Epidemiology, control and surveillance of Chagas disease - 100 years after its discovery

José Rodrigues Coura[1]/+, João Carlos Pinto Dias[2]

[1]Laboratório de Doenças Parasitárias, Instituto Oswaldo Cruz-Fiocruz, Av. Brasil 4365, 21040-360 Rio de Janeiro, RJ, Brasil
[2]Instituto de Pesquisas René Rachou-Fiocruz, Belo Horizonte, MG, Brasil

Chagas disease originated millions of years ago as an enzootic infection of wild animals and began to be transmitted to humans as an anthropozoonosis when man invaded wild ecotopes. While evidence of human infection has been found in mummies up to 9,000 years old, endemic Chagas disease became established as a zoonosis only in the last 200-300 years, as triatomines adapted to domestic environments. It is estimated that 15-16 million people are infected with Trypanosoma cruzi *in Latin America, and 75-90 million are exposed to infection. Control of Chagas disease must be undertaken by interrupting its transmission by vectors and blood transfusions, improving housing and areas surrounding dwellings, providing sanitation education for exposed populations and treating acute and recently infected chronic cases. These measures should be complemented by surveillance and primary, secondary and tertiary care.*

Key words: Chagas disease - epidemiology - control and surveillance

Since Carlos Chagas discovered American trypanosomiasis in 1909, a disease that subsequently received his name, knowledge about the epidemiology of the disease and its control has evolved in three well-defined phases: the discovery phase, the phase of knowledge dissemination and the phase of applying this knowledge to the control and surveillance of human infection. The discovery phase corresponds Chagas's pioneering studies of *Trypanosoma cruzi* in *Conorhinus megistus* (*Panstrongylus megistus*) and in experimentally infected laboratory animals and his description of the first acute cases of the disease (Chagas 1909, 1911).

In 1912, Chagas discovered that the armadillo (*Dasypus novencinctus*) is a wild reservoir for *T. cruzi*. Concomitantly, in the same ecotope, he found *Triatoma geniculata* (*Pantrongylus geniculatus*) infected with the parasite, thereby defining the wild cycle of Chagas disease. This was subsequently complemented (Chagas 1924) with the description of *T. cruzi* among naturally infected monkeys in Pará (PA). The clinical, anatomopathological and pathogenic descriptions of the acute form by Chagas (1916), along with those of the chronic form by Chagas and Villela (1922), added further to knowledge of the disease. The following other studies during the discovery phase should also be highlighted: Arthur Neiva (1910), on the biology of "Conorhinus", Gaspar Vianna (1911) and Magarinos Torres (1917), on the pathology of the disease, Brumpt (1912a, b, 1914), on the biology of *T. cruzi* in vectors, its penetration through the ocular mucosa and xenodiagnosis, Guerreiro and Machado (1913), on the serology of the Bordet and Gengou reaction (complement fixation), Evandro Chagas (1930, 1932), on the cardiac form, including electrocardiographic studies, and, finally, Emmanuel Dias (1933, 1934), on infection by *Schizotryponum cruzi* in vertebrates and invertebrates, thereby completing the studies on the parasite, its vectors, its reservoirs and human infection.

Carlos Chagas publicised his discoveries in speeches in Brazil and abroad, and in various papers published in Portuguese, Spanish, English, French and German, including his first one (Über eine neue trypanosomiasis des Menschen) in the latter language. Nonetheless, according to the collection organised by Prata (1981), the dissemination of knowledge about Chagas disease and its expansion to other countries began in the 1930s. It was then that Salvador Mazza set up a study group for regional pathology (MEPRA) in Argentina, publishing numerous studies with descriptions of many acute cases of the disease (Mazza 1937), including in the region where Kraus had denied its existence. Many epidemiological and clinical aspects of the endemic area of Argentina were studied, such as the geographical distribution of the disease and its manifestations in the acute phase, including those of the ophthalmic-ganglionic complex (Romaña 1935) and of "Schizotrypanides" (Mazza 1941). The 9th meeting of the Society of Regional Pathology of Argentina was organised by Mazza, in 1935, in the city of Jujuy, as a tribute to Carlos Chagas, who had died the previous year. At this meeting, Evandro Chagas, Emmanuel Dias and Magarinos Torres, the representatives from Brazil, proposed the name "Romana's Sign" for the ophthalmic complex, which was of great value for recognition of the acute phase of the disease in other countries within the continent.

