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Modelling congenital transmission of Chagas' disease

Silvia Martorano Raimundo[a,*], Eduardo Massad[a,b], Hyun Mo Yang[c]

[a] School of Medicine, University of Sao Paulo and LIM 01-HCFMUSP, Rua Teodoro Sampaio, 115 CEP: 05405-000 - São Paulo, S.P., Brazil
[b] London School of Hygiene and Tropical Diseases, UK
[c] Universidade Estadual de Campinas, IMECC – Departamento de Matemática Aplicada, Brazil

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ABSTRACT

The successful elimination of vectorial and transfusional transmission of Chagas' disease from some countries is a result of the reduction of domestic density of the primary vector *Triatoma infestans*, of almost 100% of coverage in blood serological selection and to the fact that the basic reproductive number of Chagas' disease is very close to one (1.25). Therefore, congenital transmission is currently the only way of acquiring Chagas' Disease in such regions. In this paper we propose a model of congenital transmission of Chagas' disease. Its aim is to provide an estimation of the time period it will take to eliminate this form of transmission in regions where vetorial transmission was reduced to close to zero, like in Brazil.

1. Introduction

On June 9, 2006, the Pan American Health Organization (PAHO) presented the Minister of Health of Brazil with the International Elimination of Transmission of Chagas' Disease Certificate (Ministério de Saúde, 2007; PAHO, 2007). This act was the culmination of an intensive process that begun in 1991 with the Southern Cone Initiative, a joint agreement between the governments of Argentina, Bolivia, Brazil, Chile, Paraguay, Uruguay and Peru, to control Chagas' disease by the elimination of the main vector, *Triatoma infestans*. This initiative has been highly successful and the prevalence area of the vector plummeted in the last years (Esgolts, 1970). As a consequence, the current seroprevalence of children between 0 and 5 years in Brazil is of the order of 10^{-5}, a clear indication that transmission, if it is occurring, is only accidental (Massad, 2008).

The successful elimination of vectorial and transfusional transmission of Chagas' disease from Brazil was a result of the reduction of domestic density of the primary vector *T. infestans* and of almost 100% of coverage in blood serological selection. As mentioned in Kirchhoff (2000), the basic reproductive number (R_0) of Chagas' disease was very close to one (1.25) (Kirchhoff, 2000), that is, not far from the elimination threshold. So, an average reduction of 25% in the vector life expectancy (feasible thanks to the domestic habits of *T. infestans*) was enough to reduce R_0 below unit, and to achieve the elimination of this form of transmission. Therefore, congenital transmission is currently the only way of acquiring Chagas' Disease in Brazil.

American trypanosomiasis (Chagas' Disease) is a zoonosis caused by the protozoan parasite *Trypanosoma cruzi* [4]. The disease is characterized by two phases: acute and chronic.

The principal mechanism of Chagas' disease transmission in humans is through the bites of insect vectors called Triatoma sp bugs (CDC, 2007). These blood-sucking bugs, in turn, get infected by biting an infected animal or person. This vector belongs to the subfamily Triatominae (Hemiptera: Reduviidae) (Lent et al., 1994; Schofield, 1994, 2000) comprising 130 recognized species, of which about a dozen are commonly involved in transmission of the trypanosome to humans. Other forms of transmission include: consumption of uncooked food contaminated with faeces from infected bugs; congenital transmission (from a pregnant woman to her baby); blood transfusion; organ transplantation; and accidental laboratory exposure (CDC, 2007).

Congenital transmission may occur at any time of pregnancy, in successive gestations and may affect twins. The infection may produce pathology in the growing foetus. The consequences on the newborn are variable, ranging from asymptomatic to severe clinical manifestations. Congenital transmission cannot be prevented, but early diagnosis of the newborn enables prompt treatment, achieving cure rates close to 100% (the treatment regimen should include benznidazol between 5 and 10 mg/kg/d for 30–60 days or nifurtimox at 10–15 mg/kg/d for 60 days) and thus avoiding progression to chronic Chagas' disease (Massad, 2008). It is a consensus that congenital Chagas disease will be a pressing public health concern until the pool of infected women of childbearing age decreases to

* Corresponding author.
E-mail address: silviamr@dim.fm.usp.br (S.M. Raimundo).

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insignificant levels, which may happen only 30 years from now (Massad, 2008).

In this paper we propose a model of congenital transmission of Chagas' disease. The model is divided into core and non-core groups. The idea of a core group is a small, highly active segment of the population which can, in some cases, propagate the disease so effectively that it cannot be eradicated (Kribs-Zaleta, 1999). The "core group" is defined as the set of individuals who had a level of risk behavior sufficient to generate viable chains of transmission in a population and the infection would die out or maintain into the population in the absence of this core group. Since core group individuals contribute to disease transmission they are very important targets for effective prevention. Borrowing this idea we define the infected subpopulations, that is, the infected children and their mothers with Chagas' disease as a core group. Our aim is to provide an estimation of the time period it will take to eliminate this form of transmission in regions where vetorial transmission was reduced to close to zero, like in Brazil.

The paper is structured as follows. In the next section we describe the model, in Section 3 we analyse its equilibrium and its stability, Section 4 we illustrate the theoretical results of model giving numerical simulations and a final discussion of the results conclude the paper.

2. The Model

As mentioned above the core group is comprised by individuals infected with the chagasic parasite. Our goal is to follow-up this core group in order to investigate the trend of the core population. The total population (N) of our model is, then, divided in core-non-core groups which are partitioned into eight classes according to their epidemiologic significance: G_i, women with Chagas' disease; Bw_i, infected female children born to chagasic mothers (vertically infected children); Bw_{int}, untreated and infected female children; G_{un}, uninfected pregnant women; Bw_{un}, uninfected female children born to chagasic mothers; ; Bm_i, infected male children born to chagasic mothers; Bm_{int}, untreated and infected male children; Bm_{un}, uninfected male children born to chagasic mothers. Therefore our core group comprises the infected females (G_i^*, Bw_i^* and Bw_{int}^*) and the infected males (Bm_i and Bm_{int}); while the non-core group is constituted by the females and males uninfected (G_{un}, Bw_{un} and Bm_{un}).

