Occupational Medicine Forum

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How to Evaluate a Positive Tuberculin Skin Test in the Workplace

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Tuberculosis has afflicted mankind for over 3000 years. Deformities noted in the skeletons of mummies had been suggestive of tuberculosis (TB), but it was not until 1997 that DNA evidence of tuberculosis in Ancient Africa was produced.[1] The Greeks were also familiar with tuberculosis, calling the disease Phthisis, meaning "consumption," because of the dramatic wasting that resulted from active disease. TB's infectious etiology was recognized in 1885 when Koch discovered the tubercle bacillus. In 1906, Albert Calmette and Camille Guerin developed the bacille Calmette-Guerin (BCG) vaccine, first used on humans in 1921, and in 1946, streptomycin was found to be effective against the disease.[2] Other antimycobacterial medications were subsequently developed.

Tuberculosis, a chronic granulomatous disease caused by the microorganism *Mycobacterium tuberculosis*, can lead to significant morbidity. Although it is treatable and curable, it is the most frequent cause of death in humans from an infectious agent worldwide,[3,4] leading to approximately 2 million deaths each year.[5,6] One third of the world's population is infected with tuberculosis,[5,6] and 8.3 million new tuberculosis infections occur worldwide each year.[3,4] During the Industrial Revolution, TB was epidemic in Europe and was responsible for 20% of deaths in England.[2] As a result of improved socioeconomic status and public health measures, as well as the subsequent arrival of antimycobacterial agents during the first half of the 20th century,[2] TB had been decreasing worldwide. However, TB saw a global resurgence in the latter half of the 20th century felt to be partially the result of the human immunodeficiency virus epidemic and the arrival of multidrug-resistant TB. Most of the new cases (80%) are seen in 23 countries with more than half being concentrated in Bangladesh, China, India, Indonesia, and Nigeria.[7] The United States saw a 20% increase in cases between 1955 and 1992, after which the upward trend started to reverse[8] as a result of effective TB control programs. Between 1992 and 2001, TB incidence in the United States decreased 40% and continues to steadily decline.[9]

Infectious patients disseminate disease by sneezing, coughing, or talking, expelling small infectious droplets in the air that remain suspended for several hours. Susceptible individuals inhale the particles and may become infected. The risk of being infected depends on exogenous factors such as intimacy and duration of contact, degree of infectiousness of the case, and the environment of contact.[10] The incubation period is 4 to 12 weeks, after which the infection may remain subclinical and dormant. The Mantoux tuberculin skin test (TST) using purified protein derivative (PPD) will be positive at this point. The organism can become activated at any time causing pulmonary or other localized or systemic disease.[10] Those infected have a 10% chance of developing active disease during their lifetime and most of this subset develops active disease within 1 to 2 years of infection. The risk of developing active disease depends on endogenous factors such as HIV infection, diabetes, silicosis, prolonged corticosteroid or immunosuppressive treatment, malignant neoplasms, and conditions associated with malnutrition.[2]

Tuberculosis is a disease of concern in occupational settings. The most notable at-risk occupational groups are those who work in healthcare facilities, correctional facilities, and homeless shelters.[11–14] However, occupational exposure to TB has been documented in many other occupational settings, including factories, funeral homes, churches, and hair dressing establishments.[15–18] Animal workers on farms, in research settings, or in zoos and circuses may also be at risk as a result to exposure to infected animals. Animals such as cows, goats, elephants, rhinoceroses, and monkeys[19,20] are susceptible to TB and can transmit

TB to humans. We also live during a time when TB is a global health problem and international travel is common. As a result, expatriate workers, aircraft personnel, and workers who travel frequently as a consequence of their employment are also at risk. Most cases of TB in the United States occur in recent immigrants from high TB prevalence countries who have been in the United States for less than 5 years[21]; as such, workplaces that employ a large proportion of recent immigrants may be at higher risk than those that do not.[22]

The occupational medicine (OM) physician with a high index of suspicion can play an important role in early detection of infectious cases and in the recognition of latent TB by identifying cases whose first presentation is at the workplace. New latent infections, which remain undiagnosed are a potential source of TB infection for years to come[23] as individuals with latent infections, may develop active disease over time and go on to infect others before they are diagnosed. TB transmission often occurs before the index case is diagnosed.[3,24] Treating latent TB infection (LTBI) derives public health benefit by decreasing the pool of latently infected individuals who can go on to active disease.[6] Occupational physicians who are conversant with the guidelines regarding placement and reading of a PPD, conducting a contact investigation, and diagnosing and treating latent TB infection, while collaborating with and referring to pulmonary or infectious disease specialists as indicated, can play an important role in helping to reduce the national burden of the disease.

