Research Directly Linked With Current Vector Control Strategy

Working paper for the Scientific Working Group on Chagas Disease Research, convened by the Special Programme for Research and Training in Tropical Diseases (TDR) and the Pan American Health Organization (PAHO)

Buenos Aires, Argentina, 17-20 April 2005. Updated 23 September 2007

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This review focuses on aspects related to current vector control strategies that deserve more attention and research. It is selective in nature and somewhat biased toward *Triatoma infestans*, partly because there has been more research on this species and partly because of my own personal experience. Although each of the species of Triatominae adapted to the domestic environment (and relevant for public health) has its own specificities, there are many shared issues among them.

Objectives of a control program. A clear definition of the ultimate goal of the vector control program is a crucial initial step; it will also help to assess whether the program has been successful or not. A Dahlem Workshop on the Eradication of Infectious Diseases established these definitions [17]: (a) Control is the reduction of disease incidence, prevalence, morbidity or mortality to a locally acceptable level as a result of deliberate efforts; continued intervention measures are required to sustain the reduction (e.g., diarrhoeal diseases); (b) Elimination of infection: reduction to zero of the incidence of infection caused by a specific agent in a defined geographical area as a result of deliberate efforts; continued measures to prevent re-establishment of transmission are required (e.g. measles, polio); (c) Eradication: permanent reduction to zero of the worldwide incidence of infection caused by a specific agent as a result of deliberate efforts; interventions are no longer needed (e.g. smallpox). Chagas disease is clearly only apt for control or elimination of infection.

The type of the control program varies with the vector species implicated and the structure of the transmission cycle. For *Triatoma infestans*, careful consideration of its biological features (i.e. lack of sylvatic foci throughout most of its geographic range), recognized public health relevance as vector, available intervention tools, and levels of societal and political commitment suggested that this species was a candidate for elimination. Similar arguments were applied to *Rhodnius prolixus* in Central America but not in Venezuela or Colombia, where it has sylvatic foci and more genetic variation. *Triatoma dimidiata*, a highly variable species with a very wide geographic range that includes numerous types of sylvatic, peridomestic and domestic habitats, is clearly a candidate for a control program throughout of most of its current distribution from northern Peru to Mexico. Similar arguments apply to other more sylvatic vector species showing different degrees of domestication, such as *Panstrongylus megistus*, *Triatoma brasiliensis* and *Triatoma pseudomaculata* in Brazil, *R. pallescens* in Panama, and *Triatoma pallidipennis* and other species in Mexico.

Current control interventions. Vector control programs may be vertically or horizontally structured. Traditionally, vector control programs had a centralized, vertical structure borrowed from malaria and yellow fever programs, with a specific and time-limited goal, and a highly motivated organization of professional spray workers. Horizontal control programs specifically train local human resources (local householders, community leaders, primary health care agents) to spray and conduct surveillance actions, with the purported aims of increasing coverage and sustainability while decreasing operation costs. The main method of Chagas disease vector control involves residual house spraying with insecticides, with environmental management and housing improvement having a marginal role in almost all public health programs.

Vertical control programs are divided into three successive phases: preparatory, mass attack, and surveillance [67]. Major activities conducted during the preparatory phase include geographical reconnaissance, mapping, assessment of baseline infestation levels in domestic and peridomestic habitats, and informed consent of local authorities and householders. In the attack phase, professional spray teams travel to distant rural areas and conduct mass spraying of all houses and dependencies with wettable or suspension concentrate formulations of pyrethroid insecticides diluted in water applied with manual sprayers. Standard procedures include spraying with insecticides walls, roofs and each and every piece of furniture and boxes, as well as other peridomestic structures such as chicken coops, corrals and sheds. Professional insecticide sprays are labor-intensive and time-demanding. For example, in northern Argentina a three-person team may take up to 3 h to spray rigorously a typical rural dwelling with extensive peridomestic structures; during the 1990s the insecticide cost averaged us$ 24 per house compound, to which salaries, per diem, gas and vehicle expenses should be added, totaling US$ 65 per house [3]. Operations are to be conducted under the universal dictum of spatial contiguity and temporal continuity, again demanding high levels of organization and prolonged efforts.

