TUBERCULOSIS: A NEW LOOK AT AN OLD DISEASE

An Honors Thesis (ID499)

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INTRODUCTION

Tuberculosis (TB) is an age old disease. Heralded in the beginning of the twentieth century as the number one cause of mortality in the United States, the disease itself dates back to the earliest ancestors of modern man. Pulmonary tuberculosis, the version usually referred to in common usage, is characterized by symptoms such as increased fatigue, night sweats, chronic productive cough, and weight loss. The disease is caused by a mycobacterium and is important as an agent of death and disability throughout the world.

Unfortunately, in recent years, interest in tuberculosis has waned among the people of the United States. Once feared as the greatest single killer in the nation, the disease has taken a back seat to chronic diseases such as cancer and heart disease, and more recently -- Acquired Immuno Deficiency Syndrome (AIDS). But in 1989, there were 13.58 cases of AIDS per 100,000 population in the United States. There were 9.46 per 100,000 cases of TB in that same year. In this author's opinion, our nation has forgotten about TB and that situation needs to be changed. As long as members of society are unaware of the symptoms, and doctors are no
longer testing for it, the nation is blatantly inviting a potentially fatal, contagious disease to spread unchecked in our population.

**HISTORY**

Some authors speculate that bovine (cow) tuberculosis was first introduced to mankind in the Neolithic Period between 7000 and 6000 BC when cattle were first domesticated (4). Positive identification of tuberculosis of the bones has been made on skeletal remains dating as far back as 3700 BC. Putting these events into perspective, the earliest record of Greek civilization on the island of Crete with the remains of the palace of King Minos dates only to approximately 2000 BC, and by the year 2150 BC the great pyramids of Egypt stood fully constructed.

Hippocrates (470-376 BC), acclaimed as the father of medicine, first identified tuberculosis in Egypt by the name of "phthsis" meaning "to waste away." Over the course of history, TB has been known by many different names. In England, it was known as Consumption or the White Plague. Other historic names have been "the white swelling" and "dropsy of the lungs." Bone samples from
Iroquois Indians living in Ontario, Canada also have been positively identified with cases of TB dating back to Indian civilizations there in 128 AD(4).

The first person to recognize the contagious nature of the disease was Girolama Fracastoro (1483-1555). Fracastoro was a highly persuasive man who practiced medicine in the Italian city-state of Verona. In 1546, he published a book known as De Res Contagiosa. This document, highly significant historically from the standpoint of epidemiology, was the first to break the transmission of disease into three possible means. The first was by direct contact, meaning that a diseased person physically touched, and thereby spread the disease. The second was transmission by inanimate objects (fomites), such as drinking glasses or articles of clothing. The third method was by so-called indirect contact. Fracastoro stated that these indirectly spread diseases could infect "at a distance"(7). TB belonged to the third category. Unfortunately, the idea of distinct methods of disease transmission was largely ignored for more than 200 years after Fracastoro's death(7).
A preacher, John Bunyan, wrote in one of his fables on morality, nearly a century later, that TB was "The captain of all these Men of Death that came against him [man] to take him away, was the consumption, for it was that that brought him down to the grave" (17). Indeed, many famous historical figures were stricken by and perished due to tuberculosis. Among these were: St. Francis of Assisi; Antoine Watteau, a noted French painter (d. 1721); John Keats, an English poet (d. 1821); Frederic Chopin, a Polish composer (d. 1849); Henry David Thoreau, an American philosopher (d. 1862); Anton Chekhov, a Russian writer (d. 1904); and Vivian Leigh, star of "Gone with the Wind" (d. 1967).

During the colonial period in the United States, between 18-25 percent of all deaths were due to TB. In a five-year period between 1768-1773 in Salem, Massachusetts, 117 of 642 deaths were a result of tuberculosis (4).

However, it was not until 1865 in a report to the French Academy of Medicine that Jean-Antoine Villemin showed conclusively that TB was a communicable disease. On March 24, 1882, Robert Koch successfully isolated the tuberculosis bacillus under his
microscope and demonstrated that it was the sole cause of TB.

Along with Koch's discovery of the bacillus itself, a substance that could be used to test individuals for tuberculosis was created with the supernatant (the fluid found on top of the culture after settling has occurred) of the tubercle bacilli. This substance became known as a tuberculin. The tuberculin allowed physicians to test individuals for tuberculosis reactivity. However, the usefulness of the test was questionable due to the high percentage of the population who were, in fact, infected. In 1930, 80% of all thirty-year-old persons tested had positive skin test reactions to the tuberculin test. Until 1940, it was thought to be a waste of time to test for TB in the population (8).

It was also believed at that time that a positive test for infection indicated that the individual was "diseased." While that assumption was not clinically accurate, there were no reliable treatment therapies (medication, surgeries) to prevent infection from becoming disease at that time. The consensus was that once a person tested positive for TB infection, they would always be an infected/diseased person. The distinction between infection and
disease had not been made, nor was there a medical cure.

In the early 1930s TB was once again the number one killer in the United States as it had been back in the colonial period. The most common victims of the disease were children under one year of age. During the 1930s, the first concerted public effort at controlling the spread of TB emerged in the form of sanatoriums. Sanatoriums were large institutions often located on spacious, beautiful land far removed from the cites. Tuberculosis patients were taken to the sanatoriums to be isolated from the uninfected population. Often these patients would remain at the sanatoriums for a number of years, even the rest of their lives. The death rate in most sanatoriums was around 50 percent (11). The sanatoriums were usually long, narrow buildings with porches running the length of both sides. It was on these porches that the TB patients resided. The belief was that the fresh air and sunshine was all that was necessary to cure the dreaded disease. Therefore, the patients were allowed to come indoors only once per day to bathe and otherwise were not allowed inside. Summer and winter alike the residents of the sanatoriums ate, slept,
socialized and died on these porches. The cost of keeping a person in a sanatorium in 1951 was six dollars per day.(11).

