South African Thoracic Society Congress 2023

Abstracts of the SATS Congress
Durban International Conference Centre
10 - 13 August 2023

ADULT PULMONOLOGY

A tale of two waves: Characteristics and outcomes of COVID-19 admissions during the Omicron-driven fourth wave in Cape Town, South Africa, and implications for the future

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Objectives. To describe the pattern of admissions during the fourth wave of COVID-19 in order to inform future public health policies.

Methods. This was a retrospective descriptive study of an early cohort of all adult patients with SARS-CoV-2 infection admitted to a tertiary hospital in Cape Town, South Africa, at the start of the country's fourth wave. The cohort was compared with an early cohort from the first wave at the same institution.

Results. In total, 121 SARS-CoV-2-positive admissions from the fourth wave were included. Thirty-one patients (25.6%) had COVID-19 pneumonia, while 90 (74.4%) had incidental SARS-CoV-2 infection. (In the first wave all 116 patients had COVID-19 pneumonia.) Thirty-two patients (26.4%) self-reported complete or partial COVID-19 vaccination, of whom 12 (37.5%) were admitted with COVID-19 pneumonia. Twenty-nine patients (24.0%), including 20 (64.5%) with COVID-19 pneumonia, received oral or intravenous steroids, which were not routinely prescribed in the first-wave cohort. Compared with the first wave, there were fewer intensive- or high-care admissions (n=18/121 (14.9%) v. 42/116 (36.2%); p<0.001), and mortality was lower (n=12/121 (9.9%) v. n=31/116 (26.7%); p=0.001).

Conclusion. Admissions to the COVID-19 wards during the fourth wave primarily comprised patients with incidental SARS-CoV-2 infection. There was a reduction in the need for critical care and in-hospital mortality. This changing epidemiology of COVID-19 admissions may be attributed to a combination of natural and/or vaccination-acquired immunity.

Comparison of patients with severe COVID-19 admitted to an intensive care unit in South Africa during the first and second waves of the COVID-19 pandemic

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Background. The second wave of COVID-19, dominated by the SARS-CoV-2 Beta variant, was reported to be associated with increased severity in South Africa (SA).

Objectives. To describe and compare the clinical characteristics, management and outcomes of COVID-19 patients admitted to an intensive care unit (ICU) in SA during the first and second waves.

Methods. In a prospective single-centre descriptive study, we compared all patients with severe COVID-19 admitted to the ICU during the first and second waves. The primary outcomes assessed were ICU mortality and ICU length of stay (LOS).

Results. In 490 patients with comparable age, comorbidities and degree of hypoxaemia, no difference in mortality was demonstrated during the second compared with the first wave (65.9% v. 62.5%, respectively; p=0.57). ICU LOS was longer in the second wave (10 v. 6 days; p<0.001). More female than male admissions (67.1% v. 44.6%; p<0.001) and a greater proportion of patients managed with invasive mechanical ventilation compared with non-invasive respiratory support (39.0% v. 14.0%; p<0.001) were noted in the second wave. No difference in the administration of corticosteroids (85.8% v. 81.5%; p=0.32) or anticoagulants (92.2% v. 86.4%; p=0.092) was noted between the two waves. Less empirical antibiotic and antiviral therapy was administered in the second wave (18.5% v. 72.1%; p<0.001 and 2.5% v. 21.4%; p<0.001). No vitamin C was administered in the second wave (0% v. 58.9%; p<0.001), and less thiamine was prescribed (6.1% v. 80.1%; p<0.001).

Conclusion. While clinical characteristics were comparable between the two waves, a higher proportion of patients were invasively ventilated and ICU stay was longer in the second wave. ICU mortality was unchanged. Drugs that lacked evidence of efficacy in the management of severe COVID-19 were used less frequently in the second wave.

An autologous human dendritic cell vaccine from extensively drug-resistant tuberculosis patients polarises antigen-specific polyfunctional and cytotoxic T-cell responses that are bactericidal to Mycobacterium tuberculosis

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Background. Extensively drug-resistant tuberculosis (XDR-TB) is an increasing public health concern, as drug resistance is outpacing the drug development pipeline. Alternative immunotherapeutic approaches are needed.
Methods. Dendritic cells (DCs) were cultured from XDR-TB patient-derived peripheral blood monocytes (N=30) by maturation with *Mycobacterium tuberculosis* (MTB)-specific antigens, with/without a maturation cocktail (interferon-γ, interferon-α, CD40L, interleukin (IL)-1β, and TLR3, TLR7 and TLR8 agonists). Two peptide pools were evaluated: (*i*) an ECAT peptide pool (ESAT6, CFP10, Ag85B and TB10.4 peptides); and (*ii*) a PE/PPE peptide pool (PE and PPE peptides). A sonicated lysate of HN878 served as an antigen control. DCs were assessed for the expression of key maturation markers and the secretion of Th1-polarising cytokines. The ability of the DC-primed peripheral blood mononuclear cells to restrict the growth of MTB-infected monocyte-derived macrophages was evaluated using an *in vitro* mycobacterial containment assay.
Results. In patients with XDR-TB, DCs matured with MTB antigen + cocktail, compared with DCs matured with MTB antigen only, showed significantly higher upregulation of key co-stimulatory molecules, CD80, CD83, CD86, and CCR7 (p<0.001 for all comparisons), and higher secreted levels of the IL-12p70 (0.67 v. 0.01 ng/mL/10^6 cells; p<0.001). The matured DCs enhanced antigen-specific CD8+ T-cell responses to ESAT6 (p=0.05) and Ag85B (p=0.03). Furthermore, containment was significantly higher with MTB antigen + cocktail v. antigen alone (p=0.0002 for PE/PPE). PE/PPE + cocktail-matured DCs achieved a higher magnitude of containment compared with ECAT + cocktail-matured DCs (50% (interquartile range 39 - 75) v. 46% (15 - 62); p=0.02).
Conclusion. In patients with XDR-TB, an effector response primed by the PE/PPE peptide pool and cocktail-matured DCs was capable of restricting the growth of MTB *in vitro*. These data support the generation of a DC-based immunotherapeutic intervention for therapeutically destitute patients with drug-resistant TB. Further mechanistic studies and future phase 1 human clinical studies are warranted.

