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WPQC UPDATE:

WPQC Spotlight: Matt Huppert

Fitchburg Family Pharmacy Tuberculosis Dispensing Partnership and Guideline Review

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Tuberculosis (TB), caused by *Mycobacterium tuberculosis*, is one of the most common infectious diseases worldwide, infecting roughly 23% of the global population.[1] However, in the United States, TB infection is much less prevalent, impacting only 2.2 per 100,000 people.[2] According to the Wisconsin Department of Health Services (DHS), there were only 66 reported cases of TB in Wisconsin in 2021, 6 of which occurred in Dane county.[3] It is imperative that these patients be treated appropriately, so DHS assumes full responsibility for the management of care for these patients, from diagnosis to cure.

Given the relative rarity of TB in Wisconsin, coordinating the dispensing of the medications to treat TB can be challenging. Many pharmacies do not regularly carry the medications necessary to treat TB. Having to order these medications as needed from a distributor can result in delays in treatment initiation. In addition, pharmacists who do not routinely dispense TB treatment may not be prepared to assess the safety and efficacy of regimens involving medications such as isoniazid or rifapentine.

Considering these challenges, DHS partners with a single regional pharmacy to dispense treatment for the small number of its patients with TB. This helps prevent delays in treatment, ensures appropriate turnover of TB medications from pharmacy shelves, and allows the pharmacists on site to become regional experts in evaluating TB treatment. When the Wisconsin DHS sought a new pharmacy partner in the Dane County area, they reached out to Fitchburg Family Pharmacy (FFP) based on both agencies' previous experience collaborating to address the COVID-19 pandemic. In the following Q&A, Matt Huppert, PharmD, shares his experience establishing this TB dispensing partnership with DHS.

Q&A with Matt Huppert

Q: How did the idea for this partnership come about?

A: We received an email from the Public Health Supervisor for Dane County asking Thad Schumacher, the owner, if we at Fitchburg Family Pharmacy could provide dispensing services for the TB program. We said we could help to ensure the patient was getting the medications they needed.

Q: What previous experiences prepared you for this partnership?

A: Our pharmacy has been working with other branches of Wisconsin DHS to provide COVID vaccinations and testing. We also felt that we could provide medications to patients in an efficient manner based on the culture of our pharmacy.

Q: What steps did you take to get started?

A: We called the coordinator to set up a date to meet. We then set up a meeting to meet with all the nurses involved with the TB drug dispensing program.

Q: How does this partnership work and what is your role in the partnership?

A: The TB nurses send us prescriptions for TB medications. They provide us with insurance information, labs, and other information for us to provide safe and effective medications. Our role is to provide the medication in a logistically efficient manner to treat TB.

Q: What barriers did you face with implementing the partnership?

A: We hadn't stocked or dispensed TB drugs previously. We also were unsure about reimbursement and payment of patient copays. We needed to be reimbursed for the medication and the time it takes to ensure the medication is safe and effective for the patient.

For another perspective on partnerships with local health departments, consider listening to PSW's 2022 Emerging Leaders Podcast episode "Working with Your Local Health Department." Here, Joshua Davis, PharmD, BCACP, discusses his experience building a relationship with the Iowa Department of Public Health and providing services such as HIV testing and COVID immunizations. The Emerging Leaders Podcast series can be found on PSW's website: https://www.pswi.org/Communications/PSW-Podcasts

Q: How did you overcome these barriers?

A: We utilized 4th-year pharmacy students to ensure our staff was updated on how to provide TB medications safely and effectively. We also did a cost analysis on how much medication we would need to stock in the pharmacy. We wanted to make sure that our pharmacy would not be spending too much money on inventory to provide this service for patients.

Q: How will this partnership help FFP and the community?

A: We want to ensure patients are receiving their medications in a timely fashion to reduce risks of disease progression. We feel this partnership is important to ensure we are taking care of patients in our community. Access to healthcare is a major barrier for patients. Both adherence and safety can be affected due to low access to healthcare. Our pharmacy is attempting to provide as much access as possible to improve this social determinant of health. Providing services like this to patients may help our pharmacy by showing what pharmacists are able to do to help our communities.

Tuberculosis Guideline Review

Most commonly, TB affects the lungs, but the bacteria can attack anywhere in the body.[4] Symptoms can include cough, fever, fatigue, or night sweats. However, it is important to recognize that not everyone infected with TB becomes sick, due to latent TB infections (LTBI). Along with LTBI, there are other factors that impact the treatment of TB, including drug susceptibility and resistance, as well as human immunodeficiency virus (HIV) status. As a result, multiple guidelines exist to aid in the treatment of TB.

