Photo: Flat Earth

Elimination of Chagas disease

AN END IN SIGHT?

Over 80% of Chagas infections in Latin America are passed on by domestic insect vectors. Chris Schofield outlines how eliminating these on a very large scale would stop disease transmission, as well as the risk of insect vectors spreading elsewhere in the world. Early disease detection and treatment combined with continued surveillance for insect re-infestation are also essential to meet the challenge of eliminating Chagas disease as a public health problem.

Chagas disease (American trypanosomiasis) is a terrible affliction, caused by infection with protozoon parasites (*Trypanosoma cruzi*) mainly transmitted to humans in the fecal deposits of large blood-sucking insects of the subfamily Triatominae. It can be fatal in its early acute stage, but more usually progresses to a lifelong debilitating condition during which the parasites cause progressive tissue destruction as they multiply in infected cells. When the tissue affected is the heart, the patient is lethargic, with cold extremities, and quite unable to work. It is this long-term debility that, in epidemiological terms, is mainly responsible for the high socio-economic cost of the disease.

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Continually molested by bugs

Even without the infection however, living in a house infested with Triatominae is very unpleasant. The bugs typically live in cracks and crevices of rural homes, emerging at night to feed on the sleeping occupants. There may be a few hundred, or several thousand individual bugs – the "record" is a house in Colombia, dismantled to reveal over 11,300 bugs.[1] The bugs are large, adults usually about 2.5 cm long, and they suck a lot of blood, contributing to chronic iron-deficiency anemia. Their black fecal streaks mark the walls and furniture, sometimes making a thick congealed patina over the walls of heavily infested houses. At times, people can no longer sleep in their houses, continually molested by the bugs. They become tired, stressed, investing scarce resources to try to get rid of the bugs. And sometimes the families divide, unable to continue under such conditions. In 1984, it was estimated that over 100 million people in Latin America were suffering this way, and that 24 million were already infected with Chagas disease.[2]

Treatment of the disease is difficult. Two drugs – nifurtimox made by Bayer in El Salvador, and benznidazole now made by LAFEPE (under license from Roche) in Brazil – can be used during the acute phase of infection. These are gradually being introduced for treatment of early chronic infections (up to 14-15 years old). Neither is completely effective, and both are toxic, risking severe side-effects – especially in adult patients. But by contrast, elimination of the domestic insect vectors is a relatively simple task – at least on a small-scale, and using adequate products applied by well-trained professionals (*see box on page 11: Spraying procedures*). The problem is how to do this on a very large-scale, because the endemic area for Chagas disease covers well over 12 million km^2 of Latin America (*see map on the right*).

Chagas disease vector control

Since the pioneering work of Carlos Chagas and colleagues in Brasil, and Salvador Mazza and colleagues in Argentina, a very wide range of vector control methods has been trialed with a view to eliminating domestic infestations of Triatominae – including biological control and insect pathogens, as well as a range of physical and chemical

Serious lesions

Around 30% of those suffering from Chagas disease will develop serious lesions, mainly of the heart, but in some cases also involving other vital organs such as the intestinal tract. Destruction of heart tissue can lead to severe arrhythmias, repeated heart attacks, and sudden death due to cardiac arrest or ventricular fibrillation. More common, however, is simple pump failure due to extensive pancarditis with muscle fiber destruction.

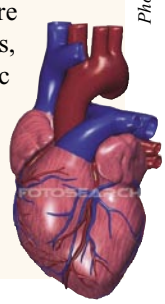


Photo: Pure Stock

THE MAP SHOWS the various initiatives where countries in different regions have joined forces to bring Chagas disease under control. Each region has to deal with different vectors and problems requiring specific strategies.

methods. The resulting experience accumulated from experiments and field trials in most countries of Latin America has led to a basic vector control approach with three main components:

- indoor residual spraying (IRS) by trained professionals (*see box on page 11*)
- householder and community participation in monitoring and surveillance
- rural house improvement

By itself, rural house improvement seems insufficient to eliminate an established domestic bug population[3] and it tends to be a relatively slow process that rarely reaches all the poorest householders. By contrast, well-managed IRS programmes can reach all domiciles, and can usually treat 2-10 houses per man per day – depending on terrain, size and distribution of houses, and the extension of peridomestic structures that are included in the treatment. However, community agreement and householder participation are essential, both to assist in preparing the premises for spraying, and also to participate in post-control monitoring and surveillance to ensure that the domestic bug population has indeed been eliminated and to provide early warning if any subsequent infestations are found.

