Your Name

Instructor Name

Course Number

Date

**Individual Essay**

**Introduction**

It has been sixty years since the treatment for tuberculosis has been developed which mainly includes vaccination and chemotherapy; still, it remains the major cause of casualty around the world occurring from a single infectious agent. It has even surpassed the prevalence of human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS) for the first time in the history of medicine (Bloom et al.). According to the World Health Organization, It is estimated that the year 2018 contributed to the death of almost one and a half million individuals with Tuberculosis as the sole cause of these casualties (*Tuberculosis (TB)*). An estimated number of individuals that were diagnosed with tuberculosis are ten million including five million males, three million females and the rest of them comprising, children. Among these cases, almost one-third remain untreated due to not having proper knowledge of the new forms of disease (Snider and Roper). Tuberculosis refers to the disease of the respiratory system which is caused by bacterial infection of *Mycobacterium tuberculosis* (Mtb). An infection is a communicable disease that is transmitted through the air to other human beings. During cough, spitting or sneezing, the bacteria is transmitted into the air from where it enters into the respiratory tract of other human beings and causes infection in the lungs (Bloom et al.). The symptoms include a cough that persists for two to three weeks, fever, chills, loss of appetite, weight loss, and lethargy. Treatments of tuberculosis involve the use of various antibiotics over a different course of time depending upon the type of tuberculosis. There are mainly three types of Tuberculosis: Latent Tuberculosis, Active Tuberculosis, and Multiple Drug-Resistant Tuberculosis. The treatment for all these forms require different drugs due to the phenomena of antimicrobial resistance (Gillespie). The essay will focus on tuberculosis associated antimicrobial resistance phenomena in detail.

**Discussion**

Latent tuberculosis is a stage where the infection is present in your body but remains inactive. This inactive infection can be activated later in life and develop into tuberculosis. Anyone of these two antibiotics: [Isoniazid](https://www.webmd.com/drugs/drug-8665-isoniazid+oral.aspx) (INH), [Rifampin](https://www.webmd.com/drugs/drug-1744-rifampin+oral.aspx) ([Rifadin](https://www.webmd.com/drugs/2/drug-5662-65/rifadin/details), [Rimactane](https://www.webmd.com/drugs/2/search?type=drugs&query=rimactane)) or a combination of Isoniazid and [rifapentine](https://www.webmd.com/drugs/drug-8317-rifapentine+oral.aspx) varying in duration are used to treat this form of infection (Bloom et al.). Active Tuberculosis is a form in which active infection can spread to others. It is treated with various antibiotics such as Ethambutol (Myambutol), Isoniazid, Pyrazinamide and Rifampin over six to nine months. These medications are prescribed to the patient based upon the ability of bacteria to develop a resistance against a certain drug. These initially formulated drugs are used in combinations so, if one or two drugs are resisted by a strain of bacteria, others can have a possible effect on inhibiting the growth and development and prevent antimicrobial resistance (Lew et al.). In most cases, through plasmid, bacteria can pass the gene of antibiotic resistance to other organisms. There are three main mechanisms through which bacteria acquire resistance towards a certain antibiotic. First, through the cell wall which acts as a barrier to the entry of drugs into cells. Second, through the drug inactivating enzymes, present on its surface which can inactivate the drugs. Third, through the drug efflux systems which expel the drug out of system actively. Final, through mutations, which changes the target proteins thus rendering it inactive (Sandhu and Akhter).

As opposed to several other bacteria, *M. tuberculosis* does not exhibit plasmids of resistance however; drug resistance emerges by acquiring particular chromosome mutations (Müller et al.). The demographic orientation of *M. Tb* is predominantly clonal, indicating a minor role throughout the genetics of *M. tuberculosis* for horizontal gene transfer (HGT). The latest survey has criticized this view but it is continuously illustrated that HGT serves a presumed function in the development of antibiotic resistance in *M. tuberculosis* (Müller et al.). Drug-resistant genetic changes in *M. tuberculosis* were identified in genetic makeup that encode proteins that are specifically aimed by antibiotic treatment, in the gene regulatory regions, or in gene product lines that activate anti-drugs. Traditional evolutionary scientists predict that immunity-conferring variants occur quantum mechanically and regardless of medication intake within bacterial communities (Müller et al.). The mean level of incidence of isoniazid and rifampicin random tolerance alterations in M*. tuberculosis* was measured at 10−8 and 10−9 mutations/bacterium/cell division, correspondingly (Müller et al.).⠀ It suggests that considering the average percentage of estimated 108 enteric bacteria present in person Tuberculosis tumors, the presence of resistant strains will almost eventually occur throughout monotherapy (Müller et al.). Tuberculosis must, therefore, be handled with combination therapy with at least four antibiotic drugs.

