1382. Acid-Fast Bacilli Testing Trends at 43 In- and Outpatient Facilities and Nontuberculous Mycobacterial Pulmonary Isolation Rate, United States, 2009–2015

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Background. The prevalence of nontuberculous mycobacterial pulmonary disease (NTM PD) is increasing in the United States and globally. The reasons for this increase are not clear but could be related to both gained awareness leading to increased mycobacterial testing, or to a true NTM PD increase. To further examine the role of testing rates in the observed increase, we studied trends in Acid-Fast Bacteria (AFB) testing and NTM isolation positivity using a large Electronic Health Record (EHR) dataset in the United States.

Methods. Using the Cerner *Health Facts* EHR dataset, we extracted microbiologic, demographic, and clinical data for patient encounters (inpatient or outpatient), with ≥1 orders for AFB respiratory cultures. The analysis was limited to the 43 facilities reporting continuously for the period 2009–2015. A patient with at least one AFB test was considered tested (AFB) and a patient with at least one pathogenic NTM respiratory isolate was considered positive. Trends in AFB testing and NTM positivity were estimated using log-linked Poisson regression ($P < 0.05$).

Results. From 2009 through 2015, of 14.8 million patients, 65,010 had 142,315 AFB tests, averaging 2.2 AFB tests/patient, for an overall testing prevalence of 0.43%; the annual testing prevalence remained unchanged during the study period ($P = 0.44$) (Figure 1). Of the 65,010 patients with AFB tests, 3,942 (6.1%) had ≥1 pathogenic NTM species, for an overall pulmonary NTM isolation prevalence of 2.7/10,000 patients represented in Cerner *Health Facts* dataset. Of the patients that had at least one pathogenic NTM, 3,094 (78%) had *M. avium* complex, and 265 (7%) had *M. abscessus/chelonae*, (Figure 2). Among patients with at least 1 NTM-positive culture, 138 patients had concomitant growth of *M. tuberculosis*.

Conclusion. Increases in NTM PD are not explained by increases in AFB testing, which remained constant in the population represented here.

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Figure 1. Rate of AFB Tested Patients per 1000 Patients

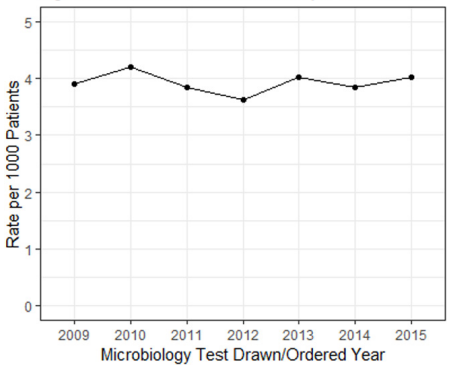
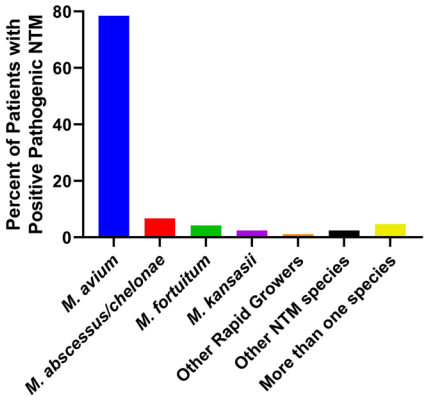


Figure 2. Distribution of NTM Species



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

1383. Everolimus is Associated with an Increased Risk of Tuberculosis in Solid-Organ Transplant Recipients

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Background. Tuberculosis (TB) is an important post-transplant infection. Everolimus has been documented to reduce the risk of cytomegalovirus infection in transplant recipients, but its impact on other infections is less known. The present study aimed to assess immunosuppressive regimens on TB risk in solid-organ transplant (SOT) recipients via a matched case–control study.

Methods. From May 2005 to December 2018, SOT recipients with TB were retrospectively identified, and those without TB undergoing transplantation at the same university hospital were selected as controls. Controls and cases were matched by age (±5 years), transplant type and year (±5 years) at a ratio of 4:1. Conditional logistic regression was used to analyze the risk factors of TB.

