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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 the 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.

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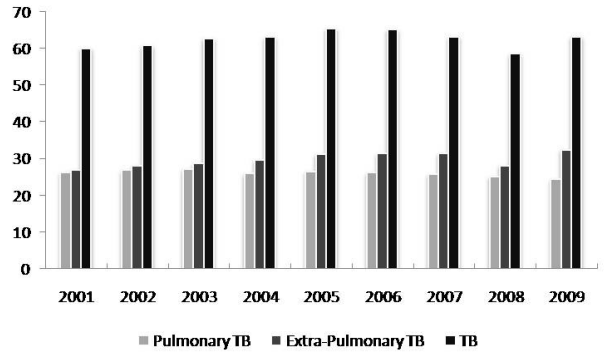

Fig. 1 Incidence of tuberculosis in Algeria $2001 - 2009$

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 tuberculous (the national average being of 10 individuals by household) are examined in order to identify among them the possible cases of TB disease. It is requested to the adults a radiological examination and from children of less than 14 years a tuberculinic test. If the examination is negative, they 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 $(\mathbf{S})$, 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 $(\mathbf{L}_1)$, and (2) later stage at low risk of developing active TB, referred as persistent LTBI $(\mathbf{L}_2)$. Likewise, we consider two classes of infectious individuals : smear positive pulmonary TB individuals, referred as $(\mathbf{I}_p)$, they can infect others and smear negative pulmonary TB individuals, referred as $(\mathbf{I}_n)$, who have TB disease and can not transmit it.

Infected individuals initially progress through recent LTBI, either, to active TB at rate $\phi\delta$, or, to persistent LTBI at rate $(1-\phi)\,\delta$. 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 $\sigma_L\beta I$. 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 $(\mathbf{T})$ 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 $\sigma_T\beta I$. The factor reducing the risk of infection, as a result of acquired immunity to a previous infection, is taken fixed for persistent latent individuals, $\sigma_L = 0.5$ (any value between 0 and 1 would lead to the same conclusions), contrary to that for treated individuals where it was considered variable.

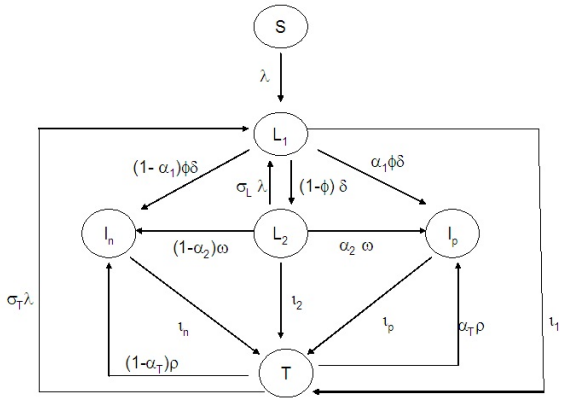

Fig. 2 Flows between the compartments of the model

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)

$$\begin{cases} \dot{S} = \mu - \beta I_p S - \mu S \\ \dot{L}_1 = \beta I_p S + \sigma_T \beta I_p T + \sigma_L \beta I_p L_2 - (\delta + \tau_1 + \mu)\, L_1 \\ \dot{L}_2 = (1-\phi)\,\delta L_1 - \sigma_L \beta I_p L_2 - (\omega + \tau_2 + \mu)\, L_2 \\ \dot{I}_p = \alpha_1 \phi \delta L_1 + \alpha_2 \omega L_2 + \alpha_T \rho T - (\tau_p + \mu)\, I_p \\ \dot{I}_n = (1-\alpha_1)\,\phi\delta L_1 + (1-\alpha_2)\omega L_2 + (1-\alpha_T)\,\rho T \\ \qquad - (\tau_n + \mu)\, I_n \\ \dot{T} = \tau_1 L_1 + \tau_2 L_2 + \tau_p I_p + \tau_n I_n - \sigma_T \beta I_p T - (\rho + \mu)\, T \end{cases}$$

