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WHO Expert Committee on the Control of Chagas Disease

Buenos Aires, 16–21 October 1989

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1. Introduction

A WHO Expert Committee on the Control of Chagas Disease met in Buenos Aires from 16 to 21 October 1989. Dr R. Bektimirov, Assistant Director-General, opened the meeting on behalf of the Director-General.

Chagas disease is a permanent threat to almost a quarter of the population of Latin America. It occurs throughout the subcontinent, but the disease manifestations and epidemiological characteristics are highly variable from one endemic area to another. There is a wide variety in prevalence rates, modes of transmission, parasite characteristics, clinical pathology, vectors, and reservoir hosts. More than any other parasitic disease, Chagas disease is related to social and economic development: the triatomine bugs and the disease they transmit will persist so long as poor housing, frequent migration of people, and rapid urbanization are common features in Latin America. It will be many years before these conditions change. Until that time, efforts to control Chagas disease must continue.

At an estimated total of 100 million people at risk and 16-18 million infected, Chagas disease represents a serious health problem in 17 countries. In many others, although the vectors are present and the parasite (*Trypanosoma cruzi*) may be isolated from animal reservoirs, humans seem only sporadically infected. Transmission by blood transfusion has increasingly been reported as the cause of new infections outside the foci of natural transmission.

In the past two decades, awareness of Chagas disease has grown considerably, among both scientists and public health authorities. Investments in research programmes have increased with national and international support. At all levels, international exchange of scientific ideas, materials, and technical standards has been intensified. Notably, the UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases has contributed to coordinating various research activities and to mobilizing human and financial resources.

At the same time, several countries have initiated or reinforced national control programmes, some with impressive success. These programmes serve as convincing evidence that the current control methods, if sustained, can be effective. The investments made in terms of national skill, health facilities, and finance reflect a political and technical commitment at national level that is of crucial importance for the development of long-term control programmes. In other countries, pilot programmes originating from local initiative exist without forming part of a structured national strategy. Finally, there are countries where the distribution and prevalence of Chagas disease are unknown and no control programmes exist.

Establishing a national policy or programme for Chagas disease control requires the multisectoral involvement of sociologists, economists, engineers and biologists – and, above all, a commitment of the country's

political leaders. Definition of a national control strategy is a complex decision-making process, and, inevitably, national strategies must be a compromise between the ideal control needs and the restricted resources.

In this report of the first WHO Expert Committee on Chagas Disease an effort is made to provide technical guidelines relevant to the planning, implementation, and evaluation of national control programmes; and current knowledge of the disease and its pathogenesis, the parasites and criteria for their identification, and the vectors and reservoirs of infection is critically reviewed. The options for control and their cost-effectiveness are discussed, and strategies for a variety of circumstances are outlined.

2. Basic information on Chagas disease

Chagas disease, or American trypanosomiasis, is a chronic parasitic disease caused by a flagellate protozoan, *Trypanosoma cruzi*. This parasite is normally transmitted to humans or other mammals by triatomine bugs, of the family Reduviidae, at the time when they pierce the skin to suck the blood on which they feed. It is not, however, inoculated directly through the bug's mouth-parts by the action of biting, as is the case in the African trypanosomiases, but is passively deposited in the bug's faeces on the skin, and penetrates into the body through the bite wound or through other abrasions in the skin or mucosa. *T. cruzi* can also be transmitted congenitally or by the transfusion of contaminated blood or the transplantation of contaminated organs. The life cycle of the parasite is long and complex, with several developmental stages both in the triatomine vector and in the vertebrate host.

2.1 Clinical stages and forms

Three stages are recognized in Chagas disease: a short acute stage and a long-lasting chronic stage, separated by a long clinically asymptomatic phase, called the indeterminate stage. Different organs may be involved at any time in the first and third stages, and the disease can be fatal in either.

2.1.1 *Infection transmitted by triatomine vectors*

Acute stage

The acute stage is characterized by general malaise with a variety of clinical manifestations. The symptoms can be very mild and atypical and consequently the disease is often not recognized at this stage; indeed, it is diagnosed in only 1% or 2% of all patients, passing unnoticed in the remaining cases. Acute Chagas disease can develop at any age, but in the highly endemic areas the cases that are recognized are usually detected in persons less than 15 years old, and mostly in children under 10. The younger the patient is, the more important are the clinical manifestations, with very severe and even fatal disease occurring below the age of 2 years.

The local inflammation at the portal of entry of *T. cruzi* is called a chagoma. The signs and symptoms are different according to the site of infection. When an infection occurs through the conjunctiva or the skin of the eyelid, a reddish, painless, periophthalmic cellulitis develops with characteristic unilateral and bipalpebral oedema of the eyelids and regional lymphadenitis. Chagoma of the eye (Romaña's sign) is seen in more than 90% of the patients diagnosed as recently infected. Infections in other parts of the body are less characteristic: they may resemble erysipelas or skin tumour or take the form of one or several furuncles or subcutaneous nodules. Such lesions may also be associated with regional lymphadenitis.

General symptoms of acute Chagas disease are fever, enlarged liver and spleen, generalized oedema, and swollen lymph-nodes. Sometimes, a generalized exanthematous rash, anorexia, diarrhoea, and vomiting may also occur. Up to 30% of cases show electrocardiographic or radiological abnormalities due to acute myocarditis of different degrees. The main abnormalities observed in electrocardiographic readings are sinus tachycardia, prolongation of the P-R interval, primary T-wave changes, and low QRS voltage. Chest X-ray can reveal cardiomegaly of varying degrees of severity. Mortality from acute myocarditis occurs in 2-3% of cases, mostly at less than 2 years of age. In the remaining cases, the symptoms subside spontaneously within 4-8 weeks without clinical sequelae in the short or medium term. A severe complication of the acute stage is meningoencephalitis, which, again, is mainly seen in children under 2 years old; the clinical picture consists of convulsions, with or without fever, and varying degrees of loss of consciousness. The mortality in cases with meningoencephalitis can be as high as 50%.

Indeterminate stage

The indeterminate stage begins some 8-10 weeks after the acute stage, whether there have been clinical manifestations or not. This stage may last several years or persist indefinitely. It is characterized by the absence of clinical symptoms, the subjects being fully capable of normal physical activity and showing normal electrocardiograms and chest X-rays. However, serological tests for Chagas disease remain positive, and parasitaemia, though not detectable by direct parasitological methods, can be recognized by xenodiagnosis (see section 7.1.1) in 20-60% of cases. During the indeterminate stage, most patients are unaware of their infection with *T. cruzi* and over this long interval form an important reservoir of infection and contribute to maintaining the life cycle of the parasite.

Chronic stage

It is estimated that up to 30% of persons with the indeterminate form of the infection will suffer from cardiac, digestive, or neurological damage 10-20 years after having contracted the disease, while the remainder will never exhibit any manifest organ involvement.

Cardiac form. The cardiac form of chronic Chagas disease is the most studied, the best known, and the easiest to diagnose. The clinical manifestations depend on the degree of myocardial damage, the presence of arrhythmias, and the degree of heart failure. The most frequent symptoms are palpitations, dizziness, syncope, dyspnoea, oedema, and chest pain. By chest X-ray the degree of heart enlargement can be determined and electrocardiography shows typical ventricular conduction defects and arrhythmias. The most frequent ventricular conduction defects, which may be either isolated or combined, are block of the right bundle branch and left anterior hemiblock. Different degrees of atrioventricular (A-V) conduction defects and even complete A-V block can also be seen. The most important complications are systemic and pulmonary embolism and sudden death (*1*).

In chronic Chagas disease almost any variety of arrhythmia may occur. Sick sinus syndrome with sinus bradycardia and sinoatrial block is frequently seen, as are ventricular premature beats. These are usually polymorphic and appear isolated, in couplets, or in episodes of ventricular tachycardia of variable duration. Sustained ventricular tachycardia can cause life-threatening haemodynamic disorders. Of the ventricular arrhythmias, ventricular fibrillation is the most important and probably the most frequent mechanism of sudden death in patients with chronic Chagas disease. Primary T-wave changes and pathologically abnormal Q waves are also seen. Nuclear imaging and cineangiography show different degrees of ventricular dyskinesia or akinesia, and in many cases a typical aneurysm at the apex of the left ventricle. The coronary arteries are not affected.

Digestive form. Any portion of the digestive tract can be involved in chronic Chagas disease but the most commonly affected segments are the oesophagus and the colon. Significant lesions in the intramural nervous plexus are associated with peristaltic disturbances. There may be progressive dilatation of the oesophagus, accompanied by variable degrees of regurgitation and dysphagia. Radiological examination of the oesophagus may show contraction abnormalities in the initial stages of the disease. Similarly, coordination of colonic movement is lost, leading to severe constipation and dilatation. The most important complications of the megacolon are faecaloma and acute volvulus. Mega-oesophagus and megacolon may coexist with various degrees of heart lesion (*2*).

Neurological symptoms. Chronic Chagas disease can lead to involvement of the central, peripheral, or autonomic nervous system. These neurological changes have been the least studied and are therefore the least well known of the chronic forms of the disease. In certain endemic areas, pareses, functional disturbance of the cerebellum, convulsions, and psychiatric abnormalities have been observed as a consequence of lesions of the central nervous system or of secondary lesions after an acute episode of meningoencephalitis as part of the acute stage.

Recent studies have shown that in the chronic stage of the disease there may be a definite involvement of the motoneurons of the spinal cord. In such patients, involvement of the sensory peripheral nervous system, with alteration of dorsal root ganglia and a generalized loss of the sensory axons, has also been observed.

Alterations of the autonomic nervous system have been recognized in histological as well as in functional studies. The histological studies have shown neuronal damage in the intestine and heart.

Various functional tests that analyse the behaviour of physiological indicators of autonomic nervous system activity – such as heart rate, blood pressure, gall-bladder contractility, skin temperature, and skin conduction level – have shown alterations of the sympathetic and parasympathetic nervous systems. These alterations have been demonstrated early in the chronic phase of the disease, even before any heart or intestinal damage has become evident. The early appearance of irreversible alterations in the autonomic nervous system suggests that this is part of a pathogenic mechanism common to all the manifestations of chronic Chagas disease.

2.1.2 *Infection acquired through blood transfusion*

Most of the more than 200 cases of *T. cruzi* infection caused by transfusion of contaminated blood that have been reported to date have been in adults. It is suspected that many more cases are either inapparent or unrecognized.

The incubation period varies from 3 weeks to more than 3 months. Patients are sometimes unsuccessfully treated with antibiotics because of a persistent fever. General lymph-node enlargement and splenomegaly are frequent among infected patients, but eventually the fever and other signs will disappear, even without treatment, after 1-2 months (*3*).

2.1.3 *Congenital Chagas disease (4)*

Intrauterine *T. cruzi* infection can cause abortion or premature birth, in which case symptoms may appear soon after delivery. The most common finding is hepatosplenomegaly. Other less frequent observations concern neurological symptoms such as convulsions, hyporeflexia, hypotonia, tremors of the arms and legs, and apnoea. Fever, icterus, and oedema may occur, and metastatic haemorrhagic chagomas are sometimes seen in the skin and/or mucosa. There are usually no signs of cardiac involvement, but when they are present, cardiac failure is rare.

Serological findings have included anaemia, leukocytosis with lymphocytosis, hyperglobulinaemia, hypoproteinaemia and, on several occasions, hyperbilirubinaemia. The cerebrospinal fluid may be normal or may show lymphocytes and an increase in globulins, independently of the presence of symptoms indicating lesions of the central nervous system.

The electrocardiogram is usually normal, although it may show low-voltage complexes, a decreased height of the T wave, and a prolonged A-V conduction time.

The prognosis is not favourable in cases with involvement of the central nervous system, haemorrhagic tendency and gastrointestinal, pulmonary or urinary infections. About 50% of the prematurely born die as a consequence of the infection.

Although most reported cases are in the premature, cases of transplacental infection are now increasingly being reported in full-term deliveries. In such cases, the only symptoms may be a mild hepatomegaly or hepatosplenomegaly, without involvement of the central nervous system. Sometimes, the infection is well tolerated and remains symptomless, even in the presence of parasitaemia and other positive serological findings.

2.2 Pathology

Lesions are found during the acute as well as the chronic stage of the disease.

2.2.1 *Acute stage*

Portal of entry. Lesions at the portal of entry are similar whether they occur in the conjunctiva or in the subcutaneous tissue. Early reactions are mainly nonspecific, such as vascular congestion, oedema, and peripheral leukocyte infiltrations; later, lymphocytes and monocytes predominate; and later still, an invasion of the tissue by fibroblasts, giant cells and lymphocytes may be observed. In the few cases in which a biopsy of satellite nodes has been made, the lesions have been compatible with an acute nonspecific adenitis with proliferation of histiocytes in the sinusoids; sometimes multinucleated giant cells (with or without parasites) may be seen.

Heart. The pathology may vary from no alteration in the heart muscle fibres to muscle cells parasitized with amastigotes (the intracellular stage of the trypanosome), with or without a peripheral inflammatory reaction. Findings have included muscle fibres full of parasites with signs of myocytolysis, penetration of macrophages into the fibres, free parasites or macrophages with phagocytosed parasites, and infiltration of lymphocytes, monocytes, and/or polymorphonuclear cells and sometimes eosinophils.

Nervous system. The histopathological lesions are those of acute meningoencephalitis. The meninges show vascular congestion, haemorrhagic microfoci, and inflammatory infiltration with polymorphonuclear cells, lymphocytes, plasmacytes, and macrophages, with or without amastigotes. Parasites may be found free in the perivascular spaces or nestled within the glia or neuronal cells. Similar tissue manifestations may also be found in the cerebellum and in the medulla.

