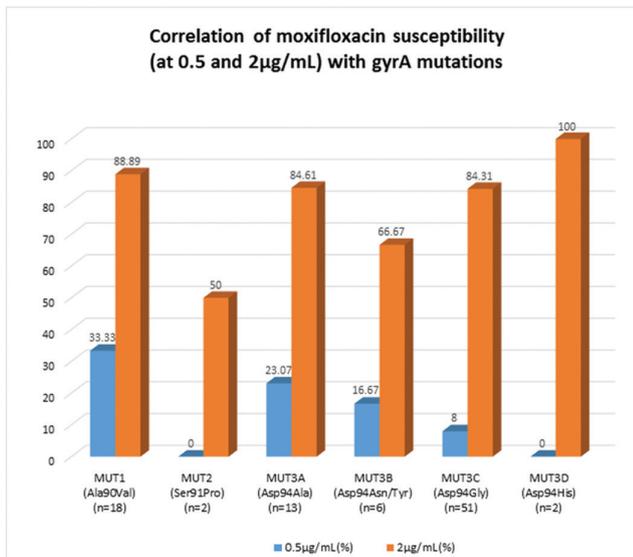


**Background.** This study was done to investigate the utility of specific fluoroquinolone mutations in LPA in predicting the susceptibility in DST at WHO recommended Critical Concentrations of 0.5 and 2 µg/dL of moxifloxacin within a short time frame as provided by LPA.

**Methods.** In a retrospective study performed at a tertiary care hospital of Mumbai, India from October 2015 to February 2017, consecutive samples demonstrating fluoroquinolone resistance by LPA were selected. The LPA kit used was Hain Lifescience Genotype MTBDRsl (Version 1). It detects the following mutations in gyrA gene: MUT1: Ala90Val, MUT2: Ser91Pro, MUT3A: Asp94Ala, MUT3B: Asp94Asn/Tyr, MUT3C: Asp94Gly, MUT3D: Asp94His. The causal mutation was noted. For 89 of these samples, DST had been requested and results with Critical Concentration of 0.5 µg/dL and 2 µg/dL for moxifloxacin were available

**Results.** The 89 samples studied were as follows: Sputum (n = 60), paravertebral soft tissue (n = 2), bronchoalveolar fluid (n = 2), cerebrospinal fluid (n = 1), endotracheal tube secretion (n = 1), pleural fluid (n = 1) and site not recorded (22). 3 of these samples had double mutations. Results are as follows.

Mutation in gyrA gene	Number of samples (n)	Susceptible at 0.5 µg/dL [n (%)]	Susceptible at 2 µg/dL [n (%)]
MUT1 (Ala90Val)	18	6(33.33)	16(88.89)
MUT2 (Ser91Pro)	2	0(0)	1(50)
MUT3A (Asp94Asn)	13	3(23.07)	11(84.61)
MUT3B (Asp94Asn/Tyr)	6	1(16.67)	4(66.67)
MUT3C (Asp94Gly)	51	4(8)	43(84.31)
MUT3D (Asp94His)	2	0(0)	2(100)



**Conclusion.** This study showed a higher proportion of *M. tuberculosis* susceptibility at 2 µg/dL rather than at 0.5 µg/dL, to moxifloxacin for gyrA mutations Ala90Val (MUT1), Asp94Ala (MUT3A), Asp94Gly (MUT3C), Asp94His (MUT3D) but not for Ser91Pro (MUT2) and Asp94Asn/Tyr (MUT3B). However, the number of samples with Ser91Pro (MUT2) and Asp94Asn/Tyr (MUT3B) mutations was too small for meaningful conclusion. This susceptibility at a higher critical concentration of moxifloxacin may have clinical implications for use of high dose moxifloxacin. Since this information is available within a short time frame as provided by LPA, a more effective regimen could be devised 4 to 8 weeks earlier than after results of DST. This may result in faster sputum conversion and prevent amplification of resistance.

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

**2108. Lateral Flow Urine Lipoarabinomannan Assay (LF-LAM) for Diagnosis of Active Tuberculosis in HIV-Infected Adults: a Prospective Cohort Study**  
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**Background.** Early diagnosis and treatment of active tuberculosis (TB) in HIV-positive patients is challenging. Tests based on the detection of mycobacterial lipoarabinomannan (LAM) antigen in urine have emerged as potential point-of-care tests for TB. However, limited data exists on their performance among HIV-TB co-infected patients from Southeast Asian countries.