where the rate of infection $\lambda = \beta I_p$ 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), $Y = (L_1, L_2, I_n)$ (the number of infected individuals who do not transmit the disease), $Z = (I_p)$ (the number of infected individuals capable of transmitting the disease), $U_0 = (1, 0, 0, 0, 0, 0) \in \mathcal{R}^{2+3+1}$ the disease free equilibrium and

$$\widetilde{g}(X^*, Z) = (\widetilde{g}_1(X^*, Z), \widetilde{g}_2(X^*, Z), \widetilde{g}_3(X^*, Z))$$

with

$$\begin{cases} \widetilde{g}_1(X^*, Z) = \frac{(\sigma_L \beta I_p + c_2)\beta I_p}{c_1(\sigma_L \beta I_p + c_2) - (1-\phi)\delta\sigma_L \beta I_p} \\ \widetilde{g}_2(X^*, Z) = \frac{(1-\phi)\delta\beta I_p}{c_1(\sigma_L \beta I_p + c_2) - (1-\phi)\delta\sigma_L \beta I_p} \\ \widetilde{g}_3(X^*, Z) = \frac{\delta\beta I_p[(1-\alpha_1)\phi(\sigma_L \beta I_p + c_2) + (1-\phi)(1-\alpha_2)\omega]}{c_n[c_1(\sigma_L \beta I_p + c_2) - (1-\phi)\delta\sigma_L \beta I_p]} \end{cases}$$

gives

$$M = \left(\frac{\alpha_1 \phi c_2 + \alpha_2 \omega (1-\phi)}{c_1 c_2} \delta\beta \right) \text{ and } D = (c_p).$$

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

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

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 $\left(S^*, L_1^*, L_2^*, I_p^*, I_n^*, T^*\right)$ of system (I) we have to solve the following system on I_p^*

$$\begin{cases} \mu - \beta I_p^* S^* - \mu S^* = 0 & (1) \\ \beta I_p^* S^* + \sigma_T \beta I_p^* T^* + \sigma_L \beta I_p^* L_2^* - c_1 L_1^* = 0 & (2) \\ (1-\phi)\,\delta L_1^* - \sigma_L \beta I_p^* L_2^* - c_2 L_2^* = 0 & (3) \\ \alpha_1 \phi \delta L_1^* + \alpha_2 \omega L_2^* + \alpha_T \rho T^* - c_p I_p^* = 0 & (4) \\ (1-\alpha_1)\,\phi\delta L_3^* + (1-\alpha_2)\omega L_2^* + (1-\alpha_T)\,\rho T^* & \\ -c_n I_n^* = 0 & (5) \\ \tau_1 L_1^* + \tau_2 L_2^* + \tau_p I_p^* + \tau_n I_n^* - \sigma_T \beta I_p^* T^* & \\ -c_T T^* = 0 & (6) \end{cases}$$

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

Equations 1, 3, 4 and 5 give S^*, L_1^*, I_n^* and T^* as function of I_p^* and L_2^*.

$$\begin{cases} S^* = \frac{\mu}{(\beta I_p + \mu)} \\ L_1^* = \frac{\left(\sigma_L \beta I_p^* + c_2\right)}{(1-\phi)\delta} L_2^* \\ T^* = \frac{c_p}{\alpha_T \rho} I_p^* - \left[\frac{\alpha_1 \phi \sigma_L}{\alpha_T \rho (1-\phi)} \beta I_p^* + \frac{(\alpha_1 \phi c_2 + (1-\phi)\alpha_2 \omega)}{\alpha_T \rho (1-\phi)} \right] L_2^* \\ I_n^* = \frac{(1-\alpha_1)\phi\left(\sigma_L \beta I_p^* + c_2\right)}{(1-\phi)c_n} L_2^* + \frac{(1-\alpha_2)\omega}{c_n} L_2^* \\ -\frac{(1-\alpha_T)\rho}{c_n} \left(\frac{\alpha_1 \phi \sigma_L \beta I_p^* + (\alpha_1 \phi c_2 + (1-\phi)\alpha_2 \omega)}{\alpha_T \rho (1-\phi)} \right) L_2^* \\ +\frac{(1-\alpha_T)\rho}{c_n} \frac{c_p}{\alpha_T \rho} I_p^* \end{cases}$$

