The Impact of Treatment of Latent Tuberculosis on the Incidence: The Case of Algeria

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Abstract—We present a deterministic model which describes the dynamics of tuberculosis in Algerian population where the vaccination program with BCG is in place since 1969 and where the WHO recommendations regarding the DOTS (directly-observed treatment, short course) strategy are in application. The impact of an intervention program, targeting recently infected people among all close contacts of active cases and their treatment to prevent endogenous reactivation, on the incidence of tuberculosis, is investigated. We showed that a widespread treatment of latently infected individuals for some years is recommended to shift from higher to lower equilibrium state and thereafter relaxation is recommended.

Keywords—Deterministic model, reproduction number, stability, tuberculosis.

I. INTRODUCTION

HUNDRED and thirty-one years after the identification by Robert Koch in 1882 of the Mycobacterium tuberculosis, pathogenic of tuberculosis (TB), the disease is still a problem of public health world. In 2012, an estimated 8.6 million people developed TB and 1.3 million died from the disease. The number of TB deaths is unacceptably large given that most are preventable [7].

As many countries, Algeria is concerned by TB; the annual number of new cases of TB is around 21,000 cases of which more than 48% are cases of contagious pulmonary TB. In spite of a relatively significant medical cover for the country, more than 180 patients died yearly of smear positive pulmonary TB. Since 1969, vaccination by Bacille Calmette Guerin (BCG) is compulsory. Tuberculosis is a notifiable disease in Algeria and benefit from the total exemption from payment of cares; individuals with TB disease get their drugs from special centre implanted in each area of the country. A national program based on WHO recommendations was set up and several efforts were made in order to take charge of individuals with TB disease [5]. The various actions undertaken allowed a significant reduction of the incidence of this disease and this from the Seventies. In Fig. 1, the recorded pulmonary TB and extra-pulmonary cases per 100,000 inhabitants in Algeria extracted from [6] are plotted from 2001 to 2009.

An understanding of the dynamics of TB at the population level will lead to a better revitalization of the control program of this disease [1]. Since people with TB infection are considered at highest risk of developing TB disease in the 2 years which follow the infection, during which approximately 5 to 10 percent develop TB disease, an intervention that targets people with recent latent TB infection could be effective as control measure. Nevertheless to provide treatment for a large fraction of the population is costly and not feasible besides which the identification of LTBI individuals is not an easy task. We propose then to quantify how much treatment of recent TB infection individuals, of all close contacts of smear positive pulmonary cases, reduces the incidence of TB; an intervention would consist in keeping a watch on these close contacts.

The paper is organized as follows: In section III a deterministic model which describes the dynamics of tuberculosis is proposed. The dynamic of the model is governed by ordinary differential equations; therefore the analysis of the disease free equilibrium and the endemic equilibrium and conditions for local and global stability of these points is investigated in this section. Intervention that alter reactivation and re-infection as well as treatment of carries and the impact of treatment of TB infection on the incidence of TB over time are examined in this section. Section IV includes some numerical simulations of the proposed model and discusses the obtained results.

II. TUBERCULOSIS

Tuberculosis is an infectious disease caused by bacteria called Mycobacterium Tuberculosis (MTB). The bacteria usually attack the lungs (pulmonary TB), but can also affect other parts of the body through the blood (extra-pulmonary TB). The MTB is transmitted quasi exclusively by air. The infecting droplets are produced in the form of aerosol by the contagious patients at the time of cough, speech or sneezes. These droplets remain in suspension in the ambient air; ninety percent of them are inactivated as soon as their emission and only a fraction of 1% survive for few hours. The inhalation into the lungs of some bacteria suspended in the air constitutes,
in practice, the only mode of contamination. The individual becomes infected by breathing in the bacteria. The immune system is sometimes able to kill TB bacteria. If not, either, the bacteria remain alive but inactive in the body and the person contracts a TB infection, or, they become active and begin to multiply in the body and cause TB disease. Infected individuals who did not progress to TB disease may remain infected, non-infectious, for their lifetime unless endogenous reactivation or exogenous re-infection occurs [4]. Note that only the contamination by smear positive TB individuals has an epidemiologic importance.

