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An Unequal Consumption? Sex and Gender Differences in Tuberculosis

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AN UNEQUAL CONSUMPTION? SEX AND GENDER DIFFERENCES IN TUBERCULOSIS

by

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In the developing world today, tuberculosis (TB) accounts for 26% of avoidable deaths (Holmes et al 1998). Poverty is considered to be a main risk factor for TB, and since some estimates show that women make up 70% of the world's poor (Thorson and Diwan 1998:11), one might conclude that the incidence of TB worldwide would be much higher for women than men. However, reports reviewed in this thesis show the reverse to be true, with an adult annual male notification ratio for TB at 1.5 to 2.1 times higher than that of females. Both biological reasons and social factors have been presented by researchers in an attempt to explain this discrepancy, but no one set of literature has looked at both biological and social factors together.

In this literature-based thesis, I explored two disparate sets of literature: those that examine the biological differences in TB by sex and those that study the social context and cultural aspects of TB. After reviewing these studies, I do believe that there is most likely a slight biological resistance to tuberculosis for women. However, when studying the biological and social factors together, I feel that the social factors that work against women may be concealing a higher rate of TB in women than is being reported.

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CHAPTER I

INTRODUCTION, STATEMENT OF THE PROBLEM, AND OVERVIEW

The "eradication" of tuberculosis (TB) was prematurely thought to be one of the great triumphs of modern medicine as the disease had all but disappeared from public view in the global North by the 1960s (Feldberg 1995). However, in the developing world at present, tuberculosis accounts for 26% of avoidable deaths and approximately 80% of people who succumb to tuberculosis are in the most economically productive ages of 15 to 54 years (Holmes et al 1998:96). Not only is tuberculosis still a major health issue, but as Snider (1997 in Gandy and Zumla 2003:7) states, "tuberculosis was a major world health problem 50 years ago, and it is an even greater problem today".

In general, infectious disease is still the most common cause of death in the world (Thorson and Diwan 2003), and TB has been one of the most rampant and destructive. In recent years, the development and spread of multi-drug resistant tuberculosis (MDR-TB)[1] has hindered even more so our ability to respond to this infection. Addressing the inaccurate reference of tuberculosis as a disease of the past and of its reappearance, Gandy and Zumla state that "the resurgence of a disease is one of the most telling indictments of the failure of global political and economic institutions to

improve the lives of ordinary people" (2003:7). The failure of social institutions that Gandy and Zumla refer to has helped to produce some of the largest risk factors corresponding with tuberculosis infection: poverty and social inequality.

Statement of the Problem

Poverty is considered to be a main risk factor for tuberculosis, and since some estimates show that women make up 70% of the world's poor (Thorson and Diwan 1998:11), one might conclude that the incidence of tuberculosis worldwide would be much higher for women than men. However, reports such as Dolin's (1998), Holmes et al (1998), Diwan and Thorson's (1999), Borgdorff et al (2000), Martinez et al (2000), Uplekar et al (2001), and Salim et al (2004) have actually shown the reverse to be true, with the adult[2] annual male notification ratio for tuberculosis at 1.5 to 2.1 times higher than that of females. To date, this difference has not yet been satisfactorily explained. Statistics such as these raise the question of whether this difference is due to a biologically higher resistance to tuberculosis in women, less exposure of women to the disease, an under-diagnosis of tuberculosis in women, skewed reporting and treatment, or a combination of these factors.

At present, most of the research conducted regarding sex differences in TB has taken either a biological or a social stance. Because of this "either/or" focus, the current literature fails to make sufficient connection between the biological sex differences in tuberculosis and the social variables that affect this disease. Additionally, researching diseases such as tuberculosis by concentrating only on biological or on social factors could inadvertently lead to a misrepresentation of the actual disease prevalence. Not connecting both realms in tuberculosis research may in fact result in a statistical disparity between male and female notification rates when in actuality, this disparity may not be so severe on a practical level. In this literature-based thesis, I will present the main arguments of both sets of research, and will attempt to bridge the gap in the research between the social and biological reasons for the disparity in tuberculosis notification data between the sexes. I argue that examining both the biological as well as the social factors affecting tuberculosis may actually unveil a TB notification rate that is much more similar between the sexes than is currently reported.

Origins of the Question

Although some sources cite a 2:1 ratio of male tuberculosis notifications to female, tuberculosis is still a serious disease for women. Worldwide, tuberculosis is one of the major killers of girls and young women,

causing an estimated 800,000 deaths each year (Liefooghe 1998:89). In the developing world today, TB kills more women than all causes of maternal mortality combined (Grange, Ustianowski, and Zumla 1998:77). Ngamvithayapong-Yanai et al (1998:127) state that tuberculosis is the leading infectious killer of women in the world. Perhaps by discovering the reasons behind why tuberculosis notification rates are lower for women than for men, the overall prognosis of both sexes in regards to tuberculosis will benefit.

As with many aspects of medicine and health, sex and gender related inequalities in infectious diseases have been neglected research areas. In general, most clinical research is based on males and adheres to the unstated assumption that apart from reproduction, men and women are physiologically the same (Doyal 1998). This way of thinking already gives women a health disadvantage because women's unique biology is not taken into account. It is assumed that what will work clinically for the man will also work for the woman. A greater emphasis needs to be placed on women's health in general.

Fortunately, the topic of sex differences in health is increasingly recognized for its importance in furthering the understanding of epidemiology and treatment of infectious diseases (Thorson and Diwan 1998). Previously, studies on women and disease have mainly focused on how

childbearing affects disease. Yet, even the existing literature on tuberculosis and pregnancy is inconclusive, as is much of the general literature on sex and gender differences in tuberculosis. According to Snider (1984, in Grange et al 1998:77):

> Very little can be said about this subject [tuberculosis and pregnancy] that is not controversial. There is a surprisingly large body of literature, but much of it is quite old and many of the studies were not designed or analysed [sic] in a manner which permits definite conclusions.

Some recent research is now examining how women's reproductive systems as a whole, specifically sex-based hormones and other sex-related biological factors, affect disease. For example, several authors cite growing evidence that sex-related biological factors such as differential immune responses, differing levels of antibody production, and T cell differences can affect both the susceptibility and immunity to infectious diseases (Doyal 1998, Dolin 1998, Bothamley 1998, Rook 1998, Grange et al 1998). Furthermore, epidemiological evidence points to biological sex-based differences in the incidence, risk, histology, and pathogenesis of certain lung diseases (including tuberculosis) in women compared to men (Caracta 2003). Caracta's work as well as the work of other researchers who pose biological reasons for the increased incidence of tuberculosis in males versus females will be explored further in Chapter 3.

Indeed, it appears as though there may be biological differences in the way men and women are affected by tuberculosis. However, tuberculosis is not just a disease in the medical sense of the word; diseases are also social entities. Dubos and Dubos (1992) call tuberculosis a "social disease" as it is so closely linked to the welfare of the population. Social factors such as gender differences in behavioral patterns, social roles, and different access to resources influence both the degree of exposure to infections as well as the available options for those who do become infected (Doyal 1998, Thorson and Diwan 1998, Liefooghe 1998, Rangan and Uplekar 1998, Ngamvithayapong-Yanai 1998). The elimination of tuberculosis will be seemingly impossible as long as poverty, overpopulation, poor access to health care, and malnutrition characterize a large portion of the world.

The rapid spread of tuberculosis and other infections in places such as jails, orphanages, and poor neighborhoods of large cities in much of the developing and post-socialist world can be attributed to the above-mentioned factors. These factors are by no means exclusionary; nor are developing and post-socialist countries the only areas of the world to still be affected by this disease. The United States, Canada, and many parts of Europe also have higher than desirable rates of tuberculosis infection in jails, prisons, shelters, and other high-density urban areas. Although there are several treatments

for tuberculosis, there are still inadequate detection techniques, and overall, the best way to eradicate this disease seems to be through prevention of the social environment that aids in its easy transmission.

According to Barnett and Casper, in the realm of public health there has been an upsurge in interest in how social environment influences population health (2001), especially related to disease. These authors define "social environment" as encompassing "the immediate physical surrounding, social relationships, and cultural milieu within which defined groups of people function and interact (2001:465)". Barnett and Casper pose that the components of social environment include:

> built infrastructure; industrial and occupational structure; labor markets; social and economic processes; wealth; social, human, and health services; power relations; government; race relations; social inequality; cultural practices; the arts; religious institutions and practices; and beliefs about place and community. The social environment subsumes many aspects of the physical environment, given that contemporary landscapes, water resources, and other natural resources have been at least partially configured by human social processes. Embedded within contemporary social environments are historical social and power relations that have become institutionalized over time. Social environments can be experienced at multiple scales, often simultaneously, including households, kin networks, neighborhoods, towns and cities, and regions (2001:465).

Considering the above definition, it would be obviously erroneous to say that the social environments that contribute to tuberculosis are the same all over the world. Indeed, social environment can differ for people living

within the same city, the same neighborhood, the same street, or even the same family. Because one's social environment is dependent on factors such as age, ethnicity, occupation, health status, socioeconomic status, biological sex, and gender, a thorough investigation of the spread of disease should also consider these factors.

Holmes et al (1998) demonstrate that the examination of social differences between males and females in the epidemiology of other tropical diseases has yielded useful insights. For example, when passive case-finding techniques were used to determine malaria and leishmaniasis[3] infection rates, it was found that women were under-represented at the clinics compared to the actual community prevalence rates. As stated by I. Smith (1994, in Thorson and Diwan 2003:55): "Gender of itself is not the cause of morbidity and mortality in tuberculosis, but it is a powerful indicator of disadvantage, a marker of the many factors that influence health and the utilization of health services". Uplekar et al (2001) make the point that the mere availability of health care services (physical access) may not ensure its use. Services must also be acceptable (socio-cultural access) and affordable (economic access). These barriers to health care access generally affect women more so than men. Other social differences regarding men, women, and tuberculosis will be discussed in Chapter 4.

Tuberculosis: Understanding the Disease

Tuberculosis is an unrelenting infection that has survived the ages and currently has higher morbidity and mortality rates than any other infection in the world. In 1993, the World Health Organization (WHO) determined that the magnitude of tuberculosis infection was so high that it declared tuberculosis a "global emergency," the first time in WHO history that a single infectious disease was given such priority (Ollé-Goig 2000). In 1996, the WHO (quoted in Farmer 1999:184) stated that, "In 1995, more people died of tuberculosis than in any other year in history". This alarmingly high rate is primarily due to the high prevalence of tuberculosis in the densely populated developing countries, as well as overall low detection rates and poor cure rates.

In 1996, it was estimated that 7.4 million people developed tuberculosis, but only 3.8 million were reported to the WHO (Thorson and Diwan 1998:9). Even more recently, the WHO has selected a goal of the reversal of the trend of tuberculosis by the year 2020 as one of the top ten global health targets in the new WHO policy "Health for All in the 21st Century" (Ollé-Goig 2000). According to Blanc and Uplekar (2003:95), currently two billion people, or approximately one-third of the global population, are infected with tuberculosis and are at risk of developing the

disease and Borgdorff et al (2000:123) states that approximately two million people die from tuberculosis annually.

Clearly, tuberculosis is a disease that still demands world attention. A communicable infection primarily caused by *Mycobacterium tuberculosis*, (also called the tubercle bacilli), tuberculosis is typically transmitted through the inhalation of tiny airborne particles called droplet nuclei that are expelled by a person who has infectious tuberculosis (U.S. Dept. of Health and Human Services 2000). Some of these bacilli reach the alveoli of the lungs, where they are ingested by macrophages (U.S. Dept. of Health and Human Services 2000). Actual infection begins with the multiplication of tubercle bacilli within these alveolar macrophages. Most healthy people have immune systems that can contain the bacilli and will prevent the development of active tuberculosis, resulting in a latent infection. Persons who have a latent infection are asymptomatic and not infectious but such persons usually have a positive reaction to the tuberculin skin test (U.S. Dept. of Health and Human Services 2000). Statistically, only about 10% of these infected persons will develop active tuberculosis at some time in their life, but the risk is considerably higher for persons who are immunosuppressed, especially those with HIV infection, young children, the elderly, and those whose basic nutritional and sanitary needs are not met (U.S. Dept. of Health and Human

Services 2000). However, tuberculosis is not only limited to the lungs. Although the majority of tuberculosis cases are pulmonary, and the lung is almost always the portal of entry into the body, tuberculosis can occur in almost any anatomical site, in any organ of the body, or it may manifest as a disseminated disease such as Potts disease[4] and scrofula[5] (Stead and Dutt 1994).

Today in the United States, there are several areas of concern in regard to tuberculosis: tuberculosis cases continue to be reported in every state, drug-resistant cases are reported in almost every state, and an estimated 10 to 15 million persons in the United States are infected with *Mycobacterium tuberculosis* and without intervention, about 1 to 1.5 million of these people will develop the disease at some point in their life (U.S. Dept. of Health and Human Services 2000). Global migration has also changed the international landscape of infectious disease, affecting the United States especially. It is estimated that today in the United States, half of all cases of tuberculosis occur in foreign-born persons (mainly from Mexico, Haiti, sub-Saharan Africa, South Asia, and developing nations in East Asia and the Pacific), who represent just 10% of the total United States population (Khan et al. 2002). Although this surge and resurgence of tuberculosis in the United States is quite alarming, the fact of the matter is that much of the rest of the world is

even worse off in regard to the disease. In the next chapter I will look more in depth at the history of tuberculosis, its epidemics, as well as some worldwide tuberculosis trends.

CHAPTER II

BRIEF HISTORY OF TUBERCULOSIS, ITS EPIDEMIC WAVES, AND CURRENT SEX TRENDS

Tuberculosis is a disease with many guises throughout its history. The name of the disease, its description and afflictions, and the perception and treatment of tuberculosis have all changed over time, and are in some ways are still evolving. No matter the guise, few other diseases have caused human suffering on the same scale as tuberculosis. In this chapter, a brief history of tuberculosis will be explored, mainly citing from Rothman's "Living In the Shadow of Death" (1994). I will also delve into this disease's epidemic waves and some current worldwide TB sex trends.

Brief History of Tuberculosis

Hippocrates (460-370 BCE), the classic medical scholar, considered "phthisis" (or pulmonary tuberculosis as it is known today) to be the "greatest and most terrible disease" (in Gandy 2003:15). Indeed, tuberculosis is one of the oldest and most persistent diseases known to civilization (Rothman 1994, Gandy 2003) - a combination of historical and archaeological evidence shows that tuberculosis was widespread in early Hindu, Greek, and Roman societies, and gradually spread for over 2,000 years (Gandy 2003).

Skeletons found in Neolithic burial grounds and mummified bodies preserved in ancient Egyptian tombs reveal evidence of the disease (Rothman 1994:14), and it has been suggested that infected humans introduced the contagion to the New World sometime between the last ice age (15,000 to 35,000 years ago) and the completion of deglaciation (approximately 6,000 years ago) (McKinney et al 1998:52).

Although it is known that tuberculosis has affected the human condition for ages, little is known about the actual impact of tuberculosis from the medieval to the early modern period, as its prevalence was not well documented (Rothman 1994:14). By the seventeenth century, however, this disease had become very common. Whatever its antecedents, it was not until the beginning of the nineteenth century that this disease became insidious and feared (Rothman 1994). For most of the 19th century, tuberculosis was referred to as "consumption" or the "great white plague" and was considered by physicians to be a hereditary and non-contagious condition (Rothman 1994). In this era, the symptoms of consumption were defined in terms of the readily observable physical changes – the body was literally consumed by the disease (Rothman 1994:4). Descriptions of the symptoms of tuberculosis in medical texts focused on the physical attributes and progression of the disease: the cough developed from "frequent and harassing" to "hollow

rattles" and "graveyard coughs" (Rothman 1994:4). The initial "ruddiness" of the face eventually gave way to the "deathlike paleness", which was masked by a "glowing hectic flush" in the last stages of the disease (Rothman 1994:4).

During the early 19th century, those who contracted consumption were considered "invalids," a term that was as much social as it was medical (Rothman 1994:4). To be classified as an invalid was by definition to be excused from fully complying with social expectations, "invalids" were allowed to modify or even avoid obligations of earning an income or becoming a wife or mother (Rothman 1994:22). However, "invalids" were also expected to have a life long occupation of improving their health (Rothman 1994:23). Persons with consumption were not patients, they were "health-seekers" (Rothman 1994).

At this time, physicians believed that the disease originated in "irritations," which were believed to be caused by an interaction between an inherited constitution and particular life-styles and environment (Rothman 1994:4). The most "irritating" occupations were ones that were considered to be sedentary and "bookish," like law, ministry, and teaching. Climates that were the most "irritating" were those with cold, wet, and windy weather (Rothman 1994:4). Physicians in the United States "prescribed" ways to reverse the course of the disease, namely countering the "irritants" by

changing diet to a "mild" and "unstimulating" one, altering routine to follow a regimen of "gentle exercise," and moving to a "mild and uniform" climate (Rothman 1994:4). Diet, exercise, and climate affects much of a person's life, and so it seems that tuberculosis did not just consume the bodies of persons affected, but also consumed their uncertain lives as well. For those affected, all efforts were put forth to try to reverse the disease, whether it meant choosing a less "irritating" job or moving cross-country to a better climate, and they were unable to know the course their disease, and therefore their life, would take (Dormandy 1999).

In 1882, a discovery revolutionized both the medical and the social history of tuberculosis (Rothman 1994). Through a novel staining method, Robert Koch identified the tubercle bacillus and was able to distinguish it from other bacteria: "Under the microscope all constituents of animal tissue...appear faintly brown, with the tubercle bacilli, however, beautifully blue" (in Rothman 1994:179). Based upon his discovery, Koch was then able to quickly prove that tuberculosis was an infectious disease, and it was now possible to define its boundaries. Koch also came to understand that the bacteria entered the body and that "the great majority of all cases of tuberculosis begin in the respiratory tract, and the infectious material leaves

its mark first in the lungs or in the bronchial lymph nodes" (Rothman 1994:179).

