory syndrome (IRIS). Immune restoration has been postulated to have a role in the development of endobronchial lesions in MAC infection.

**Objectives.** To report the unusual finding of an endobronchial lesion in a patient with AIDS presenting with MAC-associated IRIS, and to investigate the relationship between endobronchial lesions in MAC infection and reconstituted immunity.

**Methods.** A 29-year-old HIV-positive woman was referred to our centre for bronchoscopy and lavage. She reported a 1-month history of cough productive of yellow sputum, as well as fevers, weight loss of 15 kg and fatigue. Repeated sputum samples had identified acid-fast bacilli, but the GeneXpert was consistently negative. Four months prior to presentation she had commenced combination antiretroviral therapy with a baseline CD4 cell count of 18 cells/ $\mu$ L.

**Results.** The repeat CD4 cell count was 103 cells/ $\mu$ L. On bronchoscopy, a single polyp of 0.5 cm was found at the entrance to the right upper lobe bronchus. Biopsies of the lesion showed necrotising and non-necrotising granulomatous inflammation surrounded by a chronic inflammatory cell infiltrate. Acid-fast bacilli were observed. Molecular studies confirmed the presence of *Mycobacterium avium*.

**Conclusion.** Endobronchial lesions are a rare manifestation of MAC infection. This unusual complication is typically reported in patients with AIDS who were recently initiated on antiretroviral therapy, and appears to be a feature of MAC-associated IRIS.

## Bronchial thermoplasty for severe persistent asthma: Experience from Cape Town, South Africa

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**Introduction.** Bronchial thermoplasty (BT) is a Global Initiative for Asthma-recommended step-5 therapy for severe persistent

asthma in patients who are uncontrolled despite optimal medical therapy. However, there are no outcome data for severe asthma in resource-limited settings.

**Objectives.** To examine the effect of BT on severe asthma.

**Methods.** Patients with severe persistent asthma undergoing BT (three treatments, 1 month apart) at Groote Schuur Hospital and the University of Cape Town Academic Hospital were enrolled prospectively. The primary outcome was a decrease in the number of exacerbations – defined as the need for adjunct oral corticosteroids or antibiotics – recorded in the 12 months before the procedure, compared with the number of exacerbations in the 12 months after completion of the final BT treatment. Secondary outcomes included differences in Asthma Control Test (ACT) scores, overall chronic oral corticosteroid (OCS) dose (in mg/month), number of asthma classes of medications used pre- and post BT, and the need for admission post-procedure. Patients also underwent bronchial biopsies after each procedure, but the relevant results are not reported here.

**Results.** Twelve patients (50% male; median age (interquartile range (IQR)) of 59 (46 - 64); 10/12 (83%) on OCS and 8/12 (66%) with previous ICU admission) underwent BT (36 procedures) and completed the 12-month post-procedure follow-up period. The median (IQR) number of exacerbations decreased significantly post-BT 12 (6 - 12) v. 2 (0.3 - 3);  $p=0.0002$ ). ACT scores post-BT were also significantly higher (7.5 (6.0 - 11.8) v. 14.5 (11.25 - 17.75);  $p=0.012$ ). There was a reduction in the median (IQR) monthly OCS dose before and after BT treatment, 300 mg (200 - 450) v. 240 mg (40 - 450). The number of classes of asthma medications was unchanged. BT was well tolerated, but 8% ( $n=3$ ) of patients developed post-procedural bronchospasm requiring overnight admission, one of whom developed a pneumothorax that was managed conservatively.

**Conclusion.** In this small single-centre study in a resource-poor setting, which enrolled patients with disease more severe than in published clinical trials, BT reduced exacerbations and improved asthma control.

## The utility of endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) for the diagnosis of mediastinal lesions in a resource-limited TB- and HIV-endemic setting

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**Introduction.** Diagnostic evaluation by mediastinoscopy is associated with increased risk, cost and hospitalisation. Although endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) may be a useful alternative, there is limited data from tuberculosis (TB)- and HIV-endemic settings with limited access to surgical facilities.

