

costs. Categorical variable data were summarized in absolute and relative frequency tables. Quantitative variables were described with median and Interquartile range. Proportional differences were calculated with Z test, risk opportunities and difference of medians with Mann Whitney's U test were performed. We take p values < 0.05 as significant.

Results. Adherence to S-VOT monitoring strategy was 99.8% in first phase of treatment and 98.2% in second phase. All patients completed treatment, achieving 100% cure criteria in patients with pulmonary TB. Most adverse drug effects were reported on first month (31.6%, p=0.003). Skin changes were the most frequent complaint at the beginning of management (16.4%) and epigastralgia at the end (20%). The likelihood of adverse effects was significantly reduced when patients started maintenance phase on third month (OR: 0.29, p = 0.0003). The experience of the strategy was generally positive for patients. Time savings was major advantage. Travel costs in S-VOT were lower than DOT for patients, as well as the daily time investment in TB treatment.

Conclusion. S-VOT strategy was well tolerated and accepted by all patients, allowing an excellent level of adherence, with reduction in travel costs and investment of time for treatment. S-VOT is proposed as a viable alternative to DOT in selected patients.

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1639. Lung Transplant Outcomes in Patients with Chronic Respiratory Disease and Pre-Operative Nontuberculous Mycobacterial Disease

Sarah McGuffin, MD¹; Erika D. Lease, MD¹; Lauren E. Bartlett, BS¹; Chris Goss, MD¹; Luke M. Johnson, B.S.²; Haya Jamali, PhD¹; ¹University of Washington, Seattle, WA; ²University of Washington School of Medicine, Seattle, Washington

Session: P-72. Tuberculosis and other Mycobacterial Infections

Background. Pulmonary infection secondary to nontuberculous mycobacteria (NTM) is associated with significant morbidity and mortality, especially in individuals with underlying structural lung disease. Such infections are challenging to treat due to high virulence, antibiotic resistance, and the lack of effective and tolerable therapies. At many transplant centers, the isolation of NTM may be considered a contraindication for lung transplantation.

Methods. Institutional and referral medical records, microbiology, radiology and pathology databases were reviewed for patients who underwent lung transplantation at the University of Washington between 2006-2020. 8 patients with NTM disease were identified according to the American Thoracic Society (ATS) guidelines. 9 patients with sputum cultures positive for NTM, but not diagnosed with NTM disease were also evaluated.

Results. Patients with NTM disease continued antimycobacterial therapy pre- and post-operatively. NTM organisms isolated included *M. avium* complex, *M. fortuitum*, *M. abscessus*, *M. kansasii*, and *M. fortuitum*.

In the cohort with NTM-disease, one patient died within a year of transplantation (14%), three died within 1-5 years (43%), and four (51%) are still alive 1-9 years post-transplantation. Only one patient clearly died as a direct cause of the NTM infection, and this occurred early post-transplantation due to disseminated *M. abscessus* infection. Of the other deceased patients with pre-existing NTM disease, one died due to graft rejection at 3 years, one died due to graft rejection with concomitant non-NTM pneumonia at 2 years, and one died due to cardiac arrest at 4 years. In the cohort without NTM disease, none died within 1 year of transplantation, 22% died within 1-5 years, 11% died more than 5 years post-transplant, and 66% are still alive 1-14 years post-transplant.

The probability of survival more than 1 year and more than 5 years post-transplant and 38% in patients with NTM-disease, and 100% and 56% in patients without NTM disease.

Conclusion. NTM infection in the lung transplant candidate is uncommon and challenging, however successful treatment can occur, perhaps in the setting of certain subspecies and with prolonged combination antimicrobial therapy.

Disclosures. All Authors: No reported disclosures

1640. A Clinical Audit and Cost Analysis of Tuberculosis Management at a Tertiary Referral Centre in the Republic of Ireland

James A. O'Connell, MB BCH BAO MSc MRCP¹; Eoghan de Barra, MB MD²; Samuel McConkey, MB MD²; ¹Department of International Health and Tropical Medicine, Dublin, Dublin, Ireland; ²Royal College of Surgeons in Ireland, Dublin, Dublin, Ireland

Session: P-72. Tuberculosis and other Mycobacterial Infections

Background. Ireland is a low tuberculosis (TB) incidence country. Effective TB services are important in the efforts to meet WHO End TB Targets. A dedicated TB clinic was established in our tertiary referral centre in 2018. Our aim is to describe the patients with TB attending our service and evaluate the care provided to them in terms of cost and clinical effectiveness.

