LTBI Videos-Treatment

This program is presented by the Global Tuberculosis Institute and is based on recommendations from the Centers for Disease Control and Prevention. This is the third in a series of videos for community health providers. In this video, you will learn about treatment for latent TB infection, also called LTBI. Other videos discuss the screening and diagnosis of TB infection.

There are several treatment plans available for TB infection. Medications used are isoniazid, rifapentine and rifampin. Treatment of TB infection greatly lowers the risk that TB infection will progress to TB disease. Treating a patient for TB infection when they really have TB disease can lead to poor outcomes, including drug resistance.

Which treatment regimen you choose depends on several factors, including co-existing medical conditions and potential for drug interactions. For people who are close contacts to an infectious case of TB, base the treatment regimen on the drug susceptibility pattern of that case.

Consider directly observed therapy, in which a healthcare worker observes a patient swallowing their TB medication, particularly for patients who may have trouble adhering to their treatment plan. Directly observed therapy, or DOT, is also recommended for people on an intermittent dosing regimen, and children under 5 who are close contacts. Check your state's standards of practice about any DOT requirements.

Treatment for Latent TB Infection

The first treatment regimen is isoniazid, also called INH. The preferred length of this regimen is 9 months of daily isoniazid, because it's more efficacious. An alternative regimen is 9 months of isoniazid twice weekly using DOT. A 6 month regimen of daily INH is an acceptable alternative, but is estimated to be only 70 percent efficacious, and isn't indicated for children and people living with HIV. For children ages 2 to11 and HIV infected individuals taking anti-retroviral medication, the preferred treatment regimen is 9 months of INH daily.

The second treatment regimen, and the newest regimen recommended by CDC, is a

12-dose regimen of isoniazid and rifapentine. This regimen is recommended as an option equal to the standard 9-month daily regimen of isoniazid in specific populations. This includes otherwise healthy people, aged 12 and older, who either were recently in contact with someone with infectious TB, or are *recent convertors*, that is, had a positive TST or IGRA within 2 years of getting a negative result. For all others, consider this regimen on a case-by-case basis, such as when it's more likely the patient will complete this regimen than other options. All doses of this regimen must be given by DOT.

Don't use this 12-dose regimen for children younger than 2; pregnant women or those expecting to become pregnant; people living with HIV or AIDS who are on anti-retroviral treatment; or people who may be infected with TB that is resistant to isoniazid or rifampin.

A third treatment regimen is 4 months of Rifampin daily. This regimen is used with people who cannot tolerate isoniazid or have been exposed to TB that's mono-resistant to isoniazid. This regimen may also be considered when a shorter course of treatment is preferred in order to enhance treatment completion. This regimen should not be used for people living with HIV taking anti-retro-viral therapy. A 6-month regimen of daily Rifampin is recommended for infants, children, and adolescents.

When determining which regimen to use, n addition to the clinical factors, consider what resources you have, the patient's preferences, and other influences that might affect their adherence. We'll discuss these factors later.

General Treatment Guidelines

Let's talk about some general treatment guidelines. In general, dosage is based on weight. For more information about dosage, please see this website, (www.umdnj.edu/ntbcweb/products/ltbimultimedia.htm).

Someone who is exposed to drug-susceptible TB and diagnosed with latent TB infection should be treated with isoniazid, or if they meet the requirements identified previously, with the 12-dose isoniazid or rifapentine regimen.

Someone exposed to TB mono-resistant to isoniazid, and who tests positive for TB infection should be treated with rifampin for 4 months or, 6 months for children.

For someone exposed to multidrug-resistant TB who tests positive for TB infection, you must consult an expert. Contact your local TB program for guidance.

Special Circumstances

Important considerations when treating TB infection include whether the patient is a contact, is living with HIV, is pregnant or breastfeeding, or is an infant or child.

A contact is someone recently exposed to infectious TB. Evaluate contacts immediately for TB infection and TB disease, and treat any who are diagnosed with TB infection. Retest a contact who has a negative test for TB infection 8 to 10 weeks after the last exposure to the infectious case. Work closely with your local health department to evaluate contacts.

Start treating contacts under age 5 or who are immunocompromised, even if they have a negative test for TB infection, as long as their chest radiograph is normal and TB disease has been ruled out. Continue their treatment until you know the results of their second test for TB infection. Treatment may be discontinued in a healthy child if the second test is negative. Treatment is sometimes continued in HIV positive and other immunosuppressed individuals, even if the second test is negative. Consult with your local TB program for these cases.

For those living with HIV who are taking anti-retroviral treatment, use a 9 month regimen of isoniazid. Rifampin is contraindicated in people living with HIV who are taking certain anti-retro-viral drugs. Consider the 12 dose regimen for people living with HIV who are otherwise healthy and not on anti-retro-viral therapy.

Rule out TB disease if a woman is pregnant. Consider immediate treatment if the woman has HIV, or is a recent contact. If a pregnant woman has no other risk factors, wait to treat until 2 to 3 months post-partum. The preferred regimen is isoniazid daily or twice weekly using DOT. Also give a vitamin B6 supplement. There is a risk of increased hepatotoxicity during pregnancy and 2-3 months after delivery. The 12 dose regimen is not recommended for pregnant women or women expecting to become pregnant.

Breastfeeding is not contraindicated in women taking isoniazid. Give vitamin B6 supplements to nursing women on isoniazid and their breastfed infants. The amount of isoniazid in breast milk is very small, so if a breastfed infant has TB infection, he or she needs to be given isoniazid.

