Chapter 6

Eco-Epidemiology of Chagas Disease in Chile

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Additional information is available at the end of the chapter

http://dx.doi.org/10.5772/intechopen.74744

Abstract

There are four vector species of Chagas disease in Chile: *Triatoma infestans*, responsible for the domestic cycle; *Mepraia spinolai*, the main wild vector; and *M. gajardoi* and *M. parapatrica*, two coastal wild species whose importance as vectors is not well known. They are species of dry environments of the central-north region of Chile, whose best predictors of distribution are warm average temperatures and low rainfall. They are found in rock quarries, nests of birds, and small mammals, and *T. infestans* has sylvatic foci associated with a Bromeliaceae species. While human blood represents 70% of the diet of *T. infestans*, in *M. spinolai* this value is 7%, which means that a large part of Chagas disease in Chile is due to *T. infestans*. However, all species have high percentages of *T. cruzi* infection. Chagas disease in Chile follows the distribution of *T. infestans*, and although the cycle of domestic transmission by this vector is interrupted, there is still a constant prevalence and mortality and ascending incidences. Models predict that although climate change will not vary greatly the north-south distribution of vectors, it could increase the reproductive number of the disease, increasing risk areas of Chagas disease.

Keywords: Chagas disease, ecology, vectors, epidemiology, Chile

1. Introduction

American trypanosomiasis or Chagas disease is caused by the flagellated protozoan *Trypanosoma cruzi*, transmitted by several hematophagous insect species (Hemiptera, Reduviidae, and Triatominae) which in Chile are known as vinchucas. This protozoan species undergoes part of its development cycle (epimastigotes and trypomastigotes) in the insect vector, and when it ingests blood of a vertebrate host, the infectious trypomastigotes are eliminated with the

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dejections on the host; these are able to enter the bloodstream through the small wound or scratch lesions. Inside the *T. cruzi* continues its development with intracellular forms (amastigotes) and extracellular forms (trypomastigotes), producing damage which may be manifested in an acute form, although it generally does so after many years as a chronic form that compromises the digestive tract (megacolon or megaesophagus) and/or heart disease.

Two cycles of vector transmission in Chagas disease are described: (1) the domestic cycle maintained by domestic vectors, in Chile *Triatoma infestans*, which includes a man and an animal reservoir constituted by domestic and peridomestic animals such as cats, dogs, cows, horses, and others, and (2) the wild cycle maintained by wild vectors (such as *Mepraia spinolai*) and the wild animal reservoir composed of rodents, small marsupials, rabbits, etc. These cycles are not completely separated, since there are species that transit between the peridomestic and wild environments such as dogs, cats, goats, and other farm animals (**Figure 1**) [1–3]. In addition, wild vectors can penetrate into domestic environments and feed on humans [4], and domestic vectors can form wild colonies [5–7].

Its discovery is due to the Brazilian doctor Dr. Carlos R. J. Chagas, who in 1907 was the director of the Oswaldo Cruz Institute and director of the National Malaria Control Program. Dr. Chagas examined huts, finding a large number of insects that he named *Conorrhinus sanguessuga* (now *Panstrongylus megistus*) that contained "*Crithidia*." After experiments of inoculation

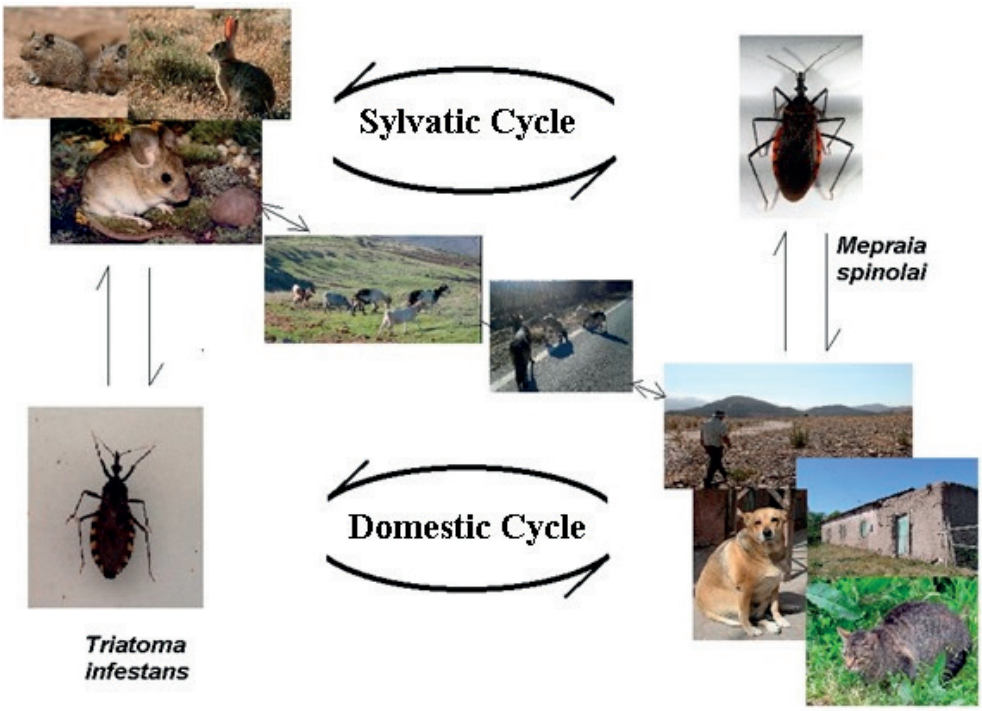

Figure 1. Domestic and wild cycles of Chagas disease.

in monkeys, he found a great quantity of flagellates, calling the new species *Shyzotrypanum cruzi* (today *Trypanosoma cruzi*) in honor of Dr. Oswaldo Cruz. Later, in 1909 he found a naturally infected cat and on April 14 found in the village of Santa Rita a 2-year-old girl named Berenice who lived in a house infested with *P. megistus* with a feverish condition and found in her blood the protozoan *T. cruzi*, describing the disease in 1909 [8]. Later, Carlos Chagas wrote about acute and chronic forms of the disease (1911) and the life cycle of *T. cruzi* (1931) [9], among other topics.