Early in the 1940s, various other radical cures for the disease were proposed such as treatment with calcium, tuberculin, mercury, or gold injections.(17). In 1941, Dr. Minaldi introduced an operation which involved puncturing the TB cavity in the lung and attempting to "suck out" the TB germs. The intent was to accelerate the healing process by removing all of the germs present in the lung. Unfortunately, the tuberculosis bacilli rapidly reproduced after the surgery and thus no benefit was achieved.

Two other procedures that came into vogue in the early 1940s were the surgical removal of one lung and the surrounding ribs (thoracoplasty), and the placement of a ping-pong ball in the TB cavity of the lung. The former procedure was believed to have removed the TB germs from the body entirely and thereby cured the patient. However, it failed to take into account the TB bacilli circulating in the body that served to infect (if it was not already involved) the other lung after the operation, and continued to function destructively in the other organs of the body. The
procedure, in addition to being traumatic, also produced a scoliosis-type posture in its recipients.

The second procedure, that of insertion of a ping-pong ball, was intended to arrest the disease process and give the lung time to rest. While the resulting collapse of the lung did deny the tuberculosis bacilli the same degree of oxygen they had previously been receiving and thereby slowed the reproduction of the germs, as soon as the ping-pong ball was removed and the lung reinflated the process resumed as before (11).

In 1945, Waksman discovered the first antimicrobial drug effective in the treatment of TB -- Streptomycin (8). Two other antimicrobials arrived soon after, P-aminosalicylic acid (PAS) in 1946 and Isoniazid (INH) in 1952 (17). These three were the first drugs used to treat TB. They were extremely effective.

These drugs, however, produced common side-effects such as fever and skin rash, which appeared three to four weeks after treatment onset, but did represent the first successful medical treatment for TB. After the effectiveness of the chemotherapy was
proven, the radical surgical procedures became a thing of the past.

These early drugs were given to the residents of the sanatoriums. The problem with the regimen was that it required the patients to take anywhere from 20-30 pills at one sitting. The pills themselves coupled with the quantity of water necessary to swallow them, ruined the patients' appetites and resulted in extreme compliance problems. For the patients of the sanatoriums, eating was one of their few pleasures and they, not having confidence in the drug therapy, had no desire to spoil that. This compliance problem was only uncovered when the shrubbery surrounding the sanatoriums began to turn brown and die. Investigation into the problem revealed that the patients had been spitting their medications into the bushes instead of swallowing them! After that, the porches of the sanatoriums were enclosed.

However, owing to the discovery of effective drug therapy, the need and desire for the sanatoriums diminished. The prevalence of tuberculosis in the nation began to decline steadily, and by 1970 doctors quit looking for TB in their patients. Eventually the last
of the sanatoriums closed.

ESTABLISHING THE CAUSE

Today, when we hear the word tuberculosis we think of disease that affects the lungs, and we recall sometime in our lives when we have been tested for it -- no big deal. However, according to some, tuberculosis is the most serious granulomous infection known to man (4).

The disease is caused by a bacterium known as Mycobacterium Tuberculosis. There are actually five strains of M. Tuberculosis, human, bovine, murine, avian, and piscine. Only the human and bovine strains are pathogenic to man.

Bovine TB is most often contracted by drinking the milk of infected cows. In 1886, Marfan discovered that much like the relationship of small pox and cow pox, persons who were infected with bovine tuberculosis did not contract human TB (8). Bovine TB manifests itself as fever and lumps found in the neck of the infected individuals as a result of the swollen lymph nodes. The focal point for bovine TB is usually in the tonsils. With the widespread use of pasteurization, the incidence of bovine TB in humans is practically nonexistent.
The M. Tuberculosis bacteria itself is a slender, rod-shaped bacteria measuring four microns in length and one micron in diameter. The bacteria are transmitted through the air in droplets of saliva from a diseased person. Therefore, an individual need only breathe the "wrong" air to contract the infection. If left untreated tuberculosis kills two-thirds of its victims in two to three years (23).

While TB's means of transmission lends its primary effect on the body as pulmonary, its effects do not have to be limited to the lungs. Tuberculosis of other parts of the body is known as extra-pulmonary TB (6). The bacilli, once they have entered the lungs, are transported throughout the body via the blood vessels and lymph system (8).

**INFECTION AND REINFECTION**

The process of becoming an active case of TB has two stages, primary infection and reinfection (24). Primary infection is the process in which a person first comes in contact with the TB bacilli and takes it into his lungs. Reinfection is the process when the infected individual's body begins to function as an active case of tuberculosis. This distinction is important. Tuberculosis
infection is not the same as tuberculosis the disease. Only active cases of TB can spread the disease.

Upon primary infection or the time of TB's initial entry into the body, the primary complex of the disease appears in the lungs (8). The primary complex consists of the primary focus or initial parenchymal lesion, and the slight enlargement of the hilar lymph nodes located near the affected area of the lung. The initial lesion is usually less than one centimeter in length. The lymph nodes swell in an increased attempt to drain the affected lung. Most primary complexes are not visible with chest x-rays and the person infected will skin test negative at this point.

Occasionally, more than one lesion will occur in the lungs at the time of primary infection. This condition is known as segmental lesioning or epituberculosis. Multiple lesions are commonly seen in children because of the fact that their bronchi are smaller, more pliable, and thus more easily broken down by the TB bacillus. The segmental lesioning usually begins at the time the individual's skin test converts from negative to positive at the end of the period of primary infection, and continues for about six months. The appearance of segmental lesioning after six months
is rare(8). The prognosis for persons whose primary infection results in segmental lesions is the same as for a person with only one primary parenchymal lesion.