Children under 5 with TB infection are at high risk of progressing to TB disease. Consider testing adults who are close to the infected child to see if they have infectious TB disease. The preferred regimen for children aged 2 to 11 years is 9 months of daily isoniazid. Monitor serum liver enzymes only if the child is at risk for hepatotoxicity. The risk of isoniazid-related hepatitis in infants, children and adolescents is minimal. Consider DOT for children of all ages, especially those on the 12-dose regimen, although the 12-dose regimen isn't recommended for children younger than 2. There are many adherence strategies, such as crushing pills and mixing them with food, to get children to complete treatment.

You may have some concerns about treating patients for TB infection. Common concerns of community providers include the length of treatment, potential side effects, as well as the need for monthly clinical evaluation. As with any treatment, you must weigh the risks and benefits for each individual patient. Visit the CDC's website and call your local TB program if you have any questions about side effects and drug interactions.

Adverse Effects

Let's talk now about some adverse effects of medications for TB infection, as well as how to monitor patients and ensure adherence.

There are several possible adverse effects of isoniazid. Asymptomatic elevation of serum liver enzyme concentrations occurs in 10 to 20 percent of people, and usually returns to normal when treatment is discontinued. It's generally recommended to withhold isoniazid if transanimase levels exceed 3 times the upper limits of normal with symptoms, and 5 times the upper limit if patients have no symptoms .

A very small percentage of people taking isoniazid may develop hepatotoxicity. The risk factors include alcohol use, liver disease, or the risk of liver disease, and the use of other medicines that are broken down in the liver.

A very small percentage of people taking isoniazid may develop peripheral neuropathy. This is more likely with other conditions such as diabetes, HIV infection, renal failure, and alcoholism. Give a vitamin B6 supplement if a patient has any of these conditions.

Now, let's talk about possible adverse effects of rifampin and rifapentine. A small percentage of patients may experience hepatotoxicity. Patients may also experience gastrointestinal symptoms, such as nausea, anorexia and abdominal pain. However,

gastrointestinal symptoms are not usually severe enough to stop treatment. Some patients taking rifampin may also experience skin reactions, such as pruritus, and flu-like symptoms.

Hypersensitivity is a rare side effect associated with an intermittent Rifapentine regimen. Hypersensitivity may cause fever, headache, dizziness, pain, petechiae, and pruritis. Keep vigilant for more severe hypersensitivity reactions, such as hypotension and thrombocytopenia.

Tell patients taking rifampin or rifapentine they will notice a normal orange discoloration of body fluids, including urine and tears. Contact lenses may be permanently stained. Get a list of all other medications a patient is taking. Rifampin and rifapentine can interact with many other drugs, such as methadone, warfarin, hormonal contraceptives and phenytoin. Patients on these medications require close monitoring. Tell women to use a barrier method of birth control while they are taking either rifampin or rifapentine, because their hormonal contraceptives may not be as effective.

To make sure treatment for TB infection is safe and effective, periodically check on your patient. To assess the patient's progress, conduct clinical monitoring, provide education and order appropriate lab tests. Vigilance for hypersensitivities is important. See the patient on a monthly basis to look for signs of hepatitis, assess adherence and review symptoms of adverse effects.

Some patients need baseline liver function tests. Get baseline testing for patients with liver disease, regular alcohol use, HIV infection, risk factors for liver disease, patients on other hepatotoxic medications, and women who are pregnant or post-partum. Periodic retesting is recommended for people with initial abnormal results and for those who are at risk of liver disease. Get lab tests if a patient develops any symptoms of hepatitis. These symptoms include fatigue, weakness, malaise, anorexia, nausea, vomiting, abdominal pain, pale stools, dark urine, chills and jaundice. Tell patients to stop treatment and seek medical attention immediately if they develop any of those symptoms.

Regular patient education is vital. Clearly explain TB infection and why treatment is critical. Be sure to communicate in language the patient can understand. Educate patients and caregivers about the importance of good adherence. Emphasize possible side effects and adverse reactions. Provide patients with written instructions for adverse effects, and tell patients to stop treatment and promptly seek medical evaluation if any adverse effects occur. Report any adverse events to the

CDC Division of Tuberculosis Elimination by email to this address (LTBIdrugevents@cdc.gov)

Adherence

Many things can affect a patient's adherence to their treatment for TB infection. Barriers to completing treatment can involve clinic services, the patient, or the medications. If patients have to wait a long time to get an appointment, or to actually see the doctor, they may have difficulty completing treatment. Patients may face other barriers, including poverty, transportation, cultural differences, language, and other medical conditions. The medications themselves can be a barrier, including length of treatment, side effects, getting refills, the number of clinic visits and co-pays. Talk to your patient about any concerns he or she has. Discuss together how to address them before starting treatment.

Work with your local health department to provide DOT, case management, free or low cost medicines, incentives and other assistance. Use DOT for high risk patients and people on the 12 dose regimen.

Follow-up with patients after they finish treatment for TB infection. Provide documentation that includes name, TB test and radiograph results, dates, and dosage and duration of medication. Review the signs and symptoms of TB disease, and tell patients to contact you if they develop any of them. Remember, diagnosing and treating TB infection is an important part of preventing TB disease in our community.

Thank you for viewing this video on treatment of TB infection, which is the third in a series. The other videos discuss screening and diagnosis. For more information, visit this website www.umdnj.edu/ntbcweb/products/ltbimultimedia.htm.