**Objectives.** To investigate the utility of EBUS-TBNA for the diagnosis of mediastinal lesions in a resource-limited TB- and HIV-endemic setting.

**Methods.** We prospectively evaluated 154 patients who underwent EBUS-TBNA between March 2013 and July 2017 at Groote Schuur Hospital, Cape Town, South Africa. The indications for EBUS-TBNA were undiagnosed mediastinal lesions and assessments for staging of lung cancer. Patients without diagnostic clarity underwent mediastinoscopy or appropriate surgical biopsy.

**Results.** The diagnostic accuracy of EBUS-TBNA, regardless of the indication, was 68.7% (95% confidence interval (CI) 57.7 - 75.7) with a positive predictive value of 100% (95% CI 94.7 - 100), and negative predictive value of 63.9% (95% CI 52.1 - 71.9). Overall, EBUS-TBNA diagnosed TB in 19/24 patients (79.2%). Sarcoidosis was diagnosed in 6/16 (62.5%) patients with EBUS-TBNA alone, and 11/16 patients (68.8%) when combined with transbronchial biopsy. Malignant disease was diagnosed in 39/54 (72.2%) patients. False negative results were obtained in 31 (20%) patients, of whom 15 had malignancy, 5 had TB, and 5 had sarcoidosis. On subgroup analysis, 14/154 (9.1%) referred patients were HIV-positive, of whom EBUS-TBNA diagnosed TB in 5 patients, sarcoidosis in 1 patient, and benign disease in 7 patients, with 1 false-negative diagnosis in a patient with lymphoma. The overall sensitivity of EBUS-TBNA in HIV-positive persons was 92.9%. The procedure was well tolerated in 149/154 patients (96.7%), with reversible complications occurring in five patients.

**Conclusion.** EBUS-TBNA is a safe and valuable diagnostic tool for benign and malignant disease, even in HIV-positive persons. Overall, surgical intervention was avoided in ~70% of patients, thereby improving the time to treatment initiation, and reducing associated risk, cost and hospitalisation rates. These data inform clinical practice in resource-limited TB- and HIV-endemic settings.

## A human lung-orientated approach to correlates of risk in tuberculosis

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**Introduction.** Currently tested vaccines against tuberculosis (TB) have been ineffective. Evidence suggests that a robust Th1 immune response is insufficient to prevent disease progression. Immunological correlates of risk are poorly understood within the human lung, the organ of initial contact with *Mycobacterium tuberculosis*.

**Objectives.** To investigate, in a comparative, first in man study, local in vivo pulmonary immune responses in HIV-negative individuals with different risk susceptibility profiles based on clinical, radiological and immunodiagnostic profiles, including immunodiagnostic test negative despite exposure, presumed latent tuberculosis infection (LTBI), previous active TB, recurrent TB, and self-cured TB, using a lung antigenic challenge model (purified protein derivative (PPD) and live-Bacillus Calmette-Guérin (BCG)).

**Methods.** PPD, live BCG, and saline (control) were instilled into different lung segments via bronchoscopy. Initial experiments were performed to determine the immunomechanical effect of saline instillation and to optimise BCG and PPD concentrations. Bronchoalveolar lavage was performed prior to antigenic challenge, i.e. at baseline, and 72 hours' post-challenge. Peripheral blood samples



and BCG-challenged skin biopsy samples were collected concurrently. Flow cytometry was used to analyse BAL and peripheral blood cells for cell surface markers and cytokine/chemokine expression profiles associated with innate and cell-mediated immune pathways.

**Results.** The bronchoscopic instillation of saline alone in healthy controls ( $n=4$ ) induced an immune response. Antigenic challenge using BCG (104 colony-forming units) and PPD (0.5 tuberculin units) was optimal in generating measurable alveolar immune responses, i.e. an increase in total cell numbers from the baseline (BCG-driven,  $p=0.03$ ; PPD-driven,  $p=0.004$ ). PPD challenge in those with previous TB showed significantly increased TLR2+IL6+ coexpression in macrophages ( $p=0.01$ ), but decreased biomarker-specific T-cell expression (CD4+TNF $\alpha$  ( $p=0.05$ ), CD8+TNF $\alpha$  ( $p=0.02$ ), and Th17 homing cells (CD4+IL17+CCR6+;  $p=0.004$ ). However, a high degree of inter-patient variability was observed.

