Tuberculosis

Tuberculosis (TB) is a potentially fatal contagious disease that can affect almost any part of the body but is mainly an infection of the lungs. It is caused by a bacterial microorganism, the tubercle bacillus or *Mycobacterium tuberculosis*. Although TB can be treated, cured, and can be prevented if persons at risk take certain drugs, scientists have never come close to wiping it out. Few diseases have caused so much distressing illness for centuries and claimed so many lives.

Overview

Tuberculosis was popularly known as consumption for a long time. Scientists know it as an infection caused by *M. tuberculosis*. In 1882, the microbiologist Robert Koch discovered the tubercle bacillus, at a time when one of every seven deaths in Europe was caused by TB. Because antibiotics were unknown, the only means of controlling the spread of infection was to isolate patients in private sanatoria or hospitals limited to patients with TB—a practice that continues to this day in many countries.

The net effect of this pattern of treatment was to separate the study of tuberculosis from mainstream medicine. Entire organizations were set up to study not only the disease as it affected individual patients, but its impact on the society as a whole.

When streptomycin, the first antibiotic effective against *M. tuberculosis*, was discovered in the early 1940s, the infection began to come under control. Although other more effective anti-tuberculosis drugs were developed in the following decades, the number of cases of TB began to rise again in the mid-1980s. This upsurge was in part again a result of overcrowding and unsanitary conditions in the poor areas of large cities, prisons, and homeless shelters.

An additional factor is the AIDS epidemic. AIDS patients are much more likely to develop tuberculosis because of their weakened

immune systems. There still are an estimated 8-10 million new cases of TB each year worldwide, causing roughly 3 million deaths.

High-risk populations

Tuberculosis is more common in elderly persons. More than one-fourth of the nearly 23,000 cases of TB reported in 1995 developed in people above age 65. Many elderly patients developed the infection some years ago when the disease was more widespread. The aging process itself may weaken the body's immune system, which is then less able to ward off the tubercle bacillus. Finally, bacteria that have lain dormant for some time in elderly persons may be reactivated and cause illness.

TB also is more common in blacks and Asiatic population, who are more likely to live under conditions that promote infection. As of late 2002, TB is a major health problem in certain specific communities. In some cases, the vulnerability to tuberculosis is increased by occupational exposure, as a recent outbreak of TB among poultry farm workers indicates.

The high risk of TB in AIDS patients extends to those infected by human immunodeficiency viruses (HIV) who have not yet developed clinical signs of AIDS. Alcoholics and intravenous drug abusers are also at increased risk of contracting tuberculosis. Until the economic and social factors that influence the spread of tubercular infection are remedied, there is no real possibility of completely eliminating the disease.

Causes and symptoms

Transmission

Tuberculosis spreads by droplet infection. This type of transmission means that when TB patient exhales, coughs, or sneezes, tiny droplets of fluid containing tubercle bacilli are released into the air. This mist, or aerosol as it is often called, can be taken into the nasal

passages and lungs of a susceptible person nearby. Tuberculosis is not, however, highly contagious compared to some other infectious diseases. Only about one in three close contacts of a TB patient, and fewer than 15% of more remote contacts, are likely to become infected. As a rule, close, frequent, or prolonged contact is needed to spread the disease. Of course, if a severely infected patient emits huge numbers of bacilli, the chance of transmitting infection is much greater. Unlike many other infections, TB is not passed on by contact with a patient's clothing, bed linens, or dishes and cooking utensils. The most important exception is pregnancy. The fetus of an infected mother may contract TB by inhaling or swallowing the bacilli in the amniotic fluid.

Progression

Once inhaled, tubercle bacilli may reach the small breathing sacs in the lungs (the alveoli), where they are taken up by cells called macrophages. The bacilli multiply within these cells and then spread through the lymph vessels to nearby lymph nodes. Sometimes the bacilli move through blood vessels to distant organs. At this point they may either remain alive but inactive (quiescent), or they may cause active disease. Actual tissue damage is not caused directly by the tubercle bacillus, but by the reaction of the person's tissues to its presence. In a matter of weeks the host develops an immune response to the bacillus. Cells attack the bacilli, permit the initial damage to heal, and prevent future disease permanently.

Infection does not always mean disease; in fact, it usually does not. At least nine of ten patients who harbor *M. tuberculosis* do not develop symptoms or physical evidence of active disease, and their x-rays remain negative. They are not contagious; however, they do form a pool of infected patients who may get sick at a later date and then pass on TB to others. It is thought that more than 90% of cases of active tuberculosis come from this pool. Whether or not a particular infected person will become ill is impossible to predict with certainty. An estimated 5% of infected persons get sick within 12-24 months of being infected. Another 5% heal initially but, after years or decades,

develop active tuberculosis either in the lungs or elsewhere in the body. This form of the disease is called reactivation TB, or post-primary disease. On rare occasions a previously infected person gets sick again after a later exposure to the tubercle bacillus.

