Chagas Disease as a Neglected Zoonosis in the American Continent

14

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ABSTRACT

In this chapter, the authors analyze the epidemiology, associated risk factors, worldwide prevalence, host range, life cycle, and treatment of Chagas Disease or American Trypanosomiasis. This disease is caused by an infection to human and other mammals with the hemoprotozoan Trypanosoma cruzi, which is transmitted by infected insect vectors (Hemiptera: Reduviide, subfamily Triatominae). The presence of wild reservoirs and vector insects naturally infected with T. cruzi has only been reported from the American Continent. Some cases of natural transmission to the human have been recognized in the southern half of the United States. The transmission of T. cruzi to the humans was mainly associated with the presence of triatomine bugs in rural dwellings and poor sanitary conditions. However, in recent years, there have been changes in the epidemiological landscape, where infection in humans has increased by contact with reservoirs, wild vectors, climate changes and the migratory phenomenon. The presence of T. cruzi in the insect vector and its ability to experimentally infect rodents were described in 1908 by Carlos Chagas. Scientific researchers described the disease first, and the etiological agent and the mechanisms of transmission later. The discovery of Chagas disease has been so crucial in advancing science and enhancing public health benefits that it serves as an outstanding illustration to comprehend the intricate dynamics intertwining science and society. From 2019, the World Health Organization inaugurating World Chagas Disease Day on April 14, the date on which Carlos Chagas identified the first human case of a T. cruzi infection. Authors conclude that in the control of Chagas Disease, the climate change must be taken into account.

Key words: Chagas Disease, American Continent, Trypanosoma cruzi, Triatomines, zoonosis

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1. INTRODUCTION

Chagas Disease or American Trypanosomiasis is caused by an infection to human and other mammals with the hemoprotozoan *Trypanosoma* (*Schizotrypanum) (T.) cruzi*, transmitted by contamination with faeces and/or urine of infected insect vector. The presence of wild reservoirs and transmitting triatomine insects naturally infected with *T. cruzi* has only been reported from the American Continent (Fig. 1) (from the south of the United States to northern Chile and Argentina). Recently, some cases of natural transmission to the human have been recognized in the southern half of the United States (CDC 2020). Historically, the transmission of *T. cruzi* to the human was mainly associated with the presence of triatomine bugs in rural dwellings and poor sanitary conditions. However, in recent years, there have been changes in the epidemiological landscape, where infection in humans has been favoured by contact with reservoirs, wild vectors, climate changes and the migratory phenomenon (Guhl et al. 2020).

Fig. 1: Distribution of *T. cruzi* in the American Continent (in red). Figure made by Carlos Ramón Bautista Garfias

Curiously, the presence of *T. cruzi* in the insect vector and its ability to experimentally infect rodents were described in 1908 by Carlos Chagas. Historically the microbe hunters first described the diseases, later the etiological agent and the mechanisms of transmission (Reyes 2009).
The discovery of Chagas disease has been so crucial in advancing science and enhancing public health benefits that it serves as an outstanding illustration to comprehend the intricate dynamics intertwining science and society (Petraglia and Trindade 2022). From 2019, the World Health Organization inaugurating World Chagas Disease Day on April 14, the date on which Carlos Chagas identified the first human case of a *T. cruzi* infection (WHO 2023).
At present, the World Health Organization classifies this disease as the most prevalent of poverty-promoting neglected tropical diseases and the most important parasitic disease of humans in Latin America, which affects between six to eight million people. It is also true that climate change is a serious hurdle for controlling this zoonotic disease and the migratory phenomenon of people from endemic zones to areas where natural transmission occurs between reservoirs and Triatomine insects (Kreier and Baker 1987; Martín-Escolana et al. 2022).

2. EPIDEMIOLOGY

In addition to vector transmission of *T. cruzi*, it can also be transmitted transplacentally, through infected blood transfusions or organ donations, laboratory accidents, needle sharing among intravenous drug users (IVDU), and orally through food and drink contaminated with triatomine insect or their feces or urine. Due to increased population mobility over previous decades and the possibility of transmission without the participation of the insect vector, the infection has been increasingly detected in the United States of America, Canada, and many European, African, Eastern Mediterranean and Western Pacific countries. The presence of infected people means that there is transmission of the parasites in other continents as well. The transmission of *T. cruzi* to the vertebrate host can be considered as a fortuitous event, an accident that can occur due to the repeated contact of the host with the vector when the triatomine feeds and defecates on, near or in human food (WHO 2023).
Reservoir infection occurs mainly through the oral route, where the metacyclic trypomastigote present in faeces, urine, and the hindgut of the triatomine insect is ingested or by contact of the droppings with mucous membranes. While in man, oral infection is less frequent compared to transmission by contamination from exposed skin (wounds), mucous membranes (eye, mouth), blood transfusion, congenital transmission, organ transplants and by laboratory accidents. The detection of the distinctive DNA of T. cruzi in mummies dating back approximately 4,000 years in the region where the initial human settlements existed in Chile, which are at least 7,000 years old, suggests that human infection didn't solely result from the presence of the vector/host. This finding implies that various factors influenced and increased the likelihood of the parasite's transmission to humans (Guhl et al. 2020).