**Conclusion.** These preliminary findings demonstrate the feasibility of using an in vivo mycobacterial-specific human lung antigenic challenge model. The emerging data will likely have implications for the design of vaccines and immunotherapeutic interventions.

## Diagnosing tuberculosis in hospitalised HIV-positive individuals who cannot produce sputum: Is urine-lipoarabinomannan testing the answer?

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**Introduction.** Up to one-third of HIV-positive individuals with suspected tuberculosis (TB) are sputum-scarce. The Alere Determine TB LAM Ag lateral-flow strip test can be used to diagnose TB in HIV-infected patients with advanced immunosuppression. However, how urine-LAM testing should be incorporated into testing algorithms, and in the context of specific patient subgroups, remains unclear.

**Objectives.** To clarify the role of urinary LAM in tuberculosis diagnostics.

**Methods.** This study represents a post hoc subgroup analysis of data from a randomised multicentre parent study. The study population consisted of hospitalised HIV-infected patients with suspected TB who were unable to produce sputum and who underwent urine-LAM testing. The diagnostic utility of urine LAM for TB in this group was compared with the performance of urine LAM in patients who did produce a sputum sample in the parent study.

**Results.** There was a total of 187 and 2 341 patients in the sputum-scarce and sputum-producing cohorts, respectively. In comparison with those who produced sputum, sputum-scarce patients were younger, had a lower Karnofsky performance score, and a lower weight and body mass index at admission. A greater proportion of sputum-scarce patients were urine-LAM-positive, compared with those who were able to produce sputum (31% v. 21%, respectively;  $p=0.04$ ). A higher proportion of sputum-scarce patients died within 8 weeks of admission (32% v. 24%, respectively;  $p=0.013$ ).

**Conclusion.** Urine-LAM testing can effectively identify TB in HIV-infected patients who are at a higher risk of mortality and unable to

generate a sputum sample for diagnostic testing. Our findings support the use of urine-LAM testing in sputum-scarce, hospitalised HIV-infected patients, and its incorporation into diagnostic algorithms for this patient population.

## Early-morning urine collection to improve urinary lateral flow lipoarabinomannan (LAM) assay sensitivity in hospitalised patients with HIV-TB co-infection

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**Introduction.** The HIV pandemic has fuelled a resurgence of tuberculosis (TB), which is the leading cause of death in HIV-infected persons in sub-Saharan Africa. Rapid initiation of TB treatment may reduce mortality in these vulnerable patients. Urine-LAM testing has been approved by the World Health Organization for use in hospitalised patients with advanced immunosuppression. However, the sensitivity of the test remains suboptimal.

**Objectives.** To examine the incremental diagnostic sensitivity of early morning urine (EMU) v. random urine sampling using the Determine lateral flow lipoarabinomannan assay (LF-LAM) in HIV-TB-coinfected patients.

**Methods.** Consenting HIV-positive inpatients, screened as part of a larger prospective, randomised controlled trial, who were treated for TB and could donate matched random and EMU samples were included. Thus, paired samples were collected from the same patient, and LF-LAM was graded using the pre-January 2014 grade 1 and 2 manufacturer-designated cut-off points (the latter was designated grade 1 after January 2014). Single sputum GeneXpert-MTB/RIF- and/or TB-culture positivity served as the reference standard (definite TB). Those treated for TB but not meeting this standard were designated as cases of probable TB.

**Results.** A total of 123 HIV-infected patients commenced anti-TB treatment and provided matched random and EMU samples. A total of 33% and 67% had definite and probable TB, respectively. Among those with definite TB, LF-LAM sensitivity using the grade 2 cut-off point increased from 12% to 39% with random v. EMU respectively ( $p=0.005$ ). Similarly, among probable TB cases LF-LAM sensitivity increased from 10% to 24% ( $p=0.001$ ). LF-LAM specificity was not determined.

