Journal of the Nigerian Association of Mathematical Physics
Volume **20 (March, 2012), pp 119 – 124**

Stability Analysis of Equilibrium States of an SEIR Tuberculosis Model

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Abstract

We extend the tuberculosis model proposed by Blower etal. [1] by incorporating factors such as rates of detection and treatment of active tuberculosis (TB), proportions of recruited individuals due to immigration, rate at which susceptible individuals become infectious and the recovered class. We prove that the solution to the model is positive and bounded. We examine the stability and equilibrium states of the extended model with respect to the basic reproductionnumber R_0. We show that the disease-free equilibrium (DFE) is globally asymptotically stable if $R_0 \leq 1$ and that there exists at least one endemic equilibrium which is globally asymptotically stable if $R_0 > 1$.Finally, based on our results, we discuss optimum treatment strategies for tuberculosis epidemics.

Keywords: Tuberculosis; Mathematical model; Global stability; Equilibrium; Epidemics; Basic reproduction number.

1.0 Introduction

Tuberculosis (TB) is an ancient disease that continues to cause epidemic and pandemic infection despite ongoing efforts to limit its spread [2, 3, 4, 5, 6]. Despite many decades of study, the widespread availability of a vaccine and more recently, a highly visableWHO efforts to promote unified global control strategy, TB remains a leading cause of infectious mortality
[6, 7, 8, 9, 10]. Although, TB is currently well-controlled in most countries, recent studies show that the overall global incidence of TB is rising as a result of resurgence of the disease in Africa and parts of Eastern Europe and Asia [2, 3, 8, 11, 12, 13]. In these regions, the emergence of drug-resistant TB strains and the convergence of HIV (human immunodeficiency virus) and TB epidemics have made TB control very difficult [2, 9, 14, 15, 16].

Tuberculosis is an infection of the lung caused by Mycobacterium tuberculosis [3,4]. Untreated individuals suffer severely from loss of energy, poor appetite, fever, loss of weight, night sweats and chest pain [2, 3, 4, 5, 6, 12]. Individuals with active disease may infect others if the airborne particles they produce when they cough, sneeze, talk or sing are inhaled by others. A newly infected person may take 3 to 4 weeks before transmitting the disease to others. Many people may not realize they are infected as TB infections are often asymptomatic for the first few years. The first infection is usually latent but may develop later into active TB.

Many mathematical models have already been proposed to investigate the complex transmission dynamics of tuberculosis. See for example Blower etal. [1], Castillo-Chavez and Feng [17], Chika and Ezeofor [18], Cohen and Murray [19], Colijn etal. [3], Gomes etal. [20], Keeling and Eames [21], Murray and Salomon [22], Salpeter and Salpeter [15], Song et al. [13],Vynncycky and Fine [5], Waaler and Piot [6], among others. In this paper, we consider the model of Blower etal. [1]. We shall improve on this model by incorporating certain factors that play very important roles in understanding the spread and control of the disease.

2. The Model of Blower etal. [1]

Considering a three sdimensional model consisting of susceptible (S), latently infected (E) andactively Infected (I). Susceptible individuals are infected at a rate βIS and move either into the latent class E or directly into the infectious class I. In the infectious state, individuals do not recover but suffer an increased death rate due to disease. Then, the Blower etal. model is given by the following equations

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$$\left.\begin{aligned} S' &= \pi - \beta IS - \mu S \\ E' &= (1-\rho)\beta IS - (v+\mu)L \\ I' &= \rho\beta IS + vL - (\mu+\mu_T)I \end{aligned}\right\} \quad (1)$$

where
π =recruitment rate of susceptible individuals
μ =natural death rate
μ_T = death rate due to TB infection
v = rate of slow progression
ρ =rate of fast progression
In their analysis, the model is matched to TB mortality data and R_0 is used to derive a population threshold below which the disease cannot take hold.