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

$$L_2^* = \frac{a_2 \beta I_p^{*2} + a_1 I_p^* + \mu a_0}{b_3 \beta^3 I_p^{*3} + b_2 \beta^2 I_p^{*2} + b_1 \beta I_p^* + \mu b_0} \beta I_p^*$$

where

$bb = \rho\alpha_T c_1 \sigma_L - \rho(1-\phi)\delta\alpha_T \sigma_L + (\phi\alpha_1 c_2 + (1-\phi)\omega\alpha_2)\delta\sigma_T$

$a_2 = (1-\phi)\delta c_p \sigma_T$, $a_1 = a_2 \mu$, $a_0 = (1-\phi)\delta\alpha_T \rho$,

$b_3 = \phi\delta\alpha_1 \sigma_L \sigma_T$, $b_2 = bb + \mu b_3$, $b_1 = b_0 + \mu bb$,

$b_0 = \rho\alpha_T c_1 c_2$.

Finally, substituting L_1^*, L_2^*, I_n^* 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

$$P(I_p) = p_3 I_p^{*3} + p_2 I_p^{*2} + p_1 I_p^* + p_0$$

therefore the possibility of existence of endemic equilibria. The coefficients of P are

$$\begin{aligned} p_3 &= (\mu a_2 d_2 + a_2 d_1 + b_2 e_2 + b_3 e_1)\,\beta^3 \\ p_2 &= (\beta\mu a_0 d_2 + \mu a_2 d_1 + a_2 d_0 + b_1 e_2 + b_2 e_1)\,\beta^2 \\ p_1 &= (\beta\mu a_0 d_1 + \mu a_2 d_0 + \mu b_0 e_2 + b_1 e_1)\,\beta \\ p_0 &= \mu a_0 d_0 \beta + \mu b_0 e_1 = -\mu a_0 d_0 \beta_\rho (1 - R_\rho) \end{aligned}$$

where

$e_1 = (\tau_n(1-\alpha_T)\rho - c_n c_T)(1-\phi)\delta c_p + \alpha_T \rho (1-\phi)\delta c_n \tau_p$

$e_2 = -c_n a_2$

$d_0 = f_2 c_2 + \alpha_T \rho (1-\phi)\,\delta\,[c_n \tau_2 + \tau_n(1-\alpha_2)\omega] - f_3 f_1$

$d_1 = f_2 \sigma_L - \delta f_3 \alpha_1 \phi \sigma_L + c_n \sigma_T f_1$

$d_2 = c_n b_3$

$f_1 = \delta(\alpha_1 \phi c_2 + (1-\phi)\alpha_2 \omega)$

$f_2 = \alpha_T \rho [c_n \tau_1 + \tau_n(1-\alpha_1)\phi\delta]$

$f_3 = (\tau_n(1-\alpha_T)\rho - c_n c_T)$

and where

$$\beta_\rho = \frac{c_1 c_2 c_p c_n c_T - \rho((1-\alpha_T)c_p \tau_n + \alpha_T c_n \tau_p) c_1 c_2}{d_0}$$

and $R_\rho = \frac{\beta}{\beta_\rho}$ defining a new reproduction number. Note that for $\rho = 0$, letting $\beta_0 = \frac{c_1 c_2 c_p}{(\phi\alpha_1 c_2 + (1-\phi)\omega\alpha_2)\delta}$ we find again the basic reproduction number $R_0 = \frac{\beta}{\beta_0}$.

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

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

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

$$J_1 = \begin{pmatrix} -c_1 & 0 & \beta & 0 & 0 \\ (1-\phi)\delta & -c_2 & 0 & 0 & 0 \\ \alpha_1\phi\delta & \alpha_2\omega & -c_p & 0 & \alpha_T\rho \\ (1-\alpha_1)\phi\delta & (1-\alpha_2)\omega & 0 & -c_n & (1-\alpha_T)\rho \\ \tau_1 & \tau_2 & \tau_p & \tau_n & -c_T \end{pmatrix}$$