Cough aerosol sampling of tuberculosis patients indicates that highly infectious 'super-spreader' individuals can be accurately identified through predictive modelling of GeneXpert cycle thresholds

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Background. To control the spread of tuberculosis, particularly at community level, it is critical to identify highly infectious individuals, who should be isolated and their contacts traced. Given the current resource limitations, it would be desirable to target the most infectious individuals, especially in the context of screening (active case finding) programmes. In a previous study, we used a cough aerosol sampling system (CASS) to identify individuals who exhaled culturable and presumably contagious *Mycobacterium tuberculosis* (MTB) in their cough aerosols (particles <10 μM).
Objectives. To rapidly identify highly infectious super-spreader individuals.
Methods. In the previous study, of 452 tuberculosis patients, 310 did not emit any culturable cough aerosols (CASS negative), while 142 had culturable MTB (CASS positive) in their respirable cough droplets. Here, we performed a more granular analysis by dividing the CASS-positive patients into two groups, those who emitted 1 - 9 (n=100) and those who emitted ≥10 (the 'super-spreaders', n=42) colony-forming units in their cough aerosols. We compared various demographic, clinical, physiological and diagnostic characteristics between the three groups and performed predictive linear modelling (with bootstrapping) to evaluate whether super-spreaders could be accurately identified.
Results. Compared with CASS-negative patients, super-spreaders were significantly more likely (p<0.05 for all comparisons) to be male (79% v. 55%; relative risk (RR) 2.6 (1.3 - 5.3)), to be HIV negative (79% v. 54%; RR 2.8 (1.4 - 5.6)), to be smokers (76% v. 60%; RR 1.97 (1 - 3.9)), to have a persistent cough (86% v. 69%; RR 2.5 (1.1 - 5.7)), and to have better lung function. In addition, super-spreaders had a significantly (p<0.0001 for all comparisons) shorter time to sputum culture positivity (6.1 (0.5) v. 21.2 (1.1) days), a lower GeneXpert cycle threshold (CT) average (CT 16.1 (0.5) v. 22.4 (0.3)), and higher average smear grade (3.6 (0.2) v. 1.4 (0.1)). Predictive modelling using the Xpert CT alone (preferred for its fast turnaround time) revealed that super-spreaders could be distinguished from CASS-negative patients with a sensitivity of 0.83 (0.78 - 0.86) and specificity of 0.73 (0.63 - 0.78).
Conclusion. Tuberculosis super-spreaders can be accurately identified using readily available demographic, clinical and GeneXpert results, showing great potential to inform isolation and contact tracing protocols that could considerably limit the transmission of tuberculosis.

SARS-CoV-2 viral replication persists in the human lung for several weeks after symptom onset in mechanically ventilated patients with severe COVID-19: A prospective tissue-sampling study

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Background. The immunopathogenesis of severe COVID-19 is incompletely understood. Remdesivir is not recommended in mechanically ventilated (MV) patients. In the upper respiratory tract (URT), replicating (culturable) SARS-CoV-2 is recoverable for ~ 4

- 8 days after symptom onset; however, there is a paucity of data on the frequency or duration of replicating virus in the lower respiratory tract (i.e. the human lung).

Methods. We undertook lung tissue sampling (needle biopsy), shortly after death, in 42 MV decedents during the Beta and Delta COVID-19 waves. An independent group of 18 ambulatory patients served as a comparative control. Lung biopsy cores from decedents underwent viral culture, histopathological analysis, electron microscopy, transcriptomic profiling, immunohistochemistry and cell-based flow cytometry of deconstructed tissue.

Results. Of MV decedents, 38% (n=16/42) had culturable virus in the lung for a median of 15 days (persisting for up to 4 weeks) after symptom onset, compared with ≤~5 days in the URT of ambulatory patients. Lung viral culture positivity was not associated with comorbidities or steroid use. Delta but not Beta variant lung culture positivity was associated with accelerated death and secondary bacterial infection (p<0.05). NP culture was negative in 23.1% (n=6/26) of decedents despite lung culture positivity. This hitherto undescribed bio-phenotype of lung-specific persisting viral replication was associated with an enhanced transcriptomic pulmonary pro-inflammatory response, but concurrent with viral culture positivity.

Conclusion. In a sizeable subset of patients with acute COVID-19, concurrent rather than sequential active viral replication continues to drive a heightened pro-inflammatory response in the human lung beyond the 2nd week of illness (despite lack of viral replication in the URT), and was associated with variant-specific increased mortality and morbidity. These findings have potential implications for the design of interventional strategies and clinical management of patients with severe COVID-19 disease.

Funding. South African Medical Research Council.

Frequency, kinetics and determinants of viable SARS-CoV-2 in bioaerosols from ambulatory COVID-19 patients infected with the Beta, Delta or Omicron variants

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Background. Airborne transmission of SARS-CoV-2 aerosol remains contentious. Importantly, whether cough- or breath-generated bioaerosols can harbour viable and replicating virus remains largely unclarified.

Methods. We performed size-fractionated aerosol sampling (Andersen cascade impactor) and evaluated viral culturability in human cell lines (infectiousness), viral genetics, and host immunity in ambulatory participants with COVID-19.

Results. Sixty-one percent (n=27/44) and 50% (n=22/44) of participants emitted variant-specific culture-positive aerosols <10 µm and <5 µm, respectively, for up to 9 days after symptom onset. Aerosol culturability was significantly associated with lower neutralising antibody titres, and suppression of transcriptomic pathways related to innate immunity and the humoral response. A nasopharyngeal Ct <17 ruled in ~40% of aerosol culture positives and identified those that were probably highly infectious. A parsimonious three transcript blood-based biosignature was highly predictive of infectious aerosol generation (positive predictive value >95%). Only 29% of participants produced culture-positive aerosols <5 µm at ~6 days after symptom onset, therefore supporting the super-spreader hypothesis.

Conclusion. These data, the first to comprehensively confirm variant-specific culturable SARS-CoV-2 in aerosol, inform the targeting of transmission-related interventions and public health containment strategies emphasising improved ventilation.

Comparison of the effects of electronic cigarette vapours and tobacco smoke extracts on human neutrophils in vitro

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Background. Electronic cigarettes (ECs) are aerosol delivery systems composed of nicotine and various chemicals, widely used to facilitate smoking cessation. Although ECs are considered safer than cigarettes, their vapours contain chemical toxicants that may interact with cells of the host's innate immune system such as neutrophils, adversely affecting the innate immune system and potentially predisposing EC users to respiratory infections.

Objectives. To compare effects of aqueous EC aerosol extracts (ECEs, with or without nicotine) with cigarette smoke extract (CSE) on neutrophil and platelet reactivity *in vitro*.

Methods. Neutrophil reactivity is characterised by generation of reactive oxygen species (ROS), degranulation (elastase release) and release of extracellular DNA (neutrophil extracellular trap (NET) formation: NETosis), which were measured using chemiluminescence, spectrophotometric and microscopic procedures, respectively. Platelet reactivity was measured according to the magnitude of upregulated expression of the adhesion molecule CD62P using flow cytometry.

Results. Exposure of neutrophils to ECEs or CSE significantly inhibited ROS generation and elastase release by N-formyl-L-methionyl-L-leucyl-L-phenylalanine (1 µM)-activated neutrophils. Pretreatment of neutrophils with CSE also resulted in a marked attenuation of phorbol 12-myristate 13-acetate (6.25 nM)-mediated release of extracellular DNA, which was unaffected by the ECEs. Similarly, CSE, but not the ECEs, inhibited the expression of CD62P by platelets activated with ADP (100 µM).