The transmission model is shown schematically in Fig. 1.

In this study, we consider a cohort of chagasic pregnant women that can generate uninfected and infected newborns. Clinical studies show that most women refuse being tested, and consequently, most positive cases are diagnosed at pregnancy, during the prenatal routine hospital care (Massad, 2008). We also assume that the infant females who were not infected with the parasite (but are born to chagasic mothers) are recruited into the uninfected pregnant class and can generate uninfected newborns.

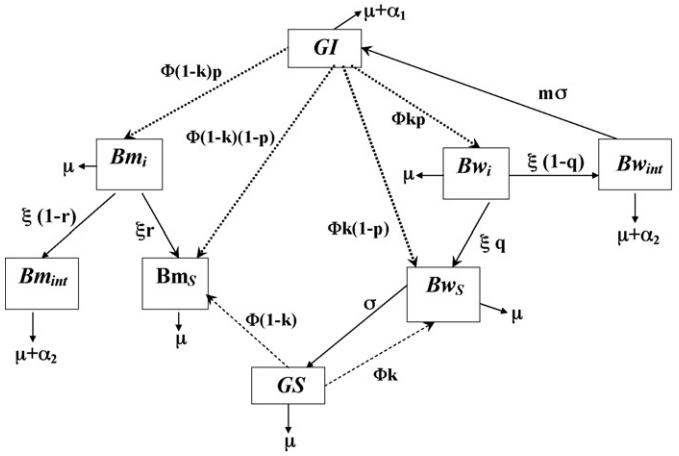

Fig. 1. The flow diagram of the Chagas' disease transmission.

We assume that: all the parameters of the model are positive; the vital dynamics includes a birth process given by natality rate ϕ and a death process given by natural mortality μ; the parameter α_i is the disease-related death rate, where α_1 is the disease-related death rate of women with Chagas' disease, while α_2 is the disease-related death rate of untreated children. Let p $(0 \le p \le 1)$ be the proportion of chagasic children born to chagasic mothers and $(1-p)$ the proportion of uninfected children born to chagasic mothers. Let us define k $(0 \le k \le 1)$ as the proportion of female children among all newborns. We assume that women with Chagas' disease have lower fertility rate than uninfected women, named, respectively, ϕ' and ϕ. This assumption is based on the observation by Bittencourt (1976), according to whom in 24 placentas of chagasic women, the most consistent findings were villous and intervillous inflammatory infiltrates. Amastigotes of *T. cruzi* were found mostly in the chorionic villi and in the chorionic plate, and less frequently in the fetal membranes, which would be responsible for an important number of miscarriages. We have, then, ϕk as the proportion of female children born to uninfected mothers. On the other hand, we have $\phi' k$ as the proportion of female children born to mothers with Chagas' disease; among them we have $\phi' kp$ as the proportion of chagasic newborns and $\phi' k(1-p)$ as the proportion of uninfected newborns.

Sexually immature female children (Bw_{un} and Bw_{int}) reach the reproductive ages at constant rates σ and $m\sigma$. So σ^{-1} is the average age at which the uninfected children are sexually active and eventually become pregnant. Note that we have $\sigma > \mu$, that is, the average age to generate the first descendant (σ^{-1}) is lower than the surviving time (μ^{-1}). Let us assume that chagasic female children reach the reproductive age later than uninfected children, which delay is given by the parameter m, $0 \le m \le 1$. Since $\phi' < \phi$ and $m\sigma < \sigma$, it easy to see that the chagasic women generate less descendants than the uninfected one.

The model includes the treatment of infected children (Bw_i and Bm_i) born to chagasic mothers. The treated patients are cured at a constant rate ξ, with ξ^{-1} being the average period of time of healing. Let q $(0 \le q \le 1)$ and r $(0 \le r \le 1)$ be the proportions of treated female and male children, respectively. Consequently, $(1-q)\xi$ and $(1-r)\xi$ are the probability that treatment failure occurs for whatever reason.

The dynamics of vertical transmission are formalized by the following homogeneous linear system of ordinary differential equations with constant coefficients

$$\begin{cases} \frac{dGi}{dt} = m\sigma\, Bw_{int} - (\mu+\alpha_1)\, G_i \\ \frac{dBw_i}{dt} = \phi'\, k\, p\, G_i - (\mu+\xi) Bw_i \\ \frac{dBw_{int}}{dt} = \xi(1-q)\, Bw_i - (m\sigma+\mu+\alpha_2) Bw_{int} \\ \frac{dG_{un}}{dt} = \sigma\, Bw_{un} - \mu\, G_{un} \\ \frac{dBw_{un}}{dt} = \phi'\, k(1-p)\, G_i + \phi\, k\, G_{un} + \xi\, q\, Bw_i - (\mu+\sigma) Bw_{un} \\ \frac{dBm_i}{dt} = \phi'(1-k)\, pGi - (\mu+\xi) Bm_i \\ \frac{dBm_{int}}{dt} = \xi(1-r)\, Bm_i - (\mu+\alpha_2) Bm_{int} \\ \frac{dBm_{un}}{dt} = \phi'(1-k)(1-p)\, Gi + \phi(1-k)\, G_{un} + \xi\, r\, Bm_i - \mu Bm_{un}, \end{cases} \quad (1)$$

where the total population is $N = G_i + Bw_{un} + Bw_i + Bw_{int} + G_{un} + Bm_i + Bm_{int} + Bm_{un}$, and

$$\frac{dN}{dt} = \phi'\, G_i + \phi G_{un} - \mu N - \alpha_1 G_i - \alpha_2 (Bw_{int} + Bm_{int}).$$

These equations represent the rates of change of each class and are expressed in terms of the parameters described previously.