**TB control program in Algeria**

The priorities for TB control program in Algeria are:

- The vaccination at birth in order to reduce the incidence of childhood TB knowing that is relatively ineffective in protecting against adult TB and does not prevent MTB infection.
- The identification in a permanent way of active TB cases and their treatment in order to break the transmission chain of the MTB and thus the sterilization of the sources of infection.

The cases of TB are only detected in the infectious stage; this is due to a lack of efficient system of detection at early stages of infection. People living under the same roof as a contagious household (non-family) are examined in order to identify among them the tuberculous (the national average being of 10%).

People living under the same roof as a contagious individual are informed of the possibility of late appearance of the disease and informed of the clinical signs which will have to lead them to consult as soon as possible [5].

**III. MODEL DESCRIPTION AND ANALYSIS**

**A. Model description**

Although the population is vaccinated, this does not avoid infection. Susceptible (S), individuals who have never encountered the natural mycobacterium, can be infected only through contact with individuals having smear positive pulmonary TB disease. Latent TB infection (LTBI) is divided into two stages: (1) an early stage at high risk of developing active TB, referred as recent LTBI (I_1), and (2) later stage at low risk of developing active TB, referred as persistent LTBI (I_2). Likewise, we consider two classes of infectious individuals: smear positive pulmonary TB individuals, referred as (I_p), can they infect others and smear negative pulmonary TB individuals, referred as (I_n), who have TB disease and can not transmit it.

Infected individuals initially progress through recent LTBI, either, to active TB at rate φ, or, to persistent LTBI at rate (1 − φ) δ. From persistent LTBI class, individual can progress at low risk and slowly to infectious class either, by endogenous reactivation at rate ω, or, by exogenous re-infection at rate σ_1 β I. All detected infectious individuals receive 6 months treatment; 90% have a full recovery and the remaining 10% including 1% for disease-induced death and 9%, gathering the relapses, the failures and those which fail to comply with the treatment, return to infectious class at rate ρ; they receive a treatment of second line. Treated (T) individuals acquire some immunity not fully which reduces the risk of re-infection. They can return to the recent LTBI class only by exogenous re-infection at rate σ_T β I. The factor reducing the risk of infection, as a result of acquired immunity to a previous infection, is taken fixed for persistent latent individuals, σ_L = 0.5 (any value between 0 and 1 would lead to the same conclusions), contrary to that for treated individuals where it was considered variable.

We incorporate into the model treatment of recent LTBI at a variable rate τ_1 and persistent LTBI at a variable rate τ_2. The model is schematically illustrated in Fig. 2, and the interactions of the compartments are specified by the following system (I)

\[
\begin{align*}
\dot{S} &= μ - β I_p S - μ S \\
\dot{L}_1 &= β I_p S + σ_T β I_p T + σ_L β I_p L_2 - (δ + τ_1 + μ) L_1 \\
\dot{L}_2 &= (1 - φ) δ L_1 - σ_L β I_p L_2 - (ω + τ_2 + μ) L_2 \\
\dot{I}_p &= α_3 φ δ L_4 + α_2 δ L_2 + α_T T - (τ_p + μ) I_p \\
\dot{I}_n &= (1 - α_1) φ δ L_1 + (1 - α_2) ω L_2 + (1 - α_T) ρ T
\quad - τ_n + μ) I_n \\
\dot{T} &= τ_1 L_1 + τ_2 L_2 + τ_T I_p + τ_n I_n - σ_T β I_p T - (ρ + μ) T
\end{align*}
\]

where the rate of infection λ = β I_p depends on the number of cases of smear positive pulmonary TB in the population and where

\[
S + L_1 + L_2 + I_p + I_n + T = 1.
\]

so that the total population size is constant. The natural death term (μ) represents the per capita rate at which individuals die of causes other than TB.

**B. Analysis of The model**

1) **Determination of the Basic Reproduction Number:** The basic reproduction number R_0, which is defined as the average
number of secondary infections produced by an infected individual in a completely susceptible and homogeneous population [3], is computed with the help of the next generation operator approach [2].

