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Tuberculosis: A New Screening Recommendation and an Expanded Approach to Elimination in the United States:

A review of risk assessment, testing, and treatment.

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Abstract

Nurses play a critical role in the diagnosis and treatment of tuberculosis and in the prevention of tuberculosis transmission through infection control practices. To eliminate tuberculosis in the United States, however, an expanded approach to testing and treating people with latent tuberculosis infection must be implemented. Recently, the U.S. Preventive Services Task Force (USPSTF) issued a new recommendation statement on latent tuberculosis infection testing that expands nurses' opportunities to identify at-risk populations for tuberculosis prevention. In combination with newer testing methodologies and shorter treatment regimens, implementation of the USPSTF recommendation has the potential to remove previously existing barriers to screening and treatment of both patients and health care providers. This article provides a general overview of tuberculosis transmission, pathogenesis, and epidemiology; presents preventive care recommendations for targeted testing among high-risk groups; and discusses the USPSTF recommendation's applicability to public health and primary care practice in the United States.

Keywords

latent tuberculosis infection; tuberculosis; tuberculosis disease; tuberculosis testing; tuberculosis treatment

A nurse at your clinic had been coughing for a few months, but dismissed it as seasonal allergies. The nurse's annual tuberculosis test was positive, and after a chest X-ray, medical examination, and sputum laboratory results, the nurse was diagnosed with tuberculosis. The health department estimates that the nurse may have been infectious for two months prior, exposing patients, visitors, and staff to *Mycobacterium tuberculosis*. Immuno-compromised adult patients and children who had been in close contact with the nurse are of special concern to the health department. Clinic staff members are concerned about the risk of transmitting tuberculosis to their own families.

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Health workers from the Duval County Health Department and other Florida health agencies test homeless citizens for tuberculosis in downtown Jacksonville. Photo by Bob Mack, AP Photo /The Florida Times-Union.

This fictional scenario describes one way tuberculosis can present a risk to health care workers, their families, and their patients. Tuberculosis in health care workers is not common, but still occurs too frequently in the United States. According to data from the National Tuberculosis Surveillance System, approximately 350 health care workers were diagnosed with tuberculosis in 2015, accounting for 3.9% of total cases.[1] Tuberculosis transmission involving health care workers has been seen in hospitals, clinics, and long-term care facilities.[2–4] The adoption of tuberculosis infection control measures has decreased the number of tuberculosis outbreaks and incidents of tuberculosis transmission to patients and health care workers. Proven tuberculosis control practices, such as infection control measures and active tuberculosis case finding and treatment, are essential elements of a tuberculosis elimination strategy. This article will discuss preventing tuberculosis disease from developing through targeted testing and treatment of latent tuberculosis infection to provide an even greater impact on reducing future cases of tuberculosis disease.

Background

Tuberculosis was a leading cause of death in the United States in the early 20th century. Medical and public health interventions resulted in a steady decline in cases that began in the mid-1950s and continued until the early 1990s, when a tuberculosis resurgence occurred. The resurgence was associated with the emergence of the HIV epidemic, increased immigration from countries with high tuberculosis rates, and declines in funding of tuberculosis control programs in many jurisdictions. After a major reinvestment in tuberculosis control activities at all levels of government, tuberculosis cases began to decline again in 1993. However, after two decades of decline, tuberculosis incidence in the United

States has now stalled at approximately three cases per 100,000 persons. In fact, after having declined yearly from 1993 to 2014, the overall number of tuberculosis cases in the United States increased slightly in 2015, from 9,406 to 9,557.[1] (See Figure 1.)

Epidemiologic modeling suggests that tuberculosis elimination, defined as less than one tuberculosis case per 1 million persons per year, will not occur by the end of this century given the annual declines observed over the past two decades.[5] Achieving tuberculosis elimination in the United States will require a substantial improvement in identification and treatment of latent tuberculosis infection among high-risk groups who live in this country, while at the same time continuing to focus on active tuberculosis case finding and treatment. New and expanded approaches to and partnerships for tuberculosis prevention and control are necessary to achieve this goal.[1]

In 2016, the U.S. Preventive Services Task Force (USPSTF) issued a recommendation statement on testing asymptomatic adults ages 18 and older who are at increased risk for tuberculosis.[6] This was the first USPSTF recommendation statement issued on tuberculosis testing since 1996.[7] It urges health care providers to assess their patients' risk of latent tuberculosis infection by considering the country of origin of foreign-born persons and whether patients live or have lived in high-risk congregate settings such as homeless shelters and correctional facilities. The USPSTF assigned a "B" grade to its screening recommendation, meaning that the recommended service has more potential benefits than potential harms for the population covered.[6] Under the Affordable Care Act, services recommended by the USPSTF with grades of "A" or "B" should be provided with no co-pay or deductible costs for insured persons.[8]