Conclusion. These observations suggest that EC aerosols may inhibit some immunoprotective activities of neutrophils such as ROS production and elastase release by activated cells, the effect of which was not enhanced by nicotine. The inhibitory effects of CSE were significantly more pronounced than those of ECEs, especially for suppression of NET formation and platelet activation. If operative *in vivo*, this may compromise intrinsic pulmonary antimicrobial defence mechanisms, albeit less so than cigarette smoke.

Early experience and outcomes of novel generic cystic fibrosis transmembrane conductance regulator protein modulator drugs in South Africans with cystic fibrosis: A real-world study to challenge Big Pharma patent monopoly in low- and middle-income countries

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Background. Cystic fibrosis (CF) transmembrane conductance regulator protein modulator drugs (CFTRm) have transformed the prognosis of people with CF (pwCF), but they are not available in South Africa (SA). Some pwCF in SA are personally obtaining a cheaper generic elexacaftor/tezacaftor/ivacaftor (ETI).

Objectives. To describe and compare patient outcomes after initiating standard (daily) generic ETI dosing or off-label 'modulator-sparing' dosing (twice weekly), in combination with a strong CYP3A-inhibitor.

Methods. This was a multicentre descriptive study from December 2021 to March 2023, using SA CF registry data. Uni- and multivariable repeated measures analyses were conducted to describe changes in sweat test, forced vital capacity in 1 second (FEV1pp) and body mass index (BMI) over the 12-month follow-up period, for different dosing schedules.

Results. Forty-three pwCF (median age 25 years; 41 with ≥1 copy F508del) initiated ETI with standard (n=31) or modulator-sparing doses (n=12). One patient died during the study period. Mean (standard deviation) pretreatment sweat chloride, BMI and FEV1pp were 92 (21) mmol/L, 19.1 (2.4) kg/m^2 and 58 (29.4), respectively. The overall mean reduction in sweat chloride over the first month of ETI treatment was 52 mmol/L (p<0.01), with improvements in FEV1pp and BMI of 15.1 (p<0.01) and 0.98 kg/m^2 (p<0.001), respectively. Improvements in FEV1pp and BMI were sustained or improved further throughout follow-up, with no difference between dosing groups (p>0.1).

Conclusion. The treatment effect of generic ETI appears similar to real-world data reported using the original product. There was no significant difference in response between modulator-sparing and standard dosing; reduced dosing may therefore be considered as an interim measure to reduce cost and increase access to CFTRm in SA.

Management and outcomes of community-acquired sepsis in patients admitted to medical wards at a tertiary academic hospital: A 6-month prospective study

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Background. Sepsis is a life-threatening organ dysfunction secondary to the dysregulated body's immune response to infection, and it is a significant cause of morbidity and mortality worldwide.

Objectives. To describe the management and outcomes of community-acquired sepsis among medical admissions at Dr George Mukhari Academic Hospital (DGMAH), Pretoria, South Africa.

Methods. A prospective cross-sectional review of medical records of consecutive adult patients with community-acquired sepsis admitted to the internal medicine wards at DGMAH between 1 August 2022 and 31 March 2023 was performed. Clinical outcomes were measured by mortality, length of hospital stay and intensive care unit (ICU) transfer.

Results. A total of 169 patients fulfilled the study inclusion criteria, representing 7.3% of the total admissions. Their mean (standard deviation) age was 43.4 (16.5) years (range 18 - 91), and more than half (52.7%) were <40 years of age. Most of the patients (63.3%) were male. The most prevalent diagnoses were community-acquired pneumonia, infective endocarditis and tuberculosis. More than eighty percent (86.4%) had at least one comorbid condition. Retroviral disease (HIV), diabetes mellitus, acute kidney injury and hypertension were the most frequent comorbidities. The most common samples submitted for investigation were blood cultures (72.8%), and 74 of 123 samples (60.2%) were found to be positive for one or more microbial pathogens. The two most common bacteria isolated from blood cultures were *Staphylococcus aureus* and coagulase-negative staphylococci. The most common antibiotics prescribed were augmentin and azithromycin. Of the study cohort, 15.4% of patients died, over half (55.0%) stayed in the hospital for over a week, and 16.6% were transferred to the ICU for escalation of care.

Conclusion. The study suggests that overall mortality due to community-acquired sepsis was high, particularly in patients admitted with infective endocarditis and community-acquired pneumonia who were co-infected with HIV. Bacteraemia, especially from *S. aureus*, was associated with increased hospital mortality.

The diagnostic performance of unstimulated IFN-γ (IRISA-TB) for pleural tuberculosis: A prospective study in South Africa and India

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Background. Tuberculous pleural effusion (TPE) is the most common form of extrapulmonary tuberculosis in many settings. The diagnostic performance of frontline rapid nucleic acid amplification tests, such as GeneXpert MTB/RIF, remains suboptimal (sensitivity ~30%). However, a more sensitive version (GeneXpert MTB/RIF Ultra), and alternative newer assays, are now available.

Objectives. To evaluate the diagnostic performance of Xpert Ultra and the newer interferon-gamma rapid immunosuspension assay (IRISA-TB), a rapid (same-day) diagnostic test, in patients with presumed TPE (the pleural fluid sample remains unprocessed and there is no overnight stimulation step, and this is therefore not an IGRA).

Methods. In this multicentre, observational study, a total of 218 participants with suspected TPE were recruited (110 and 108 from South Africa and India, respectively). Participants underwent routine diagnostic testing and pleural biopsy. IRISA-TB testing was performed concurrently. Performance was compared with other available same-day diagnostic tests (adenosine deaminase (ADA) and Xpert Ultra).

The reference standard for tuberculosis (TB) was microbiological and/or histopathological confirmation of TB using the fluid and/or pleural biopsy sample.

Results. Results for this preliminary analysis were available for 133/218 participants (61.0%). The sensitivity of IRISA-TB (cut point 20.5 pg/mL) was significantly better than that of Xpert Ultra (81.9% v. 34.6% (25.2 - 45.5), respectively; $p<0.001$). The specificity of IRISA-TB was significantly higher than that of ADA (97.5% v. 84.7% (76.5 - 90.4); $p=0.029$), but was similar to Xpert Ultra (97.5% v. 99.1% (94.9 - 99.9)). The negative predictive value (NPV) of IRISA-TB (88.4% (80.0 - 93.7)) was higher than that of ADA (86.3% (78.3 - 91.7)) and Xpert Ultra (66.7% (59.1 - 73.6)) ($p=0.036$). The positive predictive value (PPV) of IRISA-TB was 88.4% (80.0 - 93.6).

