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# A Mathematical Model for Tuberculosis

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**ABSTRACT**
Tuberculosis is a disease which is caused by the bacterium Mycobacterium Tuberculosis. Incomplete treatment of patients with infectious tuberculosis may not only lead to relapse but also to the development of antibiotic resistant TB, one of the most serious health problems the society facing today. The different types of research are one, theoretic to practical. This method is concerned with formulating mathematical models. These models describe the dynamics of the disease. Sometimes numerical simulation gives a good insight. Mathematical modeling also aids the discovery of the underlying assumptions involved in the dynamics of the different epidemics. Modeling identifies necessary constraints to enable one to predict. Thus modeling is a tool not only to prevent the disease but also to control it. Modeling will also aid in the development of epidemiology, and help mankind to design more effective methods to control infectious diseases. In this paper we investigate a model of Pulmonary Tuberculosis. The total population is divided into five categories where individuals are placed according to their status regarding Pulmonary Tuberculosis. This model can be analyzed for the stability of its various equilibrium points and as well as the eigen values for their stability.
**Key words:** Tuberculosis, Mathematical Model, Dynamical Behavior, Eigen values, Stability of equilibrium point.

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## I. INTRODUCTION

Tuberculosis is a disease which is caused by the bacterium Mycobacterium Tuberculosis. With nearly 3 million deaths each year (Figure 1), tuberculosis has the dubious distinction of being the one and only cause of death from a single infectious agent in the entire world [1]. The magnitude worldwide of this problem calls for a renewal of tuberculosis management programmes. This can be done very well if it is based on an understanding of the dynamics of the infection at the level of infected individuals. Bacterial diseases show features that make a description of their dynamics much more complex than it is for the case of directly contracted viral infections. In bacterial infections, the periods of infectiousness are longer, usually recovery is slower and more evasive than in viruses. Such infections do not usually guarantee immunity against being re infected with the same bacterium. Hence a greater number of epidemiological classes are to be considered in the population [2]. This implies an increase in the number of equations and more rate parameters to be utilized in the corresponding mathematical models.

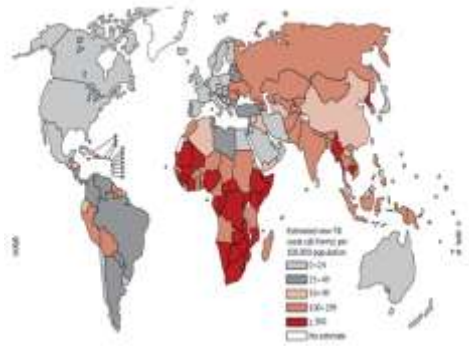

**Figure 1: Estimated TB incidence rates by India**

The mortality associated with TB in the U.S.A. continues to exhibit a downward trend. The annual rate of cases of TB had been declining but raised in the 1980s and early 1990s in the U.S.A. The change in this trend had been called as a period of TB reemergence. TB reemergence over the past decade has tested the existing prevention and control TB programs in developing nations to their limit [3].

**Early dynamical models of Tuberculosis:**

Waaler was the first to model Tuberculosis in 1962 [4]. Waaler made a division of the population into three groups: susceptible, latent and infectious. He framed the infection rate as an unknown function of the number of infectious persons. He used a particular form of a linear

function to model infection rates in the execution of his model. The model used a pair of uncoupled equations. The equations are

$$E_{t+1} = E_t + aI_t + \varepsilon I_t - d_2 E_t - \gamma E_t$$
$$I_{t+1} = I_t + \gamma E_t - d_3 I_t - \varepsilon E_t$$

where the incidence rate $aI_t$ is proportional to the number of infectious, $\varepsilon$ is the per-capita progression rate from latent-TB to infectious-TB cases; $\gamma$ is the per capita treatment rate (treated individuals will become members of latent-TB class again), $d_2$ is the per-capita death rate of the latent-TB class, and $d_3$ is the per capita death rate of the infectious-TB class.

Using statistics from the Indian subcontinent, Waaler [5] estimated the parameters of this linear model to be $a = 1$, $\varepsilon$ = 0.1, $d_2 = 0.014$, $\gamma$ = 0.10085, $d_3$= 0.07. Because the Eigen values all have norms close to 1 (1.04), Waaler envisaged that the time trend of TB is not likely to increase (it could decrease, but slowly). This linear model did not model the mechanics of the spread of the disease. But the parameters obtained from a specific place in India, gave useful information for other countries.

A model developed by Brogger [6] improved upon Waaler's. Brogger introduced age into the model and changed the method for calculating the rates of infection. This rate in Brogger's model consisted of both linear and nonlinear infection terms, given by the term βS (1 − Z + Z $\frac{1}{N}$ ), where Z is an adjusting parameter. Z differentiates between normal infection, super infection, and direct leaps in infection. There were two extreme cases that were covered in this model due to Brogger: Z = 1 which makes the incidence = βS $\frac{1}{N}$.

