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(City, State)

## Introduction

Tuberculosis or TB refers to a common, deadly, and infectious disease that is caused by a number of mycobacteria strains (Kumar, et al., 2007). The most common mycobacterium that causes TB is the Mycobacterium tuberculosis. TB usually affects the lungs, although it is also possible for the other body parts to be affected. The disease uses air as the medium of spreading the infection when infected people sneeze, cough or transmit fluids from the respiratory organs through air. Some of the symptoms associated with the different TB variant, as well as TB stages, include chills, loss of appetite, fever, fatigue, loss of body weight, and night sweats (Gerald, et al., 2010). Most of these symptoms overlap within the different variants, with some being specific for specific variants. There are also chances that multiple variants of TB may be present at the same time in a patient. The kind of tuberculosis that affects the lungs is normally referred to as the pulmonary tuberculosis. On the other hand, the TB that takes place outside the lungs is known as extra pulmonary TB. Both pulmonary and extra pulmonary TBs may be present at the same time in a single patient (Gerald, et al., 2010).   
In pulmonary TB, the infection becomes active almost immediately and is associated with symptoms such as prolonged cough with sputum production and chest pain. A small portion of individuals may be asymptomatic and in other incidents of coughing blood may be observed (Lawn & Zumla, 2011). In rare occasions, patients may experience corrosion of the pulmonary artery leading to excessive loss of blood. Although most TB cases are pulmonary TB, few of the active cases (15–20%) occur outside the lungs, leading to other forms of TB. These forms of TB that occur outside the lungs are referred to as extra pulmonary tuberculosis (Golden & Vikram, 2005). These forms of TB are common in individuals who are immunosuppressed especially those with HIV or in children. Some of the sites where extra pulmonary TB may affect include the central nerves system, the pleura, lymphatic system, bones, genitourinary system, and joints (Golden & Vikram, 2005).   
The Mycobacterium tuberculosis (MTB), which is the major causative factor of TB, is a small organism in shape, aerobic, and non-motile in nature (Gerald, et al., 2010). Test for TB may be done using histological stains using the sputum as the sample and viewed under a light microscope. Because of the increased amount of lipid in cell wall of MTB, staining the pathogen with a gram stain gives a weak positive result or no positive results at all (Niederweis, et al., 2010). MTB has the ability to withstand dry conditions for several weeks and when exposed to weak disinfectants. The MTB bacteria are only able to grow when in the cell of a host organism. The bacterium is, however, able to grow in cultures in the laboratory (Parish & Stoker, 1999). Other mycobacteria that cause TB include M. canetti, M. africanum, M. bovis, and M. microti.

## Transmission

TB is basically an airborne disease with the causing bacteria being spread form an infected person in another person in very small droplets. The pathogens may be introduced in the air after when a person with active TB speaks, sneezes, laughs or sings. These actions release aerosol droplets that are infectious with a diameter of between 0. 5 and 5. 0µm. In a single sneeze, the amount of droplets may be as high as 40, 000 droplets (Cole & Cook, 1998) with each of the droplets having a chance to cause TB. The high chances of causing infection are contributed by the fact that the infectious dose of TB is very low with less than 10 bacteria causing an infection (Nicas, et al., 2005).   
People who have frequent and prolonged close contact with TB patients are at an increased risk of getting an infection. Patients who have active TB and have not been treated have a chance of infecting at least 10 other people every year and the transmission takes place from those who have an active TB. There are no reports of infection by those with a latent infection. The chances of infection being transmitted from an infected person to another depend on the infectious droplet number, ventilation effectiveness, exposure time, the virulence of the pathogen. In addition, environmental factors such as the concentration of the infectious droplets in the air, size of the space and whether open or closed, Ventilation, air circulation, specimen handling, as well as air pressure are other factors that may determine the success of TB infection.