Letting \( X = (S, T) \) (the number non-infected individuals), \( Y = (I_p, I_s, I_n) \) (the number of infected individuals who do not transmit the disease), \( Z = (I_b) \) (the number of infected individuals capable of transmitting the disease), \( U_0 = (1, 0, 0, 0, 0, 0) \in \mathbb{R}^{2+3+1} \) the disease free equilibrium and \( \tilde{g}(X^*, Z) = (\tilde{g}_1(X^*, Z), \tilde{g}_2(X^*, Z), \tilde{g}_3(X^*, Z)) \) with

\[
\begin{align*}
\tilde{g}_1(X^*, Z) &= \frac{(\sigma_1, \sigma_2) \beta I_p}{c_1(\sigma_1, \beta I_p + c_2) c_3} (1 - \phi)(\sigma_1, \beta I_p + c_2) c_3,
\tilde{g}_2(X^*, Z) &= \frac{\sigma_2(\sigma_1, \beta I_p + c_2) (1 - \phi) \sigma_1, \beta I_p}{c_1(\sigma_1, \beta I_p + c_2) c_3},
\tilde{g}_3(X^*, Z) &= \frac{\beta(\sigma_1, \beta I_p + c_2) (1 - \phi) \sigma_1, \beta I_p}{c_1(\sigma_1, \beta I_p + c_2) c_3},
\end{align*}
\]

gives

\[
M = \left( \frac{\alpha_1 \phi c_2 + \alpha_2 \omega (1 - \phi)}{c_1 c_2 p} \right) \delta \beta.
\]

Hence \( R_0 \), defined as the spectral radius of the matrix \( MD^{-1} \) is

\[
R_0 = MD^{-1} = \frac{\alpha_1 \phi c_2 + \alpha_2 \omega (1 - \phi)}{c_1 c_2 p} \delta \beta.
\]

2) Steady States: In qualitative analysis of the model, the existence of steady states and their stability will be determined and analyzed.

To find an equilibrium \((S^*, L_1^*, L_2^*, I_p^*, I_n^*, T^*)\) of system (1) we have to solve the following system on \( I_p^* \)

\[
\begin{align*}
\mu - \beta I_p^* S^* - \mu S^* &= 0 \\
\beta L_1^* S^* + \beta \phi T^* L_1^* + \sigma_1 \beta I_p^* L_2^* - c_1 L_1^* &= 0 \\
(1 - \phi) \delta L_1^* - \sigma_1 \beta I_p^* L_2^* - c_2 L_2^* &= 0 \\
\alpha_1 \phi L_1^* + \alpha_2 \omega L_2^* + \alpha \rho T^* - c_3 I_p^* &= 0 \\
(1 - \phi) \omega L_2^* + (1 - \alpha_2) \omega L_2^* + (1 - \alpha_1) \omega T^* - c_4 I_n^* &= 0 \\
-\alpha_1 I_p^* &= 0 \\
\tau_1 L_1^* + \tau_2 L_2^* + \tau_3 I_p^* + \tau_4 I_n^* - \sigma \beta I_p^* T^* &= 0 \\
-\tau_5 T^* &= 0
\end{align*}
\]

where \( c_1 = \delta + \tau_1 + \mu, c_2 = \omega + \tau_2 + \mu, c_p = \tau_p + \mu, c_n = \tau_n + \mu \) and \( c_T = \rho \).

Equations 1, 3, 4 and 5 give \( S^*, L_1^*, I_p^* \) and \( T^* \) as function of \( I_p^* \) and \( L_2^* \)

\[
\begin{align*}
S^* &= \frac{\mu}{(\beta I_p^* + \mu) - \mu S^*} \\
L_1^* &= \frac{(\sigma_1, \beta I_p^* + c_2) c_3}{(1 - \phi) \sigma_1, \beta I_p^* + c_2} c_3 \\
T^* &= \frac{\alpha_1 \phi L_1^* + \alpha_2 \omega L_2^* + \alpha \rho T^* - c_3 I_p^*}{(1 - \phi) \delta L_1^* + \alpha_1 \phi L_1^* + \alpha_2 \omega L_2^* + \alpha \rho T^* - c_3 I_p^*} L_2^*
\end{align*}
\]