In the surveillance phase of vertical programs, vector control staff visit the houses on a regular schedule to conduct timed searches for bugs and re-spray selectively the reinfested houses. When more than 5-10% of reinfested houses are found, the whole community is re-sprayed again as in the attack phase. In practice, control teams may experience logistical difficulties in revisiting the houses with the desired frequency, and the villages may go through a new reinfestation cycle at a rate that varies according to the local force of reinfestation. Determinants of reinfestation, including environmental and demographic factors operating at various spatial scales, are context-sensitive and need extensive research with the aim of optimizing control operations.

Detection of infestation. Detecting the presence of low-density populations of triatomine bugs in mud-and-thatch houses or peridomestic ecotopes during the surveillance phase is a difficult task. Timed manual collections, in which trained personnel aided with an irritant spray search for bugs during a fixed searching time per house, has been the standard method to assess the occurrence and intensity of infestation by triatomine bugs. Because this method is costly, requires skilled staff and lacks sensitivity and precision, several types of shelter boxes made of cardboard and sheets of typing-paper or calendars (fixed to bedroom walls for long periods) have been devised and used to detect domestic infestations. Recycled tetra brik boxes providing internal refuges and insulation from weather agents were more sensitive and cost-effective than timed manual captures with an irritant spray in peridomestic structures [31,73]. A new generation of detection devices combining the use of sticky paper and bug attractants (e.g., hexanal, nonanal) has shown promising results in preliminary field trials [61] and merit enhanced application in community-based vector surveillance. When adequately instructed and stimulated, householders and school children have proved very effective in collecting bugs during the surveillance period. The number of domestic bugs collected per person-hr and other proportional correlates of bug abundance (such as the number of signs of infestation in sensing devices) constitute suitable indices that may be measured routinely by vector control programs for risk assessment and for prioritizing field operations.

Impact of control actions. In the Southern Cone countries, vertical control programs accomplished a high degree of success in reducing domestic infestation by *T. infestans* and human prevalence of *T. cruzi* in extensive rural areas between the 1960s and 1980s, although at a differing pace. More recent progress under the aegis of the Southern Cone Initiative has been highly significant and led to the certification of free from transmission of *T. cruzi* mediated by *T. infestans* in Uruguay, Chile, Brazil, four provinces in Argentina and one department in Paraguay (see reviews by country in Silveira et al. 2002). In some regions, the elimination of *T. infestans* from most of its past distribution is a foreseeable goal, but in other high-risk areas such as the Gran Chaco, the situation is far less complacent [35].

Argentina provides a study case in point regarding the complexities of vector control, organizational issues, program goals, socio-economic and political changes. The vertical control program in Argentina set up in 1962 brought about a large decrease in human prevalence of *T. cruzi* but failed to achieve a complete coverage of the affected areas and reach a sustainable surveillance phase by the early 1980s [71]. At that time, the disorganized decentralization of the national program (transfering the burden and reduced budgets to the affected provinces) determined a diminishing operational capacity (staff, vehicles), reduction in insecticide spraying rates, and a repeated domestic recolonization by *T. infestans* throughout most of its distribution range. The national vector control program maintained regional delegations in some of the affected provinces, but unfortunately not in provinces with the highest human prevalences with *T. cruzi*, such as Santiago del Estero, Chaco, Formosa and La Rioja. To remediate the absence of effective surveillance, primary health care agents were included in the control scheme. This showed positive impacts in some provinces, but the primary health care system suffered a gradual deterioration over the 1980s [70]. The successive political and economic crises left residual provincial vector control programs. A new national Chagas control program launched in 1994 ("Programa Dr. Ramón Carrillo"), mostly based on extensive community mobilization, training, and house spraying with pyrethroid insecticides (provided by the federal government) conducted by householders, exerted a tremendous impact on domestic infestation rates and notifications of acute Chagas cases down to very low levels [70]. This program faced the recurrent challenge of domestic reinfestation that suffered its predecessors and is described below. Discontinuation of intense control efforts combined with worsening socio-economic conditions and the acute crisis started in late 2001 determined a gradual deterioration of the control status in endemic rural areas. Outbreaks of dengue in 1998 and 2002 diverted the scarce human resources available away from Chagas vector control and virtually stopped control actions. On a more positive note, some provinces appropriated enough resources to maintain effective vector control actions (including the use of the primary health care system), whereas other provinces at higher risk, with less resources and greater areas to cover, practically depended completely on the central vector control program or its delegations to spray houses with insecticides. With an average age of 56 years as of 2005, skilled field staff is on the way to retirement during the next 10 years and so is their valuable experience unless it is transferred promptly. Field vehicles >20 years old are also longing for retirement. The basic spatial heterogeneity of Chagas vector control status reflects in areas under effective, sustained surveillance coexisting with areas where control actions have been irregular over time, with areas under a persisting reinfestation problem where symptomatic Chagas acute cases (the tip of the iceberg) are being increasingly notified since 2001 in at least eight provincial states [35].