Koch's discovery inspired a new scientifically derived terminology for the disease. "Consumption" rapidly became an arcane term, for it no longer seemed suitable to define a disease by its most dramatic symptom. The new designation, tuberculosis, linked the disease directly to its causative agent. Diagnosis now depended on the presence of the tubercle bacillus in the sputum, not the hollowness of the cough or the loss of weight (Rothman 1994). However, even with the new biological definition of the disease, the concept of tuberculosis was still seen as a disease born and bred of poverty, and by 1903, the fear of tuberculosis and of those who had the disease had its own term: phthisiophobia (Rothman 1994). Men and women with tuberculosis now referred to themselves as "tbs" or "lungers" - their diseased organ represented their persona (Rothman 1994). The afflicted were still considered to be invalids in a sense; a "special species" who were morally as well as physically disabled (Rothman 1994). Even early in its definable life, it was very difficult to separate biology and social factors when it came to tuberculosis.

In contradistinction to the American prescriptions of travel for health for tuberculosis sufferers, the first institutional treatment for consumption

took place in Germany in the middle of the nineteenth century (Rothman 1994). The promoters of the sanatorium were convinced that confining people afflicted with tuberculosis in facilities would promote both societal well-being (by isolating those with the disease), but also individual well-being by implementing a therapeutic regimen with medical supervision (Rothman 1994). The German system of sanatoriums triumphed over the American prescriptions, and by 1900, thirty-four tuberculosis sanatoriums with 4,485 beds had opened in the United States (Rothman 1994). Twenty-five years later, there were 536 sanatoriums with 673,338 beds in the United States (Rothman 1994). However, both methods of tuberculosis "treatment" - changing one's social conditions or entering a sanatorium - could only be utilized by those who were economically comfortable.

Today it is still difficult to separate biological and social factors when discussing the reasons why tuberculosis has not been eradicated. However, two biological diseases have further hindered the abolition of tuberculosis: the emergence of HIV and multi-drug resistant strains of TB (MDRT). The great number of people who are co-infected with both tuberculosis and HIV/AIDS and the increased spread of drug-resistant tuberculosis render some cases unresponsive to standard treatment and other cases completely untreatable (Blanc and Uplekar in Gandy and Zumla 2003), not to mention

the creation of new social barriers and implications due to these biological developments. In combination, these factors indicate that there could be an unprecedented global health catastrophe fueled by tuberculosis infection in the near future. In the next section, I will discuss the epidemic waves of TB that have occurred in the past.

Tuberculosis Epidemics

Because of the viability of latent tubercle bacilli in the tissue of healthy persons (U.S. Dept. of Health and Human Services 2000), tuberculosis poses both an immediate and a delayed threat to the population at large. A delayed threat is possible when a significant percentage of any population carries latent tuberculosis infection. When the bacilli produce disease, the disease course is chronic and protracted giving ample time for transmission to susceptible hosts (Stead and Dutt 1994). Therefore, tubercle bacilli infection can produce disease in a human being after decades of dormancy. Conversely, tuberculosis can produce an epidemic when introduced into a new population where only a small number carry the immunological protection of a previous latent infection (Stead and Dutt 1994). When a new tuberculosis infection is introduced into a susceptible population, the morbidity and mortality rates take the predictable form of an epidemic wave (Stead and Dutt 1994).

As is the case with all epidemic waves, there is a sharp rise to a peak followed by a more gradual descent in the numbers of persons affected by the disease. For many other infectious diseases, this epidemic curve is measured in weeks or months, but for tuberculosis, this curve is measured in decades and centuries (Stead and Dutt 1994). According to Stead and Dutt (1994), the wave form of the tuberculosis epidemic occurs by natural selection of susceptible persons and runs its course in about 300 years. Tuberculosis sufferers did not usually succumb to the disease within a matter of days, as occurred with other infectious diseases. Acute attacks alternated with remissions, and the process of wasting away and dying could take several years to several decades (Rothman 1994:13).

In the U.S., the first available mortality figures were from Massachusetts in 1786, and they indicated that tuberculosis was responsible for 300 deaths per 100,000 population (Rothman 1994). The gradual urbanization of human populations, with increases in community sizes resulting in crowding was probably one of the main causes for the peak mortality figure in New England to reach 1,600 deaths per 100,000 people per year in 1800 (Rothman 1994, McKinney et al 1998). Tuberculosis was the leading cause of death in the United States throughout the nineteenth century

and well into the twentieth (Rothman 1994). From 1800 to 1870, tuberculosis caused one out of every five deaths (Rothman 1994:2).

In general, tuberculosis spread throughout the United States and other countries with the Industrial Revolution. In many countries there was an explosive increase and peak of tuberculosis incidence between 1790 and 1840 (Dormandy 1999). These dates are transposable with appropriate adjustments for countries like France, Germany, Scandinavia, and countries in Eastern Europe where the Industrial Revolution was delayed or more protracted (Dormandy 1999). Additionally, the peak of tuberculosis spread throughout different areas of the United States and followed the path of industrial development. The peak of the tuberculosis epidemic was reached in New Orleans in 1840, and the West in 1880 (Rothman 1994). Until the advent of public health measures such as modern sewage systems, towns and cities in both the United States and Europe were places of demographic decay and could not sustain themselves without a steady influx of immigrants from the healthier countryside (McKinney et al 1998:53). After 1870, the mortality rates in the general population declined, but the disease became endemic among immigrants living in crowded housing in the poorer neighborhoods (Rothman 1994). The urban death rate (deaths per 100,000 population per annum) from pulmonary tuberculosis in the U.S. remained at a fairly constant

high level throughout the first half of the nineteenth century (McKinney et al 1998). After about 1880, the urban death rate finally entered a period of steady decline (McKinney et al 1998).

The disease also spread throughout various ethnic groups at different rates and times. For instance, TB occurred in blacks at a lower rate than in whites before the Civil War. After the war, the increase was massive among blacks, with a peak of 650 per 100,000 people per year in 1890 when increased mobility and urbanization created an ideal atmosphere for the transmission of tuberculosis (Stead and Dutt 1994). There is also controversial evidence of the presence of the disease in American Indians prior to the arrival of whites, but it is generally thought that American Indians did not have a problem with tuberculosis until they were concentrated in reservations. Peak prevalence in this group was reached about 1910 as a consequence of urbanization and crowding, which again favored the easy spread of the infection (Stead and Dutt 1994).

Social issues such as urbanization, industrialization, and warfare, which were countered by implementation of public health measures, would cause tuberculosis rates to wax and wane, even in the middle of a fairly predictable epidemic wave. For example, there was a steady decline in tuberculosis death rates in England and Wales from 1904 through 1945

(McKinney et al 1998). This steady decline was temporarily interrupted and the TB rates once again rose between 1914 and 1918 during World War I, and again during 1939 and 1945, the period of World War II (McKinney et al 1998).

The United States public health service mounted a crusade against tuberculosis in the 1930s through 1950s based upon hygienic measures and chemoprophylaxis rather than vaccination[6], and the tuberculosis rates started to drop (Rothman 1994). At the time, penicillin or streptomycin were used as the main TB drugs until the introduction of isoniazid in 1952 and rifampin in 1974[7] (Reichman and Tanne 2002). There have been no new class of drugs for treating tuberculosis since the 1970s (Reichmann and Tanne 2002), and for several years, it appears as these drugs were very effective, as the TB rates dropped.

However, in New York City in 1979, rates for tuberculosis began to climb again, and between 1980 and 1991, the number of cases increased 145% (Rothman 1994). One of the main causes was that alarmingly, 19% of the microorganisms were resistant to the two most effective and least toxic drug treatments - rifampin and isoniazid (Rothman 1994). Resistance is often a result of the fact that many people affected with tuberculosis begin a course of therapy, but fail to complete it, thereby fostering the emergence of drug-

resistant strains. In 1991, public health officials "sounded the alarm," acknowledging that the disease was back with a new force and deadliness. In keeping with past trends, tuberculosis continued to show itself as a disease of those without social privilege - in this case, African Americans and other minorities, the homeless, and those people infected with HIV (Rothman 1994).

Reports in recent years of tuberculosis in the United States mainly associated with immigration, new drug resistant strains, and HIV/AIDS have challenged the image of tuberculosis as a disease of history. To many, the resurgence of tuberculosis, like the advent of AIDS, represents a failure of biomedicine - a failure to adapt to changing biological strains or new population bases (Feldberg 1995). Since 1981, another epidemic that is closely related to and has increased the dangers of tuberculosis has been in progress, HIV/AIDS (Stead and Dutt 1994). Since HIV kills T-helper cells (T4 lymphocytes[8]), it renders its victims without defense against mycobacterial infection (Stead and Dutt 1994). Because of the loss of these T-lymphocytes and macrophages, the only defense the body has against *M. tuberculosis* is lost. HIV infection not only increases the risk of reactivation of dormant tuberculosis infection, but it also greatly increases the risk of progressive disease from a new infection (Stead and Dutt 1994).

The wave of tuberculosis in relatively recent history reached its peak at points in time when industry and urbanization caused overcrowding, coupled with a public health system that could not support the demographic growth. War also caused spikes in tuberculosis rates. In much of the developing world, TB may still be considered an emerging infection as the disease spreads to previously unaffected regions and case rates continue to rise. Tuberculosis was apparently rare in India and China until the end of the nineteenth century, and did not reach the island of Papua New Guinea until the middle of the twentieth century (McKinney et al 1998). In the remote interior of sub-Saharan Africa, TB was virtually unknown well into the twentieth century (McKinney et al 1998).

With the development of chemoprophylaxis, especially the rifampin class of drugs, it was thought that tuberculosis would be totally eradicated in the foreseeable future. However, the resilience of the disease and the difficult and long treatment program for tuberculosis caused strains of the bacteria to develop resistance to several of the first line drugs that are used to treat TB. These multi-drug resistant strains, coupled with the advent of the age of HIV and AIDS, have perhaps placed us on the cusp of a new, different tuberculosis epidemic. In this next section, I will review the current trends of tuberculosis in the literature from various cultures and countries, with a

special focus on the difference in tuberculosis rates between males and females.

Current Worldwide Tuberculosis Sex Trends

A striking feature of tuberculosis which is apparent in both incidence[9] rates and prevalence[10] surveys from most parts of the world is that tuberculosis seems to affect more men than women (Borgdorff et al 2000, Holmes et al 1998, Martinez et al 2000, Uplekar et al 2001). Many separate studies in varying parts of the globe and throughout different eras have found that the general worldwide prevalence of infection with tuberculosis is similar in males and females until early adolescence, after which the prevalence is higher in males (Holmes et al 1998). Unfortunately, although this trend is evident through various cultures, the age at which the prevalence of TB increases in males compared to females is very inconsistent, as is indicated by the following study results.

An analysis of tuberculin prevalence surveys from mass bacilli Calmette-Guérin (BCG) vaccination campaigns in 15 countries worldwide conducted by the International Tuberculosis Campaign in 1948 through 1951 suggested that the prevalence of tuberculosis infection was nearly equal in males and females before about 10 years of age (Holmes et al 1998). However, between the ages of 10 and 16, the male prevalence began to

exceed that of females (Holmes et al 1998). These findings are similar to those done by the WHO in Africa during the same era (Holmes et al 1998). Additionally, two studies in India, one conducted in the Bangalore District consisting of four surveys of randomly selected villages between 1961 and 1968, and one conducted in Chingleput, India, found that males and females had roughly a similar prevalence of infection until the age of 14, after which the prevalence among males was 20% to 71% higher than among females (Holmes et al 1998). A study with similar results was carried out with the Korean Prevalence Surveys. In these surveys, tuberculin testing was performed along with chest x-rays and bacteriological screening. It was found that among unvaccinated persons aged 0 to 9, the prevalence of the tuberculosis skin test positivity was about the same in both sexes. However, males older than age 15 had a 3% to 30% higher prevalence of skin test positivity than females (Holmes et al 1998).

Uplekar et al (2001) also performed a literature review and carried out field visits to tuberculosis programs. They used prevalence data and notifications from 29 surveys in 14 countries. Notification rates varied strongly among countries, but the female to male ratio was below 1.0 and decreased with increasing age in almost all of the countries from which the data was reviewed. Borgdorff et al (2000) found similar results in their

comparison of prevalence surveys. The authors found that the female to male ratio was less than 1.0 in all countries except Samoa. The female to male notification rate ratio decreased with increasing age in all countries except Syria. They also found that in Kenya, Malawi, and Tanzania the HIV epidemic, although accounting for an overall substantial increase in tuberculosis case-load, led to only a minor shift in the female to male notification ratio (Borgdorff et al 2000). However, the authors do not seem to take into account the fact that HIV notification could also have a stigma, leading to less accurate notification numbers.

From the research reviewed above, it does seem nearly universal that the prevalence of tuberculosis is higher in males than females. Martinez et al (2000) also looked at TB incidence rates in the United States, and found a similar pattern. The authors conducted a retrospective epidemiologic analysis of sex-specific tuberculosis incidence rates in San Francisco from 1991 through 1996 using all reported cases of tuberculosis (pulmonary and extra-pulmonary) (Martinez et al 2000). A stratified analysis was performed on the age at tuberculosis diagnosis, ethnic group, HIV status (when known), and place of birth. Molecular fingerprinting data was also used to show sex differences in the incidence of disease for recently transmitted versus reactivated cases of tuberculosis. San Francisco was chosen because the

current tuberculosis epidemiology at the time in that area reflected a blend of ongoing transmission in the U.S.-born population and a reactivation of the disease in the foreign-born population (Martinez et al 2000).

The results of the Martinez et al (2000) study also yielded remarkably similar results to other studies and surveys performed all over the world. The researchers found overall that the male to female ratio for the reported incidence of tuberculosis was 2.1 and that in both the U.S.-born and the foreign-born populations, the ratio was close to 1.0 until the age of 14. Additionally, higher male to female ratios were seen in the U.S.-born Caucasian and African American populations (Martinez et al 2000). After the age of 14, the difference between male and female incidence rates increased. In these populations, after the age of 25, the incidence of tuberculosis in males was generally 2 to 3 times higher than in females. The increased incidence in males in these populations remained even in the HIV-negative stratum, suggesting that HIV infection could not be the sole explanation for the difference (Martinez et al 2000).

Another pattern that has been documented in the literature is that females have a higher tuberculosis mortality rate than males at certain ages. There is again inconsistency though, regarding exactly what ages these are, depending on the time and place where the studies were conducted. For

example, Frost (1939) observed that females in the birth cohort of 1880 in Massachusetts had a higher mortality rate than males from ages 5 to 19 years. From the ages of 20 and 29 years, the rates were equal, after which the men's rates were higher (Frost 1939). Holmes et al (1998) also cited several studies that observed a very similar pattern, suggesting that females had higher tuberculosis mortality than males through approximately age 29 (conducted in China in 1990, in Denmark and Iceland in the mid-1900s, in the non-caucasian population of the United States in 1962 and in 1990) or age 35 (conducted in Nagpur, India from 1957-1976). After these ages, the men's rates were several times higher than that of the women.

All of the above papers and studies do seem to present a valid argument that through recent history and in various countries and cultures, the consistent sex-based pattern of tuberculosis incidence, prevalence, and mortality is very similar. It overwhelmingly appears as though adult males have a higher incidence and prevalence of tuberculosis than females, regardless of country or even time period studied. On the other hand, it seems as though females have a higher tuberculosis mortality rate than males up to approximately 19-35 years of age. None of these studies or statistics, however, explains *why* these sex-based differences exist. Next I will look more in-depth at the specific studies that have tried to assess the biological

and social factors that may cause the sex differences in tuberculosis notification ratios.

CHAPTER III

THE BIOLOGICAL EVIDENCE FOR SEX DIFFERENCES IN TUBERCULOSIS

When discussing male and female patterns of health, one of the most noticeable differences is that women as a group tend to live longer than men of the same social status as themselves (Doyal 1998). Clearly the extent of women's greater longevity varies between countries, and in some societies, types of gender discrimination may eliminate the difference altogether. However, broadly speaking, women appear to be the biologically stronger sex when it comes to life expectancy. Yet at the same time, some reports suggest that women also report more sickness and distress than do men (Doyal 1998). Undoubtedly there are great benefits to be found in examining and understanding the impact of gender and sex on human health in general, as well as how sex affects diseases such as tuberculosis. Unfortunately, this area of research has not been as active to date as it should be.

Despite the lack of comprehensive or conclusive research into the biological differences between men and women affected by tuberculosis, there has been some important work conducted in the general area of the intersection of sex and disease. The various biological factors that may play a role in producing a male-female divide in tuberculosis notification and in

other diseases can be broken down into several subsets: the effects of pregnancy on disease and differential susceptibility to disease (Caracta 2003, Gerberding 2004, Rook 1998, and Grange et al 1998), differential tuberculosis presentations and response to tuberculosis testing (Bothamley 1998, Diwan and Thorson 1999, Caracta 2003, and Kivihya-Ndugga et al 2005), and tuberculosis and HIV/AIDS co-infection (Harries et al 2003, Corbett et al 2003, Kumar et al 2001, and Gerberding 2004). I will explore each of these subsets individually.

Effects of Pregnancy on Disease and Differential Susceptibility to Disease

Although it is not accurate to describe the differences in male and female health risks based solely on reproductive capabilities, it does seem that pregnancy has specific effects on certain diseases. The question as to whether pregnancy and/or childbirth have adverse, beneficial, or no significant effects on the clinical course of tuberculosis has been the topic of considerable debate for almost as long as tuberculosis has been a known disease. According to Miller and Miller (1996), Hippocrates and Galen held the view that pregnancy had a beneficial effect on tuberculosis. This view persisted until the early 19th century, leading some physicians to advise pregnancy as a tuberculosis remedy (Grange et al 1998). Aside from a postulated hormonal cause for the supposed beneficial effect, some physicians hypothesized that the raising of

the diaphragm in pregnancy caused closure of the pulmonary cavities, discouraging tuberculosis infection (Grange et al 1998). Around 1835, there was a considerable shift in medical opinion as reports of an adverse effect of pregnancy on tuberculosis began to appear, and many physicians began to advocate therapeutic abortions (Grange et al 1998). However, one century later the general view was that pregnancy had no effect at all on mild tuberculosis (Grange et al 1998).