From (2) we get \( L_2^* \) as function of \( I_p^* \)

\[
L_2^* = \frac{b_3 \beta I_p^* + a_1 I_p^* + \mu a_0}{b_3 \beta I_p^* + b_2 \beta I_p^* + b_3 I_p^* + \mu b_0 \beta I_p^*}
\]

where

\[
bb = \rho c_T c_1 c_2 c_3 - \rho (1 - \phi) \delta c_T c_1 c_2 c_3 + (\alpha_1 c_2 + (1 - \phi) \phi c_2) \sigma_T c_1 c_2 c_3
\]

Finally, substituting \( L_1^*, L_2^*, I_p^* \) and \( T^* \) in (6) we get either \( I_p^* = 0 \), from which it may be concluded that system (I) always has the disease free equilibrium (DFE), or, \( I_p^* \) is a root of the third degree polynomial

\[
P(I_p) = p_3 I_p^3 + p_2 I_p^2 + p_1 I_p + p_0
\]

together with the possibility of existence of endemic equilibria. The coefficients of \( P \) are

\[
p_3 = (\mu a_2 d_2 + a_2 d_1 + b_2 e_2 + b_2 e_1) \beta^3
\]

\[
p_2 = (\beta a_2 d_2 + \mu a_2 d_1 + a_2 d_0 + b_2 e_2 + b_2 e_1) \beta^2
\]

\[
p_1 = (\beta a_2 d_1 + \mu a_2 d_0 + \mu b_0 e_2 + b_2 e_1) \beta
\]

\[
p_0 = \mu a_2 d_0 \beta + \mu b_0 e_1 - \mu a_0 d_0 \beta (1 - R_p)
\]

where

\[
e_1 = (\tau_1 (1 - \alpha_T) - c_4 c_T) (1 - \phi) \delta c_p + \alpha_T \rho (1 - \phi) \delta c_n \tau_p
\]

\[
e_2 = c_n a_2
\]

\[
d_0 = f_2 e_2 + \alpha T \rho (1 - \phi) d [c_n \tau_2 + \tau_n (1 - \alpha_2) \omega] - f_3 f_1
\]

\[
d_1 = f_2 \sigma_T - \delta f_2 \alpha_T \phi \omega c_n + c_n \tau_T f_1
\]

\[
d_2 = c_n b_3
\]

\[
f_1 = (\alpha_1 \phi c_2 + (1 - \phi) \alpha_2 \omega) c_1 c_2 c_3
\]

\[
f_2 = \alpha_T \rho \left[ c_n \tau_1 + \tau_n (1 - \alpha_1) \phi \delta \right] c_1 c_2 c_3
\]

\[
f_3 = (\tau_1 (1 - \alpha_T) - c_4 c_T) (1 - \phi) \delta c_p
\]

where

\[
\beta_p = c_1 c_2 c_3 c_4 c_T - (\rho (1 - \alpha_T) c_T \tau_n + \alpha_T c_n \tau_T) c_1 c_2
d_0
\]

and

\[
R_p = \frac{\beta_p}{\rho} \text{ defining a new reproduction number. Note that for } \rho = 0, \text{ letting } \beta_0 = (\sigma_1 c_2 + (1 - \phi) \sigma_2) c_3, \text{ we find again the basic reproduction number } R_0 = \frac{\beta_0}{\delta c_p}
\]

3) Stability of the disease-free equilibrium (DFE): At the disease free equilibrium DFE, we have \( I_p^* = 0 \) and previous computation yields \( S^* = 1 \), \( L_1^* = L_2^* = I_n^* = T^* = 0 \). Hence \( DFE = (1, 0, 0, 0, 0, 0) \).

