LTBI Videos-Treating Latent TB Infection

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 primary care providers. In this video, you'll learn about treatment for latent TB infection, also called L-T-B-I or TB infection. We'll discuss the rationale for treating LTBI, general treatment guidelines, available treatment regimens, special circumstances, and patient education and adherence. Other videos discuss screening, diagnosis, and monitoring patients on LTBI treatment.

Why treat LTBI?

Although people with LTBI are not sick and cannot spread TB to others, there *is* a risk that if untreated, the bacteria can overcome the person's immune defenses and multiply, causing TB disease. Treating LTBI prevents infected people from getting sick with TB disease and becoming infectious to others, which helps prevent transmission.

Treatment is recommended for almost all patients with LTBI. However, if resources are limited, treatment *should* be prioritized for those with a higher risk for progression to TB disease, or for developing severe disease, if infected. Groups at higher risk are listed in the boxes on the screen. This includes those with immunosuppression, organ transplant recipients, and children younger than 5 years of age, who can progress to TB disease very quickly. Others at higher risk include people who were recently infected, known as contacts, those with a history of untreated or inadequately treated TB disease, and those with certain health conditions, such as diabetes and chronic kidney disease.

It is important to exclude TB disease *before* beginning LTBI treatment, since treating a person for LTBI when they really have TB disease can lead to poor outcomes including drug resistance. View the video on diagnosing LTBI for more information.

Common concerns about treating patients for LTBI include the length of treatment, potential adverse drug reactions, and the need for monthly clinical evaluation. However, treatment regimens are safe *and* effective. Serious adverse drug reactions are rare, and the risk of hepatotoxicity is minimal in most patients and should not deter treatment. Certain patients *are* at a higher risk for hepatotoxicity, so this can be considered in both regimen selection and in the monitoring plan. More information can be found in the video on monitoring and in the resource link at the end of this video. As with any treatment, you must weigh the risks and benefits for individual patients.

General Treatment Guidelines

In general, dosage for LTBI regimens is based on weight. For more information about dosing for the regimens described in this video, please see this website. Baseline laboratory tests, such as LFTs, are *not* routinely indicated before initiating treatment, however, they should be obtained for the groups listed on your screen. More information can be found in the video on monitoring.

Although most treatment regimens for LTBI can be self-administered, directly observed therapy, or D-O-T, can be considered for patients who have a high risk of progression to TB disease, including the groups listed on your screen. With D-O-T, a healthcare worker observes a patient swallowing their TB medication. Some health departments may have guidelines for use of D-O-T for certain individuals, such as children less than five years of age who have been exposed to a person with infectious TB or anyone who is a contact to someone with multi-drug resistant TB, however this may not be possible outside of public health settings. Some health departments *may* be able to assist with D-O-T, including video-based D-OT, for these individuals. Contact your health department for information on local guidelines and resources.

Treatment Regimens

There are several treatment regimens available for LTBI. While all the recommended regimens listed on your screen are effective at preventing TB disease, CDC and the National Tuberculosis Controllers Association now indicate that shorter, rifamycin-based regimens are preferred over longer regimens of 6 to 9 months of monotherapy with isoniazid, which is often called I-N-H. These short-course regimens are effective, safe, *and* have higher completion rates than the longer regimens. They also generally have a lower risk for hepatotoxicity than isoniazid monotherapy.

For many patients there are several acceptable regimens. Regimen selection will depend on clinical factors, such as other medical conditions or drug-drug interactions as well as availability, patient preferences, resources available to providers, state and local recommendations, and other variables that might affect adherence. We'll discuss these factors later. Remember, shorter regimens help patients finish treatment!

The 12-dose regimen of once weekly isoniazid and rifapentine is one of the preferred regimens and can be used in adults and children 2 years of age or older, including people with HIV, as drug interactions allow.

Rifamycins can have significant drug interactions with other medications, including, but not limited to those listed on your screen. Since rifamycins can reduce concentrations of some medications, dose adjustments of the companion medications may be needed. Drug interactions with weekly rifapentine are fewer than with rifampin. Thus, the 12-dose, once-weekly regimen can be considered when rifampin is contraindicated.