The first studies of Chagas disease in Chile were carried out by Dr. Juan Noé in 1921, with appreciation of *T. cruzi* in the vector *Triatoma infestans* around Santiago. Subsequently, the Argentine Dr. Salvador Massa, led by Noé, demonstrated the specificity of *T. cruzi* in cardiac fibers in experimental animals. With the creation of the Department of Parasitology of the State Health Office in 1937, systematic investigations led to the demonstration of the first case in Chile [10].

Knowledge of this disease has been progressively increasing in Chile thanks to the contribution of numerous researchers. Schenone, in 1980, [11] recognized three stages in the investigation of this disease. In the first stage, from 1937 to 1943, research focused on detecting the disease and tried to determine the endemic areas, detecting vector species and reservoirs. Important studies in this stage included those of Drs. G. Gasic, V. Bertín, *S. Massa*, and R. Gajardo Tobar. In the second stage, from 1944 to 1952, there was a more systematic study, determining the magnitude of the problem and conducting systematic surveys to determine the epidemiology better. The remarkable work of Dr. Amador Neghme was published in this period. The third stage can be established from 1953 to 1994 where there was a fruitful work of many researchers who have helped to clarify clinical aspects, congenital transmission, blood banks, epidemiology, distribution of endemic areas, the reservoir, natural history, ecology, physiology, and behavior of vectors. In this stage, the contributions of Drs. H. Schenone, W. Apt, and A. Atías and their teams stand out in epidemiological and clinical aspects. The fourth stage subsequent to 1995 had been added in which the investigation has focused more on specifying aspects not revealed in the previous periods and that has been marked by the acknowledgment of the interruption of the home transmission chain by *Triatoma infestans* which occurred in 1999. Research was focused mainly on laboratory and diagnostic improvement, on congenital and transfusion treatment and transmission, and on the study of the ecology of Chagas disease vectors and *T. cruzi*. There were important improvements in the detection of the disease, the control of blood banks and the success of domiciliary disinfestation carried out by the vector control area of the Ministry of Health. A negative effect of the declaration of the interruption of the vector transmission chain has been less interesting and resources for the study and control of this disease contributes to perpetuate it as an unattended disease.

2. Eco-epidemiology of vectors

Four species of insect vectors of Chagas disease have been described in Chile. The species responsible for the domestic cycle is *Triatoma infestans*, and the species involved in the wild cycle are *Mepraia spinolai* (**Figure 2**), *M. gajardoi*, and *M. parapatrica*.

Figure 2. *Triatoma infestans* and *Mepraia spinolai*, the main vectors of Chagas disease in Chile.

2.1. Distribution and niche

The vector *T. infestans*, a bug with characteristic yellow spots in the connexivum, has the widest distribution in Chile, between 18 and 34°S (**Figure 3**). It is found in domestic habitats, but foci of reproductive populations have also been detected in wild habitats [5–7]. In the domestic habitats, it is found in cracks of adobe walls or in "quincha" (wooden branches covered with mud), roofs of branches, and dwellings and chicken coops of the peridomiciliary zone. In sylvatic habitats it has been found forming colonies associated with plants of *Puya chilensis* (Bromeliaceae).

Mepraia spinolai is a wild species endemic to Chile with high polymorphism, with apterous females, and apterous, winged, and brachypterous males with red spots in the connexivum [12–14]. It is found between 26 and 34°S, from the sea level to 3000 m (**Figure 3**) [11]. Their habitat is made up of rocky areas such as quarries and cracks, bird nests, and animal caves [15] and sometimes peridomiciliary pens and walls and in human dwellings [16, 17].

Mepraia gajardoi is a coastal, wild species that lives between latitudes 18 and 26°S, feeding on small reptiles and mammals in the area. The males have generally blackish coloration with small reddish lateral spots in the dorsal part of connexivum. Male brachypterous and female micropterous.