The stability of the disease free equilibrium is achieved through the determination of the sign of the eigenvalues of the Jacobian matrix \( J_0 \) of system (I) evaluated at \( DFE \):

\[
J_0 = \begin{pmatrix}
-\mu & 0 & 0 & -\beta & 0 & 0 \\
0 & -c_1 & 0 & \beta & 0 & 0 \\
0 & (1 - \phi) \delta & -c_2 & 0 & 0 & 0 \\
0 & \alpha_1 \phi c_2 & \alpha_2 \omega & -c_0 & 0 & \alpha_T \rho \\
0 & (1 - \alpha_1) \delta & (1 - \alpha_2) \omega & -c_n & 0 & (1 - \alpha_T) \rho \\
0 & \tau_1 & \tau_2 & \tau_n & -c_T & 0
\end{pmatrix}
\]

one negative eigenvalue \((-\mu)\) of \( J_0 \) is straightforwardly determined, the other five eigenvalues are those of the matrix

\[
J_1 = \begin{pmatrix}
-\alpha_1 \phi c_2 & \alpha_2 \omega & -c_0 & 0 & \alpha_T \rho \\
\alpha_1 \phi c_2 & \alpha_2 \omega & -c_0 & 0 & \alpha_T \rho \\
(1 - \alpha_1) \delta & (1 - \alpha_2) \omega & -c_n & 0 & (1 - \alpha_T) \rho \\
\tau_1 & \tau_2 & \tau_n & -c_T & 0
\end{pmatrix}
\]
The stability conditions of \( J_1 \) are determined by use of the following result of M-matrices theory.

**Proposition**

Let \( A = [a_{ij}] \) be a \( n \times n \) matrix. The real part of each of the eigenvalues of \( A \) is greater than zero if and only if all diagonal entries of \( A \) are positive, and there exists a positive diagonal matrix \( D \), such that \( AD \) is strictly diagonal dominant, that is,

\[
a_{ii}d_i > \sum_{j=1, j \neq i}^{n} |a_{ij}|d_j \quad i = 1, ..., n.
\]

Since the matrix \( J_1 \) has negative diagonal entries, we consider the matrix \( -J_1 \). According to the previous proposition, \( J_1 \) has negative real part if and only if there exists a positive diagonal matrix \( D = (d_i^*)_{1 \leq i \leq 5} \) such that \( -J_1D \) is strictly diagonal dominant, namely,

\[
(I) \quad \begin{align*}
& c_1d_1^* > \beta d_1^* \\
& c_2d_2^* > (1 - \phi)\delta d_1^* + \alpha_2\omega d_2^* + \alpha_T\rho d_2^* \\
& c_3d_3^* > (1 - \alpha_1)\rho d_1^* + (1 - \alpha_2)\omega d_3^* + (1 - \alpha_T)\rho d_3^* \\
& c_4d_4^* > \gamma_1d_1^* + \gamma_2d_2^* + \gamma_Td_3^* + \gamma_n d_4^* \\
& c_5d_5^* > (1 - \alpha_1)\phi d_1^* + (1 - \alpha_2)\omega d_5^* + (1 - \alpha_T)\rho d_5^* + \varepsilon
\end{align*}
\]

Let \( d_1^* = 1 \)

\( d_1^* = \frac{\beta + \varepsilon}{c_1} \)

\( d_2^* = \frac{(1 - \phi)\delta + \varepsilon}{c_1c_2} + \frac{(1 - \phi)\delta + c_1}{c_1c_2} \)

\( d_4^* = \frac{(1 - \alpha_1)\phi d_1^*}{c_4} + \frac{(1 - \alpha_2)\omega d_3^*}{c_4} + (1 - \alpha_T)\rho d_3^* + \varepsilon \)

\( d_5^* = \frac{\gamma_1d_1^*}{c_5} + \frac{\gamma_2d_2^*}{c_5} + \frac{\gamma_Td_3^*}{c_5} + \frac{\gamma_n d_4^*}{c_5} + \varepsilon \)

where \( \varepsilon > 0 \), \( t = c_1[(1 - \alpha_2)\omega c_T + (1 - \alpha_T)\rho_T] + c_Tc_1c_2 \)

\[ y = (1 - \alpha_T)c_1e_2 + (1 - \alpha_T)\rho_T e_2 \]

\[ z = (1 - \alpha_T)\rho_T e_2 + (1 - \alpha_T)\omega_T e_2 \]

\[ \begin{align*}
& x = a_1d_1^* + a_2d_2^* + a_3d_3^* + a_4d_4^* + (1 - \alpha_T)\rho_T e_2 \\
& + (1 - \alpha_T)\omega_T e_2 + (1 - \alpha_T)\rho_T e_2 + (1 - \alpha_T)\omega_T e_2
\end{align*} \]