The total population is divided into three groups: the core group formed by the infected females (G_i^*, Bw_i^* and Bw_{int}^*), the uninfected group formed by the health females (G_{un} and Bw_{un}) and the male group (Bm_i, Bm_{int} and Bm_{un}). To simplify we assumed that the analysis of the system (1) is reduced to women groups only. The core group presents a special dynamic. The healthy newborns are removed from the core group going to the uninfected population. However, there is not external input to the core group because we are disregarding chagas vector transmission. Hence the source of individuals in this core group is the infected new borns generate by chagasic mothers due to vertical transmission. We analyse the behavior of these two subpopulations.

With no vaccine available for large-scale public health interventions, the main control strategy relies on prevention of Chagas transmission by eliminating the domestic insect vectors and controlling the transmission by vertical transmission and blood transfusion. Our model deals with intervention by drug treatment of infection described by the parameter q.

3. Analysis of the Model

Here our main objective is to follow-up the core group to estimate the elapsed time required to decrease the pool of infected women to insignificant levels or eradicate it. Note that there are three ways to exit from the core group: (a) by the disease induced mortalities, α_1 and α_2; (b) by treating effectively the proportion of female infected newborns, q, who are cured (in the case, $q = 1$ means that all infected newborns are cured); and (c) by avoiding or interrupting the congenital transmission (when $p = 0$, all newborns are uninfected) through effective treatment of pregnants. In order to reach our goal, we performed the analysis for the homogeneous linear system (1) in matrix form as $\dot{\mathbf{x}} = M\mathbf{x}$, where $\mathbf{x} \in R^7$, $dot\mathbf{x} = (d\mathbf{x}/dt)$ and M is a 7×7 constant matrix (Esgolts, 1970; PAHO, 2007).

The algebraic technique of diagonalizing the square matrix M is used to reduce the linear system (1) to an uncoupled linear system. We define the linear transformation of coordinates $\mathbf{y} = \tilde{M}^{-1}\mathbf{x}$, where $\tilde{M}$ is the invertible matrix. Then $\mathbf{x} = \tilde{M}y$, $\dot{\mathbf{y}} = \tilde{M}^{-1}\dot{\mathbf{x}} = \tilde{M}^{-1}M\mathbf{x} = \tilde{M}^{-1}M\tilde{M}\mathbf{y}$, where $\tilde{M}^{-1}M\tilde{M}$ is diagonal matrix. This uncoupled linear system has the solution $y(t) = diag\,[e^{\lambda_1 t}, \ldots, e^{\lambda_7 t}]\,y_0$, where y_0 is the initial condition and λ_i are eigenvalues of the matrix M. Thus, the general solution of the system $\dot{\mathbf{x}} = M\mathbf{x}$ is of the form $X = \sum c_i^{(i)}\tilde{M}e^{\lambda_i t}$, $i = 1, \ldots, 7$. Investigating the trajectories of the some solutions $X_i = \overline{X_i}(t)$, $i = 1, \ldots, 7$ of the system $\dot{\mathbf{x}} = A\mathbf{x}$ may be reduced to investigating the stability of a trivial solution, that is, the point of the system of equations located at the origin, $X_i = 0$, $i = 1, \ldots, 7$. This point is asymptotically stable when all roots λ_i of the characteristic equation are negative (if real) or have negative real parts (if complex). Thus, due to the presence of factors $e^{\lambda_i t}$, the trajectories whose initial values lie in any δ—neighborhood of the origin enter an arbitrarily small ε—neighborhood of the origin and, as $t \to \infty$, they approach the origin. Otherwise, if at least one root λ_i is positive (if real) or has positive real parts (if complex), the trajectories have the same shape as in the preceding case, but they evolve in the opposite direction. Now, as t increases, trajectories originating at points that are arbitrarily close to the origin recede from it without bound, and so the trivial solution is unstable. In this way all the possibilities for the roots $\lambda_i \neq 0$ can be analysed; note that the case $\lambda_i = 0$, is excluded by the condition $\det M \neq 0$.

However, if $\det M = 0$ then the characteristic equation $|M - \lambda I| = 0$ has a zero root. Assuming that $\lambda_1 = 0$, then the general solution will be the form $X_i(t) = c_1^{(1)}\tilde{M} + \sum c_i^{(i)}\tilde{M}e^{\lambda_i t}$, $i = 2, \ldots, 7$. If one of these roots has negative real parts, then as $t \to \infty$, the points on every trajectory approach to the point $X_i(t) = c_1^{(i)}\tilde{M}$, lying on this trajectory. The trivial solution is stable, but there is no asymptotic stability. Indeed, in that case, the trivial solution is a singular point. To find singular points one must first find a set of points in which the conditions of existence and uniqueness theorem are violated. Of course, not every point at which these conditions are violated is a singular point, since the conditions are sufficient for the existence and uniqueness of the solution, but are not necessary.

In order to make a real phenomena compatible to its mathematical description we studied the position of trajectories in the neighborhood of the trivial solution $X_i = 0$, $i = 1, \ldots, 7$ of the system (1). The matrix M is given by

$$A = \begin{bmatrix} a_{11} & 0 & 0 & m\sigma & 0 & 0 & 0 & 0 \\ \phi' k(1-p) & a_{22} & \xi q & 0 & \phi k & 0 & 0 & 0 \\ \phi' kp & 0 & a_{33} & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \xi(1-q) & a_{44} & 0 & 0 & 0 & 0 \\ 0 & \sigma & 0 & 0 & a_{55} & 0 & 0 & 0 \\ \phi'(1-k)p & 0 & 0 & 0 & 0 & a_{66} & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & \xi(1-r) & a_{77} & 0 \\ \phi'(1-k)(1-p) & 0 & 0 & 0 & \phi(1-k) & \xi r & 0 & a_{88} \end{bmatrix},$$

where

$$\begin{cases} a_{11} &= -(\mu + \alpha_1) \\ a_{22} &= -(\mu + \sigma) \\ a_{33} = a_{66} &= -(\mu + \xi) \\ a_{44} &= -(m\sigma + \mu + \alpha_2) \\ a_{55} = a_{88} &= -\mu \\ a_{77} &= -(\mu + \alpha_2). \end{cases}$$