The multiplication of the bacilli proceeds most rapidly in the lung tissue because of the available oxygen supply. The body offers very little resistance to the multiplication of the bacilli in the lung and as soon as the number of bacteria is large enough, the bacteria begin to disseminate throughout the body. This usually occurs via the hilar lymph nodes, which are attempting to drain the affected lung and thereby allow the bacteria into the lymph system. The lymph system facilitates the bacteria's entrance into the blood and allows the bacilli to reach all the other organs of the body. Again, the various organs and tissues offer little resistance to the growth process of the bacilli. In a minority of people the rapid multiplication that occurs at primary infection will proceed and become tuberculosis disease. However, in most cases, the process naturally ceases within a few weeks. Mysteriously, the reproduction of TB bacilli throughout the body slows and ceases, the dissemination of bacilli from the lungs to the rest of the body stops, and the unusual quantity of fluid
present in the infected lung dissipates(24). In most people, especially children, all that remains a year or two after primary infection are the residual swollen lymph nodes and a small calcified lesion in the lung. This calcification occurs where the primary focus was located, and contains tuberculosis germs that have been "walled in" by the body's immune system.

The entire process usually requires anywhere from four to eight weeks to complete itself. At the end of this period, the individual's body has created a resistance to virulent TB bacilli. Soon the body will begin the process of destroying those bacilli present in other organs outside of the calcification in the lung. Eventually, most of the body tissues will return to normal.

The second result of a primary infection is that the person will now skin test positive for TB. It is important to remember that this positive test does not indicate that the person is necessarily an active case of TB. The majority of people are symptom free when their skin test converts to positive. Only a minority of individuals experience even minor flu-like symptoms such as a dry cough and fever. The time of reinfection is when the
disease process begins.

Reinfection can occur as a result of the infected person once again inhaling the tuberculosis bacilli from a diseases person (exogenous reinfection), or as a result of the virulent germs contained within the calcified node in the lung once again escaping into the body (endogenous reinfection). Endogenous reinfection occurs when the immune system of the infected individual is suppressed or weakened to such a degree that the protective calcification in the lungs begins to break down. In either case, it is a result of the body's cellular reaction to the bacilli the second time that causes the death of the healthy body tissues. During primary infection the cells of the body learned to fight off the tuberculosis bacilli as the person developed an immunity to the disease. Whereas the multiplication of the bacilli was allowed to continue during primary infection due to the original lack of immunity, during reinfection the acquired antibodies attempt to prevent the disease from taking hold. This cellular "war" results in the necrosis (death) of the tissue involved "at the sight of the battle." This is how the damage to the body by tuberculosis
manifests itself (24). In other words, the body's immune response to TB upon reinfection is so violent that even healthy tissue is destroyed.

**RELATED DISEASES**

As mentioned earlier, TB bacilli locate anywhere in the body. Therefore, this necrosis-producing disease process can begin in any of the body's organs. These other forms of TB are known as Extra Pulmonary (beyond the lungs) Tuberculosis. The more common examples of Extra Pulmonary TB are tuberculous meningitis, tuberculous lymphadenitis, tuberculosis of the bones and joints, and genitourinary tuberculosis.

Approximately one-fifth of all cases of TB are Extra Pulmonary. Curiously, the specific types of Extra Pulmonary TB seem to have a predilection for certain races. For example, Asians tend to develop tuberculosis lymphadenitis; southern Europeans, genitourinary TB; and South African blacks, tuberculous pericarditis (8).

Tuberculous meningitis is the most serious form of Extra Pulmonary TB and it is the single most important factor in
tuberculosis-related death in children. TB meningitis results from the dissemination of the TB bacilli through the blood to the brain. Early symptoms include vomiting and headache. These symptoms later progress to fever, neck rigidity, drowsiness, and even convulsions. Twenty-five percent of all people infected with TB meningitis show a normal chest x-ray and the disease is not usually diagnosed until two weeks after the onset of symptoms. Prior to the development of antimicrobial drugs, TB meningitis was fatal in most cases. Today, complete cure is usually possible. However, if diagnosis is not made early enough, neurological deficits are evident upon the patient's recovery.

The TB bacilli are isolated in a sample of the patient's cerebrospinal fluid for positive identification of TB meningitis. Due to the fact that tuberculosis bacilli require four to ten weeks to be evident in a laboratory culture, all patients suspected of TB meningitis should be treated as verified cases. If not, the patient will have expired before positive TB diagnosis can be made (8).

Tuberculous lymphadenitis is often contracted by drinking milk
from cows with bovine tuberculosis. Because of this, lymphadenitis was much more common in the past. The use of pasteurization (process of sterilization by heating) has eliminated the usual means of transmission. The disease typically results today from the hematogenous dissemination of the bacilli from the lungs to the glands of the neck and specifically the tonsils. The disease symptoms are much like those experienced with bovine TB. In fact, the primary focus of tuberculosis bacilli in the body is often found in the tonsil instead of the lung in TB lymphadenitis.

Symptoms of the disease include fever and lumps in the neck. The patient will skin test positive for TB infection. Lymphadenitis onset can occur one month after primary infection. If it has not appeared within the first few years following infection, it is unlikely that lymphadenitis will develop. Twenty-five to thirty percent of all immigrants to North America from China, India, and the Philippines who suffer from TB disease have tuberculous lymphadenitis (8).

Tuberculosis of the bones and joints is yet another form of Extra Pulmonary TB. Patients with TB of the bones and joints are
usually not diagnosed for a number of years and normally suffer from one of the other forms of TB as well. The disease tends to destroy intervertebral disks much like other agents such as typhoid, brucella, or staphylococci. It is not possible to determine the cause of disk destruction with x-rays. If tuberculosis of the bones and joints goes undetected long enough it can lead to paraplegia or permanent deformity of the patient. The disease can settle in and eventually destroy the movement of any joint of the body. A possible identification of TB of the bones and joints can be made from a culture of synovial fluid from an affected joint. Therapy with antimicrobial drugs and temporary immobilization of the affected body part can cure the disease and thus curtail the progressive destruction. However, damage done during the active disease process cannot be reversed. Tuberculosis of the bones and joints is very similar to TB arthritis and can be handled in the same manner (8).