**Methods.** We prospectively recruited HIV-positive adult patients with CD4 count less than or equal to 200/mm<sup>3</sup> and symptoms suspected of active TB from two tertiary hospitals between December 2015 and March 2017. Freshly collected urine was applied to the Determine<sup>®</sup>-TB LAM Ag test strip (4 bands of graded intensity), using grade 1 cutoff. Diagnostic accuracy of urine LAM strip test were assessed against microbiological reference standard, defined as positive *Mycobacterium tuberculosis* cultured from one or more clinical specimens (definite TB) or composite reference standard including definite TB and probable TB, defined as those have symptoms consistent with TB and response to anti-TB treatment.

**Results.** A total of 280 patients were enrolled. Of whom, 72 (25.7%) and 65 (23.2%) had definite and probable TB. Amongst those with definite TB, LF-LAM test gave a sensitivity of 75.0% (95% CI 63.9–83.6), specificity of 86.0% (95% CI 79.4–90.8) and accuracy of 82.3% (95% CI 76.7–86.8). When compared with the composite reference standard, the test yielded a lower sensitivity (61.3%, 95% CI 53.0–69.1) and accuracy (73.9%, 95% CI 68.5–78.7), with equal specificity. The test showed the highest sensitivity (90.5%, 95% CI 77.9–96.2) and accuracy (85.9%, 95% CI 79.2–90.7) but lower specificity (84.0%, 95% CI 75.6–89.9) in HIV-infected patients with CD4 count less than 50/mm<sup>3</sup>. The sensitivity of the combined LF-LAM or sputum microscopy was higher than that of either test alone (86.1% vs. 75.0%, 61.1%, respectively). *Mycobacterium avium* complex (MAC) was cultured in 7 out of 20 with false positive result. Urine LAM strip test can remain positive for up to 4 weeks even after anti-TB treatment.

**Conclusion.** Urine LAM assay gave the best performance for diagnosis of active TB in advanced HIV-infected patients and provide an additional benefit of a greater simplicity, speed, with a more easily obtainable sample.

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

**2109. Improved Detection and Accuracy of *Mycobacterium* Species Identification from Paraffin Embedded Tissues of Patients by Using Multigene Targeted PCR and Sequencing**

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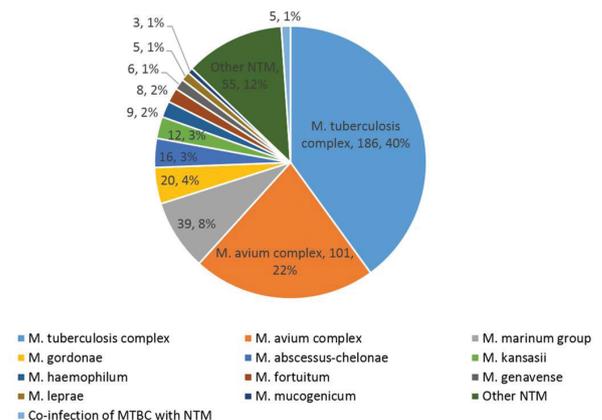
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**Background.** Prompt and accurate identification and differentiation of *Mycobacterium tuberculosis*-complex (MTBC) from non-tuberculous mycobacteria (NTM) is crucial for the selection of antimicrobial treatment and appropriate public health response. Diagnosis and characterization of mycobacteria is challenging due to diverse clinical presentations, lack of sensitivity of smear microscopy, and fastidious culture identification. Moreover, because of clinical suspicion of noninfectious conditions, specimens are often not processed for culture and formalin-fixed, paraffin-embedded (FFPE) tissues are the only specimens available. For rapid and accurate identification of *Mycobacterium* spp. from patient tissues, sensitive and specific molecular assays combined with other tissue-based methods are vital.

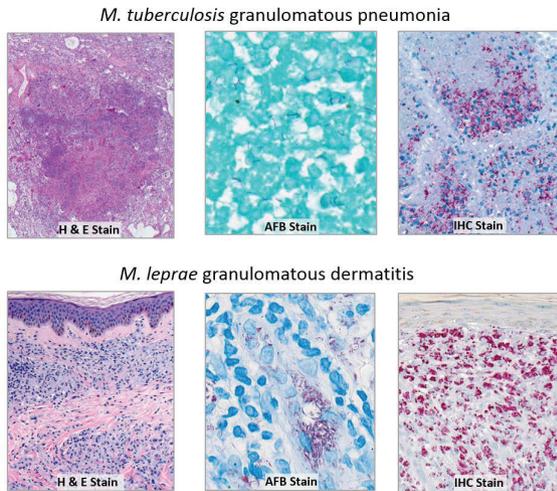
**Methods.** We extracted DNA from FFPE tissues from 931 patients with clinical and histopathological suspicion of mycobacterial infection (received during 2013–2016) and evaluated by multistage, multigene targeted *Mycobacterium*-genus, complexes-and species-specific PCR assays (targets including 16S rRNA, rpoB, groEL, IS6110, RLEP) and sequencing. Tissues were also examined by acid-fast bacilli (AFB) stains and mycobacteria immunohistochemistry (IHC). Assays to detect mutations associated with drug resistance were performed on MTBC cases.