substituting in the inequality \( c_1d_1^* > \alpha_1\phi d_1^* + \alpha_2\omega d_2^* + \alpha_T\rho d_3^* \) we get

\[ \varepsilon < \frac{d_0\beta_0\rho_T}{B} (1 - R_\rho) \]

where \( B = [e_1c_T - (1 - \alpha_T)\rho_T]C + \tau_n(x + y + t)\alpha_T\rho \)

and \( C = a_1\phi c_T + (a_2\omega_T c_T + \alpha_T\rho_T e_2) + (1 - \alpha_T)\delta \)

Thus for \( R_\rho < 1 \) all inequalities of system (II) are satisfied; this implies that the real part of each of the eigenvalues of \(-J_1\) is greater than zero and therefore the DFE is locally asymptotically stable. Otherwise, it is unstable and an epidemic is triggered. The special case \( R_\rho = 1 \) implies that \( p_0 = 0 \) and the disease free equilibrium loses its stability and becomes unstable for \( R_\rho > 1 \).

Looking on the expression of \( R_\rho \), we note that it is independent of the parameters \( \sigma_T \) and \( \sigma_L \); although the exogenous re-infection does not affect the stability, it affects the effort to reduce the TB incidence.

4) **Endemic equilibrium:** The existence of endemic equilibria for system (I) is linked to the existence of real positive roots of the polynomial \( P; (L^*_p > 0 \) must be biologically feasible).

A numerical computation of the polynomial discriminant \( Disc \) of \( P \)

\[
Disc = \left( \frac{3p_1p_3 - p_2^2}{9p_3^2} \right)^3 + \left( \frac{9p_1p_2p_3 - 27p_0p_3^2 - 2p_2^3}{54p_3^2} \right)^2
\]

yields \( Disc < 0 \), consequently all roots of \( P \) are real and unequal. Using the fact that the sign of the product of all roots of \( P \) is that of \( -sign(p_0)sign(p_3) \) and Since \( p_3 < 0 \) and \( p_0 = \mu a d_0 \beta_0 (R_\rho - 1) \) we deduced that the polynomial \( P \) has at least one positive real root if \( p_0 > 0 \), that is, \( R_\rho > 1 \) and therefore the existence of one endemic equilibrium. Using Descartes’ Rule of signs we proved that \( P \) has three real negative roots for \( 0 < R_\rho < 1 \) and thus non equilibrium.

5) **Expected population after eradication of the disease:** Eradication of the disease occurs when there are no more exposed and infectious individuals in the population, namely \( L_1 = L_2 = I_p = I_n = 0 \). Therefore \( S + T = 1 \) and the system (I) is reduced to

\[ \begin{align*}
& S = \mu - \mu S \\
& T = -(\rho + \mu)T
\end{align*} \]

solving these equations we get

\[ \begin{align*}
S(t) &= 1 + (S(0) - 1)e^{-\mu t} \\
T(t) &= T(0)e^{-(\rho + \mu)t}.\end{align*} \]

where \( S(0) \) and \( T(0) \) are the initial number of susceptible, treated individuals respectively. As \( t \to +\infty \), \( S(t) \to 1 \), and \( T(t) \to 0 \). Hence, in such situation, the whole population will be comprised of susceptible individuals.

6) **Model without exogenous re-infection:**

Case \( \sigma_T = \sigma_L = 0 \)

We investigate the situation where the re-infection is not possible or does not occur in the population. Equation (1) becomes

\[ b_1e_1\beta I_p + \mu a d_0 \beta + \mu b_0 e_1 = 0 \]

We have \( p_1 = b_1e_1 < 0 \).

Indeed \( b_1 = \alpha_T\rho e_2 > 0 \) and \( e_1 < 0 \) where

\[ e_1 = -\mu (1 - \phi) \delta_1 \rho_T \tau_n + \mu \rho_T \tau_n + \mu \rho + \mu c_3 \]

Moreover we have proved that \( p_0 = \mu a d_0 \beta + \mu b_0 e_1 = \mu a d_0 \beta (R_\rho - 1) \), therefore for \( R_\rho > 1 \), we have one real positive root then one endemic equilibrium and for \( R_\rho < 1 \) there exist no equilibrium.

case \( \sigma_T = 0 \)

Now let us assume that individuals who followed a treatment acquired a full immunity against re-infection; so \( \sigma_T = 0 \).

