795. Review of Treatment of Latent Tuberculosis Infection at VA Portland Healthcare System

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Background. Treatment of latent tuberculosis infection (LTBI) is important for tuberculosis elimination in low-incidence countries. Currently, the VA Portland Healthcare System (VAPORHCS) offers both 3HP (12-dose rifapentine plus isoniazid directly observed therapy [DOT]) and 9H (9-month daily isoniazid) for treatment of LTBI. Majority of veterans are treated with 9H despite increasing evidence showing higher rates of completion with 3HP. We reviewed the rates of completion and adverse events (AE) between veterans treated with 3HP and 9H.

Methods. We performed a retrospective chart review on all patients within the VAPORHCS who initiated LTBI treatment with 9H or 3HP between January 2011 and December 2016. LTBI was diagnosed through tuberculin skin testing or interferon-γ release assay. 9H treatment was self-administered while 3HP was under DOT. Collected data included demographics, co-morbid conditions, immunosuppression, treatment completion, and AE. Treatment completion was determined through chart documentation.

Results. A total of 93 patients were treated for LTBI. Most patients were white (71%), and male (86%). The median age was 57 years old. Seventy-two patients (77%) were treated with 9H, and 21 (23%) were treated with 3HP. The overall completion rate was 86%. Completion rates between 9H (91%) and 3HP (86%) were not significantly different (P = 0.46). Twenty-three patients (31.9%) on 9H and six patients (28.6%) on 3HP were on chronic immunosuppression with TNF inhibitors and/or corticosteroids (P = 0.78) with an overall completion rate of 86%. Nine patients (13%) on 9H and two patients (10%) on 3HP had HIV. P = 0.90 when overall rates of AE were similar between groups. (4%, 14%, 0.11), including hepatitis toxic (2%, 0%, P = 0.57) and neurotoxicity (4%, 5%, P = 0.94).

Conclusion. The overall treatment completion rates were high and statistically similar between 9H and 3HP groups, even with immunosuppressive therapy. There were no significant differences in rates of adverse events. While the majority of patients were treated with 9H, these results suggest an opportunity for more use of the 3HP, possibly without the need for DOT regimen going forward.

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796. Treatment of Latent Tuberculosis Infection in a Refugee Population

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Background. As tuberculosis (TB) rates decline in the United States, many new cases are among individuals who migrated from countries with a high incidence of TB. Public Health – Dayton & Montgomery County (PHDMC) screens in immigrants and refugees for active TB. The objective of this study was to estimate the number of active cases of TB prevented through screening and treatment of LTBI.

Methods. Data were collected through retrospective chart review of refugee patients seen between July 1, 2011, and June 30, 2015. Refugee status was verified. Tuberculin skin tests were reviewed for cases in refugees. The number of expected new, active TB cases was calculated. We counted 2,771 cases of LTBI. There were 59.5% cases with extra pulmonary (n = 1,650) forms and 40.5% with pulmonary forms (n = 1,121). The median age was 38 years (IQR = [25–55 years]) with a male predominance (n = 1,508; 54.4%). We noted that 72.9% of patients (n = 1,985) received the DF, 26.2% (n = 714) received the CF and 0.8% (n = 23) received both forms of treatment. DF was significantly more prescribed in patients with extra-pulmonary tuberculosis (75.4% vs. 72%; OR = 0.837; P = 0.043) whereas CF was significantly prescribed in patients with pulmonary tuberculosis (28% vs. 24.6%; OR = 0.837; P = 0.043). DF was more used in patients with primary tuberculosis infection (30.3% vs. 21.6%; OR = 0.632; P < 0.001). The duration of treatment was significantly higher in patients who received DF (9 months vs. 8 months; P < 0.001). We did not find a difference in the evolution between patients treated with DF and those treated with CF.

Conclusion. DF are of a great importance to ensure better compliance and sympathetic effects of different durations.

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798. The Role of Whole-Genome Sequencing in Characterizing the Mechanism of Action of Anti-Tuberculosis Compounds: Demonstrated With Para-Amino Salicylic Acid and Its Analogue

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Background. Para-aminosalicylic acid (PAS) was one of the first antibiotics to be used against tuberculosis (TB) and is still one of the last remaining drugs available to treat extensively drug-resistant (XDR) disease. Despite being on the market for decades, the mechanism of action of PAS is not completely understood yet. Sixteen new compounds against Mycobacterium tuberculosis were created in the laboratory as salicylate analogues (based on their chemical structures) and their antimycobacterial activity had never been tested before. The main aim of this project was to test the activity of these new analogues and to understand their mechanism of action (including PAS).

Methods. The compounds were tested using three different methods (spot culture, resazurin, and MGT system). Additionally, resistant mutants were created against PAS and the most promising analogue, whole-genome sequencing (WGS) was performed to understand their mechanism of action.

