

ARTIGO DE OPINIÃO

THE CONTROL OF LATIN AMERICAN TRYPANOSOMIASIS

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The author presents his personal point of view on the present situation of Chagas' disease control in Latin America countries. He compares the situation with African trypanosomiasis. He comments on the existence of cases in other Continents. He emphasizes the success of the fighting against domiciliated triatomine bugs by using residual insecticides. He discusses other forms of Trypanosoma cruzi transmission.

Key-words: Chagas' disease. Latin American trypanosomiasis. African trypanosomiasis. Control.

Since its discovery⁸ Chagas' disease has become one of the most important endemic infections in Latin America. Its subtle clinical presentations influence medical practice like holoendemic *Falciparum* malaria in subsaharan Africa. Like African trypanosomiasis human acute *Trypanosoma cruzi* infections occur in poor people in rural areas. The vector geographical distribution is responsible for disease occurrence in both infections. Infection is life long.

We live in an age where international travellers may have been reared in bug infested houses. For example an Australian child with leukemia recently develops acute *T. cruzi* infection after a unit of Bolivian blood. Even children rarely forget the colour of the adult bug which are winged and blackish with one dominant colour: white (*Triatoma infestans*), red (*Panstrongylus megistus*), brown (*Rhodnius prolixus*) and yellow (*T. dimidiata*). Suitable specimens for display should be available in every outpatient department and blood transfusion centre in the New World. Chagas' disease in the USA is associated with Latin American immigrants^{19 20} though at least three indigenous infections have been documented.

Triatomine bugs are adventitious blood feeders; living syringes that pump blood into their crops from intraluminal blood vessel penetration. Any blood will do to pass through the five larval stages rapidly and secure the next generation. Like most insects a newly emerged female is virgin only for a matter of hours. Their other great need is a place to hide

during the day. Most of the more than 100 species known²¹ are nocturnal. A few have domiciliated in illconstructed rural housing attracted by biomass concentration and man's sedentary nocturnal habit. Poor domestic hygiene and large families encourage bug colonisation.

Brasília was built in one of the largest transmission foci in the world (Goiás, Minas Gerais, Bahia states³⁵). Bugs do not colonise concrete apartment blocks and if transmission occurs in cities it is the result of rural migrant workers squatting in peripheral shanty towns with *T. cruzi* and bugs¹⁰. Our problems with Chagas' disease in the hospital service continue today among adults from the interior before the Nacional Control Programme began in 1985¹⁴. We have not seen a child infected by bug faecal contamination for over a decade and we saw at least one a week before 1985. Acute infection with *T. cruzi* in childhood frequently passes unrecognised. Cardiopathy is usually manifested in the third or fourth decade especially in males who have families to support and do harder physical work. That is the tragedy, many dependants but short of breath he can't work.

An aspect of great confusion regarding this subject is the distinction between *T. cruzi* sylvatic cycles, domestic cycles and consequent human infection. Only a minority of the latter develop clinically declared Chagas' disease. This confusion has rendered calculations of incidence and prevalence of speculative value³³. Regarding Figure 1 bugs determine disease endemicity; *T. infestans* in the Cone Sul, *P. megistus* in Northeast Brazil, in Venezuela, Colombia and Eastern Central America *R. prolixus* and *T. dimidiata* in Western Central America and Ecuador. I have worked in Trinidad where there are sylvatic cycles but no human

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Figure 1 - Map of South America purporting to show Chagas' disease distribution.

infection, and demolished houses full of *T. infestans* but with no *T. cruzi* infection in transmission. I have seen 8 year old children always living in houses with active transmission develop the Romana's sign of acute disease. Thus infection is not always easily acquired.

