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Control measures for Chagas disease

Gustavo Cruz-Pacheco [a], Lourdes Esteva [b,*], Cristobal Vargas [c]

[a] IIMAS-UNAM, México, D.F. 04510, Mexico
[b] Facultad de Ciencias, UNAM, México, D.F. 04510, Mexico
[c] Depto. de Control Automático, CINVESTAV-IPN, México, D.F. 07000, Mexico

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ABSTRACT

Chagas disease, also known as American trypanosomiasis, is a potentially life-threatening illness caused by the protozoan parasite, *Trypanosoma cruzi*. The main mode of transmission of this disease in endemic areas is through an insect vector called triatomine bug. Triatomines become infected with *T. cruzi* by feeding blood of an infected person or animal. Chagas disease is considered the most important vector borne infection in Latin America. It is estimated that between 16 and 18 millions of persons are infected with *T. cruzi*, and at least 20,000 deaths each year.

In this work we formulate a model for the transmission of this infection among humans, vectors and domestic mammals. Our main objective is to assess the effectiveness of Chagas disease control measures. For this, we do sensitivity analysis of the basic reproductive number R_0 and the endemic proportions with respect to epidemiological and demographic parameters.

1. Introduction

Chagas disease, also known as American trypanosomiasis, is a life-threatening illness caused by the protozoan parasite, *Trypanosoma cruzi*. The main mode of transmission of Chagas disease in endemic areas is through an insect vector called a triatomine bug. During the day, most domestic triatomines hide in crevices in walls and rustic roofs. The bugs emerge at night, when the inhabitants are sleeping, altough in Mexico there is at least is one that is diurnal. Because they tend to feed on peoples' faces, triatomine bugs are also known as *kissing bugs*. Triatomines pass *T. cruzi* parasites (called trypomastigotes) in feces left near the site of the bite wound. Scratching the site of the bite causes the trypomastigotes to enter the host through the wound, or through intact mucous membranes, such as the conjunctiva. Once inside the host, the trypomastigotes invade cells, where they differentiate into intracellular amastigotes. The amastigotes multiply by binary fission and differentiate into trypomastigotes, which are then released into the bloodstream. The triatomine bug becomes infected by feeding on human or animal blood that contains circulating parasites [1]. All the species of Triatominae are capable of transmitting Chagas disease, but the most important from an epidemiological point of view are *Triatoma infestans*, *Rhodnius prolixus*, *Triatoma dimidiate*, *T. brasiliensis*, *Triatoma barberi*, and *Panstrongylus megistus*. Given its wide distribution and ability to domestic and peridomestic invation, *T. infestants*, is the major cause of infection of *T. cruzi* in South America, meanwhile, *T. barberi*, and *T. dimidiate* are the most important transmitters in Mexico [2,3].

Chagas disease may also be spread through blood transfusion, organ transplantation, ingestion of food contaminated with parasites, and from mother to fetus. The proportion of trans–placental transmission from mothers with chronic *T. cruzi* infection to their newborns is 2–10% [4]. Risk factors for vertical transmission are not fully understood, but effectiveness of the adaptive immune response and the genetic susceptibility of both the mother and the child are suspected. Neonatal infection by *T. cruzi* causes an acute form of Chagas disease, which may be accompanied by a severe infectious syndrome that can causes death if not treated early. This form of the disease is frequent, severe, identifiable and curable. Indeed, almost all newborns diagnosed and treated before the end of their first year of life can be definitely cured [5].

In the early acute stage of the disease, the symptoms are mild and usually produce no more than local swelling at the site of infection, in general around the eyes in children. Current treatment consist of benznidazol and nifurtimox that in the acute phase may result in cure rates between 60% and 90%, but have limited efficacy in the chronic phase, toxic side effects, and are not readily accessible to patients due to difficulty for the supply [6].

* Corresponding author. Tel.: +52 5556224858; fax: +52 5556224859.
E-mail addresses: cruz@mym.iimas.unam.mx (G. Cruz-Pacheco), lesteva@lya.fciencias.unam.mx, lesteva@matematicas.unam.mx (L. Esteva), cvargas@ctrl.cinvestav.mx (C. Vargas).

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There is an asymptomatic middle stage in which the infection can not be detected at all, even blood test results are negative, and the length of this period is not well determined. After around 4–8 weeks, individuals with active infections enter the chronic phase of Chagas disease which has a variable duration that goes from 10 to 20 years, and around 60–80% of chronically infected individuals remain asymptomatic through their lifetime. The antiparasitic treatment also appears to delay or prevent the development of disease symptoms during the chronic phase of the disease, but 20–40% of chronically infected individuals will still eventually develop life-threatening heart and digestive system disorders [7].

T. cruzi infection has been found in more than 150 mammalian species throughout Latin America, and south of the United States. Mammals typically involved in wild cycles of transmission include opossums, armadillos, raccoons, monkeys, wood rats, and coyotes, among many others [2,8]. In some situations, dogs have been shown to be an important link in the maintenance of the domestic cycle and consequently in the transmission to humans [9]. Livestock have occasionally been found to be infected with *T. cruzi*, but the parasite is not known to affect the health of livestock. Birds, amphibians, and reptiles are naturally resistant to *T. cruzi* infection; however, in some situations, birds may be important sources of blood meals for triatomines [9].

