Tuberculosis (TB)

Tuberculosis is curable, yet is the second most deadly infectious disease due to detection difficulties and poor patient compliance during the 6 month antibiotic regimen.

Contraction, Spreading and Disease Progression: Tuberculosis (TB) is the result of bacterial infection primarily found in the lung. The bacteria (*Mycobacterium tuberculosis*) is transmitted most commonly through the transfer of small amounts of bacteria when coughing or sneezing (CDC 2013). In most cases the disease does not cause noticeable symptoms and is known as latent TB. This type of TB cannot be easily detected and the disease cannot spread in this state (WHO 2013). If a patient has a compromised immune system, the disease can replicate and the person can spread it to those they contact. As a result, patients co-infected with HIV, which have a weakened immune system, are 21 to 34 times more likely to have an active TB infection (WHO 2013). If the disease is not treated, 70% of people with active cases die within 10 years and 20% of people with latent cases die within 10 years (Tiemersma, 2011).

Detection: Detection based on clinical symptoms of such as chronic cough, chest pain and weight loss is very difficult and thus other methods are needed (CDC 2013). Most resource poor countries rely on sputum smear microscopy to visually detect the bacteria. Chest X-rays can also be used to detect TB in the lungs. Though effective, these tests cannot detect the latent form of the disease (CDC 2013). Alternative tests include tuberculin skin test, sputum culturing and interferon blood tests that are able to detect the latent form of the disease and are more commonly used in developed countries (CDC 2013).

Epidemiology: It is estimated that 1/3 of the world population is infected with the disease but the large majority of the cases are latent (US DHHS 2013). The active form of the disease is most prevalent in Sub-Saharan Africa and Southeast Asia (Figure 1). In 2011 there were 8.7 million TB incidences of active TB and 1.4 million deaths due to TB (WHO 2012). In addition, TB caused the largest number of deaths for those living with HIV (430,000 deaths in 2011) (WHO 2012). Additional risk factors for TB include smoking and diabetes (CDC 2013).

Map removed due to copyright restrictions. See Figure 2.5, Estimated TB incident rates, 2011 from *Global Tuberculosis Report*, 2012. WHO.

Treatment and Prevention: TB is a generally curable disease with a 6 month antibiotic regimen (CDC Treatment 2013). Through effective drug distribution and education, the rate of TB has decreased slightly since 2005, though, as stated before, the burden is still very significant (WHO 2012). The drop in the rate shows the power of collaboration between governments, aid agencies and pharmaceutical companies to educate and deliver therapies (WHO 2012 Report). The largest

risk to these treatment gains comes through the emergence of multiple drug-resistant TB (MDR-TB). MDR-TB is characterized by TB infections that do not respond to the first line drugs isoniazid and rifampin. This resistance is commonly caused by inappropriate treatment, non-compliant patients or poor quality medicine (WHO 2012). MDR-TB incidence is growing and in 2011 310,000 cases were reported (WHO 2012). It can be treated with more expensive therapies with more side effects, but its recent emergence underscores the importance of patient supervision and support by a healthworker to ensure completion of the 6 month antibiotic regime (Rowland, 2013). Recently new forms of TB that are even more drug resistant have developed. One called extensively drug-resistant TB (XDR-TB) is estimated to be present in 9% of MDR-TB cases (WHO 2012) and another called totally drug-resistant TB (TDR-TB) is much more rare, though potentially much more dangerous due to the ineffectiveness of current treatments (Udwadia, 2013).

Difference in Care Across Settings: Due to the role of HIV in TB mortality there are significant efforts in places with high levels of HIV, such as Sub-Saharan Africa, to actively screen TB patients for HIV and thus allow for treatment as soon as possible (WHO 2012). In addition, preventative therapy against TB is recommended to those with HIV to limit TB contraction. In 2011 half a million people received preventative therapy against TB, mainly in South Africa (WHO 2012).

Potential Disruptive Innovations:
Diagnosis: The introduction of the Xpert MTB/RIF nucleic acid amplification assay in 2010 has allowed for more sensitive and accurate diagnoses, less human error and the direct ability to test for MDR-TB (WHO 2012). By 2012 the new detection method was present in almost half of the 145 countries that were eligible for a reduced price. Quickly scaling this technology will allow for faster diagnosis of MDR-TB and therefore more effective treatment of this deadly condition. Current detection techniques take weeks to determine MDR-TB status and thus the disease can potentially spread.
Treatment: Current TB drugs are over 50 years old and the MDR-TB treatment regimen requires patient compliance for up to two years. There are 11 therapies in PhII and PhIII trials with many testing 4 month treatment regimes and also new therapies for MDR-TB (WHO 2012). Bedaquiline was recently approved by the FDA to treat MDR-TB (Walker, 2013). Another exciting development is the potential for future TB vaccines, however preliminary results from one potential vaccine (MVA85A) were disappointing (Tameris, 2013).
Collaboration: As stated before, the collaboration and data sharing by government with organizations such as WHO has allowed for tracking of the disease, standardized testing and implementation of treatment programs (e.g. DOTS) with proven track records (WHO 2012). The FDA fast-track and orphan drug programs also have the potential to enable the development of novel TB therapies by enabling financial returns even though the large majority of TB patients are in less-developed countries (Walker, 2013).

Future Challenges: Future challenges focus around the development of new therapies for the growing threat of MDR-TB. Ideally these therapies would have a shorter treatment times, thus greatly reducing healthcare worker burdens, medicine delivery burden and costs. The WHO also has made significant efforts to scale up HIV/TB treatment collaboration which is essential to slow the co-morbidities, spread and progression of the disease.

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