National evidence-based guidelines for evaluating an individual exposed to an infectious case and treatment of LTBI have been developed by the Centers for Disease Control and Prevention (CDC), the American Thoracic Society (ATS), and the Infectious Disease Society of America (IDSA).[22] After exposure to an individual with infectious TB, a Mantoux TST should be performed on exposed persons. This intradermal injection of purified protein derivative (0.1 mL of five tuberculin units), derived from killed tubercle bacilli, is to be examined for induration by a trained health care worker 48 to 72 hours after placement. The presence of erythema without induration is not considered a positive test. TST results should be recorded as millimeters of induration. Multipronged (Tine) tests are not considered acceptable for testing.[25]

The ability to react to a TST diminishes over time in certain TB-infected individuals. Therefore, if one TST is performed many years after exposure, the result may be negative. However, if retested a week or 2 later, the test may be positive. This booster phenomenon is seen more commonly in BCG-vaccinated individuals and in those over 55 years of age. In healthcare settings, where serial TSTs are performed, a booster response resulting from a remote infection acquired years ago may be mistaken for a new conversion (recent infection). As a result, it is recommended that a baseline two-step PPD be administered to workers who will undergo serial skin tests for TB. This entails performing a second TST (second-step) approximately 2 weeks after an initial negative TST (first-step) is performed using the same dose and strength of tuberculin solution. If the second step of the two-step PPD test is negative, the individual may be considered noninfected. For employees who had a TST within the preceding 12 months, a one-step PPD test may suffice, because the earlier test may qualify as the first step of the two-step test.[26]

The ATS/CDC cutoff levels for positive TSTs are based on risk groups. An induration of 5 mm transverse diameter) or more over a 2-year period is considered a positive test for persons with human immunodeficiency virus disease, immunosuppressed patients (bone marrow or organ transplant recipients), recent contacts of persons with active disease, and persons with fibrotic changes on chest radiograph (CXR) consistent with prior TB. An induration of 10 mm or more is considered the cutoff for a positive TST in healthcare workers (HCWs), employees, and residents of prisons or long-term care facilities, recent immigrants (immigrated in the past 5 years) from countries with a high prevalence of TB, workers in a mycobacteriology laboratory, injection drug users, as well as persons with silicosis, chronic renal failure, diabetes mellitus, malnutrition, and other chronic conditions. An induration of 15-mm reaction is considered positive in other individuals.[21] A negative TST does not mean a person does not have TB infection. Reasons for a false-negative reaction include immunocompromised conditions, recent TB infection, and overwhelming TB disease. Live attenuated vaccines such as the measles, mumps, rubella vaccine administered 4 to 6 weeks before a TST may lead to a false-negative result. The use of anergy testing along with the PPD is no longer routinely recommended for screening for TB infections.[25] False-positive tests may occur as a result of crossreactivity of the PPD solution with other nontuberculous mycobacterial antigens or in individuals who had prior BCG vaccination. The TST is not contraindicated for persons vaccinated with BCG,[22] and the effect of BCG on the TST wanes over time.[27]

After the initial baseline TST after an exposure to an infectious case, follow-up skin testing should be conducted 8 to 12 weeks later. Those who develop a new positive TST should be evaluated for active versus latent TB and treated accordingly. Isoniazid (INH) is the drug of choice for the treatment of latent TB infection (regardless of age) with an efficacy of approximately 90% in persons who are compliant with the medication. The recommended duration of treatment is 9 months, but 6

months is an alternative in HIV-seronegative adults.[28] Baseline and monthly liver function tests are not routinely recommended, except for those who are HIV-positive, those who have chronic liver disease, pregnant and postpartum women (up to 3 months), and regular alcohol users. Pyridoxine (vitamin B6) at a dosage of 25 mg per day is recommended along with INH in patients who use alcohol, are pregnant, or breast feeding, or have HIV or other chronic disease, including preexisting peripheral neuropathy. Guidelines recommend discontinuing INH if transaminase levels are over three times upper limit of normal in symptomatic patients and five times upper limit of normal in asymptomatic patients.[21]

More than one commercial PPD solution is available for TST,[29,30] and more recently, blood tests for the diagnosis of latent TB have been introduced. One such test, the QuantiFERON-TB test, a T-cell-based interferon gamma assay, was approved by the U.S. Food and Drug Administration (FDA) in 2001. It may be more sensitive (up to 89%) and specific (>99%) than the TST and does not crossreact with BCG. As such, it may be useful for testing individuals with prior BCG vaccination. Another advantage of this test would be that it requires one patient visit, and eliminates the need for two-step testing.[31] The T SPOT-TB test is another blood test currently available in Europe. It is highly specific for *M. tuberculosis* and uses an enzyme-linked immunospot assay to quantify the number of mononuclear cells producing interferon gamma in response to stimulation with certain antigenic proteins.[2,23]

Occupational medicine physicians can play a role in helping to contribute to the Institute of Medicine's call to eliminate TB in the United States[32] by considering active TB in workers who have suggestive symptoms or latent TB in workers in high-risk categories. Although healthcare environments, correctional facilities, homeless shelters, long-term care facilities for the elderly, and drug treatment shelters are traditionally considered as high-risk occupational groups for TB,[11–14] many other workplaces are potentially at risk. In having a high index of suspicion and being able to identify, treat, and refer TB cases as needed, occupational medicine physicians can help to reduce transmission of the disease with the attendant disruption to the workflow, lost workdays, and reduced productivity, and help to decrease the burden of TB in the workplace.

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