The characteristic equation related to the matrix A has eight eigenvalues; three of them, $\lambda_1 = -(\mu + \xi)$, $\lambda_2 = -(\mu + \alpha_2)$ and $\lambda_3 = -\mu$ are straightforwardly calculated while the other four are related to the matrix

$$A_0 = \begin{bmatrix} a_{11} & 0 & 0 & m\sigma & 0 \\ \phi' k(1-p) & a_{22} & \xi q & 0 & \phi k \\ \phi' kp & 0 & {}_{33} & 0 & 0 \\ 0 & 0 & \xi(1-q) & a_{44} & 0 \\ 0 & \sigma & 0 & 0 & a_{55} \end{bmatrix}. \quad (2)$$

The matrix A_0 has the following characteristic equations:

$$P_1(\lambda) = \tilde{a}_0\lambda^2 + \tilde{a}_1\lambda + \tilde{a}_2 = 0, \quad (3)$$

with

$$\begin{cases} \tilde{a}_0 = 1 \\ \tilde{a}_1 = (\mu + \sigma) + \mu \\ \tilde{a}_2 = \sigma k\left[\phi^{th} - \phi\right], \end{cases} \quad (4)$$

where ϕ^{th} is given by

$$\phi^{th} = \frac{\mu(\mu + \sigma)}{k\sigma}, \quad (5)$$

and

$$P_2(\lambda) = a_0\lambda^3 + a_1\lambda^2 + a_2\lambda + a_3 = 0, \quad (6)$$

with

$$a_0 = 1$$
$$a_1 = (m\sigma + \mu + \alpha_2) + (\mu + \alpha_1) + \left(\mu + \xi\right)$$
$$a_2 = (m\sigma + \mu + \alpha_2)(\mu + \alpha_1) + [(m\sigma + \mu + \alpha_2) + (\mu + \alpha_1)]\left(\mu + \xi\right)$$
$$a_3 = \xi(1-q)kpm\sigma\left(\phi^* - \phi^{'}\right), \tag{7}$$

where ϕ^* is given by

$$\phi^* = \frac{(\mu + \alpha_1)\left(\mu + \xi\right)(m\sigma + \mu + \alpha_2)}{\xi(1-q)pm\sigma k}, \tag{8}$$

if $q \neq 1$ and $p \neq 0$. When $p = 0$, or $q = 1$, we have $\phi^* \to \infty$. In both cases, the three eigenvalues corresponding to (6) are negatives, given by $\lambda = -\left(\mu + \xi\right)$, $\lambda = -(\mu + \alpha_1)$ and $\lambda_3 = -(m\sigma + \mu + \alpha_2)$.

We now show that the signs of roots of both characteristic Eqs. (3) and (6) determine the behavior of the trajectories of system (1).

First, it is straightforward to note that the characteristic Eq. (3) has negative real parts if $\phi < \phi^{th}$, where ϕ^{th} is given by Eq. (5). However, to show that the roots of the characteristic Eq. (6) have a negative real part we apply M-matrix criteria (see Appendix A). Hence, to ensure the roots of the characteristic Eq. (6) have negative real part, it is necessary $\phi < \phi^{th}$ and $\phi' < \phi^*$, where ϕ^{th} and ϕ^* are given by (5) and (8), respectively.

Finally, showing that $\phi^{th} < \phi^*$ implies in that if $\phi < \phi^{th}$, then the roots of both characteristic Eq. (3) and (6) always have negative real part. In addition for $\phi = \phi^{th}$, one gets $\bar{a}_2 = 0$, such as the characteristic Eq. (3) has a zero and negative roots; while for $\phi > \phi^{th}$, it has positive and negative roots. We point out that for $\phi > \phi^{th}$ the roots of the characteristic Eq. (6) always have negative real part. In particular, for $\phi = \phi^*$ the polynomial (6) has a zero and complex roots with negative real part.

Therefore, for $\phi < \phi^{th}$ the trajectories of system (1) converge asymptotically to the trivial solution, that is, all populations go to extinction. For $\phi = \phi^{th}$ the trajectories converges asymptotically to finite value, such that the uninfected populations reach to finite values G^*_{un}, Bw^*_{un} and Bm^*_{un}; while the populations with Chagas' disease go to zero. For $\phi > \phi^{th}$ the nature of the trajectories have two different behaviors. For $\phi^{th} < \phi \leq \phi^*$ the uninfected populations increase unbounded, G^*_{un}, Bw^*_{un} and Bm^*_{un}; while the populations with Chagas' disease go to zero. For $\phi > \phi^*$ all trajectories increase without limit, that is, all populations increase unbounded.

Table 1
Parameter values used in simulations.

	Definition	Value
μ	Death rate	0.01667 years^{-1}
$\phi = \phi'$	Natality rate	Variable, years^{-1}
σ	Reproductive age	0.0667 years^{-1}
α_1	Disease-related death rate of chagasic pregnant women	0.01 years^{-1}
α_2	Disease-related death rate of untreated children	0.01 years^{-1}
ξ	Treatment rate	0.1 years^{-1}
p	Proportion of chagasic children born to chagasic mothers	0.1
k	Proportion of female children among all newborns	0.5
m	Likelihood of chagasic sexually immature female children become pregnant	0.9
q, r	Proportion of treated female and male children	0.5

The polynomial $P_1(\lambda)$ is related to the dynamical behavior of uninfected women classes (G_{un} and Bw_{un}), while $P_2(\lambda)$, is related to the core group (G^*_i, Bw^*_i and Bw^*_{int}). The male classes (Bm_i, Bm_{int} and Bm_{un}), being decoupled from the dynamical system, do not affect the dynamical behavior of the system (the negative eigenvalues are linked to these groups).

The main objective is to show that if ϕ^* increases then the persistence of the core group in the population is avoided. According to Eq. (8), ϕ^* increases when (a) the disease induced mortality rates, α_1 and α_2, increase; (b) the proportion p of infected children who are treated increases; and (c) the successful treatment of pregnants that avoids the vertical transmission increases such that the probability of vertical transmission p decreases.