## Epidemiology

Approximately a third of the population worldwide has had an M. tuberculosis infection with new infections taking place in 1% of the population every year. Most of these infections, however, do not lead to TB disease, and more than 90% of infections do not show any TB symptoms. In the year 2012, an estimated 8. 6 million people were diagnosed with chronic active TB cases (WHO, 2013). More than 8. 8 million new cases of TB and about 1. 45 million deaths were reported in 2010. Most of these cases were recorded in developing countries. Out of the 1. 45 million deaths, more than 0. 35 million deaths involved patients who were co-infected with HIV.   
TB is rated as the second most common death cause after the infectious diseases such as HIV/AIDS. Since the year 2005, the overall number of TB cases has been reducing while the number of new cases started reducing since 2002 (WHO, 2011). Incidents of TB are more prominent in developing countries compared to the developed countries. In most of the Asian and African countries, approximately 80% of people give positive results when tested for TB compared to less than 10% of people in the United States (Kumar, et al., 2007). The urge to have a total control of TB has been made impossible by the fact that development of an effective vaccine is difficult, long and expensive diagnosis of the disease, prolonged treatment, incidents of drug resistance, as well as high incidents of HIV-associated TB (Lawn & Zumla, 2011).   
In 2007, Swaziland recorded the highest TB incidence rate with 1200 cases in every 100, 000 individuals. On the other hand, India had the highest total incidence recording a total of 2. 0 million new cases. Incidents of tuberculosis in developed countries are rare, and the few cases are found mainly in the urban areas. In general, in 2010, the rates of TB globally are at 180 per 100, 000. In Africa, America, Europe, and south Asia are 332, 36, 63, and 278 respectively. Both in Australia and Canada, the cases are high in Aboriginals especially those who live in remote areas (FitzGerald, et al., 2000). Similarly, in the US, the Aborigines are five times more likely to suffer from TB while the ethnic and racial minorities accounted for more than 80 per cent of all TB cases that are reported. TB incidents vary with age where, in Africa, the disease mainly affects young adults while, in developed countries, the disease affect the old group as well as those who are immunocompromised.

## Pathogenesis and Immune Response

TB infection takes place after a person breath in droplet nuclei that contain the bacilli. The inhaled bacilli then get into the alveoli of the lungs where most of them are ingested and destroyed by the alveolar macrophages. A few of the bacilli may undergo multiplication intracellularly after which they are released after the death of macrophages. The bacilli that are still alive in the lungs may then spread through the bloodstream and the lymphatic channels and move into other distant organs and tissues. These organs and tissues include those organs that are best fit for TB development such as the apex of the lung, lymph nodes, brain, kidneys, and the bone. The movement of the bacilli to these organs and tissues trigger the immune system to initiate a systemic immune response (CDC, 2013).   
In a period of between 2 to 8 weeks, the macrophages are able to ingest and engulf the tubercle bacilli and the cells built a barrier shell, known as a granuloma. This keeps the bacilli in a contained position enabling the body to control the spread of the infection. In case the immune system is unable to control the tubercle bacilli, the pathogen continues to with the multiplication process leading to the development of TB disease. These processes may occur in varying areas of the body such as the lungs, brain, kidney, and bones among others (CDC, 2013).   
The TB causing bacteria may stay in the body without causing any sickness to the body. This condition is known as latent TB infection and people in this condition do not experience any TB symptoms and do not feel sick. These individuals are also noninfectious and have no ability to spread the disease to other individuals. However, in case the disease causing pathogen is activated, the pathogen is able to attack the body and lead to the patient suffering from the disease. In most cases, the TB bacteria are activated when the immune system is not able to stop their growth. It is when the TB bacteria are active or multiplying in the body that the condition is referred to as a TB disease. Once the bacteria are active, the person is now able to transmit the bacteria to other uninfected individuals surrounding them (CDC, 2012).   
Many people with latent TB manage to keep it suppressed and do not develop TB disease. To others, the infection develops to TB disease soon after infection even before the body could fight the bacteria. Others in latent TB condition may develop TB disease years later after the immune system is weakened due to other reasons such as infections that compromise of the immune system. People having a weak immune system such as those who are HIV positive are at a greater risk of developing TB disease compared to normal individuals (CDC, 2012).

