with surgical debridement, and functional loss. Herein we describe our experience with such infections.

**Methods.** Records for adult patients from two academic, tertiary facilities with culture-proven NTMI involving the upper extremity were retrospectively reviewed. Demographic information, co-morbidities, laboratory and microbiological evaluation, management, and outcomes were extracted. Patients were analyzed based on pathogen identified and immune suppression.

**Results.** 77 patients were identified. The mean age was 59 years and 65% of patients were male. 48% reported a preceding injury, with the hand being most frequently involved (58%). 41% were considered immune-compromised; 19% of them were organ transplant recipients. Mean symptom duration prior to presentation was 203 days. Mean time to culture identification was 33 days, and 25 different species of NTM were identified (subcategorized as rapid or slow growers). 77% had solitary lesions, with cutaneous/subcutaneous location as the most common site. All patients underwent surgical debridement with four undergoing amputation to control infection. 69% received combination antimicrobial therapy for a mean duration of 184 days. Immunosuppressed patients were treated with antifungal therapy for a longer duration (mean 243 vs 155 days). One-third of patients experienced complications and/or recurrence regardless of organism type.

**Conclusion.** NTMI of the upper extremity is often misdiagnosed leading to significant delays in appropriate management. Knowledge of its protean manifestations and early consideration in the differential diagnosis of chronic, painful swelling of the hand or wrist, nodular or inflammatory lesions, or septic arthritis is crucial. A low threshold for surgical or biopsy with specimens sent for histopathology as well as microbiologic analysis is warranted. A combined approach with surgical debridement and prolonged combination antimicrobial therapy is necessary for optimal outcomes; however, adverse reactions from such therapy are commonly encountered.

**Disclosures.** All Authors: No reported disclosures

### 1390. Durlobactam, a Diazabicycloctane (DBO) β-lactamase Inhibitor (BLI), Inhibits BlaC and Peptidoglycan (PG) Transpeptidases of Mycobacterium tuberculosis (Mtb): A Novel Approach to Therapeutics for Tuberculosis (TB)?

**Background.** Novel therapies for multidrug-resistant TB are needed and new BLIs against BlaC and PG transpeptidases with the ultimate goal of repurposing these drugs for the treatment of TB.

**Methods.** Methods. Mass spectrometry was performed to capture acyl-envelope complexes (AECs) of purified BlaC and PG transpeptidases (PonA1, LdtK, LdtG, LdtL, and LdtS) with β-lactams and BLIs. Steady-state enzyme kinetics were determined using nitrocefin as a substrate, MICs with amoxicillin (AMX), meropenem (MER), CLA, and DUR alone and in combination against Mtb H37Rv were assessed using a microdilution method.

**Results.** DUR alone had a MIC of 2 µg/mL with Mtb H37Rv (Table 1). BlaC formed AECs with all carbapenems and BLIs. BlaC had lower $K_i$ and higher $k_2/K_1$ values than those with AVI and REL and comparable to those with CLA; however, with a period of pre-incubation, AVI fully inhibits BlaC (Table 2). The carbapenems and DUR formed the most AECs with PG transpeptidases of the β-lactams and BLIs respectively; PG transpeptidases had lower $K_i$ values with DUR than those with AVI (Table 3).

| Antibiotic | MIC (µg/mL) |
|------------|-------------|
| AMX        | 0.125       |
| Meropenem  | 32          |
| Clavulanate| 32          |
| Dorbacum   | 2           |
| Amoxicillin| 2           |
| Amoxicillin+4 µg/mL Clavulanate| 0.5 |
| Meropenem  | 2.5         |
| DUR        | ≤0.125      |

**Table 1. Minimum Inhibitory Concentrations for Mycobacterium tuberculosis H37Rv**

**Conclusion.** DUR alone has some antimicrobial activity against Mtb H37Rv. The likely mechanism that underlies this activity is inhibition of BlaC and several PG transpeptidases. Inhibition of enzyme targets with DUR was more potent and efficient than AVI and REL. DUR in combination with β-lactams lowered MICs but the DUR concentration used was higher than its MIC. Our findings support the exploration of novel BLIs against BlaC and PG transpeptidases with the ultimate goal of repurposing these drugs for the treatment of TB.