From the mid-1940s onwards, three underlying events stimulated interest in studying and renewing the knowledge of Chagas disease in Brazil: (i) the creation of the Oswaldo Cruz Institute's "Prophylaxis and Study

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+ Corresponding author: coura@ioc.fiocruz.br
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Centre" for Chagas disease in Bambuí, in the midst of the endemic area of Minas Gerais (MG), which was placed in the hands of the dynamic leadership of Emmanuel Dias; (ii) the creation of Medical Schools in Ribeirão Preto, Goiânia, Uberaba and Uberlândia, within the endemic triangle of the disease, in the states of São Paulo (SP), Goiás (GO) and MG, and especially the scientific influence of the School in Ribeirão Preto; (iii) International Congress commemorating the 50th anniversary of the discovery of Chagas disease, which was held at the Oswaldo Cruz Institute, in Rio de Janeiro, in 1959, under the organization of Carlos Chagas Filho, from which five volumes of studies totalling 1,886 pages were published.

The research centre in Bambuí, created in 1943, was a major source for spreading knowledge of not only the epidemiology and prophylaxis of Chagas disease, but also of Chagas cardiopathy, which was the subject of an excellent study by Laranja et al. (1956) in *Circulation*.

The new, modern Medical School in Ribeirão Preto, in the interior of the State of SP, brought together a notable group of researchers on Chagas disease. This group created an epidemiological and vector control model in Cássia dos Coqueiros (Freitas 1946, Freitas et al. 1959), started a new line of ecological studies on reservoirs and vectors (Barretto 1964, 1967) and developed original serological techniques (Almeida et al. 1959). The group also conducted novel clinical and epidemiological studies (Ramos et al. 1949) and pathogenetic and pathological studies (Köberle 1957, 1959) on Chagas disease.

In GO, the studies by Rassi et al. (1956, 1958) on the chronic and acute cardiac forms, and by Rezende (1956, 1959) on the digestive form, led to the creation of a vigorous group. In Bahia, Andrade (1956, 1958, 1959) and Prata (1959) opened original fields of study on the pathology and prognosis of chronic Chagas cardiopathy.

The International Congress on Chagas disease, held in Rio de Janeiro in 1959 with more than 500 participants from various countries around the world, opened up new avenues for developing research on Chagas disease internationally over the ensuing decades.

Also in 1959, a major advance in diagnosing Chagas disease was achieved through the technical application of immunofluorescence by Fife and Muschel (1959) and Camargo (1966), in research on antibodies against *T. cruzi*. With regard to clinical diagnosis, the study by Rezende et al. (1960) stood out, providing proof of contrast retention in megaesophagus evaluations.

In the 1960s, several studies on the immunological, morphological, pathogenic and therapeutic aspects of *T. cruzi* marked the evolution of these fields. At the beginning of that decade, Brener (1961) demonstrated for the first time that a parasitological cure for experimental Chagas disease was possible. This finding opened up new prospects for treating the acute phase of the disease and stimulated studies in the field of specific therapy. Coura and Silva 1961 and Coura et al. 1962 reviewed the problem of specific therapy among human beings and applied nitrofurazone to chronic cases of human Chagas disease for the first time.

Nussenzweig et al. (1962, 1963) found antigenic differences in strains of *T. cruzi* isolated from humans, bats, triatomines, *Didelphis* and wild rodents and classified them into at least three immunological types. During this same period, analysis of seven samples of *T. cruzi* from different origins allowed Brener and Chiari (1963) to group them into three morphological patterns, according to the width of the predominant forms (thin, wide and very wide or "stout" forms), previously described by Chagas (1909) as sexual dimorphism. However, Deane et al. (1963) did not find pathogenic differences regarding the morphology and origin of the strains of *T. cruzi* in wild animals. Subsequently, Brener (1965) correlated some of these morphological variations with the phases of the infection, which had already been observed by Silva (1959). Hoare (1964, 1972) carried out an important morphological and taxonomic review of trypanosomes in mammals and placed *T. cruzi* in the *Stercoraria* group, subgenus *Schizotripanum*.

T. cruzi exhibits morphological, immunological and pathogenic diversity, depending on the host and other as yet undetermined factors, as well as regional and individual variations of the human disease and of the natural and experimental infection. Consequently, Coura (1965) and Coura et al. (1966) proposed the name "cruzi complex*"* for this etiopathogenic combination.

The 1970s and 1980s were marked by a series of advances in knowledge about the disease, especially within the fields of the immunology and immunopathology of Chagas disease and of the biochemistry, ultrastructure and interaction of *T. cruzi* with host cells. These advances were synthesised by Brener (1973, 1980) with excellent reviews on the biology and immunology of the parasite. A complete survey on Chagas disease, from the parasite to prophylaxis, was carried out by 16 Brazilian authors and published as a book entitled "*Trypanosoma cruzi* and Chagas disease", edited by Brener and Andrade (1979).