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,

$$a_{ii}d_i > \sum_{\substack{j=1 \\ j\neq i}}^{n} |a_{ij}|\, d_j \qquad i = 1, ..., n.$$

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 $-J_1 D$ is strictly diagonal dominant, namely,

$$(II) \begin{cases} c_1 d_1^* > \beta d_3^* \\ c_2 d_2^* > (1-\phi)\delta d_1^* \\ c_p d_3^* > \alpha_1\phi\delta d_1^* + \alpha_2\omega d_2^* + \alpha_T\rho d_5^* \\ c_n d_4^* > (1-\alpha_1)\phi\delta d_1^* + (1-\alpha_2)\omega d_2^* + (1-\alpha_T)\rho d_5^* \\ c_T d_5^* > \tau_1 d_1^* + \tau_2 d_2^* + \tau_p d_3^* + \tau_n d_4^* \end{cases}$$

Let

$$\begin{aligned} d_3^* &= 1 \\ d_1^* &= \frac{\beta+\varepsilon}{c_1} \\ d_2^* &= \frac{(1-\phi)\delta\beta}{c_1c_2} + \varepsilon\frac{(1-\phi)\delta + c_1}{c_1c_2} \\ d_4^* &= \frac{(1-\alpha_1)\phi\delta d_1^* + (1-\alpha_2)\omega d_2^* + (1-\alpha_T)\rho d_5^* + \varepsilon}{c_n} \\ &= \frac{(x\beta + y\tau_p) + \varepsilon\,(x+y+t)}{z} \\ d_5^* &= \frac{\tau_1 d_1^* + \tau_2 d_2^* + \tau_p d_3^* + \tau_n d_4^* + \varepsilon}{c_T} \end{aligned}$$

where $\varepsilon > 0$, $t = c_1\left[(1-\alpha_2)\omega c_T + (1-\alpha_T)\rho\tau_2\right] + c_T c_1 c_2$
$y = (1-\alpha_T)\rho c_1 c_2$, $z = \left[c_n c_T - (1-\alpha_T)\rho\tau_n\right] c_1 c_2$,
$x = \left[(1-\alpha_1)\phi\delta c_T + (1-\alpha_T)\rho\tau_1\right] c_2$
$+ \left[(1-\alpha_2)\omega c_T + (1-\alpha_T)\rho\tau_2\right](1-\phi)\delta$,
substituting in the third inequality $c_p d_3^* > \alpha_1\phi\delta d_1^* + \alpha_2\omega d_2^* + \alpha_T\rho d_5^*$ we get

$$\varepsilon < \frac{d_0\beta_p c_T}{B}\,(1 - R_\rho)$$

where $B = \left[c_n c_T - (1-\alpha_T)\rho\tau_n\right] C + \tau_n\,(x+y+t)\,\alpha_T\rho$ and $C = \alpha_1\phi\delta c_2 c_T + (\alpha_2\omega c_T + \alpha_T\rho\tau_2)\,(c_1 + (1-\phi)\delta) + (\tau_1 + c_1)\,\alpha_T\rho c_2$.

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_ρ, we note that it is independent of the parameters σ_T and σ_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; ($I_p^* > 0$ must be biologically feasible).

A numerical computation of the polynomial discriminant $Disc$ of P

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

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 $p_0 = \mu a_0 d_0 \beta_\rho\,(R_\rho - 1)$ we deduced that the polynomial P has at least one positive real root if $p_0 > 0$, that is, $R_p > 1$ and therefore the existence of one endemic equilibrium. Using Descartes' Rule of signs we proved that P has three real negative roots for $0 < R_p < 1$ and thus non equilibria.