This new screening recommendation complements existing guidelines for latent tuberculosis infection testing, including those of the Centers for Disease Control and Prevention (CDC), the American Academy of Pediatrics, and the American Thoracic Society.[9–12] In addition to removing cost barriers, newer testing methodologies and shorter treatment regimens have the potential to remove previously existing barriers such as multiple clinic visits for testing and long months of treatment. (For recommendations from the USPSTF and the CDC, see *Latent Tuberculosis Infection Screening Recommendations*.)

Latent Tuberculosis Infection Screening Recommendations

U.S. Preventive Services Task Force

Screening for Latent Tuberculosis Infection in Adults

Foreign born

People who were born in, or are former residents of, countries with increased tuberculosis prevalence: http://jamanetwork.com/journals/jama/fullarticle/2547762

Congregate settings

People who live in, or have lived in, high-risk congregate settings (such as homeless shelters and correctional facilities): http://jamanetwork.com/journals/jama/fullarticle/2547762

Centers for Disease Control and Prevention

Recommendations for Tuberculosis Testing

Health care workers

Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health care settings: www.cdc.gov/mmwr/preview/mmwrhtml/rr5417a1.htm?s_cid=rr5417a1_e

People exposed to someone with tuberculosis disease

Guidelines for the investigation of contacts of persons with infectious tuberculosis: www.cdc.gov/mmwr/preview/mmwrhtml/rr5415a1.htm

People with weakened immune systems

Targeted tuberculin testing and treatment of latent tuberculosis infection: www.cdc.gov/mmwr/preview/mmwrhtml/rr4906a1.htm

Children

Recommendations for preventive pediatric health care: www.aap.org/en-us/Documents/periodicity_schedule.pdf

TRANSMISSION, PATHOGENESIS, EPIDEMIOLOGY

Transmission

Tuberculosis is most commonly spread from person to person through the air. When a person with infectious tuberculosis disease coughs, speaks, or sings, tiny particles containing *M. tuberculosis* are expelled into the air.[13] These particles, called droplet nuclei, are about 1 to 5 microns in diameter—less than 1/5000th of an inch. Droplet nuclei can remain suspended in the air for several hours, depending on the environment.[14] If another person inhales air that contains these droplet nuclei, infection may occur; but not everyone who is exposed to a person with infectious tuberculosis disease becomes infected with *M. tuberculosis*. The probability that tuberculosis will be transmitted depends on patient characteristics and environmental factors. For example, a person who has tuberculosis disease of the lung or throat is most infectious when chest radiographs show cavitation, and the person doesn't cover her or his mouth and nose when coughing. Environmental factors, such as exposure to *M. tuberculosis* in a small, enclosed space with recirculated air containing infectious droplet nuclei, increase the probability of transmission of *M. tuberculosis*.[10]

Pathogenesis

When a person inhales air with droplets containing *M. tuberculosis*, most of the larger droplets become lodged in the upper respiratory tract, where infection is unlikely to develop. Infection most often occurs when smaller droplet nuclei containing tubercle bacilli reach the alveoli of the lungs. In the alveoli, most of the tubercle bacilli are killed by the immune system. However, the few remaining live bacilli can multiply and spread throughout the body via the bloodstream. Tuberculosis disease is most likely to develop in the apex of the

lung, but can also occur in the kidneys, the brain, and bone. Tubercle bacilli can also spread through lymphatic channels to the lymph nodes.

In people who have a healthy immune system, the body is able to stop the multiplication of the bacilli within weeks after infection, preventing further spread. At this point, the person has latent tuberculosis infection, which can be detected by a tuberculosis test two to eight weeks after infection. A person who has latent tuberculosis infection isn't considered a case of tuberculosis and isn't infectious—that is, she or he cannot spread the infection to others.[15]

When the immune system can't stop tuberculosis bacteria from growing, latent tuberculosis infection progresses to tuberculosis disease. Without treatment, approximately 5% of people with latent tuberculosis infection develop tuberculosis disease within one to two years after becoming infected. Another 5% of people with untreated latent tuberculosis infection will get sick years later, when their immune system becomes weak for another reason. Therefore, without treatment, approximately 10% of people with latent tuberculosis infection will progress to tuberculosis disease.[16] For the differences between latent tuberculosis infection and tuberculosis disease, see Table 1.