Several questions emerge, and they demand elaboration and research at various dimensions and scales, including how to scale up successful pilot vector control trials. Schmunis and Dias (2000) stressed the loss of effectiveness in malaria, dengue and Chagas vector control programs brought about by irresponsible, disorganized decentralization throughout Latin America. A workshop sponsored by TDR/WHO, the Interamerican Development Bank and the University of Buenos Aires, on the effects of decentralization on disease control programs identified several areas of research interest [76]. Is a vector elimination program compatible with a horizontal control approach? Background experience casts serious doubts. When the ultimate program goal is control, how can we improve the sustainability of the surveillance phase? Is this independent of the eco-epidemiologic setting (i.e. risk-independent)? That is, do we need a control strategy specifically tailored to high-risk areas and their socio-cultural characteristics? What are the roles of the central government, provinces, districts, and the community in the surveillance phase? What are the pros and cons of integrating vector surveillance into primary health care activities? What were the goals, promises and consequences of decentralization in different countries? How can we mitigate the untoward effects of decentralization in vector control programs that traditionally had a vertical structure?

The reinfestation process. Following a single community-wide residual spraying with pyrethroid insecticides applied by professional personnel, the typical pattern recurrently observed in high-risk settings over the past two decades is that domestic bug infestations are apparently eliminated for 1-2 years [30]. This perception of complete success tends to slow down the continuation of surveillance and control actions, the so-called "punishment of success" experienced by successful vector control programs. The false elimination of triatomine bugs is in part accounted for by the difficulty in detecting the presence of low-density populations of triatomine bugs, which demands skilled staff, motivated householders or sensing devices to facilitate bug detection (see below). In addition, depending on the extent of treatment coverage and eco-epidemiological context, bugs need some time to arrive from source sites and recolonize the treated area.

In the absence of surveillance activities in high-risk regions such as the Gran Chaco, a single house or peridomestic structure left infested implies a fast reinfestation of the whole community in 3-5 years [9-11] and the appearance of new human cases of *T. cruzi* during such period [33]. The few longitudinal studies that combined serological and entomologic data at the household level have shown that transmission of *T. cruzi* may occur even at low infected bug densities [48,55]. Indeed, human acute cases of *T. cruzi* transmitted by dispersing adult triatomine bugs flying into houses in Acapulco [14] or the Amazon [12] and USA [50], among others, or by very low-density *T. infestans* populations in Paraguay [61], Argentina [33] and Peru [44] demonstrate that the probability of transmission of *T. cruzi* given a potentially infective contact with a bug is considerable and should leave little room for complacency. Domestic dogs and cats apparently also become infected at low infected-bug densities [34]. The sparse evidence available also suggests that the threshold domestic abundance of *T. infestans* below which transmission of *T. cruzi* to humans is unlikely would be very low, if any threshold exists at all, and undetectable within the imprecision of current vector sampling methods. Given the multiple sources of uncertainty underlying the estimation of transmission probabilities and insufficient empirical data, a prudent approach would promote no tolerance of domestic triatomine infestations [33]. The relationship between domestic bug abundance and risk of transmission, including transmission thresholds, merits more research in different settings.