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

$$\begin{aligned} \dot{S} &= \mu - \mu S \\ \dot{T} &= -(\rho+\mu)\,T \end{aligned}$$

solving these equations we get

$$\begin{aligned} S(t) &= 1 + (S(0)-1)e^{-\mu t} \\ T(t) &= T(0)e^{-(\rho+\mu)t} \end{aligned}$$

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

$$b_1e_1\beta I_p + \mu a_0 d_0 \beta + \mu b_0 e_1 = 0$$

We have $p_1 = b_1e_1 < 0$.
Indeed $b_1 = \alpha_T\rho c_1 c_2 > 0$ and $e_1 < 0$ where

$$e_1 = -\mu\,(1-\phi)\,\delta\left[\rho\tau_p\,(1-\alpha_T) + \rho\alpha_T\tau_n + c_p\tau_n + \rho\mu + \mu c_p\right]$$

Moreover we have proved that $p_0 = \mu a_0 d_0\beta + \mu b_0 e_1 = \mu a_0 d_0 \beta_\rho\,(R_\rho - 1)$, 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

$$p_2 I_p^2 + p_1 I_p + p_0 = 0$$

where $p_2 = b_2e_1\beta^2$, $p_1 = (\beta\mu a_0 d_1 + b_1e_1)\,\beta$, $p_0 = \mu a_0 d_0\beta + \mu b_0 e_1$. 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 (μ) 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 β is variable. The treatment period by the program being 6 months which gives a recovery rate of 2 per individual per year, so $\tau_p = \tau_n = 2$ (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 towards the class I_p were taken from algerian data. The rate of endogenous reactivation for treated individuals $\rho = 0.00002yr^{-1}$, the rate of endogenous reactivation for persistent latent infection $\omega = 0.0002yr^{-1}$, 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 σ_T is variable. The rate of progression to active TB is estimated from $\phi\delta \approx 0.6$ [4]; if we assume that $\phi = 5\%$ of the latent population eventually develops active TB then $\delta = 12year^{-1}$. 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_n is $\phi = 0.05$. The incidence in Algeria for the year 2006 being 26.1 per 100000 inhabitants [6], the corresponding values of infectious I_p is 8834 cases and of the transmission coefficient β is 150.42 and reproduction number $R_\rho = 1.9$; we used the system (I) to compute these values.

Fig. 3. describes the incidence of TB at equilibrium as function of the reproduction number R_ρ in the absence of treatment of LTBI individuals $(\tau_1 = \tau_2 = 0)$; the circle $\circ$ corresponds to the incidence in Algeria for the year 2006.

Fig. 4., Fig. 5, and Fig. 6 describe the proportion of individuals with smear positive pulmonary TB at equilibrium as a function of the transmission coefficient β in the absence of treatment of individuals with LTBI $(\tau_1 = \tau_2 = 0)$ with heavy line and with treatment of recent LTBI at rate $\tau_1 = 1$ and persistent LTBI at various values of τ_2 with dashed line. Through these figures, we see how the proportion of active TB individuals changes if the susceptibility to re-infection of treated individuals differs from that of persistent LTBI individuals.

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 $\sigma_T \leq \sigma_L$.

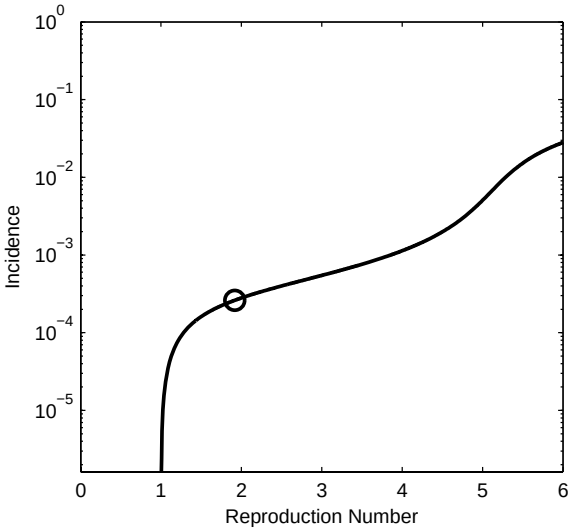

Fig. 3. Incidence at equilibrium as function of the reproduction number R_ρ in the absence of treatment of LTBI individuals; the circle $\circ$ corresponds to the incidence in Algeria for the year 2006.