Trypanosoma cruzi sylvatic cycles are ancient and may have coincided with marsupial evolution. These animals have transmitting bugs in their nests and tolerate high *T. cruzi* parasitaemias with few pathological effects (eg. *Didelphis sp*). Such infected marsupials exist from Washington D.C. to Patagonia. Mans entry into these cycles resulted from the violent ecological changes he made with wild animal predation. It is possible that areas of Latin America where sylvatic cycles were already precarious predisposed to triatomine invasion

of the peridomicile when man arrived (eg. Argentina chaco, Brazilian cerrado etc). The cerrado region on the high upland plateau of Brazil covers an area the size of Western Europe²³. Such a hypothesis would explain why Chagas' disease has never been a problem in the Amazon basin where there are many stable sylvatic cycles²⁹. Also the Amazonian indian often builds his shelter without walls which could provide hiding places for bugs to escape their many enemies². House construction is a major factor in insecticide control. A flimsy Brazilian structure of roof palm and adobe walls is easier to render bug free than a Bolivian stone hut with a metre thick vegetable roof.

It is stated baldly that the solution to Chagas' disease is domiciliated bug control. Brazil has led in this field. From the discovery of the power

of residual insecticides on walls of triatomine infested houses¹² to the National Control Programme¹¹. A nation wide serological survey⁵ was undertaken at the same time. The Ministry of Health had entomological data on the presence of triatomines for all states. *T. cruzi* transmission to man is variable even in endemic localities. For example the author works in an area of pure *Leishmania viannia braziliensis* transmission chosen because there is no Chagas or kala azar to confuse serology. Yet less than 100 miles away is *T. cruzi* transmission in houses. Thus careful geographical mapping and planning are essential before costly control³⁴. House spraying in our area (Mambáí) cost 5 American dollars per house in 1980. A control programme has three phases. First the identification of afflicted households and cost calculation. Second attack with a residual insecticide and finally vigilance to prevent vector return. Brazil controlled Chagas' disease with Brazilian money voted as a result of Brazilian knowhow. Research workers are proud of this sequence as the annual meetings at Caxambu and Uberaba remind us.

The State of São Paulo mounted effective control to combat *T. infestans* before the national programme³¹. Various pilot areas where field research on control have been reviewed²⁵. The object is to break contact between the sleeping child and the vector in the wall or bed. Eradication of *T. cruzi* transmission is not possible because of sylvatic cycles and potential house invading triatomines in the area. In our study area of Mambáí, Goiás these are in order of importance *T. sordida*, *P. megistus*, *R. neglectus* and *T. pseudomaculata*²⁷.

Careful manual demolition of bug infested houses²⁸ yields valuable information on the behavior of bug colonies which can help in control. For example *T. infestans* and *R. prolixus* tend to colonise the upper wall and roof. *P. megistus* and *T. dimidiata* are lower wall frequenters. All may be found in the bed near the blood meal source. Dogs are a most important domestic reservoir for they often sleep in the house. Cats have a high *T. cruzi* infection rate since they eat mice which eat bugs but since they hunt at night rarely infect bugs. Other domestic animals acting as reservoirs are Andean guinea pigs especially if kept under the bed and goats in wall leantoos in the chaco region. Pigs, cows and horses can be infected but develop low parasitaemias. The importance of mammalian *T. cruzi* sources in the peridomicile

relates to their capacity to infect domiciliated bugs. Thus *Didelphis marsupialis* which builds nests in the kitchen roof to raid the stove at night area is a risk. Armadillos with their own bugs (*P. geniculatus*) in their own burrows are of little importance.