Results. One compound in particular, AD2SA, showed the lowest critical concentration (0.04 µg/mL) among the salicylate analogues. The WGS analysis identified a total of 28 single nucleotide polymorphisms (SNPs) in the AD25a-resistant mutants. There were 59.5% males (77%) were treated with 9H, these results suggest an opportunity for more use of the 3HP, possibly without the need for DOT regimen going forward. Conclusion. These new analogues and to understand their mechanism of action (including PAS).

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799. Genetic Diversity of Mycobacterium tuberculosis StrainsCausing Drug-Resistant Tuberculosis in Central Region of Mozambique: The Whole-Genome Sequencing

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Background. Knowledge the genetic diversity of M. tuberculosis strains causing drug-resistant tuberculosis (DR-TB) in high burden TB and low resources countries such as Mozambique is a key factor to TB disease spread control and world TB epidemic control. Whole-genome sequencing (WGS) better describes molecular diversity,
lineages and sub-lineages, relationship between strains, underline mutations conferring drug-resistant TB, which may not be shown by molecular and phenotypic tests. As far as we know this is the first study that describes genetic diversity of M. tuberculosis strains causing DR-TB and using WGS in central region of Mozambique. We aim to describe genetic diversity of M. tuberculosis strains causing DR-TB in central Mozambique.

**Methods.** A total of 35 strains from Beira Mozambique were evaluated with genotypic tests (Genotype MTBDRplus; and MTBDRs) and phenotypic (MGIT-SIRE™) and DST. All isolates resistant to isoniazid (H) or rifampicin (R) or both were submitted to WGS. Illumina HiSeq 2000 was used and analyzed with TB profiler database and phylogenetic tree was done using Figtree tool. This was a descriptive cross-sectional study. Results. WGS shown that strains analyzed, belongs to three of six major lineages, with Lineage 4: 25(71.4%); Lineage 1: 5(14.3%); and Lineage 2 Beijing family: 5(14.3%). All pre-XDR strains 3(8.6%) were from lineage 4.3. By WGS, all 35 strains had any mutations conferring DR-TB while in one strain, mutation was not shown by genotypic neither phenotypic DST. Compared with genotypic tests, WGS had best performance in showing mutation conferring resistance to ethambutol 12/35 (34.3%) and 7/35 (20%). Conclusion. The DR-TB disease in Beira Mozambique is mainly caused by M. tuberculosis strains of Lineage 4, sub-lineage although lineage 1 and 2 are also present. WGS shows underline mutations causing DR-TB which are not detected by genotypic and phenotypic DST. Disclosures. All authors: No reported disclosures.

***800. Drug-Resistant TB: An Experience From Qatar***

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**Session:** 70. Tuberculosis and Other Mycobacterial Infections

**Background.** Drug-resistant tuberculosis (DR-TB) is an important issue for public health. This study was conducted to evaluate the characteristics, treatment outcome, and risk factors associated with 223 DR-TB cases in the State of Qatar.

**Methods.** A descriptive records-based retrospective study was conducted on patients registered at Communicable Disease Centre (CDC), Qatar to all consecutive microbiologically confirmed tuberculosis cases for the period January 2010–March 2015. Demographic and clinical data extracted included: patient’s age, sex, and country of origin; disease type (pulmonary or extra-pulmonary); presence of comorbidities, HIV/AIDS status, previous chemoprophylaxis and/or previous treatment for TB, and anti-TB drug resistance the resistance pattern of isolated mycobacteria. The sputum culture conversion rate and treatment outcome was assessed for the patient who completed their treatment in Qatar.

**Results.** Of 330 patients with positive M. tuberculosis culture were analyzed; 223 (6.7%) were resistant to one or more first-line drugs, to isoniazid in 3.1% (n = 102), streptomycin in 1.2% (n = 41), rifampicin in 0.2% (n = 6), ethambutol in 0.15% (n = 5), and multi-drug resistance in 1.2% (n = 38) of patients. Among the resistant TB patients, more common demographic characteristics were being resident of Indian subcontinent (64.1%). A history of anti-TB treatment was not a risk factor with drug resistance in our cohort. Only 111 (49.7%) patients were tested for HIV antibodies and the results were all negative. There was significant correlation between the type of drug resistance and Mantoux test findings (23.3% used was Mantoux ≥8 mm p<0.001). Sputum culture conversion to negative at 2 months of therapy was 94% (n = 101), whereas 122 cases lost follow-up. The outcome of treatment was assessed for 85 resistant cases with follow-up after completion of treatment, show cure rate of 96.7%, and relapse of 2.4%. However, 137 cases (61.4% from total) they left the country before completion of therapy.

