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Modelling congenital transmission of Chagas' disease

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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

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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.

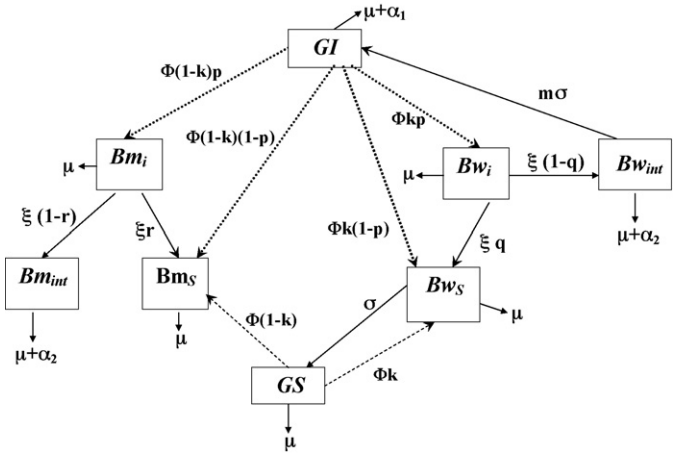

Fig. 1. The flow diagram of the Chagas' disease transmission.

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

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