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CHAGAS' DISEASE

(American Trypanosomiasis)

by

Robert J. Tonn, Ph.D., MPH

March 1991

VBC Tropical Disease Paper No. 6

Other papers in the VBC series include:

Malaria
Schistosomiasis
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African Trypanosomiasis
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Life cycle illustrations: Taina Litwak
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The blue square shows a triatomine, or "kissing" bug, which transmits Chagas' disease. The other symbols depict essential components of vector-borne disease control: the environment, communities and research.

Author

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Executive Summary

Chagas' disease is found in the Western Hemisphere from Argentina to the United States. Some 90 million people live in the endemic areas. An estimated 16 million people are infected and 27 percent of them are likely to develop the chronic cardiac phase of the disease. Chagas' disease causes severe incapacitation during peak working years, premature death in the chronic phase and childhood mortality during the early acute phase.

The disease is transmitted by infected triatomine or "kissing" bugs, through blood transfusions, or from mother to child during pregnancy.

The intensity of infestation by the triatomine vectors is very high in rural areas where housing conditions are poor. Close association of humans to wild and domestic mammals in animal shelters adjacent to houses exacerbates transmission. Socioeconomic advancement is probably as important for control as medicine and vector control. It is possible to control the domestic transmission cycle by indoor house spraying with residual insecticides, but this method is costly and difficult to evaluate because of the extended nature of the infection.

Widely applicable chemotherapy is not available because nothing eliminates the intracellular parasites. Current drugs are only effective during the early acute phase and cause gastrointestinal and neurological side effects that require medical supervision.

Most Chagas' disease research is being conducted in Latin America and coordinated by the UNDP\World Bank\WHO Special Programme for Research and Training in Tropical Disease (TDR). These efforts are producing results that better clarify geographic differences in pathology and the biology of the parasite. Some improved control methods have been developed, but there has been little success in reducing the intensity of transmission.

Contaminated blood bank supplies and infection through transfusion or use of other blood products are increasing problems in Latin America. It is possible to clear the blood of infection, but many places do not have blood banks or facilities to screen and hold the blood for 24 hours for treatment. Studies report contaminated blood levels of five to 50 percent in certain regions. Sale of blood by people migrating to cities from infected areas is an important concern.

Major areas for assistance include: improved rural housing, improved blood banks (most likely in association with HIV screening), better diagnosis in early phases when chemotherapy is effective, and more efficient methods of insecticide application.

1. Introduction

American trypanosomiasis, or Chagas' disease, is caused by a protozoan parasite, *Trypanosoma* (*Schizotrypanum*) *cruzi*, which is transmitted to humans by triatomine bugs. Carlos Chagas, a Brazilian physician, found the parasite in the hindgut of the bug *Panstrongylus megistus* in 1907. Two years later, he found the same trypanosome in the blood of three sick children and in an armadillo. Chagas believed transmission occurred through the bite of the vector, but in 1912 Brumpt demonstrated that the parasite was transmitted when vector feces contaminated the skin of a host.