Pulmonary tuberculosis

Pulmonary tuberculosis is TB that affects the lungs. Its initial symptoms are easily confused with those of other diseases. An infected person may at first feel vaguely unwell or develop a cough blamed on smoking or a cold. A small amount of greenish or yellow sputum may be coughed up when the person gets up in the morning. In time, more sputum is produced that is streaked with blood. Persons with pulmonary TB do not run a high fever, but they often have a low-grade one. They may wake up in the night drenched with cold sweat when the fever breaks. The patient often loses interest in food and may lose weight. Chest pain is sometimes present. If the infection allows air to escape from the lungs into the chest cavity (pneumothorax) or if fluid collects in the pleural space (pleural effusion), the patient may have difficulty breathing. If a young adult develops a pleural effusion, the chance of tubercular infection being the cause is very high. The TB bacilli may travel from the lungs to lymph nodes in the sides and back of the neck. Infection in these areas can break through the skin and discharge pus. Before the development of effective antibiotics, many patients became chronically ill with increasingly severe lung symptoms. They lost a great deal of weight and developed a wasted appearance. This outcome is uncommon today—at least where modern treatment methods are available.

Extrapulmonary tuberculosis

Although the lungs are the major site of damage caused by tuberculosis, many other organs and tissues in the body may be affected. The usual progression is for the disease to spread from the lungs to locations outside the lungs (extrapulmonary sites). In some

cases, however, the first sign of disease appears outside the lungs. The many tissues or organs that tuberculosis may affect include:

- *Bones.* TB is particularly likely to attack the spine and the ends of the long bones. Children are especially prone to spinal tuberculosis. If not treated, the spinal segments (vertebrae) may collapse and cause paralysis in one or both legs.

- *Kidneys.* Along with the bones, the kidneys are probably the commonest site of extrapulmonary TB. There may, however, be few symptoms even though part of a kidney is destroyed. TB may spread to the bladder. In men, it may spread to the prostate gland and nearby structures.
- *Female reproductive organs.* The ovaries in women may be infected; TB can spread from them to the peritoneum, which is the membrane lining the abdominal cavity.
- *Abdominal cavity.* Tuberculous peritonitis may cause pain ranging from the vague discomfort of stomach cramps to intense pain that may mimic the symptoms of appendicitis.
- *Joints.* Tubercular infection of joints causes a form of arthritis that most often affects the hips and knees. The wrist, hand, and elbow joints also may become painful and inflamed.
- *Meninges.* The meninges are tissues that cover the brain and the spinal cord. Infection of the meninges by the TB bacillus causes tuberculous meningitis, a condition that is most common in young children but is especially dangerous in the elderly. Patients develop headaches, become drowsy, and eventually comatose. Permanent brain damage is the rule unless prompt treatment is given. Some patients with tuberculous meningitis develop a tumor-like brain mass called a tuberculoma that can cause stroke-like symptoms.
- *Skin, intestines, adrenal glands, and blood vessels.* All these parts of the body can be infected by *M. tuberculosis*. Infection of the wall of the body's main artery (the aorta), can cause it to rupture with catastrophic results. Tuberculous pericarditis occurs when the membrane surrounding the heart (the pericardium) is

infected and fills up with fluid that interferes with the heart's ability to pump blood.

- *Miliary tuberculosis.* Miliary TB is a life-threatening condition that occurs when large numbers of tubercle bacilli spread throughout the body. Huge numbers of tiny tubercular lesions develop that cause marked weakness and weight loss, severe anemia, and gradual wasting of the body.

Diseases similar to tuberculosis

There are many forms of mycobacteria other than *M. tuberculosis*, the tubercle bacillus. Some cause infections that may closely resemble tuberculosis, but they usually do so only when an infected person's immune system is defective. People who are HIV-positive are a prime example. The most common mycobacteria that infect AIDS patients are a group known as *Mycobacterium avium* complex (MAC). People infected by MAC are not contagious, but they may develop a serious lung infection that is highly resistant to antibiotics. MAC infections typically start with the patient coughing up mucus. The infection progresses slowly, but eventually blood is brought up and the patient has trouble breathing. In AIDS patients, MAC disease can spread throughout the body, with anemia, diarrhea, and stomach pain as common features. Often these patients die unless their immune system can be strengthened. Other mycobacteria grow in swimming pools and may cause skin infection. Some of them infect wounds and artificial body parts such as a breast implant or mechanical heart valve.