3. EXTENSION AND MODIFICATION OF BLOWER MODEL

In this section, we extend the model system (1) to a four dimensional model which consists of the susceptible individuals (S), latently infected individuals (E), actively infected individuals (I) and recovered individuals (R). We add certain factors such as proportions of recruitment due to immigration, detection and treatment rates of active TB and rate at which susceptible individuals recover. Our modified model equations are as follows

$$\left.\begin{aligned} S' &= (1-\gamma)\pi + sI - \beta IS/N - \mu S \\ E' &= (1-\rho)\beta IS/N - (\mu+v+\varepsilon)E \\ I' &= d\rho\beta IS/N + dvE - (\mu+\mu_T+s)I \\ R' &= s\varepsilon E + sI - \beta IR/N - \mu R \end{aligned}\right\} \quad (2)$$

where$N = S + E + I + R$ is the total size of the population and
γ =proportion of recruitment due to immigration
d = detection rate of active TB
s =treatment rate of active TB
ε = rate at which susceptible individuals recover
Other parameters are as defined in [1].

Lemma 3.1: The basic reproduction number $R_0$for model (2) is

$$R_0 = \frac{\rho\beta\pi}{(\mu+\rho)(\mu+s)} \quad (3)$$

From (3) above, we derive the following.

Lemma 3.2 [23].

If $R_0 < 1$, the disease-free equilibrium $P_0$is locally asymptotically stable; If $R_0 = 1$, P_0 is stable; if $R_0 > 1$, P_0 is unstable.

Lemma 3.3 [23]. Let $f: [0,\infty) \to \mathbb{R}$ be a bounded C^2 function with a bounded second derivative and let $f(t_k) \to r^*$ or r_* as $k \to \infty$ where

$$r^* = \lim_{t\to\infty} \sup_{\theta \geq t} f(\theta)$$

$$r_* = \lim_{t\to\infty} \inf_{\theta \geq t} f(\theta)$$

then $\lim_{t\to\infty} f'(t_k) = 0$.

Theorem 3.1 [23]. If $R_0 < 1$, then the DFE P_0 is globally asymptotically stable. Combining this theorem with Lemmas 3.2 and 3.3, we have that the DFE P_0 is globally asymptotically stable if $R_0 < 1$.

4. EXISTENCE, UNIQUENESS AND POSITIVITY OF SOLUTION

Here, we prove that all solutions of system (2) are positive and bounded in $\mathbb{R}^4$.

Let $\mathbb{R}^n = (0,\infty)$ denote the set of positive vectors $x = (x_1, x_2, \dots, x_n)$ with $x_i > 0$ for all $i = 1,2,\dots,n$. We will use the following results as stated in Appendix A of Thieme [24].

Lemma 4.1. Let $F: \mathbb{R}_+^n \to \mathbb{R}^n$

$F(x) = \big(F_1(x), F_2(x), \dots, F_n(x)\big),\ \ x = (x_1, x_2, \dots, x_n)$

be continuous and have partial derivatives $\frac{\partial F_i}{\partial x_j}$ which exist and are continuous in $\mathbb{R}_+^n$, for all $i, j = 1,2,\dots,n$. Then, F is locally Lipschitz continuous in $\mathbb{R}_+^n$.

Theorem 4.1. Let $F: \mathbb{R}_+^n \to \mathbb{R}^n$ be locally Lipschitz continuous and for each $i = 1,2,\dots,n$ satisfy$F_i(x) \geq 0$whenever $\in \mathbb{R}_+^n$, $x_i = 0$.

Then, for every $\in \mathbb{R}_+^n$, there exists a unique solution of $x' = F(x),\ x(0) = x_0$ with values in $\mathbb{R}^n$ which is defined in some interval $(0, a)$ with $a \in (0,\infty)$. If $a < \infty$, then

$$\sup_{0\leq t\leq a} \sum_{i=0}^{n} x_i(t) = \infty$$

We prove the following theorem

Theorem 4.2. Suppose Lemma 1 holds. Then for all $S(0) > 0,\ E(0) > 0,\ I(0) > 0,\ R(0) > 0,$ there exists $(S, E, I, R);\ (0,\infty) \to (0,\infty)$ which solve system (2) with initial condition $S = S(0), E = E(0),\ I = I(0),\ R = R(0)$.

Proof. We will apply Theorem 4.1, we define

$$\left.\begin{aligned} F_1(x) &= (1-\gamma)\pi + sI - \beta IS/N - \mu S \\ F_2(x) &= (1-\rho)\beta IS/N - (\mu + v + \varepsilon)E \\ F_3(x) &= d\rho\beta IS/N + dvE - (\mu + \mu_T + s)I \\ \mathrm{F_4(x)} &= s\varepsilon E + sI - \beta IR/N - \mu R \end{aligned}\right\} \qquad (4)$$

where$x = (S, E, I, R)$.