In Brazil, annual meetings were organised in Caxambu, beginning in 1974, and annual meetings were held in Araxá, from 1984 onwards (subsequently transferred to Uberaba). These conferences reviewed the basic and applied research on Chagas disease and the results of these reviews were published each year, respectively, in the journals *Memórias do Instituto Oswaldo Cruz* and Revista da Sociedade Brasileira de Medicina Tropical. In addition, starting in 1974, special programs for supporting research on Chagas disease were established by the Brazilian National Research Council (PIDE-CNPq) and the Tropical Disease Research Program of the World Health Organization, created a specific section for supporting research on trypanosomiasis/Chagas disease.

In 1948, Dias and Pelegrino demonstrated that gamexane was able to control domesticated vectors of Chagas infection in areas of MG, in Águas Cumpridas. Subsequently, in Bambuí, Dias (1945, 1957) demonstrated the need for at least two sprayings with BHC, separated by an interval of 30-60 days, for the eradication of *Triatoma infestans*. This finding was corroborated by Freitas et al. (1959) in Cássia dos Coqueiros, SP, and, as a result, the basis for controlling vector transmission

of Chagas infection was established. These experiments were initially extended by the National Malaria Service and then, starting in 1956, were conducted on a large scale by the Department of Rural Endemic Diseases, which was created that year. However, the actions were sporadic and restricted to small areas, due to the priority given to malaria control at that time. It was only in 1983 that Chagas disease control was established in Brazil in a regular and continuous manner, and this was extended to other countries through the creation of the "Initiatives" of the Southern Cone, in 1991, of the Andean countries, in 1997, of Central America and Mexico, in 1998, and of the Amazon countries, in 2004. More recently, an initiative among non-endemic countries was created, in response to the intense migration of patients from endemic countries to non-endemic ones.

Epidemiology of Chagas disease

The geographical distribution of Chagas infection, including its reservoirs and its vectors, extends from the Southern United States to Southern Argentina and Chile. Thus, it covers all of the Americas, and 90 million people in this region are exposed to infection. It is currently estimated that 15 million people present *T. cruzi* infection or carry the disease. Fig. 1 shows the distribution of Chagas infection in the Americas, emphasising the endemic and anthropozoonotic zones of Brazil.

More than 130 species have been found to be potential *T. cruzi* vectors. In Brazil, 52 species of triatomines have been described, but five have particular epidemiological importance because they are domesticated: *T. infestans, P. megistus, T. brasiliensis, T. pseudomaculata and T. sordida*. The other 47 species are wild and maintain a natural cycle only with wild mammals. *T. infestans*, which is the only strictly domesticated species, has been eliminated in Brazil, Chile and Uruguay, and its eradication or control in other South American countries is in progress (Lent & Wigodzinsky 1979, Forattini 1980, Dias & Coura 1997, WHO 2002, Dias & Macedo 2005, Coura 2008).

More than 100 wild reservoirs of *T. cruzi* have been described among marsupials, xenarthra, bats, carnivores, lagomorphs, rodents and non-human primates. Among the domestic reservoirs, it is important to highlight dogs, cats, domestic rats, mice and guinea pigs, in countries where they are reared in houses. Other animals, such as pigs and caprines, have also been found to be infected. Birds, reptiles and fish do not become infected because they have "lysines" that destroy *T. cruzi* (Barretto 1964, Deane 1964, Dias & Macedo 2005, Coura 2008).

In nature, *T. cruzi* maintains wild, peridomestic and domestic cycles. The latter is maintained by means of domesticated triatomines that transmit the infection from domestic animals to humans and between humans as well. The wild cycle is enzootic and is maintained by triatomines and wild animals, while the peridomestic cycle originated from the wild cycle and maintains the infection among domestic animals in areas surrounding human dwellings through the action of peridomestic triatomines, and occasionally through exchanges with the wild cycle (dogs and cats hunting wild animals, and wild animals, such as rats and *Didelphis,* invading areas surrounding human dwellings). Deane et al. (1984) described a double cycle of *T. cruzi*: vertebrate and invertebrate cycles in the same mammalian host, *Didelphis marsupialis*, which is the most important wild reservoir of this parasite. The interrelation of these cycles can be seen in a simplified manner in Fig. 2.

The wild cycle of Chagas infection has existed in nature for millions of years. Some accidental human cases might have occurred at the time when mankind lived in