**Conclusion.** Drug-resistant TB in Qatar is influenced by migration, especially from the Indian subcontinent, where the patients were probably infected. Rapid sputum sampling performed in the early stages of the disease, patient isolation, and drug susceptibility testing should be the standard of care to avoid further transmission and improve TB control.

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

***801. Emergence of Multi-Drug Resistance Tuberculosis During the Treatment***

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**Session:** 70. Tuberculosis and Other Mycobacterial Infections

**Background.** Successful treatment of tuberculosis (TB) requires monitoring for clinical, radiographic, and microbiologic improvement. Even after negative cultures are obtained, there should be continued monitoring of sputa. If cultures become positive during treatment of drug susceptible TB (DS-TB), there should be concern for multi-drug-resistant tuberculosis (MDR-TB). We present two cases diagnosed with DS-TB who developed MDR-TB during treatment.

**Case Report.** Case 1 is a 33-year-old male who was incarcerated in Peru. During incarceration in 2008, three of his cellmates had MDR-TB and he was diagnosed with DS-TB and treated with directly observed therapy (DOT) for 7 months. In Texas in 2015 he was diagnosed with DS-TB and was initiated on rifampin, isoniazid, pyrazinamide, and ethambutol (RIPE). Five months into DOT, his sputa became culture positive with molecular detection of drug resistance (MDRDR) and drug susceptibility testing (DST) revealing resistance to all of RIPE. Repeat MDRDR and DST of the 2015 isolate showed no resistance. Genotyping of the two isolates were identical by mycobacterial interspersed repetitive units (MIRU) and spoligotyping. However, while genome sequencing showed two different isolates. Case 2 is a 63-year-old female diagnosed with DS-TB in Saipan and started on RIPE in April 2017. She was on DOT until July when she moved to Texas and was lost to follow-up until September. She claims adherence with rifampin and isoniazid during this time. All sputa collected between diagnosis and September were smear and culture negative. Six months into therapy, she had sputa that was culture positive with MDDR DST showing MDR-TB. Her isolates from Saipan and Texas were sent for genotyping. The MIRU and spoligotyping showed two different isolates.

**Conclusion.** These cases show the importance of following cultures throughout treatment. Traditionally, MDR-TB is thought to be due to poor adherence. However, in high prevalence areas, heterogeneous infection with two different strains is an important consideration for the cause of MDR-TB. Concomitant infection of DS and MDR-TB can occur with MDR-TB not being detected until far into therapy. These cases represent heterogeneous exogenous infection of DS and MDR-TB—only discovered through genotyping of culture monitoring.

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***802. Use of N-Acetylcysteine for Prevention and Treatment of Isoniazid Induced Liver Injury During Treatment of Mycobacterial Infections***

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**Background.** Hepatotoxicity secondary to therapy for Mycobacterium tuberculosis (MTB) is a common complication that may lead to treatment interruption. N-Acetylcysteine (NAC) exerts a hepatoprotective effect by repleting glutathione stores and enhancing the cellular antioxidant defense mechanism. NAC has been found to be protective against liver toxicity in animals treated for MTB infection. Randomized controlled trials have shown that its use in humans also decreases the risk of hepatotoxicity associated with anti-MTB treatment but there is minimal data regarding its utility for treatment of liver toxicity.

**Methods.** Patients who received NAC from January 2012 to March 2018 for prophylaxis and treatment of increasing liver function tests (LFTs) while on isoniazid (INH) were included. A retrospective review of the medical record system was performed.

**Results.** Nineteen patients were included. Eight received NAC for treatment. The average age was 49 years. Seventy percent of patients were male. The mean BMI was 25. Five patients had underlying liver cirrhosis and two had hepatic steatosis. Eleven patients had Hepatitis C (HCV) and one had active Hepatitis B infection. Ten patients had MBT pulmonary infection, thee had latent TB infection, two meningitis, and three had disseminated disease. One patient was treated for atypical mycobacterial infection. The mean LFT values of the group receiving NAC were not significantly different than the group not receiving NAC—p > 0.05. The prophylaxis group had stable LFTs during treatment, except for two patients whose enzymes increased more than three times the upper limit of normal. These two patients had underlying HCV and liver cirrhosis. Only one required discontinuation of INH. Both those patients reported unacceptable side effects of NAC. The treatment group had a favorable trend of liver enzymes after NAC initiation, with levels significantly improving by day 14 (Figures 1 and 2). Three patients did not require discontinuation of antibiotics. INH was stopped prior to NAC initiation in four patients. No side effects of NAC were documented in any patient.

**Conclusion.** NAC is a safe and effective measure to prevent and treat hepatotoxicity secondary to INH therapy. More studies are needed to determine its optimal dose and duration for this indication.

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***Figure 1.***