Methods. We performed a retrospective review of patients attending our service from 01/07/2018-31/12/2019. We included patients who were referred for assessment of symptoms of active tuberculosis. We collected data on patients risk factors for TB, time from illness onset to diagnosis and resources utilized (including hospital admissions, outpatient appointments, investigations and drug treatment). We estimated the productivity losses due to TB in our cohort following the Hanover Consensus. Using national TB notifications data we used our estimate treatment cost and productivity losses to estimate the total national cost of TB in Ireland in 2019.

Results. Fifty-four patients were assessed for TB in our clinic. Most patients (68.5%) referred had a diagnosis of TB made, 5.6% had a non-tuberculous mycobacterial infection and the remainder had no mycobacterial infection diagnosed. Over half (51.4%) of patients with TB had respiratory TB. The most prevalent risk factor was being from a country of high TB incidence (59.5% of TB patients). Five patients (13.5%) had drug resistance. Patients were referred most frequently from the emergency department (54.1%). The median time from symptom onset to diagnosis was 14.1 weeks (IQR 5.3-30) in patients with respiratory TB compared to 25.9 weeks (IQR 6.3-55.9) in patients with non-respiratory TB. Out of 35 patients who remained within our service 97.1% (34/35) completed treatment and 2.9% (1/35) are still on treatment.

We estimate that the median cost of managing a case of TB in our centre was €6088 (€1,003-17,588). The estimated cost of managing all 267 cases of TB in Ireland in 2019 was €9,048,380 which incurred productivity losses of €791,421. The total cost of TB to Ireland in 2019 was €9,839,801.

Conclusion. Our clinic had a high rate of treatment success. Interventions to reduce diagnostic delay and cost are needed.

Disclosures. All Authors: No reported disclosures

1641. A Comparative Analysis Of Lymph Node Tuberculosis Between Children And Adults

Fatma Hammami, MD¹; Makram Koubaa, MD¹; Amal Chakroun, MD¹; Khaoula Rekiq, MD¹; Fatma Smaoui, MD¹; Emma Elleuch, MD¹; Chakib Marrakchi, MD¹; Mounir Ben Jemaa, MD¹; ¹Infectious Diseases Department, Hedi Chaker University Hospital, University of Sfax, Tunisia, Sfax, Tunisia

Session: P-72. Tuberculosis and other Mycobacterial Infections

Background. Lymph node tuberculosis (LNTB) represents the most common site of extrapulmonary tuberculosis. Among children, due to non-specific clinical features, the diagnosis is often delayed. We aimed to compare the clinical, therapeutic and evolutionary features of LNTB between adults and children.

Methods. We conducted a retrospective study including patients hospitalized for LNTB in the infectious diseases and pediatric department between 1993 and 2018. Children aged ≤18 years were included.

Results. Overall, we encountered 231 cases of LNTB. There were 40 children (17.3%) with a mean age of 11±4 years and 191 adults (82.7%) with a mean age of 42±16 years. As to gender, females were more affected (adults: 67% vs children: 70%), with no significant difference (p >0.05). A family history of tuberculosis was significantly more frequent among children (20% vs 6.3%; p=0.01). Raw milk consumption (38.2% vs 30%; p >0.05) and close contact with animals (29.8% vs 35%; p >0.05) were noted among both adults and children. Fever (53.4% vs 32.5%; p=0.01), night sweats (35.8% vs 10%; p=0.001), loss of appetite (38.2% vs 17.5%; p=0.01) and weight loss (35.1% vs 15%; p=0.01) were significantly more frequent among adults. Tuberculin skin test was positive in 75.8% of the cases among adults and in 86.2% of the cases among children (p >0.05). Multifocal tuberculosis was significantly more frequent among adults (23.8% vs 5.7%; p=0.01). Antitubercular therapy was prescribed for a mean duration of 10±4 months among adults and for 9±3 months among children, with no significant difference (p >0.05). Side effects of antitubercular drugs were more frequent among adults (33% vs 10.3%), with a significant difference (p=0.004). Comparison of the disease evolution showed no significant difference between adults and children, regarding recovery (94.8% vs 90%), relapse (5.2% vs 5%) and death (0.5% vs 2.5%).

Conclusion. The clinical presentation of LNTB among children was less common and misleading. A family history of tuberculosis and a high index of suspicion might shorten the diagnostic delay.