By the properties of continuity over operations, we have the continuity of F_i for all $i = 1,2,3,4$.

Further,

$$\left.\begin{aligned} \frac{\partial \mathrm{F_1}}{\partial x_1} &= -\mu \\ \frac{\partial \mathrm{F_1}}{\partial x_2} &= s \\ \frac{\partial \mathrm{F_1}}{\partial x_3} &= s - \beta S/N \\ \frac{\partial \mathrm{F_1}}{\partial x_4} &= 0 \end{aligned}\right\} \qquad (5)$$

These partial derivatives exist and are continuous. In the same way, the other partial derivatives exist and are continuous. In consequence, by Lemma 4.1, $F$is locallyLipschitz continuous.

Let $x_1 = S = 0$ and $x_2 = R > 0,\ x_3 = I > 0,\ x_4 = E > 0$, then $F_1(x) = (1-\gamma)\pi + sI > 0$. Now, let$x_2 = E = 0$and $x_1 = S > 0,\ x_3 = I > 0,\ x_4 = R > 0,$

then $F_2(x) = (1-\rho)\,\beta IS/N > 0$.Let $x_3 = S = 0$ and $x_1 = E > 0,\ x_2 = R > 0,$

$x_4 = I > 0$ then$F_3(x) = dvE - (\mu + \mu_T + s)I > 0$. Finally, let $x_4 = R = 0$ and $x_1 = S > 0,\ x_2 = E > 0,\ x_3 = I > 0$, then$F_4(x) = s\varepsilon I + sI > 0$.

By Theorem 4.1 for every $x_0 = \big(S(0),\ E(0),\ I(0),\ R(0)\big) \in \mathbb{R}_+^4$, there exists a unique solution of $x' = F(x),\ x(0) = x_0$ with values in $\mathbb{R}_+^4$ which is defined in some interval $(0, a)$ with $a \in (0,\infty)$.If $a < \infty$, then

$$\sup_{0\leq t\leq a} \big(S(t) + E(t) + I(t) + R(t)\big) = \infty \qquad (6)$$

Now, suppose that $a < \infty$ and set

$$U(t) = S(t) + E(t) + I(t) + R(t) \qquad (7)$$

Then,

$$U' = -\mu S + [dv - (\mu + v)]E - (d\rho\beta S/N)I - \mu R + rU^2 \qquad (8)$$

such that

$$U' \leq \beta I \leq \beta U \qquad (9)$$

in consequence

$$\frac{U'}{U} \leq \beta \tag{10}$$

Integrating the both inequality, we obtain

$$InU(t) \leq InU(0) + \beta(t)$$

which implies that

$$U(t) \leq U(0)e^{\beta t}, \quad t \in (0, a) \tag{11}$$

So, $S(t) + E(t) + I(t) + R(t) = U(t)$ is bounded, a contradiction with Theorem 4.1. In consequence, $a = \infty$.It follows then that the solutions of the model (2) are positive and defined on $(0, \infty)$.

5. EXISTENCE AND STABILITY OF EQUILIBRIUM STATES

In this section, we discuss the existence and stability of the equilibria of model (2). To study the case where eradicating TB is a possibility, we restrict our attention to a closed population where there is no immigration. We assume there is no immigration. Then, at equilibrium our model becomes

$$\left.\begin{array}{c} \pi + +sI - \beta IS/N - \mu S = 0 \\ (1-\rho)\,\beta IS/N - (\mu + v + \varepsilon)E = 0 \\ d\rho\beta IS/N + dvE - (\mu + \mu_T + s)I = 0 \\ s\varepsilon E + sI - \beta IR/N - \mu R = 0 \end{array}\right\} \tag{12}$$

If a population is free of tuberculosis infection (i.e.$E = I = 0$), system (12) reduces to

$$\left.\begin{array}{c} \pi - \mu S = 0 \\ -\mu R = 0 \end{array}\right\} \tag{13}$$

Solving (13), we see that the disease-free equilibrium of model (12) is

$$P_0 = \left(\frac{\pi}{\mu}, 0, 0, 0\right) \tag{14}$$

The other equilibrium points are as follows

$$\left.\begin{array}{c} E = \dfrac{(1-\rho)\beta I}{\mu + v + \varepsilon} \\ S = \dfrac{(\mu + \mu_T + s)I - dvE}{(1-\rho)\beta I} \end{array}\right\} \tag{15}$$