Conclusion. Xpert Ultra has poor sensitivity for the diagnosis of pleural TB. In contrast, IRISA-TB demonstrated high sensitivity, specificity, NPV and PPV for the diagnosis of TPE in TB-endemic settings.

High rates of cavitary disease, detected during community-based active case finding, in individuals with subclinical v. symptomatic active tuberculosis

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Background. Subclinical tuberculosis (TB; asymptomatic individuals with microbiologically proven TB) represents a large proportion of the global TB burden. Whether these individuals contribute to disease transmission is unclear. Lung cavitation is associated with infectiousness and disease transmission.

Objectives. To compare radiological findings, including cavitary disease, in individuals with subclinical v. symptomatic active TB during community-based active case finding.

Methods. Participants with microbiologically confirmed TB (GeneXpert and/or culture positivity; $N=77$), recruited from two ongoing, prospective community-based active case-finding studies in South Africa, underwent a chest x-ray (CXR) and fluorodeoxyglucose positron emission tomography computed tomography (^{18}F FDG PET-CT).

Results. A total of 1 013 participants were enrolled, of whom 77 (7.6%) had microbiologically confirmed TB (43 (55.8%) had subclinical TB and 34 (44.2%) had symptomatic active TB). CXRs and PET-CTs were available for 72/77 participants (93.5%), of whom 61.1% ($n=44/72$) had cavitary disease on CXR (significantly higher in those with symptomatic active TB than in those with subclinical TB (78.8% v. 46.2%, respectively; $p=0.005$)) and 75.0% ($n=54/72$) had cavitary disease on PET-CT (similarly higher in symptomatic active TB v. subclinical TB (84.8% v. 66.7%)). Compared with PET-CT, CXR correctly identified 74.1% ($n=40/72$) with cavitary disease (~25% of cavitary disease was therefore missed on CXR). Of participants with TB, 27.3% ($n=21/77$) were smear positive (44.1% of symptomatic active TB v. 14.0% of subclinical TB; $p=0.005$). Of smear-positive participants, 17/21 (81.0%) had cavitary disease on PET-CT. This pattern of findings remained largely unchanged when individuals with a history of previous TB were excluded from the analysis.

Conclusion. Among community-based individuals who did not self-report to healthcare facilities, the rates of cavitary disease were substantial (even in those with subclinical TB). To our knowledge, these data are the first to compare community-based CXR and PET-CT findings, thus informing future active case-finding strategies that seek to detect almost all probably infectious persons with TB.

Feasibility of concurrent COVID-19 screening during community-based active case finding for tuberculosis in symptomatic individuals in South Africa

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Background. Tuberculosis (TB) is a global public health threat. The COVID-19 pandemic resulted in extensive resource reallocation, disrupting healthcare services and reversing years of TB control efforts.

Objectives. To evaluate the feasibility of concurrent COVID-19 screening during community-based active case finding (ACF) for TB in symptomatic individuals in South Africa (SA).

Methods. In this cross-sectional study, we recruited participants with clinical symptoms suggestive of TB and/or COVID-19 from the SA site of an ongoing, European and Developing Countries Clinical Trials Partnership-funded, community-based ACF study (XACT-19 (RIA2020S-3295)). Participants underwent simultaneous point-of-care (POC) testing; for TB, we tested sputum using GeneXpert MTB/RIF Ultra, and for COVID-19, we tested nasopharyngeal swabs using Xpert SARS-CoV-2. Diagnostic accuracy was compared with sputum culture and reverse transcription polymerase chain reaction at a central laboratory (reference standards for TB and COVID-19, respectively). To assess feasibility and usability of POC Xpert testing, minimally trained study personnel completed the System Usability Scale (SUS, a Likert-based questionnaire with a score ranging from 0 (negative) to 100 (positive)).

Results. Between February 2022 and March 2023, a total of 490 participants were enrolled, of whom 123 (25.1%) were symptomatic and included in this analysis; $n=16/123$ (13.0%) participants tested positive for TB, $n=9/123$ (7.3%) tested positive for COVID-19, and $n=2/123$ (1.6%) had concurrent TB and COVID-19. Sensitivity and specificity of POC Xpert Ultra was 75.0% (42.8 - 94.5) and 96.4% (91.0 - 99.0), respectively, whereas those of POC Xpert SARS-CoV-2 were 66.7% (22.3 - 95.7) and 97.4% (92.6 - 99.5), respectively. Five study personnel completed the SUS with a mean (standard deviation) score of 77.5 (17.2), indicating POC Xpert to be acceptable and to have 'good' usability.

Conclusion. When performing ACF for TB, concurrent screening for COVID-19 using POC molecular tools is feasible and has a moderate diagnostic yield. Further research may establish the optimal distribution of resources for potential future COVID-19 waves or pandemics.

Evaluating the impact of computer-assisted X-ray diagnosis and other triage tools to optimise GeneXpert-orientated community-based active case finding for tuberculosis and COVID-19 (XACT-19)

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Background. Almost 40% of persons newly diagnosed with tuberculosis (TB) are unreported. Detecting cases in TB/HIV-endemic communities has been restricted by a lack of sensitive and user-friendly point-of-care (POC) diagnostic tools. Computer-aided detection (CAD) has been recommended by the World Health Organization for screening for TB; however, implementation of CAD in community-based active case finding (ACF) is unclear.

Objectives. To determine the adjunctive role of CAD in GeneXpert-orientated community-based ACF for TB.

Methods. In this ongoing, European and Developing Countries Clinical Trials Partnership-funded (RIA2020S-3295), open-label randomised controlled trial, high-risk persons (symptomatic and/or HIV-infected) with presumed TB were recruited from TB/HIV-endemic communities in South Africa (SA) and Zambia (Zimbabwe is an additional site). Using a low-cost mobile van staffed by three healthcare workers and equipped with an ultra-portable X-ray and GeneXpert system, participants were randomised into either 'CAD + POC Xpert' (arm 1: CAD followed by Xpert MTB/RIF Ultra in CAD-positive participants using a CAD4TB v7 threshold of 10 (South Africa) and 50 (Zambia) based on prior population-specific calibration), or 'POC Xpert alone' (arm 2: POC Xpert MTB/RIF Ultra only). The primary outcome was time to detection of microbiologically proven TB (Xpert and/or culture positivity). We present an interim trial progress report.

Results. From February 2022, a total of 505 participants have been enrolled (256 (50.7%) from SA and 249 (49.3%) from Zambia). Of the 505 participants, 26.9% (n=136) were HIV infected (median CD4 count 609 cells/μL) and 33 (6.5%) tested positive for TB (n=25/256 (9.8%) in SA and 8/249 (3.2%) in Zambia). Fifteen participants underwent screening to detect 1 case of TB. Of TB-positive participants, 7/33 (21.2%) were smear positive.