Pregnancy does seem to have certain affects on different diseases. There is now a generally accepted view that many infectious diseases, including varicella, malaria, leprosy, coccidioidomycosis[11], and listeriosis[12] have an increased incidence or clinically worsen during pregnancy (Grange et al 1998). For instance, according to the World Health Organization and United Nation's Children's Fund (in Gerberding 2004), malaria causes serious illness during pregnancy, and pregnant women also suffer a decreased immunity to malaria that more than doubles their chance of contracting and dying from malaria. On the other hand, some autoimmune diseases such as rheumatoid arthritis and multiple sclerosis often show an improvement during pregnancy (Grange et al 1998).

However, as mentioned previously, studies on pregnancy and disease are oftentimes at odds. In studies cited in Caracta (2003) exploring the

connection between pregnancy and asthma, asthma improves in one-third of pregnant women, worsens in one-third and is unaffected in the remaining third. Nevertheless, positive clinical observations of asthma in pregnancy are thought to be due to depressed T-cell function, and changes in levels of sex hormones, changes in other steroid hormones and pregnancy-related anti-inflammatory factors, which are similar to the factors cited in Rook (1998) regarding tuberculosis and pregnancy.

According to Rook (1998), immunity to tuberculosis depends on the presence of an effective Th1 lymphocyte response which is accompanied by cytotoxic T-cells[13] and activated macrophages[14]. As a general rule, the *rate* of tuberculosis infection is lower in women in the childbearing years, but several studies have indicated that the *risk of progression* from infection to disease is higher during this period of time (Grange et al 1998), and that women of reproductive age have higher TB-related mortality rates than men of the same age (Dolin 1998). However, there is contradictory evidence as to whether this is due to pregnancy (Grange et al 1998). If it is due to pregnancy, it is postulated that these changes in disease manifestation could be due to T cell[15] function, specifically a Th1 to Th2 drift that can occur in pregnancy that allows for a successful pregnancy while at the same time stopping the fetal

implant from being recognized by the mother's body as an invasive tumor (Rook 1998).

Generally speaking, a predominately Th1 response is associated with disease protection, while a significant differentiation of Th1 cells into Th2 cells may trigger inappropriate immune responses that can induce tissue destruction and progression of diseases such as tuberculosis (Grange et al 1998). This Th1 to Th2 drift could very well explain why women of reproductive age are at a higher risk than men of the same age of progressing from tuberculosis infection to clinical disease (Dolin 1998). However, if indeed women have a higher risk of progressing to clinical disease during their childbearing years, why do the statistics show that men still have a higher tuberculosis notification rate during these ages? Perhaps the T cell drift to a predominately Th2 response does not occur for all women during pregnancy, or other hormonal changes compensate for T cell drift. Also, as mentioned by Grange et al (1998), the studies to date on pregnancy and tuberculosis have yielded conflicting results. This is definitely an area that has been grossly neglected, that has contradictory results from studies performed, and that could greatly benefit from further research.

The differences in the male and female reproductive systems do clearly generate specific health issues for each sex[16]. However, differences in

disease susceptibility between men and women extend beyond differences in their reproductive systems. For example, men are more likely to die from heart disease than women, while women suffer more from autoimmune disorders, musculoskeletal disorders, anxieties, and depression than do men (Doyal 1998). Sex variations in disease susceptibility may be the reason for some of these differences.

Sex-related differences have been noted especially in diseases of the lungs. A lung disease that is very undoubtedly sexually dimorphic is lymphangioleiomyomatosis (LAM), a rare disease occurring exclusively in women that can lead to progressive loss of lung function (Caracta 2003). LAM mainly affects premenopausal women and is characterized by smooth muscle cell proliferation, occurring primarily in the lung, but also in extrapulmonary sites such as lower cervical, thoracic, abdominal, and pelvic lymph nodes (Caracta 2003). Caracta suggests an involvement of female sex hormones in the pathogenesis of LAM based on the occurrence of LAM in women during their childbearing years as well as the development of symptoms or an increase in the extent or severity of symptoms during pregnancy (2003). Moreover, there are reports of LAM worsening when exposed to exogenous estrogen (Caracta 2003). Finally, estrogen and progesterone receptors have been found in proliferating LAM cells but not in

normal smooth muscle cells in the lungs of women with LAM (Caracta 2003). The aforementioned factors are indicative that sex hormones influence this disease.

Epidemiological evidence also points to sex-based differences in the incidence, risk, histology, and pathogenesis of other lung diseases (Caracta 2003). For example, asthma and wheezing are more common in prepubertal boys than girls. The odds ratio[17] for asthma in boys between the ages of 2 to 5 is 1.8 compared to the odds ratio for asthma in girls (Caracta 2003:216). By age 14, the risk of chronic asthma is four times greater for boys than girls, and the risk of hospitalization due to asthma three times greater (Caracta 2003:216). It is hypothesized that these differences may be attributed to boys' relatively smaller airway size and caliber compared to girls of the same age (Caracta 2003). By age 20, however, there is a reversal of this incidence and a distinct female predominance in asthma. At this age, the odds ratio for hospitalization is 2.5 to 3.0 for females compared to males. Additionally, there is a greater prevalence of atopy[18] in female asthmatics and a longer duration of hospitalization and morbidity with increasing age in women versus men (Caracta 2003:216). To some extent, these differences may be related to smaller relative airway caliber in women versus men after puberty,

but Caracta also suggests changes in hormonal status occurring naturally with aging as a plausible hypothesis (2003).

Caracta (2003) proposes that sex differences in asthma may be related to both cyclical and age-related changes in sex hormones, resulting in an age-related increase in asthma rate in females as compared with males. Age-related changes in sex hormones may also lead to premenstrual asthma[19] (PMA) syndrome, as well as fluctuations of asthma symptoms during pregnancy (Caracta 2003). Because asthma severity also seems to vary with short-term reproductive processes such as the menstrual cycle and pregnancy, major female sex hormones (progesterone and estrogen) may also play a role. Caracta (2003) suggests that cyclical fluctuations in asthma symptoms may specifically be related to a reduction in premenstrual serum estrogen levels. One additional factor that may link sex hormones to diseases such as asthma and PMA is the fact that it has been found that oral contraceptive pills may reduce dynamic fluctuations in women with PMA and decrease menses-associated asthma (Caracta 2003).

In terms of infectious diseases, Doyal (1998) and Gerberding (2004) indicate that men appear to be biologically more vulnerable to malaria than women[20]. Caracta (2003) postulates that the role of sex hormones may be central to this difference in vulnerability, as sex hormones may either

contribute to the pathogenesis of disease or serve as protective factors. Graham A.W. Rook (1998) agrees with Caracta (2003). In *Steroid Hormones and the Immune Response; Sex and Gender Differences* (1998), Rook proposes that there are very clear sex-related differences in immune function that may lead to the variability in disease susceptibility in men versus women.

Rook (1998) applies the hypotheses in the above examples to tuberculosis, agreeing that sex differences indicate hormone-related and steroid-related causes for sexually dimorphic responses to tuberculosis. Additionally, Rook suggests some antibody and steroid-related causes that could also result in sex differences in tuberculosis response (1998). One specific argument the author makes is that women have higher levels of IgM[21] antibodies and therefore make a more vigorous antibody response to many vaccines, including the vaccine for tuberculosis (Rook 1998). This increase in antibody response could enable a woman's defense system to better protect against tuberculosis compared to a man's immune system, leading to a higher male notification rate for tuberculosis than females. However, this would mainly be the case only in countries where the tuberculosis vaccine is readily used.

On the other hand, Rook (1998) also suggests cortisol levels are crucial for tuberculosis immunity because when T cells are activated in the presence

of raised cortisol levels, these Th1 cells can differentiate into Th2 cells, which are detrimental in tuberculosis. The release of cortisol has been linked with stress reaction, and Rook (1998) alludes to the fact that women may have more stressors than men. These stressors in turn release cortisol, resulting in a T cell differentiation in women more often than in men. This explanation may rationalize why men and women have different responses to tuberculosis infection; however, it would lead one to believe that women should have higher tuberculosis notification rates than men, which is not reflected in the tuberculosis notification rate trends.

Other researchers concur that T cell shift and hormonal differences may explain differences in tuberculosis for males and females. Grange et al (1998) agree with Rook's suggestion of the T cell differentiation theory as they also cite T cell shift or T cell differences as possibly explaining sex differences in tuberculosis susceptibility. Additionally, Dolin (1998) suggests that the higher prevalence of tuberculosis infection in post-adolescent males than in post-adolescent females may be explained by "female" hormones (such as estrogen and progesterone) that might protect females in this stage of life from infection. However, Dolin does not further explain this point in his paper.

It appears as though the research regarding the possible biological reasons for the sex differences in tuberculosis notification rates are at times contradictory and a bit vague. Grange (1998) and Rook (1998) pose that T-cell differentiation (caused by pregnancy or stress) may cause women of childbearing years to have an increased progression of the disease than men of the same age. This should result in more women than men with tuberculosis during these ages, which is a statistic that is not reflected in the data. On the other hand, Rook also suggests that females have a more vigorous antibody response resulting in a stronger immunity to tuberculosis (1998). Rook and Dolin (1998) also pose that female hormones may help to protect women in their childbearing years from tuberculosis infection. These theories would in fact support the lower female (versus male) tuberculosis notification rate. Finally, the results from studies performed on pregnancy and tuberculosis have also yielded contradictory results. These are all areas that could undeniably benefit from further research and investigation, as it does seem that there are definite biological differences in tuberculosis susceptibility between the sexes. In the next section, I will review studies that present biological differences in the presentation of tuberculosis and testing response.

Differential Tuberculosis Presentation and Response to Testing

As suggested in the previous section and chapter, the comparison of infection rates with disease rates in some settings indicates that females may have a higher rate of progression to disease in their reproductive years, whereas males have high progression rates at prepubescent and older ages (Holmes et al 1998). Similar age and sex patterns in progression to disease were observed in different countries and in areas with drastic differences in economics (Holmes et al 1998). Aside from these patterns, there may also be differences in the type and presentation of tuberculosis for males versus females. As mentioned previously, although the majority of reported tuberculosis infections are pulmonary, tuberculosis actually represents a broad spectrum of disease and not just a single clinical entity. Tuberculosis can also be classified as either primary or post-primary[22], and pulmonary tuberculosis can be described as smear-positive or smear-negative[23].

Bothamley's work states that males are more susceptible to the type of tuberculosis (post primary) that is responsible for the continuing the spread of the disease (1998). In general, post primary tuberculosis is usually responsible for disease transmission, has a high male-to-female ratio, and is usually found in individuals aged 20 to 39 years (Bothamley 1998). On the other hand, women more often present with the other forms of tuberculosis that are not as common or as contagious (Bothamley 1998). In a large study

of extrapulmonary tuberculosis, females were represented more frequently than males (Bothamley 1998). Additionally, in adults, females were also as likely as or more likely than males to present with miliary tuberculosis[24], tuberculous meningitis, lymph node tuberculosis, abdominal tuberculosis, and tuberculous pericarditis (Bothamley 1998). A pertinent consideration is that much of the tuberculosis data does not separate (or perhaps even consider) cases of extrapulmonary tuberculosis. If extrapulmonary tuberculosis is more common in females than in males, and if extrapulmonary tuberculosis cases are not consistently counted in tuberculosis statistics, it could help explain why it appears as though there is a higher male notification rate for tuberculosis.

Besides the fact that extrapulmonary tuberculosis seems to be more common in females than males, Diwan and Thorson (1999) and Caracta (2003) state that 70% more smear-positive male than female TB patients are diagnosed every year and notified to the WHO. This is significant because the prognosis for smear-negative tuberculosis is worse than smear-positive (Corbett et al 2003). This does not mean anything in terms of the overall male to female tuberculosis notification ratio, but it does affect the progression of disease for males versus females. If more women indeed are smear-negative,

more women will potentially have a more severe tuberculosis infection, or a greater risk of contracting other debilitating or fatal diseases.

Aside from differential responses to the disease itself, males and females may react differently to the common tuberculosis diagnostic tools. Kivihya-Ndugga et al (2005) found that the performance of a tuberculosis diagnostic tool contributes to the sex differences in notification rates and therefore may influence male and female tuberculosis notification rates. In their study, a total of 998 persons in Nairobi, Kenya suspected of being infected with tuberculosis gave sputum samples to establish if they were culture-positive (2005). Of the 998 persons, 600 (60%) were male and 398 (40%) were female and it was found that 60% of the males and 51% of the females were culture-positive (Kivihya-Ndugga et al 2005:295). Two main forms for diagnoses were used: routine Ziehl-Neelsen (ZN) staining and fluorescent microscopy (FM). In cases where persons had three negative ZN results, they were also given chest x-rays (CXR) (Kivihya-Ndugga et al 2005). The authors found that the sensitivity for detecting a culture-positive case using ZN was significantly higher among men than women, and ZN performed on sputum from women was able to detect on average 10% fewer culture-positive tuberculosis cases than among men (Kivihya-Ndugga et al 2005). Additionally, males are more likely to exhibit positive skin tuberculin

tests compared to females (Dolin 1998, Diwan and Thorson 1999, Caracta 2003). A positive response has always been attributed to tuberculosis infection, but it could equally indicate simply a greater or more dramatic physical response in males on the skin, or even a greater exposure to cross-reacting environmental mycobacteria. These differences in immune response could be part of an explanation of differences in symptoms, signs, forms, and outcomes of tuberculosis. However, both studies make it clear that different, more sensitive diagnostic tools may be needed in order to accurately diagnose both sexes.

Based on the literature reviewed in this section, clearly there are differences between men and women in regards to both the manifestation of tuberculosis, as well as their reaction to the common methods of tuberculosis testing. Because women generally present with the less common (and oftentimes statistically ignored) forms of tuberculosis, this could result in the higher male than female tuberculosis notification rates. Additionally, if the testing that is typically performed to diagnose tuberculosis is not as sensitive to female patients as it is to males, there is a greater chance that female cases of tuberculosis are being missed entirely, and therefore not being treated or counted statistically. These issues compound the complexity of trying to get accurate tuberculosis statistics, especially for women. Another factor that

adds to this complexity is co-infection of both tuberculosis and HIV/AIDS, which will be discussed in the next section.

Tuberculosis and HIV/AIDS Co-infection

Currie et al (2003) assert that tuberculosis and human immunodeficiency virus (HIV) are the leading causes of death from infectious diseases among adults, and a staggering number of people are affected by one or both diseases worldwide. At the end of the 20th century, the Joint United Nations Programme [sic] on HIV/AIDS (also referred to as UNAIDS) estimated that 33.6 million people worldwide were living with HIV or autoimmune deficiency syndrome (AIDS) (Harries et al 2003:112). This is a staggering statistic, especially given the fact that AIDS was recognized as a disease only in 1982 and that the virus responsible for causing AIDS was identified only in 1983 (Harries et al 2003).

Originally thought to be a "disease of men" (Farmer 1996, 1999), the face of HIV and AIDS has rapidly changed in recent years. With enormous increases in incidence among women in both the global North and the developing world, researchers such as Simmons et al (1996), Gerberding (2004), and Kumar et al (2001) affirm that HIV/AIDS is now a highly gendered disease, and that the majority of new infections affect underprivileged females. For example, in South Africa, one of the countries

hardest hit by HIV, the HIV incidence rate among South African girls is 3 to 4 times higher than that of boys (Kumar et al 2001). In sub-Saharan Africa, women are 30% more likely than men to be HIV-infected (Gerberding 2004). In the United States, new HIV infections are also on the rise in women versus men. An analysis of newly diagnosed HIV infections that occurred in 29 states in the U.S. from 1999 to 2002 showed that 35% of cases resulted from heterosexual contact, and among these, almost two thirds (64%) occurred in women (Gerberding 2004). A recent report of HIV reporting data in New York City similarly found that 35% of new HIV diagnoses in 2001 were in women, an increase from 25% before the year 2001 (Gerberding 2004).

Kumar et al (2001) attribute the increase in overall HIV infection among women to the fact that biologically, young women are more vulnerable to HIV infection than young men. In fact, the risk of HIV infection during unprotected vaginal intercourse is as much as 2 to 4 times higher for women (Kumar et al 2001). One of the reasons for this increased risk is because during heterosexual sex, the exposed surface area of the vagina and labia is larger in women than the vulnerable surface area in men (Simmons et al 1996). Additionally, semen that is infected with HIV contains a much higher concentration of the virus than the sexual excretions of females (Kumar et al 2001). All in all, the male to female transmission of the infection

is much more efficient than female to male transmission. Worldwide, more than four-fifths of all HIV-infected women have contracted the virus through heterosexual transmission (Larkin 2000, Wingood and DiClemente 1996).

For people living with HIV, and from a public health perspective, tuberculosis is the most important opportunistic infection observed (Harries et al 2003). In the last 10 to 15 years, tuberculosis case numbers have increased by 300 to 400 percent in countries with a high prevalence of HIV infection (Harries et al 2003). HIV infection impairs the body's immunity to diseases and therefore the actual impact of HIV on tuberculosis (and vice versa) depends on the degree of overlap between these infections (Harries et al 2003). However, it is a fact that individuals living with HIV are more likely to become infected with tuberculosis upon exposure as compared to individuals without HIV infection (Thorson and Diwan 1998, Harries et al 2003, Corbett et al 2003). Corbett et al (2003:1009) state that approximately 9 percent of all new tuberculosis case in adults[25] is directly attributable to HIV infection, although the proportion was much greater in parts of Africa (31%) and some industrialized countries, notably the United States (26%).

When a person is infected with HIV as well as tuberculosis, the prognosis is dismal, especially because of the proliferation of associated risks. For a person who is co-infected with both HIV and tuberculosis, there is an

increased and accelerated risk of developing active tuberculosis[26] (Thorson and Diwan 1998, Harries et al 2003), experiencing tuberculosis reactivation (Harries et al 2003, Corbett et al 2003), experiencing adverse reactions to anti-tuberculosis drugs which can lead to treatment interruption and fatalities (Harries et al 2003), and dying from other opportunistic infections during the 6 to 8 months of their tuberculosis treatment (Corbett et al 2003). Although many people who are co-infected with HIV and tuberculosis die *with* tuberculosis rather than *from* tuberculosis (Corbett et al 2003), tuberculosis is among one of the top killers of people living with HIV and AIDS (Thorson and Diwan 1998).