It follows then tha

$$S = \frac{(\mu + \mu_T + s)(\mu + v + \varepsilon) - dv(1-\rho)\beta}{(1-\rho)\beta} \tag{16}$$

Substituting (16) into the 1st equation of the model gives the following which is a function of I. So,

$$G(I) = \left(\frac{\mu[\mu + \mu_T + s)(\mu + v + \varepsilon)] - dv(1-\rho)\beta - \pi(1-\rho)\beta}{(\mu + \mu_T + s)(\mu + v + \varepsilon) - dv(1-\rho)\beta - s(1-\rho)\beta}\right)I \tag{17}$$

For I very large, $G(I) > 0$ always so there is always a positive equilibrium for the system.
Now,

$$G'^{(I)} = \frac{(\mu + \mu_T + s)(\mu + v + \varepsilon) - dv(1-\rho)\beta - \pi(1-\rho)\beta}{s(1-\rho)\beta - (\mu + \mu_T + s)(\mu + v + \varepsilon) - dv(1-\rho)\beta} \tag{18}$$

which is negative given the condition that the numerator in $G(I)$ is less than zero and we can now have the following.Let

$$R_1 = \frac{\rho\beta\pi}{(\mu + s)(\mu + \varepsilon + \rho + \mu_T)} \tag{19}$$

We observe that $G(0) > 0$for $R_0 > 1$, then G has a positive zero. It then follows that our modified model (2) has a positive equilibrium for $R_1 > 1$. Therefore, if $R_1 > 1$, then the unique positive root of $G(I) = 0$ always exist. So, from equation (15), it implies that model (2) has a unique positive endemic equilibrium$P^* = (S^*E^*I^*R^*)$for $R_1 > 1$.

6. STABILITY OF EQUILIBRIUM STATES

We recall that the DFE P_0 from model (5.1) is given by $\left(\frac{\pi}{\mu}, 0, 0, 0\right)$. Linearizing our system about the DFE gives the following characteristics equation

$$(\mu + \lambda)\left[(\varepsilon + \mu + v + \lambda)(\mu + \mu_T + s + \lambda) - \frac{\rho\beta}{(\mu + s)(\mu + \varepsilon + \rho + \mu_T)}\right] = 0 \tag{20}$$

Thus, we have

$$(\mu+\lambda)\left[\lambda^2+(2\mu+\varepsilon+\mu_T+s+v)\lambda+(\varepsilon+\mu+v)(\mu+\mu_T+s)-\frac{\rho\beta}{(\mu+s)(\mu+\varepsilon+\rho+\mu_T)}\right]=0 \quad (21)$$

We note that $\lambda=-\mu$ is one of the eigenvalues and it is always negative. To obtain the other eigenvalues, we consider

$$\lambda^2+(2\mu+\varepsilon+\mu_T+s+v)\lambda+(\varepsilon+\mu+v)(\mu+\mu_T+s)-\frac{\rho\beta}{(\mu+s)(\mu+\varepsilon+\rho+\mu_T)}=0 \quad (22)$$

From equation (21) we see that all roots have negative real parts iff

$$(\varepsilon+\mu+v)(\mu+\mu_T+s)-\frac{\rho\beta}{(\mu+s)(\mu+\varepsilon+\rho+\mu_T)}>0 \quad (23)$$

That is, if $R_1<1$. If $R_1=1$, one eigenvalue of (6.2) is zero.If $R_1>1$, one of the roots of equation (22) has a positive real part. Hence, by Lemmas 3.2 and 3.3, we obtain global asymptotic stability of the DFE. We thus have the following theorem.

Theorem 6.1.If $R_1\leq 1$, then the DFE P_0 is globally asymptotically stable (GAS).