Pyrethroids have proven much more effective in human habitations than in peridomestic ecotopes housing domestic animals and various species of triatomine bugs. Lack of recognition of this limitation implied recurrent cycles of reinfestation, increased cost and frustration. In peridomestic habitats, the effectiveness of pyrethroids decreased with the abundance of *T. infestans* per site before spraying [8,11,30,32]. Resurgence of peridomestic triatomine populations after spraying with pyrethroid insecticides has frequently been reported by official control programs in Argentina, especially in semiarid rural areas, before the appearance of any insecticide resistance to pyrethroids. Early and persistent peridomestic reinfestation after spraying with pyrethroids has been reported for *T. sordida*, *T. brasiliensis* and *T. pseudomaculata* in Brazil [15,16,52], *T. dimidiata* in Central America [49,20] and *T. pallidipennis* in Mexico [57]. For species other than *T. infestans*, reinfestations may also be driven by invasion from sylvatic foci. Clearly, pyrethroids are very effective but they are no magic bullets.

In Argentina, several pieces of evidence clearly suggest that most of the infestations found after spraying originated from *T. infestans* that survived exposure to the insecticides at each site (i.e. residual foci) [11,32] (but see below). Most importantly, the very short-lasting residual effects of pyrethroids in peridomestic sites was well below the time taken for *T. infestans* eggs to hatch at local ambient temperatures. The insecticidal activity of pyrethroids is inversely temperature-dependent, and is reduced by marked exposure to sunlight and high temperature, which induce photolysis of pyrethroid molecules [62]. In spite of extensive field evidence right at the outset of the use of deltamethrin and other pyrethroids in the early 1980s, these factors and the differential effectiveness of pyrethroids in domestic and peridomestic ecotopes have been mostly overlooked by vector control programs and most reference publications [77,79]. Blanket or selective insecticide sprays are frequently conducted during the hot season, when triatomine bugs increase in numbers and become more apparent, but unfortunately under these conditions the effectiveness of pyrethroid sprays is strongly reduced. The problem is even compounded in community-based control programs against *T. infestans* because rural villagers do not perceive peridomestic infestations as a direct nuisance or hazard to their animals or themselves. This issue needs to be further assessed by social scientists. The performance of two successive community-wide rounds of spraying with pyrethroids within 6-12 months holds promise of success if applied by professional spray workers, although at the expense of increased operational costs. Unlike the standard treatment, the application of a double dose of pyrethroid insecticides in infested peridomestic sites such as animal corrals was more effective in eliminating local populations of *T. infestans* than the standard treatment [11]. Operational research on targeted control measures is needed to improve the efficiency of current procedures.

In summary, the current tactics and procedures fail to eliminate peridomestic populations of *T. infestans* in semiarid rural areas from the Gran Chaco and need to be revised. This appears to be a generalized problem with triatomine species having extensive peridomestic or sylvatic foci, such as *T. brasiliensis* and the Mexican *Triatoma* species. Specific tactics tailored to the peridomestic environment may include determination of optimal insecticide doses, frequency and timing of spraying; reinforced surveillance of key structures using simple detection devices, and development of environmental management methods aimed at rendering house structures less susceptible to triatomine colonization. This should include replacement of peridomestic enclosures for animals with appropriate designs and materials adapted to the local context. This is an area where very little research has been made. Housing improvement (including plastering of walls and replacement of thatched roofs) requires linking rural development agencies that promote improvements in agriculture and livestock production to housing and health ministries at national and provincial levels for long-term support. Development of novel peridomestic control approaches, such as biological control agents or xenointoxication of bugs by spraying insecticides to domestic animals or using insecticide dog collars [58] would seem to merit attention for some triatomine species where standard procedures have shown limited effectiveness.

<u>Sources of reinfestation.</u> A key question still unresolved is whether the triatomine bugs appearing after blanket insecticide spraying are (1) survivors or the offspring of previously existing bugs; (2) immigrants from untreated domestic or peridomestic foci, or (3) brought by passive transport from other villages. This distinction is relevant because the first alternative demands improved spraying procedures, higher insecticide doses or more effective insecticides, whereas the remainder calls for increased geographic coverage of insecticide spraying [67]. The potential sources of reinfestants differ between species of Triatominae: *T. infestans* (considered mostly domestic or peridomestic, with either no or exceptional sylvatic foci, but see below) and *R. prolixus*, *T. dimidiata* or *P. megistus* (with known sylvatic foci at least in some areas). Even in district- or community-wide insecticide trials in which external sources of reinfestants may be virtually excluded, the appearance of extensive peridomestic foci shortly after spraying gives support to the notion that reinfestant bugs are survivors or offspring of those existing prior to insecticide spraying. Biochemical markers and traditional morphometry were used to assess the origins of reinfestants [18,19]. More recently, wing geometric morphometry showed

increased power of resolution [64] and evidence of bug dispersal between sylvatic and domestic habitats [22]. However, to provide conclusive evidence that may help distinguish between potential sources of reinfestations, we also need to make full use of recently developed molecular markers [2,24,36,45,53,59] combined with carefully collected bug samples before and after insecticide spraying, geographic information systems and spatial analysis.