Undoubtedly, the combination of HIV and tuberculosis is devastating. However, the hardest hit by the co-infection of these diseases is women, and there is strong evidence that young girls are particularly at risk (Kumar et al 2001, Wingood and DiClemente 1996). HIV and tuberculosis may have a particularly severe impact on young women in low-income settings because of their higher risk of HIV infection at a time when they appear to be at an increased risk of progression from tuberculosis infection to disease (Holmes et al 1998). According to Holmes et al, sex- and age-specific HIV prevalence in the general population peaks in women aged 15 to 24 and in men several years later (1998:101). In Tanzania, for example, the prevalence of HIV

infection among smear-positive tuberculosis cases was significantly higher in females than males in the age group of 15 to 34 years (Holmes et al 1998:101). Similar results were found in a study in Zambia where 74% of women with tuberculosis aged 14 to 24 were also HIV positive versus 45% of the men (Holmes et al 1998:101).

The ages of females who seem to be most affected by the dual-pandemic of tuberculosis and HIV/AIDS fall within the most reproductive years, and therefore can cause some additional issues. In a sample from the country of Zambia, for example, more than 1 in 4 pregnant women who receive prenatal care is living with HIV and AIDS (Grange et al 1998). The authors postulate that if around 50% of people of child-bearing age in the sub-Saharan Africa regions carry an *M. tuberculosis* infection and up to 25% are living with HIV and AIDS, then conceivably as many as 1 in 8 pregnant sub-Saharan African women could be co-infected (1998:81).

On a highly interrelated note, HIV and tuberculosis infection in women has obvious implications for the health and well-being of children. HIV can be transmitted perinatally, leading to a large number of children with HIV infection. Also, an estimated 12 million children are orphaned by the disease (Gerberding 2004). Although the prevention of HIV transmission from an infected mother to her infant is feasible due to effective antiretroviral

therapy, many mothers just do not have access to this treatment, especially since services that prevent mother-to-child transmission are severely limited in developing and low-income populations (Gerberding 2004). This leads to a staggering rate of HIV infection (and in turn, possibly tuberculosis) in children as well. In the countries of Zambia and Côte d'Ivoire, for example, HIV infection in children living with tuberculosis aged from one month to fourteen years is between an unimaginable 10 to 40 percent (Harries et al 2003). Currently the best way to prevent tuberculosis and HIV in children in these populations is to treat and prevent these diseases in adults, particularly in women.

In summary, it appears as though there is biological evidence that women and men are in fact affected differently by tuberculosis. Indeed, the biological changes that a woman goes through during pregnancy may affect her immunity and progression of tuberculosis, although the literature regarding tuberculosis and pregnancy is inconclusive and contradictory. On the one hand, it is suggested that the Th2 drift that typically occurs in pregnancy may cause a clinical worsening or greater susceptibility to tuberculosis during this period of a woman's life. Raised cortisol levels due to stressors may also cause this Th1 to Th2 cell drift resulting in the same susceptibility. However, there is no evidence of this clinical worsening of TB

or of this greater susceptibility in the tuberculosis statistics. On the other hand, it is also thought that female hormones and an increase antibody response in females may result in a greater TB immunity than in males.

Women and men present with different forms of tuberculosis, as well. Since men oftentimes have the "typical" tuberculosis presentation, could that be a reason as to why more men are recognized as having tuberculosis than women? Tuberculosis testing also seems to be more sensitive to forms of tuberculosis that are more typically seen in males than in females. Finally, the sex differences in the contraction of rate of infection of HIV could then in turn also impact tuberculosis rates. But, if HIV is increasingly becoming a "disease of women and children," and if tuberculosis co-infection goes hand-in-hand with HIV, why is the male tuberculosis notification ratio higher than that of females?

I found many of the biologically-based studies regarding sex differences in tuberculosis to be flawed, which may result from the confusing and varied nature of the disease. It is very difficult to get an accurate count of persons exposed and infected with tuberculosis, and I feel there currently are no accurate means by which to accurately assess the numbers of people truly affected by this disease. Furthermore, there are many imperfections with the various tuberculosis tests, and the results can be unreliable.

Obviously there are still a lot of questions to be answered and a lot of work that can be done regarding the biological explanations for the potential sex difference in tuberculosis. Many other authors agree, and do not feel these biological factors are sufficient, do not feel they are accurate, or do not believe that they get to the root of the issues of tuberculosis. These authors focus instead on the many social variables that can lead to differentials in this disease. In this next chapter, I will look at the social evidence that has been suggested that supports why male tuberculosis notification rates are higher than the rates of females.

CHAPTER IV

THE SOCIAL EVIDENCE FOR SEX DIFFERENCES IN TUBERCULOSIS

The relationship between social factors, health-related beliefs, and the resulting health behaviors is very complex, but it is necessary to understand these relationships in order to successfully eradicate health problems. Specific to tuberculosis, existing literature on the connection between social issues and disease suggests several social factors which may cause the perceived disparity in the tuberculosis notification rates between men and women. These factors include differential disease exposure, work environment, labor migration, various risk behaviors, the stigma associated with tuberculosis, and issues related to access to healthcare. However, despite the fact that there have recently been entire symposiums geared towards tuberculosis and gender, there has not been, nor is it truly feasible to perform, one comprehensive study that analyzes all of the possible social variables in a given area for an extended period of time. So although the studies that have been conducted regarding the social aspects of tuberculosis have provided some pertinent information, the modern picture of how social factors affect tuberculosis and gender remains dismally incomplete. The nature of the literature that has been conducted to date on these topics is

often confusing and inconclusive, examining only pieces of the greater issue within a relatively small community or area without placing these pieces in a larger theoretical, social, or global framework.

Nonetheless, the information made available by the studies reviewed in this chapter provides a starting point for a more comprehensive examination into the social factors affecting tuberculosis. In this chapter I will look at social factors such as work and migration (Holmes et al 1998, Suarez-Varela et al 1999, Gaston 1993), risk behaviors (Reichman and Tanne 2002, Bothamley 1998, Farmer 1996), stigma and social perception of tuberculosis (Goffman 1963, Sontag 1977, Eastwood and Hill 2004, Liefooghe 1998, and Diwan and Thorson 1999), and medical inequalities (Doyal 1998, Uplekar et al 2001, Borgdorff et al 2000, Thorson et al 2000) that have been linked to differences in tuberculosis notification rates between men and women. I will sum up the chapter by exploring the writings of researchers such as Lock and Scheper-Hughes (1996), Briggs (2001), Nguyen and Peschard (2003), and Farmer (1996, 1999, 2003, 2005) who attest that most of the existing explanations and studies of inequalities are too simplistic and need to be considered in a much larger social framework. These researchers suggest that these explanations that have been posed may actually be using constructs of culture to disguise the real reason for the underreporting of women with

tuberculosis: social inequalities, namely poverty. First, however, I will examine the different ways men and women may be exposed to tuberculosis through labor and migration.

Differential Disease Exposure: Work, Migration, and Gender

In cultures with clearly defined gender roles, everyday tasks lead to different types of health risks based on typical day to day activities. As an example, women in certain age groups who have the gender delineated role of collecting water for the household have a higher risk than men of developing schistosomiasis[27], since they are more exposed to the infectious agent through the water source they visit daily (Thorson and Diwan 1998). Furthermore, the particular nature of "female" versus "male" work can affect health. Countless women worldwide are subjected to at least a dual responsibility of caring for the home and children as well as carrying out agricultural work, and many women also participate in wage labor in addition to these responsibilities (Thorson and Diwan 1998). Consequently, many women have little time or resources for rest, which is very detrimental when they become ill. Additionally, women tend to be the primary caretakers of the ill and overall usually have a poorer nutritional status. All of these demands negatively affect a woman's overall health. Taking all of these responsibilities and factors into consideration, one may be led to believe

that women would be more compromised in terms of health in general and therefore also be more prone to tuberculosis infection. Unfortunately, I did not find studies that delve into the relationship between women's care giving, tasks at home, and other responsibilities, with tuberculosis exposure and infection. Instead, the majority of the studies I reviewed regarding labor and gender focus on factors that may lead to an increased rate of tuberculosis infection, or at the very least, reported tuberculosis cases, for males, not females.

One area related to work where there seems to be a difference between men and women is the number of personal contacts made on a daily basis. Holmes et al (1998) assert that because globally, women are generally responsible for the care of the home, whereas men tend to work outside of the home, this dichotomy of work environments and tasks leads to a disparity in the numbers of external personal contacts in men and women. The authors hypothesize that this differential exposure could explain why males and females show roughly similar prevalence rates of tuberculosis infection until adolescence, after which the male tuberculosis prevalence is higher than that of females. For example, in a study by Holmes et al (1998) that takes place in the Bangalore District of India, males and females had roughly the same prevalence of tuberculosis infection until the age of 14, after

which the male prevalence was 20% to 71% higher. These findings are also consistent with studies carried out in Chingleput, India and in the Korean Prevalence Surveys[28], also reviewed in Holmes et al (1998). The authors hypothesize that these results are due to the fact that until adolescence, males and females have a similar number of personal contacts (Holmes et al 1998). After adolescence however, males have more frequent external contacts, both socially and through their work environment, possibly providing them with more opportunity to be exposed to contagions. Therefore, this differential exposure to personal contacts could lead to the reported higher tuberculosis rate in males than females.

It is a fact that the majority of men work outside of the home and may therefore come into contact with more people than women do on a daily basis. Because these men work in close proximity to other male workers, they do have an increased chance of becoming infected with viruses and other infectious diseases, including tuberculosis. However, I find this explanation to be a bit simplistic. Although this relationship may in and of itself be true, this study does not even begin to consider how tuberculosis may spread to family members when these men return home. It is reasonable to think that men infected with tuberculosis would also spread the infection to their wives and children with whom they live in close quarters. In my research, I did not

find any studies regarding the spread of tuberculosis from male workers to their families. This is an area that I feel requires further exploration.

A substantial amount of research has been done, however, regarding the associations between certain types of "male work" and the contraction of tuberculosis and other diseases. Labor that is considered to be traditionally "male" can pose some particular risks and may help to explain the higher rate of tuberculosis in males, if indeed this disparity does exist on a practical (and not just statistical) level. In "Tuberculosis related to labor activity in an area of Valencia, Spain" (Suarez-Varela et al 1999), the authors conduct a descriptive study of five year case histories of individuals with tuberculosis that were reported to La Fe University Hospital in Valencia. The authors gathered information from the individual records regarding these individuals' sex, age, civil status, cohabitation, and rural or urban origin. Spain was chosen for this research because it is one of the countries in Europe most affected by tuberculosis[29]. Overall, the population of tuberculosis cases that were reported to the La Fe University Hospital had significantly more males (73%) than females (27%) (Suarez-Varela et al 1999).

Agriculture, industry, and service employment account respectively for 10.8 percent, 42.0 percent, and 46.2 percent of the labor force in this Valencian community (Suarez-Varela et al 1999). Workers in many of these

types of jobs are faced with inherently dangerous situations which may affect their general health status. For example, these workers deal with threats of mine cave-ins, inhalation of dust in mining and construction that could lead to other general disorders and pulmonary diseases[30], working with heavy machinery, exposure to the weather, exposure to noise, and being transported to and from job sites in crowded, unsafe vehicles (Gaston 1993).

In regard to tuberculosis, the authors state that among the people infected, miners and construction workers are the most numerous, followed by agricultural and farm workers. All of these types of labor are considered to be mainly "male" jobs. There are also a considerable number of cases that occurred in the so-called "passive" individuals: housewives, students, and pensioners (Suarez-Varela et al 1999). While a small proportion of women work in all of the professional areas represented in this study, most of the women with tuberculosis in this study work at home (and would therefore fall into the "passive" category listed above). Interestingly, it was found that the aforementioned group exhibited the highest percentage of extrapulmonary tuberculosis (Suarez-Varela et al 1999). These findings are consistent with the findings of Bothamley (1998), where in a large study of extrapulmonary tuberculosis, females were represented more frequently than were males. Unfortunately, extrapulmonary tuberculosis infections and other

tuberculosis manifestations tend to not be separated from cases of pulmonary tuberculosis in the data. Furthermore, oftentimes extrapulmonary and other tuberculosis forms may not even been reported at all in tuberculosis trend data. Because this type of tuberculosis seems to affect women more than men, not counting these cases could lead to a disparity in tuberculosis rate statistics by sex. It would then appear statistically that more men than women are affected with tuberculosis when in fact, women may have a different form of tuberculosis that not as readily reported or counted.

Due to the poor economic prospects in rural areas, people who work in jobs in agriculture, mining, and construction commonly have to migrate to another area to find work. Labor migration to urban areas occurs more frequently by men and is another central consideration when dealing with the possible connection of "male" labor and tuberculosis. Research has posed some correlations between labor migration and infections with diseases such as HIV and tuberculosis. For example, Decosas et al (1995) examine African migration patterns and HIV infection. Because HIV and tuberculosis are very highly related, this article also has relevance to tuberculosis infection. As has been stated, once a person is infected with HIV, they also have a higher chance of developing a tuberculosis co-infection.

As a specific example of how labor migration may affect HIV and tuberculosis infection, Decosas et al (1995) studied the migration of workers (primarily men) to Cote d'Ivoire. West Africa has a highly mobile population of fishermen, traders, farmers, and prostitutes (Decosas et al 1995). A main destination of migrants is Cote d'Ivoire, as can be delineated from the fact that among its population of about 12 million people, one quarter are migrants from neighboring countries, and in the capital, the proportion is as high as 40% (Decosas et al 1995). Cote d'Ivoire also has the highest HIV prevalence rates in West Africa, but despite the rising morbidity and mortality of tuberculosis patients with HIV infection, the epidemiology of tuberculosis in the Cote d'Ivoire remains under-documented (Ngom et al 1999).

As is the case in many other areas and countries, seasonal migration in West Africa is a predominantly male practice; a large agricultural enterprise in Cote d'Ivoire may have a camp of as many as 2,000 young male migrant workers living there (Decosas et al 1995). The workers in these camps are most likely subjected to close, unsanitary living quarters which facilitate the spread of diseases such as tuberculosis, and because of the already high rate of HIV in this area, tuberculosis has an even more fertile ground on which to spread. Because the majority of these migratory workers are males, this may

explain why males have an increased chance of being exposed to HIV and therefore tuberculosis, versus females who work in the home or who do not migrate for work.

As the world's population grows, differential pressure on ecosystems and economic factors will invariably lead to larger and larger population movements. With these population movements, one can expect the movement of diseases as well. Marilyn Gaston (1993) explores the disease patterns of the migrant farm worker population in the United States, and also finds a significant level of parasitic, chronic, and infectious diseases, including tuberculosis. In fact, a study in 1992 of four migrant health care centers in three states points out that the disease patterns of this population are similar to those that were found in the general United States population well over 60 years ago. This means that the migrant farm worker population in this study has high rates of parasitic and infectious diseases including food and water borne disorders and tuberculosis as well as chronic and dermatological diseases (Gaston 1993).

Gaston also reports that the Centers for Disease Control indicate that farm workers are approximately six times more likely to develop tuberculosis than the general population of employed adults, given their substandard and over crowded living conditions (1993). Furthermore, according to the

National Agricultural Workers Survey, the average farm worker in the early 1990s earned less than $7,500 per year (Gaston 1993). This is not enough money to live on, much less to use to treat a disease such as tuberculosis. This study, like Decosas et al (1995) also suggests that people who are involved in migrant labor (who are usually males) are habitually forced to live in insalubrious living conditions - a social environment in which diseases such as tuberculosis have a higher rate of spread of infection.

One's work environment should be expected to influence the incidence of tuberculosis simply because the majority of individuals spend a large portion of their lives in the settings in which they participate in labor. The studies reviewed in this section suggest that one of the reasons the tuberculosis notification ratio seems to be higher in men than in women is because of various factors related to labor. It is suggested that because men typically have more external contacts both socially and in their work environment than do women, they then would have the potential for more tuberculosis exposure and increased rates of tuberculosis than women. Additionally, men who work in "male" jobs such as mining and construction have increased rates of pulmonary tuberculosis infection than men in other types of work such as administrative or managerial positions. Finally, the act of labor migration, which also is usually performed by men, may lead to

increased tuberculosis exposure and infection in men through the unsanitary and crowded living conditions of migrant camps, as well as the increased possibility of exposure to HIV, and the introduction of these men into new communities.

All of these factors may indeed lead to an increased exposure and rate of tuberculosis infection in men versus women. However, as I pointed out, there are also several issues that have not been explored in this research, especially pertaining to women in particular. There was no investigation of women as caretakers of the ill and how this may affect their tuberculosis exposure. Also, why is extrapulmonary tuberculosis and other tuberculosis manifestations that seem to be more prominent in women than men oftentimes not included in tuberculosis notification statistics, and what needs to change in order to include them? Finally, how does male tuberculosis infection affect the women who live in the households with these men? These are areas that would benefit from additional exploration, and would help to provide a more complete picture of how labor factors actually affect tuberculosis infection of both men and women. In the next section, I will review the research that pertains to the connection between various risk behaviors in which men and women participate, and tuberculosis rates.

Risk Behaviors and Gender

Certain risk behaviors and the resulting consequences may be attributed to the genders unequally. For instance, Brooke Schoepf explains how AIDS, which originally was described as a "gay man's disease," has now "transformed many women's survival strategies into death strategies" (1993b:24 in Farmer 1996:24):

> Women, who often lack access to cash, credit, land or jobs, engaged in 'off-the-books' activities in the informal sector. Some exchange sex for the means of subsistence. Others enter sex work at the behest of their families, to obtain cash to purchase land or building materials, to pay a brother's school fees, or to settle a debt. Still others supplement meager incomes with occasional resort to sex with multiple partners.

The above quote shows how women in many countries have to use sex to sustain or to provide for their families. However, because of HIV and AIDS, the very acts these women use to try to survive, may also kill them. Although men can also contract HIV and AIDS through sex and drug use, the difference between men and women and this disease is that generally women are socially more at risk simply due to the fact that they cannot control the social variables that put them in this situation. For example, according to Farmer (1996), it is estimated that up to 50% of Bombay's prostitutes are recruited through trickery or abduction. This is probably the case for hundreds of thousands of poor girls in India, Nepal, and elsewhere. For these women, this way of life is not a choice, and the women cannot control

the variables. Additionally, as mentioned previously, women are at a higher risk of HIV infection through sexual intercourse than are men (Kumar et al 2001). This lack of control and higher overall risk can result in the proliferation of HIV, AIDS, and tuberculosis in women who have no means of protection at all.