2.2.2 *Indeterminate stage*

It is difficult to evaluate the pathological findings that have been described for this stage of *T. cruzi* infection since autopsy-based studies may include individuals who are already in the chronic stage. The relatively small amount of biopsy material collected from people during the indeterminate stage of the disease may not be sufficient to obtain a representative picture of its pathology. The available information, however, including that from experimental studies, shows that the following changes may occur: (a) fibrosis, periganglionitis, and reduction in the number of neurons in the autonomic nervous system, especially in the parasympathetic sector; (b) focal fibrosis (cicatricial) involving the sinus node and the A-V conduction system; and (c) mild focal myocarditis. However, there may also be a complete absence of lesions (*5*).

2.2.3 *Chronic stage*

The main lesions associated with human Chagas disease are chronic cardiomyopathy and visceromegalies. Either or both may occur in a patient.

Cardiomyopathy

This is a dilated type of cardiomyopathy, often with mural endocardial thrombosis, which may be the source of embolism, both pulmonary and systemic. Over half the patients present typical focal thinning of the myocardium or aneurysm at the left ventricular apex, which is considered to be pathognomonic for chronic Chagas heart disease.

The most important histological findings are: (a) diffuse, severe, active chronic myocarditis, with lymphocytes and macrophages as the predominant cell types, but with variable numbers of plasmacytes and eosinophils; (b) hypertrophy of myocardial fibres, sometimes accompanied by focal atrophy and myocytolysis; (c) replacement of myocardial fibres by focal and interstitial fibrosis; and (d) inflammatory, fibrotic, and vascular changes of the conductive tissue.

Advanced histopathological reactions can be observed on systematic, serial examination of the conducting tissue. The sinus node frequently shows condensation of the fibrous stroma, atrophy, and fragmentation of specific fibres. Alterations in the A-V conduction system are frequent. There is usually a good correlation between the electrocardiographic and histopathological findings. The right bundle branch is the most damaged part of the system, probably owing to its long and undivided intramyocardial course. Cases with a total persistent A-V block do not show a unique disruptive lesion, but rather a series of changes scattered throughout the conduction system, sometimes giving morphological evidence of a progressive destructive process. Fatty tissue sometimes replaces the damaged conducting tissue. Its low electrolyte content makes it the least conductive tissue of the body. In addition to chronic inflammation and fibrosis, there are vascular lesions, such as

phlebosclerosis, thickening of the intima, telangiectasia, arterial muscular hypertrophy, and, occasionally, small-vessel thrombosis.

Demonstration of parasites in the myocardial lesions can be made in only about 15-30% of the cases, on thorough examination by routine light microscopy. In positive cases, rare parasites can occasionally be demonstrated in the tissues of other organs (intestines, oesophagus, uterus, kidney, adrenals, urinary bladder, etc.). Outside the heart, the parasites seem to provoke only mild lymphocytic infiltrations or no reaction at all.

The changes summarized above are found in patients dying from progressive cardiac failure, but there is now pathological evidence that patients with *T. cruzi* infection but without apparent signs of heart failure may, after sudden death from causes other than Chagas disease, present either minor pathological changes or the fully developed picture of chronic cardiomyopathy described above. Advanced myocardial lesions may therefore occur during the indeterminate stage in the absence of evident clinical symptoms (*6*).

Megaviscera

There are no specific gross or microscopic findings that can differentiate chronic mega-oesophagus or megacolon associated with *T. cruzi* infection from intestinal dilatations due to other causes (congenital, ulcerative, etc.) except for the extremely rare demonstration of *T. cruzi* amastigotes in smooth muscle cells. The few microscopic changes observed in mega-oesophagus and megacolon are mild, focal, mononuclear-cell infiltrations in the muscular coat and in the myenteric plexus. There is also fibrosis in the plexus and disappearance or considerable reduction in the number of neurons. Less marked but similar changes without distension can sometimes be observed in the oesophagus or colon of asymptomatic individuals.

Severe inflammation accompanied by degenerative and necrotic lesions of the neurons of the myenteric plexus has been described during the acute phase of *T. cruzi* infection, both in humans and in experimental animals. However, these lesions are not comparable to the high degree of inflammatory lesions and fibrosis seen in the heart in chronic disease.

2.2.4 *Congenital infection*

The organs with the most lesions in congenital infections are the heart, oesophagus, intestines, brain, skin, and skeletal muscle. The inflammations, which are sometimes perivascular, consist of mononuclear cells and often polymorphonuclear leukocytes. *T. cruzi* has been found in the skin, skeletal muscle, oesophagus, and heart of fetuses and stillborn children, and of full-term infants who have died shortly after delivery. Amastigotes are mostly found in the skeletal and cardiac muscle fibres or in the cells of the reticuloendothelial system, often associated with giant cells with a single lobulated hyperchromatic nucleus and cytoplasm full of parasites, but with no inflammatory reaction.

2.3 Pathogenesis

Several attempts have been made to explain the fact that the pathological changes in the heart and hollow viscera that are characteristic of chronic Chagas disease can occur when few or no parasites are present. The fact that there seems to be no relationship between the localization of the tissue lesions and the concentrations of parasites, and that the mononuclear inflammatory foci in the myocardium do not necessarily correspond to the sites where parasites are present, has been interpreted as an indirect indication that an "allergic reaction" might be involved in the pathogenesis of the tissue lesions. According to another hypothesis, *T. cruzi* may be directly responsible for the destruction of the autonomic nervous system and consequently for the pathological alterations in the myocardium or the hollow viscera. In recent years, it has also been suggested that *T. cruzi* may share antigens with host tissues and thus trigger an autoimmune response. Yet another possibility is that parasite antigens bind to host cells and that these cells become targets of the host's immune response. Present knowledge is based on human and experimental studies on cell-mediated and humoral responses to parasite and host tissues, but it is difficult to correlate the findings in human infections with the experimental data, and therefore no satisfactory hypothesis on the pathogenesis of Chagas disease has yet been proposed (*7*).

2.3.1 *Megaviscera*

Digestive "mega" conditions seem to result from massive neuronal destruction in the myenteric plexus during acute infection as a consequence of parasite-related inflammatory reactions. Apart from the incapacity of the neurons to regenerate, the intensity of destruction, which is probably related to the tropism and pathogenicity of the *T. cruzi* strains, is apparently important since mega-oesophagus can already be observed in the acute phase of the disease, or shortly thereafter. Usually, however, "mega" organs are observed during adult life, when, it is assumed, the progressive physiological loss of neurons in an already damaged plexus reaches critical levels. Subsequently, severe dysperistalsis and greater organ dilatation follow.

2.3.2 *Chronic myocarditis*

Chronic myocarditis seems to depend on a highly complex pathogenesis. The only clear point is that it is not directly parasite-related. There is general agreement on its being induced by delayed-type hypersensitivity. The histological picture of active chronic inflammation, with immunologically competent cells, a rich vascular component, a fibrosing tendency, and a scarcity or absence of parasites, is compatible with such an interpretation. The role played by *T. cruzi* antigens, by neoantigens, or by autoimmunity is a matter of considerable importance and controversy.

2.3.3 *Congenital infection*

It is still not known at what stage of development the fetus becomes infected. Transplacental transmissions have been reported both when the mother has acquired an acute infection with *T. cruzi* during pregnancy and years after an acute infection has occurred. Although parasitaemia is higher during the acute phase, this period does not last long. This is probably the reason why most cases originate from mothers with a chronic or indeterminate-stage *T. cruzi* infection.

The effect of pregnancy on parasitaemia is not clear. It has been reported on the one hand that the frequency of positive xenodiagnosis increases during the third trimester of pregnancy, and on the other that the overall rate of positivity of xenodiagnosis is higher in nonpregnant than in pregnant women. Mothers delivered of congenitally infected fetuses or liveborn children may be either positive or negative for parasitaemia. Moreover, pregnant women with an acute infection and positive parasitaemia do not necessarily pass the infection to their offspring. Therefore, patent parasitaemia in the mother seems to have little relation to the development of congenital *T. cruzi* infection.

An attempt has been made to relate the regional differences in the incidence and clinical picture of congenital Chagas disease to the characteristics of *T. cruzi* isolates from patients, but with inconclusive results so far.

3. The parasite

3.1 Taxonomy

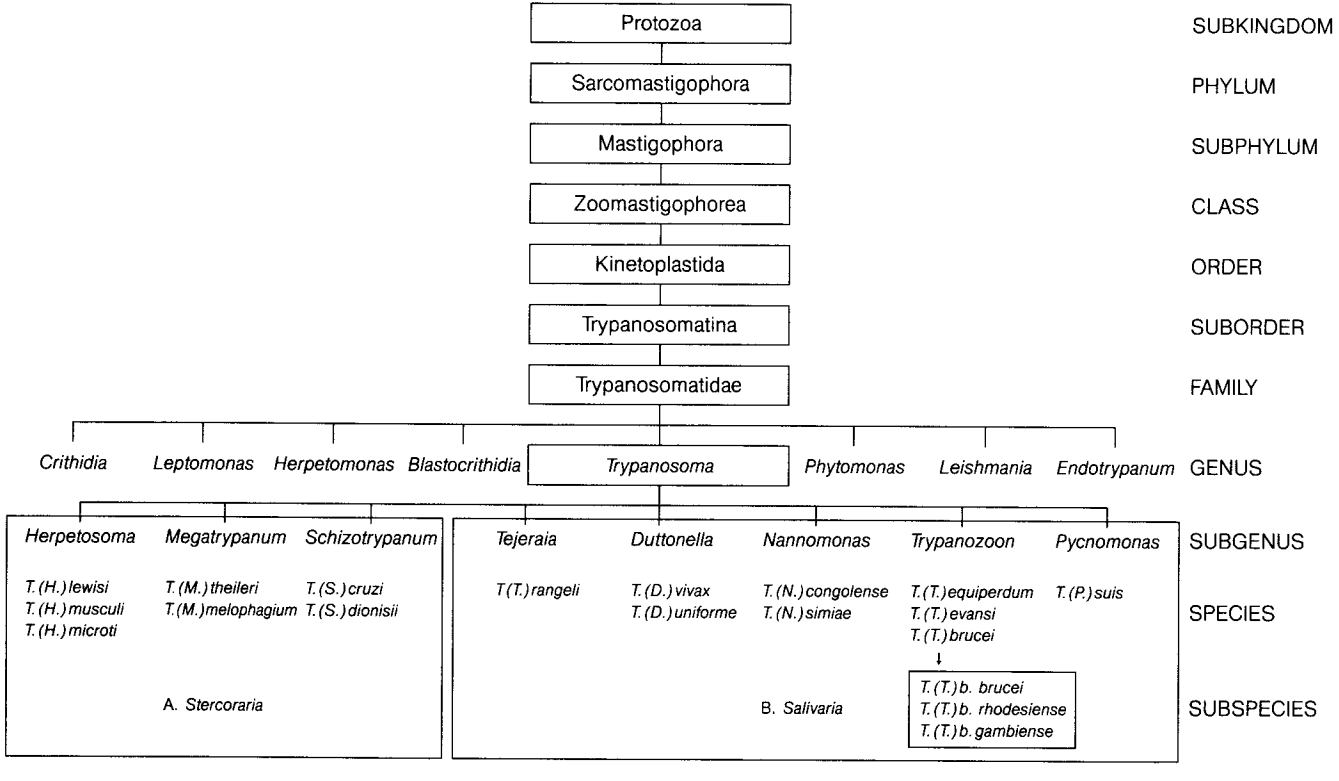
Trypanosoma cruzi belongs to the Mastigophora subphylum of the phylum Sarcomastigophora, order Kinetoplastida, which comprises flagellar organisms with a kinetoplast, an organelle located in the cell mitochondrion which contains a fibrous network of DNA. *T. cruzi* is included in the stercorarian section, together with the group of trypanosomes whose infective stages develop in the vectors' digestive tract and contaminate the mammalian hosts through faeces. The subgenus *Schizotrypanum* has been adopted for trypanosomes that multiply in vertebrates via intracellular stages. Hence the full taxonomic name is *Trypanosoma (Schizotrypanum) cruzi* (see Fig. 1).

3.2 Isolation and maintenance of *T. cruzi* strains

T. cruzi strains can be isolated by xenodiagnosis, by blood culture, and in acute cases by inoculation of blood into newborn mice. Amplification of the isolated populations is made by serial passages through animals and cultivation in axenic and tissue-culture media. As an alternative, large numbers of strains can be maintained, protected from external influences

Figure 1

Classification of mammalian trypanosomes[a]



[a] Reproduced from WHO Technical Report Series, No. 739, 1986 (*Epidemiology and control of African trypanosomiasis:* report of a WHO Expert Committee).

or experimental manipulation, by cryopreservation (-70 to -196 °C). The use of an adequate standard international code for isolated and preserved parasite populations is strongly recommended (see Annex 1).

3.3 Identification criteria

T. cruzi consists of a pool of populations, which circulate among humans, domestic and sylvatic insect vectors, and animal reservoirs. The geographical distribution of *T. cruzi* in the sylvatic cycle extends far beyond that of the human disease. In the process of geographical and biological dispersion the parasite has evolved a great diversity of subpopulations or strains, which, when isolated from the various hosts and experimentally studied in the laboratory, display distinct strain characteristics.

Identification of the *T. cruzi* species is relatively easy by morphological and biological criteria – except for its distinction from *Trypanosoma rangeli,* a trypanosome that is not associated with human pathogenicity and that is found in Colombia, Venezuela, and Central America. In some areas *T. rangeli* shares the same vectors and reservoirs as *T. cruzi.*

Characterization of *T. cruzi* at strain level is much more difficult and is currently being extensively investigated. Comparative studies on *T. cruzi* strains are important to determine the possible role played by different strains in such aspects as the pathogenesis of the different clinical forms, the geographical variations in clinical forms and morbidity, and the differences in cure rates observed after treatment. For this reason the investigation of intraspecific variation involves a large range of criteria based on biological methods and biochemical characterization at the molecular level.

3.3.1 *Biological characterization*

Biological characterization is based on differences in the development of the parasite in mammalian hosts (course of infection) and on differences in sensitivity to chemotherapeutic agents. In addition, immunological and biochemical characteristics are used for strain identification.