Genitourinary tuberculosis usually occurs several years after the primary infection. It is found unisexually in the kidneys, bladder and ureters of affected individuals. In men, it can also be found in the epididymis, and in women in the endometrium and
fallopian tubes. The disease results in the swelling and eventual blockage of the diseased reproductive or urinary tract. This can lead to sterility or uremic poisoning. Diagnosis is made with either a biopsy or urine culture. Individuals with genitourinary TB will skin test positive for tuberculosis infection and can be cured with the use of antimicrobial drug therapy (8).

Aside from these few mentioned, other organs of the body could also become the focus of TB infection and disease. The organ most commonly affected by tuberculosis is the lung. Seventy percent of all active cases of TB are pulmonary and it is the only form of human tuberculosis that is communicable. All other forms of TB arise from primary complexes brought on by a primary infection in the lungs. Owing to this, TB is classified as an airborne pathogen. This simply means that the tuberculosis bacilli gains access to the body by entering through the respiratory system. Historically, pulmonary TB was the only form of the disease attributed to the TB bacilli. Extra Pulmonary disease, due to its unique symptoms, was considered a different pathogen entirely.

Pulmonary tuberculosis is uncommon in children because of their
strong immune systems. This form of TB relies on reinfection to become active. Again, the time of initial infection is generally not the time when the body succumbs to disease. When a person with a strong immunity contracts the disease a primary complex is formed in the lungs and then calcified over. At the time when that person's immune system is compromised due to stress, pregnancy, AIDS, cigarette smoking, other disease infection, pollution, or old age the protective calcification breaks down and in essence, the individual acquires the disease from himself.

The number of bacteria present in a person with pulmonary TB is large relative to other forms of TB because of the oxygen-rich conditions present in the lungs. It is estimated that for every four to six centimeter cavity in the lung anywhere from one to ten billion TB bacilli are present.

Symptoms of pulmonary TB include chronic productive cough (indicative of fluid in the lungs and sputum is coughed up), occasional shortness of breath or chest pain, general achiness, loss of weight, and night sweats(11). In the United States the presence of a productive cough and shortness of breath is common in
the population among cigarette smokers and makes the diagnostic use of such symptoms highly unreliable. Additionally, smokers often suffer from other forms of degenerative lung disease such as emphysema and bronchitis. Both diseases serve to weaken the patient's immunity increasing their chances of developing TB and equally increasing their chances of the disease perpetuating undiagnosed.

Looking at the number one and two causes of mortality, we find heart disease and cancer. Both disease are considered chronic and essentially lifestyle induced. Scientific speculation, particularly in the case of cancer, seems to indicate that environmental irritants, chemicals, work habits, and certain behavior patterns predispose certain individuals to cancer by weakening the immune system and thus allowing the disease process to begin. In fact, the number of lung cancer cases currently outnumber the case of TB by two to three times for older males in the western world. Symptoms for both diseases can be similar and very often TB and cancer co-exist in the same patient. Cancer, however, usually only affects one lung, while TB often affects both
lungs. Because of the fact that both cancer and TB depend on the presence of weakened immunity to take hold in a victim's body, the presence of one disease process may provide the perfect conditions for an attack by another disease. Such is the case with AIDS patients. The disease AIDS weakens the body's natural defense system and provides the ideal conditions for other diseases to flourish.

AIDS was first reported in the United States in 1984 with 4,445 cases. In that same year, there were 22,255 reported cases of TB, down 6.7 percent or 1,591 cases from 1983 statistics. The previously steady decline in cases of TB slowed to an amazing .7 percent, with only 54 fewer cases of TB reported in 1985 as compared to 1984. Then, just two years after the arrival of AIDS, the number of cases of tuberculosis actually increased by 2.6 percent (567 cases) in 1986. It was the first year since 1948 that our nation saw a rise in the number of cases of TB. As would be expected, deaths from tuberculosis were up in 1986 (18).

AIDS is a result of the infection and progressive action of the Human Immunodeficiency Virus (HIV) in the human body. The
condition known as AIDS does not in itself kill a human being. HIV works to destroy the body's ability to fight off infection from all other disease organisms. AIDS is the syndrome produced by the action of the virus. Given a host without the benefit of a strong immune system, all other diseases, including tuberculosis, flourish and eventually result in the death of the individual. Persons with compromised immunity are at a much greater risk of developing TB disease from an initial primary infection. Equally, persons who are already infected with TB, but whose immune systems have put the disease process into remission, who contract HIV have a much greater chance of suffering from an endogenous reinfection. The HIV virus appears to be one of the strongest known determinants for the progression of TB infection to TB disease (19). In some areas it has been found that up to 25 percent of all TB patients test positive for HIV. Tuberculosis, if diagnosed, is one of the few diseases specifically associated with HIV infection that can be treated and cured. One potential problem of diagnosis is the possibility that a person positive yet undiagnosed for HIV may not react to a routine TB skin test. The reason for this is the
immunosuppressive capability of HIV could prevent the body from reacting to the presence of the tuberculin. Thus, the test would appear negative, and because the patient was as yet asymptomatic for AIDS, no follow-up would be done.

Recent reports by the CDC seem to indicate that AIDS-related tuberculosis may in some cases serve as a precursor to full-blown AIDS. TB tends to appear early in the course of the progression of AIDS and could serve as an indicator of the presence of HIV infection (23). The current recommendation is that all AIDS patients and those known to be HIV infected be tested for TB. Also, all individuals tested positive for tuberculosis should be tested for the presence of HIV. Curiously, AIDS patients appear to have higher incidence of extrapulmonary tuberculosis.

Additionally, due to the nature of AIDS transmission and the prevalence of homosexual behavior and drug use in prisons, infection with the HIV virus, presence of ARC (AIDS-related complex), and actual AIDS victims are markedly more common in prisons. Bob Gore, assistant director of the California State Department of Corrections, stated that he felt that out of the
67,200 inmates of California's prisons, an estimated 2-3,000 were either HIV positive, ARC, or AIDS(23).