Clearly, note that when $p = 0$ or $q = 1$, we have $\phi^* \to \infty$ as pointed above. Hence, the core group goes to extinction for all values of the natality rate ϕ'. The curve of ϕ' with respect to these parameters takes a hyperbolic shape, showing asymptotes when $p \to 0$ and $q \to 1$. On the other hand, when the effective treatment decreases the disease induced mortality rates α_1 and α_2, result in a linear decreasing in ϕ^*. As a consequence, the core group could be maintained in the population.

In the next section we will perform the numerical simulations to determine the velocity in which the trajectories of the subpopulations of the core group tend to the extinction.

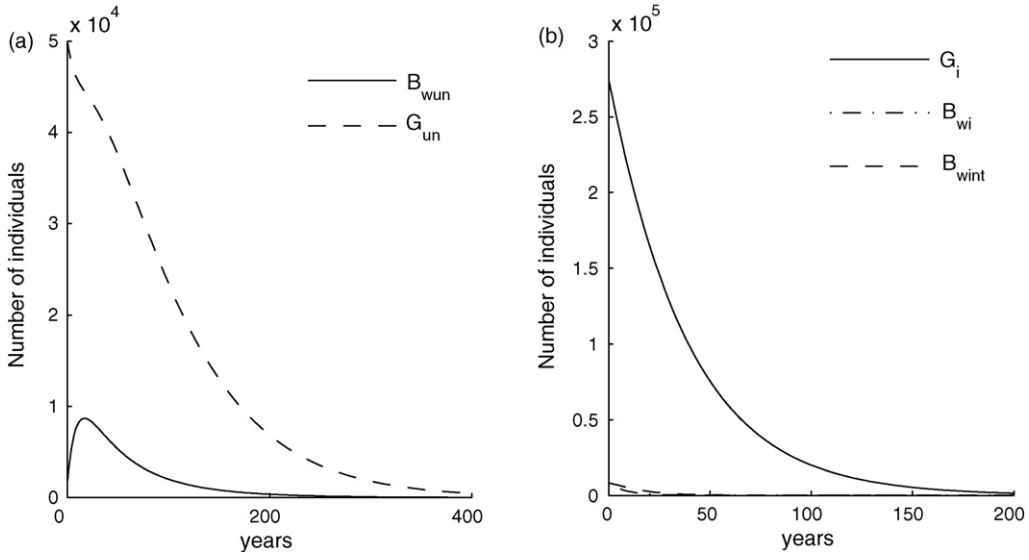

Fig. 2. The profiles of populations for number of individuals, where $\phi < \phi^{th}$. (a) The variation of both uninfected and chagasic pregnant women populations. (b) The role of vertical transmission.

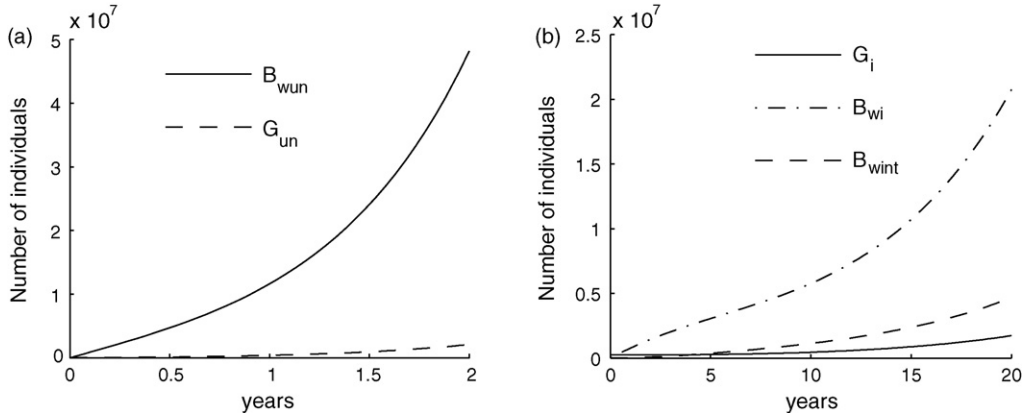

Fig. 3. The profiles of populations for number of individuals for $\phi > \phi^*$.

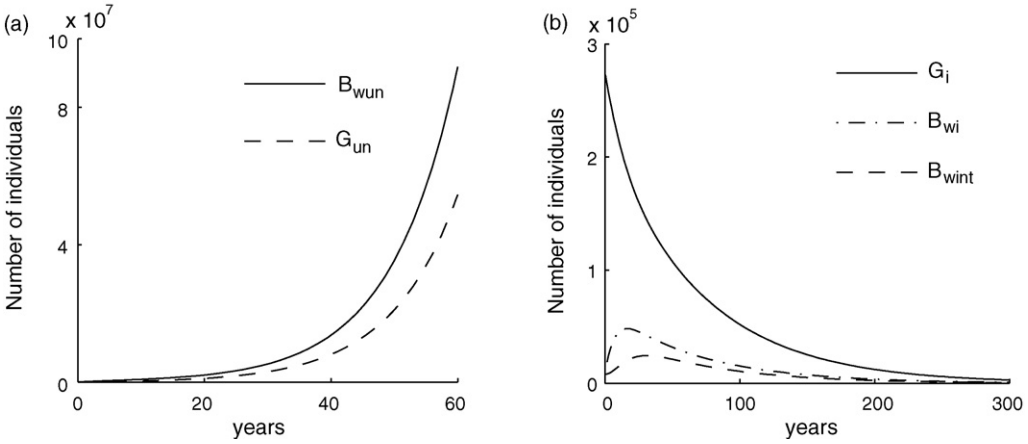

Fig. 4. For $\phi^{th} < \phi < \phi^*$, (a) shows the profiles of women uninfected populations G_{un} and Bw_{un} reaching finite values; while (b) shows the profiles of women with Chagas' disease G_i, Bw_i and Bw_{int} going to zero.