A first instar bug infected with *T. cruzi* remains so for two years in the authors laboratory though flagellate density in its intestine varies with time depending on parasite and host factors. A most efficient vector compared with tsetse flies. The attack phase of control cannot be discussed in detail. This is done elsewhere^{25 31}. Spraying coverage can be checked by timed bug application to wall surfaces. These vary in their residual retention of insecticide effect depending on the material constituting the surface. Chlorinated hydrocarbons (which are non biodegradable) have been abandoned in favour of pyrethroids which have little smell, good knockdown and more persistent residual effect¹. Brazil has a research unit testing insecticides in Rio de Janeiro and evaluating triatomine resistance. Triatomine turnover in field settings is low (1-2 generations a year) with the exception of *R. prolixus* (2-4). It is in this species that the most insecticide resistance has been documented in Venezuelan field control schemes. On reviewing Chagas control programme²⁵ the vigilance phase was usually poorly documented. Our field work has concentrated on this aspect since insecticide attack in Mambáí in 1980¹⁷. We have published on the field situation in Mambáí sequentially¹⁶. At the time of writing *T. infestans* has not been captured in the municipality for 3 years but it may arrive in a visitors baggage tomorrow. As an example this species caused acute Chagas' disease in an apartment on Copacabana beach after arriving in a sack of Goiás rice. Such passive transport is more frequent than direct flight.

Since we discovered that people knew little of the implication of household bugs³ we have concentrated on health education and community vigilance¹⁷. Today many of our vigilance posts are based at schools for children are the best bug spotters. The labelled plastic bag with bug occupant arriving at our base laboratory in the village produces a house visit and a decision regarding insecticide application. In a few remote farms a responsible community member has been trained and equipped in bug identification and insecticide application. Vigilance

continues indefinitely to prevent vector return to house. An important factor favourable to bug control cannot be measured, namely community development. When we arrived in Mambaí in 1974 there was no bridge over the river which we forded on foot, nor was there a school teacher in the municipality.

House improvement to avoid bug colonisation comes at the end of a control programme when persistent bug presence becomes evident. This procedure is expensive. The householder must be involved in the project instructed and helped by the field team. Then house pride returns with better hygiene and even flowers on the table. We have recently found that practical binding agents for plastering in a mixture of Mambaí soil sand and cement are rice straw and maize husk¹⁵. These best prevent plaster cracking and using such formulations bug colonisation is discouraged.

The most important vector bug is *Triatoma infestans* because of its wide distribution in Cone Sul countries, the high domiciliated population achieved. its vector efficiency and its capacity to dislocate other house vectors as it did in Mambaí where previously *P. megistus* transmitted *T. cruzi* in houses. The origin of *T. infestans* may have been the Cochabamba valley in Bolivia. From here it migrated to become the principal vector in Northern Chile, Southern Peru, Argentina, Paraguay and Uruguay. Essentially a domiciliated vector it was captured in houses in Maranhão State, Brazil before national control. Climatic factors could explain why this bug constantly travelling in baggage up the Brasília-Belém highway never established house colonies in Pará State.

Both *T. infestans* and *P. megistus* in Northeast Brazil were highly domiciliated and house annex invasion (eg. chicken houses) was from the domestic colony. *P. megistus* in the South of Brazil inhabits sylvatic ecotopes occasionally flying into light to join even São Paulo dinner parties. *R. prolixus* and *T. dimidiata* colonise the peridomicile requiring increased vigilance to prevent reinvasion. Casually throwing a palm frond on a leaky roof in Venezuela may introduce *R. prolixus* again. No more space can be devoted to triatomine *T. cruzi* vectors although others are important (eg. *T. braziliensis*, *R. pallidus*).

The infection can be transmitted in many other ways. Protozoologists are not used to handling high risk organisms and there have

been over 50 laboratory infections²⁴. The Mechanism may be obscure as in a skilled laboratory worker or animal house cleaner. Aerosol transmission is the probable answer as animals can be infected by this route (DJ Winslow: personal communication, 1975). Blood transfusion infection is a constant risk in endemic areas. The safest precaution is not to accept Latin American blood from endemic areas. If such blood has to be used sero negative donors without a history of house bugs should be chosen. If this is not possible due to shortage 1:4000 gentian violet should be added to the blood 24 hours before transfusion. Patients sometimes complain about turning blue but the author has not seen this technique fail. *T. cruzi* can also be transmitted congenitally, by breast milk and organ transplant. Many types of oral infection have been documented including pipetting cultures in the laboratory, eating under cooked infected meat or food contaminated by *Didelphis* urine, cold soup in which infected triatomine have defaecated, sugar cane juice with homogenised triatomines or simply eating infected Mexican bugs as we eat grasshoppers, termites, and bumble bees. A real risk from such accidents is an immediate indication for Rochagan therapy. This can only be stopped after negative serology six weeks later.