This is the type of infection term which is familiarly used. Secondly for Z = 0 one obtains an infection rate which is proportional to the number of susceptibles. The prevalence term $\frac{1}{N}$ was used to make an adjustment to flow rates. Brogger's aim was to compare different control methods that included treating and locating more cases, the use of vaccination, as well as mass roentgen graph.

Using Brogger and Waaler's model as a model template, ReVelle brought in a nonlinear system of ordinary differential equations that models TB transmission dynamics [7] [8]. He did not follow the usual mass action law, of the function βSI of Kermack and McKendrick [9] in modeling the infection rate. It was ReVelle who indeed in this context of the disease dynamics, explained rigorously the reason as to why the infection rate depends linearly on the prevalence. He used a probabilistic approach to do this. Most epidemic models use the form βS$\frac{1}{N}$ for the infection rate. Mathematically speaking the use of an infection rate proportional to SI does not change the qualitative properties of the model provided the total population size N remains constant over time or it asymptotically approaches a constant. As ReVelle did with his model, however when modeling epidemics with respect to developing countries, βS $\frac{1}{N}$ seems a better form for modeling the infection rate. ReVelle modeled TB dynamics with a system of non-linear differential equations ignoring population structure. Nine compartments were used in ReVelle's model. The entire population was Malthusian because he wanted to apply it to developing countries.

**Modeling Tuberculosis**:

India is second in the world for population numbers (Table 1 & 2) with more cases of TB than other countries [10].

**Table 1: Estimated global epidemiological burden of TB, 2009 [10]**

TABLE 1: Estimated global epidemiological burden of TB, 2009

| WHO region | Incidence[a] | | | Prevalence[b] | | Mortality (excl. HIV) | |
|---|---|---|---|---|---|---|---|
| | No. in thousands | % of global total | Rate per 100,000 pop[c] | No. in thousands | Rate per 100,000 pop[c] | No. in thousands | Rate per 100,000 pop[c] |
| Africa | 2,800 | 30% | 340 | 3,900 | 450 | 410 | 50 |
| The Americas | 270 | 2.9% | 29 | 350 | 37 | 20 | 2.1 |
| Eastern Mediterranean | 660 | 7.1% | 110 | 1,000 | 180 | 99 | 18 |
| Europe | 420 | 4.5% | 47 | 560 | 63 | 62 | 7 |
| South-East Asia | 5,100 | 55% | 280 | 4,900 | 280 | 480 | 27 |
| Western Pacific | 1,900 | 21% | 110 | 2,900 | 160 | 240 | 13 |
| Global total | 9,400 | 100% | 140 | 14,000 | 164 | 1,300 | 19 |

a Incidence is the number of new cases arising during a defined period.
b Prevalence is the number of cases (new and previously occurring) that exists at a given point in time.
c Pop indicates population.

**Table 2: Estimated burden of tuberculosis in India [10]**

TABLE 2: Estimated burden of tuberculosis in India

| | Number (Millions) (95% CI) | Rate Per 100,000 Persons (95% CI) |
|---|---|---|
| Incidence | | |
| All cases (2009 WHO estimate) | 2.0 (1.6-2.4) | 168 |
| Period Prevalence (2000 GoI estimate) | | |
| AFB positive | 1.7 (1.3-2.1) | 165 (126-204)† |
| Bacillary* | 3.8 (2.8-4.7) | 369 (272-457)† |
| Prevalence, all cases (2009 WHO estimate) | 3.0 (1.3-5.0) | 249 |

* Defined as a person with at least one AFB smear positive by sputum microscopy, or at least one sputum culture positive for M. tuberculosis.
† Prevalence rate calculated from estimated number of persons with disease in 2000, divided by 2000 population estimate.

In this paper we investigate a model of Pulmonary Tuberculosis.

The total population is apportioned into five categories where individuals are placed according to their status regarding Pulmonary Tuberculosis.

$x_1(t) =$ Number of susceptible individuals not protected by BCG vaccine at time t
$x_2(t)$ = Number of latent unprotected individuals at time t
$x_3(t) =$ Number of infectious individuals with PT at time t
$x_4(t) =$ Number of treated and fully recovered ex-infectious individuals at time t
$x_5(t) =$ Number of incompletely recovered ex-infectious individuals at time t
The individuals are born at rate $b$ directly into category $X_1$, and die in all categories also at rate b. The total number of individuals is $N = \sum_{i=1}^{5} X_i(t)$ and as births balance deaths, $N$ is constant over time. The proportion of individuals in category $X_i(t)$ at time t, is denoted by $x_i(t) = X_i(t)/N$. Individuals within each category are not discriminated by age and in order to build a deterministic model, we consider average rates of transfer among categories, assumed constant over time.
A further explanation for the five categories is now provided.