## Animal Models

The fact that TB is an infectious disease and could be transmitted from one species to another was initially proven in 1865 when it was transmitted from human to rabbit (Parsons, 2010). The disease outcome is, however, different depending on the pathogen that causes the infection and species of the host. Through experiments, it has been established that rats, mice, rabbits and guinea pigs are some of the common animal models that can be used to study TB pathogenesis (Gupta & Katoch, 2005). Rabbit strains have been shown to be the one that are relatively resistant to TB and results to a greater rate of antibody production compared to other more susceptible strains. There has been, however, limited insight into the actual mechanisms of the TB disease using these animal models. Tools necessary for the examination of the immune response are also not available for use with the animal models. Although sophisticated models for doing TB experiments have been developed, examination of the comparative susceptibility in different host species still use the basic infection models (Parsons, 2010).   
Other than in the understanding of TB pathogenesis, animal models have also been used in testing for various vaccine candidates. This has been made possible by the great similarity between the physiologies of animals with that of human. These animal models provide information that is valuable about human systems. In the understanding of the host response to an infection in the lungs, immunopathological changes and the effectiveness of new vaccines in protecting the body, the mouse and guinea pig models are used as the main animal models (Gupta & Katoch, 2009).   
Use of animal models in studying TB has several advantages including the ease of infecting the animal with TB through the pulmonary route making sure that only few of the virulent tubercles are added in the alveolar space just like in human. In addition, using animal models makes it easy to study progression stages of the disease such as the liquefication, cavity formation, granuloma formation, as well as the hematogenous spread of the disease. Through animal models, it is also possible to see symptoms such as fever, weight loss, respiratory distress, and abnormal X-rays. The fate of the animal if left untreated is also similar to that in human patients where the animal dies due to pulmonary insufficiency (Gupta & Katoch, 2009).

## Treatment

Medications for TB treatment involve the use of antibiotics that are able to eliminate the bacteria. Having an effective treatment for TB has been difficult due to the abnormal structural and chemical composition of the cell wall surrounding the mycobacteria. The cell wall is made up of thick lipid layers that make it difficult for the drug to penetrate rendering most drugs ineffective (Brennan & Nikaido, 1995). Two antibiotics that are mainly employed in the treatment of TB are rifampicin and isoniazid with their treatment taking up to several months.   
Treatment of the latent TB uses just a single antibiotic while active TB is treated using a combination of a number of antibiotics. This is with the aim of reducing development of resistance to antibiotics. Treatment of latent TB conditions is essential since it prevents the patients from progressing to active TB conditions later in their life. According to the WHO recommendations, having a directly observed therapy are the best treatment strategy in order to reduce the number of those taking antibiotics inappropriately (Gantz, 2001).   
The recommendations for the treatment of new cases of pulmonary TB involve taking a six month medication. In the first two months, the combined dose of isoniazid, rifampicin, ethambutol and pyrazinamide is taken followed by a combination of isoniazid and rifampicin for four months. In the areas where isoniazid resistance is high, addition of ethambutol to the combination may be done for the four months (Lawn & Zumla, 2011). In cases where there is a recurrent of the disease, it is recommended that a test to determine the antibiotics that are effective in eliminating the bacteria be done before giving the treatment. Where the bacteria show multiple drug resistance, treatment may involve a combination of at least four effective antibiotics for a period of 18-24 months (Lawn & Zumla, 2011).   
In 2006, a global plan to stop TB was launched as a roadmap to enhance TB prevention as well as treatment. The plan also aimed to enhance research on TB, development ion. The global plan was started in 2006 and is aimed to be accomplished by 2015. The plan also has a goal of reducing the deaths caused by TB by half by 2015. The plan was later updated in 2010, which marked the mid-point of the plan, with the aim of revising the plan in order to take into account the progress that had been made since 2006. The plan is divided into the implementation component and research and development component. The implementation component focuses on the transformation of TB control by enhancing the existing diagnosis and treatment interventions and by introducing recent technologies in developing diagnostic tests. The research and development component was intended to show the necessary tools for the development of new tools needed to have an effective prevention methods and treatment choices. The research and development component is made up of five topics, new drugs, new diagnostics, new vaccines, as well as operational research (WHO, 2011).

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