Drug Susceptible TB Treatment

The American Thoracic Society (ATS), Centers for Disease Control and Prevention (CDC), and Infectious Diseases Society of America (IDSA) released a clinical practice guideline in 2016 regarding the treatment of drug-susceptible TB.[5]

Preferred Treatment Regimen

The preferred regimen for drug-susceptible TB in adults caused by organisms that are not known or suspected to be drug-resistant consists of an intensive phase for 2 months, followed by a continuation phase of 4 months, as outlined in tables 1 and 2.

When using isoniazid (INH), pyridoxine (vitamin B6) is added to prevent neuropathy. Doses of 25-50 mg daily are appropriate if the patient does not already have neuropathy. This is especially important in those at high risk of neuropathy, such as those pregnant or breastfeeding, patients with HIV, diabetes, alcoholism, malnutrition, chronic renal failure, or advanced age. If the patient experiences neuropathy, the dose may be increased to 100 mg per day.

Administration Schedule

The preferred frequency of this treatment regimen is once-daily dosing for both the intensive and continuation phases; however, there have been a variety of studies that have looked at the administration of antituberculosis drugs using directly observed therapy (DOT). This is the practice of observing the patient swallow their medications 5-days-a-week. Experts believe that both approaches to treatment are appropriate and should be decided on based upon patient-specific factors and preferences. Treatment regimen medications typically are administered together at one dosing period and the bioavailability of all the medications is greatest when taken on an empty stomach.

Alternative Treatment Regimens

When patients are intolerant to first-line medications or there is a presence of mono-resistance, alternative regimens may be used.

- If pyrazinamide (PZA) cannot be used, INH, rifampin (RIF), and ethambutol (EMB) should be used for 2 months followed by 7 months of RIF and INH.

For treatment of latent TB, please see: Guidelines for the Treatment of Latent Tuberculosis Infection: Recommendations from the National Tuberculosis Controllers Association and CDC, 2020

TABLE 1. Intensive Phase Regimen

Intensive Phase	*Dosing*	*Duration*
Rifampin* (RIF)	10 mg/kg/day (typically 600 mg)	7 days/week for 8 weeks (56 doses) or 5 days/week for 8 weeks (40 doses)
Isoniazid (INH)	5 mg/kg/day (typically 300 mg)	
Pyrazinamide (PZA)	40-55 kg: 1000 mg daily 56-75 kg: 1500 mg daily 76-90 kg: 2000 mg daily	
Ethambutol (EMB)	40-55 kg: 800 mg daily 56-75 kg: 1200 mg daily 76-90 kg: 1600 mg daily	
**Rifampin analogs rifapentine and rifabutin can be used in select patients*		
Rifabutin	5 mg/kg/day (typically 300 mg)	
Rifapentine	10–20 mg/kg/day	

TABLE 2. Continuation Phase Regimen

Continuation Phase	*Dosing*	*Duration*
Rifampin (RIF)	10 mg/kg/day (typically 600 mg)	7 days/week for 18 weeks (126 doses) or 5 days/week for 18 weeks (90 doses)
Isoniazid (INH)	5 mg/kg/day (typically 300 mg)	

- If EMB or INH cannot be used, moxifloxacin or levofloxacin can be used in their place for a minimum of 6 months in duration. It is also important to note that the use of moxifloxacin and levofloxacin has not been established in clinical trials.
- If RIF or its analogs cannot be used, it is recommended to follow the Official ATS/CDC/ERS/IDSA Clinical Practice Guideline for the Treatment of Drug-Resistant Tuberculosis.[5]

For treatment in special situations including HIV infection, tuberculous pericarditis, tuberculous meningitis, culture-negative pulmonary tuberculosis in adults, or other special situations, please see the full drug-susceptible tuberculosis treatment guidelines.

Follow-up & Monitoring

At baseline, it is recommended that patients with suspected TB have 3 sputum specimens collected for evaluation and culture, with at least 1 specimen for rapid molecular testing. Susceptibility testing should also occur for INH, RIF, EMB, and PZA if the initial culture is positive, regardless of the source. Patients also should receive a chest radiograph or similar imaging. Baseline liver function tests are obtained and if results are normal, continued monitoring does not need to occur unless symptoms consistent with hepatotoxicity develop, or for patients who chronically consume alcohol, take other hepatotoxic medications, have viral hepatitis or liver disease, or HIV. At baseline, patients should also be screened for HIV, hepatitis B and C, and diabetes. For patients being initiated on EMB, it is important that baseline visual acuity and color discrimination tests are completed, followed by monthly monitoring.