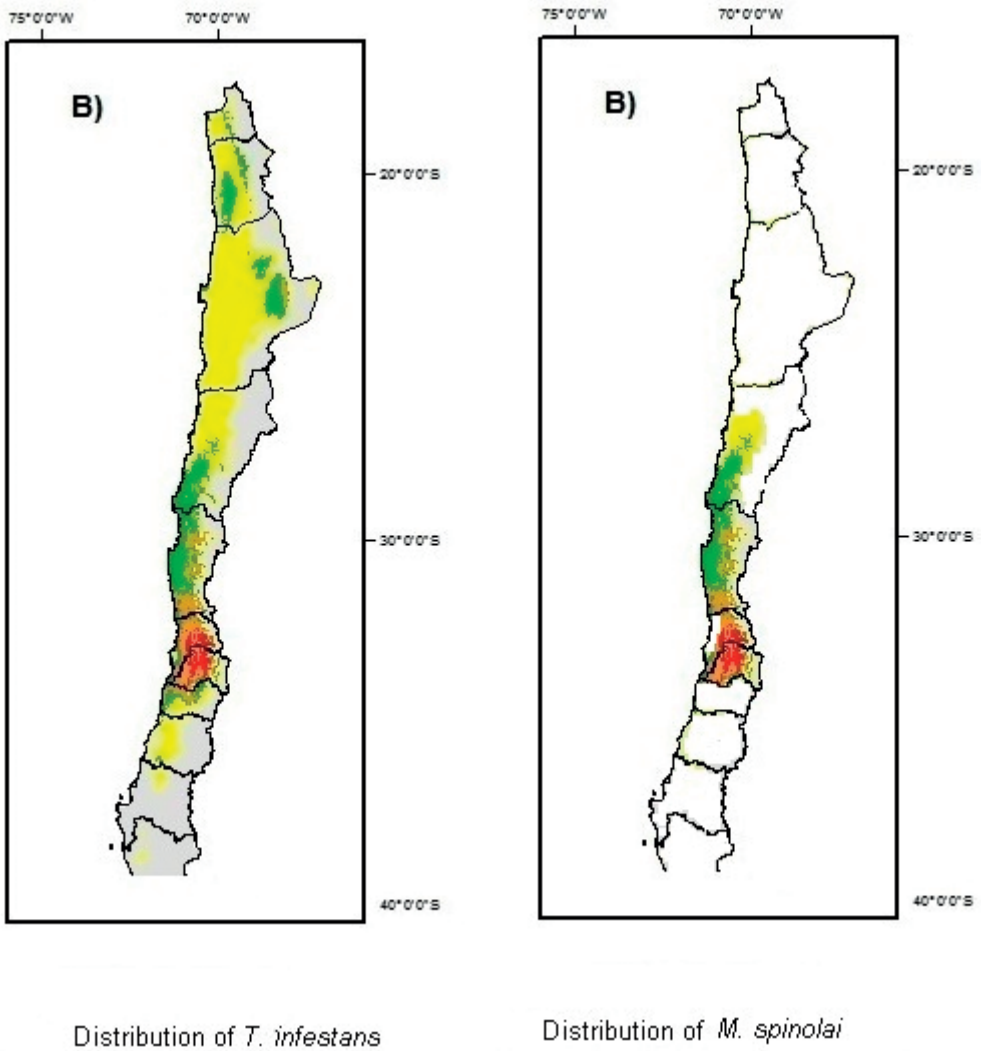

Figure 3. Approximate distribution of the two main vectors of Chagas disease (modified from [18] and [19]).

Mepraia parapatrica is a blackish species with red-orange spots in the connexivum, which only lives at 25°S. The females are micropterous, while the males are brachypterous and macropterous. It also lives on the coast, feeding on rodents and reptiles in the area.

Climate change predictions in Chile include an increase in temperature, with a gradient of higher to lower temperatures from north to south and from the Andes to the Pacific Ocean. During the 2011–2030 period, the temperature increase would be about 0.5°C in the southern

zone and 1.5°C for the north and the Chilean altiplano. A decrease in precipitation of 5–15% is expected during the same period. The distribution of *T. infestans* and Chagas disease is associated with maximum temperature and the precipitation during the driest month [18]; thus, the distribution of *T. infestans* would be little affected by climate change. This is consistent with the decrease in suitable areas proposed for *M. spinolai* in the same area and is in contrast to the high impact on the distribution of *M. gajardoi*, a species with a small distribution on the coast of northern Chile [19]. Under the assumption of niche conservatism, the latter species would suffer disappearance of its habitat, while *M. spinolai*, a species with distribution similar to *T. infestans* from 25°S southward and with similar preferred environmental conditions, would decrease its distribution area in the interior valleys while increasing its distribution on the coast [19]. Since *T. infestans* is a species residing in arid and semiarid habitats, its distribution area would not be affected significantly. However, the transmission risk of Chagas disease in this zone could be increased because of changes in metabolism, survival, reproduction, biting rates, or densities of the insects.

2.2. Ecology and population dynamics

There are very few attempts to estimate the population density of vectors. A useful measure is the so-called triatomine index used for domestic vectors such as *T. infestans*, which is defined as the number of insects captured by a person in a house in 1 hour. Schenone estimated in these species indices of 54.5 for the Antofagasta Region in 1980, 19.8 for the Atacama Region, 26.7 for the Coquimbo Region, 37.0 for Valparaíso Region, 50.5 for the Metropolitan Region, and 17.2 for the O'Higgins Region. Later, Canals et al. [20] estimated the densities of vinchucas per human in high endemic rural areas, calculating for these zones an average of 25.3 individuals/humans, with a maximum in the Coquimbo Region of 39.1 individuals/human. For the case of *M. spinolai*, the maximum triatomine index in peridomiciliary zones was 64 vinchucas/person/hour, and the estimated maximum density was 4.59 vinchucas/human [21]. The density per square meter has been estimated in this species between 15 and 364 vinchucas/m^2, with an average of 79 vinchucas/m^2 in areas of rock walls in Colina [22]. This species can be found in high densities [22–26], even in mixed colonies with *T. infestans*, and has been found in human habitations [14, 17, 27, 28]. For example, Schenone et al. [27] reported the presence of 288 specimens in 50 rural dwellings in regions III, IV, V, and Metropolitan. In this sense *M. spinolai* is a potentially dangerous species, especially in areas where the usual contact with humans occurs, as in quarry areas, and in some areas around Santiago where it is currently being urbanized, such as Colina, Lampa, and Til-Til. Also, from the perspective of its food sources, *M. spinolai* is in the phase of domiciliation [4, 29, 30], with 7.4% human blood in its diet [29, 31].