Men may participate in different risk behaviors that may lead to an increased chance of tuberculosis infection. For instance, Bothamley (1998) suggests that male and female differences in alcohol abuse may contribute to a higher frequency of pulmonary tuberculosis in men. Low levels of tumor necrosis factor-α (TNF[31]) are found in individuals with excessive alcohol consumption, and these low levels of TNF are also associated with smear-positive pulmonary tuberculosis (Bothamley 1998). Although Bothamley gives a biological correlation that lower levels of TNF are found in both groups, it is the social behavior of excessive alcohol consumption that may lead to an increased risk of tuberculosis.

Both excessive alcohol use and smear-positive tuberculosis are more often found in men than women, suggesting a possible causative effect of excessive alcohol use in men leading to low levels of TNF, which in turn may lead to easier transmission and infection with tuberculosis (Bothamley 1998). Evidence from other cross-sectional studies also indicates that heavy alcohol

consumption depresses immune function and is strongly associated with tuberculosis (Brown and Campbell 1961 and Lewis and Chamberlain 1963).

In the Suarez-Varela et al study (1999) mentioned earlier, the authors also researched the association between persons with tuberculosis and their personal habits of using tobacco, alcohol, and intravenous drugs (Suarez-Varela et al 1999). These researchers also found a statistically significant relationship between tuberculosis incidence and these typically "male" behaviors. For example, in response to questions regarding smoking in this study, 68.8% of the participants with tuberculosis reported that they smoked, compared to approximately 54.7% of the general Spanish population and 62.8% of the Valencian population (Suarez-Varela 1999). These statistics are congruent with those of Kenneth et al (1996) which also states that cigarette smoking, as well as the consumption of alcohol have been significantly associated with a risk of tuberculosis. These habits are also regarded as predisposing to a number of diseases, including chronic obstructive lung disease and liver pathology, both of which are in turn frequently associated with tuberculosis (Kenneth et al 1996). Risk behaviors such as excessive alcohol use and smoking are more often engaged in by males (rather than females), and therefore could potentially lead to an increased rate of tuberculosis among men.

Several risk behaviors in which a person participates may result in the person being incarcerated. In these cases, it is not necessarily the risk factor that may lead to an increased chance of tuberculosis infection, but rather the incarceration. The population in most jails and prisons is typically gender specific (mainly men are incarcerated) and prisons are hot spots of rapid and dangerous tuberculosis infection. Because these settings have living conditions that are unsanitary and overcrowded, they also pose specific health risks and promote spread of infections. In "Timebomb: The Global Epidemic of Multi-Drug-Resistant Tuberculosis," authors Lee B. Reichman and Janice Hopkins Tanne and their team of experts (including Dr. Paul Farmer) travel to Russian prisons to investigate the spread of tuberculosis, especially the multi-drug resistant strains (2002). Russia's prison system is enormous, crowded, and dirty. Not surprisingly, malnutrition[32] is common among inmates, especially considering the fact that the prison system only spends about $26 per year on caring for each prisoner (Reichman and Tanne 2002).

It is thought that tuberculosis is so common in Russia's prison system that almost everyone who has spent time in a Russian detention center or prison either has latent or active tuberculosis (Reichman and Tanne 2002). Of the 300,000 people (again, the vast majority are men) released from the

Russian prison system each year, the best estimate is that 30,000 of them have active tuberculosis and at least 10,000 of these probably have a multi-drug resistant strain (Reichman and Tanne 2002). Additionally, each year about 300,000 new prisoners enter the prison system where they will also experience the same conditions and will have an increased chance of becoming infected with tuberculosis (Reichman and Tanne 2002). Tuberculosis experts call the Russian prison system "a pump that spews TB into Russia's towns and cities, and then to countries that were formally part of the Soviet Union...to western countries...and around the world though the magic of fast airline transportation" (Reichman and Tanne 2002:90).

Although the Russian prison system seems to be one of the worst for the spread of tuberculosis, it can be imagined that other prison systems also do their share to spread this disease as well. Since it is an almost universal fact that the majority of inmates in prisons are men, this may be another factor as to why men have higher tuberculosis notification rates than women. Furthermore, because these men are in a governmental institution, their cases of tuberculosis may be counted more readily versus a woman who works at home who does not go to a health clinic for her symptoms, which may help to explain discrepancies in the tuberculosis notification rates of men and women.

The research reviewed in this section mainly provides suggestions as to why the tuberculosis notification ratio seems to be higher in men versus women. The dismal picture of the Russian prison systems and its male prisoners definitely present a good case for a resulting large number of men with both active and latent tuberculosis. Additionally, risk behaviors such as smoking and excessive alcohol use have also been tied to an increased risk of tuberculosis, and these behaviors are more often practiced by men. All of these factors could mean that more men than women actually are infected with tuberculosis, reinforcing the existing higher male to female TB notification ratio. In this next section, I will explore how the stigma surrounding tuberculosis affects women more so than men, which could also result in more men than women with tuberculosis being counted in tuberculosis notification data.

Beliefs, Social Stigma, and Denial

According to Goffman, a stigma is an attribute that a person possesses that makes them different from others in a less desirable way (1963:3). In social perception, this attribute reduces the person from a whole person to a tainted, discounted, and discredited one (Goffman 1963, Sontag 1977). A stigma is also defined as a failing, shortcoming, or a handicap (Goffman 1963). By definition, a person with a stigma is thought of as not quite human,

with a disconnect between their personal identity and their social identity (Goffman 1963). The individual's identity is now more defined by his or her stigma. Therefore, a central feature of a stigmatized individual's situation in life is looking for acceptance, which may manifest in the individual trying to conceal what is causing the stigma (Goffman 1963).

It is logical, then, that stigma and perception of disease affects medical behaviors, especially related to diseases such as tuberculosis. Eastwood and Hill (2004) and Johansson et al (1999) describe the two types of stigma that are associated with tuberculosis: perceived and enacted. Enacted stigma concerns discrimination due to social inferiority, which is usually seen when family members or the community shun people with tuberculosis. Perceived stigma, on the other hand, is a sense of inferiority that results from *fear* of enacted stigma, often acted out by people with tuberculosis by hiding their diagnosis from others and delaying voluntary presentation of symptoms (Eastwood and Hill 2004:73).

A fair amount of research has been conducted regarding the effects of stigma related to disease on females versus males. In general this research leads to a consensus that women seem to be affected more so than men by the stigma and societal beliefs surrounding diseases such as tuberculosis. According to Diwan and Thorson (1999), there are considerable gender

differences in the stigma associated with tuberculosis and its social consequences. Although an entire family may suffer from the social stigma of tuberculosis, the negative consequences are many times harsher for female family members (Diwan and Thorson 1999). Uplekar and Rangan (1996, in Liefooghe 1998) found that society's attitude towards females infected with tuberculosis was almost always rejection, probably resulting in part from the perception in many cultures that women are "second-class" citizens. The only exception seemed to occur if these females were significant contributors to the household income. It seems in this situation, the fact that they were monetarily contributing to the family trumps some of the stigma associated with tuberculosis. Furthermore, Rangan and Uplekar (1998) suggest that while males with tuberculosis are usually supported and cared for by their families, married females with tuberculosis do not receive the same type of support from their husbands, and are many times divorced and sent back to their natal homes. Unmarried females with tuberculosis are usually cared for by their families. However, because women with tuberculosis may find it difficult to find a marriage partner, the families often hide the illness from the public eye (Rangan and Uplekar 1998).

George et al (1997 in Uplekar et al 2001) also study how stigma affects women with tuberculosis. They found that in India, there was a greater use

of the private medical sector versus public clinics by women aged 15 to 24 years, indicating a tendency of women of marriageable age to avoid public health services (George et al 1997 in Uplekar et al 2001). In countries where women are not only expected to marry but where marriage is a main source of women's social identity, tuberculosis may impact their chances of finding or keeping their spouse. The fear of stigma can be so great that many of these women will not seek health care for diseases such as tuberculosis, or their families will seek alternative sources of care that are not as public or stigmatizing.

In Eastwood and Hill's (2004) study, health care workers and people with tuberculosis both acknowledged the negative perceptions and lack of basic knowledge surrounding the disease, and both types of stigma were widely reported to be worse for females (versus males) with tuberculosis. For individuals with tuberculosis, this fear of isolation and segregation has a very negative impact on effective tuberculosis control because it can prevent a timely diagnosis of tuberculosis, delay voluntary presentation of symptoms, and lead to non-compliance in treatment (Liefooghe 1998).

Across cultures, there are also some differences in beliefs between men and women regarding the etiology of tuberculosis. In turn, these beliefs also affect how the disease is viewed by the general public. Interestingly, many of

the beliefs regarding tuberculosis etiology held by males in various cultures are consistent with the idea that hard work causes the disease. For example, male migrant workers from Mexico attribute their tuberculosis symptoms to hard work and lack of sleep (Rubel and Garro 1992). These workers also believe that a treatment regimen consisting of rest and refraining from smoking and alcohol may delay the need for medical intervention (Rubel and Garro 1992). Similarly, in Netrakona, Bangladesh significantly more men than women attribute tuberculosis to hard work and smoking whereas women in that culture more often attributed the disease to germs or a common cold (Liefooghe 1998). Hard work and production are considered to be very admirable traits in society, and when men attribute tuberculosis to hard work, it may lessen the tuberculosis stigma for them.

According to the above studies, in general, the stigma of tuberculosis is a greater burden for women than men across most cultures. Unfortunately, none of the studies that I reviewed explained *why* this stigma was worse for women than men, and from where the stigma stems. It seems that it is just to be an accepted and understood point that this stigma still occurs, without further explanation. Regardless, tuberculosis stigma can be detrimental to the diagnosis, treatment, outcome and spread of the disease, and therefore may lead to fewer women with tuberculosis infection actually coming

forward to get treated. In turn, this trend would also lead to fewer women with tuberculosis being counted statistically. These situations would further the hypothesis that the gender disparity in tuberculosis notification rates is valid only on a statistical level.

Denial is also connected with stigma (especially perceived stigma), and in terms of tuberculosis, denial is observed at two levels: denial of being a tuberculosis suspect, and denial of a tuberculosis diagnosis (Liefooghe 1998). These forms of denial can be harmful to the individual's health, and also perpetuate the stigma associated with the disease. Research also suggests that women may deny association with tuberculosis more than men (Liefooghe et al 1997). For example, in Korea, the rate of those who admitted to concealing their tuberculosis diagnosis was highest in the urban, younger, female strata (Leifooghe 1998). Young tuberculosis patients in Sailkot and Netrakona expressed difficulty in finding a partner, broken engagements, and/or divorce (Leifooghe 1998). Potential situations such as these may make parents of these children (especially marriageable girls) reluctant to send them for treatment for tuberculosis. Also in Sialkot, physicians report that women frequently plead to have their diagnosis concealed from their husbands and some women even hide their tuberculosis treatment drugs (Liefooghe 1998).

The social perception and resulting stigmas and denial surrounding disease play an integral role in how the disease is portrayed and viewed in a society. In turn these perceptions may affect a person's medical seeking behaviors as well as the acceptance of a person by their community once they are known to be affected. This disparity in how tuberculosis stigma affects men and women differently may be a reason why there are fewer women than men reported to be infected with tuberculosis. The stigma of tuberculosis may be too much to bear so women choose to deal with the disease in private, or deny that they have the disease at all. Additionally, factors such as the means by which tuberculosis is often identified and reported, as well health system access may create barriers that also could cause discrepancies between the actual number of women affected with tuberculosis, and the number reported. These factors will be discussed in the next section.

Medical Treatment Issues and Inequalities

In general, simply being male is socially advantageous since men generally have greater power, wealth, and social status than women in the same social situation (Doyal 1998). These factors may also result in better healthcare and access to resources for men versus women. This inequity as it relates to infectious disease appears even more unforgiving in the poorest

parts of the world, where women are often constrained in their use of healthcare. Inadequate resources, lack of appropriate care, transportation, rights, education, social status, political climate, and religious or traditional customs such as their husband's refusal to give permission to receive care (Doyal 1998, Hudelson 1996) all are barriers women with tuberculosis may face in seeking diagnosis or treatment.

It has been shown that especially in conditions of poverty, preference is usually given to males in access to education (Doyal 1998). It is oftentimes thought that offering resources such as education to male children (over female children) will increase the likelihood that the male child will go on to enhance the power, wealth, and status of the family. Therefore it may seem to the family to be a more prudent investment when resources are constrained to "invest" in their male children (Doyal 1998) rather than offering the same resources to their female children, where the anticipated outcome is not as great. Therefore, especially in situations of poverty, it is women and young girls who are repeatedly given lower priority, especially if their needs are not directly connected to reproduction (Doyal 1998). Likewise, under these circumstances, should a female family member become ill, it is unfortunately generally seen as not the best use of the family's limited resources to treat the illness through a medical center. These factors could

mean that many young females with tuberculosis are not being treated, and are then also not being reported as tuberculosis cases.

Among adults, there are several factors that affect care-seeking and treatment behavior for tuberculosis in males and females. These factors include self-image, status in family and society, access to resources, and the manifestation and expression of symptoms. Also, gender differences in choice of the provider, provider bias, interpretation of sputum examination, and non-acceptance of a diagnosis of tuberculosis have all been noted and will be discussed. One treatment issue regarding disease in general is the possible gender bias in the levels and types of treatments that are offered to men and women.

In recent years, it has become evident that men and women are frequently offered different levels of treatment for the same clinical conditions (Doyal 1998), even when controlled for socioeconomic constraints. For example, in the United States and the United Kingdom, women are less likely than males to be offered certain diagnostic procedures and treatments for heart disease (Doyal 1998, Annandale and Hunt 2000, and Ostlin et al 2002) and women on kidney dialysis are less likely to be offered transplants than men of the same age (Doyal 1998). Gender bias, whether intentional or not, has been shown to affect the diagnosis and treatment of other diseases as

well. Caracta (2003) found that gender bias may underestimate the rates of chronic obstructive pulmonary disease (COPD) in women, for example, and the author found that physician rates of diagnosis of asthma versus COPD in one study were indeed gender-dependent. In this United States study, if the patient is female, physicians are more likely to diagnose asthma. If the patient is male (with the same symptoms), the patient was more likely to be diagnosed with COPD (in 58% vs. 42% of the time), but rationale was not given (Caracta 2003). This finding raises questions: is this discrepancy because diseases manifest themselves differently in men and women, or is there differential treatment based on gender?

In an attempt to resolve the issue of why women and men are sometimes offered different levels of treatment for tuberculosis, Uplekar et al (2001) studied a tuberculosis program run by a voluntary organization in Western India. In their study, the authors report that 64% of men presenting with respiratory symptoms were given a sputum examination, versus only 34% of women with similar symptoms (Uplekar et al 2001). When asked about the clinical reasoning behind this discrepancy, the program workers were unable to explain the disparity, but were eager to explore the possible explanations (Uplekar et al 2001). When investigated further, it was discovered that according to the program worker records, all sites showed a

lower prevalence of *sputum positivity* among females compared to males when both sexes were given the sputum examinations. Because historically at this clinic the workers had witnessed this trend, it became common practice to administer sputum examinations to males more often than women (Uplekar et al 2001). However, this practice also would lead to an under-diagnosis of women with tuberculosis.

Additionally, the type of screening used to detect, track, and diagnosis tuberculosis has been considered to be very gender-biased and may also lead to the statistical discrepancy seen between tuberculosis notification rates in men and women. Borgdorff et al (2000) acknowledges that a prevalence survey is the technique typically used to estimate tuberculosis disease burden in a given area. Using a prevalence survey may be the best available method at this time, although it is definitely not without limitations. For instance, these surveys have only been carried out in a few countries (Borgdorff et al 2000). However, a major limitation of the survey is that it is most likely not entirely free of gender bias. For example, women with symptoms of tuberculosis may manage to avoid being screened by the survey due to fear of being diagnosed as a tuberculosis patient (Borgdorff et al 2000). Kivihya-Ndugga et al (2005) also discuss the fact that although sex differences found in prevalence surveys are similar to those found in notification data, this does

not exclude the possibility that there is the same gender bias in case detection affecting both prevalence and notification data. The gender bias found in these surveys again could lead to an under-notification of female cases of tuberculosis.

On a similar note, using active versus passive case-finding[33] for cases of tuberculosis and other diseases also seems to be gender-biased. Cassels et al (1982) compared the utility of active and passive case-finding methods in Nepal. The authors found that females made up 28% of the 159 tuberculosis cases who came to the clinic, which would be considered passive case-finding for tuberculosis. When active case-finding was implemented, however, the percentage of female cases detected rose to 46% of 111 identified cases. The sex differential in outcome of active and passive case-findings that Cassels et al (1982) found in their study is also consistent with findings of studies examining other infections such as malaria and leishmaniasis (Holmes et al 1998). It seems possible that due to a harsher stigma attached to women with tuberculosis (versus men), using passive case-finding instead of active case-finding to define tuberculosis rates may also lead to the under notification of women with tuberculosis.

Delays in seeking care for tuberculosis and delays in the actual diagnosis of tuberculosis also have gender trends. For example, Thorson et al

(2000) studied individuals with long standing cough in rural Vietnam and report more women than men delay seeking care. Long delays in tuberculosis diagnosis may lead to adverse effects on the patients, their families, their communities, and tuberculosis control in general. Long et al (1999) also report that a number of studies on tuberculosis diagnosis have reported long delays both in the patient seeking care as well as in the health care provider making a correct diagnosis of tuberculosis. Both of these types of delays also showed gender trends. The women in the Long et al (1999) study did not receive a correct tuberculosis diagnosis by their health care provider as quickly as the men did. In addition, in order to receive a correct diagnosis of tuberculosis, women in this study had to visit more providers than men, which also caused delay in diagnosis and treatment (Long et al 1999).