Tuberculosis has long been associated with persons of lower class, thus poor nutrition and health habits, living in close proximity to one another. These conditions provide an excellent opportunity for airborne disease transmission. No where do these conditions exist quite as dependably as they do in a prison setting. As stated by Barry Dorfman, chief of California State Department of Health Services' Tuberculosis Control Unit in Sacramento, California:

Who goes to prison? Poor people and disproportionately minority groups that have higher prevalence of tuberculosis. And then if you put them all together, crowd them together, and then you stress them out -- stress is definitely a factor -- you shouldn't be surprised if you get TB(23).

In conditions such as these with large numbers of people at increased risk of succumbing to tuberculosis disease, in a population perfectly suited for effective continued transmission of the TB bacilli, tuberculosis may present itself once again as a
significant public health problem. The prisons serve as a specific community of at-risk individuals. The reverberations of an AIDS-TB partnership in such a community could spread throughout the non-institutionalized population as well. Dixie Snyder, chief of the Centers for Disease Control's division of tuberculosis control stated:

Most people who are infected with the tubercle bacilli have a latent or subclinical infection, and most of them will not develop the disease unless something stresses the immune system—something like AIDS. [With an estimated 10-15 million people in the United States alone being TB infected] there is this tremendous potential for TB to reemerge as a much larger problem than it is right now(23).

The essence of the threat from AIDS in regard to prevalence of tuberculosis in society is that we now have young, highly active members of our society immunosuppressed to the point that TB infection rapidly becomes TB disease, and TB disease is airborne and contagious. The contagious spend their time with other immunosuppressed young people and tuberculosis receives the best
chance to thrive it has had in several years. Even in light of the often fatal consequences of AIDS, it must not be forgotten that while HIV is transmitted in the blood and therefore does not warrant social isolation, TB is transmitted through the air and can be equally as fatal if undetected.

In 1930, when the majority of 30-year-olds in the nation were infected, it was mostly senior citizens who became TB diseased. That was the time in their lives when their immunity was compromised to such a point that TB could take hold in their bodies and endogenous reinfection could occur. Exogenous reinfection was uncommon because those members of society who became ill were usually older, less active, and often homebound. Most young people who contacted the germ had strong immune systems that suppressed the disease until they, too, weakened with age.

Today, we have a nation with already compromised immunity due to its lifestyle. Add to that a disease process that kills by completely destroying the body's immune system and which is primarily claiming as its victims the young and active, and we have an interesting problem. The immunosuppressive activities of the
HIV virus can go undetected for several years while the person gradually contracts and spreads multiple communicable diseases. Many of these are easily conquered by persons not infected with HIV such as the common cold, or influenza. Other diseases such as tuberculosis can also be unwittingly spread by the compromised victim of AIDS and can pose serious threats to other immunosuppressed, but not necessarily AIDS, victims.

Dixie Snyder cites the fact that relatively few people in our society today recognize TB as the formidable threat that it is as being yet another reason why tuberculosis could make a resurgence in our population. He says:

Instead of 84,000 cases that we had in 1953, now we're down to 23,000 [in 1988]. As infectious diseases go, that's still a heck of a lot of cases, but it's still a 75 percent decrease. So it has gone out of our minds, but it certainly never went away.
TESTING METHODS

The usual methods for diagnosis of tuberculosis infection are the skin test, the chest x-ray, and the examination of sputum for the presence of the tuberculosis bacilli.

Following Robert Koch's invention of a supernatant of the culture of Tubercle bacilli and the resulting tuberculin, it became possible to test individuals for tuberculosis infection. Around 1930 in the United States, a man by the name of Siebert was working with a batch of highly refined protein derivative tuberculin and created what became the international standard for tuberculins used in testing for TB. His derivative became known as PPD-S or Purified Protein Derivative-Siebert. The tuberculin is used to perform the Mantoux skin test for tuberculin reactivity. One milliliter of diluted tuberculin, or the bio-equivalent to five International/Tuberculin Units, is injected intradermally into the skin on the underside of the forearm. The amount of induration (swelling) that results is measured approximately 48-72 hours later (2). The diameter of the swelling is dependent on the body's immune response to the presence of the tuberculin in the skin. A
large amount of swelling (usually considered to be a diameter of greater than 10 millimeters) generally indicates that the person has antibodies for TB present in their system. These antibodies would be present as a result of a primary infection. Swelling of greater than or equal to 10 millimeters of actual induration indicates a positive reaction, but it is important to remember that it is an arbitrary cut-off point. It is possible for individuals who are TB infected to display induration of 5-20 millimeters or more (2). The test, however, is not specific to only tuberculosis mycobacteria. Other strains of mycobacteria can produce significant induration in response to a tuberculin test. Also, an individual's degree of sensitivity to the tuberculin, while high immediately following the primary infection, begins to wane after the first year. In areas where the prevalence of other forms of mycobacteria including tuberculosis is high, it is a common practice to retest persons who tested negative on first test one week later. An increase of greater than or equal to six millimeters of induration is usually thought to negate the findings of the previous test and indicate that the individual is TB.
infected. The reason for the retest is that persons living in the presence of higher concentrations of mycobacteria often display decreased reactivity to the tuberculin on first exposure. The second exposure usually generates a "boosted" and more accurate immune response.

Overall, a Mantoux tuberculin reactivity test is considered significant when the initial test renders a greater than or equal to 10 millimeter response or the second test produces a greater than or equal to six millimeter increase in induration as compared to the initial test (2). There is no danger of TB infection as result of repeated Mantoux tests. But because of the limitations of the test's reliability, the usefulness of the Mantoux has been questioned. Despite the criticisms, however, the test remains a simple, inexpensive, reasonably dependable means of diagnosing tuberculosis infection.

Another more definitive testing procedure for TB is the use of chest x-rays. The primary complex caused during the primary infection usually appears as a cloudy, many-fingered obstruction in the lung on an x-ray. Multiple lesions and the extent of damage
are also visible with x-rays. Unnecessary radiation, inconvenience, and expense are all drawbacks to the use of x-rays for detection. But despite this, x-rays are the second most reliable method for the detection of TB. As such, x-rays are used when a case is strongly suspected or a Mantoux test returns positive.