All new borns are assumed to take the BCG vaccine at birth [11] . As the vaccine does not always confer protection [12], a constant proportion $(1-y)$ of new borns is placed in the category of unprotected individuals $X_1$. The constant input rates for $X_1$ is $c_1 = (1-y)b$. BCG does not avoid primary infection with Tuberculosis, thus individuals in $X_1$ may become infected. BCG acts, at least in part, by limiting the spread of infection from an initial site of implantation in the lung. The most severe systemic (example meningitic or miliary) forms of disease are avoided by the vaccine and, despite the controversy [13], we assume that BCG also imparts some degree of protection against pulmonary disease. Those in $X_1$ who are to become ill and infectious (smear-positive) first go to a latent state (category $X_2$) that inevitably leads to the state of infectiousness $X_3$ at a rate $g$.

These active cases of PT are all assumed to undergo some sort of chemotherapy. Full compliance to an adequate therapy removes individuals from the transmission process, taking them from $X_3$ to $X_4$. Recovery from infection provides stronger protection against future tuberculosis than BCG , poor adherence of infectious individuals to the prescribed therapy, and/or an ineffcient therapy, moves individuals from $X_3$ to the compartment of treatment failures $X_5$. These chronic cases are not contagious (smear-negative) but because they are not fully recovered either, they relapse to $X_3$ at a constant rate r. The rate of transfer out of the $X_3$category is denoted by $h$. It will be assumed that only half of those who undergo therapy become fully recovered, thus $c_6 = h/2$ is the rate of transfer that applies both from $X_3$ to $X_4$ and from $X_3$ to $X_5$ .

Infection with Tuberculosis is caused by inhalation of aerosol droplets produced by individuals in $X_3$. It is assumed that on an average an infectious person will meet $'a'$ number of contacts per unit time. An adequate contact results in a new infectee if the other individual is susceptible. Assuming that the population is homogenously mixed, the average number of susceptibles infected per infectious individual per unit time in categories $X_1$, $X_4$ are respectively $ax_1$ and $ax_4$. The total number of individuals infected by the infectious class with size $X_3$ are thus $ax_1X_5$ and $ax_4X_5$ respectively.

Let the proportion of those infected who evolve to latent states be u and w respectively for categories $X_1$ and $X_4$.

It is assumed that $u \geq w$ because, as stated above, the vaccine hinders progression to PT and a previous history of disease is assumed to confer yet greater protection. We thus define the following rates of conversion to latent individuals:
$c_3 = ua$ And $c_5 = wa$. The total number of new latents on average per unit time, which gives the incidence of the disease, is equal to $c_3x_1X_5 + c_5x_4X_5$.

**Mathematical Model for Tuberculosis:**

The mathematical formulation for the dynamics of the model is the system of ordinary differential equations

$$\dot{x}_1 = c_1 - bx_1 - c_3x_1x_3$$
$$\dot{x}_2 = -(b+g)x_2 + c_3x_1x_3$$
$$\dot{x}_3 = gx_2 + g - (b+h)x_3 + rx_5$$
$$\dot{x}_4 = c_6x_3 - bx_4 - c_5x_3x_4$$
$$\dot{x}_5 = c_6x_3 - (b+r)x_5$$

If we set $R^+ = ]0,+\infty[$ and $R_0^+ = [0,+\infty)$, then the variables $x_i = 1 \; to \; 5$ lie in $s = \{(x_1, \ldots . x_5) \in (R_0^+)^5 : \sum_{i=1}^{5} X_i = 1\}$, $c_1 = (1-y)b$, $c_3 = ua$, $c_5 = wa$ and $c_6 = h/2$. The vector consisting of parameters $p = (b, g, h, r, u, w)$ belongs to the set
$\wp = (R^+)^5 \times ]0,1[ \times \{(u,w) : u \geq w > 0\}$
The equilibrium point for the above system of differential equations is $(\frac{c_1}{b}, 0,0,0,0)$.

The corresponding eigen values of the linearized matrix at the equilibrium point are $-b, -b$ and $\frac{1}{6}[12bg^2r - 48ghbr + 72gc_5rb + 72gc_3c_1r + 12bgr^2 + 12hbr^2 + 12h^2br - 36g^2c_3c_1 + 12bg^2h + 12bgh^2 - 36c_5r^2b - 36gc_3c_1h - 8br^3 - 8bh^3]$

.

Since the two eigen values $-b, -b$ are negative and it indicates that the equilibrium point is stable.

## II. CONCLUSION:

In this paper, we formulated a model for pulmonary Tuberculosis which is based on five catogiries $x_1$, $x_2$, $x_3$, $x_4$ and $x_5$ and analysed this model by study of equilibrium points and eigen values. Further, we study the nature of the eigen values at equilibrium point. Since these two eigen values are negative at equilibrium point and it illustrate that this system of equations is having stable equilibrium point.

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