**Conclusion.** This proof-of-concept study indicates that EMU could improve the sensitivity of LF-LAM in hospitalised TB-HIV co-infected patients. These data have implications for clinical practice.

## A very unusual cause of haemoptysis: Unilateral pulmonary vein atresia in an adolescent

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**Introduction.** Unilateral pulmonary vein (UPV) atresia is a very uncommon cause of haemoptysis presenting in adults. It is

commonly diagnosed in infancy and childhood, and can present as recurrent infections and haemoptysis.

**Objectives.** To present an unusual case of a 14-year-old female with congenital UPV atresia and a review of the literature.

**Methods.** A 13-year-old HIV-negative female presented with the problem of intermittent recurrent episodes of haemoptysis. It started at the age of 3 years old, and she was treated for pulmonary tuberculosis (TB) for 6 months. However, the *Mycobacterium tuberculosis* was never detected. She had another bout of haemoptysis at age 11 and was once again treated for TB, being smear- and culture-negative and completing 6 months of treatment. A computed tomography pulmonary angiogram showed the right pulmonary vein atresia.

**Results.** UPV atresia is a rare condition and generally presents in early childhood, with haemoptysis and recurrent respiratory infections, and in later stages with worsening dyspnoea. It is associated with congenital heart disease in approximately one-third to one-half of cases. The presence of isolated pulmonary vein atresia without any structural cardiac or developmental venous abnormality presenting in adulthood is rare, with ~50 cases being reported.

**Conclusion.** This case is important in our hospital setting, as we have a high endemic pulmonary TB burden where patients can present with haemoptysis. This case highlights a delay in diagnosis for several years because pulmonary vein atresia was not considered as a differential. It also highlights that UPV atresia should always be considered as a possible cause of haemoptysis with recurrent infections, and that we should not always rush to condemn patients to 6 months of TB treatment when we do not have strong evidence to support it. The case also highlights that non-invasive methods are adequate in diagnosing this entity.

## Empyema in children hospitalised at the Chris Hani Baragwanath Academic Hospital: A retrospective study

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**Introduction.** The incidence of empyema has significantly decreased with the introduction of the 13-valent pneumococcal conjugate vaccine. Nevertheless, the management of empyema continues to be challenging in low-resourced settings.

**Objectives.** To describe the aetiology and management of empyema in a high-burden HIV-TB co-infection setting.

**Methods.** A retrospective descriptive study was undertaken between January 2012 and December 2016 in children <14 years of age at a large secondary-tertiary referral hospital. Cases of empyema were identified through pulmonology and discharge-summary databases. Clinical, laboratory and radiological data were collected from pulmonology files and patient records.

**Results.** Over a 5-year period, 66 cases met our case definition for empyema, of which 22 (33%) were referred from surrounding hospitals. The median (interquartile range (IQR)) age of presentation was 52.0 (18.1 - 103.6) months. A total of 13 (19.7%) were HIV-infected and six (9.1%) were HIV-exposed but uninfected. The most common causative organisms were *Staphylococcus aureus* (15/66; 22.7%)

and *Streptococcus pneumoniae* (5/66; 7.8%). Treatment for *Mycobacterium tuberculosis* was initiated in 28 (42.4%) cases and more frequently initiated in HIV-infected children (10/13; 76.9%;  $p=0.010$ ). Microbiological evidence of TB was present in five (7.6%) cases. Overall, seven (10.6%) children were ventilated and one died (case fatality rate: 1.5%). Forty-three (65.2%) cases had an intercostal drain, and 16 (24.2%) had a pigtail percutaneous catheter inserted; however, fibrinolytics were documented in only six cases (10.2%). Eight (12.1%) cases had a thoracotomy and seven (10.6%) had video-assisted thorascopic drainage, all of whom had a prior drain inserted and a median (IQR) of 20 (10 - 33) days from admission to surgery.

**Conclusion.** Our study showed an increased prevalence of *S. aureus* empyema compared with previous reports. In HIV-infected children with empyema, a large proportion were initiated on TB therapy, highlighting challenges in managing TB-HIV co-infection. Although fibrinolytics or early surgery is recommended, neither practice was common.