**Results.** A *Mycobacterium* species was detected in 465 (50%) cases by PCR and sequencing. Of these, 380 (82%) were positive by *Mycobacterium* PCR targeting 16S rRNA. 85 cases (18%), including 9 MTBC, 12 *M. avium* complex and 3 *M. leprae*, were positive by other PCRs. Co-infection of MTBC and NTM spp. was detected in 5 cases. Of 465 PCR positive cases, 327 (70%) showed immunostaining and 223 (48%) were AFB-positive. Molecular markers for drug resistance were detected in 9 out of 88 (10%) tested MTBC cases.

**Figure 1. *Mycobacterium* Species Identified by PCR and Sequencing**



**Figure 2. Mycobacteria IHC and AFB staining in lung and skin tissues**



**Conclusion.** FFPE tissue analysis by multigene targeted PCR assays expands the opportunities for rapid identification of *Mycobacterium* species, allows differentiation of MTBC from NTM, and helps to detect co-infections. Using multigene targeted PCRs in combination with histopathology and IHC improve the accuracy of diagnosis, particularly in the presence of commensal and environmental pathogens.

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

#### 2110. Interferon- $\gamma$ Release Assay Performance in Pediatric Tuberculosis Disease in California

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**Background.** Interferon Gamma Release Assays (IGRAs) and Tuberculin Skin Tests (TSTs) are important adjunctive pediatric TB diagnostics. This study analyzes the use and performance of IGRAs in children diagnosed with active TB disease in a high-resource, low-incidence setting.

**Methods.** We retrospectively reviewed cases of children reported with TB to the California Department of Public Health (CDPH) Tuberculosis Registry during 2010–2015. Our cohort included 778 children, after excluding 68 without an IGRA or TST reported. We analyzed case characteristics associated with test selection and performance, and measured IGRA test sensitivity in children with laboratory confirmed TB disease.

**Results.** Of the 778 cases of pediatric TB reported, 360 were laboratory confirmed. Children tested with IGRAs were more likely foreign-born, aged  $\geq 5$  years, to have extrapulmonary disease only, and be laboratory confirmed, than those tested with TST. Children aged  $< 2$  years with confirmed disease were less likely to have a positive IGRA [PRR 0.72 (95% CI 0.55, 0.93)] than children  $\geq 2$  years. Indeterminate IGRAs were associated with age  $< 1$  year [PRR 9.23, 95% CI 2.87, 29.8] and central nervous system (CNS) disease (PRR 2.69, 95% CI 1.06, 6.86) on multivariate analysis suggesting an association with severe disease. IGRA and TST sensitivity were similar in children  $< 5$  years with confirmed disease and test concordance was high in this age group, but sensitivity was  $< 87\%$  for both tests among children aged  $< 2$  years. IGRA was more sensitive than TST among children aged 5–18 years (96%, 95% CI 88%–99% vs. 83%, 95% CI 72–91%,  $P = 0.012$ ).

**Conclusion.** Children presenting with TB symptoms and disseminated disease were more likely to be tested by IGRA than TST. In children  $< 5$  years, IGRA sensitivity is similar to TST, but sensitivity of both tests are reduced in children  $< 2$  years. Indeterminate results are higher, particularly in  $< 1$  year-olds and in CNS disease. In children aged  $\geq 5$  years with laboratory confirmed TB, IGRA has greater sensitivity than TST, and should be considered the preferred immunodiagnostic test. Our data suggest that IGRA is underutilized in this population.