Don't use the 12-dose regimen for children younger than 2 years of age, pregnant women or those expecting to become pregnant, or people who may be infected with TB that is resistant to isoniazid or rifampin. This regimen should not be used in people with HIV who are taking antiretroviral medications with clinically significant or unknown drug interactions with once-

weekly rifapentine. The pill burden per dose is higher with this regimen, however the total number of doses is much lower. This regimen can be provided by D-O-T or self-administered therapy. Choose the mode of administration based on local practice, individual patient attributes and preferences, and other considerations, including risk for progression to severe forms of TB disease.

Although many patients and providers prefer the 12-dose isoniazid and rifapentine regimen due to the shorter duration, intermittent dosing, and higher completion rates, in some cases, rifapentine may not be readily available.

Four months of daily rifampin is also considered a preferred regimen and is indicated for use in HIV-negative adults and children of all ages. This regimen may be indicated for people who cannot tolerate INH or who have been exposed to TB that is resistant to INH only. It may be possible to use this regimen for other populations as well; expert consultation is recommended. If rifampin cannot be used due to drug-drug interactions, in some cases, rifabutin, another rifamycin *may* be substituted in consultation with a TB expert.

The third preferred regimen identified by CDC is 3 months of daily isoniazid and rifampin. This regimen can be used for adults and children of all ages, including those with HIV, as drug interactions allow. However, this regimen is not as widely used by TB programs in the United States, so be sure to consult your state or local guidelines.

When short-course treatment is not an option, for example due to drug-drug interactions, an alternate regimen of 6 or 9 months of isoniazid can be used in adults and children of all ages. I-N-H can be provided daily or bi-weekly, though D-O-T *must* be used for intermittent dosing. Although this regimen has good efficacy, treatment completion rates are lower than for the shorter rifamycin-based treatment options. Additionally, 6 or 9 months of daily I-N-H has a higher liver toxicity risk than shorter rifamycin-based regimens.

If you feel that none of these options are appropriate for your patient, consult your health department for other treatment options.

Pyridoxine supplementation

Some patients on isoniazid containing regimens should receive pyridoxine supplementation to prevent peripheral neuropathy. Less than 1% of people taking I-N-H at conventional doses develop neuropathy, which is more likely to occur in those with HIV infection, diabetes, alcoholism, malnutrition, pregnancy, or other conditions associated with neuropathy. Individuals with these conditions on the 12-dose isoniazid and rifapentine regimen should be given 50 milligrams of vitamin B6 per week. Individuals on other I-N-H-containing regimens should get 25-50 milligrams per day.

Special Circumstances

Children

If a child tests positive for LTBI, consider testing adults who are close to the infected child to see if they have infectious TB disease.

Treatment of LTBI in children younger than 5 is especially important, since they are at a high risk of progressing to severe forms of TB disease. The risk of isoniazid-related hepatitis in infants, children, and adolescents is minimal. Shorter rifamycin-based regimens are also preferred in children, though the 12-dose isoniazid-rifapentine regimen should not be used in children younger than 2 years of age. If possible, consider D-O-T for children, especially those younger than five, and those on the 12-dose isoniazid and rifapentine regimen. Given the increased risk of progression to severe TB disease in young children as well as the smaller number of doses in the once-weekly isoniazid and rifapentine regimen, it is important to ensure that doses are not missed.

Although a liquid isoniazid preparation is available and both I-N-H and rifampin can be compounded by a pharmacy, these preparations contain sorbitol, which can cause diarrhea, cramping, and abdominal pain and are generally not recommended. There are many strategies, such as crushing pills and mixing them with food which are very successful and can be used in most children. See the resource list for more information.

People with HIV

Treatment of LTBI in people with HIV will depend on their current or planned antiretroviral regimen. Recommendations are updated frequently, so visit this website for current guidelines and more information on drug-drug interactions with HIV antiretrovirals. LTBI treatment for people with HIV should be provided in consultation with an expert in the management of HIV and TB infection.

Contacts

A contact is someone who was recently exposed to a person with infectious TB disease. Since people who are recently infected have an increased risk of progression to TB disease, prompt evaluation and treatment is indicated. Some primary care providers may not be involved in treatment of contacts; if you are, be sure to work closely with your local health department. For more information about evaluation of contacts, view the video on diagnosis of LTBI. Remember, all contacts whose initial TB test is negative should be re-tested 8 to 10 weeks after their last exposure, since it can take this amount of time for an immune response to develop.