In general, a well applied IRS campaign is sufficient to eliminate existing domestic bug populations, although repeat treatments are sometimes given after 3-6 months.[4] Since the 1980s, WP or SC formulations of pyrethroids have been the products of choice (*see table on page 12*). Other classes of insecticide are not generally used except where donated (or against some recently reported foci of pyrethroid resistant *T.infestans* in southern Bolivia and northwestern Argentina). Throughout Latin America, IRS campaigns followed by long-term surveillance have been the primary component of Chagas disease control programs, together with improved blood-bank screening to reduce the likelihood of transfusional transmission from infected blood donors, and improved patient care, counselling, and treatment for those already infected.

Photo: Brand X Pictures

Vector populations

Domestic: live and breed in cracks in the walls of rural houses and animal shelters, feeding on the blood of the inhabitants

Peridomestic: live in areas near housing feeding on wild and domesticated animals

Silvatic: live in woods and surrounding areas, under tree bark, in birdnests, rockpiles, palmtree crowns, or burrows of small mammals, sometimes entering houses and contaminating food or drinks

Multinational control initiatives

Following a great many trials, and national control campaigns in Venezuela, Argentina, and Brazil, the enlightened response to the geographical scale of Chagas disease control came as a series of multinational initiatives. These began with the Southern Cone countries in 1991, followed by initiatives of the Andean Pact (IPA) and Central American countries (IPCA) launched in 1997, and the Amazon Initiative (AMCHA) launched in 2002.

The **Southern Cone Initiative** (INCOSUR) involved six countries (Argentina, Bolivia, Brazil, Chile, Paraguay, Uruguay) which, with southern Peru, was designed to cover the entire distribution of the main vector, *Triatoma infestans*. At the time, it was believed that *T. infestans* was almost entirely domestic throughout its range. Small silvatic foci (*see box above: Vector populations*) were only thought to occur in the Cochabamba-Sucre region of central Bolivia. The aim of the INCOSUR program was to halt Chagas disease transmission by eliminating all domestic populations of *T. infestans*, with concurrent elimination of any other domestic vector populations in the same area. This was combined with improved screening of blood donors to reduce the risk of transfusional transmission.

The idea was that simultaneous vector control programs throughout the area would prevent re-infestation of treated premises by *T. infestans* being accidentally transported from non-treated regions. In addition, the multinational nature of the program – coordinated by the Pan American Health Organization (PAHO) – should give political continuity to the interventions, making it less likely that a country would suddenly divert resources away from the Chagas disease control program.

The **Andean Pact** (IPA) and **Central American Countries Initiatives** (IPCA) had similar aims and rationale. Here, the focus was on eliminating domestic populations of their main vector, *Rhodnius prolixus*, together with control of other vectors in the region – particularly *T. dimidiata*. There was strong evidence that *R. prolixus* had been accidentally imported from Venezuela into Central America at the turn of the last century[5], so that in Central America it appeared that *R. prolixus* could be completely eliminated. Similarly, there was evidence that *T. dimidiata* had been accidentally transported from Central America to Ecuador and northern Peru during pre-colombian times, so that it could potentially be eliminated from there, even if not from Central America where it retains extensive silvatic populations.

SPRAYING PROCEDURES

How to eliminate a domestic population of Triatominae

The following points describe the recommended procedures for spraying, using adequate products applied by well-trained professionals. The recommendations are based on experience collected from control trials and programs throughout Latin America.

1 **Identify the house** – preferably using a GPS to identify the house by its geographical coordinates.

2 **Identify yourself**, and explain your objectives to the householders, seeking their permission to enter.

3 **Check for evidence of domestic infestation:** Discuss with the householders, showing them life-size pictures of the bugs; check for streaks of bug feces on the walls, exuviae (the skins cast when a triatomine bug moults to its next stage), bug eggshells and bugs themselves (using a torch and long blunt forceps to investigate for bugs in cracks and crevices). You might also use a dislodgant spray (eg. 0.2% aqueous tetramethrin) to irritate bugs to get them to emerge from their crevices.

4 **Prepare the house for spraying** (if there is evidence of infestation): Explain to the householders, and seek their cooperation; remove to the outside all foodstuffs, kitchen utensils, animals and people; move furniture away from the walls to allow access behind; hang all clothes and bed linen outside in the sun.

