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CLINICAL PEARL
Diagnosing and Managing Pulmonary Tuberculosis
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The correct diagnosis and appropriate management of tuberculosis (TB) are important, not only for the individual patient but for the health of the public. Unfortunately there can be diagnostic pitfalls and management difficulties, including patient fears and ethical dilemmas like those illustrated in this month's *Virtual Mentor* case of an immigrant worker with TB. It is important to make an etiologic diagnosis because other infections and certain noninfectious conditions can mimic TB. The classic presentation for TB is a subacute or chronic illness characterized by constitutional symptoms, including:

- Fever
- Chills
- Night sweats
- Anorexia
- Weight loss

These symptoms occur along with respiratory complaints in patients with pulmonary TB, including:

- Chronic productive cough
- Hemoptysis
- Pleuritic chest pain
- Dyspnea

Extrapulmonary TB also occurs, and its symptoms and signs depend on the particular organ system that is involved. Those diagnoses can be even more difficult. Full examination of those conditions is beyond the scope of this discussion, but most patients with extrapulmonary TB are noncontagious, so respiratory isolation is not required, although there are exceptions. These include patients with tuberculous otitis media, laryngitis, and any open wound or draining sinus tract, all of which have been associated with person-to-person transmission even in the absence of pulmonary infection.

Chest X-ray alone cannot make the diagnosis. Although there are findings that would indicate primary TB (mid-lung infiltrates with hilar lymphadenopathy) or reactivation TB (upper lobe fibro-cavitary disease), nonspecific or atypical radiographic findings occur. Microbiologic testing is essential to prove the patient

has TB and help determine the best course of treatment. There has been great progress in the field of mycobacteriology that has helped clinicians make a laboratory-confirmed diagnosis earlier than previously possible. Most labs now use fluorescent acid-fast stains (such as auramine/rhodamine) for evaluating sputum smears. This increases the sensitivity and reduces lab technician time, inasmuch as the entire slide can be evaluated at low power magnification by fluorescent microscopy. If three consecutive early morning expectorated or induced sputum samples are smear-negative, the likelihood of active TB or risk of person-to-person transmission is low. Other tests to consider when TB is still strongly suspected despite negative sputum smears would be an early morning (before breakfast) gastric lavage, or a bronchoalveolar lavage or transbronchial biopsy obtained by bronchoscopy.

Culture remains the gold standard in diagnosis and is even more sensitive than smear. Although agar slants are still set up, most labs now inoculate broth media specifically formulated for mycobacteria. All specimens can be inoculated into broth, including sputum. The time to a positive culture has been greatly reduced to an average of about 10 days for most cases. Once there is growth in liquid media, enough organisms are usually present in a few days for speciation using gene probes or sequencing. This is a great advance over speciation by culture characteristics and biochemical reactions, which were cumbersome and took a long time to complete. So decisions about isolation and initial therapy based on whether the patient has TB or a species of mycobacterium other than TB can be made much earlier in the course of disease. Even drug sensitivity results come back faster now that susceptibilities are set up in liquid media as well.

Polymerase chain reaction (PCR) is a rapid test that has been evaluated for diagnosis of TB. Currently, however, there are problems with sensitivity and specificity, and the best use of PCR is for speciation on a sputum that is smear-positive. The value of this is that patients with a nontuberculous mycobacterial infection need not be isolated, and a drug regimen designed for the species isolated can be initiated.