Both the Thorson et al (2000) and Long et al (1999) studies showed that women had more delays in various areas (both personal delays and delays in diagnosis by medical staff) than did men. Delays among women in particular may have even more adverse effects, as the health and welfare of children and other family members is closely linked to that of the mothers or other women caretakers in the family (Long et al 1999). Delaying diagnosis can be a very harmful barrier to treatment.

Other gender-specific factors may create difficulties to treatment of tuberculosis. In their study in Bangladesh, Salim et al (2004) found that the main reason for not seeking treatment was financial for both males and females (68% of females and 76% of males). Additionally, lack of awareness (i.e. not knowing where to go for curative treatment) was reported by a minority of patients, but was reported significantly more frequently by females than males. Dependence on accompanying persons or on a guardian was also mentioned more by females, but overall these factors were rarely mentioned. All of these factors posed in Salim et al's study (2004) could cause an under diagnosis or notification of tuberculosis in women.

However, based on the fact that their results did not show a relative under-diagnosis of females in their study compared to routine conditions, Salim et al (2004) came to a conclusion that the gender differences observed in routine diagnosis are real and are not due to poorer accessibility of women to health care services. Nonetheless, not seeking treatment due to financial reasons should be considered financial access. Even if the main reason listed by the subjects in this study for not seeking treatment was financial for both sexes, it has been discussed that the access to finances, especially in situations of poverty, are often more obstructed for women than for men. Also, not knowing where to go for treatment and having to depend on another person

to attend treatment was more frequently cited by females and is an access issue. If a woman with tuberculosis does not have or cannot convince someone to accompany her to the clinic, or if she is unsure where to go, these are also barriers to healthcare access. Situations like these would result in women having more difficulty utilizing community health care than men. In these cases, it is more likely that these women will not be treated at all for this disease, and in turn, will be another lost statistic in the overall tuberculosis count.

Another practice which could also possibly lead to a disparity in the actual number versus reported number of tuberculosis cases in a given area is the fact that in some cultures, there is a preference to use traditional healers over clinical medicine. In a study in The Gambia, West Africa by Eastwood and Hill (2004), health workers who treat people infected with tuberculosis were interviewed regarding the health practices of males and females. The health workers acknowledged that the use of traditional healers prior to or instead of using medical services was widespread. These workers believe that women use traditional healers more often than men due to stronger traditional beliefs as well as the fact that most of the women were of rural residence and had little formal education (Eastwood and Hill 2004). It was also supposed that women initially consult pharmacies more, as they may

feel it is more confidential and efficient than a clinic (Eastwood and Hill 2004). This information was confirmed in the interviews with the women with tuberculosis. According to these women, they may go to traditional healers either by preference, or at the suggestion of their families (perhaps due to less cost and less chance of the stigma of tuberculosis being attached to the family). As a result, many of these women may not be properly diagnosed and treated, leading to a possible proliferation of the disease and an under-notification of true tuberculosis cases in the area.

Some research has suggested changes that could be implemented that may assist women seeking medical treatment for tuberculosis and other diseases. In Eastwood and Hill's (2004) survey study, the authors found that women expressed a desire for two specific treatment implementations that they believe would possibly help in making women with tuberculosis feel more comfortable about seeking treatment: privacy and the preference for being treated by female health workers. Eastwood and Hill attributed the women's desire for privacy to be most related to the stigma associated with attending a clinic known to treat tuberculosis (2004). Regarding the preference for treatment by female health care workers, one third of the females with tuberculosis who were interviewed in this study said that they would prefer a female health worker to deliver their tuberculosis treatment

because female health workers are "more sympathetic" (Eastwood and Hill 2004:72).

A study by Johansson et al (1999) carried out in Vietnam reports similar desires by women with tuberculosis, and also addresses treatment compliance. As discussed previously, the issue of compliance is very important both at an individual level (for the health of the individual affected) as well as at the societal level (so as to not spread the disease and/or cause drug-resistant strains). This study indicated that while men reported insufficient knowledge regarding the disease and individual cost of treatment as the main obstacles to patient compliance, the main obstacles that were reported by women included sensitivity to interactions with health staff, and social stigma (Johansson et al 1999). However, the concerns of these women could be addressed if the existing health care workers were trained to be more sensitive to gender-specific needs.

In general, people with tuberculosis may encounter many different gender inequalities within the medical system. Gender differentials in diagnosing disease, the use of passive versus active case finding, the need for more sensitive diagnostic tools, and delays in diagnosing tuberculosis can all lead to differences in the way tuberculosis is reported, diagnosed, and treated for males versus females. More often we have seen that these barriers tend to

affect women more so than men. Furthermore, gender differences in financial and physical access to healthcare, delays in seeking medical care, the request for more "sympathetic" medical staff, and the use of traditional healers as opposed to clinical medicine can affect compliance with the treatment of tuberculosis.

In the final part of this chapter, I will explore the reasoning behind these social factors, that is, why do these social inequalities exist at all and how are they being perpetuated? I will also present arguments as to why I feel the study of tuberculosis needs to be examined in a more comprehensive framework.

The Need for a Comprehensive Framework and the Effects of Structural Violence

While researching this thesis, it has at times been difficult for me to distinguish whether the differences and trends that are being reported between men and women with tuberculosis are a consequence of biology or society. In fact, I believe that I had a harder time specifically sorting the causes of sex differences in tuberculosis into neat compartments than did many of the authors of the papers I reviewed. To me, the causes and effects were not always clear, and there were many pertinent questions left unanswered. It seems undeniable that social factors and biology are intricately and complexly related, and that it is a combination of both that

results in the patterns of how a disease is viewed by the society, as well as how it is contracted, reported, and treated.

Other researchers also feel that a study of disease needs to encompass both biological and social factors and the interaction of these factors. For example, Borgdorff et al (2000) suggests that observed differences in progression from infection to disease may be due to differences in the *balance* between biological need for nutrients and the gender-specific access to these nutrients provided (or not provided) by society. Although the above statement by Borgdorff would not explain why men would contract tuberculosis more often than women, it does suggest that a diseased state is not simply a function of only biology or only social factors, but rather a combination of these two areas. Dutton and Levine (1989:31) state that this relationship is not limited to disease, but may be found in all areas of health:

> One of the most striking features of the relationship between [socioeconomic status] and health is its pervasiveness and persistence over time. The relationship is found in virtually every measure of health status: age-adjusted mortality for all causes of death as well as specific causes, the severity of acute disease and the incidence of severe infectious conditions, the prevalence and severity of nearly every chronic disease, and measures of disability and restricted activity (in Farmer 2003:13).

When discussing disease, I feel that it is impossible and erroneous to separate socioeconomic status and other social forces from biological health –

they are completely intertwined and affect each other. In fact, as Farmer (2001) suggests, fundamental social forces and processes become embodied as biological events. Susan Sontag (1977) emphasizes that the reverse is also true - biological events become embodied in culture and once one is enmeshed and embodied in the other, it is very difficult to disconnect the two. For example, Sontag states that the validation and acceptance of metaphors and myths surrounding tuberculosis into public discourse, consciousness, and society turn them into cultural pieties, and in this way have provided them means of survival for nearly two centuries, despite both the indisputable human experience of the disease as well as accumulating medical knowledge (1977). Margaret Lock and Nancy Scheper-Hughes (1996) agree with Sontag. They state the metaphors and discourse about a disease are used to reinforce the cultural stigmas surrounding a biological phenomenon.

Nguyen and Peschard also affirm that a robust relationship between socioeconomic inequality and health outcomes (2003) exists. They suggest that this relationship calls for a cross-cultural and cross-disciplinary framework for understanding how social relations condition disease patterns and fashion the body in cultural, political, biological, and historical realms (Nguyen and Peschard 2003). Unfortunately, much of the work conducted up to this point regarding sex differences in tuberculosis manifestation and

tuberculosis in general, whether it be biological research or socio-cultural, has been too limited and without historical and social contexts. Many researchers agree. For instance, Paul Farmer, in the introduction to his book "Infections and Inequalities, The Modern Plagues" states that the disparities of risk and outcome are clearly embedded in complex *biosocial* realities (2001:5). Therefore, in order to understand these realities, a biosocial analysis - one which draws from disciplines such as clinical medicine, social theory, molecular epidemiology, history, ethnography, and political economy - is needed (Farmer 1999). After all, it was an intersection of biological and social factors that allowed the spread of infections such as tuberculosis, and it is the intersection, namely poverty and the health risks associated with poverty, which allows it to continue to spread and to evolve and become more threatening.

Also, Margaret Lock and Nancy Scheper-Hughes (1996) attest that when medical research is exempt from cultural or social analysis, several assumptions usually follow. These assumptions are that the categories of nature (or biology) and culture and/or society are dichotomous, that it is possible to understand the natural world logically and rationally through the application of science, and that a mastery of technology will eventually be obtained over all of nature - most importantly, over the human body (Lock

and Scheper-Hughes1996:43). But the authors also urge us to consider the three bodies – the individual body, the social body, and the body politic (Lock and Scheper-Hughes 1996). All three of theses bodies are affected by the biological and social aspects of disease.

When discussing infectious diseases such as tuberculosis, the interplay between biology and the affected society, as well as the way society perceives the disease are exposed by and expressed through the metaphors, imagery, and discourse about the body and the disease. For example, Martin suggests that the imagery used to describe the immune system in the body evokes strong descriptions of the operation of global capital (1992), reinforcing the concept that it is a factor of being poor that leads to lack of strong immunity and resulting disease. This somewhat releases responsibility at a societal level, and places even more blame on the individual affected or possibly affected with the disease.

Charles Briggs (2001) discovered the societal manifestation of this type of metaphor in his studies of a cholera epidemic in Venezuela that occurred in the early 1990s. During this time period, "El Nacional," a leading Caracas newspaper, reported a "national alert" and a "declaration of war on the Colombian Venezuelan border." At the time, there were reports describing a cooperative agreement between public health authorities of both nations

when it was becoming evident that the cholera outbreak that had scourged Colombia was heading toward Venezuela. This type of discourse enmeshed cholera in a nationalistic rhetoric even before it crossed the border into Venezuela, and was seen not only as a threat to the health of individuals, but to the citizens and institutions of Venezuela as well as the nation-state as a whole (2001:677). However, even as cholera was entrenched in this nationalistic language and identity, it was still linked closely with social inequality and particular social groups were singled out as potential bearers of the disease (Briggs 2001). This enmeshment in a larger social or nationalistic perspective may lead to even more negative reinforcement and stigma for those who are affected or seen to be affiliated with a disease.

This unintentional negative reinforcement has been called "structural violence," a construct first described by Galtung and later by Weigert as "preventable harm or damage...where there is no actor committing the violence or where it is not meaningful to search for the actor(s); such violence emerges from the unequal distribution of power and resources or, in other words, is said to be built into the structure(s) (in Lane et al 2004:320)". Structural violence can definitely be applied to diseases, especially tuberculosis and its categorization of a 'mysterious disease of the poor' (Farmer 2001).

Structural violence affects those seen to be at the lower ends of the social spectrum such as the "marginalized," the poor, and minority groups. Margaret Connors explains how structural violence can also be gendered, and how it affects women in particular, in terms of their increased risk of HIV:

> To blame the poor for their plight, when social policies reinforce the difficulties of escaping poverty, represents a kind of structural violence. Structural violence puts people at risk for poor health and social outcomes like drug use, incarceration, family dysfunction, and HIV. Poor women's HIV risk has been created not by neglect, but rather by a social planning which redistributes wealth as if the poor do not matter (1996:100).

Growing evidence indicates that social inequality contributes to ill health independent of income level and that relative poverty is just as robust a social determinant (or even more so) than absolute poverty (Nguyen and Peschard 2003). These authors state that at the same absolute level of income, an individual in a more egalitarian society will be healthier than one in a less egalitarian society (Nguyen and Peschard 2003). Furthermore, it could be said that within a family or a community, women may be relatively poorer than men and considered to be even lower on the social ladder. Therefore, poverty and structural violence is even harsher on women. Margaret Connors (1996) says that women fare worse than men not because of their gender, but because of sexism and the unequal power relations between the

sexes. She attests that more often than not, an assertion of power (no matter the context) is not even an option for women, especially women in poverty situations.

There have been a few instances that structural violence against women has been noted in the research reviewed in this thesis. One example is in the Suarez-Varela et al (1999) study cited earlier in this chapter that stated that most of the women with tuberculosis in their study work at home; employment that is considered to be "passive." Suggesting that women's employment is passive is simply another mechanism to "keep women in their proper place" in the realm of social consciousness, and furthers the metaphors about women and their bodies posed by Martin (1992)[34]. Moreover, the fact that there is a lack of literature or research regarding "women's work" and the relationship to tuberculosis is another way that women become marginalized. Furthermore, Briggs (2001) states that invoking "cultural logic" (or perhaps in this case "sexist logic") such as the idea of women as passive creatures actually masks the true cause of the issues at hand; namely social inequality in options for labor as well as the division of labor.

Another area where structural violence and the use of culture to cover up social disparity between the sexes in terms of women and tuberculosis is

in the discussions and research surrounding the use of traditional healers in lieu of clinical medicine. This is a socio-medical issue that, as we have seen, can affect delays in diagnosis of tuberculosis, as well as treatment compliance. In a study by Eastwood and Hill (2004), health workers who treat people infected with tuberculosis acknowledged that the use of traditional healers before medical services was widespread, and believed that women use the traditional healers more because of stronger traditional beliefs as well as the fact that most of the women were of rural residence and with little formal education (Eastwood and Hill 2004).

In many countries, women especially may in fact seek traditional healers for disease treatment due to reasons such as avoidance of stigma and greater levels of trust. However, for these women, the use of folk or traditional healers is also emblematic not of the culture (as it is posed), but of the unfair distribution of the world's resources. After all, as Paul Farmer says "if folk healing were so effective, the world's wealthy would be monopolizing it (2001:259)." The use of the traditional medicine in lieu of biomedicine for tuberculosis may be doubly harmful, as the traditional medicine does not cure the biological disease (but may actually worsen it or cause it to worsen due to a delay in medical treatment), and it also reinforces the negative stigma of many of the persons in the global North associate with tuberculosis:

an "exotic" disease that affects only rural, underprivileged, "native" people in other parts of the world. Additionally, the "reasoning" that a woman more often will use healers versus medical clinics because they are uneducated or more traditional simply covers up the real social inequality that is a driving force behind these actions.

Socially, the overall condition that puts people at a greater risk for contracting diseases such as tuberculosis is poverty. In turn, contracting diseases such as tuberculosis worsens poverty. Whitehead et al (2001) calls this phenomenon, whereby poverty produces ill health which then worsens poverty, the "illness poverty trap." In this chapter several other social factors were discussed that could lead to an increase in tuberculosis exposure by men (labor migration, incarceration, other "male" behaviors and work) as well as the factors that could cause women to delay treatment or to not seek it entirely (stigma, denial, issues with diagnosis). All of these social reasons provided by the research reviewed in this chapter may lead to an under-notification of tuberculosis cases in women. Many of these arguments could explain why it appears statistically that men are more affected by tuberculosis than women. However, the majority of these social factors were discussed in this chapter occur as a *consequence* of poverty and the resulting limited power for these people (especially women) to control their own lives. As Connors

states, "[Poverty] marginalizes, stigmatizes, and erodes human agency and leads to dependence and powerlessness. Poverty effectively prevents individuals and communities from reconceptualizing problems, imagining different alternatives, and creating new solutions. This is how the personalization of poverty is internalized (1996:109)."

In this chapter I reviewed many studies that provide reasonable explanations at face value as to why males have a higher tuberculosis notification than females. The research suggests that men could have higher tuberculosis rates than women because they have more external contacts than women, work in environments or jobs that promote tuberculosis infection, and participate in risk behaviors that result in situations where tuberculosis contraction is more prominent. Other studies attest that women may actually be underreported due to the fact that the stigma of tuberculosis is harsher for women and may lead to denial or delay seeking health care. Furthermore, women may not have the access to healthcare that men have, so their cases of tuberculosis may go unnoticed. All of these reasons could potentially explain the 2 to 1, male to female notification ratio for tuberculosis. However, all of these explanations may also be covering up the real social issue that is at the heart of the tuberculosis ratio disparity: gender differences in access to resources and social inequality.

It is not just any person who is likely to contract diseases such as tuberculosis because it is not any single decision of the individual person that "causes" them to be infected. Structural factors - social class and economic status - far more than individual decisions - explain the increase and continuance of tuberculosis infection. These structural factors affect women more so than men; women are usually considered lower in social class and economic status than even their own husbands or other male family members. In the case of tuberculosis, it seems quite possible that the way these structural factors act upon women causes an under-notification of women with tuberculosis as compared to men, despite any biological differences in the disease between men and women. In the final chapter, I pose questions that arose from my research, and explore suggestions as to how to investigate tuberculosis in a more holistic framework.

CHAPTER V

SUMMARY AND CONCLUSIONS

My goal in this thesis ended up being a lofty one. In this thesis, I examined some of the existing studies and statistics on tuberculosis that seemingly without regard to country, culture, or methodology, mainly reinforced the generally accepted approximate 2 to 1 male to female TB notification rate. I then examined both the biological and social reasons for this discrepancy. I looked at the statistics regarding tuberculosis both over the course of history and modern-day in several countries. I investigated the possible biological reasons that could explain the sex-based discrepancy for tuberculosis, such as sex hormones and pregnancy, differential presentation and symptoms of tuberculosis, and the ever-growing and ever-dangerous HIV co-infection. I also explored the various social reasons that could explain why the rate of notification of tuberculosis is less for women than men, such as gendered behavioral differences, the stigmas and metaphors attached to tuberculosis, and medical treatment issues at a personal and public policy level.

The amount of information about biological and social factors associated with tuberculosis was at times contradictory, sometimes

speculative, and oftentimes overwhelming. I do believe that the literature suggesting biological reasons for the discrepancy in male and female tuberculosis notification rates do present some valid points, but also present a lot of contradictions that could benefit from further research, especially in the areas of pregnancy and tuberculosis. It may also be useful to perform more research on the different responses male and female hormones can have on disease.