5 **Spray thoroughly all internal surfaces** (including furniture and the internal roof): Use a good quality compression sprayer (eg. Hudson X-pert or equivalent) with an adequate product at the specified dose (*see table on page 12*), closely following professional spray procedures to ensure complete coverage (*see: WHO Manual for Indoor Residual Spraying, below*); complete your spray recording cards. Note: all structures physically in contact with the house should be considered as domestic for purposes of spraying and recording results.

6 **Discuss with the householders:** Ask them to collect any dead bugs they find (and provide a plastic bag in which they can be stored for collection); explain safety issues, such as avoiding excessive contact with the sprayed surfaces; after 15 minutes, help the householders to replace their furniture and utensils. Pin your visit/activity card to the inside of the main door, and explain that a member of your team will return within one week to check all is well – and also to enlist the householders help in longer-term vigilance against any future infestations. Collect all used packaging from the spraying (to be returned to your supervisor).

Further details on these procedures:

WHO Manual for Indoor Residual Spraying:
http://whqlibdoc.who.int/hq/2007/WHO_CDS_NTD_WHOPES_GCDPP_2007.3_eng.pdf

WHO Field testing and evaluation of insecticides for indoor residual spraying against domestic vectors of Chagas disease: http://whqlibdoc.who.int/hq/2001/WHO_CDS_WHOPES_GCDPP_2001.1.pdf

Seven-fold economic returns

The INCOSUR, IPA and IPCA initiatives were designed primarily as vector elimination programs. At the time of writing, Brazil, Chile, Uruguay, and Guatemala have been formally declared free of Chagas disease transmission due to their main vectors. Similar declarations have been made for various provinces and departments of Argentina and Paraguay. The distribution of *T. infestans* has been reduced from its predicted maximum of 6.28 million km² to under 1 million km² (*see figure on page 15*). Moreover, *R. prolixus* appears to have virtually disappeared from Central America except for a few remaining foci in Honduras. Also, in all countries of Latin America, screening of blood donors has been improved, with coverage close to 100% in most countries (except Mexico).

TRIATOMINE BUGS as the insect vectors of Chagas disease can be eliminated in domestic settings by treating infested buildings.

Photo: WHO/TDR/Stammers

Costs averaged around US$ 30 million per year for the Southern Cone, and around US$ 4-7 million per year for the Central American countries. However, studies in Argentina and Brazil indicate economic returns equivalent to over US$ 7 for every dollar invested in the Chagas disease control programs.[6] Benefits have also accrued to those already infected, as clinicians throughout the intervened regions report reductions in the severity of chronic lesions.[7] From studies in mouse models, such reductions seem to be largely due to lack of re-infection once the domestic vectors have been eliminated.[8]

Insecticide dose rates for Chagas disease vector control

Insecticide	Formulation	Dose rate (mg a.i./m²)
Deltamethrin	SC or WP	25
Betacyfluthrin	SC	25
Lambda-cyhalothrin	WP or CS	30
Alphamethrin	WP	50
Cyfluthrin	WP	50
Cypermethrin	WP	125

SC = suspension concentrate; WP = wettable powder; CS = capsule suspension (micro-encapsulated)

Source: Schofield 1994, and WHO/CDS/WHOPES/gcdpp/2000.1

Note that bendiocarb WP (400 mg a.i./m²) and malathion WP or fenitrothion WP (both 2000 mg a.i./m²) are sometimes used, mainly in parts of southern Bolivia and NW Argentina where some pyrethroid resistance has been recently reported in T. infestans.

Disease detection and treatment

By contrast, the **Amazon Initiative** (AMCHA) – which includes parts of nine countries – was designed primarily as a surveillance program. This is because domestic vector populations are rare in most of the Amazon region (except for *T. maculata* in parts of Roraima and southern Venezuela). Instead, vector-borne transmission in the Amazon region is attributed primarily to adventitious silvatic bugs (mainly species of *Rhodnius* and *Panstrongylus*) flying into houses and contaminating food and drink. Such transmission is often described as "oral-route transmission" and has resulted in a series of so-called "family microepidemics" of acute Chagas disease in various parts of the Amazon region (and elsewhere). In such circumstances, there is little role for vector control programs. Instead, emphasis is given to detection and treatment of those occasional outbreaks of acute disease – a task where malaria slide-microscopists are now playing an increasing role, by identifying trypanosomes in the peripheral blood-smears of febrile patients originally suspected of malaria. In a sense, the Amazon Initiative may also be revealing aspects of how the future of Chagas

disease control could proceed throughout the Americas, once the existing domestic vector populations have been eliminated.