3. ASSOCIATED RISK FACTORS

3.1. HUMAN HOST

Poverty; which includes poor sanitary conditions and houses with crevices allowing the proliferation and hiding of the vector.
Lack of knowledge; Ignorance that triatomine insects are carriers of a pathological agent makes the presence of insects in dwellings seem natural and there is no attempt to eliminate them. This happens at all socioeconomic levels. Ecological tourism and staying in places where the natural conditions of the ecosystems are preserved as much possible way also favours the

attraction of triatomine insects to the light sources in the rooms of houses. Displacement of food sources of blood-sucking insects and the continuous invasion of human settlements in peri-urban areas to build houses scares away reservoirs and causes insects to move into peridomestic areas and even further into houses (De Fuentes-Vicente et al. 2023).

3.2. VECTOR

Their feeding in both sexes frequently occurs on less hardened skin sites such as the face, which is why they are commonly known as kissing bugs and barbeiros (barber). Adaptation to human habitation and movement from wild environments to peridomiciles and even more to homes, makes contact of blood-sucking insects with humans more likely. Once the insect vectors are infected, the infection with the parasite remains throughout their life, which in some species can be a year or more. This increases their probability of being infected after feeding, since the life cycle of some species can be one year or more. They can withstand long periods of fasting, have few predators and are attracted at night by the light of the houses and their flight. Although they are not the best flying insects if they are allowed short flights (Carbajal de la Fuente et al. 2022).

3.3. RESERVOIRS

Chagas disease is mainly an enzootic infection, where transmission originates via the oral route when the vertebrate host is infected by ingesting faeces or urine contaminated with trypomastigotes or by ingesting the vector. There is also the possibility of transplacental transmission route (De Fuentes-Vicente et al. 2023).

4. WORLDWIDE PREVALENCE WITH EMPHASIS IN MÉXICO

Chagas disease (or the presence of *T. cruzi* in mammals) is present in humans from South United States of America to Argentina, showing different degrees of prevalence (Carbajal de la Fuente et al. 2022; WHO 2023) (Fig. 1). Chagas disease is one of the most important human parasitic diseases in the American continent. In this context, approximately six million people are affected and that about 172,000 new infections occurred during 2019 in this continent (Rojas de Arias et al. 2021). Regarding infection scenario in Mexico, the disease is present in the whole country, showing the highest prevalence in states geographically located in the Neotropical area of the region (Dumonteil 1999; Carabarin-Lima et al. 2013; Ibañez-Cervantes et al. 2018).

5. HOST RANGE

5.1. MAMMAL HOSTS

Many mammal species are infected by *T. cruzi*, including farm animals, such as cows (Fujita et al. 1993; Correa et al. 2020), pigs, sheep, horses (Ruiz-Piña et al. 2018), goats (Correa et al. 2020), and wild animals, such as primates (Jansen et al. 2018) bats (Torres-Castro et al. 2021), opossums (Jansen et al. 2018; Cantillo-Barraza et al. 2020), and skunks (Galaviz-Silva et al. 2017). In a recent report, an American barn owl (*Tyto furcata*) was found to be infected with *T. cruzi* (Martínez-Hernández et al. 2022).
Dogs are especially important because they can die of heart failure caused by *T.cruzi* infection (Barr 2009; Hamer and Saunders 2022). In this context, It was found that dogs infected with *T. cruzi* had owners infected with the parasite too (Chan-Pérez et al. 2022).

5.2. VECTORS

There are 149 species of triatomine insects (order Hemiptera, family Reduviidae), distributed mainly in the American continent. In Mexico, there are 33 vector species. The epidemiological significance of vectors is notably high, primarily due to their infection indices and their ability to transmit *T. cruzi* (Chagas) (Carbajal de la Fuente et al. 2022).