Although TB can occur in anyone, certain groups are more likely to have been exposed to TB, including individuals who are:

- Foreign-born
- Members of an ethnic minority
- Residents of prisons, shelters, nursing homes, and other long-term facilities
- Health care workers
- Intravenous drug users
- From regions that are medically underserved

The chances that someone acquires infection depends on:

- Infectiousness of the index case (somewhat related to the organism load observed on sputum smears)
- Duration of the exposure
- Environment (crowding, poor ventilation)
- Virulence of the organism

Once an individual is exposed or latently infected (asymptomatic, but with a positive skin test indicating specific immune system activation), certain conditions increase that person's risk of developing clinical disease:

- Diabetes mellitus
- Chronic renal failure
- Malabsorption or malnutrition
- Intravenous drug use
- Cancer
- Corticosteroids and other immunosuppressive drugs
- HIV-positive status

Of all the risk factors, infection with HIV is associated with the highest risk. HIV testing is appropriate in patients with HIV-associated, although not AIDS-defining, conditions. The management may be different for patients with HIV/TB co-infection, especially those with advanced immune deficiency from HIV.

Treating TB

Treatment of TB can also be difficult; it requires taking multiple drugs for prolonged periods of time, and the medications all have side effects. The number of medications, duration of therapy, and tolerability all impact compliance. Three drugs are indicated for initial therapy in geographic areas with low incidence of multidrug-resistant TB (MDR-TB) and with patients who do not have risk factors for drug resistance (e.g., do not come from a country with a high-rate of drug resistance such as Mexico). The three drugs most frequently initiated are isoniazid (INH), rifampin (RIF), and pyrazinamide (PZA)—the components of a "short course" regimen that can be completed in 6 months.

The emergence of multidrug-resistant TB and extreme drug-resistant (XDR-TB) strains have been a major obstacle to effective therapy. These strains are a far greater problem in the developing world, but in the 1980s many urban areas in the U.S. had high rates of MDR-TB. Fortunately, with restored efforts toward TB control—mainly through public health programs—rates of MDR-TB have decreased. There are still some urban areas with high rates of MDR-TB, but many cities have rates that are well below the 4 percent level, the threshold at which initial therapy consists of at least four drugs to cover strains that would be resistant to both INH and RIF, the most common pattern of MDR resistance. The fourth drug usually added to INH, RIF, and PZA is ethambutol (EMB).

In the hospital setting, all patients with suspected pulmonary TB are placed in respiratory isolation. As for the patient in this case, isolating him from family and other contacts may not be necessary. At this point, with initiation of therapy, the risk of spread to household members or close contacts at work is lower than the risk of spread that was present prior to diagnosis and therapy. If there are very young children at home, there may be a decision to isolate the patient from them in order to limit the risk of transmission, but most children receive prophylaxis until repeated skin testing assures they have not been infected. We usually consider patients to be noninfectious in about 2 weeks, unless they have advanced HIV or do not have a prompt clinical response with resolution of fever, resolution of other constitutional symptoms, and improvement in cough. Otherwise restrictions can usually be lifted at that time.

Mandatory Reporting of TB

TB cases must be reported, and it is usually not even up to the physician to do so. Hospital labs and infection control have reporting responsibility, and they often directly report to health departments. Public health plays an extremely important role. Studies done in the 1980s showed that only 20 percent of patients completed the course of TB therapy, and this helped fuel the increased incidence of TB and increased rates of drug resistance. Directly observed therapy (DOT), with public health personnel often serving as observers, helps assure that adequate therapy is carried out, which is important for both the patient's outcome and for limiting transmission. Although medical staff can skin-test household contacts, most physicians do not have the ability to do a home visit or adequately assess potential exposures at the patient's place of employment to determine who else may be at risk. Public health professionals will complete this assessment, determine which contacts are at risk, plan how to test contacts, supply the meds, and, in most cases, deliver DOT.

In summary, TB is a disease that still occurs in the U.S., with some areas and populations being disproportionately affected. Microbiologic diagnosis is extremely important, and recent advances allow earlier diagnosis, institution of appropriate infection control efforts, and initiation of effective therapy. Public health personnel can be a great help to physicians and health care professionals by assessing the risk of transmission and identifying at-risk contacts, as well as by supplying medications and offering DOT in many cases. TB reporting is essential and greatly benefits patients as well as society as a whole.

Further Reading

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