Disclosures. All Authors: No reported disclosures

1642. A Novel β-lactamase Inhibitor (Durlobactam, DUR) and β-Lactams Enhance Susceptibility Against Multidrug-Resistant (MDR) Mycobacterium abscessus (Mab)

Khalid M. Dousa, MD¹; Sebastian G. Kurz, MD²; Christopher Bethel, MS³; Alita Miller, PhD⁴; Robert A. Bonomo, MD⁵; ¹Case Western Reserve University, Cleveland Heights, OH; ²Mount Sinai National Jewish Health Respiratory Institute, New York City, NY; ³Louis Stokes Cleveland VA Medical Center, Cleveland, OH; ⁴Entasis Therapeutics, Waltham, MA; ⁵Louis Stokes Cleveland VA Medical Center, Cleveland, Ohio

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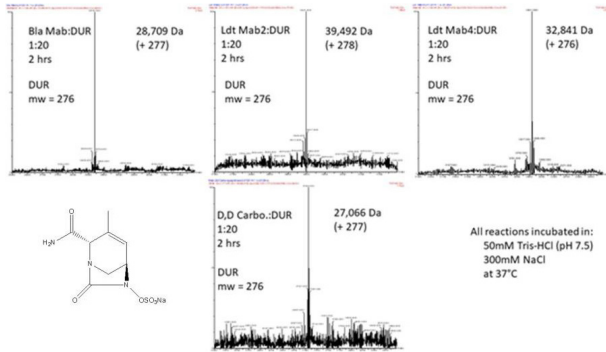
Background. *Mab* is a MDR nontuberculous mycobacterium that causes lung infections in patients with structural lung disease. *Mab* harbors a chromosomally encoded class A β-lactamase, Bla_{Mab}, able to hydrolyze penicillins, cephalosporins and carbapenems. L,D- and D,D-transpeptidases (L,D TP and D,D TP) shape peptidoglycan (PG) synthesis and contribute to cell wall structure. Select combinations of β-lactams that inhibit L,D TP and D,D TPs and Bla_{Mab} are desirable as they can potentially improve treatment outcomes. DUR is a novel DBO β-lactamase inhibitor (BLI) with broad-spectrum activity against Ambler class A, C, and D β-lactamases (Fig.). Here, we investigated the mechanism of action and efficacy of DUR alone and combined with select β-lactams in restoring susceptibility of *Mab* to β-lactam antibiotics

Methods. Minimum inhibitory concentrations (MICs) of cefuroxime (CEF), imipenem (IMI) and amoxicillin (Amox) with or without DUR were determined using microdilution. Approximately 5 x 10⁵ colony-forming units per milliliter were inoculated into Middlebrook 7H9 Broth supplemented with 10% (vol/vol) oleic albumin

dehydroxycatalase and 0.05% (vol/vol) Tween 80. When more than 2 drugs were combined, Amox was added at fixed concentration of 8 µg/ml to serial dilutions of CEF-DUR or IMI-DUR. *Mab* isolates were incubated with test agents at 30°C for 48 h, and MIC was defined as lowest antibiotic concentration that prevented visible bacterial growth. Reaction intermediates in the inactivation pathway of Bla_{Mab}, L,D-TP and D,D-TPs with DUR

Results. One hundred clinically derived and previously characterized isolates were tested in these assays. MIC₅₀ and MIC₉₀ of DUR alone was 4 and 8 µg/ml, demonstrating intrinsic activity. Combinations of DUR-IMI or DUR-CEF plus 8 µg/ml Amox lowered MIC₅₀ to < 0.06 µg/ml in all 100 clinical isolates (Table). Mass spectrometry analyses of Bla_{Mab}, L,D-TP and D,D-TPs^{Mab (2,4)} inactivated by DUR showed formation of stable adducts of DUR to Bla_{Mab}, L,D-TP and D,D-TPs (Fig.)

Chemical composition of durlobactam (DUR) and mass spectrometry of Bla_{Mab}, L,D-TP and D,D-TPs incubated with DUR



MIC50 and MIC90 of 100 *Mab* clinical strains against DUR alone and in combination with Amox, CEF and IMI

	DUR µg/mL	Amox µg/mL	Amox/DUR (1:1) µg/mL	CEF µg/mL	CEF/DUR (1:1) µg/mL	CEF/Amox +Amox 8 µg/mL	IMI µg/mL	IMI/DUR (1:1) µg/mL	IMI/DUR +Amox 8 µg/mL	IMI/Amox (1:1) µg/mL
MIC50	4	>256	2	8	1	<0.06	4	2	2	<0.06
MIC90	8	>256	4	16	2	<0.06	8	4	2	0.25

DUR (durlobactam), CEF (ceftriaxone), Amox (Amoxicillin), Imipenem (IMI)