Widespread agent and vectors

A much debated question then becomes "Can Chagas disease be eliminated?" We must be clear on terminology: the causative agent, *T. cruzi*, will not be eliminated – it is a widespread parasite of small mammals and marsupials throughout the Americas. The vectors, Triatominae, will not be eliminated – there are over 140 species distributed in the Americas (and some also in India and SE Asia). As consequence, the disease will not be eliminated, in the sense that the ubiquity of parasites and vectors in Latin America will always pose a risk of occasional transmission to humans. Such cases, without prompt diagnosis and treatment, can in turn pose a risk of onward transmission through non-vectorial routes, such as blood transfusion, organ transplant, and occasional congenital cases.

Eliminate domestic variants

But some vector populations can be eliminated: *T. infestans* over most of its original distribution in Argentina, Bolivia, Brasil, Chile, Paraguay, Uruguay and southern Peru; the central American form of *R. prolixus*, and the South American form – at least from the central valleys of Colombia; *R. ecuadoriensis* from northern Peru, and *T. dimidiata* from Ecuador. All these populations appear to have been imported – as domestic variants – from elsewhere, mainly by accidental carriage by humans, and mostly within the last 150 years. In a sense, their presence outside their original foci is aberrant, due to human accidents that should be corrected.

Photo: Iconotec

These populations have probably accounted for well over 80% of Chagas disease transmission, but they are not the only vectors. All populations of all species of Triatominae should be considered at least as potential vectors, although without human contact they can play no epidemiological role. So the focus perhaps should be to minimize that contact, and then to minimize the risk of that contact. With this perspective, outline strategies become clear. All existing domestic populations of Triatominae, of whatever species, should be eliminated, and experience accumulated from control trials and programs throughout Latin America shows that this is possible (*see box: Spraying procedures on page 11*).

Now, how do we sustain this absence of domestic Triatominae, knowing that the previously infested houses may remain susceptible to re-invasion? The technical response was to improve insecticide formulations, in an attempt to give longer protection to the treated premises. But, recognizing that no treatment can last forever, the strategic response – as illustrated by the multinational initiatives – was to try to remove source populations, to make re-infestation unlikely. Successful when dealing with an imported domestic variant (such as *R. prolixus* in Central America), this strategy is much less successful when dealing with domestic populations that also occupy extensive peridomestic habitats (such as *T. infestans* in the Chaco region of NW Argentina and southern Bolivia) or that retain local silvatic ecotopes (such as *T. dimidiata* in parts of Central America).

The challenge of peridomestic control

The control of peridomestic populations of Triatominae is seen as a major technical challenge. Conventional spraying with WP or SC pyrethroids (as used inside houses) tends to have reduced

impact, since the superficial deposits can be degraded by sunlight and/or quickly covered with dust or animal dejections. Some people report better results using a double spray[9] or using slow-release polymer formulations.[10] Others prefer physical modifications to the peridomestic habitat – for example, using higher standard fencing materials instead of piled brushwood for goat corrals in the Argentine chaco, which can greatly reduce the habitat available for peridomestic *T. infestans* and *T. guasayana*.[11] Other approaches involve the concept of "xenointoxication" – treating domestic animals with a pour-on or powder formulation of insecticide, in order to kill any bugs that may attempt to feed on them.[12] Insecticide-impregnated dog collars have been used for a similar purpose[13], and it seems likely that further technical developments will lead to improvements in the ways to control peridomestic Triatominae. But perhaps a strategic response also needs to be considered.

Photo: ?????????

SPRAYING against domestic *T.dimidiata* in Nicaragua.

Combined with surveillance strategies

The importance of peridomestic Triatominae is primarily as a potential source for re-infesting the domestic habitat. Where possible, they should be reduced or eliminated, not least, for their effects on the productivity of peridomestic animals. But more importantly, from a public health standpoint they can also be viewed as akin to silvatic populations, some of which are also potential sources for re-infesting the domestic habitat. Seen in this light, the strategy changes. It is both impractical and ecologically unacceptable to contemplate large-scale interventions against silvatic populations of Triatominae. It is also irrelevant in terms of transmission control. Only by coming into contact with humans – for example by entering a house – does a silvatic bug assume possible epidemiological significance, either by causing direct transmission or by establishing a new domestic colony. But a newly established domestic colony can be eliminated, and a transmission event can be treated – which is the basis of the Amazon surveillance strategy. Perhaps even elsewhere, peridomestic and silvatic populations should be considered similarly – focusing on the vectors only when incipient domestic colonization is apparent, but otherwise focusing only on diagnosis and treatment of possible new cases of infection.