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### 1391. Body Mass Index and Leptin Levels at Different Stages of the Tuberculosis Spectrum

**Background.** Leptin is an adipose tissue-derived cytokine that plays a role in energy regulation and immune functions. High leptin levels and obesity have been associated with decreased risk of developing active TB. We aimed to characterize the association between body mass index (BMI) and leptin levels in patients at different stages of tuberculosis (TB).

**Methods.** Data from a cross-sectional cardiovascular risk study of 40 to 70 years old individuals enrolled in Lima, Peru, and Cincinnati, US, were analyzed. Four categories based on TB and treatment status were defined: no TB infection (Quantiferon-TB test negative; n=31), latent TB infection (LTBI; Quantiferon-TB test positive; n=43), active TB on treatment (the continuation TB treatment phase; n=30), and post-TB (within one year of TB treatment completion; n=16). BMI and plasma leptin levels were compared among the four groups using the Kruskal-Wallis test, followed by Dunn’s multiple comparison test if differences were found in the Kruskal-Wallis test. Multivariate ordered logistic regression models were used to assess factors associated with leptin levels, adjusted for potential confounders.

**Results.** The median age was 53 years, and 51% were female. BMI was different between study groups (p<0.01), with LTBI individuals having the highest BMI compared to other groups; see Figure 1A. Leptin levels were marginally low in the group with active TB on treatment, but no significant differences were found between groups (p=0.44; see Figure 1B). In multivariate analysis, leptin was associated with female sex (OR 23.95%, 9.5-58), BMI (OR 1.5, 95% CI, 1.2-1.7), and coronary plaque ≥25% stenosis (OR 0.29, 95% CI, 0.08-0.99). Body mass index (BMI) and plasma leptin levels in participants with negative Quantiferon-TB test (QFN-), latent tuberculosis infection (LTBI), active tuberculosis on treatment (ATBT), and post-TB treatment (TB-treated).

**Conclusion.** NTMI involving the upper extremity are often misdiagnosed leading to significant delays in appropriate management. Knowledge of its protean manifestations and early consideration in the differential diagnosis of chronic, painful swelling of the hand or wrist, nodular or inflammatory lesions, or septic arthritis is crucial. A low threshold for surgical or biopsy with specimens sent for histopathology as well as microbiologic analysis is warranted. A combined approach with surgical debridement and prolonged combination antimicrobial therapy is necessary for optimal outcomes; however, adverse reactions from such therapy are commonly encountered.

**Disclosures.** All Authors: No reported disclosures

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**References:**

[1] Nguyen, T.V., Kreiswirth, B.N., Boom, R.H., Askar, M., Montanini, P.J., Dousa, T.P., Askar, M.D., Serjeantson, S., Askar, M.D., Serjeantson, S., Askar, M.D., Serjeantson, S. et al. (2018). *Novel therapies for multidrug-resistant TB are needed and new BLIs against BlaC and PG transpeptidases with the ultimate goal of repurposing these drugs for the treatment of TB.* *J Antimicrob Chemother.*

[2] Nguyen, T.V., Kreiswirth, B.N., Boom, R.H., Askar, M., Montanini, P.J., Dousa, T.P., Askar, M.D., Serjeantson, S., Askar, M.D., Serjeantson, S., Askar, M.D., Serjeantson, S. et al. (2018). *Novel therapies for multidrug-resistant TB are needed and new BLIs against BlaC and PG transpeptidases with the ultimate goal of repurposing these drugs for the treatment of TB.* *J Antimicrob Chemother.*

[3] Nguyen, T.V., Kreiswirth, B.N., Boom, R.H., Askar, M., Montanini, P.J., Dousa, T.P., Askar, M.D., Serjeantson, S., Askar, M.D., Serjeantson, S., Askar, M.D., Serjeantson, S. et al. (2018). *Novel therapies for multidrug-resistant TB are needed and new BLIs against BlaC and PG transpeptidases with the ultimate goal of repurposing these drugs for the treatment of TB.* *J Antimicrob Chemother.*

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Significance was determined using the Kruskal-Wallis test, followed by Dunn's multiple comparison test if the Kruskal-Wallis test p-value was <0.05.

**Conclusion.** LTBI individuals had a higher BMI compared to persons with active TB on treatment and post-TB. Higher leptin levels were associated with higher BMI, but we found no association between leptin and TB status in our cohort.