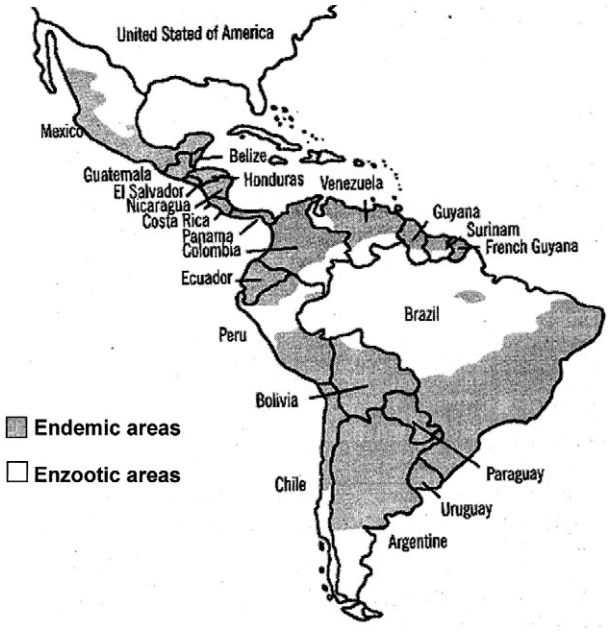

Fig. 1: distribution of Chagas disease in Latin America (adapted from WHO, Techinical Report 811).

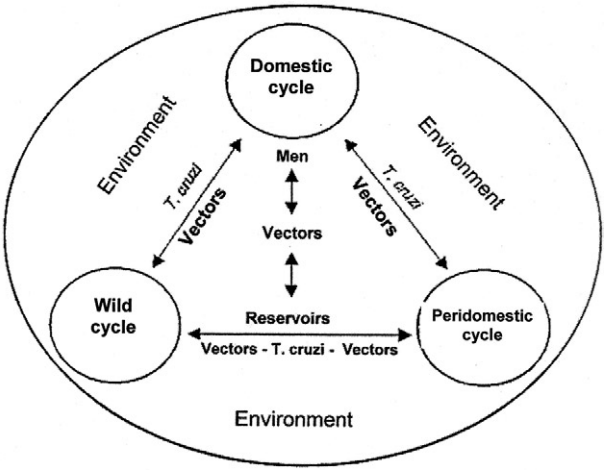

Fig. 2: interchanges between wild, peridomestic and domestic cicles (adapted from Coura 2008).

caves, but evidence of human infection has so far only been found in mummies from 4,000 and up to 9,000 years ago (Guhl et al. 1999, Afderheide et al. 2004). Although triatomines have been known since the XVI century (Lent & Wigodzinsky 1979), their adaptation to human dwellings began with the agricultural cycle and was intensified during the livestock cycle, through increasing deforestation and removal of the wild animals that were the food source for triatomines. To survive, triatomines gradually adapted to areas surrounding human dwellings and the interiors of these dwellings, and as a result underwent genetic simplification. Transmission of Chagas infection evolved from an enzootic disease of wild animals to an anthropozoonosis when mankind invaded wild ecotopes and became infected. In addition, when wild animals and vectors invaded human domiciles, man became infected by means of vector transmission or through food contamination due to the excreta of vectors or marsupials. The latter still frequently occurs in the Amazon Region, causing acute outbreaks of the disease (Pinto et al. 2008). When wild triatomines adapt to areas in and around human dwellings and Chagas infection starts to be exchanged between domestic animals and humans, as is the case in the classic endemic areas for Chagas disease, the situation is classified as a zoonosis. Finally, the infection can be characterised as an zooanthroponosis, meaning an infection that is transmitted from man to domestic animals and from these to wild animals (Aguilar et al. 2007, Coura et al. 2007, Coura 2008).

The transmission mechanisms for Chagas infection can be divided into two groups: (i) the principal mechanisms, by means of vectors (triatomines), blood transfusion, oral transmission, contaminated food and placental or birth canal transmission (ii) and secondary mechanisms, by means of laboratory accidents, management of infected animals, organ transplants, sexual transmission, wounds, contact with sperm or menstrual fluid contaminated with *T. cruzi* and, hypothetically, deliberate criminal inoculation or contamination of food with the parasite (Dias & Coura 1997, Coura 2007). Vector transmission may currently still be responsible for more than 70% of the cases in countries in which there is no systematic vector control. Likewise, transmission by means of blood transfusions may occur in up to 20% of the cases in places where there is no control over blood banks, such as in Bolivia. Congenital transmission exhibits great regional variation, from 0.5-10% of cases in places like Chile, Bolivia and Paraguay. Although oral transmission is accidental, nowadays it can be considered endemic in the Amazon Region (Fraiha et al. 1995, Valente et al. 1999, Junqueira et al. 2005, Pinto et al. 2008).