Conclusion. Community-based ACF detected a high burden of TB, of which a significant minority (~20%) was probably infectious. These data have implications for ACF strategies in high-burden settings.

The clinical profile of teenagers with asthma attending the respiratory outpatient clinic of an academic hospital

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Background. Asthma is a heterogeneous disease characterised by chronic airway inflammation. The chronic inflammation is associated with airway hyper-responsiveness. The burden of asthma is particularly high in adolescents, with an increased prevalence and mortality compared with younger children. Studies have shown that asthma management creates a particular set of challenges among adolescents, who are seeking greater autonomy, developing socially and emotionally, and experiencing changes in their relationships with friends and family. Adolescence is a time of testing limits, and often risk-taking behaviour such as experimentation with smoking.

Objectives. To describe the clinical profile of teenage asthmatics in a tertiary care centre.

Methods. A cross-sectional study of teenage asthmatics attending a respiratory clinic was performed. The study consisted of face-to-face interviews and review of clinical and laboratory records.

Results. Eighty-seven teenagers were studied. The mean (standard deviation) age was 15.5 (1.52) years. The majority (59%) were male. Forty-seven percent had been diagnosed with asthma between the ages of 3 and 5 years. Ten (11.5%) were current smokers. The mean CAT score of the group was 19.2 (2.29). Fifteen (26.7%) had had an attack requiring hospitalisation in the past 12 months, and 5.8% had had a previous intensive care unit (ICU) admission. Eighteen patients (20.7%) had access to a home nebuliser. There were no statistically significant differences in CAT scores or smoking status between males and females. Knowledge of asthma medication and appropriateness of inhaler technique did not independently affect the risk of ICU admission.

Conclusion. The majority of the participants had satisfactory asthma control as determined by the CAT score, even though inhaler technique was largely unsatisfactory. The prevalence of tobacco use in this cohort is a cause for concern.

A benign endobronchial polyp with breath-taking consequences

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Case presentation. A 30-year-old man was referred to our hospital with a 4-month history of progressively worsening dyspnoea, significant loss of weight, and night sweats. He also reported a chronic dry cough which was now productive of yellow-coloured sputum. He denied experiencing haemoptysis.

His background medical history was significant for radiation-induced hypothyroidism and previous childhood lymphoma, which was successfully cured after treatment with chemotherapy and radiation at age 12. He also reported having completed 6 months of anti-tuberculosis (TB) treatment for pulmonary TB 17 years prior to this admission. He was HIV negative. He reported a 5 pack-year cigarette smoking history.

On clinical examination, the patient was found to be in respiratory distress with generalised muscle wasting. His room air oxygen saturation was 85% with a sinus tachycardia of 144 bpm. There was finger and toe digital clubbing. There was evidence of volume loss of

the left hemithorax with a deviated trachea to the left, decreased chest expansion and decreased breath sounds. The right side of the chest was normal to examination. Cardiovascular examination was normal without features of pulmonary hypertension.

A chest X-ray confirmed left hemithorax volume loss and a dense left-sided opacification without air bronchograms. There was compensatory hyperinflation of the right lung.

A contrast-enhanced computed tomography scan of the chest revealed collapse-consolidation of the entire left lung. An endobronchial mass was noted within the left main bronchus with almost complete endobronchial obstruction. No calcification or enhancement was visualised, and there was no erosion through the tracheal walls. The right lung was normal. No significant mediastinal lymphadenopathy was noted.

Sputum cultured a *Proteus mirabilis* sensitive to amoxicillin, and GeneXpert Ultra was positive for rifampicin-sensitive TB. The patient was commenced on co-amoxiclav and anti-TB treatment.

Flexible bronchoscopy revealed a well-circumscribed multilobulated endobronchial polypoid mass, originating from the proximal left main bronchus. There was complete occlusion of the left main bronchus. Histological examination showed a benign fibroepithelial polyp.

The patient was referred for cardiothoracic surgery. A left pneumonectomy was performed with complete excision of the polyp and successful stump closure. The patient was discharged home 4 days postoperatively.

At follow-up 6 months later, the patient reported being well, with resolution of all respiratory symptoms. He reported a return to baseline weight and return to normal activities.

Discussion. Benign fibroepithelial polyps of the bronchial tree are rarely reported in the literature, and this is the first case report described in South Africa (SA).

The aetiology of fibroepithelial polyps is unclear, and the pathogenesis has not been well established. There are case reports which suggest that these lesions arise from chronic inflammatory processes.[1] This patient had multiple risk factors for chronic inflammation: he was a smoker with a 5 pack-year history, he had received radiation therapy for lymphoma as a child, he had had previous pulmonary TB, and he also had newly diagnosed pulmonary TB and bacterial co-infection of the post-obstructed lung.

Radiological findings typically show a well-defined nodule growing into the bronchus, with lobulated margins, resembling a blackberry.[2] During bronchoscopy, the lesions appear as a well-defined round, whitish pedunculated mass with a smooth surface and firm consistency.[3] The histological findings of these lesions have been reported as dense fibrovascular stroma, lacking epithelial overgrowth, covered by normal respiratory epithelium.[2]

SA has a high prevalence of pulmonary TB, and not infrequently patients are reinfected with TB. Our case highlights the importance of investigating for endobronchial obstruction in patients with persistent pulmonary infection, particularly when isolated to one anatomical area of the thorax.

This case posed a challenge when deciding on a therapeutic strategy for relieving the endobronchial obstruction, preventing polyp growth and curing the TB. The commonest treatment modality is endobronchial excision with biopsy forceps.[2] Endoscopic resection offers the therapeutic potential of lung re-expansion, allowing for improved clearance of mucus and secretions from the airways, and therefore better pulmonary hygiene and an improved chance of TB treatment success. However, the risk of contaminating the right lung was a major concern. Furthermore, re-expansion of the left lung seemed unlikely given the radiographic features of chronicity.

Although fibroepithelial polyps are slow-growing lesions with no malignant potential, and no evidence of increased mortality, our case shows that this benign lesion can result in significant endobronchial obstruction with resultant chronic pulmonary infection and structural changes, therefore posing a significant risk of morbidity and mortality if left unaddressed. Surgical treatment, including pneumonectomy for cure of infection, should be considered in order to prevent complications related to persistent pulmonary mycobacterial infection.

Conclusion. Fibroepithelial polyps are most commonly found in the skin and genitourinary tract, and benign endobronchial fibroepithelial polyps are rare.[4] While the aetiology of these lesions remains unclear, an inflammatory pathogenesis is likely. These lesions may be identified by their typical radiological findings, and by their appearance macroscopically during bronchoscopy. The diagnosis can be confirmed with a biopsy. There is no consensus on the treatment of these lesions, but as our case demonstrates, surgery may be required to provide cure of endobronchial obstruction and treatment of infection.