Epidemiology

Among the 9,557 tuberculosis cases reported in the United States in 2015, a third (n = 3,186; 33.3%) occurred among U.S.-born persons; two-thirds (n = 6,350; 66.4%) occurred among foreign-born persons.[1] Tuberculosis disease is a nationally notifiable disease: health care providers are required by law to notify state public health authorities of a case of tuberculosis disease. However, latent tuberculosis infection is not a nationally notifiable disease. Latent tuberculosis infection data collection and surveillance varies from state to state. The CDC estimates that up to 13 million people in the United States are living with latent tuberculosis infection and that more than 85% of U.S. cases of tuberculosis disease each year are the result of reactivated infection instead of recent transmission.[5, 17]

The rest of this article will focus on improving the identification and treatment of latent tuberculosis infection among high-risk populations, including foreign-born persons living in the United States, those who live or have lived in high-risk congregate settings, and those who work in health care settings. We discuss preventive care recommendations for targeted testing among these and other high-risk groups and their applicability to U.S. public health and primary care practice.

LATENT TUBERCULOSIS INFECTION RISK ASSESSMENT, TESTING, AND DIAGNOSIS

Risk assessment

People at risk for developing tuberculosis disease fall into two broad categories: those at increased risk for exposure to tuberculosis disease and those at increased risk for progression to tuberculosis disease if infected. Foreign-born persons, those who live or have lived in congregate settings, and health care workers are among those who have an increased likelihood of exposure to people with tuberculosis disease and should be tested for

tuberculosis infection.[10] In addition, people with clinical conditions or other factors associated with an increased risk of progression from latent tuberculosis infection to tuberculosis disease should also be tested.[9] For a complete list of factors associated with increased risk of exposure to or infection with *M. tuberculosis*, as well as factors associated with increased risk of progression from latent tuberculosis infection to tuberculosis disease, see *Tuberculosis Risk Factors*.[15, 18]

Tuberculosis Risk Factors[15, 18]

People at high risk for exposure to or infection with *Mycobacterium tuberculosis* include:

- close contacts of a person with infectious tuberculosis disease
- persons who are from, or who frequently travel to, areas of the world with high rates of tuberculosis
- persons who live or work in high-risk congregate settings (for example, nursing homes, homeless shelters, or correctional facilities)
- health care workers who serve patients who are at increased risk for tuberculosis disease

People at high risk for developing tuberculosis disease after infection with *M. tuberculosis* include:

- children younger than 5 years of age
- persons with any of the following:
  - HIV infection
  - substance abuse
  - silicosis
  - diabetes mellitus
  - severe kidney disease
  - low body weight
  - organ transplant
  - head and neck cancer
  - gastrectomy/gastric bypass
- persons receiving immunosuppressive therapy, including medical treatments with tumor necrosis factor-a antagonists or cor-ticosteroids, or specialized treatment for rheumatoid arthritis or Crohn's disease
- cigarette smokers and persons who abuse drugs or alcohol
- persons recently infected with *M. tuberculosis* (within the past 23years)

- persons with a history of untreated or inadequately treated tuberculosis disease

Foreign-born persons—The USPSTF recommendation statement on latent tuberculosis infection screening encourages health care providers to consider foreign-born patients' country of origin in assessing their risk of latent tuberculosis infection. The recommendation applies to asymptomatic adults ages 18 years and older who were born in or are former residents of countries with increased tuberculosis prevalence.[6, 19]

According to the CDC, the disparity in tuberculosis incidence in the United States between U.S.-born and foreign-born persons continued to increase in 2015, with a case rate among the foreign born that was approximately 13 times higher than that among the U.S. born (15.1 versus 1.2 cases per 100,000 persons).[1] More than half (57%) of all foreign-born persons with tuberculosis disease in the United States originated in five countries: Mexico, the Philippines, India, Vietnam, and China.[1] Haiti and Guatemala are also important contributors to U.S. tuberculosis disease cases. For complete and current data on tuberculosis rates by country, see the World Health Organization's *Global Tuberculosis Report 2016* at www.who.int/tb/publications/global_report/en. Because of regional variations in at-risk populations, the USPSTF encourages clinicians to consult local or state public health agencies for additional details on specific at-risk populations in their community.[6]

Cases among foreign-born persons most often occur years after their arrival in the United States, which is consistent with disease progression after years of untreated latent tuberculosis infection.[1] Treating those with latent tuberculosis infection could, therefore, have a significant impact on reducing future cases of tuberculosis disease. Health care providers who care for large numbers of foreign-born persons should, therefore, be prepared to offer testing for tuberculosis infection. In addition to offering to test those born in countries with high tuberculosis prevalence, health care providers may also consider offering testing to those who have traveled to or resided in countries with a high tuberculosis prevalence, especially those who have had exposure to local at-risk populations.