The epidemiological characteristics of Chagas infection in the Americas can be grouped into four sets of countries, according to the transmission cycles and the vector and transfusion control programs (Schmunis 1994, Carlier et al. 2002, Dias & Macedo 2005). Group I, which includes Argentina, Bolivia, Brazil, Chile, Ecuador, Honduras, Paraguay, Peru, Uruguay and Venezuela, is characterised by domestic and peridomestic cycles with zones of high prevalence of human infection; a predominance of chronic Chagas cardiopathy; the absence or rare of the digestive form in northern of the ecuatorial line; important wild cycles in various natural environments, including *T. infestans* in restricted areas in Bolivia; and vector and transfusion control programs in most countries, with prospects of eliminating *T. infestans* (already achieved in Brazil, Chile and Uruguay) and *Rhodnius prolixus*, which are eminently domesticated species. Group II, which includes Colombia, Costa Rica and Mexico, is characterised by domestic and peridomestic cycles with the presence of chronic Chagas cardiopathy; the occurrence of infected donors; the detection of wild cycles; and a lack of or only incipient control programs. Group III, which includes El Salvador, Guatemala, Nicaragua and Panama, presents domestic, peridomestic and wild cycles with little clinical information, and the beginnings of control actions in Guatemala and Nicaragua. Group IV, which includes the Antilles, Bahamas, Belize, Cuba, United States, Guiana, French Guyana, Haiti, Jamaica and Surinam, presents wild cycles with rare cases of autochthonous human cases and little clinical information; numerous infected immigrants in the United States; and an absence of control programs, with the exception of the beginning of blood bank control in the United States, where cases of transfusion transmission have already been described.

A new epidemiological, economic, social and political problem has been created with the internationalization of Chagas disease due to legal and illegal migration from the endemic countries of Latin America to non-endemic countries in North America, Europe, Asia and Oceania, in particular the United States, Canada, Spain, France, Switzerland, Japan, emerging Asian countries and Australia (Schmunis 2007). These migrations have created new epidemiological and public health problems for the countries that have received the infected migrants. These problems include risks of transfusion and congenital transmission, as well as a need for medical care for Chagas patients and additional controls over blood banks in countries with little experience in this subject. On the other hand, in addition to the medical, social and economic aspects, a political problem regarding migration control has been created, since immigration is often necessary to provide labour in more developed countries.

Chagas disease in the Amazon Region

Several acute cases of human Chagas disease have been reported in the Amazon Region, most of them by *T. cruzi* I, Z3, and hybrid ZI/Z3. In the localities where this disease has been reported, the chronic form of this disease is considered to present low endemicity. The first acute cases in the Amazon Region were reported by Floch and Tasque (1941) and Floch and Camain (1948) from French Guiana. Shaw et al. (1969) described another four acute cases in Belém, the capital of PA, in Northern Brazil. Since then, more than 400 acute cases have been reported, most of them from outbreaks likely caused by oral transmission in the states of PA, Amapá and Amazonas (AM), Brazil (Valente & Valente 1993, Valente et al. 1999, Pinto et al. 2004, 2008, Coura 2006). Serological surveys and cross-sectional studies carried out by Fundação Nacional de Saúde from 1975-1980, in different states

in the Brazilian Amazon Region, and by Coura et al. from 1971-2002 in AM showed prevalences ranging from 2.4-13.2% (Camargo et al. 1984, Coura et al. 1999, 2002). Severe chronic cases of Chagas disease have also been reported in the Brazilian Amazon Region (Albajar et al. 2003, Junqueira et al. 2005, Xavier et al. 2006).

Control and surveillance

Control over Chagas disease must be undertaken through the interruption of its transmission mechanisms, the improvement of housing and areas surrounding dwellings, sanitation education for exposed populations and the treatment of both acute cases and recently infected chronic cases. These measures should be complemented by surveillance and be based on primary, secondary and tertiary care. For such control, it is fundamentally important to permanently eliminate contact between triatomines and the areas in and around dwellings. This can be done by applying residual insecticides, improving housing, plastering walls to avoid cracks and hideaways for triatomines, improving roofing with adequate tiles and flooring with cement or tiles and emphasising the avoidance of basements, which are a frequent habitat of triatomines. In the areas surrounding dwellings, the pens, pigsties and storage places must be far from the home, and accumulations of rubble should be avoided, since these can house vectors. Likewise, there should be controls over blood donors by means of serological reactions, especially ELISA and the direct immunofluorescence test with a low cut off, at the level of 1:20. In places where serological screening cannot be performed, nearby referral centres must be used for screening and prior selection of donors according to blood groups, with negative serological tests required for emergency donations (Dias 1997, Dias & Macedo 2005).