4. Numerical Analysis

In this section, we illustrate the theoretical results of model (1) giving numerical simulations of the equilibrium and its trajectories. We integrate the system (1) by Runge–Kutta method of fourth order using the set of the parameter values given in Table 1, where one gets $\phi^{th} = 0.0417$ and $\phi^* = 1.7976$. The initial values provided to system (1) are given by $G_i(0) = 275.000$, $Bw_{un}(0) = 1.500$, $Bw_i(0) = 8.250$, $Bw_{int}(0) = 8.250$, $G_{un}(0) = 50.000$, $Bm_i(0) = 8.250$, $Bm_{int}(0) = 8.250$ and $Bm_{un}(0) = 1.500$.

The results of numerical simulations are displayed graphically in Figs. 2–7. Here, for simplicity, we are making $\phi = \phi'$.

Fig. 2 shows the profiles of number of individuals, where $\phi = 0.006$ years^{-1}, with $\phi < \phi^{th}$. It can be seen that in the absence of immigration into the community, and with the natality rate ϕ below its threshold value, the total population will become extinct after some time. Fig. 2a shows the variation of uninfected newborns and their mothers; while the role of vertical transmission is explicitly shown in Fig. 2b.

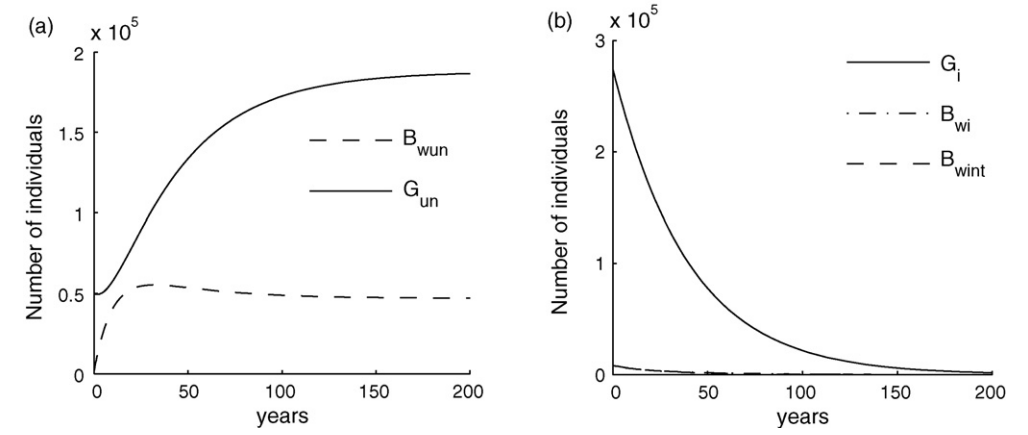

Fig. 5. For $\phi = \phi^{th}$, (a) shows the profiles of women uninfected populations G_{un} and Bw_{un} reaching finite values; while (b) shows the profiles of women with Chagas' disease G_i, Bw_i and Bw_{int} going to zero.

In Fig. 3 it is shown that for $\phi > \phi^*$, where $\phi = 60$ years^{-1}, all populations increase unbounded. It is seen that the population of susceptible female children Bw_{un} increases faster than the others.

Fig. 4 shows that for $\phi^{th} < \phi < \phi^*$, where $\phi = 0.6$ years^{-1}, the uninfected women populations, G_{un} and Bw_{un}, increase unbounded (Fig. 4a), while the women with Chagas' disease populations G_i, Bw_i and Bw_{int} go to zero (Fig. 4b).

By comparing Figs. 3nd 4 it is noted that the decrease in the rate of natality of the community decreases the population with Chagas' disease. Other way to reduce the population with Chagas' disease is by allowing the critical natality rate ϕ^* to surpass actual natality rate ϕ. This helps reducing the Chagas' disease prevalence as well. Thus, if the birth of children from chagasic pregnant is controlled or these newborns are under effective treatment or other control mechanisms, the overall infective population will remain under control and the disease can be kept under control. Consequently, the vertical transmission of the disease can be reduced significantly.

Fig. 5a and b shows that by controlling the natality rate, $\phi = \phi^{th}$, the values of women with Chagas' disease population is reduced and it would be eradicated after some time.

Fig. 6 describes the profile of chagasic women population (G_i) with increasing values of $\alpha_1 = \alpha_2 = 0$; 0.01; 0.02; 0.05 from top to bottom and $\phi = 0.05$. Observe that as the greater the disease induced mortalities, the smaller is the elapsed time to reduce the women with Chagas' disease population. However, the drug treatment of chagasic individuals and the application of effective treatment to avoid vertical transmission tend to decrease the disease induced mortality rates. Hence, the better the screening and treatment of chagasic individuals, the more they survive and the greater the time to reduce the population with Chagas' disease.

Let us now investigate the influence of treatment of infected women and the caring of pregnants to reduce the vertical transmission. Fig. 7 shows the time evolution of women with Chagas' disease when treatment is applied on the core group with values of $p = 1, q = 1$; $p = 0, q = 0$, $p = 1, q = 0.5$ and $p = 1, q = 0$ from bottom to top and $\phi = 0.05$. We disregard the variation in the disease induced mortality rates, as discussed above. Hence the impacts of treatment of chagasic individuals (q) and the caring of pregnant women to avoid vertical transmission (p), are assessed. When the proportion of treated individuals increases ($0 \le q \le 1$) or the vertical transmission is avoided ($0 \le p \le 1$), we have the increase in ϕ^*, and when $q \to 1$ or $p \to 0$, we have $\phi^* \to \infty$. As ϕ^* increases the time to reduce the population with Chagas' disease increases.