Proof. We follow the approach in Sharomi et al. [25]. We first show that the sets

$$H=\left\{(S,E,I,R)\in\mathbb{R}_+^4: S+E+I+R\leq\frac{\pi}{\mu}\right\} \quad (24)$$

and

$$H_r=\{(S,E,I,R)\in H: S\leq S^*, E\leq E^*\} \quad (25)$$

are positively invariant and attracting and we then find a Lyapunov function for the model on H. Summing the equations in the model gives

$$\frac{dQ_1}{dt}=\frac{[\mu(1-\gamma)]\pi}{\mu+\rho}-(\mu+v)Q_1-\varepsilon(E+I)-\mu_T I \quad (26)$$

Since the right hand side of (26) is bounded above by $\frac{\mu(1-\gamma)\pi}{\mu+\rho}-(\mu+v)Q_1$, it follows then that $Q_1'(t)<0$ if $Q_1(t)>$ More specifically by a standard comparison theorem [25, 26, 27, 28, 29, 30], we have that $Q_1(t)\leq Q_1(0)e^{-\mu t}+\frac{\pi}{\mu}(1-e^{-\mu t})$. In particular, $Q_1(t)\leq\frac{\pi}{\mu}$ if $Q_1(0)\leq\frac{\pi}{\mu}$. Thus$\frac{\pi}{\mu}$., H is positively invariant. If $Q_1(0)>\frac{\pi}{\mu}$, then either the solution enters H in infinite time or $Q_1(t)$ approaches $\frac{\pi}{\mu}$ asymptotically and the infected variables E and I approach zero. Hence, H is attractive. Now, using the Lyapunov function

$$D'=(\mu+\mu_T)E'+\rho(\mu+\varepsilon)I'$$

we have that $D'\leq 0$ if $R_1\leq 1$ and $D=0$ iff $E=I=0$. Then, it follows from the Lasalle Invariant Principle [31] that $E\to 0$ and $I\to 0$ as $t\to\infty$. That is, the disease dies out. Since the disease-free equilibrium P_0 is attracting as well as positively invariant, then the DFE is GAS if $R_1\leq 1$ (or $R_0\leq 1$).

Remark 6.1. Using the techniques of persistence theory [26, 29, 30, 31] we can show the uniform persistence of the disease and the existence of the endemic equilibrium $\bar{P}$ of system (2). See Ref [11], for the details.

Theorem 6.2. The endemic equilibrium of the model system (2) is globally asymptotically stable if $R_0>1$.

Remark 6.2. If we consider our model (2) and take parameter values as follows: $\rho=0.004$, $\beta=0.0238$, $\pi=0.60$, $\mu=0.01425$, $s=0.37$ then we calculate the basic reproduction number of the DFE of the model using (3) as $R_0=0.5716<1$. This shows that the DFE is GAS. Hence, infection is temporal and the disease eventually dies out. If we keep the value of μ unchanged and let $\rho=0.0088$, $\beta=0.0856$, $\pi=0.80$, $\mu=0.01425$, $s=0.14$. then the basic reproduction number is $R_0=1.1894>1$ which implies that endemic equilibrium is globally asymptotically stable. Here, an average infectious individual is able to replace itself and the number of infective rises and an epidemic results.

7. DISCUSSION OF RESULTS AND CONCLUSION

In this paper, we proposed an SEIR epidemiological model to study the transmission dynamics of TB. We have investigated the global asymptotic stability of the DFE and the unique endemic equilibrium in terms of the basic reproduction number R_0.Our results show that the basic reproduction number is a threshold parameter of the disease dynamics [27, 28]. In particular, we obtained global asymptotic stability of the DFE when $R_0\leq 1$ and global asymptotic stability of the endemic equilibrium for $R_0>1$. These results indicate that the disease eventually dies out if $R_0\leq 1$ while it persists if $R_0>1$. However, if the detection rate (d) and treatment rate(s) of TB is kept higher, a more stable DFE could be achieved for disease eradication. The global endemic equilibrium also has important implications for disease control. The study of the global endemic equilibrium is essential in predicting the evolution of the disease in the long run so that prevention and intervention strategies can be effectively designed and public health administrative efforts can be properly scaled. Undoubtedly, with improved therapies, vaccinations and strict border checks on those immigrating to make sure that no immigrant with tuberculosis infection is allowed entry, the possibility of reduction in the infection can

still be achieved. In addition, media coverage of the disease could possibly play an important role in the control of tuberculosis outbreak as people follow the reports and choose to protect themselves by reducing their social activities and direct contacts with others, especially with those high-risk groups, which could therefore lead to a reduction of effective contacts between susceptible individuals and infectious individuals. This would significantly reduce the number of infectives and its proportion to the total population.

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