Another approximation to get an idea of the density can be obtained from the number of specimens referred to the Institute of Public Health of Chile; these come in greater proportion from the regions of Antofagasta, Atacama, Coquimbo, Valparaiso, and Metropolitan (Santiago). A recent study [32] reported that 8331 triatomines have been received between 2005 and 2016. A 73.7% correspond to *T. infestans*, 24.0% to *M. spinolai*, and 2.3% to *M. gajardoi*. Their numbers increased over this period. This high proportion of *T. infestans* could be explained because this

species, once eliminated from human habitations, has been able to recolonize wild habitats with several foci whose magnitude has not been completely clarified. From the first description of a wild focus in Chile in 2006 [5] in Calera de Tango, and in Til-Til, the new outbreaks in Sahondé, Putaendo [6] to the reports of wild foci in the cities of Valparaiso 2009, Atacama 2014, and Coquimbo 2015 [7].

The data reported by the Ministry of Health show the proportion of infested dwellings (home infestation) in 1999 and annual data since 2010 and divide the information into the percentage of colonized houses, that is, colonies with evidence of active reproduction, the individual visits to houses that receive adult individuals but without colonization, and the total (the sum of both). Household infestation has clearly decreased in this period, but the proportion of houses with individual visitors has increased. Currently, domiciliary infestation is estimated at 0.05% [32].

The vinchucas in Chile are long-lived species, surviving around 18 months in the laboratory [12, 13, 24, 33]. Their development is strongly affected by temperature and relative humidity like all triatomines [34]. The development of *T. infestans* completely ceases at temperatures below 16°C, and temperatures above 40°C are lethal [35]. The effect of relative humidity (RH) and its importance in molt periods has been discussed [36]. Combinations of variable ranges of low temperature and RH affect the maturation of *T. infestans* and *M. spinolai* (**Table 1**). While at constant temperature and humidity, the pre-imago period consisting of five nymph states (N1–N5) is 6.1 months in *T. infestans* [37]; this increases to 14.3 months in variable

	T. infestans	**EC**	***M. spinolai***	**EC**
Fecundity (eggs/female/week)	1.9	(15–32/40–90)	0.25	(28/70)
	1.0	(25/75)		
	5.4	(26/60)		
Egg viability (%)	74.6	(17/70)	27.7	(24/73)
	93.7	(24/73)		
Mortality rate (death/individual/day)	0.0083	(25/75)	0.0055	(24/73)
	0.0070	(15–32/40–90)		
Reproductive number (Ro)	1.36	(15–32/40–90)	22.9	(28/70)
	25.04	(26/60)		
Generation time (months)	14.7	(15–32/40–90)	13.2	(28/70)
	7.1	(26/60)		
Intrinsic rate of growth (r)	0.021	(15–32/40–90)	0.24	(28/70)
	0.45	(26/60)		

(EC: Temperature (°C)/Relative humidity (%)). References. Canals et al. [20].

Table 1. Some population parameters of *T. infestans* and *M. spinolai* in different environmental conditions.

environments [24, 38, 39]. In the main wild vector, *M. spinolai*, this period is between 9 and 10 months under constant conditions [12, 33], while in environments with RH and T variability, only nymphs are obtained up to N5 status. With greater restriction at low temperature and humidity, they only reach the N2 status in 12 months [24]. The arrest of secondary development in unfavorable conditions (induced diapause) has been observed in both species [24, 33, 40]. Also, some parameters like the net reproductive rate (R_0) are strongly affected. Both species present survival curves with exponential decays and similar mortality rates [24, 28, 33, 41]. The mortality and fertility rates in *T. infestans* present periodic variations during the year even under relatively constant environmental conditions. For example, under laboratory conditions the mean fecundity of *T. infestans* varied from 0.39 eggs/female/week in autumn to 1.63 eggs/female/week in spring, with maximum values of 7.59 eggs/female/week in spring and 5.83 eggs/female/week in summer. Maximum mean mortality and fertility rates were in spring and summer [42].

2.3. Ecophysiology and behavior

Triatoma infestans is a diurnal insect, while all species of the genus *Mepraia* are diurnal. In the laboratory *M. spinolai* moves between 15 and 42°C with a preferred temperature of 24.8°C [43]. *T. infestans* moves between 18 and 42°C with a preferred temperature of 24.2°C [43]. Other authors have found that *T. infestans* preferred temperatures between 26 and 27°C [44] and variations from 28 to 29°C at the beginning of the night, immediately after the ingestion of blood, but 25°C 12 days later [45, 46]. The synchronization of activity patterns to the L/D cycle is similar to other triatomines [47–51]. Other activities synchronous to the L/D cycles are the rhythms of oviposition [52], molt [53], hatching [46], and aggregation [54]. The stimulus for orientation and approach to a potential prey is temperature, displaying the classic pattern of antennal movements-locomotor movement and extension of the proboscis [55, 56]. *T. infestans* decreases the frequency of antennal movements when it is within 30 to 15 cm of its prey, whereas *M. spinolai* always maintains a low frequency, which may be due to a greater distance of perception in this species [57]. Once in contact with its prey, *T. infestans* introduces its proboscis, sucking blood, being able to increase its weight from four to six times in a single ingestion [38, 39, 57]. The volume of blood ingested is estimated between 30 and 70 ml when fed on a species such as *Mesocricetus auratus* [58]. The bite frequency in *T. infestans* has been estimated at 0.0754 bites/day [21]. The bite frequency of *M. spinolai* has been estimated at 0.155 bites/day, with volumes of blood ingestion between 20 and 160 mg. The intake volume has been found to be inversely correlated with the weight prior to intake, which is an indicator of nutritional status. Thus, the volume of the intake is related to the time elapsed since the last feeding and to the degree of distension of the abdomen [59].