Diagnosis

The diagnosis of TB is made on the basis of laboratory test results. The standard test for tuberculosis—which is the so-called tuberculin skin test—detects the presence of infection, not of active TB. Tuberculin is an extract prepared from cultures of *M. tuberculosis*. It contains substances belonging to the bacillus (antigens) to which an infected person has been sensitized. When tuberculin is injected into

the skin of an infected person, the area around the injection becomes hard, swollen, and red within one to three days. Today skin tests utilize a substance called purified protein derivative (PPD) that has a standard chemical composition and is therefore is a good measure of the presence of tubercular infection. The PPD test is also called the Mantoux test. The Mantoux PPD skin test is not, however, 100% accurate; it can produce false positive as well as false negative results. What these terms mean is that some people who have a skin reaction are not infected (false positive) and that some who do not react are in fact infected (false negative).

The PPD test is, however, useful as a screener. Anyone who has suspicious findings on a chest x-ray or any condition that makes TB more likely should have a PPD test. In addition, those in close contact with a TB patient and persons who come from a country where TB is common also should be tested, as should all healthcare personnel and those living in crowded conditions or institutions.

Because the symptoms of TB cover a wide range of severity and affected body parts, diagnosis on the basis of external symptoms is not always possible. Often, the first indication of TB is an abnormal chest x-ray or other test result rather than physical discomfort. On a chest x ray, evidence of the disease appears as numerous white, irregular areas against a dark background, or as enlarged lymph nodes. The upper parts of the lungs are most often affected. A PPD test is always done to show whether the patient has been infected by the tubercle bacillus.

To verify the test results, the physician obtains a sample of sputum or a tissue sample (biopsy) for culture. Three to five sputum samples should be taken early in the morning. If necessary, sputum for culture can be produced by spraying salt solution into the windpipe. Culturing *M. tuberculosis* is useful for diagnosis because the bacillus has certain distinctive characteristics. Unlike many other types of bacteria, mycobacteria can retain certain dyes even when exposed to acid. This so-called acid-fast property is characteristic of the tubercle bacillus.

Body fluids other than sputum can be used for culture. If TB has invaded the brain or spinal cord, culturing a sample of spinal fluid will make the diagnosis. If TB of the kidneys is suspected because of pus or blood in the urine, culture of the urine may reveal tubercular infection. Infection of the ovaries in women can be detected by placing a tube having a light on its end (a laparoscope) into the area. Samples also may be taken from the liver or bone marrow to detect the tubercle bacillus.

One important new advance in the diagnosis of TB is the use of molecular techniques to speed the diagnostic process as well as improve its accuracy. As of late 2005, four molecular techniques are increasingly used in laboratories around the world. They include polymerase chain reaction to detect mycobacterial DNA in patient specimens; nucleic acid probes to identify mycobacteria in culture; restriction fragment length polymorphism analysis to compare different strains of TB for epidemiological studies; and genetic-based susceptibility testing to identify drug resistant strains of mycobacteria.

Treatment

Supportive care

In the past, treatment of TB was primarily supportive. Patients were kept in isolation, encouraged to rest, and fed well. If these measures failed the lung was collapsed surgically so that it could 'rest' and heal. Today surgical procedures still are used when necessary, but contemporary medicine relies on drug therapy as the mainstay of home care. Given an effective combination of drugs, patients with TB can be treated at home as well as in a sanitarium. Treatment at home does not pose the risk of infecting other household members.

Drug therapy

Most patients with TB can recover if given appropriate medication for a sufficient length of time. Three principles govern modern drug treatment of TB:

- Lowering the number of bacilli as quickly as possible. This measure minimizes the risk of transmitting the disease. When sputum cultures become negative, this has been achieved. Conversely, if the sputum remains positive after five to six months, treatment has failed.
- Preventing the development of drug resistance. For this reason, at least two different drugs and sometimes three are always given at first. If drug resistance is suspected, at least two different drugs should be tried.
- Long-term treatment to prevent relapse.

Five drugs are most commonly used today to treat tuberculosis: isoniazid (INH, Laniazid, and Nydrazid); rifampin (Rifadin, Rimactane); pyrazinamide (Tebrazid); streptomycin; and ethambutol (Myambutol). The first three drugs may be given in the same capsule to minimize the number of pills in the dosage. As of 1998, many patients are given INH and rifampin together for six months, with pyrazinamide added for the first two months.