Conclusion. We demonstrate that a novel DBO BLI, DUR, is an active agent with potent intrinsic activity against Bla_{Mab} and Mab L,D-TPs and D,D-TPs. We hypothesize that DUR improves β-lactam activity by protecting against the hydrolytic activity of Bla_{Mab} and by targeting multiple steps in PG synthesis

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1643. A scoping review of pediatric latent tuberculosis care cascades: Initial steps are lacking

Jeffrey Campbell, MD¹; Thomas Sandora, MD MPH¹; Jessica Haberer, MD, MS²; ¹Boston Children's Hospital; ²Harvard Medical School, Boston, MA

Session: P-72. Tuberculosis and other Mycobacterial Infections

Background. Each year an estimated 1 million children develop and ~200,000 die from tuberculosis (TB). The WHO has named identification and treatment of latent tuberculosis infection (LTBI) one of the cornerstones of efforts to eliminate TB by 2030. Identification and treatment of pediatric LTBI requires completion of a complex care cascade. While attention has been given to LTBI care cascades in adults, to date there has been no attempt to map literature on the pediatric LTBI care cascade.

Facilitators and barriers to retention in steps of the pediatric LTBI care cascade

Methods. We systematically searched PubMed, CINAHL, Cochrane and Embase databases for papers and abstracts describing screening, diagnosis, and treatment of pediatric LTBI. We categorized literature using seven step-offs in the pediatric LTBI care cascade, extrapolated from prior studies focused on adults: 1) intention to screen to initial test, 2) initial test to receipt of results, 3) receipt to referral for evaluation, 4) referral to completion of evaluation, 5) completion to treatment recommendation, 6) recommendation to treatment acceptance/initiation, and 7) initiation to treatment completion. Our aim was to assess factors that facilitated and inhibited completion of each cascade step, and to identify knowledge gaps in this literature.

Results. We identified 137 studies that met inclusion criteria. Most studies described multiple step-offs in the care cascade, although the focus of most (120/137 studies) was on initiation and completion of LTBI therapy (the final step in the care cascade). Several effective strategies to improve medication adherence were described, including selective use of nursing visits, directly observed therapy, shorter treatment regimens, and peer counseling. Reports of facilitators and barriers for retention in upstream step-offs in the cascade were scarce, revealing a lack

of published evidence for how to retain children from pre-screening to treatment initiation (Table).

Cascade step	Facilitators of retention ¹	Barriers to retention ²	Knowledge gaps
1) Intention to screen to initial testing (n = 42 studies) ³	• Contact tracing programs	• Concurrent infections • Fear of testing procedures • "Parental avoidance"	• Populations at risk for low testing uptake • Strategies to optimize testing uptake
2) Initial testing to received test result (n = 43)	• Younger age	• Non-specific loss to follow-up	• Comparison of TST and IGRA in loss to follow-up • Reasons for loss to follow-up
3) Received test result a referral for evaluation (n = 22)	• No analytic studies	• Non-specific loss to follow-up	• Reasons for loss to follow-up
4) Referral for evaluation to completion of evaluation (n = 26)	• No analytic studies	• Non-specific loss to follow-up • Refusal of TB clinic visit	• Comparison of referral to TB health department versus primary care clinics • Reasons for loss to follow-up
5) Completion of evaluation to recommendation for treatment (n = 41)	• No analytic studies	• Medical contra-indications • Moving away/transferred care before starting therapy • Patient/parent non-acceptance of therapy	• Prevalence of medical contra-indications • Strategies to shorten time between completion of evaluation and recommendation for treatment
6) Recommendation for treatment to initiation of treatment (n = 77)	• Knowledge about TB transmission, treatment and policy • Relationships with TB patients	• Lack of knowledge about LTBI therapy • Older age • Arrival at patient refusal of treatment	• Reasons for parental refusal • Strategies to improve initial treatment uptake
7) Initiation of treatment to completion of treatment (n = 120)	• Close relationship and close contact with TB index case • Established record of follow-up prior to LTBI screening • Knowledge about TB spread and prevention • Location of treatment, and use of health department clinic • Peer counseling and contingency contracting program • Psychological states (mastery, self-esteem) • Shorter period between screening and medical evaluation • Shorter therapy regimen • Selective use of nurse-led outreach programs and DOT • Socioeconomic and demographic features (income, younger age, recent immigration)	• Distance or lack of transportation to clinic • Forgetfulness • Lack of cooperation from children • Lack of insurance • Lack of understanding of how or how long to take therapy • Long-term treatment regimens • Lower parental education • Parental work conflicts • Pregnancy • Psychological states (engaging in high risk behaviors) • Side effects • Socioeconomic and demographic features (older age, lack of insurance) • Stigma about TB and links to HIV • Treatment of other TB illness	• Location of treatment (primary care clinics, health department clinics) • Scalability or durability of effective pilot programs • Socioeconomic and demographic features associated with adherence • Timing of therapy discontinuation • Use of novel adherence strategies (e.g. mobile health)

Table. Summary of facilitators, barriers, and knowledge gaps in literature about the pediatric LTBI care cascade.