During treatment, a sputum specimen is collected for an acid-fast bacilli (AFB) smear and cultured monthly until 2 consecutive specimens are negative. When initiating the continuation phase, it is crucial that the patient obtain a sputum specimen once completing the intensive phase if a negative sputum culture has not already been documented, as the culture results tend to correlate with the likelihood of relapse after completing therapy. It is also recommended that once a patient has been on treatment for 3 months or longer, drug susceptibility tests are completed to identify any treatment failures. Also, it is important to assess adherence and monitor for improvement in TB symptoms as well as the development of medication adverse effects such as jaundice, dark urine, nausea, vomiting, abdominal pain, fever, rash, anorexia, malaise, neuropathy, or arthralgias. Weight should be monitored monthly to adjust medication doses as needed.

Management of Treatment Interruptions

Treatment interruptions can lead to serious outcomes such as treatment resistance and potentially the need to restart treatment from the beginning, especially if the break is early in therapy or long in duration. In general, if the treatment interruption occurs during the intensive phase and is less than 14 days in duration, continue treatment until the planned number of doses is completed. If the interruption is greater than 14 days in duration, drug therapy will need to be restarted from the beginning. If the interruption occurs during the continuation phase, and the patient has received at least 80% of doses and had a negative AFB smear on initiation, further therapy may not be warranted. If the patient has received at least 80% of doses and the AFB smear was positive initially, continue drug therapy until all doses are complete. If the patient has not received at least 80% of doses, and the accumulative lapse is less than 3 months, the patient may continue therapy until all doses are complete. If the patient has not received at least 80% of doses and the accumulative lapse is greater than 3 months, the patient needs to restart therapy from the beginning of the intensive phase.

Management of Common Adverse Events

As mentioned previously, potential adverse effects that may develop from these treatment regimens include jaundice, dark urine, nausea, vomiting, abdominal pain, fever, rash, anorexia, malaise, neuropathy, or arthralgias.

Gastrointestinal Adverse Effects: Gastrointestinal (GI) adverse reactions are common with these treatment regimens. To minimize symptoms of nausea or epigastric distress, patients may take the medications at bedtime. When GI intolerance is not related to hepatotoxicity, antacids may be used as they interfere less with drug absorption as compared to food. If patients are still experiencing intolerances, a low-fat snack may be utilized to minimize side effects.

Rash: A rash may also be a common side effect experienced by patients using antituberculosis medications. If the rash is considered mild (mainly itchy without mucous membrane involvement or systemic symptoms (fever)), patients can use antihistamines and their TB regimen can be continued. If the rash is considered a petechial rash or a generalized erythematous rash, or if fever and/or mucous membrane involvement develops, medications should be stopped. Systemic corticosteroids may be used to treat severe systemic rashes. When symptoms have improved greatly, medications can be individually restarted in intervals of 2-3 days. RIF should be restarted first, then INH, then EMB or PZA. If at any point the rash reoccurs, the last medication added should be stopped immediately. Once 3 medications have been restarted without the recurrence of a rash, the fourth medication should not be added unless the medication is essential, and the rash was considered mild.

Fever: Drug fevers can be caused by multiple factors when treating TB. If patients have a body temperature of ≥ 39°C but feel well, superinfection is generally not suspected. Stopping the medications should resolve the fever in approximately 24 hours. Once the patient is not experiencing a fever, reinitiate medications individually every 2-3 days, similar to the process used for rechallenging medications due to a rash.

Hepatotoxicity: The most frequent serious adverse reaction to RIF, INH, and PZA is drug-induced liver injury. When alanine transaminase (ALT) is ≥ 3 times the upper limit of normal (ULN) with symptoms of hepatitis such as jaundice, dark urine, nausea, vomiting, abdominal pain, or ≥ 5 times the ULN in the absence of symptoms, drug-induced liver injury is suspected. If drug-induced liver injury is suspected, hepatotoxic medications should be stopped immediately. Once ALT is < 2 times the ULN, medications may be restarted individually, typically starting with RIF since it is less likely to cause hepatotoxicity than INH or PZA. After 1 week, if there is no increase in ALT, INH can be restarted. Similarly, if there is still no increase in ALT after 1 week, PZA can

be initiated. If at any point ALT increases or symptoms reoccur, the last medication added should be stopped immediately.

Drug-Drug Interactions

Drug-drug interactions are very common when treating TB. It is uncommon for antituberculosis drug concentrations to substantially change and affect the treatment of TB, but it is very common for antituberculosis medications to cause changes in concentrations of other medications. Many of these interactions are due to induction of CYP isozymes by rifamycins. For a detailed list of drug-drug interactions, please see the full drug-susceptible tuberculosis treatment guidelines.

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