Hospitalization is rarely necessary because many patients are no longer infectious after about two weeks of combination treatment. Follow-up involves monitoring of side effects and monthly sputum tests. Of the five medications, INH is the most frequently used drug for both treatment and prevention.

Surgery

Surgical treatment of TB may be used if medications are ineffective. There are three surgical treatments for pulmonary TB: pneumothorax, in which air is introduced into the chest to collapse the lung; thoracoplasty, in which one or more ribs are removed; and removal of a diseased lung, in whole or in part. It is possible for patients to survive with one healthy lung. Spinal TB may result in a severe deformity that can be corrected surgically.

Prognosis

The prognosis for recovery from TB is good for most patients, if the disease is diagnosed early and given prompt treatment with appropriate medications on a long-term regimen. Modern surgical methods have a good outcome in most cases in which they are needed. Miliary tuberculosis is still fatal in many cases but is rarely seen today in developed countries. Even in cases in which the bacillus proves resistant to all of the commonly used medications for TB, other seldom-used drugs may be tried because the tubercle bacilli have not yet developed resistance to them.

Prevention

General measures

General measures such as avoidance of overcrowded and unsanitary conditions are also necessary aspects of prevention. Hospital emergency rooms and similar locations can be treated with ultraviolet light, which has an antibacterial effect.

Vaccination

Vaccination is one major preventive measure against TB. A vaccine called BCG (Bacillus Calmette-Guérin, named after its French developers) is made from a weakened mycobacterium that infects cattle. Vaccination with BCG does not prevent infection by *M. tuberculosis* but it does strengthen the immune system of first-time TB patients. As a result, serious complications are less likely to develop. BCG is used more widely in developing countries than in the developed ones. The effectiveness of vaccination is still being studied; it is not clear whether the vaccine's effectiveness depends on the population in which it is used or on variations in its formulation.

Prophylactic use of isoniazid

INH can be given for the prevention as well as the treatment of TB. INH is effective when given daily over a period of six to 12 months

to people in high-risk categories. INH appears to be most beneficial to persons under the age of 25. Because INH carries the risk of side-effects (liver inflammation, nerve damage, changes in mood and behavior), it is important to give it only to persons at special risk. High-risk groups for whom isoniazid prevention may be justified include:

- close contacts of TB patients, including health care workers
- newly infected patients whose skin test has turned positive in the past two years
- anyone who is HIV-positive with a positive PPD skin test; Isoniazid may be given even if the PPD results are negative if there is a risk of exposure to active tuberculosis
- intravenous drug users, even if they are negative for HIV
- persons with positive PPD results and evidence of old disease on the chest x-ray who have never been treated for TB
- patients who have an illness or are taking a drug that can suppress the immune system
- persons with positive PPD results who have had intestinal surgery; have diabetes or chronic kidney failure; have any type of cancer; or are more than 10% below their ideal body weight
- People from countries with high rates of TB who have positive PPD results.
- People from low-income groups with positive skin test results.
- Persons with a positive PPD reaction who belong to high-risk ethnic groups.

As a form of extrapulmonary tuberculosis that impacts the spine, Pott's disease has an effect that is sometimes described as being a sort of arthritis for the vertebrae that make up the spinal column. More properly known as tuberculosis spondylitis.

Pott's disease is often experienced as a local phenomenon that begins in the thoracic section of the spinal column. Early signs of the presence of Pott's disease generally begin with back pain that may seem to be due to simple muscle strain. However, in short order, the

symptoms will begin to multiply. Night sweats may become common, along with a running a fever during the day. As the condition worsens, it is not unusual to experience a loss of appetite, resulting in an anorexic state and the resulting weight loss. There is also often periods in which there is a tingling or numb sensation in the legs, accompanied with a sense of not having much strength in the legs.

Fortunately, there are several ways to determine if Pott's disease is the root cause of the symptoms. Blood tests can help determine if there is an elevation in the rate of erythrocyte sedimentation. A bone scan will determine if there is some indication of problems, which may lead to the scheduling of a bone biopsy. Conducting a CT scan as well as a radiograph of the spine is also likely to provide valuable information about the presence and current status of Pott's disease.

Once the presence of Pott's disease is confirmed, there are several treatment options available. The first line of defense will involve the use of analgesics and various antituberculous drugs, which can help to arrest the progress of the disease, as well as begin to alleviate symptoms. In some cases, it may be necessary to insert a rod into the area of the spine, providing needed stability. This is often the case if some degree of spinal cord compression has been noted. Finally, more ambitious surgery may be required, especially in situations where there is a need to drain fluid from pockets or abscesses that have formed, or if conditions indicate impending collapse of the vertebrae in the spinal column.