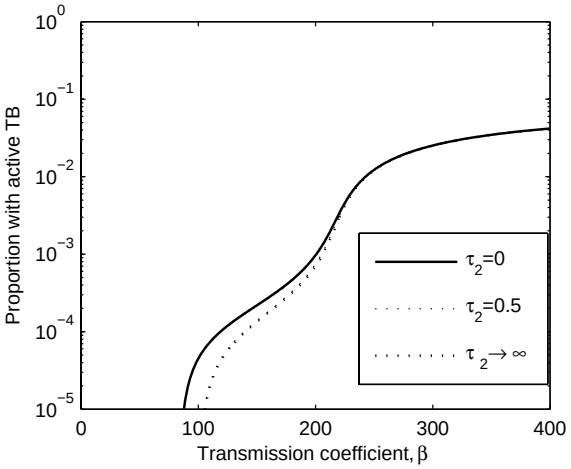

Fig. 4. The proportion of individuals with smear positive pulmonary TB at equilibrium as a function of the transmission coefficient β for $\sigma_T = \sigma_L$ and $\tau_1 = 1$.

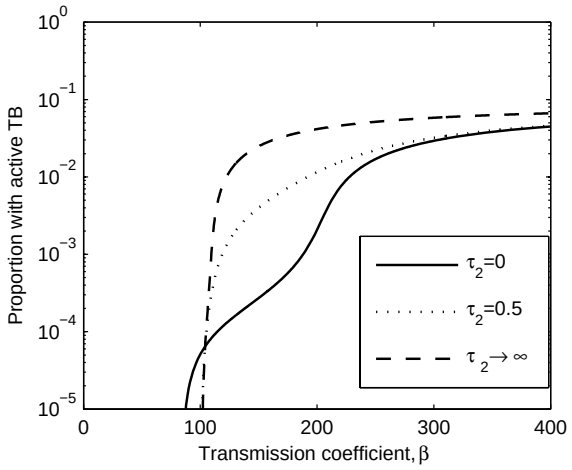

Fig. 5. The proportion of individuals with smear positive pulmonary TB at equilibrium as a function of the transmission coefficient β for $\sigma_T = 2\sigma_L$ and $\tau_1 = 1$.

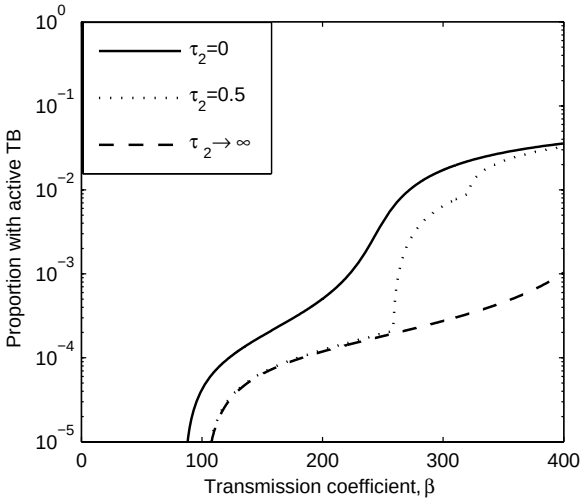

Fig. 6. The proportion of individuals with smear positive pulmonary TB at equilibrium as a function of the transmission coefficient β for $\sigma_T = \sigma_L/2$ and $\tau_1 = 1$.

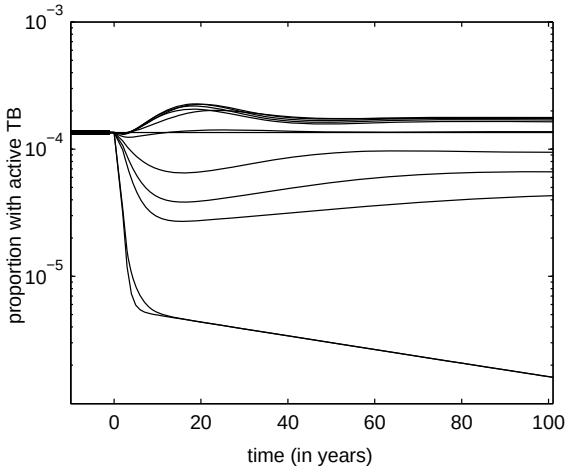

Fig. 7. The proportion of active TB individuals as function of time for different values of the treatment rate of LTBI individuals.

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