## Diagnostic performance of lung ultrasound compared with chest X-ray for pneumonia in children in the Drakenstein Child Health Study

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**Introduction.** Chest X-ray (CXR) is the first-line imaging modality for suspected pneumonia in children. However, CXR interpretation is limited by moderate sensitivity and specificity and poor inter-rater reliability (IRR), and it exposes children to ionising radiation. Lung ultrasound (LUS) may be a radiation-free, lower-cost alternative for the diagnosis of pneumonia.

**Objectives.** To compare the diagnostic performance of LUS and CXR in children with suspected pneumonia.

**Methods.** LUS was performed on 103 children in the Drakenstein Child Health Study who presented with World Health Organization - defined pneumonia and who received a CXR as part of routine care. IRR between a general practitioner and a paediatric radiologist for the interpretation of LUS findings for pneumonia were compared with CXR interpretation by two specialist paediatricians. Reliability of different LUS features was also compared.

**Results.** The study included 72 hospitalised and 31 non-hospitalised pneumonia cases with a median age of 7.3 months. The general practitioner and paediatric radiologist reported LUS findings consistent with pneumonia in 58% ( $n=60$ ) v. 52% ( $n=54$ ) of cases, respectively ( $p=0.01$ ). The overall agreement on LUS findings was

substantial ( $\kappa=0.60$ ) compared with poor agreement on CXR ( $\kappa=0.25$ ). On LUS, there was better agreement for consolidation ( $\kappa=0.67$ ) and for a normal scan ( $\kappa=0.68$ ) than for interstitial syndrome ( $\kappa=0.45$ ).

**Conclusion.** LUS demonstrated better IRR than CXR for detecting features of pneumonia in children. Consolidation is a more reliable sonographic sign of pneumonia than interstitial syndrome. LUS may be preferable to CXR for the diagnosis of pneumonia in children.

## The incremental yield of urine LAM over Xpert MTB/RIF testing in hospitalised HIV-infected sputum-expectorating patients

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**Introduction.** GeneXpert MTB/RIF and urinary lipoarabinomanan (LAM) are newer tuberculosis (TB) tests that have been shown to be effective for the diagnosis of TB in advanced HIV co-infection.

**Objectives.** The goal of this analysis was to assess the diagnostic utility of urine LAM for TB in HIV-infected patients admitted for suspected TB and for whom an Xpert MTB/RIF test result was available.

**Methods.** The analysis included patients who were able to provide a sputum sample for GeneXpert MTB/RIF, and urine for the Alere Determine TB LAM Ag lateral-flow strip test. Three diagnostic strategies were compared: using both urine-LAM- and Xpert MTB/RIF-testing for all patients suspected of TB; using urine-LAM testing only in those found to have a negative GeneXpert MTB/RIF test; and using GeneXpert MTB/RIF-testing in only those who had negative urine-LAM results. Sputum culture was used as a reference standard for the diagnosis of TB.

**Results.** Urine-LAM testing had a sensitivity of 38.1% (95% confidence interval (CI) 30.9 - 45.7) and a specificity of 88.1% (95% CI 84.3 - 91.1) while GeneXpert MTB/RIF testing was found to have a sensitivity of 75.0% (95% CI 67.9 - 81.2) and a specificity of 95.1% (95% CI 92.4 - 97.0). The combination of Urine LAM and GeneXpert MTB/RIF had a sensitivity of 78.4% (95% CI 71.6 - 84.2), and a specificity of 84.6% (95% CI 80.7 - 88.1). The incremental yield of adding urine-LAM testing after GeneXpert MTB/RIF testing (in those with a negative GeneXpert MTB/RIF test) was 4.5%, while the incremental yield of adding GeneXpert MTB/RIF testing after urine LAM testing (in those with a negative urine LAM test) was 106%.

**Conclusion.** In sputum-expectorating patients with advanced HIV, and where both molecular and antigen testing is available, urine LAM has minimal incremental yield over GeneXpert MTB/RIF.