¹Most studies described multiple steps of the cascade. Therefore, study totals do not sum to 137.

²Factors identified in literature as significantly associated with completing steps in the cascade.

³Factors listed in literature as preventing completion of steps in the cascade (assessment of statistical significance not required)

Abbreviations: TST = tuberculin skin test; IGRA = interferon-gamma release assay; DOT = directly-observed therapy; HIV = human immunodeficiency virus

Conclusion. While existing literature describes LTBI treatment initiation and completion in children, our analysis reveals a lack of data guiding retention of children from LTBI screening through treatment initiation. This review highlights the need to further understand early steps of the care cascade, in order to help alleviate the burden of TB in children.

Disclosures. Jessica Haberer, MD, MS, Merck (Consultant)

1644. "And the stick to fight TB is IPT": Perspectives on TPT Implementation Among Senior Nurses in Rural South Africa

Megan A. Grammatico, n/a¹; Amiya A. Ahmed, n/a²; Laurretta Grau, PhD³; Anthony Moll, MBChB⁴; Sheela Shenoi, MD, MPH⁵; ¹University of Connecticut School of Medicine, Wallingford, Connecticut; ²University of Maryland School of Medicine, Silver Spring, Maryland; ³Yale School of Public Health, New Haven, Connecticut; ⁴Church of Scotland Hospital, Tugela Ferry, KwaZulu-Natal, South Africa; ⁵Yale University, New Haven, Connecticut

Session: P-72. Tuberculosis and other Mycobacterial Infections

Background. Tuberculosis (TB) disproportionately affects people living with HIV (PLH). The World Health Organization (WHO) has endorsed tuberculosis preventative therapy (TPT) in resource-limited settings with high HIV and TB burdens. South Africa has led global TPT efforts, yet implementation remains sub-optimal.

Methods. In a rural, impoverished region of South Africa with high TB and HIV prevalence, primary care clinic-based senior nurses were asked to participate in anonymous, semi-structured interviews assessing TPT knowledge, beliefs, and attitudes. The currently available regimen is isoniazid preventive therapy (IPT) for 12 months. Through an iterative process, a code list was generated and applied to each transcript. The data were analyzed using thematic analysis and Nvivo 12 software to identify facilitators and barriers to IPT prescribing.

Results. Among 22 nurses at 14 primary health clinics, 86% were female, median age 39 (IQR 31-54.8) years, with median 10.5 (IQR3-18) years of health care experience. Nurses felt that TPT was effective at preventing TB. Barriers to implementation included limited time to counsel patients due to understaffing in high-volume clinics and lack of documentation of IPT prescription in patients' charts, which limited effective follow-up. Nurses certified in Nurse-Initiated Management of Antiretroviral Therapy (NIMART) expressed confidence in their IPT knowledge, but those not certified wanted additional training. Nurses identified patient-level factors impeding TPT implementation, including transportation, HIV-related stigma, mobility, particularly among men, and pill burden associated with length of IPT (12 months) with concurrent daily chronic medications. Facilitators included availability of IPT in both hospitals and primary care clinics, and capacity for task-shifting to other healthcare professionals (counselors, staff nurses). The impending rollout of 3HP (12 weeks of isoniazid-rifampentine) was viewed favorably.

Conclusion. Nurses identified limited time to counsel PLH and lack of standardized training programs as the main barriers to implementation of TB preventative therapy. Addressing these barriers will be critical to successful implementation of new TPT regimens.

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1647. Breast Tuberculosis: A Diagnostic Challenge

Fatma Hammami, MD¹; Makram Kouba, MD¹; Amal Chakroun, MD¹; Khaoula Rekiq, MD¹; Fatma Smaoui, MD¹; Emna Elleuch, MD¹; Chakib Marrakchi, MD¹; Mounir Ben Jemaa, MD¹; ¹Infectious Diseases Department, Hedi Chaker University Hospital, University of Sfax, Tunisia, Sfax, Sfax, Tunisia