Results. TB developed in 30 SOT recipients (13 kidney, 7 heart, 6 liver, and 4 lung) after a mean duration of 1,601 days after transplantation, with predominant lung involvement (87%). The diagnosis was made by culture in 70% and pathology in 17%. Rifamycins-based regimens were used in 27 cases, and 4 developed rejection without graft failure. A total of 106 controls were selected. At the time of TB diagnosis, cases were more likely to use everolimus than controls (27% vs. 11%, $P < 0.05$), but no significant differences were observed in the use of tacrolimus, cyclosporin, sirolimus, prednisolone, or mycophenolate mofetil. The median duration of everolimus use was 585 and 698 days in 8 cases and 12 controls, respectively. Multivariable analysis showed that everolimus use (adjust odds ratio [aOR] 22.3, 95% conference interval [CI] 2.5–203.0) and hemodialysis (aOR 19.6, 95% CI 1.3–287.1) were independently associated with TB.

Conclusion. TB is more likely to develop in SOT recipients on everolimus and hemodialysis. Further studies to confirm our findings are warranted, and TB risk assessment should be performed for those receiving everolimus and hemodialysis.

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1384. *Mycobacterium marinum* Infection: 21 Years of Experience at a Tertiary-Care Hospital

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Background. *Mycobacterium marinum* is a slow-growing, non-tuberculous mycobacterium responsible for skin and soft-tissue infections (SSTIs), tenosynovitis, and osteomyelitis (OM). We conducted a retrospective study describing the risk, clinical course, and outcome of *M. marinum* infection.

Methods. Adult patients with culture-confirmed *M. marinum* infections were identified from the mycology laboratory at Mayo Clinic, Rochester from January 1998 to December 2018. *M. marinum* infection was defined as uncomplicated (limited to SST) and complicated (tenosynovitis, OM, or disseminated).

Results. Forty-six cases of culture-confirmed infection with *M. marinum* were included (Table 1). Only 16 cases (35%) reported a water exposure and 22 (48%) involved finger and/or hand trauma. The median time to diagnosis was 3.6 months. Most patients (76%) presented with uncomplicated *M. marinum* infection with skin lesions mainly localized in the upper limb (Table 2). QuantiFERON and PPD were positive in 4 (8%) and 2 (4%) cases, respectively. Granulomatous inflammation and positive special stains were noted in 34 (74%) and 11 (24%) cases, respectively. Cases with complicated *M. marinum* infection had a longer duration of symptoms and length of treatment ($P < 0.05$) (Table 3). Prior to diagnosis, 63% of patients received at least one antibiotic for bacterial SSTIs. More than 50% of the patients diagnosed with *M. marinum* received a one drug regimen and 8% did not initiate therapy. Median treatment duration was 4.4 months. Twenty-six cases (56%) had susceptibilities performed and treatment modifications were made in 10 cases (38%). From the patients that started therapy, 73% completed therapy and 33% were lost to follow up. Cured was achieved in 87% of cases that completed therapy, 2 cases (6%) had a recurrence, and only one patient with active malignancy had a positive blood culture and died. Twelve (44%) and 10 cases (37%) were cured with one and two-drug regimens, respectively.

Conclusion. Most patients with *M. marinum* infection present as an uncomplicated infection in the upper limb. Classical exposure was only suspected in a third of the cases. Patients with complicated *M. marinum* infection had a prolonged duration of symptoms and lengthy treatment. Most patients were successfully treated with a one and two-drug regimen.

Table 1. Baseline characteristics

	N = 46
Male (%)	28 (60.9)
Age, median (range)	59 (19-86)
Immunosuppression (%)	8 (17.4)
Comorbidities	
Diabetes (%)	5 (11)
Chronic kidney disease (%)	2 (4.4)
Autoimmune disorder *(%)	5 (11)
Active malignancy (%)	1 (2.2)

*Autoimmune disorder: Crohn's disease, DM type 1, Rheumatoid arthritis, Ulcerative Colitis and Polymyalgia rheumatica.