People who live or have lived in congregate settings—The USPSTF recommendation statement includes those who live or have lived in high-risk congregate settings, such as shelters, prisons, nursing homes, and residential institutions. In 2015, among those in the United States ages 15 years and older with tuberculosis disease, the CDC found that 5.5% had been homeless within the past year, 1.9% had been long-term care facility residents, and 3.6% had been in a correctional facility at the time of diagnosis.[1] Published prevalence rates of latent tuberculosis infection in these settings vary widely, ranging from 23.1% to 87.6% among prisoners, and from 18.6% to 79.8% among the homeless.[20] Therefore, providers may find additional opportunities for testing by asking patients whether they live or have lived in congregate settings.

Health care workers are potentially at increased risk for exposure as a result of their work with people who have undiagnosed tuberculosis disease. Recommended tuberculosis testing

programs in health care settings include initial two-step tuberculosis skin testing or a tuberculosis blood test upon hire, and annual or serial testing as determined by state regulations and facility risk assessment.[10] As a result of these testing programs, many health care workers are aware that they're infected with tuberculosis. For their own health and because active tuberculosis disease puts patients, coworkers, and family members at risk, these health care workers should consider latent tuberculosis infection treatment to prevent progression to disease.

Health care workers who have had a positive test result for tuberculosis infection should be promptly evaluated for tuberculosis disease. Of special concern are health care workers with a newly positive test result for tuberculosis infection, as recent infection is a risk factor for progression to tuberculosis disease. In fact, the greatest risk for progression occurs within the first two years after infection. Once tuberculosis disease has been ruled out, treatment for latent tuberculosis infection should be offered to health care workers who are eligible through employee health services or in coordination with a private physician. Results from tuberculosis tests and records of completed treatment for latent tuberculosis infection should be documented as part of the employee's health record. Regulations on tuberculosis testing, treatment, and infection control for health care workers vary from facility to facility. For assistance with the planning and implementation of tuberculosis control activities in the health care setting, and for information on state and local regulations, health care facilities should coordinate with a local or state tuberculosis control program. A complete list of state tuberculosis control programs can be found at www.cdc.gov/tb/links/tboffices.htm.

People who have been exposed to someone with tuberculosis disease— Contact investigations are used to identify people exposed to those with infectious tuberculosis disease (referred to as contacts), assess exposed contacts for tuberculosis infection, and provide appropriate treatment for contacts found to have latent tuberculosis infection or tuberculosis disease. Tuberculosis patients in the United States have, on average, 11 contacts who may be at risk for tuberculosis infection; and of those, an average of three contacts become infected and may develop disease if not diagnosed and treated.[21] Public health departments make every effort to identify those who have been in close contact with someone who has infectious tuberculosis disease, and they can provide information on exposure risk to concerned individuals who know someone who has been included or have themselves been included in contact investigations.

People with weakened immune systems—Certain clinical conditions can weaken the immune system and, therefore, increase the risk of progression to tuberculosis disease among those with latent tuberculosis infection. People who have HIV, patients receiving immunosuppressive medications such as chemotherapy or tumor necrosis factor-α inhibitors, and organ transplant recipients are at increased risk. Other medical conditions associated with an increased risk of progression from latent tuberculosis infection to tuberculosis disease include silicosis, diabetes mellitus, chronic renal failure or hemodialysis, gastrectomy, jejunoileal bypass, and head and neck cancer.[18] Tuberculosis testing in these populations is recommended as part of standard disease management for these conditions or as indicated prior to the use of certain medications.[9]

Children, especially those younger than five years of age, who test positive for tuberculosis infection are likely to be in the early stage of infection and are at high risk for progression to active disease, with potential for disseminated tuberculosis and tuberculosis meningitis.[9, 22] Adolescents' and young adults' risk of developing active tuberculosis disease after exposure is less than that of young children, but greater than that of middle-aged and older adults.[9] A diagnosis of latent tuberculosis infection or tuberculosis disease in children younger than 15 years of age is a public health problem of special significance because it is a marker for recent tuberculosis transmission.

The American Academy of Pediatrics recommends annual tuberculosis infection testing for children infected with HIV and incarcerated adolescents. Children who are known contacts of a person with confirmed or suspected tuberculosis disease and children who were born in or have traveled to a high-risk country should also be tested for tuberculosis infection.[11] Clinicians may also want to consider the potential risk of tuberculosis infection in children who live in homes with visitors from high-risk countries who may have active tuberculosis disease.