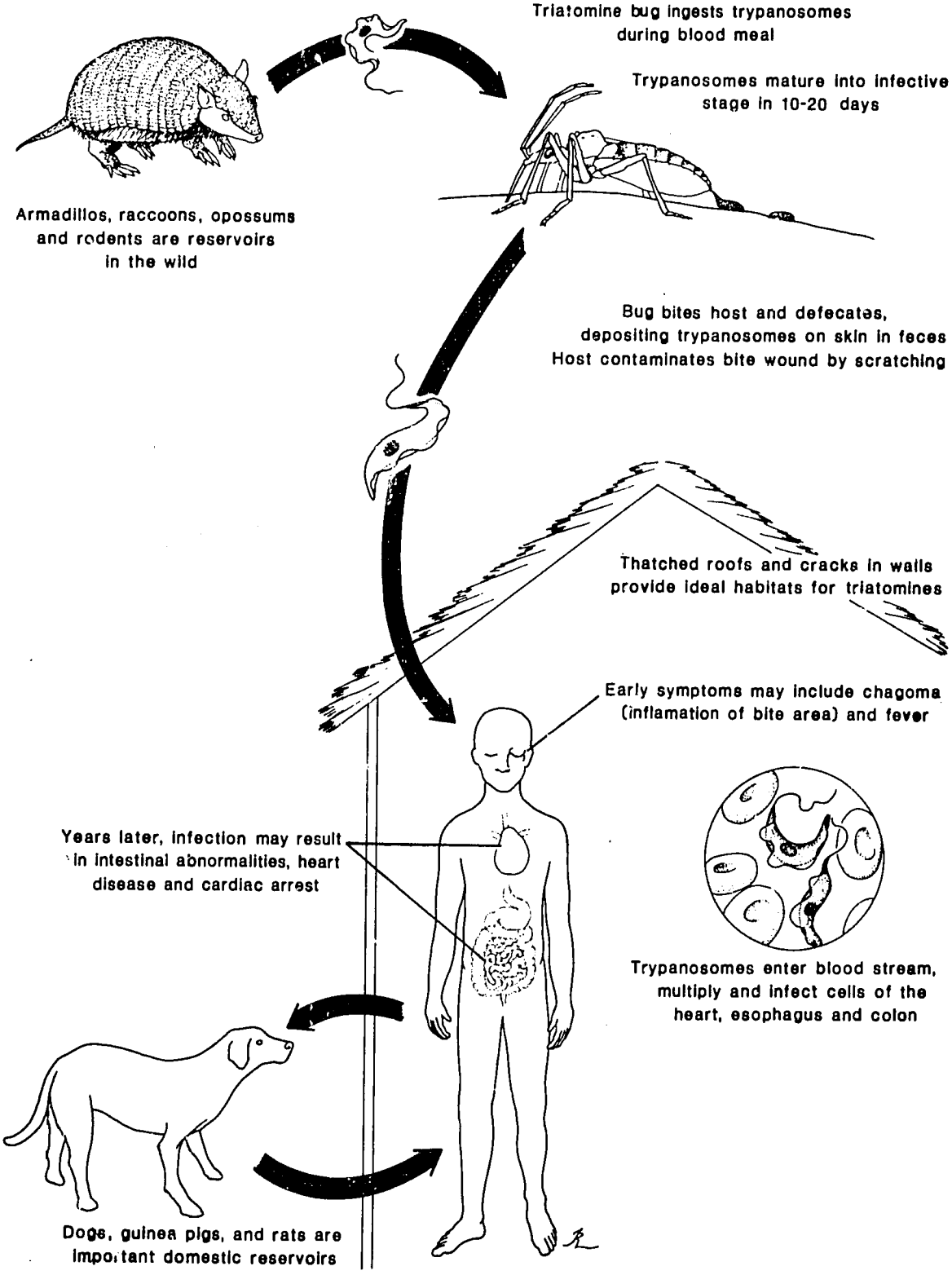
Chagas' disease is associated with poverty in rural areas and its prevention depends as much on socioeconomic advancement as medicine. Between 15 and 20 million people are estimated to be infected.

Humans make contact with the sylvatic *T. cruzi* cycle when they invade the habitats of wild vectors and reservoirs. As these areas become dominated by humans, wild reservoirs are forced out and people and domestic animals become a stable source of blood for some of the vectors. Construction of houses and outbuildings provides a dark, humid, protected environment for the vectors.

Chagas' disease has three ecological cycles: 1) sylvatic in the natural environment between wild vector and wild host; 2) a transitional or peridomestic cycle in which wild vectors or reservoirs enter the human environment, gaining an opportunity to pass the parasite to other vectors and domestic or farm animals; and 3) the domestic cycle, which includes vectors that have adapted to the human environment and feed on people (see life cycle, p. 3).

Transmission also occurs through transfusions of infected blood, organ transplants, from mother to child during pregnancy, in laboratory accidents, and possibly in mother's milk during breast-feeding. Sale of blood by people migrating to cities has become an important problem in Latin American cities because about 28 percent of donors may be positive for *T. cruzi*. Even in countries where *T. cruzi* is uncommon, it is possible to acquire the infection through blood transfusion because of migration of infected people from endemic areas. It is estimated that about two percent of children born to seropositive mothers may have congenital Chagas' disease. Ingestion of infected bugs or uncooked infected animal tissue are also possible means of transmission.

Life Cycle of Trypanosoma cruzi



a. Symptoms

The acute stage of Chagas' disease occurs with the first wave of parasitism a few weeks after infection and may resolve or pass into a subacute or chronic stage. For the most part, the acute stage is either asymptomatic or presents mild symptoms, but death in young children is not uncommon. In some cases there is a chagoma, or inflammation, at the site of the bite wound where parasites entered the host. Symptoms, which may include fever, sweating, muscular pain, raised pulse rate, enlargement of the liver and spleen, and inflammation of the lymph nodes, occur primarily in children. About fifty percent develop a swelling of the eyelids known as Romaña's sign.

Recent studies indicate that some degree of cardiac involvement occurs in any Chagas' infection. An indeterminate phase with no visible symptoms may last a lifetime. Patients in this latent phase of the illness, however, are still capable of transmitting the infection.

It is not clear what causes the chronic phase, but it may be related to the host's immunity. The role of reinfection is unknown. The chronic phase can cause circulatory problems, damage to the central nervous system and the heart muscle, and enlargement of the digestive track (megaesophagus and megacolon). Sudden death due to acute cardiac arrest is common among those infected in the 20 to 50 age group.

Many people older than 65 who are seropositive for Chagas' infection have no evidence of pathology, but up to 27 percent of seropositive populations develop cardiac abnormalities as demonstrated by electrocardiogram (ECG). Geographic differences in pathology occur. For example, the megasyndrome (megacolon and megaesophagus) is absent in Venezuela, but is common in Brazil, Bolivia and central Argentina.