Table 2. Clinical presentation and laboratory findings at initial presentation

Clinical presentation	N = 46
Upper extremity	44 (95)
Redness (%)	28 (61)
Pain (%)	25 (54.3)
Abscess (%)	9 (19.6)
Skin manifestations* (%)	34 (74)
Lymphangitis (%)	12 (26.1)
Complicated (%)	11 (23.9)
Constitutional symptoms (%)	4 (8.7)
Time to evaluation (days), median	24 (0-366)
Laboratory findings	
WBC, mean ± SD	6.14 (2.23)
Platelets, mean ± SD	252 (94.5)
Creatinine, mean ± SD	1.08
ESR, median (range)	5 (0-60)
CRP, median (range)	3 (0.3 -190)
Time of positive culture, mean ± SD	28.2 ± 15.3

*Skin manifestations include nodules, papules and plaques

Table 3. Complicated versus non-complicated

	Uncomplicated n = 35	**Complicated n =11**	P value
Gender			
Male (%)	19	9	0.160
Female (%)	16	2	
Immunosuppression	7	1	0.658
DM	5	0	0.317
WBC, mean	6.14	6.42	0.731
Platelets, mean	253.1	251.3	0.959
ESR, median	5	9	0.825
CRP, median	2.4	3	0.417
Duration of symptoms prior to diagnosis (months), median	2.9	4.7	**0.026**
Number of drugs used, mean	1	2	0.070
Length of treatment (months), median	3.6	5.7	**0.031**

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1385. Mechanism-Based, *In Vitro* Inhibition of *Mycobacterium abscessus*: Assessing β-Lactam Therapy

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Background. *M. abscessus* (*Mab*) is an emerging pathogen, a highly drug-resistant rapidly-growing nontuberculous mycobacteria. Mab L, D transpeptidases ($Ldt_{Mab\ 1–5}$), D,D carboxypeptidase and Bla_{Mab} β-lactamase are important targets. Herein, we tested the susceptibility of ceftaroline (TAR) and imipenem (IMI) alone and in combinations with two diazabicyclooctanone β-lactamase inhibitors (BLI), relebactam (REL) and avibactam (AVI), against representative clinical isolates belonging to the *Mab* complex and assessed the mechanism of inhibition using mass spectrometry (QTOF-MS)

Methods. Minimum inhibitory concentrations (MICs) of TAR and IMI with or without AVI and REL and a TAR-IMI combination with and without REL were determined using microdilution. Approximately 5 x 10^5 colony-forming units (CFU) per milliliter were inoculated into Middlebrook 7H9 broth supplemented with 10% (vol/vol) oleic albumin dextrose catalase and 0.05% (vol/vol) Tween 80. AVI or REL were added at fixed concentration of 4 μg/mL to serial dilutions of TAR or IMI. For the TAR-IMI combinations, IMI at 1 μg/mL, and serial dilutions of TAR were used. *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. (QTOF-MS) was used to assess intermediates of $Bla_{Mab,}$ Ldt_{Mab1} and Ldt_{Mab2} with TAR, IMI, AVI, and REL

Results. *In-vitro* susceptibility testing on representative clinical *Mab* strains (table). MIC_{90} was > 128 μg/mL for TAR and 8 μg/mL for IMI. Combination of TAR and IMI lowered MIC's of all clinical isolates to <0.06 μg/mL. Addition of REL or AVI lowered TAR MICs but had minimal or no impact on IMI or TAR-IMI MICs. Mass spectrometry analyses of Bla_{Mab}, $Ldt_{Mab\ (1–2)}$ alone and incubated with IMI, TAR, REL and AVI (figure). Bla_{Mab} β-lactamase bound the AVI and REL, but acyl complexes with TAR or IMI were not detected. $Ldt_{Mab\ (1–2)}$ form stable acyl complexes with AVI, REL, TAR, and IMI.