6. LIFE CYCLE

The life cycle of *T. cruzi*, the protozoan parasite responsible for Chagas disease, unfolds through a complex interplay between insect vectors and mammalian hosts. Initiated when an infected triatomine bug feeds on a mammalian host, the cycle begins in the insect's midgut, where bloodstream trypomastigotes transform into epimastigotes. These epimastigotes multiply through binary fission and eventually transition into infective metacyclic trypomastigotes (Fig. 2). During subsequent blood meals, these metacyclic trypomastigotes are excreted with the bug's feaces, leading to their deposition near the bite wound or mucous membranes of the host. Entry into the mammalian host may occur through various routes, including breaks in the skin or mucous membranes. Inside the host cells, metacyclic trypomastigotes transform into amastigotes, multiplying within the host cell's cytoplasm. The host cell may rupture, releasing amastigotes into the bloodstream, where they transform into bloodstream trypomastigotes. Circulating in the bloodstream, these trypomastigotes can infect various cells and tissues,

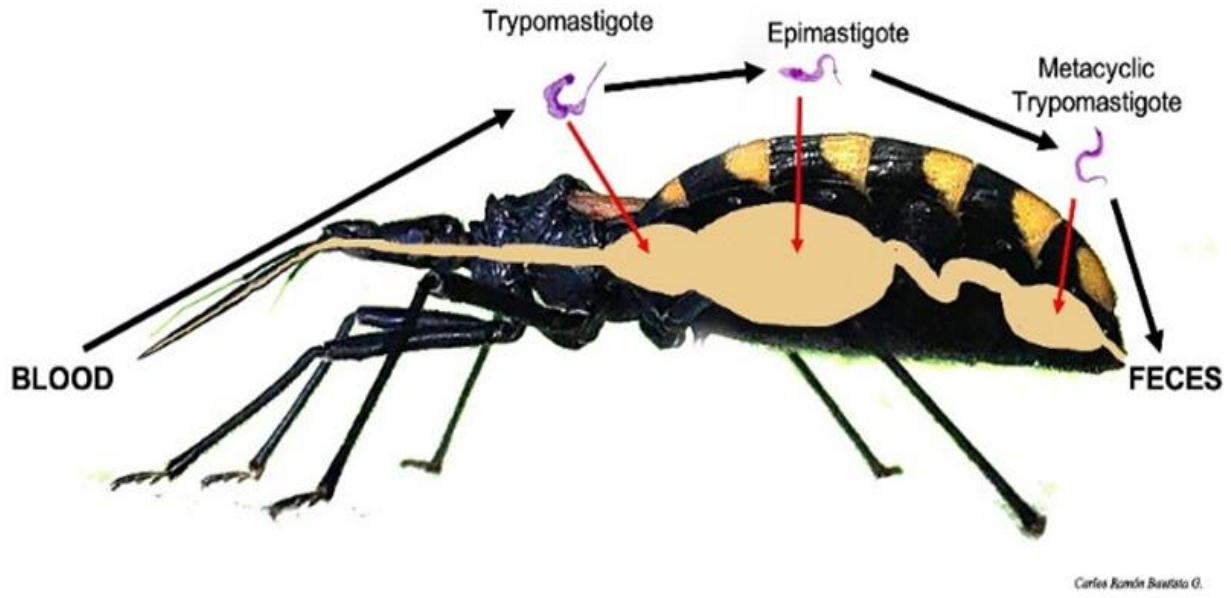

Fig. 2: *T. cruzi* life cycle in the vector *Triatoma pallidipennis*. Figure made by Carlos Ramón Bautista Garfias based on a photography of Benjamin Nogueda Torres.

perpetuating the infection (Fig. 3). The cycle may repeat when another triatomine bug feeds on an infected host, taking up bloodstream trypomastigotes and initiating the transformation back into epimastigotes in the insect's midgut. This intricate life cycle, involving both insect vectors and mammalian hosts, contributes to the persistence and transmission of Chagas disease in endemic regions of the Americas (Bern et al. 2019).