Severe reactions to the bite of triatomine bugs may produce intensive itching and other skin problems. These are usually reactions associated with antigens in the saliva of the bugs. Transmission occurs when a person contaminates the bite wound by scratching it and inadvertently rubbing in the infected bug's feces.

b. Biogeography

Every country in Latin America has reported cases of Chagas' disease, as have Texas and California's Sacramento Valley. The disease does not occur naturally outside of the Americas, although triatomine bugs are found throughout the Western Hemisphere and the Orient. The vectors occur in the Caribbean, but apparently the disease does not, except in Trinidad and Tobago. *T. cruzi* has been found in raccoons, rodents, other reservoirs and potential vectors as far north as Maryland.

Because notification of authorities is not compulsory and reliable mortality data are scarce, the exact distribution is difficult to determine. Map 1 provides an estimate of distribution.

c. Agent

T. (Schizotrypanum) cruzi, the parasite that causes Chagas' disease, may be a biological complex of species with many characteristic traits. Strain and antigenic differences have been noted from different geographic areas. These variations may explain the geographic differences observed in the pathology of Chagas' disease.

T. cruzi develops into forms infective to mammals in the vector's gut. Although infective parasites may develop in the vector as early as day seven, it usually takes about 15 to 20 days for infective forms to appear in the feces.

Trypanosomes are transmitted to a vertebrate host via the feces of a triatomine bug, usually when the bug is feeding or immediately afterwards. Therefore, the feeding and defecation habits of species of triatomine bugs are important in determining their effectiveness as a vector.

Two life-cycle phases occur in the vertebrate host. In the first phase, the parasite is found in circulating blood. During the second phase, trypanosomes multiply in the cells of the host's tissue. The parasite is intracellular during an asymptomatic incubation stage of one to three weeks.

Triatomine bugs, particularly those of the genus *Rhodnius*, may transmit another trypanosome, *T. rangeli*, to humans and other

Map 1. Distribution of Chagas' Disease

Prepared by the Vector Biology and Control Project
Source: PAHO, 1986

animals. Its range is northern and western South America, Panama and Central America. Although *T. rangeli* does not appear to cause disease in humans, its presence may complicate diagnosis of *T. cruzi*.

d. Vectors

Triatomine bugs or "kissing bugs," are the vectors of American trypanosomiasis. It is unlikely that other biting insects transmit the infection. More than 50 species are found naturally infected with *T. cruzi*, but only about 12 species are considered of epidemiological importance. The important vectors are those that infest human dwellings, either actively by being attracted to light and flying into houses or passively by being brought into houses with building materials, personal possessions or firewood.

The genera *Triatoma*, *Rhodnius* and *Panstrongylus* contain the most important domestic vectors: *T. infestans*, *T. dimidiata*, *R. prolixus* and *P. megistus*. These are epidemiologically important species because of their wide geographical distribution, close association with humans, and blood-feeding and defecation habits.

Nymphs and adult triatomines take blood meals and can become infected with *T. cruzi*. Once a bug is infected, it tends to remain so for life. Consequently, the percentage of bugs infected with *T. cruzi* increases with each developmental stage. There are times, however, when few parasites are passed or the infection may be lost during metamorphosis.

Certain sylvatic species may be becoming established in peridomestic and domestic habitats. Bugs are found in houses in racks, behind wall hangings, and in other sheltered places in walls, roofs, floors, boxes, clothing and beds, where darkness offers protection from enemies. *T. dimidiata* is usually found in the lower third of a wall, on dirt floors, or in woodpiles. *T. infestans* is more frequently located in upper walls or roofs.

e. Reservoir Hosts

Armadillos, raccoons, opossums and rodents are important sylvatic reservoirs because they enter human environments.

More than 150 wild mammals have been found infested with *T. cruzi*. Transmission also may take place when a reservoir animal eats an infected bug.

In human environments, domestic animals replace wild animals as hosts. Dogs and cats are considered important reservoirs in most endemic areas. The guinea pig is particularly important in Bolivia and Peru, where it is raised in households for food. The common rat is a major domestic reservoir in Panama and Costa Rica. Goats, pigs and other domestic mammals have been found infected.

2. Distribution and Severity

About 90 million people, or 25 percent of Latin America's population, are at risk of infection and at least 16 million of them are estimated to be infected with *T. cruzi*. After the latent phase, 27 percent of those infected develop heart problems that may lead to sudden death, six percent develop digestive system abnormalities, and three percent present damage to the central nervous system. Chagas' disease is believed to be the most common cause of congestive heart failure in South America.

a. Geographic distribution

Few systematic studies have been conducted to provide adequate information about the distribution and severity of Chagas' disease in Latin America. The following list is not exhaustive, but summarizes the information available from a number of the A.I.D.-assisted countries in the endemic area (see map, p.6).