Since the end of the 1940s, control over *T. cruzi* transmission to man has been accepted as the most promising way to combat Chagas disease. From the outset, control over the vector was seen as the first and greatest priority, followed by the target of control over transfusional transmission (Dias & Schofield 1999). In the 1940s, especially through the work of Emmanuel Dias, the fight against triatomines took place not only through chemical methods, but also through attempts to improve housing and sanitary education, in experiments carried out in Bambuí and in the Triângulo Mineiro. This was followed by important studies by Pedreira de Freitas, in SP, which together demonstrated the feasibility of control over domesticated vectors, with consequent interruption of the transmission of Chagas disease to new generations of susceptible individuals (Dias 1945, 1957, Dias & Coura 1997, Dias & Schofield 1999, WHO 2002). Although the inputs and strategies for controlling transfusional transmission originated from a group of scientists in SP at the beginning of the 1950s, widespread control did not occur until the 1980s, with the emergence of AIDS and the generalization of measures throughout Brazil (Moraes Souza et al. 1997). Because of the lack of inputs and strategies, congenital transmission could never be targeted through primary prevention, and its management consisted of the diagnosis and early treatment of infected newborns (Dias 1997, Moya & Moretti 1997, Carlier et al. 2002). National control programs were solidly implemented from the 1960s onwards in many countries, with priority given to vector and blood bank control. As a result, today there are many extensive areas in which transmission has practically ceased (WHO 2002).

Vector control is applied particularly to areas with domesticated insects (colonising human homes) or with high rates of infestation in areas surrounding dwellings. This is fundamentally undertaken by means of the continuous application of chemical insecticides with residual action, combined with housing improvement and sanitary education activities (Dias 1957, 1997). Unfortunately, in most countries (except Uruguay, some locations in Bolivia, and, in the past, Venezuela), there are no rural housing policies that fully meet the needs of Chagas disease areas. Similarly, there continues to be a lack of programs within the official education systems, including university degree programs (Dias & Schofield 1999), or else they are extremely timid with regard to combating Chagas disease. Thus, the basic strategy for vector control is to combat them chemically. Operationally, this involves demarcation and planning (including triatomine surveys), massive attack, review stages, selective attack and, finally, epidemiological surveillance. Improvements have been achieved in relation to the pioneering studies that used chlorates (BHC, Dieldrin, Lindhane) or phosphates (Malathion). Today, chemical combat against the vector is by means of synthetic pyrethroids derived from chrysanthemum acid, with substitution of an alpha-cyan radical. These chemicals have a residual effect lasting 3-9 months within domestic environments. They are usually applied to the internal walls of the house and to outhouses surrounding the home where foci of triatomines might be found, usually by means of manual air pressure pumps for final volumes of 10-15 L of the formula. As a rule, these pyrethroids are efficient against many harmful arthropods and are practically harmless to humans and domestic animals (but with undesirable effects, such as skin or mucosa irritation, caused by direct contact). However, they are highly toxic to fish and therefore must not be disposed of in natural water supplies (nor can the pumps be washed in this water). Other strategies and formulations have been tested in an attempt to increase the residual action of the pyrethroids and other insecticides, such as dispersion in microcapsules, incorporation in paint and slow-release matrixes, association with theoretical enhancement products (piperonyl butoxide, for example), microdrop aerosols etc. However, there are usually issues relating to the cost, operational problems and formulation on an industrial scale. For example, a formulation of some insecticides for use in fumigation pots has been widely used in surveillance areas in Argentina, with easy application and good immediate effects on adults and nymphs, but with high cost and minimal residual effect (Dias 1997). In general, the specified pyrethroids have not encountered resistance from triatomines, either in the field or in the laboratory. However, over the last few years, a monitoring and vector control laboratory in Buenos Aires has detected focal populations of *T. infestans* (Southern Bo-

livia and Salta, Argentina) and *R. prolixus* (one focus in Venezuela) with strong evidence of resistance to the usual pyrethroids, which is requiring extra care on the part of the sanitary authorities.

Alternatively, the carbamate chemical group (propoxur, bendiocarb) can replace pyrethroids, usually with slightly lower efficiency and higher cost. Phosphate compounds are practically never used against triatomines because of their toxicity and lower residual effect. Chlorates are banned from agricultural and sanitary use because of undesirable environmental and sanitary effects. Numerous other alternatives for directly combating triatomines have been tested, generally with slight effects, unmeasured costs and difficulties in application to extensive endemic areas. The following examples can be cited: hormones (juvenilising, precocenes), biological control (nematodes, fungi and predator hymenoptera), genetic control (sterile males) and traps (with light or pheromones). There are also recent experiments with physical controls, by means of heating houses to more than 50°C, or with xenointoxication using fipronil. All of these strategies are still experimental and present problems regarding their application on a public health scale (WHO 2002, Dias & Schofield 2004). In general, areas that have been treated chemically, with proper continuity, exhibit drastically reduced rates of domestic infestation over periods ranging from 3-6 years. The remaining triatomines usually comprise separate and focal populations, derived from operational failures or active migration from the wild cycle to the environment (secondary ubiquitous species). Under these circumstances, the great challenge is to keep infestation to a minimum level through surveillance, thereby preventing domestic colonization (Silveira 2000, Dias & Schofield 2004). Today, surveillance involves community participation, with the basic objective of keeping homes clean and difficult for triatomines to colonize, making it possible for the people living in these homes to detect suspicious insects and report them to the local health services. The surveillance system in Brazil and in other countries is now strongly decentralised to municipalities, thus making it easier to report the presence of "triatomine bugs" and elicit an immediate response (house inspection, education and insecticide) from the local health units. This scheme is usually complemented by installing small notification posts at strategic locations and implementing regular supervision of these areas by subregional inspectors (Dias 1991). Since most of the residual foci are restricted to areas surrounding dwellings, the basic strategies for such situations include adequate management and hygiene, with selective insect eradication in outhouses with positive findings, at regular intervals (every 6 months-2 years). For the periodic evaluation and for directing prophylactic actions, it is becoming widespread among endemic countries to use serological-epidemiological surveys, usually among individuals in young age groups (Dias 1997). It is worth highlighting, in the context of putting policies into action, the way in which shared initiatives for Chagas disease control between countries have succeeded.