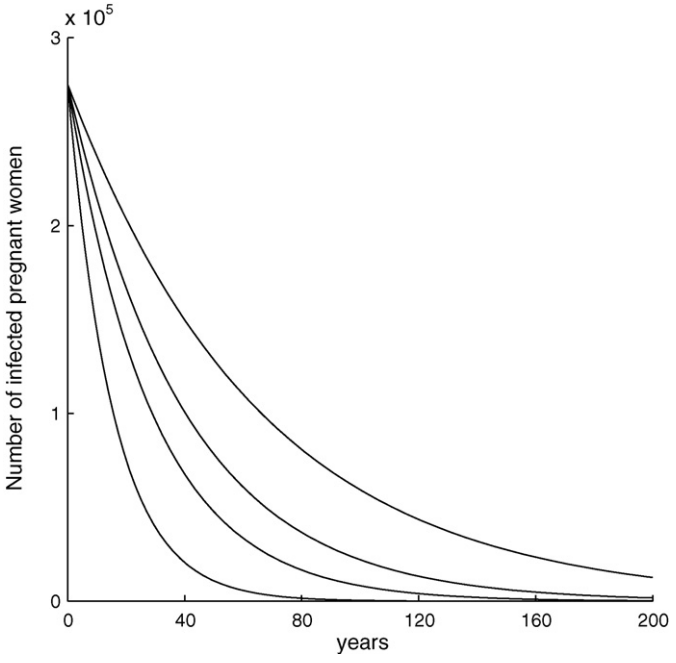

Fig. 6. The profile of women with Chagas' disease population (G_i) with increasing values of $\alpha_1 = \alpha_2 = 0$; 0.01; 0.02; 0.05 from top to bottom and $\phi = 0.05$.

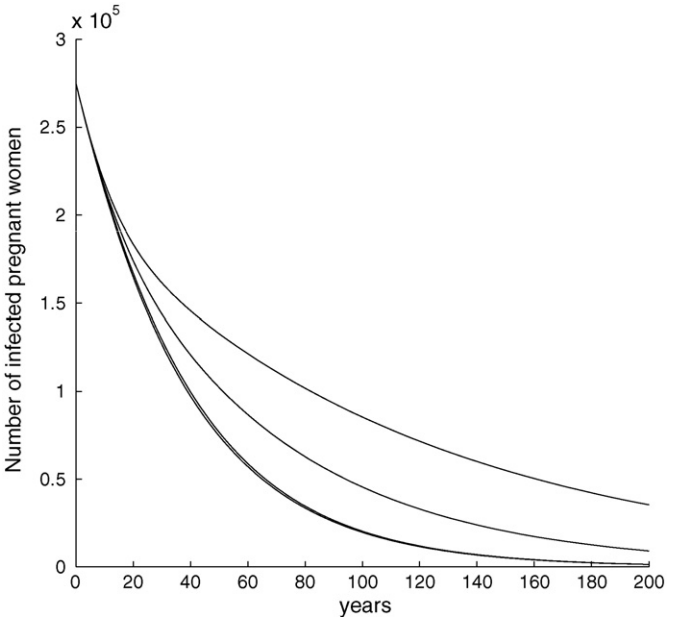

Fig. 7. The time evolution of women with Chagas' disease when treatment is applied on the core group with values of $p = 1, q = 1$; $p = 0, q = 0$, $p = 1, q = 0.5$ and $p = 1, q = 0$ from bottom to top and $\phi = 0.05$. By increasing the treatment rate ($p = 1$) and the proportion of treated female and male children ($q = 1$), the spread of the disease can be reduced more quickly.

5. Conclusion

In this paper, a linear mathematical model is proposed and analysed to study the transmission of Chagas' disease in a population of varying size without recruitment into the infected women population. Here, we allowed only the vertical transmission, since the vectorial transmission was eliminated in Brazil and many other countries. The model was, then, divided in core-non-core groups and we studied the decreasing trend of the core population.

By analysing the model, we have found a critical parameter that regulates the size of core group population, the threshold natality rate ϕ^*, which depends on mortality rate, average age at which the chagasic children are sexually active and eventually become pregnant, and proportions of female children among all newborns and of treated individuals. This threshold shows that infected babies continuously maintains the infective population, but if the threshold value is higher than the natality rate ϕ', then the core group decreases.

The screening and treatment of the infected pregnants result in: (a) decrease in the vertical transmission (p decreases), (b) increase in number of the infected individuals under treatment (q increases), and (c) decreases the disease induced mortality rates (α_1 and α_2 decrease). The overall effect on the threshold parameter ϕ^* is its increasing, because the decrease in the mortality rates is less sensitive than the variation in the proportions p and q.

The decrease in the parameter ϕ^* leads the core group to follow a decreasing trend in the size. And, as we have shown, much lower this value, more quickly the infected population goes to extinction. Thus, the spread of the disease should be controlled by way of promoting effective treatment to keep the infected population under control.

Congenital transmission of *T. cruzi* infection is the last way of acquiring the disease in Brazil. The success in the control of vector-transmitted Chagas' disease and screening programmes in blood banks has uncovered the public health relevance of congenital transmission, which has been gradually emerging in vector-free suburban areas and non-endemic cities (Schijman, 2006). The main difficulty in controlling it is due to the lack of a proper pre-natal programme that could diagnose the infection in candidate mothers and a safe chemoprophylaxis that could reduce the likelihood of vertical transmission. This is the greatest challenge in eradicating Chagas' disease from Brazil since there still remain an estimated 8000 to 16,000 new cases per year of congenital transmission (Schijman, 2006). Although congenital transmission cannot be prevented, early diagnosis enables prompt treatment of newborns, achieving cure rates close to 100% (Schijman, 2006).

Presently there are about 3.5 million people living with Chagas' disease in Brazil (Kropf et al., 2003). It would be very convenient to have an estimate of the time when the disease can be considered eradicated, that is, when there is no individual living with the disease. For this, it is necessary to project the current number of individuals considering the age-dependent prevalence and mortality rates.

Assuming the estimated age distribution of Chagas' disease prevalence (WHO, 2007) and mortality rate (IBGE, 2007a), Massad (2008) calculated, with demographic models (Smith and Keyfitz, 1977), the half-life of each age cohort. In the age cohort of 15–29 years, for instance, the half-life was estimated to be 30 years. This implies that, from the current 480,000 estimated cases in this cohort, 240,000 will still be alive in 30 years from now. Also, from the current 227,500 estimated cases for the age cohort of 0–4 years, in 40 years there will be 113,750 alive individuals, and so on. Therefore, even if the transmission were completely interrupted now, it would take several decades before complete eradication of cases.