Belize

Several species of vectors infected with *T. cruzi* have been found in houses and human cases of Chagas' disease have been reported.

Bolivia

Chagas' disease is endemic in about 83 percent of the country, where 47 percent of the population lives. Chagas' morbidity and mortality are believed to be highest in Bolivia. The Ministry of Health estimates that six pregnant women and seven newborns die from acute Chagas every day.

In five surveys conducted since 1977, seroprevalence has ranged from 45 to 70 percent. Seroprevalence in pregnant women ranged from 25 to 50 percent, with rates as high as 80 percent in some surveys, and rates of infection in infants born to chagastic mothers from 8 to 36 percent. Of 268 blood donors in Santa Cruz, 63 percent had *T. cruzi* antibodies. The Bolivian government is establishing the first national control program under A.I.D.'s child survival project, with technical assistance from the VBC Project.

Costa Rica

It is estimated that 12 percent of the population is infected and as many as 45 percent live in the endemic area. Of 1,420 people examined in one study, 11.7 percent were seropositive and 24.3 percent of the infected population had ECG abnormalities compatible with Chagas's disease. This study also found that 24.6 percent of houses were infested and 30.9 percent of bugs dissected were infected with *T. cruzi*. Socioeconomic changes, including installation of cement floors and removal of firewood stored near houses, reduced infestations. In another study in San José, 7.6 percent of 221 blood samples examined were seropositive.

Ecuador

Although it is estimated that only one percent of the population is infected, about 41 percent live in endemic areas. Control activities begun in 1980 have been discontinued. Chagas' disease occurs in the provinces of Manabi and Guayas. The largest number of cases is reported from Guayaquil. A survey that did not include Guayaquil found that 1.2 percent of 3,602 houses were infested and 10.7 percent of 532 people had antibodies for *T. cruzi*. Of 1,057 blood samples from blood banks, 3.2 percent were seropositive.

El Salvador

Approximately 43 percent of the people live in endemic areas. Vectors have not been reported below 120 meters or above 1400 meters. Between 30 percent and 80 percent of houses in small villages and rural areas in endemic zones may be infested, with 25 percent of the bugs infected with *T. cruzi*. One survey showed that 38.9 percent of 211 houses were infested and 14.0 percent of the bugs examined had *T. cruzi*. Of 487 people sampled in rural communities, 20.5 percent had *T. cruzi* antibodies. In San Salvador, 8.7 percent of 537 blood samples from blood banks were seropositive.

Guatemala

Eighteen percent of the population is estimated to be seropositive and 52 percent live in the endemic areas. The departments of Chiquimula, Jalapa, El Progreso, Santa Rosa and Zacapa are most endemic for *T. cruzi*. A survey by the Univer-

sity of San Carlos found house infestations of 31.0 percent and *T. cruzi* antibodies in 16.6 percent of those tested. Of 1,052 blood donors tested in Guatemala City, 110 (10.4 percent) were seropositive. Other blood bank surveys showed 7.8 percent of 1,132 samples and 11.4 percent of 551 samples positive.

Honduras

A study indicated the following degrees of infestation with triatomine bugs: 14.8 percent of houses in a high mountain region near the Pacific; 3.6 percent of houses in a lower mountain region, including the Caribbean coast; and no houses in low swampy regions and Caribbean islands. Seropositivity in the sampled population was 16.3 percent for high mountains, 4.4 percent for low mountains and 0.2 percent for swampy areas. Fifty nine (15.6 percent) of 378 blood donors from the high mountains and 28.0 percent of 50 donors from Tegucigalpa were seropositive.

Panama

Vectors are found in seven provinces and the Canal Zone, with house infestation rates up to 16 percent. In a serological survey, 303 (22.3 percent) of 1,361 people in central Panama were seropositive. The estimate for the entire country is 24 percent. No *T. cruzi* antibodies were found in children younger than 10 in western Panama.

Peru

Chagas' disease is most prevalent in the southwest and northeast of the country. One-third of the people live in the endemic zone and about 10 percent are seropositive. A sample of 329 bloods from the department of Tacna yielded 12.9 percent with *T. cruzi* antibodies. More than 13 percent of houses in the department of Arequipa were infested and 27.6 percent of the bugs examined had *T. cruzi*. In the department of Moquegua, 19.1 percent of houses were infested and 27.5 percent of the bugs infected. For Tacna, 3.6 percent of the houses were infested and 7.1 percent of the bugs infected.

A control program covering 119,500 square kilometers began in the southeast in 1965. Control reduced house infestation by 90.1 percent in Moquegua.