Vector control of Chagas disease is heading towards some predictable trends and challenges (Dias 1991, Dias & Schofield 2004). Species that are exclusively domesticated, such as *T. infestans* and *R. prolixus*, tend to become eliminated from their dispersion areas due to continuous efforts in contiguous spaces, particularly in the regions to which they had been introduced. Ubiquitous species that are present in the wild and that are capable of becoming domesticated (*T. brasiliensis, T. pseudomaculata, T. sordida, T. dimidiata* and *P. megistus*) tend to persist, sporadically invading human housing and therefore demanding continuous surveillance. Consequently, it will be of enormous importance to have a technical and political-administrative setup enabling a permanent and sustainable epidemiological surveillance system, with a decentralised organization, constant supervision and wide-ranging community participation. Other native wild species with some potential for invasion (*R. neglectus, R. ecuadoriensis, R. pallescens, T. vitticeps, T. rubrovaria, T. tibiamaculata and T. maculata*) can under some circumstances transmit the disease and even achieve incipient colonisation. The surveillance needs to be able to detect, monitor and resolve these problems. Particular attention must be given to areas surrounding dwellings, which is where the greatest and most frequent foci of domesticated triatomines in Brazil are now found and where the action of insecticides currently in use is poorest. In terms of overall policies regarding land occupation and proactive surveillance of possible human cases of schizotrypanosis, special care must be given to areas in which the agricultural frontiers are expanding, as well as to areas of invasion and entry into wild environments, such as the Amazon Region and the Atlantic Forest. On the other hand, programs and projects for housing improvements must also be encouraged, combined with mandatory sanitary education and insect eradication, especially in rural or poor urban peripheral areas that present constant triatomine reinfestation. A series of operational investigations will naturally be necessary for improving the program and enabling route changes in the light of new situations. Plans for managing pesticide resistance, searches for more adequate insecticides and formulations, management of areas surrounding dwellings, improvements to detection of low-density triatomines and new strategies for community participation are today considered priority issues for better control over the vector transmission of Chagas disease (Dias 1997, Silveira 2000, WHO 2002). Fig. 3 shows the progressive reduction of infestation and elimination of *T. infestans* from Brazil through chemical combat.

The control situation regarding transfusional transmission in most countries is very comfortable, due to the rigorous and wide-ranging serological control over blood. In areas without controls, such as some regions of Bolivia, chemoprophylaxis using gentian violet or other similar pigments is indicated. These are capable of eliminating the parasite within 24 h (Dias & Coura 1997, Moraes Souza et al. 1997, Silveira 2000, WHO 2002). In general, in the countries and regions that are under vector control, the trend is towards a progressive reduction in the number of infected donor candidates (in Brazil

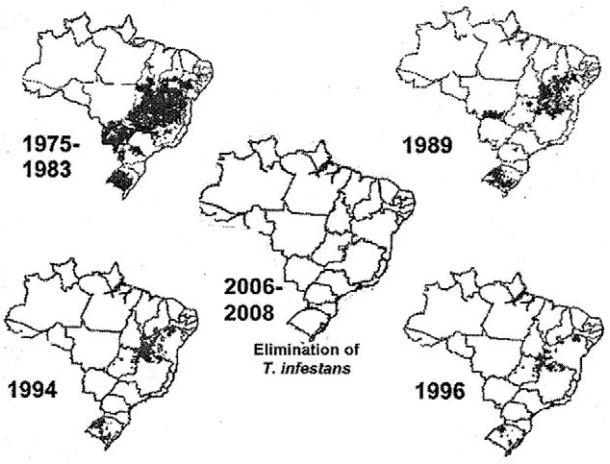

Fig. 3: control of *Tripanosoma infestans* in Brazil - 1975-2008 (adapted from Secretaria de Vigilância em Saúde, Ministry of Health, Brazil).

the current mean is about 0.6%) and a shifting of the infected individuals to older age groups. In fact, there is already a consensus regarding the possibility of selection by means of only one test (ELISA), as long as the laboratory reaches international quality standards.