The final testing procedure for tuberculosis infection is the examination of the patient's sputum for TB bacilli. This is considered to be the most important and conclusive method for diagnosis. The sputum is examined in two ways. One method, termed "smear" testing, is simply examining the sputum under a microscope for the presence of the bacilli. Smear positive tests indicate advanced stages of the disease because of the large number of bacilli needed in order to be detected with a microscope. An estimated 100,000 tubercle bacilli per milliliter of sputum must be present to be detected with a smear test.

The second method, sputum "culturing", can detect even subtle cases of tuberculosis. The drawback to culturing is that it requires anywhere from 4 to 10 weeks of culture growth in a
suitable laboratory media to produce the bacilli. Evidence indicates that only a few hundred bacilli per milliliter of sputum are needed to detect TB if culturing is used.

To clarify, "sputum" is not the same as saliva. Sputum is considered the "phlegm" that can be coughed up directly from the lungs. The substance is often associated with the chest congestion involved in almost any case of cold or flu(24). In the presence of TB, the sputum will contain the bacilli that are thriving in the lungs. The combination of these three methods of detection can accurately diagnose tuberculosis in nearly every case. With the advent of drug therapy, diagnosis becomes the first step to curing the patient.

**DRUG TREATMENTS**

Around 1950, the first antimicrobial drug therapies were used in the treatment of tuberculosis. While these therapies were effective, they were unpleasant for the patients and were compromised by extreme non-compliance problems. These early treatments did yield some very important discoveries for use in modern day. One important discovery was the necessity of using a
combination of two or more drugs in order to prevent the patient from becoming "drug-resistant." Also, the drugs had to be taken daily and regularly for up to eighteen months to be effective (17).

Thirdly, chemotherapy converted TB-diseased individuals from sputum-positive to sputum-negative in a very short period of time.

The significance of sputum-positive versus sputum-negative is that once negative the patient is no longer infectious. The rapidity of conversion is an indication of the effectiveness of the treatment therapy and understandably varies from person to person. In most cases, sputum conversion (both smear and culture) occurs within the first few months of chemotherapy.

Since the invention of Streptomycin in 1945, several other antimicrobials have been found to be effective in the treatment of TB. Among those tried are p-aminosalicylic acid (PAS), ethambutol, pyrazinamide (PZA), rifampin, and isoniazid (INH). All of these drugs do have side effects as well as advantages. The current recommendation for drug treatment of TB by the Centers for Disease Control is 300 milligrams of isoniazid, 600 milligrams of rifampin, and one gram of pyrazinamide daily. After two months of treatment,
the PZA is discontinued. After six months of treatment the patient is re-evaluated and if necessary the therapy is redesigned.

PZA, the most expensive of the drug trio at $150 per month was once considered a secondary choice in the treatment of TB. The drug was believed to have highly toxic side effects which have in recent years been discounted as inaccurate. PZA is always prescribed in combination with other drugs, and has been found highly effective (8). Nausea has been linked to PZA, and due to the tendency of the drug to cause an increase in uric acid, gout is also a risk. Some studies have found PZA to have a damaging effect on the liver leading to possible loss of appetite and even jaundice (6).

Rifampin is used to treat leprosy, endocarditis, meningitis, osteomyelitis, and tuberculosis. Comparatively, rifampin is the second most expensive drug costing an estimated $60 per month. While highly effective, rifampin has also been linked with liver toxicity and interferes with the functioning of birth control pills. The drug has been found to be a teratogen (capable of producing birth defects) in pregnant rats, but no evidence of this
relationship has been found to exist in humans. Research has
discovered that patients who are treated with drug combinations
that include rifampin have a faster sputum conversion rate than
those treated with combinations lacking rifampin. Possible
side-effects from the drug are fever, shortness of breath, skin
rash, and abdominal pain. A recent concern has been the increased
use of rifampin to treat conditions other than TB. The possibility
of a patient's system becoming resistant to rifampin is increased
with the greater prevalence of its use in treating other diseases.
Also, there is the possibility that these other uses can limit the
effectiveness of rifampin in treating tuberculosis by allowing drug
resistance to occur sooner in the course of treatment.

The third and least expensive drug in the trio, isoniazid,
costs a mere $2 per month and is clearly the antimicrobial mainstay
of tuberculosis treatment. Isoniazid has been determined to be the
most effective drug available today against the tuberculosis
bacilli. The major drawback to INH is the rapidity with which the
bacilli become resistant to the drug. If drug resistance occurs,
the most valuable treatment for TB will become useless. In order
to prevent resistance, INH must be administered in combination with other drugs, and the administration must be consistent from the beginning of the treatment regimen until the time of complete eradication of the bacilli from the patient (8). The most serious side effect of INH is hepatitis. The incidence of hepatitis seems to be related to age, occurring rarely in children and increasing over the years. Some experts believe that it is the combination of INH and rifampin that causes hepatitis while most believe that the use of INH alone is the culprit (8). INH tends to cause the body to lose large quantities of pyridoxine (vitamin B6) and thus supplements of vitamin B6 are given during treatment to prevent nerve damage (6).

Chemotherapy for TB must be maintained for at least one year to prevent relapse. Still, even in cases where the regimen is followed exactly, relapse does occur. An estimated 10-15 percent of all cases of TB in North America are the result of relapse (8). Twenty to thirty percent of those cases harbor drug resistant tuberculosis germs. These individuals present two problems from a public health standpoint. The first problem is the fact that their
form of TB will be more difficult to cure because of the resistance it maintains to our treatment recommendations. Secondly, individuals with active TB who are drug resistant and sputum positive, are not only contagious in society, but the germs they expectorate are drug resistant as well. For these reasons, total compliance to drug therapy combined with continuous monitoring of the infectiousness of the patient and the effectiveness of the treatment is extremely important until the time of cure(11).