Uruguay

The endemic area covers 125,000 square kilometers, with a population estimated as high as 950,000 and seropositives varying from 4.5 to 15.7 percent. It is estimated that between one and six percent of houses are infested and 4.8 to 12.4 percent of the triatomines are infected. A sample of 329 blood samples from blood banks yielded 5.5 percent seropositives.

b. Child survival

The acute phase of Chagas' disease is far more severe in young children than in adults and can cause death in those younger than two. Therefore, the disease has a serious impact on child survival in the countries where it is endemic. Studies in Bolivia found that eight percent of newborns suffered from congenital Chagas' and 13 percent of acute cases in children developed into chagastic meningitis. The Ministry of Health estimates that seven newborns and six pregnant women die from Chagas' every day in Bolivia.

c. Economic Impact

Few studies have examined the economic impact of Chagas' disease. In Brazil, where prevalence is about four percent, annual economic productivity losses due to Chagas' are estimated at $250 million. Brazil loses an additional $5 billion a year because of absenteeism caused by Chagas' disease. These costs have not been calculated for Bolivia, where the estimated prevalence of Chagas' infection is 40 percent. A study in Brasilia estimated a loss of 2,275 working years per 100,000 men and 1,363 working years per 100,000 women due to premature death from Chagas' disease.

3. Control Measures

It is possible to control domestic cycle transmission of Chagas' disease through housing improvements and by spraying houses and outbuildings with residual insecticides. Because it may take decades for the chronic phase of the disease to be expressed, control does not stop human cases from occurring at once, but serological surveys have shown that vector control can halt transmission and ultimately reduce the caseload.

a. Diagnosis and Surveillance

Early diagnosis and treatment are essential because Chagas' disease is virtually untreatable in the later chronic phase. TDR has established a network of laboratories to facilitate field collection of blood specimens. As a rule, a single serological test may be done for field surveys, but two or more tests are recommended before declaring a patient infected. In remote areas in most countries, portable battery-driven electrocardiograph machines are used to identify heart abnormalities characteristic of Chagas' disease. Reasonably specific and standardized guidelines for interpreting ECG abnormalities suggestive of Chagas' disease have been in use for several years and provide a relatively reliable indirect measure of morbidity.

Direct blood examination is of value only during the acute phase. The chances of finding parasites are increased by centrifugation of the blood using the strout or micro-strout method. Blood and tissue cultures and animal inoculations are done experimentally. In areas with *T. rangeli*, care should be taken not to confuse it with *T. cruzi*.

Xenodiagnosis is a common diagnostic method. Uninfected triatomines are allowed to feed on suspected cases and are examined 15-20 days later for parasites. Artificial xenodiagnosis techniques have been developed so that the bug does not have to feed directly on a person. Blood is drawn from people who may be infected and "clean" vectors feed on this blood through a membrane. Because of possible allergic reactions, xenodiagnosis is used in clinics or hospitals more than for field surveys. Parasite concentration through centrifugation is replacing xenodiagnosis in some laboratories.

Control activities are evaluated by house checks for bug infestation and by serological surveys, particularly of young people.

b. Chemotherapy

Widely applicable chemotherapy is not available because nothing effectively eliminates intracellular parasites. Two drugs that diminish parasitemia and reduce the risk that an autoimmune response will trigger the chronic phase are used for the acute stage. There is no good evidence, however, that they are effective against chronic infections.

These trypanocidal drugs are nifurtimox (Lampit^{R}), which is given at a dose of 10 mg/kg body weight to adults and 15 mg/kg to children for 60 to 90 days, and benznidazole (Rochagan^{R}), given at a dose of 5 mg/kg body weight for 30 to 60 days. Both are taken orally. They produce side effects such as gastrointestinal upset and disorientation. The susceptibility of different strains of *T. cruzi* to these drugs varies. Strains from Argentina and Chile seem to be more susceptible to nifurtimox than some Brazilian ones. Treatment failures occur with both drugs. Early diagnosis and treatment seems to improve the chances for a cure.

c. Vector control

The strategy for Chagas' disease vector control consists of three phases: preparation, attack and vigilance. Until recently, control efforts have been vertical, centralized programs. This system is beginning to break down and decentralization with community involvement is being advocated.

In the preparatory phase, each house is numbered, the community mapped, demographic information gathered and a program of health education begun. Houses and outbuildings are examined for living bugs or signs of their presence. Synthetic pyrethroids or other irritants may be used to drive bugs from hiding places. Captured bugs may be dissected for parasites. Baseline data on house infestation, species of vectors involved and bug infection rates are collected.

The attack phase consists of a cycle of applications of residual insecticide to roofs, walls, floors (depending upon the vector) and furniture in houses and outbuildings. Premises are checked for bug infestations between insecticide applications or just before the next application. Frequency of applications is determined according to abundance of bugs capable of reinfestation, species of vector, type and formulation of insecticide, surface treated and climate. Fenitrothion and other organophosphate insecticides must be applied two or three times a year. Some synthetic pyrethroids are applied only once a year.

Insecticides are usually applied with hand compression sprayers, but motorized backpack sprayers also have been used. Commercial slow-release, microencapsulated formulations in paint can extend the residual life of some insecticides for two or more years. Some of the newer pyrethroid compounds that have residual action are being used or tested in some programs.