Testing

There are two kinds of tests that can detect *M. tuberculosis* in the body: the tuberculin skin test (TST) and tuberculosis blood tests. A positive TST or tuberculosis blood test only indicates infection with *M. tuberculosis*; further tests are required to rule out tuberculosis disease.

Tuberculosis blood tests are called interferon-gamma release assays (IGRAs), and they're used to determine whether a person is infected with *M. tuberculosis* by measuring the immune response to tuberculosis proteins in whole blood.[23] IGRAs require a single venous blood sample and laboratory processing eight to 30 hours after collection. According to the CDC, to conduct the tests, "Specimens are mixed with peptides that simulate antigens derived from *M. tuberculosis* and controls. In a person infected with *M. tuberculosis*, the white blood cells recognize the simulated antigens and release interferon-gamma (IFN- γ); results are based on the amount of IFN- γ released."[18] is classified as negative, a second-step TST is administered one to three weeks later. Based on the results of the second-step TST, the person will be diagnosed as positive or negative for tuberculosis infection.[18] The U.S. Food and Drug Administration has approved two IGRAs that are commercially available in the United States: the QuantiFERON–TB Gold In-Tube test and the T-SPOT.*TB* test.[6, 18]

The TST is administered using the Mantoux technique by injecting 0.1 mL (5 tuberculin units) of purified protein derivative solution intradermally, usually on the forearm.[9] A person given the TST must return within 48 to 72 hours to have a trained health care worker look for a reaction on the arm showing induration, and if present, measure its size using a ruler. Redness or erythema by itself is not considered part of the reaction. The TST result depends on the size of the induration. It also depends on the person's risk of being infected with tuberculosis bacteria and the risk of progression to tuberculosis disease if infected.[23]

Some who are infected with *M. tuberculosis* may have a negative reaction to the TST if many years have passed since infection occurred. Yet they may have a positive reaction to a subsequent TST because the initial test stimulated their ability to react to the test. This is commonly referred to as the "booster phenomenon" and may incorrectly be interpreted as a TST conversion (going from negative to positive, indicating recent infection). For this reason, the "two-step method" is recommended at the time of initial testing for those who will be tested periodically, such as health care workers. If the reaction to the first-step TST

There are several advantages of IGRAs over the TST. First, whereas the TST requires two visits (one to place the test and a second for it to be read), an IGRA requires only a single visit to draw blood. Second, IGRA results are available within 24 hours—as compared with 48 to 72 hours for the TST—and can be communicated to the patient without requiring a second in-person visit.[18] Last, bacille Calmette–Guérin (BCG) vaccination, commonly used in many countries with high tuberculosis incidence to prevent tuberculosis meningitis in infants and young children, can cause false-positive TST reactions[24]; IGRAs use *M. tuberculosis*–specific antigens that don't respond to BCG antibodies. TST reactivity caused by the BCG vaccine generally wanes with the passage of time, but periodic skin testing may prolong (boost) reactivity. In general, a positive TST result indicates latent tuberculosis infection, especially in at-risk persons.[9] Given that it is not possible to determine if a positive TST reaction is due to BCG vaccination or infection with *M. tuberculosis*, the CDC recommends that TST reactions should be interpreted based on risk stratification regardless of BCG vaccination history.[23]

The TST is considered safe in children and is preferred over IGRAs in children less than five years of age because of difficulty in getting a blood draw.[23] IGRAs are the preferred tests for tuberculosis infection in children five years and older who have been vaccinated with BCG, although the TST is also acceptable.[11, 24, 25]

These advantages make IGRAs the preferred test for people (including children five years old and older) who have received BCG vaccination, and also for those unlikely to return for a TST reading.[23] A positive IGRA or TST result should be documented and included in the patient's medical record. Additional information on the use and interpretation of the TST and IGRA is available at www.cdc.gov/tb/publications/factsheets/testing/tb_testing.htm.

Diagnosis

A diagnosis of latent tuberculosis infection is made if a person has a positive IGRA or TST result and a medical evaluation does not indicate tuberculosis disease.[23] Tuberculosis disease is diagnosed by medical history, physical examination, chest radiograph, and other laboratory tests. The presence of tuberculosis disease must be excluded before treatment for latent tuberculosis infection is initiated.