T. infestans emits its dejections during the feeding act [60], which takes on average 19.5 min [38, 39, 57], usually between 3 and 4 min from the start of feeding, while in *M. spinolai* this latency is 24.4 min and not necessarily on the prey, which decreases the probability of transmission [38, 39, 57]. The bite rate and the latency between the start of the bite and the dejection are affected by the presence of the *T. cruzi* parasite in the vector; *M. spinolai* showed a higher frequency of bite and a lower latency of dejection in infected individuals [59].

The feeding spectrum of *T. infestans* in Chile was obtained by means of ag-ac reactions and double gel diffusion [60]. The diet of this species is made up of humans 68.4%, cats 6.1%, dogs 3.2%, rabbits 5.9%, rodents 1.6%, Artiodactyla 0.3%, birds 7.2%, and amphibians 0.5%. The proportions for *M. spinolai* are humans 7.4%, cats 3.7%, dogs 12.3%, rabbits 53.1%, rodents 9.9%, Artiodactyla 12.3%, and birds 1.2% [29]. The amplitude of the trophic niche of *M. spinolai* is greater than that of *T. infestans*, and they have a niche overlap of 0.229 [29]. An increase in the amplitude of the niche in times of greater heat has also been demonstrated [29]. Introducing the information of the food profile of 15 species of triatomines with multivariate analysis techniques has shown a clear separation between species of domiciliary habits and peridomiciliary, wild, and stenophagous specialists; *M. spinolai* is among the peridomiciliary species [4]. In a later study, this species was located between wild and peridomiciliary [30].

The average percentages of *T. cruzi* infection in the vectors (trypano-triatomine indices) are *M. gajardoi* 16.92 ± 17.77%, *M. spinolai* 20.88 ± 11.51%, and *T. infestans* 41.83 ± 13.23% [32]. The trypano-triatomine indices of *M. gajardoi* have remained stable over time, although based on a small number of individuals. The same occurs with the *M. spinolai* indices, but *T. infestans* shows an increasing trend.

The high trypano-triatomine indices in *T. infestans* are interesting, since a decrease of these indices was expected once these insects were removed from human habitats. Thus, for example, in Uruguay, the indices were drastically reduced as a result of vector control actions [61]. An explanation for the lack of a decline in these indices in Chile could be that despite the change in diet that involves the elimination of the human environment, *T. infestans* can find rodents and other species with high infection rates that make high trypano-triatomine indices persist. This may be true, since there is a great diversity of infected wild, domestic, and peridomestic mammals, some reaching levels of infection higher than 10% [15, 62], but this is also probably true in Uruguay.

3. *Trypanosoma cruzi* lineages

Lineages of *T. cruzi* have been recognized for a long time. Initially, isoenzymes that differ in gel electrophoresis were classified as zymodemes Z1 and Z2, the first one mainly associated with the wild cycle and the second one with the domestic cycle [63]. Subsequently, biochemical and genetic differentiation was carried out, and two lineages, TcI corresponding to Z1 and TcII corresponding to Z2, were proposed. However, the first TcII was divided into five subgroups a, b, c, d, and e, where TcIIb corresponded to Z2, TcIIa to the new zymodeme Z3 and TcIIc, and d and e to hybrids [64]. Subsequently, subgroups were also recognized in TcI: a, b, c, and d [63, 65]. Currently, it has been simplified into six subgroups, from TcI to TcVI, where TcI corresponds to Z1, TcII to TcIIb (Z2), TcIII to TcIIc, TcIV to TcIIa (Z3), TcV to TcIId, and TcVI to TcIIe.

Only TcII and TcVI have been found in *M. gajardoi* in Chile [66, 67], TcI and TcII in *M. spinolai* [66] and subsequently TcI, TcII, TcV, and TcVI [68], while in *T. infestans*, the most important

lineage is TcI circulating in wild (93.3%) and domiciliary (100%) individuals. TcII, TcV, and TcVI have also been detected mainly in nymphs, suggesting differential adaptation of *T. cruzi* lineages between nymph states [69].

It has been proposed that in small wild mammals TcI and TcII would be associated with marsupials and placental mammals, respectively. However, the TcI, TcII, TcV, and TcVI lineages have been detected in the rodent *Octodon degus* in Chile [26, 70]. The same lineages have been detected in wild *Oryctolagus cuniculus* [71], and in 117 individuals of different infected species, TcI, TcII (TcIIb), TcV (TcIId), and TcVI (TcIIe) have been detected with frequencies of 38, 41, 26 and 9%, respectively, in wild mammals. In peridomestic mammals the frequencies of these lineages were 29, 33, 43, and 14%, respectively. More than one lineage was found in 31% of the individuals analyzed, without specific association with marsupials [72, 73]. Thus, it seems that the information on the wild mammal reservoir and the vectors *T. infestans* and *M. spinolai* is quite consistent in pointing to TcI, TcII, TcV, and TcVI as the main circulating lineages, although more studies are still missing in the other wild vectors of the genus *Mepraia*.

4. Reservoir

The animal reservoir is very extensive; it is constituted by mammals of the peridomestic environment such as dogs, cats, goats, rabbits, sheep, horses, donkeys, and cattle, some carnivores, numerous rodents, and some small marsupials. Infection in mammals by *T. cruzi* has been described in around 150 species in America [74] and is widespread in numerous orders; the most important reservoirs are dogs, cats, and goats, due both to high infection rates and to their mobility which establishes a bridge between domestic and wild cycles. Proportions of infection by *T. cruzi* have been reported 14.5% in dogs, 10.7% in cats, 9.4% in goats, 12.1% in rabbits, and 4.8% in sheep [75]. Current studies with PCR in wild mammals have reported percentages of infection between 26 and 59% in the species *Capra hircus* (goat), *Thylamys elegans* (marsupial), *O. degus*, *Phyllotis darwini*, and *Abrothrix olivaceus* (rodents) [72] and large increases in interannual infection rates from 300–400%, which could be explained by a delayed response to the El Niño weather phenomenon after the emergence of small rodents [25].