Bug-free communities are monitored for signs of reinfestation in the vigilance phase. In regions where there are abundant sources of bugs capable of reinfestation, some form of control must continue.

Residual spraying of houses with DDT for malaria control may have reduced the distribution and abundance of triatomine house infestations in some areas, even though DDT is a poor insecticide against these vectors.

d. House Improvements

Recently the contributions of improved land use and integrated rural development to reducing house infestations have gained greater recognition. Efforts in Brazil, Bolivia and Venezuela have demonstrated that housing improvement is an effective method of control. For more than 30 years, Venezuela has provided new houses to rural families who meet certain income requirements. As rural income increased, there was a tendency for palm roofs to be replaced with corrugated metal ones, which reduced *R. prolixus* infestations in Venezuela.

Most house improvement programs attempt to change roofs and make the walls free from cracks. Problems arise when the infrastructure is weak, particularly around door and window

frames. Brazilian workers have had some success coating house frames with an insecticide-impregnated black paint.

It is harder for vectors to establish colonies in new or improved houses. Infestation is affected by proximity to domestic animal shelters, wild vectors and reservoirs, type of construction materials and standards of hygiene. Personal effects and new houses should be sprayed before the houses are occupied. The old house should be destroyed and outbuildings, fences and other potential bug habitats should be repaired and treated with residual insecticides.

House modification and insecticide application strategies will not be successful or sustainable unless people understand and value their importance. Effective community-level education programs about Chagas' disease control and prevention must be developed to support these interventions and enlist community involvement.

e. Protecting blood supplies

Blood supply contamination with *T. cruzi* is increasing rapidly in Latin America. Reports of Central American residents in the United States carrying antibodies of *T. cruzi* have also caused serious concern. Some countries in Latin America, including Argentina, Brazil, Honduras, Uruguay and Venezuela, have established compulsory systems for screening Chagas'-infected blood in blood banks.

Gentian violet at a ratio of 1:4000 (125 mg/500 ml blood) can be added to clear the blood in blood banks 24 hours before it is used for transfusions. However, in most places blood is not held long enough for gentian violet to act. TDR sponsored a program to screen potential trypanocidal compounds already licensed and registered for human use as additives to sterilize blood in blood banks. Unfortunately, no compound has been found to replace gentian violet.

f. Vaccines

Development of vaccines for Chagas' disease may be slow and some approaches may be impractical because of the possibility of

an autoimmune response that could stimulate pathology as well as immunity. Another problem is that the goal of vaccination is to prevent the chronic phase, so evaluation might not be completed for decades. On the positive side, antigens that have been studied do not seem to cross-react with human heart and connective tissue components.

g. Constraints to control

Constraints on control efforts include the high cost of insecticides and their short residual effect, logistical considerations such as widely dispersed housing and the size of infested areas, public acceptance of house treatments, safety of handling insecticides, labor problems within programs and lack of supervision. Many countries do not have control programs because of the competing needs of existing malaria control activities, lack of an adequate rural health structure, scarcity of epidemiological information, and financial limitations.

Technical

Surveillance and treatment efforts are hampered by the difficulty of interpreting serological tests and the lack of a "dip stick" test for use in the field. Several serological methods are available, but the results are difficult to interpret and there is little standardization among laboratories. The older serological methods lack specificity and the more recent ELISA test requires reagents that are often difficult to obtain in endemic countries.

The alternative, xenodiagnosis, is slow because it takes two to four weeks for infective forms of the parasite to develop in the vector. Furthermore, only about 50 percent of people with *T. cruzi* antibodies are positive by xenodiagnosis. Besides allergic reactions, basic constraints include the availability of adequate triatomine bug colonies, the danger of infesting areas with exotic species when the technique is used in the field and people's understandable reluctance to being bitten by bugs.

There is no treatment for the chronic phase of Chagas' infection. Current trypanocidal drugs are estimated to be effective in treating 75 to 95 percent of recent *T. cruzi* infections in the acute phase, but few cases are seen for treatment.

Human resources

The lack of well-equipped serological laboratories and trained microscopists is also a constraint to early detection and treatment. Adequate labor is usually available in endemic countries for control activities. It is not difficult to train workers to spray houses and evaluate activities because many countries already have malaria and *Aedes aegypti* control programs. The problem is staff distribution, supervision and payment of salaries.

National programs have training courses for workers and mid-level supervisory staff. Venezuela has a senior level international course on control of rural diseases, including Chagas' disease. Several Latin American universities offer MPH courses with specialization in vector-borne diseases and epidemiology. A Master of Science in Vector Control and Medical Entomology is offered by the University of Panama and the University of Nuevo Leon in Monterrey, Mexico. Nevertheless, it is difficult to recruit professional staff members for vector control because advancement is slow, salaries are low and futures uncertain.