PREVENTION

Along with being an effective treatment drug, isoniazid (INH) is also one of the two prevention methods used against TB. INH has been used to treat TB infected individuals in order to prevent them from converting to an active case. Therapy with isoniazid for one year has been determined to decrease the likelihood of an infected person becoming diseased to less than ten percent.

The other method, a vaccine, is known as BCG or Bacillus Calmette-Guerin. BCG was invented between 1908 and 1921 in the laboratories of a man named Calmette. During that thirteen year period, Calmette worked with strains of M. Tuberculosis until he
was able to develop a strain that had no pathenogenicity for animals, but otherwise appeared unchanged. Upon accomplishing this, the modified bacilli was administered to a child in 1921(24). Since the time of the initial vaccine, BCG has been the subject of constant controversy.

The first attempts to establish the efficacy of the vaccine were thwarted by erroneous statistical and research methods. Rates of disease for groups of vaccinated persons were not directly compared with otherwise demographically identical control groups. Likewise, morbidity and mortality data on vaccinated newborns were compared to the morbidity and mortality data for the country overall. Owing primarily to these initial errors, countries such as the United States and Great Britain dismissed BCG entirely(24). Then in Lubeck, Germany, in 1930, seventy-five infants died after receiving what was believed to be the BCG vaccine, but was in fact a virulent strain of the tubercle bacillus which had accidentally gotten exchanged. Regardless of the fact that the deaths of the infants were not caused by the BCG vaccine, the publicity of the incident left negative impressions in the minds of
many in regard to BCG.

The first viable study for the efficacy of BCG was performed in 1937. Ever since that time, studies of the vaccine have been rare. Upon examining six different studies, an average efficacy of only 53.3 percent was found (24). Other evidence in the research indicated a current effectiveness rating for BCG of 80 percent (8). In any case, the major clinical drawback of the vaccine is the fact that recipients of BCG test positive for tuberculosis with a Mantoux test for reactivity. Therefore, the least expensive, most commonly employed diagnostic test for TB is rendered worthless by the administration of an only moderately effective vaccine. The question is whether the 50-80 percent reduction in disease in vaccinated persons is worth the 30-50 percent of those vaccinated that go on to become infected, can no longer rely on a skin test for diagnosis, and therefore may go undiagnosed? In a country such as the United States where TB can no longer be considered endemic, the use of BCG cannot be justified. Currently, there are around 10-15 million tuberculosis infected and approximately 20,000 tuberculosis diseased individuals in the United States out of a
population of approximately 240 million people. In conditions such as these, the important factor is to continue to be able to monitor the public for patterns of disease within small communities and families, and not to attempt to unnecessarily vaccinate over 200 million people. The need to have a quick, easy diagnostic tool outweighs the expense and only moderate effectiveness of the vaccine in the United States.

BCG may be a much more efficient method of control in developing nations where the likelihood of interacting with an infected individual is higher that in the United States. Likewise, persons living in unavoidable contact with infected/diseased individuals such as nurses, doctors, outreach and social workers, and family members of TB patients might consider the 80 percent chance of protection worth the trade off of an annual chest x-ray or sputum culture to test for the 20 percent chance of becoming infected despite the vaccine. The value of BCG remains the choice of those persons. For most residents of the United States, regular skin tests for infection are sufficient to maintain awareness and consequently good health. The true danger to the individual from
TB is as a result of the active disease going undetected. Untreated tuberculosis is fatal in over 50 percent of all cases (22). Yet, nearly one-third of all cases recover without the use of drug treatment (8).

This study now approaches a critical point in the treatment/prevention process. As was discussed earlier, the likelihood that a person would develop TB from a primary infection is very slim. The reason is that the immune system of most individuals is able to suppress the disease and contain remaining live bacilli in a calcified node in the lung. Only upon reinfection, either from the outside or from within the body, is the germ strong enough to cause disease. Rather, only upon reinfection is the body's immune system weakened enough to allow disease to occur. Any condition that lowers that body's immunity can either increase the chance of a primary infection leading directly to disease, or create the conditions necessary for an endogenous reinfection to occur in a previously infected, but not diseased person.

Such immunosuppressive factors can include: pregnancy,
diabetes (particularly of juvenile onset), chronic alcoholism, use of tobacco products, exposure to silica, under or poor nutrition, presence of concurrent disease, stress, and corticosteroid treatments. The relationship of AIDS and cancer to TB rates is a current issue of health concern due to their immunosuppressive capability.

At the time of reinfection, one-third recover without treatment and most recover with drug therapy. However, it is because of the immune system, not the treatment alone, that the disease is conquered in every case (24). Were it not for mankind's strong immunity, tuberculosis would have wiped out the human population long ago (8). As evidence of this, we are reminded of the number of 30-year-olds (80 percent) who were infected with TB in the United States in 1930. In those days, herd immunity was created because a majority of the population had an acquired immunity due to their primary infection. While these people were infected with the bacilli, their cases were suppressed by their immune systems and only active cases can spread the disease.

Today, we do not have the herd immunity produced by large numbers of infected individuals. That factor in itself does not
a problem. The problem arises when we examine the number of persons nationwide who are immunosuppressed in one form or another. In general, the so-called "state of immunity" in the United States is not very good. Owing in part to personal choices of poor dietary, exercise, sleep, and stress habits (including the use of alcohol and tobacco), combined with uncontrollable factors in our environment, the people of the United States continue even with current trends toward wellness and prevention, to focus their health on destructive behaviors in the present and medicinal "cures" in the future.

Therefore, a third and final method for prevention of all diseases, and specifically tuberculosis, would be the maintenance of the immune system by the individual. Simply put, the process of maintaining the immune system can be equated with the process for maintaining proper weight. Most individuals cannot simply ignore the maintainence of their body weight and expect it to remain at their desired level. The same is true for the immune system. Left untended, or rather allowed to deteriorate -- it will. Immunity
can be strengthened by getting six to eight hours of sleep per night, exercising aerobically three or more times per week, drinking alcohol only in moderation (if at all), not using tobacco products, drinking six to eight glasses of water per day, and dealing with stress in effective, nondestructive ways. These techniques can strengthen the immune system of any person, even someone who does not enjoy the luxuries of uncrowded houses and well-co-ordinated interior decorating.