Based on the biological literature alone, it does appear as though there could be a sex- and age-related trend that may not be able to be totally explained by societal differences alone, and that some of the hormonal or immune response differences between men and women in the reproductive years could be integral. This biological difference may cause a slightly greater resistance to tuberculosis in females than males. Certainly there appears to be different manifestations of TB and progression of the disease for males and females. Further research into these biological differences is warranted and deserves to be explored, as it is possible that the differences in the biological effects of tuberculosis on men and women would call for differences in diagnosis and treatment, such as a different sputum testing method for females versus males, or better detection of extrapulmonary tuberculosis cases.

However, when the social factors are considered with the biological factors, many of the studies suggest that women may also be underrepresented in the statistics because of reasons such as stigma, medical treatment issues, and access to resources. Therefore, when the biological and social factors are taken together, I feel that there is a higher rate of tuberculosis in females than is currently being reported. If there is indeed a higher rate of TB in females, this would also mean that tuberculosis is an even greater problem overall than is currently thought. I do also feel that ultimately it does not matter if the question of the cause of the perceived disparity is biological or social; the solution to rid the world of tuberculosis needs to be a social one.

Louis Pasteur said, "The microbe is nothing; the terrain, everything (in Farmer 1999:37)". I do not know that I would classify tuberculosis as "nothing". It is a very resilient infection and has been around for thousands of years, it has changed into new forms over the years, and can be very destructive both to an individual and a society at large. From the beginning, tuberculosis has been a biological disease that was influenced and shaped by social factors. It is speculated that tuberculosis may have originated in prehistoric humans as a zoonotic infection transmitted from tuberculous animals, most likely cows[35] (McKinney et al 1998). The disease may have been

transmitted to humans through infected dairy products (Michalak et al 1998) or may have emerged from people sleeping next to their cows in the winter in an attempt to stay warm. As diseases are very affected by social factors, I do believe that it is society, or our "terrain," that has really prevented the eradication of tuberculosis. When comparing the biological and social effects presented in this paper, to me it is clear that social factors are the most influential in the continued spread of this disease, and will be the most powerful in eliminating tuberculosis. A quote from Hans Zinsser (in Farmer 1999:37) sums this thought up well:

> However secure and well-regulated civilized life may become, bacteria, Protozoa, viruses, infected fleas, lice, ticks, mosquitoes, and bed bugs will always lurk in the shadows ready to pounce when neglect, poverty, famine, or war lets down the defenses. And even in normal times they prey on the very old, living along with us, in mysterious obscurity waiting their opportunities.

People in the global North are still amazed when they hear that tuberculosis is an active disease, much less that it is a leading killer worldwide. Just a few months ago I was listening to a local morning radio talk show where they reported on a child at a school in a neighboring state who had been infected with tuberculosis. The radio DJs could not get over the fact that this disease still existed, much less that it actually reared its head in a singular case in a local suburban American town. I toyed with the idea of

calling in to the show and telling them about the real threats and statistics of tuberculosis. Perhaps this would educate some of the thousands of other Americans listening on their morning commute, but mostly it would probably fall on deaf ears. Most of the people listening to the morning radio talk show were not directly affected by tuberculosis; after all, is it not a fact that tuberculosis is a disease known to affect the poor, the destitute, those in far away lands, the "other" and not a disease of privileged middle to upper class Americans?

In my opinion, this type of attitude is one of the greatest obstacles in the eradication of tuberculosis. Farmer (1999) poses a striking and troubling question: whether the association of tuberculosis and poverty makes the disease irrelevant in the eyes of the powerful who, after all, control the funding for everything from tuberculosis treatment to tuberculosis research. Lewontin and Levins (2003) state that in the 1950s, the common-sense view of public health leaders was that infectious disease was defeated in principle, and medical students were told to avoid specialization in infectious disease because it was a dying field. In fact, the Epidemiology Department at the Harvard School of Public Health specialized in cancer and heart disease (Lewontin and Levins 2003). In the early 1980s, Paul Farmer still observed a striking lack of interest in tuberculosis and parasitology in United States

medical training and practice (1999). In August 1994, an official of the International Union Against Tuberculosis and Lung Disease commented to a journalist that tuberculosis is never heard about in North America because of who gets tuberculosis these days: immigrants, natives, poor people, and AIDS patients (in Farmer 1999:200-201).

Health care at the public policy level also creates limitations and barriers to care, as well as (although perhaps inadvertently) places the blame on the persons with the illness, their cultural beliefs, and their socio-economic status. Rangan and Uplekar (1998) make the point that policy planners often only highlight the biased societal customs, traditions, patriarchy, and class ideologies when addressing health matters and have blatantly ignored the issues related to the grossly inadequate health-care delivery system. Similarly, Farmer (1998, 2005) and Briggs (2001) both stress that the notion of cultural-based or individual-based fault is oftentimes used as a reason for inequity to cover for the true forces that constrain and impoverish individuals. Concerns such as the concentration of health care facilities in urban areas, understaffed public health institutions, inconvenient clinic timings, long waiting hours, inadequate stocks of supplies and drugs, non-functioning equipment, poor record keeping, lack of motivation to provide meaningful health care, and the high cost and lack of regulation of the private

health sector all enormously affect tuberculosis control in a given area. However, as discussed, these concerns may be even more problematic for women than for men, which may lead to an under-notification of women with tuberculosis, resulting in a perceived higher TB rate in men.

Underprivileged women with a double or triple burden of keeping the home, caring for children, and perhaps working are less likely than men to seek care for infectious diseases at clinics or hospitals far from their home, unless the disease has progressed to quite a serious state (Rangan and Uplekar 1998). Rangan and Uplekar (1998) also state that with increasing age, the proportion of untreated illnesses increases; this too is more often the case with rural women. Furthermore, the preferred method of treating tuberculosis, Directly Observed Therapy (DOT) places a heavy burden on patients, especially the very weak and sick, women, and the elderly, as it requires regular travel, often over long distances, to get to the medical center where they need to go to receive their medication. This stretches the capacity of poor families, as they often need to spend scarce resources on transportation to reach the DOT centers (Ngamvithayapong-Yanai et al 1998) and lose hours that would have been spent on caring for home, family, or earning money to reach the center and wait to see a practitioner (Rangan and Uplekar 1998).

Even if women have the resources to travel to a medical center to participate in the DOT for tuberculosis, using a treatment method such as DOT may cause fewer women to utilize the medical center. It is difficult to hide a tuberculosis infection if one has to check in to a treatment center on a regular basis, which may cause women especially to not seek treatment due to the stigma. Also, the very act of having a trained, educated healthcare professional observe a person with tuberculosis take their medication creates a power differential that may make women uncomfortable and less likely to seek this treatment, especially if the healthcare professional is male.

Holmes et al (1998) asserts that in localities where health care systems present few barriers to care, where the population and practitioners have a high index of suspicions regarding tuberculosis symptoms, and where diagnostic and reporting services of reasonable quality are available, the notification rates should be a good approximation of the incidence rates. However, it is clear that in the areas that are hardest hit by tuberculosis, the above caveats are not met. Most areas and communities affected the most by tuberculosis do not have adequate resources to provide consistent, accurate, and barrier-free health care. There may not be access to quality diagnostic systems, or if there is, it is so far from the population affected that it makes it impossible to use. In these areas, there is oftentimes not sufficiently trained

medical staff in general, much less with knowledge of tuberculosis. Accurate statistical information is especially needed from these areas in order to get a true picture of the tuberculosis epidemic.

Some of the research I studied in this thesis proposed some gender-specific solutions that could aid in a more accurate diagnosis and treatment of tuberculosis, should the resources allow. Holmes et al (1998) suggested incorporating tuberculosis education and screening into the maternal component of maternal and child health programs as well as into HIV and AIDS prevention and care programs. Styblo (1991 in Holmes et al 1998) noted that women were more likely to use health services during their reproductive years than at other times in their lives, so perhaps this would be an implementation that would see some success. Borgdorff et al (2000) also proposed that at the time of a tuberculosis diagnosis, the person with tuberculosis would be requested to bring in other family members for a sputum examination. Although this suggestion seems like a decent one in theory, it may be a bit more difficult to implement programmatically, again, unless sufficient resources were available and the stigma surrounding tuberculosis was reduced.

There are several issues with much of the research on tuberculosis that has been conducted to this point in time. Some study limitations in general

are that much of the data are outdated, and although there may have been statistical and epidemiological work performed in many of the studies, several studies also have too small of a sample size (Holmes et al 1998). One of the main problems with tuberculosis research in general is that the data is just not available. Extracting the "last available" tuberculosis data from the PAHO website by country lists results from as long ago as 1992 as "last available", and some countries do not have data at all. Also, in many of the studies, notification rates of tuberculosis are given rather than incidence rates due to the passive collection of data. Although the notification rates, prevalence rates, and incidence rates of tuberculosis were not necessarily explicitly considered in the research to be the same thing, they were oftentimes treated as the same information, or at least suggesting the same types of results and patterns. Despite the issues with the current literature, I still feel that one blatant issue lies beneath all of the statistics and studies: there is a true inequality in healthcare and resources for much of the world that is inundated by tuberculosis.

The allocation of resources is integral to the education, diagnosis, treatment, and eradication of tuberculosis. However, today in the United States we are definitely more interested in issues such as oil, terrorism, war weapons, and bioterrorism than the defeat of diseases that are still running

rampant in parts of our country, much less in much of the world. One study of New York City welfare recipients revealed staggeringly high rates of AIDS and tuberculosis; rates well in excess of those found in some of the developing countries and seventy times higher than the United States national average (Farmer 2001:4)! However, the lack of allocation of resources, especially in the United States, to areas such as tuberculosis research prevents true disease control. Cohen and colleagues agree, stating:

> The proponents of bioterrorism programmes [sic] have it backwards. Instead of pumping more resources into ill advised and risky bioterrorism programmes [sic], we should build national and international public health systems that can adequately reduce, detect, and respond to natural disease outbreaks and industrial chemical spills. Then, in the unlikely event of a bioterrorist attack, these systems will be available to manage the challenge (in Farmer 1999:xiii).

With a better resource allocation, I feel that there could be implementation of several programs that could address the immediate needs of communities affected with tuberculosis. These programs include: consistent and better treatments and access to treatment can be established for people living in rural areas and mobile populations; treatment availability for those who cannot afford it, or who face other cultural, social, or distance barriers; reimbursement or other aid (such as food) for those people who have to miss work to visit the clinic for treatment; gender-specific treatment

programs; and better follow-up with persons with tuberculosis to ensure compliance with the treatment program.

Additionally, long term needs could start to be addressed by allocating resources to more studies in areas where medical and social study has been previously neglected, the creation and use of more specific, sensitive, and overall better diagnostic tools; a more consistent and in-depth training of more health care workers; implementing improved systems of community education that hopefully also address and combat issues of social stigma; incorporating traditional healing practices with biomedical practices; and, perhaps one of the most important, conducting research into new medications that will combat multi-drug resistant tuberculosis. In Farmer (2001:208), Cole and Telenti (1995) reported that "No new antituberculous compounds have been developed by the pharmaceutical industry since the 1970s". Furthermore, Reichman (1997 in Farmer 2001:208) stated: "Most of the drug companies that publicly announce a quest for TB drugs at the time of the recent resurgence have been noticeably quiet. Few have even shown interest in developing such drugs".

Getting pharmaceutical companies to recognize the threat of multi-drug resistant strains of tuberculosis and to then spend resources on investigating and researching new anti-tuberculosis drugs may be the most

difficult task, especially since it most likely involves a high investment with a limited commercial return. Reichman and Tanne (2002) report the results of a 1999 study conducted by Diana Chang-Blanc from the WHO's "Stop TB" program covering 19 drug companies. Only five of those companies were involved in tuberculosis research programs at all, a sign in and of itself of the lack of interest in the world's leading infectious killer. Furthermore, the drug companies did not want a drug that was earmarked specifically for tuberculosis and was not used for other, more lucrative conditions such as chest infections, urinary infections, and meningitis (Reichman and Tanne 2002). If such a new antibiotic was created to be used to treat some of the above maladies, only as an afterthought would it also be used for tuberculosis treatment.

With a better allocation of resources, academia and governmental agencies could be more involved in conducting the research needed to find new treatment measures for "old" diseases that are still plaguing much of the world. I do not see our current system of private industry in a profit-driven, market-based economy coming to the aid of those affected by tuberculosis unless (or until) the disease is rampant again in the United States and is affecting a good portion of our population. Even in this scenario, however, I predict that those who would be mainly affected by tuberculosis would be

the same people who also could not afford the treatments. On the other hand, research conducted by academia could address diseases and issues that are of concern to the health and well-being of the people of the earth, not of their own pocketbooks.

Tuberculosis should not be an afterthought. It is a disease that will continue to spread and continue to affect millions of people worldwide until it cannot be ignored any longer. The two most important reasons for controlling tuberculosis are to minimize morbidity and mortality in the individual patient and to reduce the transmission of the disease into the community (Harries et al 2003). To effectively treat and prevent tuberculosis, a biosocial approach must be taken, with an emphasis on the allocation of resources to this issue. Jean Benoist and Alice Deslcaux (in Farmer 2001:148) said it well:

> The conditions limiting or promoting transmission, illness representations, therapeutic itineraries, and health care practices - none of these subjects are captured by disciplinary approaches. They evade even the distinction between biology and the social sciences, so tightly are biological realities tied to behaviors and representations, revealing links that have not yet been fully explored.

Tuberculosis is considered by Farmer to be two things at once: a completely curable disease, and the leading cause of death for young adults in much of the world (1999). Therefore, the duality of the disease calls for a

more complex means to evaluate, treat and prevent this disease; one that transcends and incorporates multiple fields of study, research, and expertise. Rene Dubos stated:

> Tuberculosis is a social disease, and presents problems that transcend the conventional medical approach...Its understanding demands that the social and economic factors on the individual be considered as much as the mechanisms by which tubercle bacilli cause damage to the human body (in Farmer 1999:228-229).

Tuberculosis has been called "the perfect expression of an imperfect civilization" (Dormandy 1999:377). This statement is an excellent summation of the inequality in our civilization, and how this inequality affects biological disease. Additionally, Farmer (2001:15) quotes Wilkinson as saying, "It is now clear," referring to an important study of inequality in industrial societies, "that the scale of income differences in society is one of the most powerful determinants of health standards in different countries, and that it influences health through its impact on social cohesion". So, essentially, the treatment of the disease of tuberculosis is not the most important treatment needed. We need to treat poverty, the environment which causes diseases such as this to thrive and continue their spread. Tuberculosis is a treatable disease; by implementing a more bio-social approach to tuberculosis treatment, and by focusing on alleviating some of the inequities of our civilization, tuberculosis can be managed. However, I stress that the critical

point to take action against tuberculosis is now. According to Farmer, "tuberculosis and HIV, which both afflict young healthy adults...are the only infectious diseases expected to cause more life years to be lost in 2020 than they cause now (2001:212)". With a better allocation of resources, programs that are both biological and social in nature, and that treat men and women without prejudice, the privileged and the underserved equally - this is the only way that this worldwide disease that has been around for thousands of years can truly be put to rest.

WORKS CITED

Annandale, E and K Hunt
2000 Gender Inequalities in Health. London, UK: Open University Press.

Barnett, Elizabeth and Michele Casper
2001 A definition of "social environment". American Journal of Public Health. 91(3):45

Blanc, Léopold and Mukund Uplekar
2003 The Present Global Burden of Tuberculosis. In The Return of the White Plague. Matthew Gandy and Alimuddin Zumla, ed. Pp. 95-111. New York, NY: Verso.

Borgdorff , MW, NJD Nagelkereke, C Dye, and P Nunn
2000 Gender and tuberculosis: a comparison of prevalence surveys with notification data to explore sex differences in case detection. International Journal of Tuberculosis and Lung Disease. 4(2):123-132.

Bothamley, Graham
1998 Sex and Gender in the Pathogenesis of Infectious Tuberculosis: A Perspective from Immunology, Microbiology and Human Genetics. In Gender and Tuberculosis. An International Research Workshop. Report from the workshop at the Nordic School of Public Health, Göteborg, May 24-26, 1998. Pp. 41-54.

Briggs, Charles L
2001 Modernity, cultural reasoning, and the institutionalization of social inequality: racializing death in a Venezuelan cholera epidemic. Comparative Studies in Society and History. 43(4):665-700.

Brown, KE and AH Campbell
1961 Tobacco, alcohol, and tuberculosis. British Journal of Diseases of the Chest. 55:150-158.

Caracta, Cynthia F
2003 Gender differences in pulmonary disease. The Mount Sinai Journal of Medicine. 70(4):215-224.

Cassels, A, E Heineman, and S LeClerq
1982 Tuberculosis case-finding in Eastern Nepal. Tubercle 63:173-185

Connors, Margaret
1996 Sex, Drugs, and Structural Violence. In Women, Poverty, and AIDS. Sex, Drugs, and Structural Violence. Paul Farmer, Margaret Connors, and Janie Simmons, eds. Pp. 91-124. Monroe, Maine: Common Courage Press.

Corbett, Elizabeth L, Catherine J Watt, Neff Walker, Dermot Maher, Brian G Williams, Mario C Raviglione, Christopher Dye
2003 The growing burden of tuberculosis. Global trends and interactions with the HIV epidemic. Archives of Internal Medicine. 163(9):1009-1021.

Currie, Christine SM, Brian G Williams, Russell CH Cheng, Christopher Dye
2003 Tuberculosis epidemics driven by HIV: Is prevention better than cure? AIDS. 17(17):2501-2508.

Decosas, J, F Kane, JK Anarfi, KDR Sodji, and HU Wagner
1995 Migration and AIDS (Viewpoint). The Lancet. 346:826-28

Diwan, Vinod K and Anna Thorson
1999 Sex, gender, and tuberculosis. The Lancet. 353:1000-1001

Dolin, Paul
1998 Tuberculosis Epidemiology from a Gender Perspective. In Gender and Tuberculosis. An International Research Workshop. Report from the workshop at the Nordic School of Public Health, Göteborg, May 24-26, 1998. Pp. 29-40.

Dormandy, Thomas
1999 The White Death. A History of Tuberculosis. Washington Square, NY: New York University Press.