The need for more field research is exemplified by recent findings related to the occurrence of sylvatic *T. infestans*. This species was known to have true sylvatic foci in Andean Bolivia, but there were also rather anecdotal findings of sylvatic *T. infestans* in northern Argentina, Paraguay and Brazil [51]. The latter may have been feral derivatives ("spill-overs") of domestic or peridomestic bug colonies at locations and times when these colonies were very frequent [19]. By the late 1990s, sylvatic *T. infestans* were captured in hollow trees in the Bolivian Chaco; these were chromatically darker than the typical, normal phenotype of domestic or peridomestic *T. infestans*, and thus were called "dark morphs". Both normal and dark morph phenotypes of sylvatic *T. infestans* were very recently found in two different locations in the Argentine Chaco (Leonardo A. Ceballos et al., unpublished results, 2005-2006). Moreover, normal phenotypes of sylvatic *T. infestans* associated with rodents were reported to occur in the Metropolitan region in central Chile [1]. The crucial issue is whether these sylvatic foci pose a real threat of domestic or peridomestic reinfestation after insecticide spraying campaigns, as shown for *Rhodnius prolixus* in Venezuela [22,63]. Current efforts seek to define the extent of the sylvatic foci of *T. infestans* and establish the degree of gene flow between domestic or peridomestic and sylvatic populations throughout the Gran Chaco. This unresolved issue cuts across all major triatomine vector species throughout Latin America.

Vector dispersal and population structure. Surprisingly, very few studies on the flight dispersal behavior of triatomine bugs have been published, and most of them pertain to *T. infestans*. Part of this may derive from the difficulties found in conducting field studies on flight dispersal, especially when using mark-recapture methods, and from the misconception that passive transportation by humans would be the main mechanism of propagation by *T. infestans* and other domestic species, to the extent that no mention of flight dispersal has been made in a reference publication [79]. Passive transport surely plays a major role in long-distance transport, but flight dispersal is the most likely mechanism underlying house reinfestation at a village-wide spatial scale (i.e., within the putative flight range of the vector). The flight initiation chances of *T. infestans*, *Triatoma protracta* and *T. sordida* are known to depend on nutritional status, temperature and wind. Field-collected *T. infestans* bugs are able to initiate flights at higher levels of nutritional status and with higher frequencies than laboratory-bred bugs; temperature thresholds for flight initiation were around 22-23ºC at sunset (Vazquez-Prokopec et al. 2006, Gurevitz et al. 2006). Furthermore, a significant fraction of the field-collected adult *T. infestans* from northern Argentina frequently lacked flight muscles, and those that had flight muscles differed dramatically with regard to muscle mass and flight initiation [28]. These fundamental traits relevant to reinfestation dynamics may account for geographic differences in reinfestation risk and have not been assessed so far. The timing and seasonality of flights and founding of new bug colonies, jointly with estimates of distance flown, may inform vector control programs on the area around a proven source or focus that would need to be sprayed with insecticides. Experimental work on orientation mechanisms, flight capacity, field observations, and physiological studies of flight metabolism in triatomine bugs are needed [68].

Another area in which we require more research is the spatial and temporal structuring of bug populations. Concerns focusing on population boundaries, geographic distribution, dispersal, and gene flow need to be addressed by population genetic studies. In general, there is very limited knowledge on the extent of gene flow between sylvatic, peridomestic and domestic populations of triatomine bugs, and this is expected to affect such factors as the spread of insecticide resistance. Such population genetics studies should be ideally conducted jointly with research on population dynamics and dispersal of triatomine bugs.