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Bilateral catamenial pneumothoraces with a left-sided diaphragmatic defect and omental herniation: A case report

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Background. Catamenial pneumothorax is the most common presentation of thoracic endometriosis syndrome. Thoracic endometriosis syndrome is defined as recurring spontaneous pneumothorax occurring within 72 hours before or after the start of menstruation, and occurs primarily in women aged 30 - 40 years. There is no definitive aetiology, though there are currently three popular theories – the metastatic, hormonal, and diaphragmatic air passage (anatomical) theories.

Case presentation. A 35-year-old woman presented with sudden-onset shortness of breath, and a chest radiograph revealed bilateral pneumothoraces. Intercostal chest drains were inserted and the pneumothoraces resolved. Two months later she re-presented with shortness of breath, and a chest radiograph again showed bilateral pneumothoraces. Further history revealed that the first episode had

occurred at the start of her menstrual cycle, and the current cycle was also concurrent with her menstrual cycle. High-resolution computed tomography showed no underlying parenchymal lung disease.
Left-sided video-assisted thoracoscopic surgery was done, and two diaphragmatic defects were noted, with omentum herniating into the chest. The omentum was resected, the defect was closed, and the hernia was repaired. Biopsy confirmed endometriosis. While right-sided video-assisted thoracoscopic surgery was planned for 6 weeks later, the patient started menstruating in postoperative recovery and developed a right-sided pneumothorax. A right-sided pleurectomy was performed and gonadotropin-releasing hormone (GnRH)-analogue therapy was started.
Conclusion. The current literature reports only cases of right-sided hernias, so this case with a left-sided defect and omental herniation is a novel presentation of thoracic endometriosis syndrome. Additionally, the presence of diaphragmatic fenestrations contributes evidence that may support the diaphragmatic air passage theory for the aetiology of thoracic endometriosis syndrome.

Clinical audit of connective tissue disease-associated interstitial lung disease at Charlotte Maxeke Johannesburg Academic Hospital over 30 years

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Background. Connective tissue diseases (CTDs) are a heterogeneous group of diseases, with variable clinical manifestations. The individual CTDs vary in their prevalence. CTDs are among the more common causes of non-idiopathic interstitial lung disease. Almost all connective tissue diseases may be associated with interstitial lung disease (CTD-ILD).
Objectives. To review and compare the prevalence, clinical features, laboratory results, high-resolution computed tomography (HRCT) imaging patterns and treatment of patients with CTD-ILD with those in other centres.
Methods. This was a retrospective study of 1 614 CTD patients conducted between 1993 and 2022 at the Charlotte Maxeke Johannesburg Academic Hospital rheumatology clinic. CTD-ILDs were noted in patients with systemic lupus erythematosus, systemic sclerosis, dermatomyositis, polymyositis, Sjögren's syndrome and mixed connective tissue disease.
Results. Of 1 614 CTD patients, 117 (7.2%) were diagnosed with CTD-ILD during this period. There was a female predominance of 91.5% (*n*=107). The median age was 54 years and the majority (83.3%; *n*=98) of the patients were of black ethnicity. Most of the patients were diagnosed with systemic sclerosis (40.2%; *n*=47), followed by systemic lupus erythematosus (34.2%; *n*=30), these two conditions constituting the bulk (74.4%) of disease burden. More than two-thirds of the patients were antinuclear antibody positive (72.6%). Cough and dyspnoea were reported in 42.7% and 38.5%, respectively, and 61.5% of the patients had audible crackles. The most frequent comorbidities were hypertension (22.2%), diabetes mellitus (18.8%) and gastro-oesophageal reflux disease (18.8%). The predominant HRCT pattern was usual interstitial pneumonia (49.6%; *n*=58) followed by nonspecific interstitial pneumonia (46.2%; *n*=54). Approximately half of the patients had a restrictive defect on pulmonary function testing and 90.6% had low carbon monoxide diffusing capacity. Most patients were treated with corticosteroids and an additional immunosuppressive agent; <10% received only one agent throughout the course of their disease.
Conclusion. CTD-ILD has a varied incidence and prevalence across the spectrum of connective tissue disease. The clinical manifestations, serological markers, radiological patterns and histopathology vary between the different connective tissue diseases. The current study reflects similar findings compared with other national and international studies.

Evaluation and determinants of asthma control among adult asthmatic patients attending Johannesburg academic respiratory clinics: A cross sectional study

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Background. The prevalence of asthma in South Africa (SA) is among the highest in Africa, and case mortality is fifth highest in the world. Little research has been done regarding levels of asthma control and associated determinants in SA.
Objectives. To explore the level of asthma control and the perceived risk factors associated with poor control in adult asthma patients attending three hospitals in Johannesburg.
Methods. This was a quantitative, descriptive, cross-sectional study of adult patients presenting to asthma clinics in selected hospitals over a period of 6 months. Participants were given a three-section self-reporting survey, consisting of a demographic section, the Asthma Control Test (ACT), and the 8-item Morisky Medication Adherence Scale (MMAS-8) questionnaire.
Results. The prevalence of poor asthma control based on participants' ACT scores in this study was 48.6%. A significant linear regression (r=–0.41; p<0.001) was identified between the ACT and the MMAS-8 score in the uncontrolled asthma group. No significant associations between uncontrolled asthma and sociodemographic factors, including age (p=0.12), gender (p=0.60), body mass index (p=0.15) and participants' education (p=0.15), were identified. Similar clustering and increases in prevalence of certain comorbidities, such as sinusitis and gastro-oesophageal reflux disease, occurred. Of the patients, 89% used short-acting beta-agonists and 93.3% inhaled corticosteroids (ICSs), of whom 58.7% were on combined long-acting beta-agonist and ICS treatment.
Conclusion. Asthma control in this setting is poor. There is also an interesting inverse relationship between control and therapy adherence. Further research needs to be done to better understand the issues surrounding asthma control and to lay the groundwork for policies to benefit asthma patients in the future.

Interventions to reduce outdoor air pollution and its impact on asthma outcome: A systematic review

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Background. Exposure to air pollutants can lead to asthma symptoms, exacerbations and hospitalisations.
Objectives. To collate data on studies of outdoor air pollution exposure reduction and asthma outcomes.
Methods. In this systematic review, we identified studies from 6 databases, articles written in English published in the 10 years up to 31 March 2022. We included randomised and non-randomised studies. Asthma outcomes included symptom control (asthma control test (ACT), childhood ACT (c-ACT)), asthma exacerbations, forced expiratory volume in 1 second (FEV_1), and ratio of FEV_1 to forced vital capacity (FVC).
Results. Seven studies met the inclusion criteria. Participants' ages ranged from 0 to ≥65 years. In one study, 50% of patients reported improved symptoms, ACT ≥20 improving post intervention from 41.1% to 60.7%, whereas in another mean (SD) ACT increased from 20.0 (2.4) at baseline to 21.5 (2.3) after intervention. For the children, there was significant improvement and a mean difference of 3 and 4 points for c-ACT and ACT. There was a reduction in the number of asthma admissions, mean 2.8 v. 4.0 ($p<0.001$). Asthma-related emergency department visits decreased by 25%. Lung function test changes varied from none to greater changes in FVC and FEV_1. Owing to the diversity of study designs, we could not perform meta-analyses.
Conclusion. We found few studies of outdoor air pollution reduction interventions on asthma outcomes, despite the importance of this topic. This field would benefit from further high-quality randomised clinical trial evidence to inform policy and decision-making.