It is possible, with the use of mathematical models to forecast (Massad et al., 2005) the total number of Chagas cases from vertical transmission. So, assuming that from the currently estimated 2.5 million cases of Chagas' disease, 51% or 1.785 millions are women. Assuming also the estimated age distribution of Chagas' disease prevalence (WHO, 2007) and mortality rate (IBGE, 2007a), and the age distribution of women fertility (IBGE, 2007b) and general mortality rate for Brazil (IBGE, 2007c), we can estimate the time evolution of cases of congenital Chagas' disease.

Finally, we would like to point that the linear model proposed in this paper may not be the ideal one for accurate forecast. However, it explains, in a simple way the main features of the congenital transmission of Chagas' disease. In a future work we will focus on an alternative nonlinear stochastic models for this purpose.

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Appendix A.

In this appendix we shall prove, by the use of M-matrices, that for $\phi < \phi^{th}$ the trajectories of system (1) converge asymptotically to the trivial solution, that is, all populations go to extinction.

The stability properties of $A_{\mathbf{0}}$ (2) are determined by using the well-known results on M-matrices. Our reference on this topic are given in Bittencourt (1976) and IBGE (2007a).

Definition. We say that a matrix $A = [a_{ij}]_{n\times n}$ is a non-singular M-matrix if $a_{ij} \leq 0$, $i \neq j$, and there exists a matrix $B \geq 0$ and a real number $s > 0$ such that $A = sI - B$ and $s > \rho(B)$, the spectral radius of B. □

The following equivalences are well-known.

Proposition 1. *A is a non-singular M-matrix if and only if the real part of each of its eigenvalues is greater than zero.*

Proposition 2. *A is a non-singular M-matrix if and only if all diagonal entries are positive, and there exists a positive diagonal matrix D, such that AD is strictly diagonal dominant, that is,*

$$a_{ij}\, d_i > \Sigma |a_{ij}| d_j, \quad i = 1, \ldots n.$$

Looking at our matrix (2) we observe that its diagonal entries are negative. We consider the matrix $-A_{\mathbf{0}}$, so its diagonal elements are positive. According to Proposition A.2, $-A_{\mathbf{0}}$ is a non-singular M-matrix if and only if there exists numbers d_1, d_2, d_3 and d_4 bigger than zero such that the following inequalities are satisfied

$$\begin{aligned}
&(\mu+\alpha_1)\, d_1 > m\sigma\, d_4\\
&(\mu+\sigma)\, d_2 > \phi'\, k(1-p)\, d_1 + \xi\, q\, d_3 + \phi\, k\, d_5\\
&\left(\mu+\xi\right)\, d_3 > \phi'\, k\, p\, d_1\\
&(m\sigma+\mu+\alpha_2)\, d_4 > \xi(1-q)\, d_3\\
&\mu d_5 > \sigma d_2
\end{aligned} \tag{9}$$

Let

$$\begin{cases}
d_3 = 1,\\
d_1 = \dfrac{m\sigma\xi(1-q) + [m\sigma(\mu+\alpha_1) + (m\sigma+\mu+\alpha_2)]\varepsilon}{(m\sigma+\mu+\alpha_2)(\mu+\alpha_1)}\\
d_4 = \dfrac{\xi(1-q)+\varepsilon}{(m\sigma+\mu+\alpha_2)}\\
d_2 = C_1 + \dfrac{\phi k}{(\mu+\sigma)} d_5 + \dfrac{m\sigma\phi k(1-p)\varepsilon}{(m\sigma+\mu+\alpha_2)(\mu+\alpha_1)(\mu+\sigma)}\\
d_5 = \dfrac{(\mu+\sigma)(1-p)\phi'}{(\phi^{th}-\phi)} C_1 + \dfrac{m\sigma\varepsilon}{(\phi^{th}-\phi)k(m\sigma+\mu+\alpha_2)(\mu+\alpha_1)}
\end{cases} \tag{10}$$

where $\varepsilon > 0$ and

$$C_1 = \frac{\phi' k(1-p)m\sigma\xi(1-q) + \xi q(m\sigma+\mu+\alpha_2)(\mu+\alpha_1)}{(m\sigma+\mu+\alpha_2)(\mu+\alpha_1)(\mu+\sigma)}.$$

Obviously, the first three inequalities given by (9) hold and, to ensure $d_5 > 0$, we require

$$\phi < \phi^{th} \tag{11}$$

Furthermore, substituting the Eq. (10) into the third inequality of system (9) we have

$$a_4 + \varepsilon A < 0,$$

where

$$a_4 = \phi' kpm\sigma\xi(1-q) - (\mu+\alpha_1)(\mu+\xi)(m\sigma+\mu+\alpha_2),$$

and $A > 0$ given by

$$A = \frac{\phi' kp\,[m\sigma(\mu+\alpha_1) + (m\sigma+\mu+\alpha_2)]}{(m\sigma+\mu+\alpha_2)(\mu+\alpha_1)\left(\mu+\xi\right)}. \tag{12}$$

Thus the third inequality of the system (9) yields

$$\varepsilon < -\frac{1}{A} a_4, \tag{13}$$

and, to ensure $\varepsilon > 0$, we require $a_4 < 0$.

Therefore, we can take $0 < \varepsilon < -(1/A)a_4$ such that the third inequality of the system (9) is satisfied when $\phi < \phi^*$.

Finally showing that $\phi^{th} < \phi^*$, this implies that if $\phi < \phi^{th}$ the system (9) has positive solution.

This implies that $-A_{\mathbf{1}}$ is a non-singular M-matrix for $\phi < \phi^{th}$. From Proposition A.1 it follows that the eigenvalues of $A_{\mathbf{0}}$ have negative real part.

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