While drug susceptibility testing (DST) is used to determine the most effective treatment regimen for tuberculosis disease, DST is not possible for latent tuberculosis infection, as its methods require a positive patient specimen. However, if a person to be treated for latent tuberculosis infection is a contact of a known source of infection (source case), and DST

results are available for that source, and the source case has drug-resistant tuberculosis disease, the treatment regimen should be modified appropriately.[18]

LATENT TUBERCULOSIS INFECTION TREATMENT

Treatment of latent tuberculosis infection is essential to controlling and eliminating tuberculosis in the United States, because it substantially reduces the risk that latent tuberculosis infection will progress to tuberculosis disease. Treatment for latent tuberculosis infection is 90% effective in preventing activation of tuberculosis disease.[9] Once the diagnosis of latent tuberculosis infection has been made, health care providers should choose the most appropriate and effective treatment regimen, and make every effort to ensure their patients complete the entire course of treatment. Treatment regimen, adverse effects, and completion date should be documented in the patient's medical records, in case the patient has another TST or IGRA in the future.

The CDC recommends four different treatment regimens for latent tuberculosis infection (see Table 2). These four regimens use isoniazid, rifapentine (Priftin), or rifampin (Rifadin). Treatment durations range from three to nine months. Depending on the regimen, patients may receive treatment daily, weekly, or on an intermittent basis. Providers should choose the appropriate regimen based on the following:

- drug susceptibility results of the presumed source case (if known)
- coexisting medical illness
- potential for drug–drug interactions

In addition, directly observed therapy (DOT), which requires each dose to be supervised (usually by a health care worker), should be considered for people who are at especially high risk for developing tuberculosis disease and may be nonadherent; and for those given a nondaily dosing regimen, such as three months of once-weekly isoniazid and rifapentine.[26] Some health departments have also found web-based video, mobile technology, or other devices to be effective ways to conduct DOT.[9, 27]

Three-month isoniazid and rifapentine (3HP) regimen

A recent advancement in latent tuberculosis infection treatment options is a regimen that combines isoniazid and rifapentine, and is administered once weekly for 12 weeks. This regimen is often referred to as 3HP, a term that derives its initialization from the regimen duration (three months) and the last letter of the abbreviation of each of the two drugs (INH and RIP). If possible, the 3HP regimen should be administered as DOT, because missed doses or altered dosing intervals or amounts could jeopardize efficacy or safety.[26] It has been shown to be effective at reducing tuberculosis disease in otherwise healthy people, 12 years of age and older, who were recently in contact with infectious tuberculosis or who had a newly positive TST or blood test for tuberculosis infection, and in those with radiologic findings consistent with healed pulmonary tuberculosis.[26] This shorter regimen is recommended as an option equivalent to the isoniazid nine-month daily regimen for treating latent tuberculosis infection.

The 3HP regimen offers practical advantages, such as completion of treatment within a limited time frame. The regimen may be used in otherwise healthy HIV-infected people, 12 years of age and older, who are not on antiretroviral medications. It may also be considered for children two to 11 years of age if completion of the preferred regimen of nine months of isoniazid is unlikely and risk of tuberculosis disease is great.

The 3HP regimen is *not* recommended for the following individuals because of unknown safety and drug interactions or known resistance[26]:

- children younger than two years of age
- persons with HIV–AIDS who are taking antiret-roviral therapy
- persons presumed to be infected with isoniazid- or rifampin-resistant *M. tuberculosis*
- pregnant women and women expecting to become pregnant while taking this regimen

Four-month rifampin regimen

A daily four-month rifampin regimen may be considered for people who cannot tolerate isoniazid or who have been exposed to isoniazid-resistant tuberculosis.[18] It should not be used to treat HIV-infected people taking some combinations of antiretroviral therapy. Because of reports of severe liver injury and deaths, the CDC recommends that the combination of rifampin and pyrazinamide should not be offered for the treatment of latent tuberculosis infection.

Six- and nine-month isoniazid regimens

There are two isoniazid regimen options: a six-month daily regimen and a nine-month daily regimen. (The six- and nine-month regimens can also be given twice weekly under DOT.) Of the two, the nine-month regimen is preferred because it is more efficacious. However, the six-month regimen provides substantial protection and is more cost-effective.[9] The six-month regimen may also result in greater patient adherence. Every effort should be made to ensure that patients adhere to latent tuberculosis infection treatment for at least six months. The preferred regimen for children two to 11 years of age is nine months of daily isoniazid.[18]

Monitoring during treatment

Clinical monitoring, including a brief physical examination, should occur at monthly visits to assess adherence and to identify signs or symptoms of adverse drug reactions.[18] Treatment should be modified if it is determined the patient is a contact of an individual with drug-resistant tuberculosis disease. Consultation with a tuberculosis expert is advised if the known source of tuberculosis infection has drug-resistant tuberculosis disease. Additional information about treatment regimens for latent tuberculosis infection is available at www.cdc.gov/tb/publications/factsheets/treatment/ltbitreatmentoptions.htm.