The clinical aspects of Chagas' disease are treated in standard texts^{9 36} and only a few points are noted. First diagnosis and treatment are so unsatisfactory that these aspects alone reinforce the emphasis on control. It appears that we know where the scanty trypanomastigotes originate in the chronic phase that infect bugs used in xenodiagnosis namely amastigote nests in the wall of the suprarenal vein³⁷. Such subpatent parasitaemia bears no relation to electrocardiogram evolution in such patients⁷. Evolution in the chronic phase to declared cardiopathy cannot be predicted despite many suggestions. One of Carlos Chagas' first patients with acute disease never developed cardiopathy³². Perhaps Köberle's hypothesis that the severity of the acute phase determines the subsequent development of cardiopathy and aperitasis merits further consideration. It is difficult to muster sufficient observations in primate models. Many minor subclinical forms of both types of pathology have been documented. Judging by our present understanding of parasympathetic ganglia function more will be discovered¹⁸.

The best definition of the acute phase is detectable motile trypanosomes in a fresh

blood film. As in the treponematoses chronic infection relies on serology⁴. False positive serology occurs with *T. rangeli* infections, leishmaniasis, leprosy, malaria, treponematoses etc. One current serologist is recommending five tests. The polymerase chain reaction will have an application here¹³. It is not available at the time of writing in Brazil so we use indirect immunofluorescence and indirect haemagglutination techniques to detect circulating antibodies and have access to a reference laboratory to check doubtful results. For USA practitioners this laboratory is at CDC Atlanta. From here also comes the only drug available in the States to treat acute Chagas' disease namely nifurtimox (Lampit). Many years ago when the author advised CDC about a parasitic disease drug service this was the only drug available. Today Bayer have stopped Lampit production and Rochagan (benzimidazole) is preferred²². Both oral drugs are mutagenic, courses are long, side effects frequent and results variable. However some patients treated in the acute phase revert serology. Since nobody can interpret the significance of repeatedly negative xenodiagnosis benefit in the chronic phase is speculative. Our unit does not treat chronic phase chagasics with specific therapy unless there are special circumstances. These are immunosuppression, Aids or transplant programming.

As previously suggested there should be a rare drug deposit in each continent²⁶. The Australian baby mentioned at the beginning of this article only had access to CDC's Lampit. One day I shall see in Brasília African trypanosomiasis in a patient who has visited the Kruger National Park. I have no access to Suramin or Mel B. Such a rare drug deposit can be small but at a big centre with good communications. In South America Rio de Janeiro and Lima are the obvious choices.

We are in the phase of applying control programmes in known endemic areas. The Cone Sul campaign has resulted in Uruguay entering the vigilance phase while attack continues in Paraguay, Northern Argentina and Bolivia. After *T. infestans* control in these regions next will be the areas dominated by *R. prolixus* and *T. dimidiata* namely Northern Latin America. Possibly domestic transmission can be broken by the year 2009 when we celebrate Chagas' first paper⁸. A friend of mine hired by Carlos Chagas recalls the interview "I would like you to work in Neivas laboratory" said the great

man leaning back in his chair "For I believe the solution to the problem of American trypanosomiasis lies in the control of the insect vector"³⁰.

SUMMARY

O autor apresenta seu ponto de vista pessoal sobre a situação atual do controle da doença de Chagas nos países da América Latina. Compara a situação com a tripanossomíase africana. Comenta a existência de casos em outros Continentes. Acentua o êxito da luta contra os triatomíneos domiciliados, através do uso de inseticidas residuais. Defende outras formas de transmissão do *Trypanosoma cruzi*.

Palavras-chaves: Doença de Chagas. Tripanossomíase latinoamericana. Tripanossomíase africana. Controle.

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