Course of infection

T. cruzi infects a wide range of vertebrate hosts: over 100 mammalian species have been naturally or experimentally infected with this parasite. In infections in laboratory mice, blood forms may differ in morphology (slender, broad, and stout forms), and different patterns of parasitaemia may occur. Strain-dependent variations in the distribution of the intracellular amastigote forms in the tissues have been described. Certain strains display a preferential tropism for macrophages in the spleen, liver, and bone marrow, whereas others are very scarce in these organs. Some strains in which such characteristics have been firmly established are being considered as prototypes for classification. Variable degrees of virulence as evaluated by the prepatent periods, course of parasitaemia, and mortality rates are also used to classify *T. cruzi* strains.

Drug sensitivity

There is a wide range of sensitivity to chemotherapeutic agents among *T. cruzi* strains, a large number of which are naturally resistant to standard drugs used routinely in Chagas disease. Resistance related to geographical distribution has been reported; strains from some areas of southern Brazil, for instance, have been demonstrated to be much more sensitive to certain drugs than those from the southeastern areas.

3.3.2 *Immunological characterization*

A number of conventional and more advanced immunological methods have been used to detect antigenic differences within the complex pool of *T. cruzi* populations. Studies of labelled components of the parasite surface have demonstrated the existence of strain-specific antigens, in addition to the ubiquitous glycoproteins common to all strains. Monoclonal antibodies have also been used to discriminate strains. Antigens coded by *T. cruzi* cloned genes are specifically recognized by sera from different patients with acute or chronic disease, but typing of *T. cruzi* strains based on antigenic characteristics has not yet been done.

3.3.3 *Biochemical characterization*

The following intrinsic characteristics at the molecular level, which are not influenced by handling strains in the laboratory, are being used for the identification of *T. cruzi* variants.

Isoenzymes

Gel electrophoresis permits the detection among the strains of *T. cruzi* of enzymes that have similar catalytic activity but may differ in other respects (isoenzymes); this has made it possible to differentiate groups of strains into zymodemes, i.e., groups with identical isoenzyme profiles. By analysis of large numbers of strains isolated from different hosts and different endemic areas, the existence of at least three main zymodemes (Z1, Z2, Z3) has been established. Epidemiological studies showed that most Z2 strains were isolated from patients with chronic Chagas disease and domestic animals, while Z1 and Z3 were found in vectors and reservoirs of the sylvatic cycle. (In some outbreaks of acute Chagas disease Z1 was isolated from patients, probably as a result of the introduction of sylvatic *T. cruzi* strains into the domestic cycle.) Further studies have shown, however, that this correlation of epidemiological and clinical data with isoenzyme patterns is not as close as was originally thought. Genetic interpretation of the zymograms of *T. cruzi* from various hosts and over a broad geographical range (from Argentina to the United States of America) has revealed great genetic variability.

Schizodemes

Strain characterization based on genotype markers is carried out by analysis of gel electrophoresis profiles of kinetoplast DNA (kDNA) yielded by enzymes (restriction endonucleases) that recognize and

discriminate between specific sequences of DNA nucleotides. Strains showing similar kDNA restriction patterns are then grouped in schizodemes. Although qualitative and quantitative strain-dependent differences have been observed, the great heterogeneity of schizodeme profiles precludes their use as a characterization system for *T. cruzi*.

DNA probes

Labelled DNA probes (cloned DNA minicircles or total kDNA) have been successfully used in a "dot-spot" rapid hybridization test for taxonomic purposes.

3.4 Heterogeneity of *T. cruzi* strains

Recent investigations on cloned populations of *T. cruzi* strains have shown that there may be a high degree of heterogeneity of subpopulations of strains, which most likely influences the characteristics of those strains. Clone-dependent differences have been identified in relation to growth rate of culture forms, infectivity to vertebrate host, virulence, and pathogenicity, among other parameters. It is possible that in the course of experimental studies, mainly when parasite populations are amplified for further investigations, clone selection or predominance may occur as a result of overgrowth of a particular subpopulation either in culture or in the vertebrate host.

4. The vectors

Almost all triatomine species are restricted to the Neotropical and Nearctic Regions, with a few occurring in both. They are geographically distributed from Salt Lake City at 41° N latitude in the USA, where *Triatoma protracta* has been reported, to Patagonia in the South American continent, where *T. patagonica* has been encountered at 46° S.

4.1 Taxonomy

Triatomines are insects of the order Hemiptera, family Reduviidae subfamily Triatominae. The tribes, genera, species, and subspecies of the Triatominae of the Americas[1] are listed in Annex 2 with an indication of their geographical distribution, their synonyms, and whether or not they have been found naturally infected with *Trypanosoma cruzi*. The subfamily Triatominae contains over a hundred species. There is, however, no consensus among taxonomists about the exact number of tribes, genera, and species, which have ranges of 5-7, 14-15, and 109-115, respectively, according to different authorities.

[1] Within the Triatominae, the only entire genus exotic to the Americas is *Linshcosteus*, with five species. In the genus *Triatoma*, *T. rubrofasciata* occurs in many tropical and subtropical areas of the world, and seven species occur only in the Old World: *T. amicitiae*, *T. bouveri*, *T. cavernicola*, *T. leopoldi*, *T. migrans*, *T. pugasi*, *T. sinica*.

4.2 Identification criteria

The Reduviidae can be distinguished from most other Hemiptera by the presence of a three-segmented proboscis, which at rest is folded under the head, reaching a point between the first pair of legs. In plant-sucking Hemiptera the proboscis is four-segmented and usually extends beyond the first pair of legs. In predatory subfamilies of Reduviidae the proboscis is stout, rigid, and often curved, adapted to pierce the hard integument of other arthropods, whereas the Triatominae always have a straight and slender proboscis, adapted to pierce the softer integument of vertebrates. The genus *Rhodnius* is distinguished from other genera of Triatominae by its long head, with antennae inserted at the front, near the clypeus. In *Triatoma* the head length is intermediate, with antennae inserted midway between the eyes and the clypeus. The genus *Panstrongylus* has a short, robust head with antennae inserted immediately in front of the eyes. Lent & Wygodzinsky (*8*) have published keys to the determination of triatomine species, in English, Spanish, and Portuguese.

Useful identification criteria for species determination include the general body structure, colour pattern, size of antennae and eyes, and male genitalia. Adults are distinguished from nymphs by the presence of ocelli, well-developed genitalia, and two pairs of wings. Usually the female bug is larger than the male, and females have visible, pointed, external genitalia.

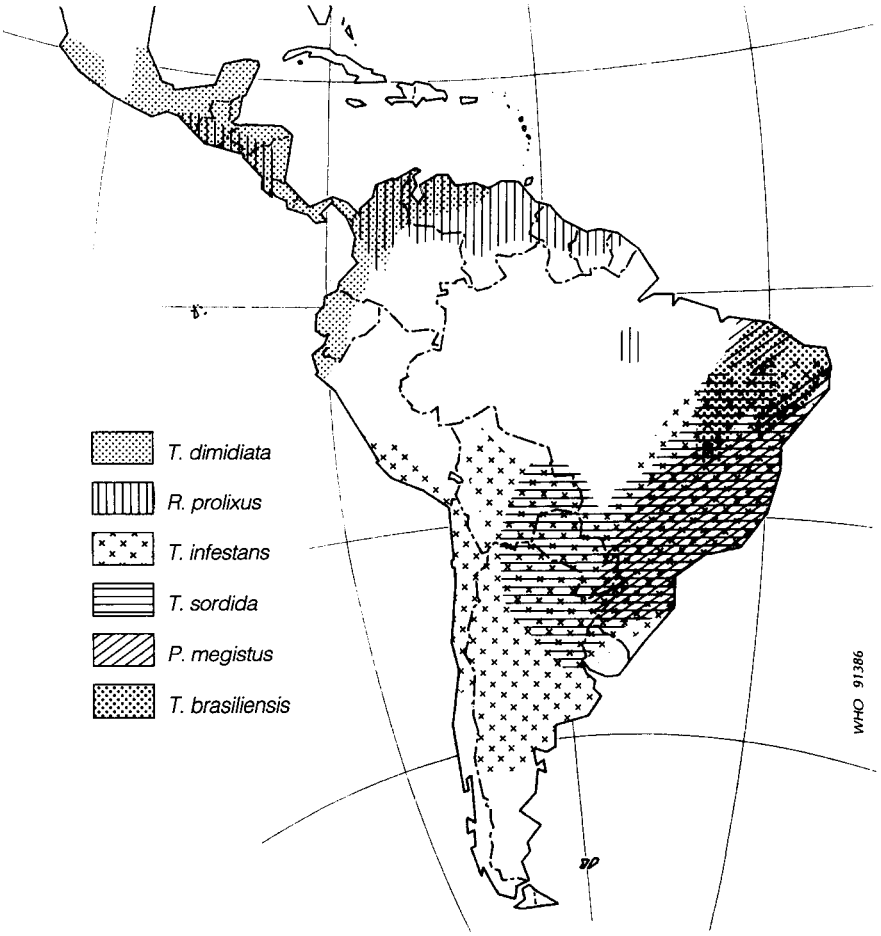
The size is a key characteristic, and varies within the subfamily from 5 to 45 mm. The colour varies from light yellow to black according to the species, with different patterns of orange, yellow, white, red, grey or green spots, principally on the connexivum. These traditional morphological characteristics may soon be complemented by such criteria as isoenzyme patterns. Cytogenetic analysis and determination of hydrocarbon composition of bug cuticles are still in a developmental stage.

4.3 Geographical distribution

The geographical distribution of the American Triatominae is shown in Annex 2, and the distribution of the six major vector species is presented in Fig. 2.

The triatomines of the USA have not adapted to household ecotopes (*9*). From Mexico to the north of South America, the most important species are *Rhodnius prolixus* and *Triatoma dimidiata;* their distribution reaches Ecuador, where *T. dimidiata* is a domiciliary species. In Colombia, French Guiana, Guyana, Suriname and Venezuela, *R. prolixus* is the main vector and has been collected at an altitude of over 2000 m. In Colombia, *T. venosa* and *T. maculata* are adapted to household ecotopes but have only secondary importance. In Peru, two main vectors are found: *Panstrongylus lignarius* in the north of the country and *T. infestans* in the southern foci. In Bolivia and Paraguay, *T. infestans* is widely dispersed, and *P. megistus* has been found in small foci. The distribution of *T. sordida* covers the eastern

Figure 2
Geographical distribution of the six major triatomine vectors of Chagas disease[a]



[a] Adapted, with permission, from Brener, Z. & Andrade, Z., ed. Trypanosoma cruzi *e doença de Chagas.* [Trypanosoma cruzi *and Chagas disease.*] Rio de Janeiro, Guanabara Koogan, 1979, p. 83.

part of Bolivia and a broad band in southern Brazil as well as areas in Argentina, Paraguay, and Uruguay. However, *T. infestans* is the most important vector in Argentina, Bolivia and Uruguay, and also in Chile. In Brazil, several species are naturally infected with *Trypanosoma cruzi,* but three are of special epidemiological importance. The most important of these is *T. infestans,* which has dispersed northwards from the south and has recently reached the northeastern states of Pernambuco and Paraíba. *P. megistus* is considered the second most important, with a wide

geographical distribution and high rates of natural infection; in parts of northeastern and eastern Brazil it is predominantly domiciliary, while in the south it is essentially sylvatic. Thirdly, in northeastern Brazil generally, *T. brasiliensis* is the main vector. *T. sordida* and *T. pseudomaculata* have low rates of natural infection with *T. cruzi*, but they replace the main domiciliary species in Brazil after the application of insecticides (*10, 11*).

4.4 Biology and behaviour

The principal biological characteristic of the triatomines is that of obligate bloodsucking by either the nymphs or the adults of both sexes. Their natural habitats are therefore the wild ecotopes that serve as nests, shelters or resting-places for mammals, birds or reptiles, where the triatomines live in easy contact with the vertebrates that constitute their natural sources of blood. Some triatomines have a marked feeding preference for a particular species, but most of them feed on a wide variety of hosts.

The association of the triatomines with *T. cruzi* and wild mammals had established natural niches within a variety of biocoenoses until the invasion and disturbance of the environment by humans. Destruction of the natural biotopes led some triatomine species to occupy peridomestic and household environments. Hunger is apparently one of the main factors in the dispersion of the insects to new ecotopes. The new epidemiological condition that has been created involves humans and domestic animals in the transmission cycle, converting the natural association of *T. cruzi* and triatomines into a true anthropozoonosis. Consequently, in addition to birds' nests, hollow trees, interstices between rocks, fallen logs, exposed roots, loose bark, palm fronds, and epiphytic bromeliads, the triatomines are now also found in peridomestic ecotopes and inside dwellings.

All species are potential vectors of *T. cruzi* but six are of special epidemiological significance in South America (*Triatoma infestans, T. brasiliensis, T. dimidiata, T. sordida, Panstrongylus megistus,* and *Rhodnius prolixus*) – with a seventh (*R. pallescens*) playing an important role in Central America and Panama.

T. infestans is the most widespread domestic species and occupies the greatest climatic range, from arid highlands (Peru) and temperate plains (Argentina) to the dry tropics (northeastern Brazil). It is also the oldest domiciliated triatomine species and is now restricted to artificial human ecotopes in most of its distribution area, although it has exceptionally been found in some sylvatic ecotopes. Its present extensive distribution has been interpreted as reflecting its wide ecological tolerance, its long-standing association with humans, and the passive dispersion that took place together with migrating human populations. *T. infestans* is most prevalent in poor adobe houses, in the thatched or straw roofs and in cracks in the mud walls, especially in the upper fringes. Nevertheless, it can also successfully colonize houses made of cement blocks or kiln-fired bricks since household belongings can act as suitable breeding and hiding places.

Feeding profiles of indoor populations indicate that 84-99% of the blood-meals are taken from resident hosts (humans, chickens, dogs, and cats), but geographical differences in the principal blood source are found. In Chile, human blood accounts for approximately 69% of this species' blood-meals, and humans act as the main reservoir host of the parasite. In Brazil, humans are the major blood source for *T. infestans* throughout its distribution area. In the highly endemic areas of central Argentina, 25-49% of feeds are upon dogs, which have become the main parasite reservoir for domestic transmission.