SUMMARY AND RECOMMENDATIONS

In April of 1989, the Centers for Disease Control (CDC) in Atlanta, Georgia, published a plan for the elimination of tuberculosis in the United States. The three part plan included an examination of current methods, the development of new technologies and methods for treatment and prevention, and an implementation approach for the new methods (1).

Step one cited surveillance, case prevention, and disease containment as the current methods used in the treatment and prevention of TB. Surveillance includes the identification and reporting of cases, suspected cases, and possible human contacts of
both. Case prevention is two-fold. One group of people included in case prevention are those already infected. Proper preventive therapy with isoniazid can stop the TB infected from becoming TB diseased in 90 percent of all persons who complete a full course of treatment(1). The other group of people included in case prevention are those people who are not infected. During step one, interventions must be designed to prevent the unaffected from coming into contact with those who are TB diseased. Methods employed to this effort can involve such things as isolation of the tuberculosis diseased patient or ensuring efficient ventilation to the outside in hospitals, nursing homes, prisons, etc.

The final portion of step one, or current methods, is disease containment. This involves the actual method or regimen used in the treatment of diseased patients. Over 25 percent of all patients are not known to have converted from sputum positive to sputum negative for six months(1). This indicates that a change needs to be made in the drug treatment the patient has been prescribed. In cases where the conversion is slow or does not come at all, the chances of drug resistance are high and should
be promptly investigated. Additionally, almost 12 percent of all known cases of tuberculosis are not receiving any form of therapy whatsoever. Finally, of those who have been diagnosed and given a prescription for medication, over 17 percent are not taking their medication consistently and according to recommendations. This behavior has been found to be the largest single determinant of the mutation of the tuberculosis bacilli to drug resistance.

The plan goes on to steps two and three which outline "improvements" on the current system. These "improvements" range from the idealistic goal of finding a reliable vaccine to simply using our current knowledge, techniques and facilities more efficiently.

In this author's opinion, the recommendations by the CDC were marvelous and complete. The CDC managed to ferret out every defect in the current system. The plan effectively advises those involved with tuberculosis treatment nationwide as to how to stop the "leaks" in their programs from ruining their entire effort. However, reading through the proposal the apt reader might question whether the CDC was taking a couple of important issues into
consideration as they composed the plan.

The first issue concerns the degree of national interest in the disease. The purpose of this document was to increase awareness that an old forgotten disease is still a viable foe in modern day. The author felt that in light of the fact that she is on the verge of finishing a degree in Public Health and knew virtually nothing about this health topic of great public concern, perhaps many others in our society were uninformed about tuberculosis as well. As she suspected, this was the case. In the course of research, she did not find anyone who knew anything of any depth about tuberculosis. Therefore, the author concludes that the strong feelings of urgency in regard to tuberculosis elimination that the CDC infers that our nation feels have been found to be lacking, nearly non-existent. Our nation wants to cure cancer, stop the spread of sexually transmitted diseases, and lose ten pounds. Overall, it would appear that the nation is not staying up nights worrying about the spread of tuberculosis.

Secondly, the CDC seemed to forget about funding. Currently, Departments of Health nationwide are having to cut back on their
programs because of funding losses. Public health personnel have a multitude of funding needs and receive only enough money to scantily service their most urgent priorities. The Delaware County Tuberculosis Society is the last one of its kind in the state. The Society works in combination with the Madison and Delaware county boards of health to effectively handle tuberculosis in this two-county area (3). In other parts of the state, tuberculosis control must be entirely funded and administered by the local health department.

All things considered, it is difficult to justify a need for precious public health dollars to go to tuberculosis education, testing, and treatment as opposed to "hot" issues such as AIDS or cancer. However, tuberculosis, unlike cancer or heart disease, is contagious—and it can be fatal. While the author does not advocate a full blown assault on the problem costing a fortune in public health dollars, including round table discussions on Oprah Winfrey, and morbid public service announcements displaying forty-year-old housewives hacking up sputum and falling defeated into their waiting caskets, she would like to present a couple of
recommendations for consideration.

[1]. TB testing in the public schools should be revived. Children, with their high degree of immunity, do not succumb to tuberculosis disease very often. But, a child who is infected provides an excellent way to find and treat an active disease case. Children are one branch of our society that public health workers have consistent access to until their sixteenth year. Those children who were found to be infected could then be put on preventive therapy for one year and the medication could be administered at school to insure compliance.

[2]. TB testing should be a requirement for all employment physicals, athletic and college physicals, routine checkups, and marriage licenses. In this way, adults in the non-institutionalized population could also be monitored with a degree of regularity.

[3]. Current testing of prison inmates should also be maintained with one exception. Instead of using the "weekly testing" method where by every "Thursday" whomever is present gets tested, the jails should be equipped to test prisoners upon admittance. This way, prisoners who are rapidly bailed or
transferred would get tested as well.

Tuberculosis is a fascinating disease. Forgotten by our society, but none the less deadly, TB is an old disease that still deserves concern. Tuberculosis thrives where immunity is weakened, such as it is in our nation's population today. Tuberculosis has been clinically linked with many other diseases including tuberculous meningitis, cancer and AIDS. As testimony to the seriousness of the disease in our nation, in 1987 TB killed more United States citizens than all the childhood and sexually transmitted diseases (excluding AIDS) combined.

Tuberculosis can be cured with a variety of antimicrobial drugs, and can be tested for with sputum testing, chest x-rays, and the Mantoux skin test. Currently, there is no way to prevent a person from becoming infected. However, with the use of prevention methods (BCG, isoniazid treatments, and total immune system strengthening) an infected individual need never become diseased. There has been tuberculosis throughout the history of mankind and all evidence indicates that it's not dead yet!
REFERENCES