When a patient is pregnant (or has delivered within the previous three months), uses alcohol regularly, has HIV infection, or has a history of liver disease, baseline and follow-up monitoring of hepatic measurements of serum aspartate aminotransferase, ala-nine aminotransferase, and bilirubin are indicated to evaluate possible hepatotoxicity.[18] According to the CDC's *Latent Tuberculosis Infection: A Guide for Primary Health Care Providers*, "Asymptomatic elevation of serum liver enzyme concentrations occurs in 10%–20% of people taking [isoniazid]; and liver enzyme concentrations usually return to normal even when treatment is continued. . . . Hepatotoxicity. . . may occur in 0.6% of persons taking [rifampin]. Hepatitis is more likely when [rifampin] is combined with [isoniazid]."[18] Laboratory testing should also be performed if adverse reactions are reported during the treatment regimen.

NURSING IMPLICATIONS

Nurses in a variety of clinical and community settings have the opportunity to incorporate testing and treatment for latent tuberculosis infection into practice. Nurses in schools, colleges, and university clinics can advise at-risk students and provide DOT if needed. ED or urgent care nurses should be aware of tuberculosis symptoms to prevent misdiagnosis. Occupational health nurses might consider offering tuberculosis testing and treatment services if employees meet the high-risk criteria. Nurses who work in community health centers and private medical practices, especially those serving high-risk populations, can provide education and awareness in addition to testing and treatment services.

State, county, and local public health agencies have the primary responsibility for preventing and controlling tuberculosis in their jurisdictions, and serve as the public health authority on tuberculosis.[28] Public health nurses perform many of the fundamental services of tuberculosis control programs. In addition to surveillance and laboratory functions, tuberculosis control programs also find tuberculosis cases in the community and conduct contact investigations as needed. Some tuberculosis control programs also provide direct medical care to patients. However, many of those at high risk for latent tuberculosis infection and tuberculosis disease and who need to be tested and treated do not traditionally receive care in public health departments; rather, they receive care from private community providers and community health centers.

The USPSTF recommendation statement provides expanded opportunities for offering testing and treatment for latent tuberculosis infection to those who may not previously have been included in testing programs or who may be newly insured and are now accessing the primary health care system. Policymakers, health systems, public health agencies, and private practitioners will need to work together to incorporate the USPSTF recommendation into practice. The role of nurses in implementing the recommended targeted testing in the private sector is critical to success. Nurses in the private sector can support efforts to address latent tuberculosis infection by

- working with local or state tuberculosis control programs to learn about at-risk populations in their communities.

- educating patients and other health care practitioners on the importance of documenting tuberculosis infection status as part of a complete medical history, especially for at-risk patients.
- providing accurate information to patients and their families about confusing issues such as the difference between latent tuberculosis infection and tuberculosis disease, the meaning of tuberculosis test results, and modes of tuberculosis transmission and prevention.
- encouraging at-risk patients to consider treatment for latent tuberculosis infection, if indicated.
- helping patients overcome treatment barriers such as complex regimens and long duration, adverse effects, obtaining refills, and collaborating with local health departments to provide DOT when appropriate.

Nurses in tuberculosis control programs are an important resource for private community providers and community health clinics. In addition to providing insight into at-risk populations in the community, tuberculosis control programs can provide technical assistance and medical consultations. Tuberculosis control programs can also connect nurses with available training opportunities, guidelines, recommendations, and patient education materials. See *Resources for Nurses and Their Patients*.

Resources for Nurses and Their Patients

RESOURCES FOR NURSES

Centers for Disease Control and Prevention

www.cdc.gov/tb/education/provider_edmaterials.htm

- Latent Tuberculosis Infection: A Guide for Primary Health Care Providers
- *Latent Tuberculosis Infection: Guide for Diagnosis and Treatment (*mobile application for health care providers)
- *Guidelines for Preventing the Transmission of* M. tuberculosis *in Health-Care Settings, 2005 (slide set)*

  Free online training: www.cdc.gov/tb/publications/webcourseswebinars/default.htm

  - TB 101 for Health Care Workers
  - Interactive Core Curriculum on Tuberculosis: What the Clinician Should Know

  Find TB Resources

  https://findtbresources.cdc.gov

New York City Department of Health and Mental Hygiene, Bureau of Tuberculosis Control

Clinical Policies and Protocols

www1.nyc.gov/assets/doh/downloads/pdf/tb/tb-protocol.pdf

Regional Training and Medical Consultation Centers' TB Training and Education Products

https://sntc.medicine.ufl.edu/rtmccproducts.aspx

RESOURCES FOR PATIENTS

Centers for Disease Control and Prevention

Patient and General Public Materials

www.cdc.gov/tb/education/patient_edmaterials.htm

- factsheets
- booklets
- brochures
- posters

Achieving declines in tuberculosis incidence will require an expanded approach, including increasing detection and treatment of preexisting latent tuberculosis infection among the U.S. populations most affected by it. The CDC's Division of Tuberculosis Elimination views the USPSTF recommendation as a springboard for a dual approach to tuberculosis elimination: strengthening existing systems that interrupt ongoing tuberculosis transmission and increasing efforts focused on targeted testing and treatment of latent tuberculosis infection, particularly in those who reside in but were born outside the United States. Nurses, especially those serving at-risk populations, are critical partners in this effort.