P. megistus is a stenohydric species, endemic to the forest of coastal Brazil. In the southern states of that country it is present in sylvatic ecotopes and sometimes in peridomestic structures, while towards the north-east, intense deforestation by humans precludes colonization of its natural ecotopes and it has become an important domiciliary species. This is reflected in the feeding profiles of *P. megistus* in some areas; in southern and central Brazil, for instance, blood-meals from humans account for only 14-30% of the total feeds of bugs collected in domestic and peridomestic sites, birds and rodents being more important blood sources.

T. brasiliensis, which is highly susceptible to infection with *T. cruzi,* is the most important vector in northeastern Brazil, where it can be found in sylvatic and peridomestic habitats, such as rocky ecotopes and cattle shelters. It has been incriminated in the transmission of *T. cruzi* to rodents and goats. The feeding patterns of peridomestic and domestic populations of this species indicate that birds are the principal blood source, followed by humans.

T. sordida is mostly a sylvatic and peridomestic species, originally from dry areas of the southern and central states of Brazil. Its range has been extended both northwards and southwards as a result of intense deforestation: the timber serves as harbourage and contributes to the dispersal of *T. sordida* populations. Although this species feeds mainly on birds, it is becoming increasingly domiciliated in southeastern and central Brazil, taking 16-32% of its blood-meals on humans.

R. prolixus is the most important vector of Chagas disease in much of tropical America and, like *T. infestans,* has evolved in adaptation to human dwellings. This species is a native of northern South America, where it also occupies many sylvatic arboreal ecotopes associated with mammals and birds that nest in palm trees or bromeliads. In a number of Central American countries and in part of Mexico, however, it is present exclusively inside houses. In the domestic environment *R. prolixus* feeds mainly on the blood of humans and chickens, although feeding on cat and dog blood has also been demonstrated. In the sylvatic environment, opossums and rodents are the main sources of blood. Inside houses, it is localized in palm-thatched roofs, cracks in the walls, and household effects.

T. dimidiata is a domiciliary species associated with wooden houses and earthen floors and present in woodpiles in peridomestic areas. It is an important vector in Central America and parts of Mexico. Although human blood predominates in its feeding profile in Costa Rica, rodents are also frequently fed on, followed by dogs and opossums. Rodents and chickens have been recorded as the main blood sources in Ecuador and Mexico.

R. pallescens is a sylvatic and peridomestic species that invades houses from its breeding places in palm trees and is becoming increasingly domiciliated. Feeding patterns of domestic populations from central Panama showed that the principal hosts were humans (59% of the feeds) followed by opossums and poultry. They are found in houses with cane walls and palm-thatched roofs. In Panama, two distinct transmission cycles of *Trypanosoma cruzi* have been described: *Triatoma dimidiata*-humans in the western areas and *R. pallescens*-humans in the central parts of the country. The higher transmission rate of Chagas disease in central Panama than in western areas has been attributed in part to the association of *R. pallescens* with the opossum (*Didelphis marsupialis*).

4.5 Ecological factors

In addition to the aspects of the interrelation of *T. cruzi* and its environment that were touched upon in the preceding section, the following ecological factors affect vectorial transmission of the parasite.

4.5.1 *Climatic factors*

Climatic factors, mainly temperature, seem to control the rate of increase of triatomine bug populations. Seasonal patterns of abundance and age structure have been established for domiciliary populations of *T. infestans* and *P. megistus* in Argentina and Brazil and of *R. prolixus* in Venezuela.

In central Brazil (Goiás), where mean maximum and minimum annual temperatures show little variation, *T. infestans* populations produce two generations a year. The moulting and development rates of nymphs, as well as the rate of female fecundity, are at their maximum in the summer. A major peak of adult emergence takes place in the summer (December-January), followed by a minor, winter, peak in June-July. The winter population is mainly composed of adults and older (4th and 5th instar) nymphs. Reproduction and moulting are resumed at the beginning of spring. Seasonal changes in density and age structure also produce changes in the proportion of infected vectors, which has been found to be higher at the beginning of the hot season. These and other features of the vectors' population dynamics must be taken into consideration when programming control operations.

Differences in the structures of vector populations have important implications for *Trypanosoma cruzi* transmission. In warm climates, transmission takes place throughout the year, with the highest level in the

summer, while in temperate regions it is concentrated in the warmer half of the year only. This is reflected in the epidemiological finding that the frequency of acute human cases of Chagas disease markedly increases during the summer months.

4.5.2 *Presence of synanthropic animals*

The ecological significance of synanthropic animals for triatomine vectors is threefold: the animals serve as blood sources and thus contribute considerably to maintaining or increasing population densities of domiciliary and peridomiciliary vectors: they can be predators of triatomines; and they can also play a role in the passive dispersal of vectors. (Their ecological significance should be distinguished from their epidemiological significance as reservoir hosts of the pathogen; see section 5).

Although it is generally accepted that triatomines are opportunistic feeders, there is some evidence of host preference in the case of peridomestic species such as *Triatoma sordida.* This has been claimed to be the main reason for some species being predominantly domiciliary and others being peridomiciliary.

Blood-meal identification studies of the six most important vector species in several endemic countries show a general pattern (although there are exceptions). After humans, birds are the most important blood sources in most areas, particularly chickens and sometimes pigeons. For *T. brasiliensis,* birds are an even more important source of blood than humans. Dogs, and to a lesser extent cats, are usually the third most important blood source, except in Argentina, where dogs may play the greatest role. The ancient custom in Peru and Bolivia of raising guinea-pigs indoors for food makes them locally important sources; generally, however, the role of rodents in this respect is limited.

Rodents, on the other hand, play a role as predators of triatomine bugs. Chickens and cats may also attack the bugs and thereby contribute to suppressing their numbers.

Animals can serve as a vehicle for the passive dispersal of vectors. For example, the migratory wood stork (*Mycteria americana*) – though not synanthropic – is considered to have carried *Rhodnius prolixus* from the north of South America to Central America and Mexico.

4.5.3 *Housing construction and housing conditions*

The nature and quality of buildings, as well as housing conditions – including the storage of goods and belongings inside and around the house – are important determinants of the colonization of human dwellings by triatomine bugs. Domiciliary and peridomestic habitats may create favourable microhabitats and provide protection from predators.

Domiciliary habitats related to construction are cracks and crevices in mud or cement walls, the junctions of adobe or cement bricks, spaces between wood or cane pieces, roofs of palm leaves, and earthen floors. Other factors that favour bug infestation include textiles (curtains, etc.), storage of the harvest in the house, collections of adobe-blocks in indoor passages and corridors, and sticks piled in the house.

The presence of animals in the dwelling house, the nature of the construction of outbuildings (for storage or for keeping animals), and the distance of such buildings from the human dwelling also have an important influence on the presence of vectors and the transmission of the parasite.

The importance of the various domiciliary and peridomiciliary factors depends on the local vector species; for instance, earthen floors are favourable for *T. dimidiata* and palm-thatch roofs for *R. prolixus*. In the latter case, not only does the roof itself provide an appropriate habitat for the vector, but the frequent repairs required entail the risk of passive transport of vector eggs from the sylvatic environment in the new thatching material. For all species, however, and especially for *T. infestans*, cracks and crevices in walls and similar constructional flaws are of great importance.

4.5.4 *Man-made environmental changes*

It is now accepted that adaptation of triatomines to the domestic environment has mainly taken place in the natural open areas of Latin America. Human settlements created drastic changes in the natural landscape, especially through intense deforestation. Colonization of human dwellings was the response by triatomine populations to overcome the scarcity of blood sources and natural shelters. Mismanagement of deforested areas led to irreversible land desertification, which favoured the spread of domestic triatomines. On the other hand, in several traditional chagasic areas agricultural development and other forms of environmental management have led to a considerable simplification of the habitat. This has greatly reduced the risk of invasion of houses and as a consequence natural foci of triatomines have become extinct. However, where human activities extend into regions with many sylvatic species, such as the Amazon basin, vector transmission of Chagas disease will spread into areas from which it may so far have been absent.

4.5.5 *Predators*

Natural enemies of triatomines include many species of predators and parasites. Among arthropod predators are many spiders, pseudo-scorpions, mites, cockroaches, ants, and other non-triatomine reduviid hemipterans. Lizards, rodents, and domestic fowl also eat triatomine bugs. Several species of tiny microhymenopteran wasps parasitize the eggs of triatomines; and some nematodes, fungi, and bacteria attack the nymphs and adults.

4.6 Vector/parasite relationships

The interaction between the different vector species and the different strains of *T. cruzi* is an important parameter affecting the susceptibility of a vector to infection. Its susceptibility and its ability to adapt to a domiciliary habitat are the two key determinants of its vectorial capacity.

The factors that influence the vector's susceptibility are:

- *Genetic factors.* In *R. prolixus,* for example, it has been shown that the susceptibility, intensity of the infection, and parasite density in the faeces are genetically regulated and that these genetic traits can be transmitted.
- *Trypomastigotes.* As with African trypanosomes, the morphological form of the trypomastigotes ingested with blood influences the level of infection: "stout" forms seem to be more infective than "slender" forms.
- *T. cruzi strains.* Local vector species are usually more readily infected with the local parasite strains than with strains from other endemic areas. The vector is capable of "selecting" subpopulations of *T. cruzi* from a natural heterogeneous population, and this could affect the parasite's pathogenicity in human hosts.
- *Others.* Other important factors include blood-meal size, the number of parasites ingested, the stage and age of the insect vector, the ability of the parasite to establish rectal gland infections in the vector, and the kinetics of parasite transformation in the insect's digestive tract.

Once infected, triatomines generally remain parasite carriers for the rest of their lives; there have, however, been a few laboratory observations suggesting that vectors may lose their infection with *T. cruzi.*

As *T. cruzi*-infected vectors show no significant biological differences from uninfected ones, there appears to be no pathogenic effect of the infection on the insect. In *T. rangeli* infections, in contrast, pathogenic effects on the insects have been demonstrated in several triatomine species.

5. Animal reservoirs

Originally, Chagas disease was strictly a zoonosis that involved numerous sylvatic triatomines and sylvatic mammals in natural foci, from which humans and domestic animals were absent. As a result of human-vector contact (e.g., in rural settlements) and modifications in the natural biotopes the disease has spread into peridomestic and domestic cycles.

Transmission cycles involving a wide range of hosts have been recorded from almost every country where *Trypanosoma cruzi* infection is endemic. At present, over 150 species from 24 families of wild and domestic or peridomestic mammals have been recorded as infected by *T. cruzi*. Dogs and in certain areas opossums and rodents are probably the most important reservoir hosts within the peridomestic cycle, opossums (*Didelphis* species) and armadillos within the sylvatic cycle (*12*).

5.1 Identification of animal reservoir hosts

The isolation of *T. cruzi* from animals aims at identifying the main reservoir hosts, at classifying them zoologically, and at evaluating the risk of introducing sylvatic strains into the domestic cycle. A list of data to be recorded for identifying and incriminating animal reservoir hosts and for characterizing *T. cruzi* strains isolated from them is presented in Annex 3. The help of an experienced zoologist is strongly recommended for the identification of animal hosts.[1]

5.2 Taxonomy, species, and geographical distribution of animal reservoir hosts

The animal reservoir hosts of *T. cruzi* have a wide geographical distribution, which broadly coincides with that of the triatomines (latitudes 42° N in the USA to 46° S in Argentina).

As a result of comprehensive studies, numerous reservoir animals have been identified in some countries of Central and South America, but in many others the hosts remain partly unknown.

A list of sylvatic and domestic or peridomestic animals that have been found to be infected with *T. cruzi* and to serve as potential reservoir hosts is given in Annex 4.

5.3 Role and importance of animal reservoir hosts within the *T. cruzi* sylvatic and domestic life cycles

The importance of the role played by an animal reservoir host in the sylvatic and domestic life cycles of *T. cruzi* is related to its species; its

[1] *Workshop on guidelines for multidisciplinary research on the epidemiology of Chagas disease.* Geneva, World Health Organization, 1979 (unpublished document TDR/EPICHA/79.1/Rev. 1; available on request from UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases, World Health Organization, 1211 Geneva 27, Switzerland).

habitat or ecotope (domestic, semi-domestic or sylvatic); its dispersal range; its population density; its geographical distribution; its availability to a vector and the degree of contact between them; the trophic preferences of vectors; and parasite/reservoir-host relationships.

In the domestic cycle of parasite transmission humans are the most important reservoir host. There is a close contact between humans and domestic triatomine bugs in the limited intradomiciliary space, and humans are frequently bitten by the bugs when asleep at night.

5.3.1 *Domestic and peridomestic animal reservoir hosts*

The domestic life cycle involves domiciliary triatomines and several domestic animals. Because of the permanent availability of blood, the density of household triatomines is high (see section 4.5.2) and human-vector contact is close. Although the probability of transmission may be low for each individual human-vector contact, a high overall rate of transmission is possible when the contact rate is high.

Most of the small domestic animal species have been found infected by *T. cruzi*, but only a few of them exhibit a high infection rate. Other larger domestic animals (e.g., pigs, horses, cows) are not often infected.

Dogs and cats

T. cruzi infection rates are especially high in dogs and cats. In areas where investigations have been carried out, they appeared to be the main domestic animal reservoir hosts when *Triatoma infestans, T. dimidiata* and *T. sordida* were the vectors. Infections in dogs have been reported from 15 countries and in cats from 7. Comprehensive studies, undertaken mainly in Argentina, Brazil, Chile, and Venezuela, showed a great variability in infection rates (from 4.5% to 100% in dogs and from 0.5% to 60.9% in cats). However, the sensitivity of the techniques (xenodiagnosis or serology) used and the different epidemiological situations have to be taken into account.