5. Distribution of the disease

Chagas disease extends in America from the Southern United States at parallel 35°N to southern South America at parallel 34°S on the Chilean side and 45°S on the Argentine side. In this zone, 21 countries report active transmission, with current prevalence very difficult to assess since most of the studies refer to the prevalence in endemic rural areas [15]. The median prevalence in these areas is approximately 8.15%. The lower extreme values probably represent Chagas disease in controlled or urban areas and the maximum Chagas disease prevalence in hyperendemic areas without protection of health systems. Currently, emergence of Chagas disease in Europe has been reported through immigrants and subsequent congenital

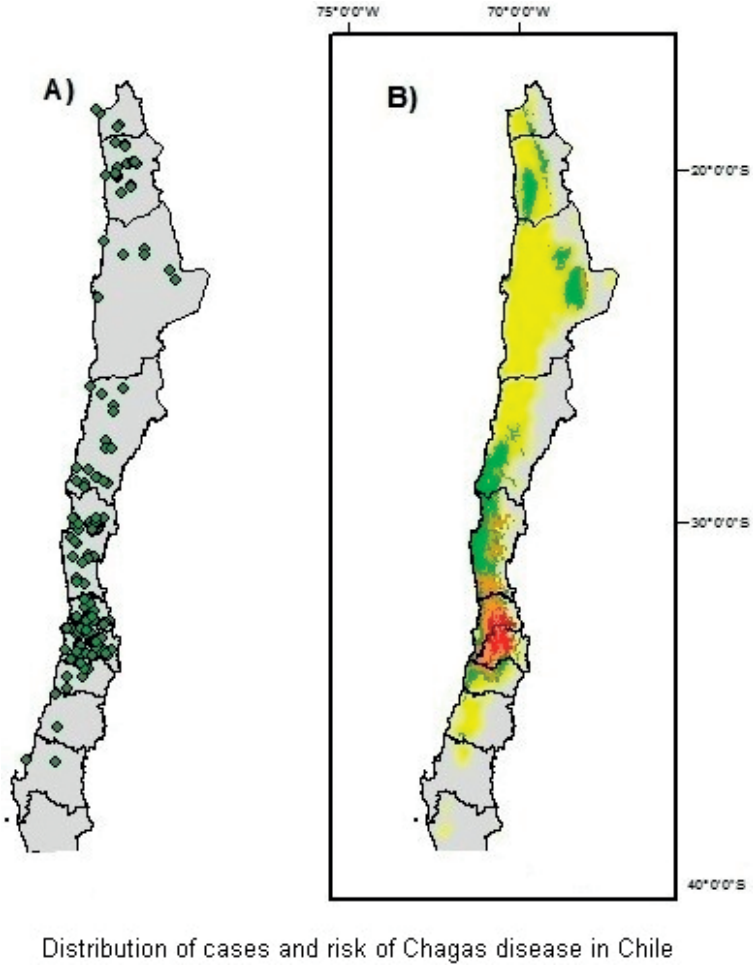

Figure 4. Distribution of cases and the risk of Chagas disease in Chile (modified from [18]).

transmission. For example, Basile et al. [76] reported more than 4000 cases diagnosed in different countries, with the highest number of cases in Spain, but Strasen et al. [77] proposed around 95% underreporting. These latter authors indicated that there could be between 14,000 and 180,000 cases in this continent.

In Chile, Chagas disease is distributed between the Arica and Parinacota Region (18°30′S) and the O′Higgins Region (34°36′S) (**Figure 4**), coinciding in large part with the distribution of the vector domestic *T. infestans* [18]. The highest incidence rates are recorded between Antofagasta and Coquimbo, with Antofagasta, Coquimbo, and Metropolitan Regions concentrating approximately two-thirds of the reported cases (**Table 2**).

Administrative region	Cases	Incidence rate (cases × 10^{-5})
Arica and Parinacota	57	23.8
Tarapacá	64	19.0
Antofagasta	223	35.8
Atacama	67	21.4
Coquimbo	292	37.9
Valparaiso	210	11.5
Metropolitan	313	4.3
O'Higgins	20	2.2
Maule	2	0.2
Bío Bío	11	0.5
Araucanía	1	0.1
Los Ríos	2	0.5
Los Lagos	0	0.0
Aisén	0	0.0
Magallanes	0	0.0
Total country	**1262**	**7.0**

Table 2. Cases and incidence rates of Chagas disease in Chile (2015) (health ministry).

6. Prevalence and incidence

Chagas disease is one of the main neglected diseases that affects the Americas and has now become an emerging disease in some parts of America and Europe [78–81], which has even been compared to the early stage of the HIV/AIDS epidemic [79]. The annual incidence varies between 28,000 and 56,000 people and between 10,000 and 14,000 deaths per year [79], affecting 6–11 million individuals [82] with 65–100 million people at risk in the world [78–80, 83]. The population at risk in Chile is 873,415 people [80, 81]. The latest national health survey (ENS) reports a prevalence of *T. cruzi* infection of 0.7% of the population, with a prevalence of 1.5% in rural areas and 0.6% in urban areas [81], and ministerial reports indicate that home infestation by *T. infestans* is practically nonexistent [80], which contrasts sharply with the data reported in the 1980s and 1990s. For example, between 1937 and 1980, a general prevalence of 16.7% was reported in endemic areas, with a maximum of 43.6% in the Coquimbo Region [11], which did not vary significantly between 1982 and 1985 [84], whereas between 1982 and1989 differences were already reported between rural areas with prevalence of 16.7% and urban areas with prevalence of 1.9% [16]. The same occurs with domiciliary infestation, in which previous reports indicated infestations between 26.8 and 33.2% of dwellings in endemic areas between Arica and the O'Higgins Regions [11, 80].