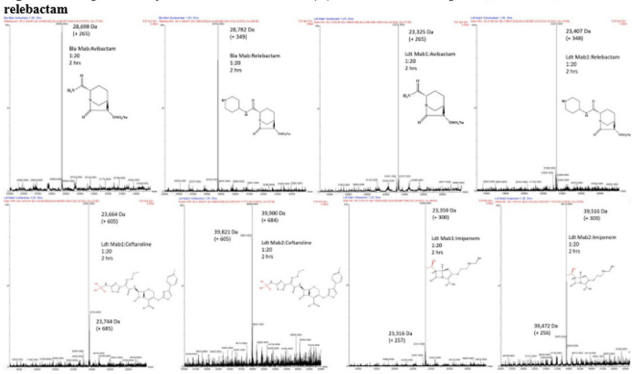
Conclusion. Addition of IMI to TAR lowers MICs of TAR against *Mab* to therapeutically achievable concentrations. It would be welcome news for clinicians who are treating patients with highly resistant *Mab* infection that the combination of TAR and IMI is commercially available and thus might be considered as part of a rescue regimen.

Table: *In vitro* activity (μg/ml) of ceftaroline (TAR), imipenem (IMI), TAR-avibactam (AVI), TAR relebactam (REL), IMI-AVI, IMI-REL and TAR-IMI-REL. REL and AVI were 4 μg/mL.

Strain	TAR	TAR + REL	TAR + AVI	IMI	IMI + REL	IMI + AVI	TAR + IMI (1 μg/mL) + REL
M.ab UHCMC 1	>128	32	32	2	2	2	<0.06
M.ab UHCMC 2	128	32	16	8	16	4	<0.06
M.ab UHCMC 3	128	32	32	2	2	4	<0.06
M.ab UHCMC 4	128	64	64	4	4	4	<0.06
M.ab UHCMC 5	>128	64	64	4	2	8	<0.06
M.ab UHCMC 7	128	32	32	4	4	4	<0.06
M.ab UHCMC 8	32	16	16	4	4	2	<0.06
M.ab UHCMC 9	16	16	16	8	8	4	<0.06
M.ab UHCMC 10	16	16	16	4	2	1	<0.06
M.ab Metro 1	64	32	32	2	2	2	<0.06
M.ab Metro 2	64	64	64	4	4	4	<0.06
M.ab Metro 3	64	32	32	4	2	1	<0.06
M.ab Metro 4	64	32	32	8	8	2	<0.06
M.ab Metro 5	>128	32	32	8	8	2	<0.06
M.ab Metro 6	64	16	16	8	8	1	<0.06
M.ab Metro 7	32	32	32	4	8	2	<0.06
M.ab Metro xx2	>128	128	128	16	16	2	<0.06
M.ab Metro xx3	128	32	64	8	8	6	<0.06
M.ab UHCMC rod I2	>128	64	64	4	4	2	<0.06

Relebactam was obtained from Achemblocks

Figure: Mass spectrometry of Bla Mab and Ldt Mab (1-2) with ceftaroline, imipenem, avibactam, and relebactam



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1386. Reduction in Expected Survival Associated with Nontuberculous Mycobacterial Pulmonary Infection

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Background. Nontuberculous mycobacteria (NTM) are emerging agents of pulmonary disease, estimated to affect >80,000 people in the United States. While the spectrum of pulmonary NTM severity is broad, some published series report 5-year mortality of up to 40%.

Methods. We conducted a retrospective cohort study to examine mortality of patients with positive respiratory cultures for NTM in the Duke Health System from January 1, 1996 to June 30, 2015, compared with the expected mortality in the US population among a cohort with the same demographic composition. We included patients with ≥2 positive NTM respiratory cultures, or 1 positive culture plus an associated ICD diagnosis. Patients with disseminated NTM, HIV, cystic fibrosis, and solid-organ or hematopoietic cell transplants were excluded, as were isolates of *Mycobacterium gordonae*. Five specific comorbidities (cancer, chronic obstructive pulmonary disease, stroke, chronic renal failure, myocardial infarction) were assessed with ICD codes. Survival was measured from the date of first positive NTM culture and censored as of 6/30/2015.

Results. We identified 653 patients who met the case definition. 451 (69%) were female; 548 (84%) were Caucasian, and the median age was 69 years (IQR 59–76). 544 (83.3%) patients had only *Mycobacterium avium* complex (MAC) isolates in cultures; 39 (6%) had only *M. abscessus*; 33 (5%) had both MAC and *M. abscessus*; 37 (5.7%) had