The best way for preventing congenital transmission is to detect the disease and provide specific treatment as early as possible (Dias 1997, Moya & Moretti 1997, Amato Neto et al. 2000, WHO 2002). Treatment for pregnant women using imidazoles (such as benznidazole) is not indicated because their effectiveness and side-effects are unknown, including in experimental models. Regarding the detection of congenital transmission, testing of pregnant women with Chagas disease should ideally begin at the prenatal stage, in order to follow up with their children from the time of their birth. This also enables better care for the infected woman. This is what takes place, for example, in regional programs in which there is good prenatal coverage, such as in Paraguay, some Argentinean provinces and Brazilian states such as GO and Mato Grosso do Sul. Diagnosis of these newborns must be carried out as a priority, using parasitological means (preferably micro-hematocrit) on the blood from the cord, and possibly additional blood culturing and PCR. Positive children should be treated as acute cases, with yearly clinical and laboratory follow-up (conventional serological tests). Investigations using conventional antibodies will obviously be positive and will not add anything in diagnostic terms. Investigations using IgM can be used, but there are difficulties in setting up the method and the sensitivity leaves much to be desired (Luquetti & Rassi 2000, Carlier et al. 2002). In practice, for endemic areas and epidemiological suspicions, newborns should undergo conventional serological tests at birth (anti-*T. cruzi* IgG testing) and seropositive children should be followed until they are around seven or eight months of age. At that age, the serological tests should be repeated, and only those who are then positive should be treated. For newborns with a strong clinical suspicion of congenital Chagas disease (prolonged fever, hepatosplenomegaly, acute myocarditis and prematurity), repeated parasitological investigation on successive days is recommended (Dias 1997, Carlier et al. 2002). To follow up on seropositive newborns, one good alternative, when possible, is to carry out new serological tests when they reach three months of age, using the shed acute phase antigen. When this test is positive, it indicates congenital transmission and favours earlier treatment (Luquetti & Rassi 2000). For all treated cases, annual clinical and serological follow-ups for 3-5 years are recommended. Cure is proven when there is a complete and persistent negative response for at least two years. At the end of the five-year period, positive serological findings signify therapeutic failure, and therefore such children would have to be treated again (with a non-imidazole, if available) and clinically followed up (Dias 1997, Luquetti & Rassi 2000).

With regard to laboratory accidents, it is fundamentally important for the technicians and researchers involved to receive rigorous preparation against such possibilities, so that they learn to deal with the parasite and to protect themselves adequately with individual protection equipment, under strictly adequate work environments and conditions. Aware and prepared, these workers must undergo serological tests before starting such work (as a baseline for subsequent evaluation), with regular external supervision. If an accident should occur, four measures are implemented (Dias 1997, Amato Neto et al. 2000). The first is immediate disinfection of the site (if it is a skin wound or eye exposure). A course of benznidazole or nifurtimox (habitual dose) lasting for 10 days should also be started immediately. The head of the service or laboratory should be notified immediately, so that the accident can be analysed and possible incorrect procedures can be corrected. New serological tests should be conducted on the victim 1-2 months after the accident. If the serological test results from a person who was previously negative become reversed, it should be concluded that chemoprophylaxis has failed and the case must be monitored as an acute one, possibly with specific re-treatment.

Before organ transplant surgery, the donor and recipient must be serologically tested, considering the following possibilities (Dias 1997, Amato Neto et al. 2000). For a negative donor and negative recipient, no action is required regarding Chagas disease. For a negative donor and positive recipient, medical-laboratory attention should be given to the recipient during the postoperative period to detect possible reactivation due to immunosuppression. If this occurs, the patient must be treated as an acute case, to minimize the risks of acute carditis and/or meningoencephalitis. For a positive donor and positive recipient, the action should be the same as for the preceding scenario. Lastly, a positive donor and negative recipient is the most important case and this occurs relatively frequently in endemic areas, particularly with kidney transplants. Usually, the need for a transplant has priority and the surgical procedure must be performed without rejecting the donor. Thus, when surgery is indicated, it is suggested that the donor should be treated with imidazole for 10 days prior to the operation (to lower his parasitemia) and the recipient should be treated prophylactically for 10 days subsequent to the operation, to prevent installation of the parasite.

The control and surveillance initiatives relating to Chagas disease in the Southern Cone in 1991, in the Andean countries in 1997, in Central America and Mexico in 1998 and in the Amazon countries in 2004 have created new expectations among the Latin American community and in non-endemic countries that have received migrants from our continent, regarding the possibility of worldwide control over Chagas disease within the next 20 years. These possibilities can be realised, but only with constant, enduring control and eternal surveillance.

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