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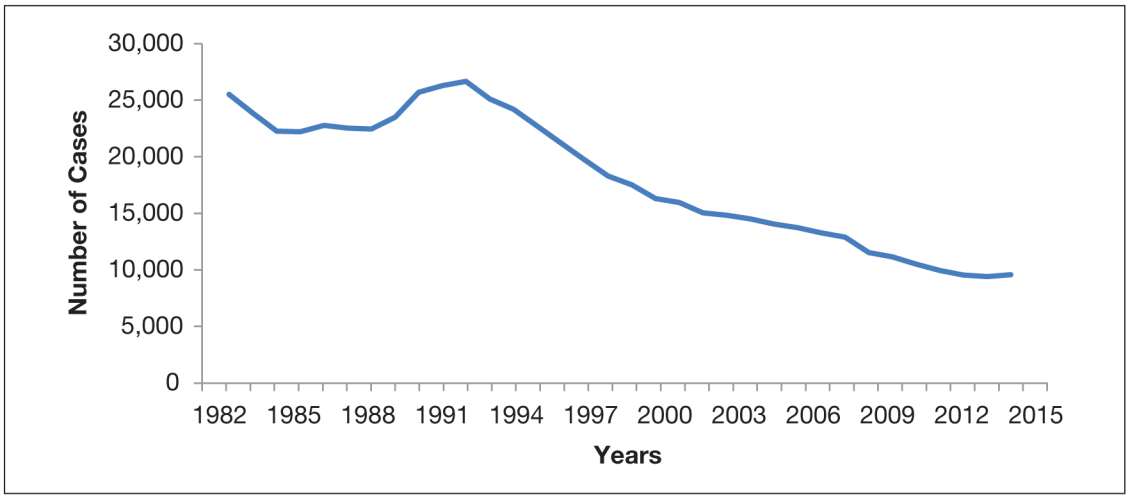

Figure 1.
Reported Tuberculosis Cases in the United States, 1982–2015

Table 1

The Difference Between Latent Tuberculosis Infection and Tuberculosis Disease

A Person with Latent Tuberculosis Infection . . .	**A Person with Tuberculosis Disease . . .**
• has no symptoms	• has symptoms that may include – a bad cough lasting 3 weeks or longer – pain in the chest – coughing up blood or sputum – weakness or fatigue – weight loss – no appetite – chills – fever – sweating at night
• does not feel sick	• usually feels sick
• cannot spread tuberculosis bacteria to others	• may spread tuberculosis bacteria to others
• usually has a skin test or blood test result indicating tuberculosis infection	• usually has a skin test or blood test result indicating tuberculosis infection
• has a normal chest radiograph and a negative sputum smear	• may have an abnormal chest radiograph, or positive sputum smear or culture
• needs treatment for latent tuberculosis infection to prevent tuberculosis disease	• needs treatment to treat tuberculosis disease

Table 2

Latent Tuberculosis Infection Treatment Regimens

Drugs	Duration	Interval	Comments
Isoniazid and rifapentine	3 months	Once weekly[a]	Treatment for: • persons 12 years old or older Not recommended for those who are: • younger than 2 years • living with HIV–AIDS and taking antiretroviral treatment • presumed to be infected with isoniazid- or rifampin-resistant *Mycobacterium tuberculosis* • pregnant or who expect to become pregnant within the 12-week regimen
Rifampin	4 months	Daily	
Isoniazid	6 months	Daily Twice weekly[a]	
Isoniazid	9 months	Daily	Preferred treatment for: • persons living with HIV • children ages 2–11 • pregnant women (with pyridoxine/vitamin B6 supplements)
		Twice weekly[a]	Preferred treatment for: • pregnant women (with pyridoxine/vitamin B6 supplements)

[a]Use directly observed therapy.

Note: Because of reports of severe liver injury and deaths, the CDC recommends that the combination of rifampin and pyrazinamide should not be offered for the treatment of latent tuberculosis infection.