In the case of Tuberculosis, the mechanism of bacterial resistance for rifampin is quite fascinating. The rpo gene is mainly involved in the synthesis of the beta subunit of RNA polymerase where rifampin acts and inhibits transcription. Rop gene mutation causes the gene to change the sequence of amino acids and thus altering the protein configuration. The configuration renders rifampin inactive because of the absence of a binding subunit (Gillespie). The bacterium is immune to other medicines by other genetic variations. For instance, there are several genetic defects in the genes katG, inhA, ahpC, and others which generate resistance to isoniazid (INH) (Gillespie). Amino acid modifications in InhA's NADH binding site seem to aid in INH tolerance by causing mycolic acid biosynthesis inhibition which occurs in the bacterial cell wall. Defects in the katG gene render it impossible for the protein catalase-peroxidase to transform INH to its pharmacologically active state. Therefore, INH is unsuccessful and bacteria develop resistance. Studies have established that to solve drug-resistant issues, the creation of new biochemical mechanisms is mandatory (Sandhu and Akhter). In certain Tuberculosis bacteria, the development of these defects can be interpreted by several modifications in the Genetic recombination, identification and repairing machinery. Genetic variations resulting in mutation enable the bacteria to have a significantly higher frequency of mutations as well as to acquire more mutations rapidly that generate antibiotic resistance (Gillespie).

The most severe form of tuberculosis corresponds to the resistance of bacteria towards several powerful anti TB drugs simultaneously and called as “Multiple Drug-Resistant Tuberculosis”(Wood and Iseman). In this case, the treatment is provided by the use of second-line anti TB drugs such as fluoroquinolones, amikacin, capreomycin, ethionamide, and para-aminosalicylic acid(Ginsburg et al.). Multi-Drug Resistant Tuberculosis can further become resilient to major categories of second-line Tuberculosis medications such as fluoroquinolones including drugs moxifloxacin, ofloxacin and intravenous aminoglycosides including amikacin, capreomycin, kanamycin. It is categorized as Extensively Drug-Resistant Tuberculosis when MDR-TB is resilient to at least one stimulant from each group (Ginsburg et al.). In a survey of MDR-TB victims in different parts of the world from the year 2005 to 2008, forty-three percent were reported to develop resistance to the minimum of one second-line medication. Approximately nine percent of MDR-TB instances were immune to both medications and were known as XDR-TB (*MDR\_TB\_FactSheet.Pdf*).

**Conclusion**

Tuberculosis is a leading cause of causalities around the world and its prevalence has now surpassed the percentage occurrence of HIV AIDS. However, the treatment of Tuberculosis is well recognized in the field of medicine still, most of the cases remain unsolved due to the emergence of the new strains. The treatment includes the use of multiple drug therapy which includes the administration of several different drug combinations because of the phenomenon of bacterial drug resistance. It has been evident from the studies that the emergence of new strains day by asks for the immediate development of new drug strategies so the prevalence of this epidemic can be taken under control.

**Works Cited**

Bloom, Barry R., et al. “Tuberculosis.” *Major Infectious Diseases*, edited by King K. Holmes et al., 3rd ed., The International Bank for Reconstruction and Development / The World Bank, 2017. *PubMed*, http://www.ncbi.nlm.nih.gov/books/NBK525174/.

Gillespie, Stephen H. “Evolution of Drug Resistance in Mycobacterium Tuberculosis: Clinical and Molecular Perspective.” *Antimicrobial Agents and Chemotherapy*, vol. 46, no. 2, Feb. 2002, pp. 267–74. *PubMed Central*, doi:10.1128/AAC.46.2.267-274.2002.

Ginsburg, Amy Sarah, et al. “Fluoroquinolones, Tuberculosis, and Resistance.” *The Lancet Infectious Diseases*, vol. 3, no. 7, July 2003, pp. 432–42. *ScienceDirect*, doi:10.1016/S1473-3099(03)00671-6.

Lew, Woojin, et al. “Initial Drug Resistance and Tuberculosis Treatment Outcomes: Systematic Review and Meta-Analysis.” *Annals of Internal Medicine*, vol. 149, no. 2, July 2008, p. 123. *DOI.org (Crossref)*, doi:10.7326/0003-4819-149-2-200807150-00008.

*MDR\_TB\_FactSheet.Pdf*. https://www.who.int/tb/challenges/mdr/MDR\_TB\_FactSheet.pdf. Accessed 10 Dec. 2019.

Müller, Borna, et al. “The Heterogeneous Evolution of Multidrug-Resistant Mycobacterium Tuberculosis.” *Trends in Genetics : TIG*, vol. 29, no. 3, Mar. 2013, pp. 160–69. *PubMed Central*, doi:10.1016/j.tig.2012.11.005.

Sandhu, Padmani, and Yusuf Akhter. “Evolution of Structural Fitness and Multifunctional Aspects of Mycobacterial RND Family Transporters.” *Archives of Microbiology*, vol. 200, no. 1, Jan. 2018, pp. 19–31. *PubMed*, doi:10.1007/s00203-017-1434-6.

Snider, Dixie E., and William L. Roper. “The New Tuberculosis.” *New England Journal of Medicine*, vol. 326, no. 10, Mar. 1992, pp. 703–05. *DOI.org (Crossref)*, doi:10.1056/NEJM199203053261011.

*Tuberculosis (TB)*. https://www.who.int/news-room/fact-sheets/detail/tuberculosis. Accessed 9 Dec. 2019.

Wood, Alastair J. J., and Michael D. Iseman. “Treatment of Multidrug-Resistant Tuberculosis.” *New England Journal of Medicine*, vol. 329, no. 11, Sept. 1993, pp. 784–91. *DOI.org (Crossref)*, doi:10.1056/NEJM199309093291108.