Rituximab therapy in connective tissue disease associated interstitial lung disease: A retrospective single-centre observational study

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Background. Connective tissue disease-associated interstitial lung disease (CTD-ILD) is a challenging clinical entity. Rituximab (RTX) is a chimeric monoclonal antibody targeted to CD20+ B cells, resulting in B-cell depletion, and has been suggested as a potential therapeutic modality in progressive disease.
Objectives. To investigate the therapeutic effects and safety of rituximab in patients with progressive CTD-ILD.
Methods. A retrospective observational analysis was performed at Wits Donald Gordon Medical Centre between January 2010 and December 2020. A total of 19 patients with CTD-ILD were treated with RTX and various combinations of immunomodulatory therapy. The effects of RTX were investigated with serial pulmonary function testing, high-resolution computed tomography (HRCT) of the chest, and the World Health Organization functional class assessment (FC).
Results. At an average of 24 months' follow-up from baseline, the mean change in forced vital capacity (FVC) was not significantly different from baseline (0.01 L; 95% confidence interval –0.13 - 0.14) ($p=0.91$). At an average of 24 months' follow-up, 17 follow-up HRCT scans were available, of which 13 showed disease stability, 3 indicated progression, and 1 indicated improvement. At an average of 24 months' follow-up, FC remained stable compared with baseline ($p=0.083$). No serious adverse drug reactions or mortalities occurred.
Conclusion. Rituximab is a potential therapeutic option in patients with progressive CTD-ILD and appears to result in stability in FVC, HRCT findings and FC over a 24 month period.

PAEDIATRIC PULMONOLOGY

The development of a multilingual health-related quality of life tool for children with bronchiectasis in South Africa

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Background. There is currently no validated health-related quality of life (HRQoL) tool for children with bronchiectasis with varying cultural and language needs in low- to middle-income settings.
Objectives. To develop a multilingual HRQoL tool and to assess the evolution of QoL measured with the developed tool over a 1-year period.
Methods. Children with bronchiectasis aged 8 - 17 years at Steve Biko Academic Hospital, Pretoria, were included. A mixed-methods approach was used, with the study in two phases. In phase 1, development of the tool involved item generation and reduction for questionnaire content, generated from semi-structured interviews, and translation into three official South African languages. In phase 2, the tool was administered to children at baseline and at 1 year.
Results. In phase 1, 49 participants were included. After item reduction (37 items) and 4 Likert scales, a final tool with 31 items (17 physical and 14 emotional) was developed. In phase 2, 78 participants were included. We found that HRQoL in physical activities was stable with light physical activity and progressively declined with higher-impact activities. Despite this, coping skills such as the ability of the children to laugh at themselves increased by 8%, and anxiety and sleep disturbance decreased.
Conclusion. Language is critical in the development of HRQoL questionnaires that are culturally appropriate in a multilingual setting. The tool showed improvements in the emotional domain and some minor decline in the physical domain. This tool still requires psychometric evaluation as a future step.

Pulmonary interstitial glycogenosis in an infant: Case report

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Background. Childhood interstitial lung diseases (ChILDs) are rare group of heterogeneous diseases affecting the lung parenchyma. Pulmonary interstitial glycogenosis (PIG) is a type of ChILD that is rare and poorly understood.

Case presentation. We present the case of a female neonate, referred from a local regional hospital, who presented with persistent tachypnoea and hypoxaemia. A chest radiograph demonstrated diffuse reticular-nodular infiltrates. ChILD was suspected, particularly in view of the findings on the chest radiograph of diffuse bilateral multiple cystic lesions and ground-glass opacities, and this diagnosis was confirmed by a high-resolution chest computed tomography scan demonstrating multiple interlobular septal thickening and diffuse areas of ground-glass opacities. The definitive diagnosis of PIG was made by a lung biopsy demonstrating expansion of the alveolar septae on reticulin stain and the presence of glycogen-laden mesenchymal cells on periodic acid-Schiff stain/D stain.

After confirmation of the diagnosis of PIG, the baby was treated with monthly cycles of high-dose intravenous pulses of methylprednisone. She was discharged home on home oxygen in a stable condition and subsequently weaned off oxygen, but unfortunately died suddenly and unexpectedly at the age of 9 months.

Conclusion. More research is still required to determine the aetiology of PIG and a quicker non-invasive method for diagnosing it. It is of paramount importance to improve understanding and knowledge in the paediatric fraternity that will in turn assist with early recognition and diagnosis of ChILD. This will contribute to improved management and prognosis.

Paediatric pulmonary Langerhans cell histiocytosis complicated by recurrent haemothoraces

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Background. Langerhans cell histiocytosis (LCH) is a rare disease in which clonal proliferation and deposition of immature dendritic cells in various tissues, including the lungs, causes inflammation and organ destruction. We report the case of a 4-year-old girl with refractory multisystem LCH complicated by recurrent bilateral haemothoraces, in a paediatric tertiary hospital in Cape Town, South Africa.

Case presentation. An HIV-negative girl aged 4 years and 11 months presented with a 4-day history of cough, runny nose and fever. She had a recurrent wheeze and night sweats and had had poor weight gain for 2 years. An initial chest radiograph showed multiple lytic rib lesions and a right pneumothorax, treated with an intercostal drain (ICD). Notable findings on presentation were decreased air entry of the right hemithorax, bilateral expiratory wheezes, and a non-tender 2 cm hepatomegaly.

Urine homovanillic acid, tuberculosis work-up, and bone marrow aspirate and biopsy were negative. Computed tomography and bone scans showed multiple lytic skeletal lesions. A diagnosis of LCH was confirmed on clavicular biopsy, classified as multifocal multisystemic disease (liver, lung and bone involvement). Treatment response was poor despite maximal chemotherapy, with a course characterised by recurrent right pneumothoraces requiring ICD insertions. She subsequently developed bilateral haemothoraces requiring fluid resuscitation and ICD drainage. The effusions were paucicellular, predominantly blood with scanty reactive lymphocytes, and no organisms were cultured.

To manage the recurrent haemopneumothoraces, a right video-assisted thoracoscopic biopsy and pleurodesis was performed, finding a small lower lobe bleb, inflammation of the parietal pleura, and upper and middle lobes adherent to the chest wall. The findings on lung biopsy were normal, but the pleura showed chronic inflammation and fibrosis. The child has continued to have pneumothoraces and pleural effusions and is currently awaiting a stem cell transplant.