A study covering 60 years of the disease in Chile of patients referred to the University of Chile and studied through xenodiagnosis revealed an average prevalence of 9.35 ± 0.1% [32]. This prevalence value of 9.35% should be considered as the level for highly endemic zones. It is in the range between 8 and 12% reported by Apt and Reyes in 1986, also based on xenodiagnosis,

and is similar to the estimated value for Latin America. This value does not present any variation in the 65 years of study, regardless of the changes in the health systems or interruption of the chain of transmission. Accurate estimation of the prevalence of Chagas disease is a difficult task since it depends not only on the sampling characteristics (random, stratified, etc.), sample size, and bias but also on the screening method used, which in the case of Chagas disease can be by xenodiagnosis, ELISA, immunofluorescence, and/or Western blot.

The values reported by the 2009–2010 ENS based on 4650 volunteers using IgG ELISA show 0.7% average prevalence, with 1.5% in the rural population and 0.6% in the urban population. These values are surprisingly similar to those reported for the urban population in 1982–1989 [85]. In this sense, the prevalence shows an evolution toward the values of an urbanized population.

The incidence in Chile shows a progressive rise from 1985 onward (**Figure 5**), without a slope change attributable to the interruption of the vector transmission chain. On the other hand, there is no appreciable effect attributable to the improvement in detection. For example, supreme decree 158 of 2004 in Chile declares Chagas disease as a notifiable disease, which is not reflected in the trend curve; later in 2008 circular four instructs blood banks to investigate the presence of *T cruzi*; law 1839 of 2009 stipulates the national policy of blood services; and in 2011 in circular B51, number 17 stipulates the surveillance of Chagas disease and establishes ways to record and inform the health authority [80, 81]. The incidence before 2009 had an average value of 2.7 ± 1.29 per 100,000 inhabitants, whereas after 2009 the average is 7.3 ± 2.02

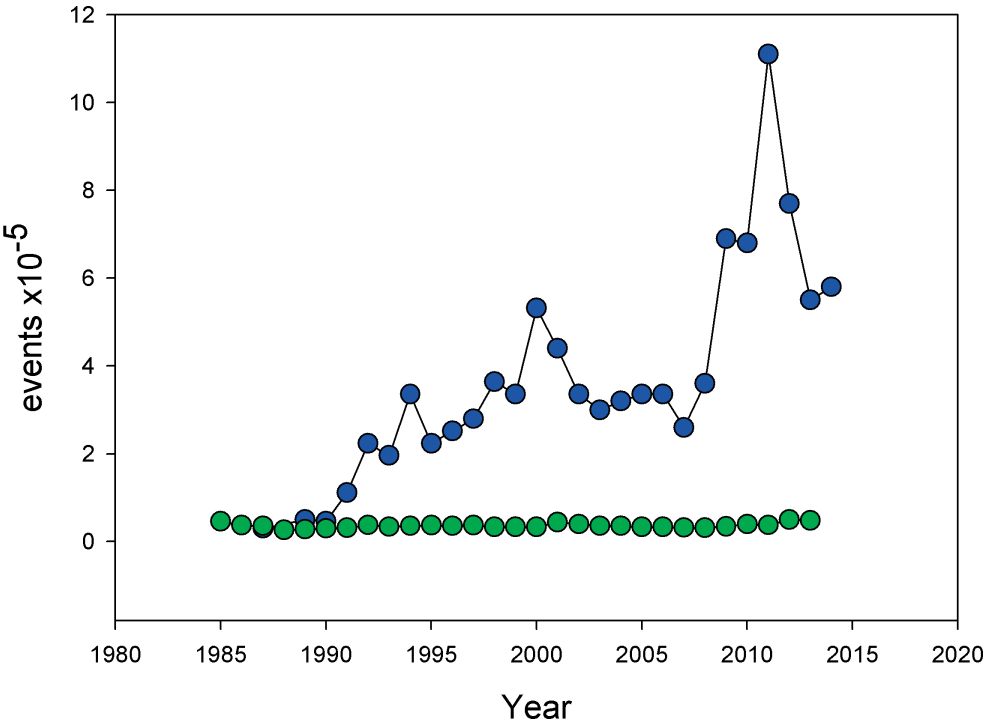

Figure 5. Incidence (blue) and mortality rates (green) of Chagas disease in Chile (Health Ministry).