Insecticide resistance. The emergence of insecticide resistance to pyrethroids in *T. infestans* in northern Argentina in 2002 added a new source of concern, as this was the first time ever that it was detected in triatomine bugs [54]. More recently, other foci of insecticide resistance have been detected in nearby and more distant areas in Bolivia (María Inés Piccolo, unpublished results). The resistant strain of *T. infestans* showed cross-resistance to other pyrethroid insecticides in use, but was susceptible to organophosphorous insecticides such as fenitrothion. However, this complicates vector control operations because organophosphorous insecticides are more toxic for mammals and its unpleasant smell makes them less acceptable in domestic sites [80].

The issue of insecticide resistance has different implications depending on whether the ultimate goal of the intervention program is vector elimination or control. Wherever significant progress toward the elimination of *T. infestans* is achieved, insecticide resistance would turn into a non-issue. But both control and elimination programs that fail to consolidate transitory achievements may have to deal with added operational problems and expense, as Bolivia has experienced in 2006-2007. Standardized molecular assays for assessing insecticide resistance merit attention.

GIS modeling. GIS allow the integration of spatial and temporal information including satellite data to describe, understand and predict the potential distribution of arthropod vectors and transmission of pathogens. Analysis of spatial data of vector-borne pathogens using spatial statistics allows for identifying clustering of vector distribution and disease cases [37,42]. GIS, satellite imagery and spatial statistics applied to eco-epidemiological research on triatomine bugs and Chagas disease may provide scientifically-based, improved tactics to vector control programs*,* particularly during the surveillance phase. Risk mapping and stratification using GIS can be used to identify priority and problem areas and target control actions. Detailed regional distribution maps of infestation or infection may also permit in-depth analysis of the progress of control interventions. Unfortunately, the very few studies on triatomine bugs or *T. cruzi* using GIS have been published very recently [9,10,20,26,47,56]. There is much to gain from these insights with the aim of understanding systems dynamics and optimizing vector control actions [78].

Domestication. The process of domestication in Triatominae lead to the simplification of genetic and phenetic characters in the process of specialization to the more stable habitat provided by human habitations, and may be a generalized current trend (Schofield et al. 1999). *Triatoma infestans* expresses the extreme of such evolutionary trend toward greater epidemiologic significance. Through loss of genetic repertoire, triatomine bugs are expected to become more vulnerable to deliberate control efforts, but the geographic spread associated with domestication may counterbalance such weakness. At present several species of sylvatic or peridomestic triatomines that were not recognized as control targets are emerging as primary vectors of *T. cruzi* in defined areas. Examples are *Rhodnius ecuadoriensis* and *Panstronlylus herreri* in northern Peru (Cuba et al. 2002) and *Rhodnius stali* in Bolivia [46], but the list may increase in the near future. Recent findings show that vector-borne transmission of *T. cruzi* to humans occurs without domestic colonization, as in the Amazon basin [12] possibly through *R. brethesi*, Panama through *R. pallescens*, and Peru through *R. ecuadoriensis*.

Systematics. Several species of Triatominae belong to a complex of species with distinct ecological, vectorial and behavioral features that determine its relevance as vectors. One example is *Triatoma sordida* and *Triatoma garciabesi*; both differ significantly in size and their epidemiologic significance. *T. sordida* is frequently found infected with *T. cruzi*, and shows a trend toward domestication in Brazil, Paraguay and Bolivia. In contrast, *T. garciabesi* is smaller; typically associated with birds; hardly ever has been found infected with *T. cruzi*; expresses less tendency to invade homes, and does not colonize human habitations to date [6]. The two species were held as synonymous by Lent and Wydgosinsky (1979) for much of the three decades that spanned between the original description of *T. garciabesi* by Rodolfo Carcavallo et al. (1967) and its final recognition as a distinct species based on cytogenetics, isoenzymes, RAPD analysis and morphometry [41]. Some of these techniques also helped differentiate between wild *R. prolixus* and *Rhodnius colombiensis* [39] and between members of the *T. phyllosoma* complex in Mexico [5]. Cuticle hydrocarbon patterns are also a helpful tool to differentiate within species complex [40]. Mitochondrial DNA is a valuable tool in studying population genetics, molecular evolution, and phylogenetic relationships due to its relatively simple genetic structure and rapid rate of change. Fragments of the mitochondrial genes encoding *cytochrome oxidase I*, *cytochrome B* and the large ribosomal subunit of some members of the Triatominae have already been sequenced and have proven useful in phylogenetic studies. Clearly, the reliable identification of target species is paramount to any vector control program, especially during the long-term surveillance phase when other triatomine species eventually fly into houses without colonizing them, or when secondary vector species may have the opportunity to replace the diminishing populations of the primary vector.