Conclusion. Paediatric LCH can present as a prolonged debilitating disease with recurrent pneumothoraces. Haemothorax, a rare complication, can result from inflammation of the pleura. Management involves a multidisciplinary approach. Thoracoscopy may be useful to confirm the site of bleeding, biopsies and/or pleurodesis.

Persistent hydropneumothorax secondary to hydatid disease

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Background. Hydatid cyst is an important parasitic zoonosis caused by echinococcus granularis that affects the lungs and can result in rupture of cysts into the pleural space, causing hydrothorax, pyopneumothorax or pneumothorax.

Case presentation. A 10-year-old boy who had previously been well presented to a referral hospital with a persistent hydropneumothorax on chest radiology that failed to drain after multiple intercoastal drain (ICD) insertions.

On arrival at our hospital, a repeat chest radiograph revealed the presence of a left-sided hydropneumothorax with a left ICD *in situ*. After re-insertion of an ICD at our institution, the hydropneumothorax persisted. Pleural fluid analysis revealed an exudate and was negative for tuberculosis (TB) (GeneXpert). Bronchoscopy revealed normal anatomy of the airways. A bronchoalveolar lavage specimen was sent off for further analysis. A computed tomography scan did not provide a further diagnosis.

The large air leak persisted despite initial treatment with broad-spectrum antibiotics and empirical TB treatment. The patient proceeded to thoracotomy for pleural clear-out and surgical treatment of a presumed bronchopleural fistula. Surgery revealed a large, complicated hydatid cyst in the left pleural space which was safely removed, with subsequent good recovery.

At follow-up at 3 months the child was well, a chest radiograph showed a fully re-expanded left lung, and lung function was normal. A liver cyst identified at diagnosis was successfully treated and the child made a full recovery.

Conclusion. This case reports an unusual presentation and cause of persistent hydropneumothorax in the paediatric population and the value of surgical intervention for both management and diagnosis.

The role of objective testing in urban adolescents with asthma symptoms in Durban, South Africa

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Background. Urban African adolescents suffer from undiagnosed and uncontrolled asthma symptoms.
Objectives. In this pilot study, to evaluate the role of objective testing and whether the European Respiratory Society Task Force (ERS-TF) diagnostic algorithm for children assisted with asthma diagnosis in urban adolescents with asthma symptoms in Durban, South Africa.
Methods. Between July 2019 and November 2021, we conducted a cross-sectional cohort study of urban schoolgoing adolescents aged 12 - 14 years as part of the Achieving Control of Asthma in Children in Africa (ACACIA) project. The study comprised two stages: (*i*) screening for asthma symptoms and diagnosis; and (*ii*) the Asthma Control Test, pre- and post-bronchodilator spirometry, and fractional exhaled nitric oxide (FeNO) measurements in those who screened positive for asthma symptoms.
Results. Of 2 093 adolescents screened, 180 were included, of whom 56% were female. Most participants had severe (*n*=128; 71%) and uncontrolled (*n*=157; 87%) asthma, while less than half (*n*=74; 41,1%) had eosinophilic asthma (EA), as shown by FeNO >25 ppb. Half (*n*=90) had a previous asthma diagnosis, but were more likely to have uncontrolled asthma (*p*=0.04). Of the 109 included spirometry measurements, the median ratio of forced expiratory volume in 1 second (FEV_1) to forced vital capacity (FVC) (FEV_1/FVC ratio), LLN and *z*-score were 88.96, 78.80 and –0.12, respectively. Spirometry measures were no different across asthma control and severity groups. Spirometry sensitivity for diagnosing asthma was 37.5% (95% confidence interval 15.2 - 64.6), and specificity was 95.7% (89.4 - 98.8). Those with EA had significantly lower FEV_1 % predicted (94.9 v. 102.0) and FEV_1/FVC ratio (86.6 v. 89.9) (all *p*-values <0.05). The prevalences of abnormal spirometry and bronchodilator responsiveness (BDR) were 9% and 12%, respectively. By performing the BDR test in those with normal spirometry, the diagnostic yield of the ERS-TF algorithm increased by 62.5%.
Conclusion. There was a high prevalence of severe and uncontrolled asthma in this cohort. FeNO may assist in phenotyping asthma where no discriminatory differences are found using spirometry. The ERS-TF diagnostic algorithm may miss adolescents with asthma if BDR testing is not performed in those with normal baseline spirometry.

THORACIC SURGERY

Surgical treatment of bronchiectasis in children: An 11-year experience at a central health facility in KwaZulu-Natal, South Africa

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Background. The surgical management of children with bronchiectasis has seldom been reported.
Objectives. To describe the presentation, surgical management and outcomes in children with bronchiectasis presenting for surgery.
Methods. We retrospectively reviewed the electronic records of 0 - 13-year-old children who underwent pulmonary resection for bronchiectasis at Inkosi Albert Luthuli Central Hospital, Durban, South Africa, between January 2004 and December 2014. Clinical, radiological and preoperative bronchoscopic findings, as well as surgical and histological outcomes, were analysed.
Results. Eighty-eight patients underwent surgical resection. The female/male ratio was 3:2, with a mean age at surgery of 8.2 (range 2 - 13) years; 39 patients were HIV infected and 39 were HIV uninfected. Tuberculosis (TB) (*n*=68; 77.2%) was the most common cause of bronchiectasis, and recurrent chest infection (*n*=45; 51.1%) was the most common clinical finding. Radiological examination confirmed isolated left-sided disease in 40 children (45.4%), isolated right-sided disease in 28 (31.8%) and bilateral disease in 20 (22.7%). Saccular disease with fibrocavitation (*n*=35; 39.7%) was the most common morphological disease type. Preoperative bronchoalveolar lavage samples confirmed a bacterial cause in 27 patients (30.6%). The most common operative procedures were primary pneumonectomy in 33 patients (37.0%), lobectomy in 30 (34.0%) and bilobectomy in 13 (14.7%). Seventy-five patients were asymptomatic after the operation, and complications occurred in 13. Two children (2.2%), one with sepsis and the other with intraoperative hypoxia, died. Seventy patients underwent complete resection. At 1 month after surgery, 89.2% of patients were asymptomatic, while 77.7% of symptomatic patients were HIV positive.
Conclusion. Complete pulmonary resection in children with advanced-stage bronchiectasis is safe, with a low morbidity and mortality. Surgery in HIV-positive patients was not associated with worse outcomes and is not contraindicated.

1. HIV- and TB-preventive measures could reduce the burden of childhood bronchiectasis. S Afr J Child Health 2022;16(3):152-157. https://doi.org/10.7196/SAJCH.2022.v16i3.1842