Dogs are important reservoir hosts of *Trypanosoma cruzi* in central and northern rural Argentina, particularly in Santiago del Estero Province (*13*); this is due to the close contact between humans and dogs (3.6 dogs per house, 50% closely associated with humans during the night), to the age-independent persistence of parasitaemia in dogs, and to the possibility of congenital or lactogenic infection in dogs. A previous study, in the same area, had shown already that dogs should be considered the principal reservoir of infection for *Triatoma infestans* and the main contributors to the maintenance of transmission in the area.

Rats

Trypanosoma cruzi infection among rats (mainly *Rattus norvegicus* and *R. rattus*) has been reported from nine countries, from the USA south to Argentina. Infection rates for *R. rattus* vary from 9.5% in an area of El

Salvador to 100% in a southwestern region of Bahia State in Brazil. Rats are usually considered to be important reservoirs because of their high population density and relatively close contact with humans as well as with domiciliary triatomines. Sometimes, rats share both sylvatic and domestic habitats, moving from one to the other.

Mice

Infections of *Mus musculus* have been reported from five countries, sometimes with a relatively high rate of infection (10-30%). It is assumed that, since mice frequently eat triatomine bugs, they can become infected and transmit their infection to cats that prey upon them.

Guinea-pigs

In Bolivia and Peru, guinea-pigs are bred indoors for food, and high rates of infection have been reported (Bolivia, 10.5-61.1%; Peru, 19.2%).

Other domestic animals

Cattle, goats, pigs, and equines have rarely been found infected and, given their low population density, their less close contact with humans than that of indoor animals, and their low parasitaemia, they are not considered to play an important role as reservoirs.

Chickens and pigeons are not susceptible to *T. cruzi* infection.

5.3.2 *Sylvatic animal reservoir hosts*

As may be seen in Annex 4, numerous species of arboreal and terrestrial mammals are involved in the sylvatic cycle; natural infections by *T. cruzi* have been reported from almost all countries of America. Some species invade peridomestic areas, where they are likely to increase the risk of transmission to humans. Their exact role in this respect, however, has not been fully assessed.

Marsupials

Opossums (especially the genus *Didelphis*) are a major reservoir of *T. cruzi* in several countries. Their importance is due to their wide geographical distribution (from Argentina to the USA), their high population densities, their nutritional habits (omnivorous, including triatomine bugs), their close contact with triatomine bugs (which are frequently found in their nests), their patent and persistent high parasitaemia, and their broad range of sylvatic and domestic biotopes (they nest in trees, bromeliads, attics, and roofs). High *T. cruzi* infection rates have been reported from a number of countries, ranging from 20% to 70%, and even up to 100% in some areas.

The possibility of opossums becoming infected by the oral route through ingestion of infected triatomines, small rodents or bats has been confirmed by oral transmission experiments.

Opossums seem to be particularly able to introduce sylvatic strains into houses and dwellings in rural and urban environments. *D. marsupialis* is

the animal most frequently associated with *Rhodnius pictipes*-infested palms in the Amazon basin, and this bug is often attracted by light into houses. *D. albiventris* invades houses and nests in roof materials. The movement of sylvatic reservoir hosts to and from domestic areas affords a link between the wild and domestic cycles of infection.

Recent observations show that some species (e.g., *D. marsupialis*) present a unique *T. cruzi* cycle in their anal glands. This internal environment seems to offer ideal conditions for the multiplication of the parasite, comparable to the internal medium of the insect's gut. This is of practical importance as it suggests that these opossums may be able to eliminate the parasite in an infective stage in gland secretions, urine, and possibly faeces.

Edentates

The order Edentata has a wide geographical distribution, ranging from Argentina to the USA. More than 20 species and subspecies have been found infected by *T. cruzi*. Armadillo species of the genus *Dasypus*, and in particular *D. novemcinctus*, are usually considered suitable reservoir hosts as they contribute to maintaining the infection in sylvatic biotopes. Armadillo burrows provide good conditions of shelter, microclimate, and food for some species of triatomines (e.g., *Panstrongylus geniculatus*). The density and dispersion range of armadillos are less than those of opossums, but their rate of infection with *T. cruzi* may be high – up to 50% in some areas of Brazil and Venezuela. Some species of sloths and anteaters are also involved. The important role of edentates as reservoir hosts has been clearly demonstrated in the sylvatic ecosystem of the Canal Area in Panama.

Rodents

More than 50 rodent species and subspecies have been reported infected with *T. cruzi*. They contribute to the maintenance of the sylvatic (enzootic) cycle. Comprehensive studies have shown very high *T. cruzi* infection rates in, for example, *Coendou prehensilis* (40%) and *Oryzomys concolor* (100%) in Venezuela.

Bats

A large number of bat species has been reported to be infected with *T. cruzi*. For years, a major problem was to differentiate infections by *T. cruzi* from those due to other *Trypanosoma* species, such as *T. dionisii*, but this has been largely overcome by the development of new techniques.

In Brazil, in the state of São Paulo and neighbouring areas, an average rate of *T. cruzi* or *T. cruzi*-like infections of 15.7% among 22 species and subspecies of bats has been reported.

Bats not only maintain the enzootic cycle in natural foci, but they can also introduce sylvatic strains into domestic areas, where they become a source of blood-meals for domestic triatomines.

Carnivores

The importance of wild carnivores as reservoir hosts of *T. cruzi* infection is not fully known but is usually considered to be fairly slight. The strictly sylvatic species have a low population density though a wide geographical distribution. A study carried out in a northeastern area of São Paulo State, Brazil, showed an average infection rate of 8.6% among approximately 100 carnivores. In Ceará State, Brazil, 3% of 10 632 carnivores were found infected with *T. cruzi*.

Primates

Some 22 species of primates have been found infected with *T. cruzi*. High infection rates have been reported in some countries: 45% among *Saimiri sciureus* monkeys in the Amazonian primary forest of Brazil; 42% among *Cebus apella* in Venezuela; and 30% in a group of Colombian monkeys and marmosets of 18 different species. Monkeys in Bolivia and Brazil have been found infected with both *T. cruzi* and *T. rangeli*. Unless *T. rangeli* is systematically searched for in triatomines, humans and animals, particularly in areas of *Rhodnius* prevalence, it will not be possible to evaluate accurately the epidemiology of *T. cruzi* infections and of Chagas disease. The presence of *T. cruzi* in wild primates also requires that strict precautions be taken regarding their use in laboratories.

5.4 Reservoir-host/parasite relationships

The relationship between animal reservoir hosts and parasites involves a very dynamic interaction. The infected sylvatic hosts usually present high parasitaemia and do not seem to be adversely affected by the parasite. In the domestic cycle of the disease, on the other hand, some animals may be affected; for example, naturally infected dogs occasionally show chronic lesions. Younger animals are usually more susceptible than adult ones. Some species, such as goats and certain species of rats, seem to be able to eliminate the infection.

6. Epidemiology

6.1 Geographical distribution and prevalence of human infection

Although baseline data on the prevalence and morbidity of Chagas disease have improved in quality and quantity during the 1980s, it is still difficult to form an accurate picture of its geographical distribution and prevalence.

Among an estimated total population in the endemic countries[1] of 360 million inhabitants, at least 90 million persons (25%) are considered at risk of infection and 16-18 million people are infected. On the basis of studies

[1] Excluding Mexico and Nicaragua, for which adequate data are not available.

conducted in Brazil, it is generally accepted that about 30% of the infected population will develop clinically overt disease; hence it can be assumed that a total of 4.8-5.4 million people have clinical symptoms attributable to Chagas disease.

As has been noted in section 5 above, Chagas disease is a zoonosis capable of perpetuation in enzootic foci, without involving human infection. Such enzootic cycles extend approximately from latitude 42° N (northern California) to latitude 46° S (southern Argentina and Chile). The geographical distribution of human infection, however, extends from the south of the United States of America to the province of Chubut in Argentina, north of latitude 44°45′ S (Fig. 3).

The country data presented below (largely based on data available to the Pan American Health Organization; *14*) are variable in coverage and are drawn from reports of different years. It should be noted that the prevalence and incidence of the disease as well as the mortality due to it are constantly changing as a consequence of population migration, control programmes, changes in socioeconomic conditions, etc.

Argentina. The area of transmission includes the zones north of latitude 44°45′ S, covering 59.5% of the country. High transmission now prevails in four provinces. In 1981 the prevalence of infection was 5.8% among 18-year-old males entering military service; however, in areas of high transmission the prevalence rate reached 30% and clinical manifestations could be found in up to 30% of those infected. The prevalence of seropositivity in blood-bank donors varies in urban areas from 5% to more than 20%.

Bolivia. The endemic area covers 80% of the more than 1 000 000 km^2 of the country's territory, involving seven of the nine departments. In 1985 it was estimated that 1 133 000 people were infected in the Cochabamba, Sucre, Tarija, and Santa Cruz areas, with electrocardiographic alterations in 26% of infected persons. The triatomine house infestation rate (see Table 3, page 52) was 41.2% and the *T. cruzi* infection rate in vectors 30.1%. Seropositivity in blood-bank donors of more than 60% has been reported in Santa Cruz Department.

Brazil. The endemic area of some 3 600 000 km^2, 44.5% of the total area of the country, is the largest in the Americas. It includes 2400 municipalities (counties) of the states of Alagoas, Bahia, Ceará, Espírito Santo, Goiás, Maranhão, Mato Grosso do Sul, Minas Gerais, Paraiba, Paraná, Pernambuco, Piauí, Rio de Janeiro, Rio Grande do Norte, Rio Grande do Sul, São Paulo, Sergipe, and the Federal District. In addition, a few autochtonous cases have recently been found in the state of Pará. The percentage of infected individuals who develop a pathological condition varies, but abnormal electrocardiographs are found in 15-30% of seropositive individuals. Most of the cases with megaviscera have been reported from Bahia, Goiás, Minas Gerais, and São Paulo, in 6% of the seropositive population.

Figure 3
Geographical distribution of human *T. cruzi* infection in the Americas

Chile. Transmission occurs in the rural and suburban areas of the northern part, which covers half of the country between latitudes 18°30′ S and 34°36′ S. The endemic area is estimated at 350 000 km^2 (46% of the country). During the period 1981-86 the triatomine house infestation rate was 37.0% and the proportion of infected persons estimated at 20% of the total population. Seropositivity in blood banks varies from 0 in the south of the country to more than 15% in the north.

Colombia. The highest transmission rates are found in the Magdalena River valley, the Catatumbo River basin and the eastern region (Macarena, Meta). In Norte de Santander Department 30% of the individuals

surveyed were seropositive in 1985 and 9% of them showed electrocardiographic changes. In the same area the triatomine house infestation rate was 15.6%, and the *T. cruzi* infection rate in vectors was 2.25%.

Costa Rica. The vectors are found in the central plain, extending primarily to the north-west and south-west regions of the country. In Alajuela Province in 1984, the triatomine house infestation rate was 34.6% and the *T. cruzi* infection rate in vectors was 30%. Seropositivity in blood banks was around 1% in 1984.

Ecuador. Transmission is highest in the coastal region, including the provinces of Manabí and Guayas. Most of the human cases have been diagnosed in Guayaquil, capital city of the province of Guayas.

El Salvador. Vectors are present in 30-80% of the dwellings in rural areas and in the small or medium urban agglomerations; these account for 70-80% of the houses in the country. The *T. cruzi* infection rate in vectors is around 25%. There are indications that 20% of the rural population are infected.

Guatemala. Human infection is frequently found in the departments of Chiquimula, Jalapa, El Progreso, Santa Rosa, and Zacapa. A triatomine house infestation rate of 31.0% for *Triatoma dimidiata* has been found, with *Trypanosoma cruzi* infection rates of 34.1% in that vector and 31.0% in *Rhodnius prolixus.* Seropositivity has been found to be about 13% in blood banks.

Honduras. Vectors are present in the departments of Choluteca, Comayagua, Copán, Francisco Morazán, Intibucá, Lempira, Ocotepeque, Olancho, El Paraíso, La Paz, Santa Barbara, and Yoro. In 1983, the highest seropositivity rates were found in the western and eastern departments and in the southern region. About two-thirds of the population are estimated to be at risk. Infection rates in the vectors of 32% or more have been found, and seropositivity in 11% of blood-bank donors.

Mexico. Vectors and infected mammals are found in the states of Chiapas, Guanajuato, Guerrero, Hidalgo, Jalisco, México, Michoacán, Morelos, Nayarit, Oaxaca, Puebla, Sonora, Yucatán, and Zacatecas. The prevalence of the disease is highest in the Pacific coast states from Chiapas to Nayarit, in the Yucatán peninsula, and in some areas surrounding the Altiplano. Although most of the manifest human infections in Mexico are considered to be mild, there have been recent reports of a few cases with megaviscera, and up to 13% of seropositive individuals show electrocardiographic changes.

Nicaragua. No recent data are available, but there are older reports of infections in the departments of Chinandega, Esteli, Jinotega, Madriz, Managua, Matagalpa, and Rivas. The mountainous zones of the north-west and central regions and parts of the Pacific coast are the principal areas of domiciliated triatomine concentrations.

Panama. Vectors of *T. cruzi* are found in seven provinces of Panama and the Canal Area. A 16.4% infestation rate with *Triatoma dimidiata* has been found in houses in Gualaca District, with a *Trypanosoma cruzi* infection rate of 3.1%. *R. pallescens,* with a *T. cruzi* vector infection rate of 10.6%, has been found in only 3.2% of houses in Chorrera District.

Paraguay. Chagas disease is considered endemic in all rural areas. Isolated studies suggest that the prevalence of human infections varies from 10% in the Misiones region, to 53% in the Cordillera, and 72% in the Paraguayan Chaco.

Peru. The highest prevalence of human infection (12%) was found in the departments of Arequipa, Moquegua, and Tacna. In Arequipa, the triatomine house infestation rate was 26.3% in 1981-86, with a *T. cruzi* infection rate of 10.6% in the vectors.

United States of America. Sylvan vectors and reservoirs of *T. cruzi* have been detected in most of southern and central states. Although only three autochthonous human infections have been reported, the large number of immigrants from countries to the south, many of whom may be infected with *T. cruzi,* could make it necessary to screen donors for blood transfusion and organ transplantation.