Environmental and anthropogenic factors affecting transmission. Climate effects linked to global warming are expected to modify current distributions of triatomine bugs and the occurrence of *T. cruzi*. In some regions, drastic changes in the natural landscape, especially through intense deforestation, habitat degradation and mismanagement of deforested areas is leading to irreversible land desertification which in turn favors the spread of domestic triatomine species by human migration in search of better living conditions. Current changes in land use (e.g. expansion of soybean crops) are determining changes in natural vegetation cover and wildlife depletion that may result in increased house invasion by sylvatic or peridomestic triatomine bugs and introduction of sylvatic *T. cruzi* strains into the domestic transmission cycle. Unstable or vanishing rural economies favor lack of land tenure, low-quality housing (which facilitates triatomine infestation), low education and labor skills, which in turn close down the cycle of poverty and disease. Migration from the rural to the urban environment, often to poor housing in slums, creates conditions for the urbanization of *T. infestans* and transmission of *T. cruzi* as recently seen in Arequipa (Peru)(Levy et al. in press) and in several small towns in Santiago del Estero (Quimilí, Tintina, Suncho Corral) and La Rioja (Olta) in Argentina. This rural to urban migration is expected to increase over the next decades. The changing eco-epidemiology of Chagas disease has multiple dimensions delineating a complex and heterogeneous scenario.

Householders are one of the main actors of the reinfestation process. How do knowledge, attitudes and practices of householders influence the process of reinfestation? What are the mechanisms underlying the reinfestation process at the household, village and regional levels, and what are their relative contributions? How can we combine standard vector control measures with modern scientific tools and multistakeholder participation [23,38] to achieve more sustainable vector control? The spray coverage and surveillance of sparsely populated, impoverished rural areas with frequent migration is complex and also contributes to persistent infestations. To understand the multiple factor dependency of the reinfestation process, the ecohealth approach provides a holistic view linking social and ecological variables and may help uncover knowledge gaps unresolved by single disciplinary approaches [4,23]. A passage from the latest call for proposals by the International Development Research Center in 2006 states it transparently: "Vector ecology and human behavior, in the social and economic context, are key factors to be considered in the control and prevention of Chagas disease… Emphasis should be placed on interacting ecological and social factors linked to the ecology of autochthonous vector species." Undoubtedly, the integration of biological and sociological research is very much needed.

"The trade-off between the desire for complete elimination of infestation and transmission and the competing demands on limited resources in Chagas-endemic countries and districts is coupled with the limited political and economic power of the neglected populations affected by the disease (Gürtler et al. in press). Sustainable social, political and economic development, allocation and utilization of resources, and political leadership are essential for sustainable Chagas disease management. In resource-limited settings, the welcome call for integrated, inter-sectoral, interprogrammatic action toward neglected disease control [38] finds very few potential local actors and many competing challenges (e.g. potable water delivery). Community-based efforts to control *T. infestans* are not sustainable unless the surveillance system is part of an established long-term national policy that mitigates the recurrent economic and political instability in the region".

Conclusion

This review sought to identify some relevant aspects of vector control that merit further consideration and intensified research. I believe that lack of well-designed and sufficiently detailed field research in the past combined with excessive optimism strongly limited our capacity to make sustained progress toward the eventual elimination of Chagas disease as a public health problem in many high-risk areas. This objective, closely related to several Millennium Development Goals, requires more resources and a greater intensity of scientifically based, coordinated efforts at multiple scales from the village to the hemisphere.

Acknowledgements

This work was supported by the NIH/NSF Ecology of Disease program through NIH Research Grant R01 TW05836 funded by the Fogarty International Center and the National Institute of Environmental Health Sciences (U. Kitron and R. E. G.), the University of Buenos Aires and Agencia Nacional de Promoción Científica y Técnica (Argentina). R. E. G. thanks the ECLAT and CDIA networks for helpful discussions, and is a member of CONICET Researcher's Career, Argentina.

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