Chagas disease is endemic in the Americas, particularly in poor, rural areas of Mexico, Central America, and South America. In 1991, the Health Authorities of Argentina, Brazil, Chile, Paraguay and Uruguay signed the 'Cono Sur Iniciative' to conduct a simultaneous campaign to stop the transmission of Chagas disease eliminating domestic *T. infestant,* and other important local species, together with screening of blood donors, and other control measures. This campaign opened the way to other similar initiatives against Chagas disease in Central America, Mexico, and countries in the Amazon region [10,11]. It has been documented that *T. infestans* has been eliminated from most of Chile, Brazil and Uruguay, and some regions of Argentina and Paraguay. However, there are still domestic populations of *T. infestans* in several provinces of Argentina, Paraguay, Bolivia, Peru, and north of Brazil [12]. Without a sustained surveillance and selective intervention against the last remaining of *T. domestic* and peridomestic infestans, this will always be a risk of renewed spread of this specie, and therefore of Chagas disease.

Despite campaigns as 'Cono Sur Iniciative', Chagas disease is still considered the most important vector borne infection in Latin America. It is estimated that between 16 and 18 millions of persons are infected with *T. cruzi*, with at least 20,000 deaths each year, and 100 millions considered at risk [13].

The nature of Chagas disease limits control measures. No vaccines to prevent the infection are available, and drugs are effective only in the acute and early chronic phase of infection, but have adverse effects. Control measures include elimination of the vector, screening blood donors, and treatment to patients in the acute phase. Since 1982, the World Health Organization has recommended the use of animals for zooprophylaxis, as a protective measure against vector borne diseases, for instance, the use of cattle in control of malaria [14]. This controversial technique consists of attracting vectors to domestic animals in which the pathogen cannot amplify (a dead-end host). However, there are two positions concerning this practice: the first one proposes that reduced feeding on people by vectors due to availability of alternative blood sources could lead to reduce the transmission of the infection. The second one claims that transmission could be increased due to an expanded vector population resulting from unlimited access to blood meals. Particular field studies on malaria support both theories [15–17].

Chagas disease is most common among people who live in substandard housing in rural and semi rural areas. Most cases are acquired by exposure to insects in domestic or peridomestic cycles, or by congenital transmission. For this reason, we focus on the study of the transmission of Chagas infection taking into account the domestic structure in rural villages, where animals and humans are in continuous contact.

In this work we present a mathematical model for the dynamics of Chagas disease in the presence of humans, transmitter and non-transmitter domestic animals. We will not include blood transmission and organ donation, since this kind of transmissions are not so important in the rural environment as vector bites and congenital transmission. The main objective is to assess the epidemiological impact of elimination of vectors, early treatment, and zooprophylaxis as a mean of control, and how this impact is influenced by changes of such measures. To this end, we will carry out sensitive analysis of the basic reproductive number of the disease with respect to the control parameters. Furthermore, the study will present a rigorous analysis of the resulting model.

Previous mathematical modeling studies have been done to understand different aspects on the transmission and spread of Chagas disease. For instance, in [18] the authors study the effect of demographic factors on the endemicity of Chagas disease. Vector dynamics and blood transfusion are considered in the transmission of the disease in [19]. A model with infection-age-dependent infectivity was developed in [20]. In [9] the authors used a model and data from villages in Argentina to demonstrate that the infection risk was reduced if domestic animals are excluded from the dormitories. The effects of insecticide spraying and of the recovery of vector population with cessation of spraying was analyzed in [21] for a model of the dynamics of transmission among humans, vectors, and domestic animals in a dwelling. The model predicts that if insecticide is discontinued, the vector population and the disease can return to the pre-spraying levels in approximately 5–8 years. The same authors presented in [22] a modified model with a delayed logistic growth term to simulate the vector carrying capacity when the blood meal supply is large.

The paper is organized as follows. The model is formulated in Section 2. Existence and stability of the equilibria of the model are investigated in Section 3. Sensitivity analysis and numerical simulations are presented in Section 4, and conclusions are given in the final section.

2. Formulation of the model

As was mentioned in the Introduction, the common transmission of the protozoan *T. cruzi* to mammals is by the bite of triatomine bugs. The disease may also be spread through blood transfusion and organ transplantation, ingestion of food contaminated with parasites, and from mother to fetus. In the model we only consider the transmission by triatomine bites and vertical transmission since these are the most common routes of infection.

We assume that the following populations coexist in the same environment:

- Humans.
- *Transmitters*: mammals that can be infected by the Triatomines, and can transmit the infection (dogs, cats).
- *Non-transmitters*: animals that can be bitten by the Triatomines, but can not be infected, and in consequence do not transmit the infection (chickens, birds).
- *Vectors*: Triatomines.

We denote by N_h, N_t, N_{nt}, and N_v, the population sizes of humans, transmitters, non-transmitters, and vectors, respectively. Since the non-transmitters population do not enter in the infection process, we consider N_{nt} as a parameter rather than a dynamical variable,