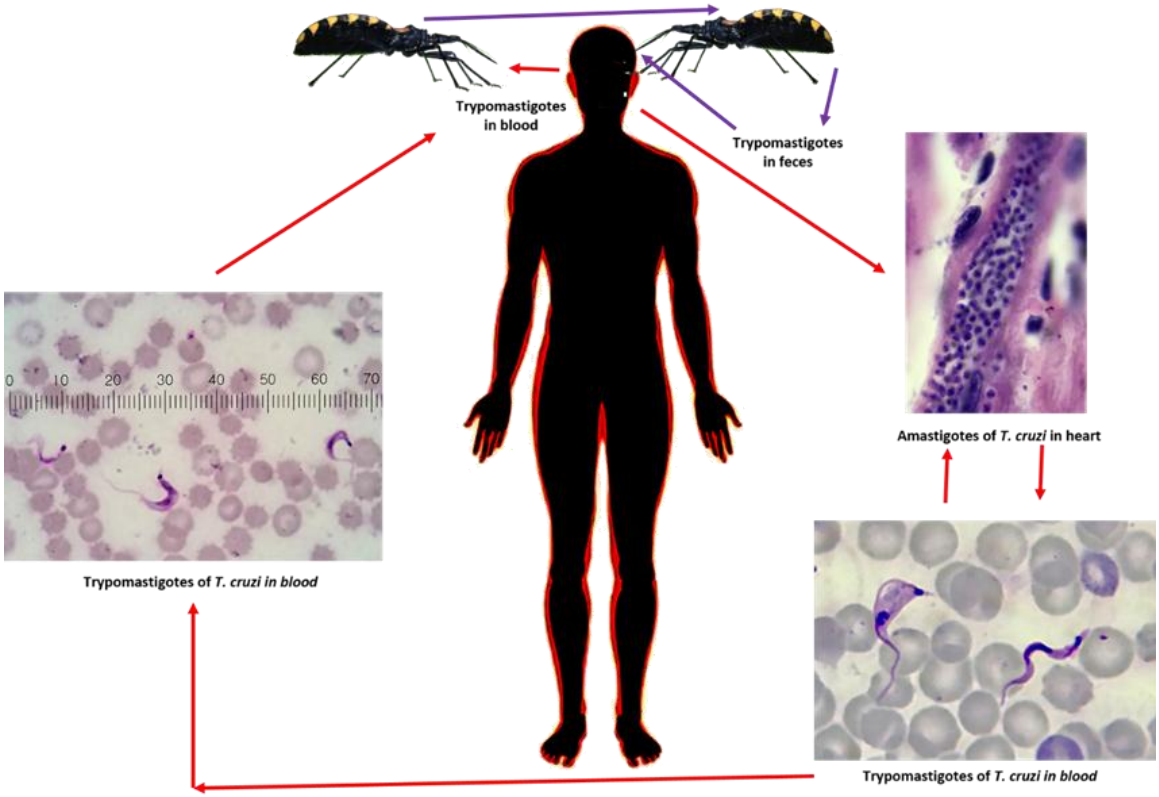

Fig. 3: *T. cruzi* life cycle in man (red arrows in man; purple arrows in vector) (Figure made by Carlos Ramón Bautista Garfias using photographs of Benjamín Nogueda Torres)

7. TREATMENT OF CHAGAS DISEASE

The parasitological treatment of Chagas disease is an unresolved issue. Currently, Benznidazole and Nifurtimox are the only two drugs that are available for the treatment of Chagas disease. There are factors that make the antiparasitic treatment of the disease unsatisfactory:
1. Very few patients receive antiparasitic treatment. Globally it is estimated that less than 1% of confirmed cases receive treatment (Arce-Vega et al. 2017).
2. The treatment is prolonged (up to 60 days), so treatment have toxic effects and induce parasitic resistance.
3. The curative efficacy of Benznidazole in the acute phase is 60 to 100% but in the chronic phase, it decreases to 8 to 20% (Reséndiz-Mora et al. 2022).

8. DISCUSSION

The first description of a wild reservoir was made by Carlos Chagas (1912) when he identified the parasite in the blood of an armadillo and in the faeces of a vector (Chagas 1912). Sometime later, it was shown that the wild cycle between reservoirs and triatomine insects with oral transmission is much more frequent than the presence of the parasite in humans and that the transition from the wild cycle to the peridomestic/domestic cycle is favoured by factors such as reservoir displacement due to the construction of new man houses, causing deforestation and increasing the probability of contact of the transmitters with man (Barretto and Ribeiro 1979). This observation is consistent with what happens today.

9. CONCLUSION

Governments in different countries of the American continent are aware of the importance of Chagas Disease in the region; however, the disease has not been controlled yet, so there is the need to carry out effective control measures. The improvement of new techniques for the diagnosis of Chagas disease and the advancement in the knowledge of its epidemiology should improve the control of the disease in the coming years. Climatic change must also be taken into account to control the infection.

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