Economic

Chemical control and house improvement require long-term support in order to be effective. Chemical control is a recurrent, short-term control tactic. Costs vary, but in most cases labor accounts for 50 percent or more of the cost of the operation. For example, because deltamethrin can be effectively applied only once a year, the annual cost of using it in Brazil is about the same as that of the much cheaper benzene hexachloride (BHC), which is applied more frequently.

House improvement is an initially expensive, but potentially more sustainable approach. In three projects in Bolivia, the cost of non-local building supplies has been US $85 to $95 per house. The community covers about 20 percent of the total cost of house modification. Housing projects, however, are constrained by migration, land ownership, lack of motivation and the inability to pay for improvements. There is criticism that new houses are not properly designed or built for rural cultures and that it is impossible to provide new or improved housing at a rate that will satisfy the demand.

4. Current Research

a. Diagnosis

Most serological tests for Chagas' infection are difficult to interpret. TDR has established a network of collaborative laboratories to develop protocols to standardize reagents, techniques and procedures for serological diagnosis and to evaluate reagents from other laboratories.

Antigens of two stages of the *T. cruzi* life cycle have been isolated and tested for serodiagnosis. Monoclonal antibodies (MAbs) and their potential for specific immunodiagnosis of Chagas' disease are being studied. Laboratories are developing MAbs that may be useful for detecting trypanosome antigens. A specific diagnostic test uses purified cell membrane antigens fixed on polyamide strips. Radioimmunoprecipitation assays are being tested by a network of laboratories in Argentina, Brazil and Venezuela.

Research to improve xenodiagnosis includes evaluations based on number and species of vectors used, frequency of tests, number of days required to hold bugs before examination and methods of dissection of vectors.

b. Chemotherapy

In addition to research on parasite clones and the ultrastructure of the parasite, studies are being conducted to determine the specific role that antibodies play in host resistance to *T. cruzi*, how immunoglobulins may limit parasitemia, and the possible therapeutic importance of metabolic pathways.

Mouse, rabbit and monkey models show promise for studies of the pathogenesis of chronic infection and for use in chemotherapeutic trials. Important research questions include the basic biochemistry and mode of action of drugs being screened.

The therapeutic efficacy of allopurinol is being evaluated. In preliminary studies, this drug was as effective as nifurtimox and benznidazole in suppressing or eliminating parasitemia, but it caused fewer and less serious side effects.

c. Vaccine development

The precise immune mechanism involved in host tissue resistance to *T. cruzi* and in control of parasitism during the chronic stage is poorly understood. Any vaccine should be effective against all stages and strains of *T. cruzi* and should produce antibodies that do not cross-react with heart or nerve tissue. Research on immunopathology and pathology is being done in Brazil, Venezuela and Argentina.

d. Epidemiology

TDR's epidemiological protocol will make it easier to compare results from various studies. Scientists in Argentina are working on epidemiological models. Emphasis on analytical epidemiological studies may help disclose possible relationships between clinical forms of the disease and different strains of parasite. Electron microscope studies, kDNA probe techniques and isoenzyme analyses are being conducted to improve our understanding of the geographical variations observed in pathology. Epidemiological studies of congenital and blood transfusion transmission are needed, particularly in urban areas where vector transmission is not important.

e. Vector control

With support from TDR, scientists at Argentina's Institute of Science and Technology of the Armed Forces have developed an insecticide fumigant canister that holds great promise for community-based vector control activities. A control program using these canisters and triatomine detection boxes for entomological surveillance in 600 houses in Santiago del Estero, Argentina, succeeded in interrupting transmission of Chagas' through vectors. In four years, seropositivity among the study population dropped from 5.5 percent to 0 percent in infants and from 12.4 percent to 0 percent in children younger than four. The total cost of the program, which was implemented with the help of primary health care workers and community members, was U.S. $4.7 per house per year, five times less than the government's traditional vertical house spraying program.

Insecticidal paints are another promising tool for community-based Chagas' control. A TDR-supported study in central Brazil tested insecticidal paints in 4,800 houses. More than 85 percent of the

treated houses were free of triatomines after 24 months, compared to 60 percent of the control group houses, which were sprayed with BHC twice during the two-year study. TDR has developed a protocol for evaluating the fumigant canister and insecticide-impregnated paints.

A.I.D. has supported the development of traps and physical barriers that may reduce house infestations. Traps are being tested in Bolivia, Brazil and Venezuela. It has been theorized that pyrethroid-impregnated pictures, calendars and papers that hang on walls would be effective in limiting bug infestations. Research on isolation of sex and aggregation pheromones in domestic vectors, the effect of pheromones of one triatomine species on another species, and biochemical analysis of possible attractant pheromones may provide means to improve all of these traps.

Research on house design and construction has been conducted for several decades in Brazil. In cooperation with the Pan American Health Organization (PAHO), Venezuela has evaluated construction materials, cost-effectiveness and the role of community participation in rural housing. Rural development projects in Bolivia, Peru, Ecuador, Costa Rica, El Salvador and Honduras include a housing component. Unfortunately, the long-term effect of housing in transmission of *T. cruzi* is not being evaluated in many of these projects.