Some contacts should be started on treatment for LTBI even if their *initial* test for TB infection is negative, as long as their chest radiograph is normal and TB disease has been excluded. This treatment, known as window prophylaxis or window period treatment, is indicated for contacts younger than 5 years of age and those who are severely immunosuppressed, because of the risk of progression to severe disease. TB disease may present differently in these individuals, so expert consultation is recommended.

Continue window prophylaxis in children younger than 5 or immunosuppressed children until you know the results of the repeat test for TB infection. If the repeat test is positive, the child should have a careful evaluation for TB disease, which should include a history, physical exam, and chest radiograph. If TB disease is excluded, LTBI treatment should be continued to the completion of therapy. Window prophylaxis may be discontinued in a healthy child if the repeat TB test is negative.

Immunosuppressed children whose repeat TB test is negative should continue LTBI treatment until the completion of therapy, after an evaluation for TB disease. Some experts may also continue treatment in very young infants, based on the individual circumstance. Consult with your local health department in these situations.

More severely immunosuppressed adults, such as people with HIV, who are receiving window prophylaxis should be treated using one of the preferred regimens, as drug interactions allow, *after* a careful evaluation to exclude TB disease. Treatment is sometimes continued in persons with HIV or other severely immunosuppressed individuals who are contacts, even if the repeat test is negative since false negative tests are more likely in these individuals.

Patient Education and Adherence

Educate your patients regularly to help ensure that those with LTBI begin *and* complete treatment. Describe the difference between latent TB infection and TB disease. Explain that people with TB infection have inactive TB bacteria in their body and that treating TB infection will kill the bacteria and prevent them from getting sick with TB disease. Focus on your patient's risk factors for progression to disease. There may be ethnic and cultural factors and health beliefs that influence a person's understanding of TB, or their willingness to be treated. Consider this while providing education about TB infection and consider patient preferences when selecting a regimen.

Be sure to communicate in language the patient can understand and use educational messages and materials that are culturally appropriate. Educate patients and caregivers about the importance of good adherence and reinforce this message at monthly monitoring visits. Links to patient education materials can be found in the resource list for this video.

Describe possible side effects and adverse reactions and tell your patients to seek medical attention if adverse reactions occur. Provide guidance on when to stop treatment in the case of serious adverse reactions and give patients written instructions and contact information for your office, so they can inform you if these occur. Potential adverse effects for specific medications and regimens are discussed in the video on monitoring.

Identifying and addressing misconceptions and barriers can contribute to adherence. Barriers can involve clinic services, the patient, or the medications. For example, treatment completion may be impacted if people have to wait a long time for an appointment or to see the doctor. Patients may face other barriers, including economic, transportation, language, and other medical conditions. Barriers related to medications include the length of treatment, side effects, getting refills, or the number of clinic visits and co-pays. Using short-course rifamycin-based regimens can

improve adherence and contribute to successful completion of treatment. Talk to your patient about any concerns they have and try to address them before initiating treatment.

Remember, your local health department may be able to assist with providing, free or low-cost medications, D-O-T, case management, or other assistance for individuals with an increased risk of progression to TB disease.

Follow up with your patients after they finish LTBI treatment. Provide documentation that includes TB test and radiograph results, dates, dose of medication, and the duration and total number of doses completed. Review the signs and symptoms of TB disease and tell your patients to contact you if they develop these symptoms.

Conclusion

Remember, treating LTBI *and* helping patients successfully complete treatment is an important part of preventing TB disease. This video presented the basics of treating LTBI, including the available treatment regimens, which are shown on your screen. The preferred shorter rifamycin based regimens are safe, effective, and have higher completion rates than isoniazid monotherapy. Consult an expert for more complex situations, such as treatment of LTBI in very young children, contacts ~~to~~ of those with drug-resistant TB, or other treatment options when rifampin cannot be used.

Thank you for viewing this video on treating latent TB infection, which is the third in a series. The other videos discuss screening, diagnosis, and monitoring those on treatment. For more information and the additional resources mentioned in this video, visit this website: globaltb.njms.rutgers.edu/