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### 1392. Nontuberculous Mycobacteria Isolated from Wisconsin Residents, 2010-2018

Bryan J. Vonasek, MD; Danièle Y. Gusland, MD; Kevin P. Hash, BA; Julie L. Tans-Kersten, MS, BSMT (ASCP); Suzanne N. Gibbons-Burgen, DVM, PhD; Elizabeth A. Misch, MD; 1University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin; 2Valley Children's Healthcare, Madera, California; 3Wisconsin Department of Health Services, Madison, Wisconsin; 4Division of Public Health, Madison, Wisconsin

**Session:** P-80. Tuberculosis and other Mycobacterial Infections

**Background.** Wisconsin is one of a handful of states in which laboratory identification of nontuberculous mycobacteria (NTM) from clinical samples is reportable to public health. The aims of this study were to characterize the demographic features of Wisconsin adults with NTM, assess the relative abundance of NTM species recovered, and describe trends in NTM isolation over the study period.

**Methods.** We conducted a retrospective cohort study of Wisconsin residents 18 years of age and older from whom NTM isolates were recovered and reported to the Wisconsin Electronic Disease Surveillance System (WEDSS) between 2010 and 2018. Isolates of *M. gordonae* were excluded. For the analysis of NTM frequency, multiple reports from the same individual were enumerated as separate isolates when non-identical or collected from different sites. Because NTM were usually reported into WEDSS without clinical data, this study couldn't discern the clinical significance of the isolates.

**Results.** A total of 9,032 NTM isolates from 7,722 adults were analyzed. The average annual number of reported NTM cases was 950 (21.7/100,000 adults) during 2011-2018. Table 1 shows the demographic characteristics of individuals with NTM isolates, stratified by specimen collection site and NTM species. *M. avium* complex (MAC) accounted for 75.7% of respiratory isolates. An important pathogenic NTM, *M. xenopi*, accounted for 8.9% of non-MAC respiratory isolates. As shown in Table 2, *M. chelonae*, a rapidly growing mycobacterium (RGM), was the most common species isolated from skin and soft tissue, head, ears, nose and throat, and eye specimens. MAC was the most common isolate from other tissue sites.

### 1393. Loss to Follow-up Rate in the Treatment of Latent Tuberculosis by Region of Origin

Hikari Yoshii, MD, MPH; Charles Bark, MD; 1Case Western Reserve University MetroHealth Medical Center, Lakewood, Ohio

**Session:** P-80. Tuberculosis and other Mycobacterial Infections

**Background.** Adherence in the treatment of latent tuberculosis infection (LTBI) is closely related to reactivation and infection control in the population. However, there has been little research on which populations are at higher risk of loss to follow-up. The aim of this study is to investigate how the adherence of LTBI patients in the United States (US) differs by region of origin.

**Methods.** A retrospective, observational study was conducted from 2001 to 2020. LTBI patients were identified from the Cuyahoga County Tuberculosis Clinic in Cleveland, Ohio. Only patients who were informed of the diagnosis of LTBI were included. Patients were discharged from the Tuberculosis outpatient clinic upon completion of treatment or when the physician decided to discontinue treatment. We defined loss to follow-up as a case where LTBI was diagnosed but the patient was not formally discharged. Patients whose treatment was interrupted due to side effects were not considered loss to follow-up. Odds ratios were calculated using a multivariable regression model with patients from North America as the reference group.

**Results.** Of 4018 LTBI patients, 1171 (28.7%) were lost to follow-up, of which 950/2314 (41.0%) were from North America. Compared with LTBI patients from North America, significantly lower loss to follow-up rates were observed for those from Middle East and North Africa 30/170 (17.7% OR 0.22, 95% CI 0.14-0.36), South Asia 60/692 (8.7% OR 0.41, 95% CI 0.21-0.78), and Sub-Saharan Africa 69/526 (13.1% OR 0.22, 95% CI 0.14-0.36).