Uruguay. The endemic area covers approximately 125 000 km^2 of the country's total area of 187 000 km^2 and includes the departments of Artigas, Cerro Largo, Colonia, Durazno, Flores, Florida, Paysandú, Río Negro, Rivera, Salto, San José, Soriano, and Tacuarembó. It is estimated that 132 000 of the more than 950 000 inhabitants of these areas are infected. In 1981-85 the triatomine house infestation rate was 1-6%, and the *T. cruzi* infection rate in vectors 4.8-12.4%.

Venezuela. The endemic area comprises 591 municipalities, covering almost 700 000 km^2 with an estimated population of 12 million in 1987. In the 1970s it was estimated that 1.2 million persons were infected.

6.2 Modes of transmission to humans

In the rural areas of Latin America, *Trypanosoma cruzi* is transmitted to humans via the faeces of infected triatomine bugs. In the cities, however, where triatomines are present only occasionally as a result of accidental introduction, the parasite is mainly transmitted by blood transfusion or congenitally; other routes are by oral contamination, by transplantation of infected organs, or, more rarely, by infection in the laboratory.

6.2.1 *Transmission by the insect vector*

In most cases of Chagas disease transmission of infection can be assigned to one of the seven main domiciliated species: *Triatoma infestans, T. brasiliensis, T. dimidiata, T. sordida, Panstrongylus megistus, Rhodnius prolixus and R. pallescens.* These species are characteristic of open

environments of Central and South America, either natural areas (savannas and grasslands, grassland-woodland mosaics such as *cerrado* and *caatinga,* dry forest, and the desert or semidesert Andean valleys) or man-made ecotopes (see also section 4).

The rate of transmission of *T. cruzi* by these and the other triatomine species is influenced by many factors, including the density of the vectors; their specific feeding frequencies; the proportion that feed on humans and on other important reservoir hosts; their longevity; their susceptibility to infection; their capacity to permit multiplication of the parasites and to excrete them; the interval between feeding and defecation; the susceptibility of the human and animal reservoir populations to infection; the distribution of the vector and animal reservoir populations in relation to human populations; the infection rates in the vectors, animal reservoir hosts, and humans; and the duration of parasitaemias.

6.2.2 *Transmission by blood transfusion*

The scope for transmission by blood transfusion is considerably greater than that for vectorial transmission since the urban areas (70% of the population of the continent) are involved, in which a large proportion of the population are migrants who have spent their first years of life in the endemic areas.

Seropositivity rates in blood donors often reach more than 20% in the highly endemic areas of Argentina and Brazil; a rate as high as 63% has been reported from Bolivia. Even in large cities outside the endemic areas, such as Buenos Aires, Caracas, Rio de Janeiro, Santiago, and São Paulo, seropositivity rates in blood banks range from 0.5% to 2%. Since it has been estimated that more than 1 million blood transfusions are made annually in Argentina and more than 4 million in Brazil, and that between 12% and 20% of the recipients of infected blood will become infected, it is probable that thousands of infections are brought about each year by this mode of transmission.

Factors related to the parasite, the recipient, the number of transfusions received by a patient, and the prevalence of infection in the area studied may be associated with the risk of *T. cruzi* transmission through blood transfusion. Another variable is the viability of the parasite and therefore its infectivity after cold storage in blood (it loses viability after 3 weeks' cold storage). A particularly high risk group are haemophilic patients, since they need numerous and frequent transfusions.

6.2.3 *Congenital transmission*

There is increasing evidence that congenital Chagas disease is more widespread than was previously believed. It is by no means restricted to the rural areas but also occurs even in cities where there is no vector transmission but to which large numbers of infected women of child-bearing age have migrated from the countryside.

In surveys in Argentina, the prevalence of infection in pregnant women has been found to vary from 6% to more than 20%, according to geographical area. In the city of Santa Cruz, Bolivia, it was 51%. In pregnant women from the lower socioeconomic levels in three Brazilian cities, a prevalence of between 5.8% and 10.9% was found. In Santiago, Chile, and three localities of the endemic area, the prevalence of seropositivity in pregnant women varied from 0.8% to 7.4%. In the city of Artigas, Uruguay, it was 8.9%.

The majority of infected mothers of congenitally infected newborn children show no clinical symptoms of chronic Chagas disease. The infection does not seem to affect fertility, nor does it seem to alter the course of pregnancy. Most authors have observed no differences between groups of infected and uninfected mothers with respect to abortion, low birth weight, premature birth, intrauterine death, and fetal development. Others, however, have reported that maternal infection can cause fetal death or premature birth.

Cases of congenital Chagas disease have been reported from Argentina, Bolivia, Brazil, Chile, Uruguay, and Venezuela (and one from Sweden in the infant of a Latin American immigrant). Studies in Argentina indicate that the prevalence of congenital infections ranges from 0.75% to 3.50% among infants of infected mothers. In Bahia, Brazil, the prevalence was 2% in infants of mothers who had not been serologically tested and 10.5% in those of seropositive mothers. The respective figures are 0.49% and 18.8% for Chile and 0.13% and 1.57% for Uruguay. In Santa Cruz, Bolivia, the prevalence of congenital transmission ranged from 5% to 8%. Transplacental infection may occur in subsequent pregnancies of the same mother but not necessarily in all of them. In newborn twins, either or both may be infected.

6.2.4 *Transmission by breast-feeding*

In 1936 in Salta, Argentina, trypomastigotes were found in the milk of a mother in the acute phase of the disease and her baby's infection was attributed to breast-feeding (*15*). This observation received little further attention until 1983, when an acute case of Chagas disease in a 2-month-old baby of a mother with the chronic disease was reported to have been acquired through breast-feeding; the case, however, appeared to be complicated by nipple bleeding. A systematic parasitological study carried out on 100 milk or colostrum samples from 78 mothers with chronic Chagas disease in Bahia, Brazil, gave negative results, even though five mothers had detectable parasitaemia at the time their milk was collected (*16*). In addition, 97 breast-fed children of infected mothers from Córdoba, Argentina, and Santa Cruz, Bolivia, born free of infection, were serologically negative. Transmission by breast-feeding therefore seems highly unlikely, and there is no reason to restrict breast-feeding by infected mothers.

6.2.5 *Accidental laboratory infection*

Laboratory contamination, though fortunately infrequent, does represent a very real risk of contracting Chagas disease. Laboratory accidents are usually due to punctures with infected needles, contact with contaminated materials, aspiration of *T. cruzi* cultures while pipetting, and splashing of *T. cruzi* suspensions on the conjunctivae. Measures for prevention and control are outlined in section 7.6.1.

6.2.6 *Oral transmission*

Acquisition of the parasite by ingestion of either infected triatomines or infected mammals has been demonstrated in experimental animals, but oral transmission of *T. cruzi* to humans has never been documented. However, epidemiological investigations of two unrelated outbreaks of acute Chagas disease have provided strongly suggestive evidence of oral transmission occurring through contaminated food (*17, 18*). If this can be confirmed, there is a potential danger of human infection through food contaminated by the secretions of house-invading opossums (see section 5.3.2).

6.2.7 *Transmission by organ transplantation*

The transplantation of organs from infected donors is a new mode of *T. cruzi* transmission that has received little attention. Patients who have received organs from donors with chronic Chagas disease have developed acute episodes of the disease and the parasite has been isolated from peripheral blood (*19*). Some fatal cases have been recognized, in whom parasites have been isolated from several organs. Since recipients are under immunosuppressive therapy, their susceptibility to infection with the donor's parasites is greatly increased. Similarly organ recipients who already have chronic Chagas disease can suffer an exacerbation of the infection as a result of the immunosuppressive treatment (*20*).

6.3 Risk factors for *T. cruzi* infection

To recapitulate what has been described in previous sections, *T. cruzi* infections are widespread in animals throughout the tropical and subtropical regions of the American continent, and Chagas disease in humans is endemic in most of Central and South America, where sociocultural conditions have brought human populations into close contact with the vector bugs. The vectors, in turn, have changed their habits and have adapted to become a natural part of the human domestic and peridomestic environment in most rural areas of Latin America. Chagas disease is the result of an interaction between *T. cruzi,* reduviid bugs, and people living in poor sociocultural conditions. It depends upon the coexistence of the etiological agent, the insect vector, the reservoir animal, and the susceptible person within a certain range of geographical and climatic factors, in combination with a range of cultural, social and economic conditions. These factors and conditions determine the

colonization, feeding and reproduction of vectors, the availability of reservoirs, and the presence of the human host.

6.3.1 *Biological factors*

Biological factors that affect the risk of human infection include the following variables related to the vector: (a) physiological habits of feeding and defecation; (b) anthropophilia; (c) adaptation to the colonization of human dwellings; (d) susceptibility to infection; (e) insecticide resistance; (f) colony densities; and (g) availability of reservoir hosts (see also sections 4.6 and 5.3).

In relation to *T. cruzi*, factors affecting the risk of human infection include: (a) reservoir availability and mobility (domestic, peridomestic, and sylvatic cycles); (b) infectivity of strains; and (c) morphological form at the time of parasite ingestion by the vector.

6.3.2 *Social factors*

In rural areas of Latin America, most human dwellings are poorly constructed or finished with materials, such as unplastered wattle-and-daub or palm-thatch roofs, that furnish excellent habitats for triatomines. This situation is rooted in the economic and cultural evolution of Latin American rural society as a whole and related to practices of household economy and individual habits and psychosocial patterns. These characteristics lead to changes in the natural ecotopes of vectors, which then invade human dwellings and transform the peridomestic area into breeding sites and foci for colony dispersion. Moreover, the sociocultural patterns also favour frequent movements of the human populations and the passive infestation of human dwellings by means of vectors lodged in objects and crops transported from a former abode to a new one. Seasonal or recurrent human migration in search of better living conditions not only enhances the risk of passive spread of the vectors with the household belongings but also increases the contamination of blood banks since poor infected migrants often sell their blood.

It is now well accepted that the natural transmission of *T. cruzi* can be interrupted by a combination of vector control measures with the promotion of social development. In addition, particularly in areas where no macrosocial development is foreseen, a better understanding is needed of the social factors that make people construct houses in such a way that they become propitious for colonization and that cause them to move frequently from one location to another; this requires microsocial analysis so that such factors may be taken into account when designing health protection strategies.

Isolation or difficulty of access makes it difficult for control programme teams to reach scattered houses and assist in their improvement. Moreover, the organization of rural work and the distribution of products and profits in rural areas lead to low incomes that prevent people from

purchasing the industrial products required for housing improvement. In some countries appropriate construction materials and supplies either are not produced or their delivery is poor in the rural areas. Since land ownership is difficult or impossible, houses are not constructed for long-term use, structures are unfinished, and hygienic standards (e.g., for cleaning and wastes disposal) are low.

The poor education of an unstable and unsettled population contributes to the perpetuation of confused beliefs about the vector and disease transmission and to a lack of self-confidence in the people's ability to control transmission; this produces passive and negative attitudes towards control activities.

The often low priority given to the control of Chagas disease by political authorities and the relatively powerless position of the population at risk, together with a shortage of resources allocated to control programmes, result in the failure or irregularity of house-spraying for vector control and of medical surveillance of the population and thus contribute to disease transmission.

Some of the social factors that need to be taken into account in relation to *T. cruzi* transmission are listed in Table 1.

Table 1
Social risk factors for *T. cruzi* infection

Social risk factors	Variables to be defined
Lack of stability; temporary nature of settlement	Modes of crop culture Agricultural practices and crop cycles Housing/land ownership
Lack of land ownership	Legal/cultural and economic aspects
High degree of human movement/migration	Domestic objects and clothing of migrants: organization, storage and disposal Kind of occupation: seasonal workers, day labourers Distance between home and workplace
Low or subsistence income	Patterns of production; occupation; temporary income Future aspirations
Low level of hygienic practices	Future aspirations Knowledge of disease transmission Supply of and demand for public health services Adequacy of furniture and fitments
Low education level; inappropriate practices and beliefs related to modes of transmission	Supply of and demand for public educational services Knowledge, attitudes and practices concerning health protection Future aspirations
Housing propitious for colonization	Housing technology Motivation for settlement Family composition
Lack of insecticide use	Regularity of house-spraying Household use of domestic insecticide High cost or difficulty of delivery of chemical products
Presence of infected domestic animals	Cultural habits, beliefs and knowledge of hygiene
Animal/storage shelters in the peridomestic area and inside houses	Knowledge of construction technology Cultural/traditional habits
Lack of low-price housing and construction materials	Industrial production Retailers in the area Autochthonous construction techniques
Isolation or difficult accessibility of houses	Existence of roads Public transportation

7. Prevention and control methods

7.1 Diagnosis

7.1.1 *Parasitological methods*

Direct methods

Direct observation of the parasite is usually made in blood. The most commonly used techniques are thin blood smear, thick blood smear, or examination of a sample of fresh blood between slide and coverslip. While examination of stained preparations allows for morphological characterization of the parasite (which is important in areas where there is also *T. rangeli*), fresh blood preparations permit easier detection of parasites because of their motility. Parasite concentration methods increase the probability of detecting parasitaemia. The simplest is centrifugation of blood. Another is to let the blood coagulate, centrifuge the serum at low speed to remove remaining red cells, and subsequently centrifuge at a higher speed (600*g*) to concentrate the parasites in the sediment (Strout method). An efficient modification of this method is to collect blood in a capillary tube, centrifuge the tube, and examine the interphase between the red blood cells and leukocyte buffy coat under the microscope. The capillary tube could be also cut at the level between red blood cells and the buffy coat and a drop examined under the microscope (see Table 2).

Centrifugation and direct microscopical observation can be also used for detecting parasites in cerebrospinal fluid.