There are several types of hand-operated, brick-making rams that can compact stabilized earth as a building material. The London School of Hygiene and Tropical Medicine, PAHO and the Southeast Center for Ecological Research (CIES, Mexico) are interested in developing field projects to evaluate this equipment for use in community-based housing improvement projects.

5. Chagas' Disease from the A.I.D. Perspective

Due to the toll taken in young lives during its acute phase, Chagas' is an important factor in child survival, second only to malaria among vector-borne diseases in endemic areas. It is widely distributed in Latin America and is a significant problem in at least six A.I.D.-assisted countries. Chagas' disease is one of the few diseases that is broadly recognized as a significant health problem in the region, yet little or nothing is being done to abate its transmission because of the extremely limited budgets of most national health programs in Central and South America.

PAHO, the international health agency that works exclusively in Latin America, also has given Chagas' disease research and control relatively low priority. The first World Health Organization (WHO) program was started by VBC/WHO/Geneva in 1973 in Venezuela with a grant from the U.S. National Institutes of Health. This program, which is now a center in Maracay, Venezuela, was subsequently turned over to PAHO. TDR has done a good job of identifying major problems and establishing scientific working groups to consider them, but has had limited resources to contribute to their resolution.

Like those of many other vector-borne diseases, the effects of Chagas' disease are most apparent in the poorest sectors of society. The least expensive forms of housing (mud walls, thatch roofs) provide harboring and breeding sites for the predominantly rural vectors. The potential benefit of linking Chagas' control with other development programs is immediately apparent. Housing that does not provide a home for the triatomid vectors will make long-term control possible with minimal additional input. Unfortunately, insecticides are the only effective intervention used in most vector control efforts. Because of the relatively short-term effect of this approach, treatments must be repeated often. The cost and number of personnel required are often so enormous that such interventions are abandoned or never started.

USAID/La Paz is mounting a large Chagas' control program as a component of its child survival program in Bolivia. The emphasis of the program will gradually shift from insecticide spraying to house improvement and health education. The VBC Project will provide a technical advisor and help train a cadre of national Chagas' control experts. Private voluntary organizations already working in Bolivia will help the program establish links with the community.

a. The Horizon

During the next decade, progress toward the control of Chagas' could be made on several fronts, including diagnosis, chemotherapy, protecting the blood supply, self-help community approaches and vector control. Linking Chagas' control efforts with housing and rural development projects could result in substantial long-term reduction of transmission. Efforts to promote community awareness of the disease, the vectors and their harborage could complement and enhance other interventions.

The advances that have been made in the fields of molecular biology and immunology have opened the door to more effective diagnosis and, in the very long run, a potential vaccine. Early diagnosis and treatment of Chagas' disease are tremendously important because the disease is essentially untreatable if it is not detected early enough. Improved diagnostics also can help remove Chagas'-contaminated blood from the blood bank supply, which is a significant source of secondary transmission.

A more "high-tech" approach to vector control through the use of pheromone and controlled-release toxicants would also increase the efficacy and efficiency of Chagas' control efforts.

b. Priorities for future action

TDR has stimulated the research community, particularly in Latin America, to coordinate its research activities in areas contributing to a better understanding of the biology of *T. cruzi* and certain aspects of the transmission of Chagas' disease. There are other critical areas of applied research that could produce significant results, including:

- Intersectoral efforts to improve housing and integrate Chagas' control with PHC or community participation. The potential for using the community to improve housing has been demonstrated in Argentina, Brazil and Venezuela. Social scientists should be encouraged to seek solutions to constraints to control that are related to human behavior.

- Pilot projects to provide information on effective ways to use health education for community-based control and surveillance.

- Assistance from primary health care systems in affected countries in implementing some of the appropriate community-based control measures mentioned above.

- Development and use of new methods of control, including insecticide-based paints for vector control and toxic-baited traps based on pheromone attractants.

- Development of cheap, accurate serodiagnostic techniques to identify contaminated blood supplies. Testing of blood supplies and products for Chagas' in endemic countries could be linked to programs to screen all blood and blood products for HIV.

- Improved insecticide application methods, particularly development of better slow-release formulations for use in paints, plastics, bug traps, bed mats and paper. Plastics that cover and seal surfaces but are not insecticidal could limit bug colonization. The private sector should be encouraged to work in this area.

- Research on use of local building materials, particularly for walls and roofing, is essential. Cane or wood used for infrastructures needs to be strengthened for protection from termite destruction and to lengthen the life spans of buildings.

- Development of inexpensive alternatives to gentian violet to clear blood and blood products of parasites. Although effective, gentian violet is not acceptable to many transfusion recipients.

- Research on providing revolving funding for low- or no-interest loans for house improvements suitable to control Chagas' disease vector infestations.

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