Doyal, Lesley

1998 Sex, Gender and Health: A Preliminary Conceptual Framework. In Gender and Tuberculosis. An International Research Workshop. Report from the workshop at the Nordic School of Public Health, Göteborg, May 24-26, 1998. Pp. 17-27.

Dubos, R, and J Dubos

1992 The White Plague: Tuberculosis, Man, and Society. New Brunswich, NJ: Rutgers University Press.

Eastwood, SV, and PC Hill

2004 A gender-focused qualitative study of barriers to accessing tuberculosis treatment in The Gambia, West Africa. International Journal of Tuberculosis and Lung Disease. 8(1):70-75.

Farmer, Paul

1996 Women, Poverty, and AIDS. In Women, Poverty, and AIDS. Sex, Drugs, and Structural Violence. Paul Farmer, Margaret Connors, and Janie Simmons, eds. Pp. 3-38. Monroe, Maine: Common Courage Press.

Farmer, Paul

2001 Infections and Inequalities. The Modern Plagues (revised edition). Los Angeles, CA: University of California Press.

Farmer, Paul, and David Walton

2003 The Social Impact of Multi-drug-resistant Tuberculosis: Haiti and Peru. In The Return of the White Plague. Matthew Gandy and Alimuddin Zumla, eds. Pp. 163-177. New York, NY: Verso.

Farmer, Paul

2005 Pathologies of Power. Health, Human Rights, and the New War on the Poor. Los Angeles, CA: University of California Press

Feldberg, GD

1995 Disease and Class. Tuberculosis and the Shaping of Modern North American Society. New Brunswick, New Jersey: Rutgers University Press.

Frost, WH
1939 The age selection of mortality from tuberculosis in successive decades. American Journal of Epidemiology. 30:91-96.

Gandy, Matthew
2003 Life without Germs: Contested Episodes in the History of Tuberculosis. In The Return of the White Plague. Matthew Gandy and Alimuddin Zumla, eds. Pp. 15-38. New York, N.Y.: Verso.

Gandy, Matthew and Alimuddin Zumla
2003 Introduction. In The Return of the White Plague. Matthew Gandy and Alimuddin Zumla, eds. Pp. 7-12. New York, N.Y.: Verso.

Gaston, Marilyn H
1993 Health needs of migrant and seasonal farmworkers. Migration World Magazine. 21(1):31-33.

Gerberding, Julie
2004 Women and Infectious Disease. Emerging Infectious Diseases. 10(11):1965-1967.

Goffman, Erving
1963 Stigma. Notes on the Management of Spoiled Identity. Englewood Cliffs, NJ: Prentice-Hall, Inc.

Grange, John, Andrew Ustianowski, and Alimuddin Zumla
1998 Tuberculosis and Pregnancy. In Gender and Tuberculosis. An International Research Workshop. Report from the workshop at the Nordic School of Public Health, Göteborg, May 24-26, 1998. Pp. 77-88.

Harries, Anthony D, Nicola J Hargreaves, and Alimuddin Zumla
2003 Tuberculosis and HIV Infection in Sub-Saharan Africa. In The Return of the White Plague. Matthew Gandy and Alimuddin Zumla, eds. Pp. 112-124. New York, N.Y.: Verso.

Holmes, CB, H Hausler, and P Nunn
1998 A review of sex differences in the epidemiology of tuberculosis. International Journal of Tuberculosis and Lung Disease. 2(2):96-104.

Hudelson, P
1996 Gender differentials in tuberculosis: the role of socioeconomic and cultural factors. Tubercle and Lung Disease. 77:391-400.

Johansson, E, NH Long, VK Diwan, and A Winkvist
1999 Attitudes to compliance with tuberculosis treatment among women and men in Vietnam. International Journal of Tuberculosis and Lung Disease. 3(10):862-868.

Kenneth, D, N Hall, and MD Rosenman
1996 Occupational Risk Factors for Developing Tuberculosis. American Journal of Industrial Medicine. 30:148-154.

Khan, Kamran, Peter Muennig, Maryam Behta, and Joshua Graff Zirvin
2002 Global drug-resistance patterns and the management of latent tuberculosis infection in immigrants to the United States. The New England Journal of Medicine. 347(23):1850-1859.

Kivihya-Ndugga, LEA, MRA vanCleeff, LW Ng'ang'a, H Meme, JA Odhiambo, and PR Klaster
2005 Sex-specific performance of routine TB diagnosis tests. International Journal of Tuberculosis and Lung Disease. 9(3):294-300.

Kumar, Nikki, June Larkin, and Claudia Mitchell
2001 Gender, Youth and HIV Risk. Canadian Woman Studies 21(2):35-40.

Lane, Sandra D, Robert A Rubinstein, Robert H Keefe, Noah Webster, Donald A Cibula, Alan Rosenthal, Jesse Dowdell
2004 Structural violence and racial disparity in HIV transmission. Journal of Health Care for the Poor and Underserved. 15(3):319-335.

Larkin, J

2000 Women, Poverty, and HIV Infection. Canadian Woman Studies. 20(3):137-141.

Lewis, JG and DA Chamberlain

1963 Alcohol consumption and smoking habits in male patients with pulmonary tuberculosis. British Journal of Preventative and Social Medicine. 17:149-152.

Lewontin, Richard and Richard Levins

2003 Prologue. The Return of Old Diseases and the Appearance of New Ones. In The Return of the White Plague. Matthew Gandy and Alimuddin Zumla, eds. Pp. 1-6. New York, N.Y.: Verso.

Liefooghe, Rose

1998 Gender Differences in Beliefs and Attitudes towards Tuberculosis and their Impact on Tuberculosis Control: What do we know? In Gender and Tuberculosis. An International Research Workshop. Report from the workshop at the Nordic School of Public Health, Göteborg, May 24-26, 1998. Pp. 89-105.

Lock, Margaret and Nancy Scheper-Hughes

1996 A Critical-Interpretive Approach in Medical Anthropology: Rituals and Routines of Discipline and Dissent. In Medical Anthropology. Contemporary Theory and Method. Revised Edition. Carolyn F. Sargent and Thomas M. Johnson, eds. Pp. 41-70. Westport, Connecticut: Praeger Publishers.

Long, NH, E Johansson, K Lönnroth, B Eriksson, A Winkvist, VK Diwan

1999 Longer delays in tuberculosis diagnosis among women in Vietnam. International Journal of Tuberculosis and Lung Disease. 3(5):388-393.

Martin, Emily

1992 The end of the body? American Ethnologist. 19(1):121-140.

Martinez, AN, JT Rhee, PM Small, and MA Behr
2000 Sex differences in the epidemiology of tuberculosis in San Francisco. International Journal of Tuberculosis and Lung Disease. 4(1):26-31.

McKinney, John D, William R Jacobs, Jr, and Barry R Bloom
1998 Persisting Problems in Tuberculosis. In Emerging Infections. Richard M. Krause, ed. Pp. 51-146. New York, NY: Academic Press.

Michalak, Kathleen, Connie Austin, Sandy Diesel, J Maichle Bacon, Phil Zimmerman, and Joel N Maslow
1998 Mycobacterium tuberculosis infection as a zoonotic disease: transmission between humans and elephants. Emerging Infectious Diseases. 4(2):283-287.

Miller, KS and JM Miller
1996 Tuberculosis in pregnancy: interactions, diagnosis, and management. Clinical Obstetrics and Gynecology. 39:120-142.

Ngamvithayapong-Yanai, Jintana, Petchawan Puangrassami, and Hideki Yanai
1998 Compliance with Tuberculosis Treatment: A Gender Perspective. In Gender and Tuberculosis. An International Research Workshop. Report from the workshop at the Nordic School of Public Health, Göteborg, May 24-26, 1998. Pp. 127-148.

Ngom, A, E Aka-Danguy, N Koffi, M Tchamran, K Moh, and B Kouassi
1999 Epidemiology of tuberculosis in Abidjan, Ivory Coast: effects of HIV infection. Medecine Tropicale: Revue du Corps de Sante Colonial. 59(2):165-168.

Nguyen, Vinh-Kim and Karine Peschard
2003 Anthropology, inequity, and disease: a review. Annual Review of Anthropology. 32:447-474.

Ollé-Goig, JE
2000 Correspondence: DOTS in Haiti. International Journal of Tuberculosis and Lung Disease. 4:282-283.

Ostlin, P, G Sen, and A George
2002 Gender Inequalities in Health. Cambridge, MA: Harvard University Press.

Rangan, Sheila and Mukund Uplekar
1998 Gender Perspectives of Access to Health and Tuberculosis Care. In Gender and Tuberculosis. An International Research Workshop. Report from the workshop at the Nordic School of Public Health, Göteborg, May 24-26, 1998. Pp. 107-126.

Reichman, Lee B and Janice Hopkins Tanne
2002 Timebomb. The Global Epidemic of Multi-Drug-Resistant Tuberculosis. New York, N.Y.: McGraw-Hill.

Rook, Graham AW
1998 Steroid Hormones and the Immune Response; Sex and Gender Differences. In Gender and Tuberculosis. An International Research Workshop. Report from the workshop at the Nordic School of Public Health, Göteborg, May 24-26, 1998. Pp. 55-75.

Rothman, Sheila M
1994 Living in the Shadow of Death. New York, NY: BasicBooks.

Rubel, AJ and LC Garro
1992 Social and cultural factors in the successful control of tuberculosis. Public Health Reports. 107:626-636.

Salim, MA Hamid, E. Declercq, A Van Deun, and KAR Saki
2004 Gender differences in tuberculosis: a prevalence survey done in Bangladesh. International Journal of Tuberculosis and Lung Disease. 8(8):952-957.

Simmons, Jane, Paul Farmer, and Brooke G. Schoepf
1996 A Global Perspective. In Women, Poverty, and AIDS. Sex, Drugs, and Structural Violence. Paul Farmer, Margaret Connors, and Janie Simmons, eds. Pp. 39-90. Monroe, Maine: Common Courage Press.

Sontag, Susan
1977 Illness as a Metaphor. New York, NY: Picador.

Stead, WW and AK Dutt
1994 Epidemiology and Host Factors. In Tuberculosis, 3rd edition. David Schlossberg, ed. Pp. 12-13. New York, NY: Springer-Verlag.

Suarez-Varela, MM Morales, MI Martinez Selva, A Llopis Gonzalez, and ML Ballester Calabuig
1999 Tuberculosis related to labor activity in an area of Valencia, Spain. Journal of Environmental Health. 62(1):36-41.

Thorson, Anna and Vinod K Diwan
1998 Background to Gender and Tuberculosis Workshop: Tuberculosis - A Global Public Health Problem. In Gender and Tuberculosis. An International Research Workshop. Report from the workshop at the Nordic School of Public Health, Göteborg, May 24-26, 1998. Pp. 9-14.

Thorson, A, NP Hoa, and NH Long
2000 Health-seeking behavior of individuals with a cough of more than 3 weeks. Lancet. 356:1823.

Thorson, Anna and Vinod K Diwan
2003 Gender and Tuberculosis: A Conceptual Framework for Identifying Gender Inequalities. In The Return of the White Plague. Matthew Gandy and Alimuddin Zumla, ed. New York, NY: Verso. Pp. 55-69.

Uplekar, MW, S Rangan, MG Weiss, J Ogden, MW Borgdorff, and P Hudelson
2001 Attention to Gender Issues in Tuberculosis. International Journal of Tuberculosis and Lung Disease. 5(3):220-224.

U.S Department of Health and Human Services
2000 Core Curriculum on Tuberculosis: What the Clinician Should Know, 4th edition. Atlanta, GA.

Whitehead, M, G Dahlgren, and T Evans
2001 Equity and health sector reforms: can low-income countries escape the medical poverty trap? Lancet. 358:833-836.

Wingood, GM and RJ DiClemente
1996 HIV Sexual Risk Reduction Interventions for Women: A Review. American Journal of Preventative Medicine. 12(3):209-213.

END NOTES

[1] The first cases of MDR-TB were described as early as the 1970s, shortly after the 1966 introduction of the drug rifampicin to treat the disease; most MDR-TB strains are now resistant to at least the drugs isoniazid and rifampicin, the two most powerful agents used in the treatment of tuberculosis and usually the basis of the first-line chemotherapy treatment (Farmer and Walton 2003).

[2] Post adolescence; present rates reviewed in these studies suggest that men have higher TB rates than women after the age of 14 (Martinez et al 2000), age 15 (Dolin 1998, Holmes et al 1998), or the age of 16 (Diwan and Thorson 1999). Prior to ages 14-16, the rates of tuberculosis are approximately equal between males and females.

[3] An infection caused by any of the flagellate protozoans of the genus *Leishmania*, transmitted to humans and animals by bloodsucking sand flies.

[4] Pott's Disease is characterized as tuberculosis of the spine with destruction of bone resulting in curvature of the spine and occas and in paralysis of the lower extremities

[5] Also called struma, scrofula is a form of tuberculosis affecting the lymph nodes, especially of the neck, that is most common in children and is usually spread by unpasteurized milk from infected cows.

[6] Although Americans rushed to vaccinate against diseases such as polio, there was a general American opposition to the BCG vaccine, even though between 1924 and 1960 extensive testing demonstrated it to be 80% effective (Rothman 1994).

[7] Rifampin was introduced in Europe in 1968 (Reichmann and Tanne 2002).

[8] Helper T-cells, or T4 lymphocytes, are T cells that stimulates B cells to produce antibody against a foreign substance

[9] The extent or rate of occurrence, especially the number of new cases of a disease in a population over time.

[10] The total number of cases of a disease in a given population at a specific time.

[11] Coccidioidomycosis is a disease caused by inhaling spores of *Coccidioides* fungi, characterized by fever, respiratory infection, and reddish bumps on the skin, common in hot, semiarid regions; also called cocci, desert fever, San Joaquin Valley fever, or valley fever.

[12] Listeriosis, or circling disease, is a serious disease of a wide variety of animals including humans that is caused by a bacterium of the genus *Listeria* (*L. monocytogenes*). It is not usually fatal in humans except in neonates, the elderly, and the immunocompromised. In neonates it is often accompanied by granuloma formation, meningitis, meningoencephalitis, and septicemia. In adults it is often accompanied by meningitis, bacteremia with chills and fever (especially in pregnant women), and sometimes endocarditis.

[13] A cytotoxic T cell is a cell that functions in cell-mediated immunity by destroying foreign cells that have a specific antigenic molecule on its surface, Also called a killer T cell, these cells are integral to the immune system function.
[14] A large white blood cell, occurring principally in connective tissue and in the bloodstream that ingests foreign particles and infectious microorganisms by phagocytosis.
[15] T cells are white blood cells that attack virus-infected cells, foreign cells, and cancer cells, as well as produce substances that regulate immune response.
[16] As an example, only women can get cervical cancer while only men can suffer from prostate cancer.
[17] "The odds ratio is a measure of association in which a value of '1.0' means that there is no relationship between variables. The size of any relationship is measured by the difference (in either direction) from 1.0, with an odds ratio less than 1.0 indicating an inverse or negative association and an odds ratio greater than 1.0 indicates a positive relation.
[18] Atopy is a hereditary predisposition toward developing certain hypersensitivity reactions, such as hay fever or asthma upon exposure to specific antigens.
[19] As many as 40% of asthmatic females report suffering from PMA.
[20] Again, except during pregnancy when the women's higher immunity seems to be compromised.
[21] IgM is short for immunoglobulin M, the class of antibodies found in circulating body fluids and the first antibodies to appear in response to an initial exposure to an antigen.
[22] Primary tuberculosis occurs predominantly in children who have not received a tuberculosis vaccination, while post-primary disease occurs when there is a pre-existing immunity towards the tuberculosis antigens (Bothamley 1998).
[23] Smear-positive TB is when a sputum sample or other bodily fluid sample is positive for mycobacteria tuberculosis on an acid fast stain. Smear-negative TB does not have a sputum or fluid sample test positive, but can be diagnosed through other means such as chest x-ray, PPD skin test, or blood work.
[24] An acute form of tuberculosis characterized by very small tubercles in various body organs, caused by the spread of tubercle bacilli through the bloodstream.
[25] "Adults" in this study included persons aged 15 to 49 years of age (Corbett et al 2003:1009).
[26] The relative risk of developing active tuberculosis in an individual who is co-infected has been estimated to be as much as 100 times higher than in an HIV negative individual (Thorson and Diwan 1998:10).
[27] Also known as bilharzia, any of various generally tropical diseases that are caused by infestation with schistosomes, is widespread in rural areas of Africa, Asia, and Latin America through use of contaminated water, and is characterized by infection and gradual destruction of the tissues of the kidneys, liver, and other organs.
[28] Males older than age 15 had tuberculin test positivity 3% to 30% higher than females.
[29] According to the official 1991 statistics, the prevalence of tuberculosis in Europe as a whole was 27 per 100,000 inhabitants, while the Spanish prevalence was 36 per 100,000 (Suarez-Varela et al 1999).
[30] Other pathologies (such as chronic obstructive lung diseases and liver disorders) had also been diagnosed in 90% of these same patients; mainly those who were working in mining and construction (Suarez-Varela et al 1999).
[31] TNF is a protein produced by macrophages in humans and other animals that is destructive to cells showing abnormally rapid growth. It has also been shown experimentally to be capable of attacking and destroying cancerous tumors.

[32] Malnutrition in and of itself is a risk factor for tuberculosis as those who are malnourished may have weakened immune systems and may be less able to fight infectious diseases (Reichman and Tanne 2002).

[33] Passive case-finding consists of the reporting of suspected or confirmed tuberculosis cases to a public health authority as they are detected when a person comes to a medical clinic with tuberculosis symptoms. Active case-finding, on the other hand, occurs when the tuberculosis program attempts to identify unreported cases of disease by actively searching through, for example, laboratory and pharmacy audit, surveys, and talking to community volunteers.

[34] In "The End of the Body?" (1992), Martin suggests that imagery in reproductive biology organizes the body around principles of centralized control and factory-based production, where men continuously produce "astonishing quantities of highly valued sperm" while women, through less efficient means, produce eggs and babies. Imagery such as this is reflected at the societal level, where "men's work" is oftentimes seen as more valuable and efficient than "women's work".

[35] *M. bovis* is a related organism to *M. tuberculosis* and is part of the *M. tuberculosis* complex.