### Table 1. Demographic characteristics of individuals with NTM isolates.

| Site          | Total N=7,722 n (%) | Respiratory N=6,357 n (%) | SST N=905 n (%) | MAC N=0,410 n (%) | RGM N=1,314 n (%) |
|---------------|---------------------|--------------------------|----------------|-----------------|-----------------|
| Gender        |                     |                          |                |                 |                 |
| Female        | 4,082 (52.8)        | 3,704 (53.2)             | 158 (51.3)     | 1,211 (59.0)    | 548 (54.9)      |
| Male          | 3,611 (47.2)        | 2,628 (40.8)             | 156 (48.7)     | 1,038 (40.9)    | 496 (45.1)      |
| Not reported  | 26 (0.3)            | 26 (0.4)                 | -              | 26 (1.0)        | (0.6)           |
| Age (years)   |                     |                          |                |                 |                 |
| Median (IQR)  | 66 (35-76)          | 67 (35-76)               | 58 (45-71)     | 67 (50-76)      | 63 (49-73)      |
| Race          |                     |                          |                |                 |                 |
| White         | 4,427 (57.3)        | 4,053 (57.9)             | 149 (48.3)     | 3,432 (57.7)    | 544 (53.6)      |
| Black         | 636 (8.2)           | 576 (8.2)                | 18 (5.1)       | 532 (8.9)       | 68 (6.6)        |
| Asian         | 269 (3.4)           | 261 (3.7)                | 10 (3.2)       | 213 (3.6)       | 37 (3.0)        |
| Other         | 75 (0.9)            | 68 (0.9)                 | 3 (0.9)        | 64 (1.0)        | 7 (0.6)         |
| Native American | 26 (0.3)         | 26 (0.3)                 | 0              | 20 (0.3)        | 6 (0.5)         |
| Multiple      | 14 (0.2)            | 12 (0.2)                 | 2 (0.6)        | 10 (0.2)        | 3 (0.3)         |
| Pacific Islander | 8 (0.1)          | 7 (0.1)                  | 0              | 5 (0.1)         | 3 (0.2)         |
| Not reported  | 2,287 (29.3)        | 1,976 (28.3)             | 136 (44.1)     | 1,862 (27.9)    | 309 (35.4)      |

Categorization was based on the initially recovered sample when multiple specimens were obtained from a given individual. "Respiratory" specimens included sputum, bronchoalveolar lavage, and tracheal aspirate specimens. IQR, interquartile range. RGM, rapidly growing mycobacteria (M. chelonae and the M. abscessus, M. chelonae-abscessus groups, and M. fortuitum groups). SST, skin and soft tissue.

### Table 2. Most common NTM species isolated from non-respiratory sites.

|M. chelonae | 102 (30.4) |
|M. fortuitum | 56 (16.7) |
|M. avium complex | 50 (14.9) |
|M. marinum | 34 (10.1) |
|M. abscessus | 24 (7.1) |
|M. avium complex | 31 (15.1) |
|M. fortuitum group | 22 (11.2) |
|M. chelonae | 11 (5.4) |
|M. abscessus group | 7 (3.7) |
|M. avium complex | 109 (53.2) |
|M. fortuitum group | 31 (15.1) |
|M. chelonae | 22 (11.2) |
|M. abscessus | 7 (3.7) |
|M. avium complex | 35 (30.3) |
|M. mucogenum | 28 (25.7) |
|M. fortuitum group | 18 (16.5) |
|M. chelonae | 8 (7.3) |
|M. avium complex | 31 (47.7) |
|M. fortuitum group | 10 (15.4) |
|M. chelonae | 6 (9.7) |
|M. abscessus group | 7 (11.4) |
|M. chelonae | 5 (7.7) |
|M. avium complex | 28 (22.2) |
|M. chelonae | 7 (29.2) |
|M. avium complex | 11 (68.8) |
|M. chelonae | 8 (85.8) |
|M. avium complex | 20 (48.8) |
|M. avium complex | 18 (45.8) |
|M. avium complex | 21 (70.0) |
|M. avium complex | 3 (10.0) |
|M. avium complex | 7 (28.2) |
|M. chelonae | 11 (44.4) |
|M. avium complex | 8 (32.0) |
|M. avium complex | 6 (12.5) |
|M. avium complex | 2 (33.3) |
|M. avium complex | 1 (2.0) |

*Respiratory specimens* were inclusive of sputum, bronchoalveolar lavage, and tracheal aspirate specimens. CNS, central nervous system; HENT, head, ears, nose, and throat; SST, skin and soft tissue.

**Conclusion.** Consistent with prior studies, MAC is the predominant NTM isolated from respiratory specimens in Wisconsin. RGM are important minority respiratory pathogens, and predominate as skin and soft tissue NTMs. We highlight *M. xenopi* as an important pathogen in Wisconsin compared to other parts of the United States. In contrast to recent reports of increasing incidence of NTM disease, we found a stable annual incidence of NTM isolation between 2010 and 2018.

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