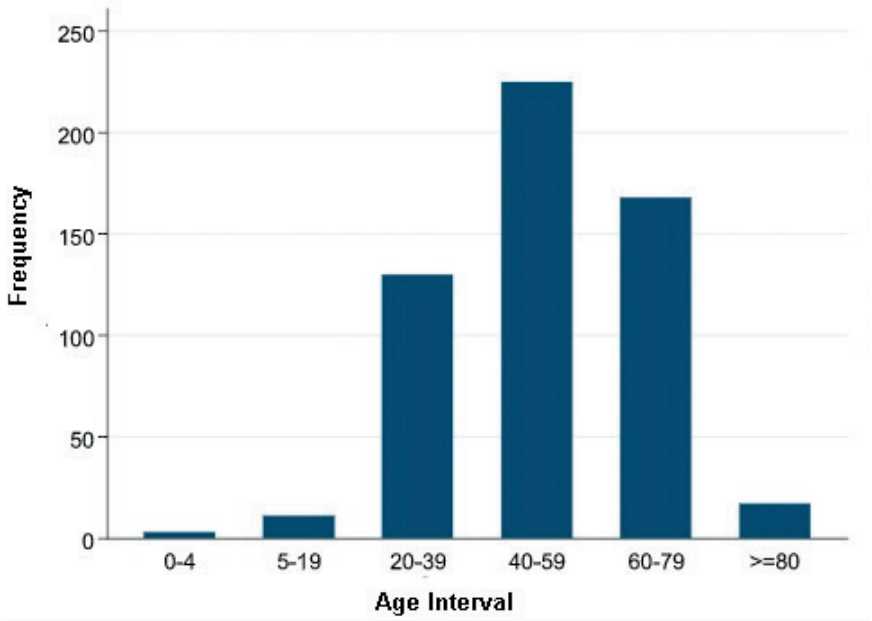

Figure 6. Age distribution of Chagas disease in 2010 (Health inistry).

per 100,000 inhabitants [32], staying relatively stable. One explanation for this temporal dynamics is that the progressive increase was not explained by a particular milestone but by a progressive improvement in the notification attributable to better staff preparation and a better notification system. Another possibility that cannot be ruled out is that this increase is real, and in this case, it should have an impact on mortality rates in the long run, a fact that is not yet evident. If the relative stability detected since 2009 persists, it would indicate that it would be reaching an adequate estimation of the endemic equilibrium, as the models predict [23, 86].

Mortality shows stability over the years (**Figure 5**). The average mortality rate is 0.36 ± 0.55 per 100,000 inhabitants [32]. Chagas disease affects the entire population in Chile, especially people of working age, with the highest rates between 30 and 65 years of age (**Figure 6**) [81].

7. Transfusion and congenital Chagas disease

The seroprevalence of *T. cruzi* in blood donors has been studied in Chile since the 1960s, with a national average of 3.7% reported between 1962 and 1988 [15]. Subsequently, this value has decreased; it was estimated between 0.5 and 1.6% according to information from the ISP between 2000 and 2005, estimated with the ELISA IgG method, and confirmed with IFI [87]. Currently, the seroprevalence of *T. cruzi* in blood donors is estimated at approximately 0.6%. The latest studies in the blood bank of the Clinical Hospital of the University of Chile were 0.4% positive out of a total of 24,568 [87].

A meta-analytic study that considered 13 case studies and 51 observational studies in ten countries estimated the rate of congenital infection was 4.7% with a CI of 3.4–5.7%. This means that in a population of mothers infected with *T. cruzi*, 4.7% of newborns are congenitally infected [88]. In this study it is proposed that in endemic areas the rate is 5% in endemic countries but lower in non-endemic countries (2.7%) and proposes a rate of 2.5% for Chile. In the same year, in a study conducted in Choapa, a highly endemic area, this rate was estimated at 4.7% [89].

8. The reproductive number (R_0)

The transmission of Chagas disease depends mainly on vector and congenital transmission. Accidental and transfusion transmissions are very rare and oral transmission only occurs in particular areas where the contact between man and nature is very close. The reproductive number of an infectious disease (R_0) corresponds to the average number of secondary infections produced by an infected individual. Thus, if R_0 is greater than 1, the disease is established in the population, and if R_0 is less than 1, the disease disappears. In the case of Chagas disease, the main component of the reproductive number is given by vector transmission, and when this is cut off, congenital transmission alone is incapable of perpetuating the disease [86, 90]. There are very few attempts to estimate the R_0 of this disease, an exception being the study by Massad [91], who estimated it at $R_0 = 1.25$ for a region of Brazil. Other estimates based on plausible approximations of many parameters obtained values of $R_0 = 7$ in Colombia [92] and $R_0 = 2.86$ [23] and $R_0 = 1.52$ in Chile [86]. However, recently in a spatial approach, a median value of $R_0 = 1.02$ has been proposed, with an approximate spatial variability between 0 and 5. The reproductive number could vary in different climate change scenarios as consequence of changes in entomological parameters such as biting rate, density, and mortality rate, increasing the Chagas risk area between 13 and 18% [93].

9. Conclusion and the way forward

Chile is in a privileged situation. It has only one domestic vector and probably only one wild vector of epidemiological importance, and the chain of domestic vector transmission by *T. infestans* is cut off. The wild reservoir is made up of small rodents, and the circulating lineages of *T. cruzi* are similar to the rest of America. However, there are some problems that persist: (1) The peri-anthropic reservoir is diverse and has bridging animals between the wild and domestic cycles that facilitate the spread of Chagas disease, such as dogs and goats; (2) housing and education conditions in Northern Chile are limited; (3) there are no control or education campaigns on wild vectors, and human dwellings are built on their territory. In addition there are wild foci of *T. infestans* and vector home intrusion; (4) prevalence, incidence, and trypano-triatomine indices still do not decrease; and (5) climate could change the epidemiological situation.

Given the obvious opportunity to eradicate Chagas disease in two generations, as predicted by the models, the way forward should be focused on (1) strengthening education campaigns of the population; (2) strengthening the monitoring of housing and peridomestic animals; (3) detection, study, and control of wild foci; and (4) reinforcing the study of the effect of climate change on the epidemiology of Chagas disease.

Acknowledgements

The authors acknowledge the financial support of Fondecyt (1150514 to MCL) and the revision of English language to Lafayette Eaton.

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