Equation (1) becomes

\[ p_2I_p^2 + p_1 I_p + p_0 = 0 \]

where \( p_2 = b_2 e_1 \beta^2, p_1 = (b_2 \mu a d_1 + b_1 e_1) \beta, p_0 = \mu a d_0 \beta + \mu b_0 e_1 \). Using Descartes’ Rule of signs we proved that \( P \) has
one real positive root and therefore one endemic equilibrium for $R_p > 1$ and two real negative roots and thus non equilibria for $0 < R_p < 1$.

IV. NUMERICAL SIMULATIONS

The simulations of the stability of the endemic equilibria as well as simulations following the proportion of active TB individuals over time were carried out using the following parameters values. The natural death rate ($\mu$) is obtained from the expression $\frac{1}{\mu}$ = life expectancy. We take the life expectancy of 75 years corresponding to the one of Algerian population. The transmission rate $\beta$ is variable. The treatment period by the program being 6 months which gives a recovery rate of 2 per individual per year, so $\tau_p = \tau_0 = 2$ (it is taken as the inverse of the time between the tuberculosis detection by the program and recovery by treatment). The proportion of individuals going to the class $I_p$ were taken from Algarian data. The rate of endogenous reactivation for treated individuals $\rho = 0.00002 yr^{-1}$, the rate of endogenous reactivation for persistent latent infection $\omega = 0.00002 yr^{-1}$, the factor reducing the risk of infection for persistent latent individuals $\sigma_L = 0.25$ were taken from the literature [4]. The factor reducing the risk of infection for treated individuals $\sigma_T$ is variable. The rate of progression to active TB is estimated from $\varphi \approx 0.6$ [4]; if we assume that $\varphi = 5\%$ of the latent population eventually develops active TB then $\delta = 12 yr^{-1}$.

The proportion of individuals going from $L_1$ (resp. $L_2$, $T$) towards $I_p$ is $\alpha_1 = 0.4$ (resp. $\alpha_2 = 0.4$, $\alpha_T = 0.9$). The proportion of individuals going to compartment $I_p$ and $I_0$ is $\phi = 0.05$. The incidence in Algeria for the year 2006 being 26.1 per 100 000 inhabitants [6], the corresponding values of infectious $I_p$ is 8834 cases and of the transmission coefficient $\beta$ is 150.42 and reproduction number $R_p = 1.9$; we used the system (I) to compute these values.

Fig. 3. Incidence at equilibrium as function of the reproduction number $R_p$ in the absence of treatment of LTBI individuals; the circle $\circ$ corresponds to the incidence in Algeria for the year 2006.

Fig. 4. The proportion of individuals with smear positive pulmonary TB at equilibrium as a function of the transmission coefficient $\beta$ for $\sigma_T = \sigma_L$ and $\tau_1 = 1$.

Finally, Fig. 7. shows how the proportion of active TB individuals changes over time when the treatment of LTBI individuals is introduced and this is done for series of rates ($\tau_1 = \tau_2 = 0; 0.1; 0.2; 0.3; 0.4; 0.5; 1; 10$ and the limit $\tau_1 \to \infty$).

A widespread treatment of LTBI individuals for some years is recommended to shift from higher to lower equilibrium state and thereafter relaxation is recommended whenever $\sigma_T \leq \sigma_L$. 

![Figure 3](image1.png)

![Figure 4](image2.png)
Fig. 5. The proportion of individuals with smear positive pulmonary TB at equilibrium as a function of the transmission coefficient $\beta$ for $\sigma_T = 2\sigma_L$ and $\tau_1 = 1$.

Fig. 6. The proportion of individuals with smear positive pulmonary TB at equilibrium as a function of the transmission coefficient $\beta$ for $\sigma_T = \sigma_L/2$ and $\tau_1 = 1$.

Fig. 7. The proportion of active TB individuals as function of time for different values of the treatment rate of LTBI individuals.

REFERENCES