Table 2
Parasitological methods for the diagnosis of Chagas disease

Methods	Type of laboratory[a]	Percentage sensitivity[b]	
		Acute stage	Chronic stage
Direct			
Thin smear	A/B	<60	<10
Thick blood smear	A/B	<70	<10
Fresh blood examination	A/B	80–90	<10
Strout	A/B	90–100	<10
Buffy coat on slide	A/B	90–100	<10
Indirect			
Xenodiagnosis	B	100	20–50
Blood culture	B	100	40–50

[a] A: Health centre laboratories located in areas at risk of vectorial and nonvectorial transmission (the infrastructure is that from the first level of medical care upwards). B: Specialized laboratories for parasitological diagnosis.

[b] As compared to xenodiagnosis for the acute stage of the infection and to serological diagnosis for the chronic stage.

Indirect methods

Xenodiagnosis requires the availability of infection-free triatomines reared in the laboratory. The technique is performed with 40 third-instar nymphs of *Triatoma infestans* or *Rhodnius prolixus* or 40 first-instar nymphs of *Dipetalogaster maxima,* distributed 10 per box, which are fed upon the patient. Thirty and 60 days after the blood-meal, their faeces and intestines are examined under the microscope for trypomastigotes or epimastigotes of *T. cruzi.* They should not be confused with *Blastocrithidia triatoma,* a trypanosomatid morphologically similar to the epimastigote of *T. cruzi.*[1] Another source of error in xenodiagnosis is the presence of *T. rangeli,* which is found (but is not pathogenic) in humans in Central America and northern South America. In this case, the haemolymph and saliva of *R. prolixus* need to be examined for *T. rangeli* in addition to their faeces, because although *T. rangeli* is, like *T. cruzi,* a stercorarian trypanosome (i.e., one that develops in the gut of the insect vector), it later migrates to the salivary glands.

Blood culture is increasingly used for amplification of parasites in the diagnosis of Chagas disease in endemic areas where laboratory colonies of vectors for xenodiagnosis have been established. Liquid media such as LIT (liver infusion tryptose) or BHI (brain-heart infusion) are used, and the effectiveness of the method can be enhanced by differential centrifugation of the blood before inoculation of the medium. In the chronic stage, parasites can be detected in about 40-50% of patients. Repeated blood cultures together with serological methods are used to assess cure after treatment.

7.1.2 *Serological methods*

Early in the course of infection antibodies against *T. cruzi* are in the IgM class; they are gradually replaced by IgG antibodies as the disease progresses. Total IgM concentrations are higher in persons with an acute infection than in uninfected individuals, but there is no increase in immunoglobulin concentrations during the chronic stage except in patients with megaviscera, in whom higher concentrations of IgA have been reported.

Among several serological tests available for the diagnosis of *T. cruzi* infection, the most widely used are the complement-fixation test (CFT or Guerrero Machado test); the indirect haemagglutination test (IHA); the indirect immunofluorescence test (IFAT); the direct agglutination test, with or without treatment of the serum with 2-mercaptoethanol (DA and 2-MEDA); and the enzyme-linked immunosorbent assay (ELISA). Other assays that have been tested, but not used routinely, are the immunoperoxidase test, which is similar to the IFAT except that a peroxidase-labelled conjugate is used instead of a fluorescent one; an

[1] Colonies of *T. infestans* infected with *B. triatoma* must be destroyed and replaced by new colonies.

immunodiffusion test; a dot-blot ELISA; and a capture ELISA using monoclonal antibodies. A latex agglutination test has been introduced for blood-bank screening.

The antigens used in these tests are the following:

- *Complement-fixation test (CFT).* Aqueous or methanol extracts of whole *T. cruzi* have been widely used but have been replaced by purified fractions of the parasite in an attempt to standardize the sensitivity and specificity.
- *Indirect immunofluorescent antibody test (IFAT).* Formol-fixed epimastigotes are stable antigens. The IFAT has the advantage that it can be used for differentiating IgM from IgG antibodies.
- *Indirect haemagglutination test (IHA).* The antigens are polysaccharide or glycoprotein fractions from epimastigotes. Red cells sensitized with those antigens can be stored lyophilized or in suspension.
- *Direct agglutination test (DA and 2-MEDA).* The antigen consists of whole epimastigotes treated with trypsin, and fixed with formaldehyde and filtered to prevent autoagglutination. The test can be used for detection of IgG or IgM antibodies.
- *ELISA.* The antigen consists of peroxidase- or phosphatase-labelled conjugates or fractions of *T. cruzi* adsorbed to polyvinyl plates or other materials, and is stable. The test can be used for detection of IgG or IgM antibodies.
- *Latex agglutination.* Polystyrene particles adsorbed with *T. cruzi* extracts are used.

Most available methods for serological diagnosis require reagents that must be stored at 4 °C. The CFT needs the greatest number of standardized reagents. Antigens for DA, IHA, and ELISA can be maintained at room temperature. The ELISA requires a reader and the IFAT a fluorescence microscope. The indirect immunoperoxidase test needs only a light microscope. For screening purposes the latex test is the simplest, but positive samples must be confirmed by other tests. If microtitration equipment is available, the combination of the 2-MEDA with DA, IHA, IFAT or ELISA for quantitative results is recommended.

The CFT, IFAT, IHA and ELISA are the most widely used diagnostic tests for Chagas disease. The reagents they require, as well as those for the DA and latex tests, are produced by public health laboratories or are commercially available. The test that becomes positive earliest during infection is the IFAT for detecting IgM antibodies, followed by the combination of the 2-MEDA and DA, also detecting IgM. Subsequently the IFAT-IgG, the CFT and the IHA become positive. In chronically infected individuals with proven parasitaemia, all the above-mentioned tests have been reported positive in more than 95% of sera. However, false-positive reactions can occur with sera from patients with leishmaniasis or persons harbouring *T. rangeli.*

Since the specificities of the tests may vary considerably, the cut-off points for positivity should be defined locally, using a standard serum panel. Discrepancies between results of the same test in different laboratories are also common. It is therefore recommended that at least two serological tests should be used for confirmation of infection.

For reliability, the techniques need to be well standardized and a stringent system of quality control must be implemented. From experience in several countries, it is recommended that a national laboratory network should be established in each of the countries in which Chagas disease is endemic. The organization of these networks could be based on any similar existing structure and coordinated by a national reference laboratory. This coordinating laboratory should be responsible for: (a) training laboratory personnel, (b) distributing the necessary reagents, and (c) setting up the requisite quality control programme. In some countries combined laboratory networks exist for blood-bank screening as well as for the diagnosis of Chagas disease; their value is widely recognized.

Reliability depends on several factors that must be controlled. Detection of errors implies testing of pools of calibrated sera, from samples of known titres, in order to obtain high, intermediate, and negative standard pools. Each time a test is performed, two known positive and two known negative sera are included together with the batch of sera to be tested. For evaluation, calibration curves are useful. They are obtained by comparing the logarithmic values of the reciprocal titres in a series of 15 tests; the geometric mean and standard deviation can thus be calculated, and a curve obtained that provides an evaluation of the laboratory's reliability.

7.1.3 *Diagnosis of acute, chronic, and congenital infections*

Acute infection

A diagnosis of recent infection with *T. cruzi* can be made by direct microscopy, with or without the help of methods for concentrating the parasites, or by indirect methods such as xenodiagnosis, blood culture, or inoculation of susceptible animals (not recommended). In endemic areas, where most cases of recent infection occur, the use of the indirect methods is unlikely. In practice, thick blood smears, fresh blood examination, and the Strout or capillary methods are the most widely used techniques. As an alternative, seroconversion can be used if periodic serum samples from the patient are available. When symptoms are not characteristic of recent *T. cruzi* infection – i.e., in the absence of "Romaña's sign" – and when parasitological examination is negative but a serological test is positive, it is difficult to conclude that a *T. cruzi* infection is recent. Seropositivity or even positive xenodiagnosis may be due to a previous infection that was not recognized. In such cases the only means of confirming the diagnosis is by detecting specific IgM antibodies by IFAT-IgM, ELISA-IgM, or the combination of the DA and 2-MEDA.

Chronic infection

During chronic infections, direct parasitological methods usually give negative results and even xenodiagnosis is positive in only about 50% of cases and may have to be repeated several times before a positive result is obtained. On the other hand, any of the serological tests mentioned above should be positive.

Congenital infection

Transplacental infection can be confirmed only by detection of parasites. Histological examination of the placenta of a fetus or of a stillborn or liveborn infant may show a villous and intervillous inflammatory reaction accompanied by different degrees of thrombosis and vascularitis, with or without amastigotes. In most cases, there is a direct relationship between the intensity of parasitaemia and the inflammatory reaction. However, the presence of amastigotes in the placenta does not necessarily indicate infection of the infant, nor is it possible to detect parasites in the placenta of all infected infants. In about half the cases in which parasites have been present in the placenta they have also been found in the umbilical cord.

Confirmation of *T. cruzi* infection in a newborn infant is usually based on the detection of the parasites in its blood. Fresh blood examination, thin or thick blood smears, blood culture, and/or xenodiagnosis are the methods most commonly used. Concentration of the parasites by the Strout method or in a capillary tube increases the possibility of finding the parasite by microscopy. Xenodiagnosis is considered a more sensitive method than direct microscopy, but it has the disadvantage that the result cannot be read for at least 30 days.

As in other transplacental infections, newborn infants infected with *T. cruzi* have higher than normal concentrations of serum IgM. In the absence of placental alterations, such a finding may indicate some intrauterine infection, but it is not sufficient to confirm *T. cruzi* infection. To do so, it is necessary to detect specific fetal IgM; for this purpose, ELISA-IgM is considered a more sensitive test than IFAT-IgM and the latter more sensitive than the DA-IgM.

Although the presence of specific IgM antibodies in the infant is indicative of immunoglobulin of fetal origin, a positive result should be considered significant only when (a) the mother does not show specific IgM antibodies in her blood or (b) placental leakage of the antibodies from the mother to the fetus can be ruled out. In addition, it has been reported that parasitaemic infants may not have specific IgM because the fetus was infected either very early during pregnancy or just before delivery. Therefore, although the presence of specific IgM may help the diagnosis, its absence does not exclude congenital infection.

As specific IgG anti-*T. cruzi* antibodies from the mother pass through the placenta, both *T. cruzi*-infected and uninfected infants will be seropositive.

However, in congenitally infected children the antibody titres will remain constant or increase, whereas in the uninfected ones they will progressively decrease.

7.1.4 *Blood-bank and organ-transplant screening*

Serum screening tests, such as the IHA or latex agglutination tests performed under controlled conditions at a dilution of 1:8, are useful for the examination of sera as a first step in blood control. Positive results should be confirmed by two tests in order to direct seropositive donors to a clinic for attention. There is still a need, however, for well-defined serological reagents providing the high sensitivity and specificity required for blood banks and for a reference test for Chagas disease diagnosis.

Infections that have occurred as a consequence of organ transplants show the need for serological studies in both donors and recipients of organs. If infection is confirmed in either individual, specific chemotherapy should be undertaken before and after the transplant. In such cases, the parasite should be isolated before the transplant and its susceptibility to antitrypanosomal drugs tested.

7.2 Clinical management and treatment

Two main aspects of the treatment of Chagas disease must be considered: trypanosomicidal treatment and symptomatic treatment of the different clinical forms.

7.2.1 *Trypanosomicidal treatment*

Trypanosomicidal treatment is indicated for patients with acute Chagas disease, most of whom are young and more tolerant than adults of the effects of the drugs used.

Nifurtimox (a nitrofuran derivative) and benznidazole (a nitroimidazole) are active against trypomastigotes as well as amastigotes. Nifurtimox is given in daily doses of 10 mg per kg of body weight to adults and 15 mg/kg to children for 60-90 days, while benznidazole is administered in daily doses of 5-10 mg/kg for 30-60 days. Acute meningoencephalitis is a severe complication for the alleviation of which trypanosomicidal treatment plays an important role. In such cases the daily dose of nifurtimox may be as high as 25 mg/kg. In the acute phase of Chagas disease trypanosomicidal treatment may turn to negative previously positive xenodiagnoses and serological tests in a considerable number of cases. However, *T. cruzi* strains from Argentina and Chile are more susceptible to the above drugs than those from Brazil.

The therapeutic efficacy of allopurinol is at present under investigation. Preliminary studies have shown it to have trypanosomicidal action at daily doses of 600 mg given for 30-60 days. If its efficacy is demonstrated, then it is possible that, given the lack of serious adverse reactions, prospects for the treatment of patients would improve.

Nifurtimox and benznidazole have also been used for treatment of congenital Chagas disease, nifurtimox in doses varying from 8 to 25 mg/kg daily for 30 days or more, and benznidazole in doses of 5-10 mg/kg daily for 30-60 days. Data from Argentina, Chile, and Uruguay suggest that both drugs are usually effective there, while data from Brazil indicate that failures also occur. Treatment is considered to be successful when both parasitaemia and serological tests become negative and remain negative for at least a year after the end of treatment. Serological tests tend to become negative from 6 to 8 months after treatment. In any case, the earlier the diagnosis is made and treatment initiated, the greater is the chance that the patient will be parasitologically cured (*21*).

Since there is no information on the effectiveness of trypanosomicidal treatment in preventing the development of chronic Chagas disease, it is not indicated during the indeterminate stage of the infection. However, in exceptional cases, when it is given for clinical investigation or at the specific request of a patient, patients must be followed up during treatment, any adverse effects treated, and the possible long-term benefit assessed. It seems that most patients cured in the indeterminate stage have been infants or children. The possible benefit of treating children in the indeterminate stage needs further study, however. Such studies can only be meaningful if clinical protocols are clearly defined and strictly followed.

At present, there is a consensus that patients in the chronic stage of the disease, with overt organic lesions, do not benefit from trypanosomicidal treatment.

7.2.2 *Symptomatic treatment*

Acute stage

Acute Chagas disease comprises three main syndromes: signs and symptoms due to the general infection, acute myocarditis, and acute meningoencephalitis (see section 2.1.1).

The generic symptoms subside spontaneously in 6-8 weeks but disappear more rapidly with trypanosomicidal treatment. In addition, it may be necessary to give antipyretic sedatives, anticonvulsants, and antiemetics or antidiarrhoeals to restore the hydroelectrolytic balance in cases of severe vomiting and diarrhoea.