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#### 2111. Diagnostic Usefulness of Bronchoalveolar Lavage Fluid Xpert MTB/RIF in Patients with Suspected Pauci-bacillary Pulmonary Tuberculosis

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**Background.** Rapid and accurate diagnosis of tuberculosis (TB) is important for appropriate treatment initiation and control of disease transmission. Xpert TB/RIF has been widely used for rapid diagnosis especially in sputum AFB smear-negative pulmonary TB. However, about one-third of patients with pauci-bacillary pulmonary TB still reveal negative Xpert TB/RIF results from sputum specimens. Theoretically, bronchoalveolar lavage (BAL) fluid can provide more sensitive specimen in those with sputum-scarce or AFB smear-negative pulmonary TB than sputum. However, there is limited data on the diagnostic performance of Xpert TB/RIF from BAL fluid in patients with pauci-bacillary pulmonary TB.

**Methods.** All patients with suspected pulmonary TB who underwent BAL due to sputum-scarcity or negative AFB smear results and underwent Xpert TB/RIF from BAL fluid were retrospectively reviewed at a tertiary hospital, Seoul, South Korea (an intermediate TB-burden country) between October 2014 and April 2017. Confirmed TB was defined to those with clinical specimens positive for *M. tuberculosis* by culture or PCR assays. Patients those with caseating granuloma in biopsy tissue and shows a good response to anti-tuberculous therapy were classified as having probable TB.

**Results.** A total of 113 patients were included in the analysis. Of these 113 patients, 30 (27%) were classified as confirmed TB, 7 (6%) as probable TB, and 76 (67%) as not TB. Of these 37 patients with confirmed or probable TB, 8 (22%) had miliary TB and 12 (32%) were immunocompromised. Only 15 (50%) of the 30 confirmed TB patients revealed positive Xpert TB/RIF results from BAL fluid. Overall sensitivity, specificity, positive predictive value, and negative predictive value of Xpert TB/RIF from BAL fluid for the diagnosis of TB were 41% (95% CI, 31%–41%), 100% (95% CI, 95%–100%), 100% (95% CI 77%–100%), and 78% (95% CI 74%–77%), respectively.

**Conclusion.** XpertTB/RIF from BAL fluid appears to be suboptimal to rule out pulmonary TB. The development of more sensitive and rapid test for pauci-bacillary pulmonary TB is needed.

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

#### 2112. Season Is Associated with Interferon Gamma Measured in QuantiFERON Gold In-Tube Test

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**Background.** The QuantiFERON Gold-in-tube (QFT) test is an Interferon Gamma Release Assay (IGRA) used to indirectly diagnose tuberculosis infection (TBI). The QFT measures Interferon gamma (INF- $\gamma$ ) released in response to specific *Mycobacterium tuberculosis* (*Mtb*) antigens. The main objective of this analysis is to determine whether there is a seasonal variation of the INF- $\gamma$  level released in QFT blood samples.

**Methods.** Data of the QFT assays conducted in health care workers (HCW) at Houston Methodist Hospital (HMH; Houston, TX) between August 2008 and April 2017 were analyzed and stratified by the season when the blood samples were drawn. Multivariate generalized linear models (GLM) controlling for age, gender and ethnicity were used to estimate INF- $\gamma$  measured in the nil and mitogen controls per season.

**Results.** Data from 10,089 QFT assays were included in the analysis. The tested HCW were primarily between the ages of 18 to 49 years (76.5%), female (65.9%), and non-Hispanic (77.0%). A significantly higher level of INF- $\gamma$  was found in the mitogen-stimulated blood (Phytohemagglutinin) in the summer (June – August) (estimate: 0.19 IU/mL;  $P < 0.001$ ) compared with the other season, and a significantly lower level of INF- $\gamma$  was found in the fall (September – November) (estimate: -0.27 IU/mL;  $P < 0.001$ ) compared with the other seasons. The INF- $\gamma$  level was significantly lower in unstimulated blood (estimate: -0.02 IU/mL;  $P = 0.038$ ) but not in the antigen-stimulated blood samples drawn in the winter (December–February) compared with those drawn in other seasons.

**Conclusion.** We observed a seasonal variation of the INF- $\gamma$  level measured in unstimulated and antigen-stimulated blood samples drawn for the QFT assays, in which seasonal factors such as airborne antigens like pollen may play a role. Clinicians should take into account the possible seasonal variation when interpreting positive QFT results, especially those on the borderline of the assay's diagnostic cutoffs. Re-testing or implementing additional diagnostic tools should be considered if necessary. Further research would be needed to identify the specific seasonal factors that may influence the QFT results.

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

#### 2113. Safety & Benefits of Directly Observed Therapy with Rifapentine and Isoniazid for Latent Tuberculosis Infection – Less is More?

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