The "end point" for elimination of Chagas disease as a public health problem can be then described when:

- all existing domestic infestations of Triatominae have been eliminated;
- local health authorities are structured and equipped to diagnose and treat occasional new infections;
- local health authorities eliminate – perhaps through contracts with local pest control operators (PCOs) – any incipient domestic vector infestation.

Epidemiologically, the situation might then resemble that of Lyme disease in Europe – the vector ticks (*Ixodes ricinus*) are present in our garden (which may be said to comprise both peridomestic and silvatic habitats) and there is a risk of *Borrelia* transmission. However, the ticks do not enter our house, and if they did, would be rapidly dealt with, and if a new infection occurs it is relatively simple to diagnose and can be treated.

The Political Commitment

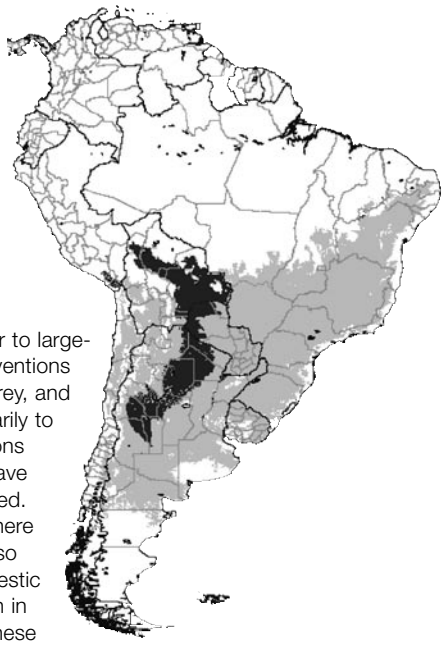
Although Chagas disease will not be eliminated, in the sense of ceasing to exist as a human disease, it could be eliminated as a serious public health problem – when all existing domestic vector populations have been eliminated, and all aspects of current control programs are adequately incorporated into routine local health programs. The products, equipment, and experience are available for this. Strategies have been developed both for the initial campaigns and their consolidation through active vigilance, and for subsequent integration of the surveillance activities into routine public health activities.[14]

But all comes to nothing without political commitment and leadership, which in turn liberates the required resources. In a few countries there is still no coherent national program. In others the national program is in disarray, with spraymen and vehicles idle, since they lack the minimum resources to mobilize. Perhaps the initial successes of the multinational initiatives were too widely hailed. But relieving some 60 million people from the molestation of Triatominae and risk of disease (as some have claimed) still leaves some 40 million with little protection – which is both inappropriate and unethical, given the demonstrated feasibility of the large-scale control interventions.

Paradoxically perhaps, a renewed urgency to complete the control interventions may come from the previously non-endemic countries now receiving migrants from Latin America. Some of these people require treatment for their chronic Chagas infection, and some pose a new risk for onward transmission by blood transfusion or organ transplant.[15] It is to be hoped that the domestic Latin American vectors can be eliminated before they too begin to arrive in Europe and elsewhere.[16]

For ECLAT (European Community – Latin American Network for Research on the Biology and Control of Triatominae) and TVRC (Trypanosomiasis Vector Research and Control Foundation) please see page 37.

Reduced distribution of *T. infestans*



THE MAXIMUM DISTRIBUTION of *T. infestans* prior to large-scale control interventions is shown in pale grey, and corresponds primarily to domestic infestations – most of which have now been eliminated. The main areas where *T. infestans* can also survive in peridomestic habitats are shown in darker grey, and these currently also represent the main areas of residual domestic infestations.

Source: Schofield C.J. & Gorla D.E. (2009) Triatominae: Biology and Control. In: Human Parasitology (ed. W.Apt) McGraw Hill.

CONCLUSION

The data and experience gathered from different geographical regions of Latin America point to the combined strategies needed to eliminate Chagas disease as a serious public health problem. First, eliminate all existing domestic vector populations, and adequately incorporate all aspects of current control programs into routine local health programs. The products, equipment, and experience are available for this. Strategies have been developed both for the initial campaigns and their consolidation through active vigilance, and for progressive incorporation of this surveillance into routine public health activities.

Article with references on the enclosed CD-ROM.