Alterations due to acute myocarditis also disappear spontaneously but they have a shorter effect when trypanosomicidal treatment is given. For treatment of the clinical manifestations of heart failure due to myocarditis, the usual therapeutic criteria are followed – that is, restriction of sodium intake and administration of digitalis and diuretics.

In acute meningoencephalitis, sedatives and anticonvulsants as well as intravenous mannitol may be needed. As has been mentioned (section 7.2.1), nifurtimox may be given in a daily dose as high as 25 mg/kg.

Chronic stage

In the chronic stage of Chagas disease cardiac, digestive or neurological lesions occur. The two first-mentioned may be improved by symptomatic treatment.

Chronic myocarditis. This causes heart failure, cardiac arrhythmias, and peripheral and pulmonary embolism (*22*).

Heart failure can be compensated by reduction of physical activity, limitation of sodium intake, and prescription of diuretics and peripheral vasodilators, mainly angiotensin-converting-enzyme inhibitors. Care must be taken to maintain the serum potassium within the normal limits. Only when such a therapeutic approach is not effective may digitalis be used, but with caution since in cases of severe myocardial damage digitalis may cause ventricular premature beats or aggravate pre-existing arrhythmia. It can also interfere with A-V conduction, mainly in patients with atrial fibrillation and slow ventricular response.

The therapeutic approach in cardiac arrhythmias depends on whether they are bradycardic or tachycardic. Patients with bradyarrhythmias respond poorly to atropine and require a permanent pacemaker when they become symptomatic. Those suffering from atrial fibrillation with slow ventricular response that is resistant to vagolytic drugs and complete A-V block also need a permanent pacemaker. Treatment of ventricular arrhythmias is indicated to prevent ventricular tachycardia or ventricular fibrillation and to prolong the life expectancy of the patient. Antiarrhythmic drugs are usually effective but such possible effects as aggravation of a pre-existent arrhythmia or negative inotropism must be watched very carefully. The antiarrhythmic drugs with recognized efficacy against ventricular extrasystoles in chronic chagasic myocarditis are lidocaine, mexiletine, propafenone, flecainide, β-adrenoreceptor antagonists, and amiodarone. Intravenous lidocaine has a rapid effect in emergencies; it is also useful to bridge the interval until oral antiarrhythmic drugs become effective. β-Adrenoreceptor antagonists can be used provided there are no signs of heart failure.

The most effective antiarrhythmic drug in Chagas disease is amiodarone. Besides its ability to suppress ventricular premature beats with more efficacy and constancy than any other antiarrhythmic drug, it is well tolerated, it does not have a negative inotropic effect, and has a long half-life and a cumulative effect. By this more uniform and constant antiarrhythmic action, it affords the patient a powerful protection that is not strictly dependent on close adherence to treatment schedules. However, careful surveillance is necessary during treatment since it may have some potentially dangerous side-effects, such as wave-burst arrhythmia or severe interstitial pneumonitis.

Antiarrhythmic drugs can cause or aggravate: bradyarrhythmias by depressing the sinus node automatism; A-V block in patients with atrial fibrillation; or intraventricular conduction defects that, again, may lead to

a complete A-V block. In this last event, the use of antiarrhythmic drugs that suppress premature ventricular beats must be combined with the implantation of a permanent pacemaker. In cases of ventricular arrhythmias that are particularly resistant to drug treatment, surgical resection of arrhythmogenic zones localized by endocardial mapping may be considered. Catheter electrofulguration, antitachycardia pacemakers, and implantable cardioverter-defibrillator devices may also be tried. When such alternatives to drug therapy are considered, it must be borne in mind that chronic chagasic myocarditis is a continuous process and that the lesions that produce ventricular arrhythmias may change or new arrhythmogenic foci may appear. Consequently, neither catheter electrofulguration, nor endocardial resection, nor implantation of a pacemaker can be considered definitive treatment of chronic chagasic myocarditis.

The presence of thrombi inthe heart chambers can easily be shown with an echocardiogram. To prevent embolism, anticoagulant therapy is indicated, but this needs careful drug titration and strict, periodic laboratory control. The practical implementation of such treatment in patients with Chagas disease is usually considered too cumbersome.

There is insufficient information on the possible benefit of surgical resection of ventricular aneurysms in chronic Chagas disease.

Mega-oesophagus and megacolon. Mega-oesophagus needs treatment when it becomes symptomatic – that is, when regurgitation or dysphagia upsets the patient. Two procedures are available: dilatation of the lower part of the oesophagus by noninvasive means or by surgical intervention. Surgical treatment has fewer complications, is effective, and produces long-lasting results.

Megacolon should be surgically treated if there is serious constipation, even before the most important complications of faecaloma or volvulus become evident. Surgical treatment consists in resecting the last part of the large intestine, mainly the sigmoid colon, different techniques being applied according to the spread of the lesion, the symptomatology, and the age of the patient. Even if faecaloma can initially be medically treated by manual or instrumental extraction or by appropriate rectal instillations, it can sometimes become necessary to remove it by surgical intervention. Acute volvulus with vascular involvement requires urgent surgical treatment.

Neurological forms. There is still no known treatment for the neurological forms of chronic Chagas disease.

7.2.3 *Assessment of cure*

The reversal of serological results from positive to negative implies the absence of trypanosomes from the organism. In patients with a recent infection, trypanosomicidal treatment often results in persistently negative

xenodiagnosis and serological tests; these changes are considered an indication of cure. In chronic cases, however, parasitological negativity is more difficult to assess. Xenodiagnosis is the standard method for parasitological diagnosis but it is of low sensitivity, and a negative xenodiagnosis therefore cannot be taken as proof of the absence of parasites. However, if serological results become negative in a chronic case, that can be considered a sign of cure.

In persons in the indeterminate stage of the disease, spontaneous reversal of serological test results has been observed, but only on rare occasions.

It has recently been proposed that detection of lytic antibodies against *T. cruzi* trypomastigotes by the complement-mediated lysis test should be a measure of active infection and therefore their subsequent absence a marker of cure. Further experience will be required to show the value of this test for the assessment of cure.

7.3 Vector control

7.3.1 *Chemical control of vectors*

Conventional insecticide spraying

Chlorinated hydrocarbons such as HCH and dieldrin were used for the control of Chagas disease vectors in the 1950s and 1960s. (DDT had a low level of effectiveness against the bugs and was discarded for this purpose.) The short residual action of the chlorinated hydrocarbons (30-180 days) made their application in two successive cycles necessary. The first application would eliminate the insects (nymphs and adults), while the second, 30-180 days later, would kill the nymphs born from eggs laid before the first application. The dosage of HCH used (in the form of the gamma-isomer, lindane) was 500 mg/m^2. The method was very slow, because the insecticide had to be applied in two accurately spaced spray rounds, and expensive, because the operational costs of the spray programmes were double those that would have been achieved with a compound needing only one application. Faster and more economical methods therefore needed to be identified that would require only a single spray round.

New insecticides with a longer residual effect and low toxicity for humans and domestic and farm animals were sought. Carbamates such as propoxur were introduced and gave good results, but their cost was too high for large-scale application. These trials were followed by the introduction of organophosphorus compounds, such as dichlorvos, applied as a "dry fog" or formulated as slow-release tablets. These compounds are still in use in devices such as the fumigant canister.

The organophosphates malathion and fenitrothion, introduced in 1975 into Chagas vector control programmes, allowed a spacing between applications of 1-2 years and therefore helped to reduce operational costs, but their disadvantage is a strong and unpleasant smell, which leads to high

refusal rates of house-spraying by villagers. These compounds are also very effective when applied to outhouses and other peridomestic structures including corrals, chicken houses and pigsties. They continue to be used for this purpose, at a dosage of 2 g/m^2.

Synthetic pyrethroids have been successfully applied since 1980 – deltamethrin in a flowable formulation at dosages of 25-50 mg/m^2 or cypermethrin and permethrin in liquid or powder form at dosages of 100-200 mg/m^2. It has been demonstrated that these products keep houses and peridomestic structures free of vectors for about 2 years. Moreover, there are few problems in their application, and apart from rare allergic reactions, their toxicity is very low. Other synthetic pyrethroids are currently under study.

Chemical vector control programmes have been successfully implemented in Argentina, Brazil, and Venezuela. In large parts of these countries, programmes have entered into the surveillance phase, characterized by monitoring of house infestation and, where necessary, focal spraying. A problem faced by the programme in Brazil is that of the replacement of *Triatoma infestans* by secondary vector species. This has drawn attention to the importance of the peridomestic habitat, where vector control can be achieved by a combination of spraying and environmental management.

Constraints on existing control programmes and resource limitations could, in part, be overcome by complementing conventional approaches with simple control and surveillance methods suitable for application in the primary health care context.

Innovative chemical control tools

In recent years, two new vector control tools have been developed for use against Chagas disease: a fumigant canister and a range of slow-release compounds, i.e., formulations of paints that incorporate insecticides. The canister, when activated, produces a gas composed of various synergistic elements, of which dichlorvos and fenitrothion are the insecticidal compounds. In slow-release paints a number of insecticides can serve as the active principle, but malathion mixed with polyvinyl acetate has been the most intensively tested.

A combination of pyrethroid spraying of the peridomicilium, the timely and well-spaced use of the canister, and community-based bug monitoring using the newly developed sensor boxes (see section 7.3.4) forms the basis of a possible alternative approach to achieving sustained and affordable vector control in areas where problems of logistics render the conventional spraying campaigns impracticable.

Field trials of a malathion/polyvinyl acetate slow-release emulsion paint in Posse (Goiás, Brazil) have shown it to be a formulation of long indoor effectiveness: after 24 months there was still a lethal effect on more than 85% of first-instar nymphs. Community acceptance was good. Further field trials in other endemic countries of Central and South America are

under way, to confirm, if possible, the use of such formulations as a cost-effective way of obtaining adequate control in remote areas.

7.3.2 *Insecticide resistance*

Resistance of Triatominae to insecticides has been well documented only in certain areas of Venezuela, where *Rhodnius prolixus* is highly resistant to dieldrin. Monitoring of the susceptibility status of the important vectors to the most commonly used insecticides should be done annually in each control area, using the standard WHO susceptibility test kit for Reduviidae.[1]

7.3.3 *Housing improvement*

Long-term control of the vectors of Chagas disease can be obtained only by modification of the houses in endemic areas in such a way as to make them unsuitable for colonization by the bugs. A number of physical features and types of use, characteristic of poor rural housing in Latin America, favour such colonization; these are related, as regards physical features, to the types of construction material used, the building technology applied, and the fact that most of the houses are poorly finished or even left unfinished, and, as regards types of use, to the habits and life-style of the *campesinos,* the country people.

Certain characteristics of the dwelling will be of greater or lesser importance than others according to the vector species concerned. Nevertheless, a house in good condition should be considered the basic goal for achieving a healthy population. The main factors concerned in the control of the vectors fall into three categories: (a) the type of construction of the dwelling itself, (b) the state of the peridomestic area and the types of peridomiciliary construction, and (c) the nature and location of objects stored inside the house.

The replacement of palm-leaf roofs by materials that are unsuitable for vector colonization is the most important measure for the control of *R. prolixus.* In the case of *Triatoma dimidiata,* however, the primary objective is to cement the dirt floor. Against both these species and *T. infestans* it is important to plaster the walls in order to prevent the formation of cracks in which the bugs may settle. Storage of materials and belongings also provides convenient hiding-places for the vector; this is particularly true where crops are stored inside the house, where clothes are piled up or stored in boxes, and where assorted objects, including firewood, are piled up in the house. The same applies to buildings in the peridomestic area, which are usually in an even worse state of repair as less care is taken in their construction.

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[1] *Instructions for determining the susceptibility or resistance of reduviid bugs to organochlorine insecticides.* Geneva, World Health Organization, 1975 (unpublished document WHO/VBC/75.587; available, on request, from Division of Control of Tropical Diseases, World Health Organization, 1211 Geneva 27, Switzerland).

Social determinants of poor housing conditions

The poor housing conditions described in sections 4.5.3 and 6.3.2 can be explained on both a macrosocial and a microsocial level. At the macrosocial level, the poverty in so much of Latin America is accentuated in the rural areas where the *campesinos* generally cannot afford a house and life-style that provide them with even minimum comfort. Moreover, the production and supply of the industrial goods necessary for the construction of adequate houses are limited – and the price is therefore high – since the demand is considered insufficient. The low demand, in turn, is attributed to a lack of cash and to the scattering of the rural population in areas often remote from the supply source.

The microsocial conditions relate to the nature of the work required for housing improvement and the family income, which restricts the amount available to be spent on this; landownership patterns and issues of ownership and market value of houses; cultural values, by which a partly finished house is considered sufficient and normal; psychosocial factors, whereby individuals feel they can do little to control their own future or the disease; and demographic factors, which underlie feelings of rootlessness and transience.

The above factors are closely linked to the technology available. Sophisticated, expensive technnology only renders more inadequate the already limited resources of the *campesinos*, thereby deepening their belief that they can do little or nothing to control the disease. Housing improvement is a matter of technology that should be suited to the social and economic realities of the population at risk. An approach based on appropriate technology will help to increase the confidence of individuals and families in their own abilities and means. If a disease control and housing improvement programme is to be successful, these microsocial factors must be taken into consideration and good relations established between the population at risk and the control programme.

Housing improvement: strategies and technology

It is not realistic to expect the *campesinos* to improve their houses on their own and at their own expense. Nor can housing improvement be considered a task for the ministry of health alone. Coordinated action is required from all parties concerned (see also section 8.3.1). The successful implementation of a joint housing improvement programme implies the ability to maintain a dialogue based on mutual recognition of the position of each of the partners and on a willingness to work together in the common interest.

If such a programme is to fit in with the actual conditions, it must be based on improving traditional construction technology as much as possible rather than on creating a substitute technology. It should permit the use of local natural resources as well as of the knowledge and skills already available in a community. The application of traditional technology (adobe and various other forms of mud construction such as *bahareque, tapia,* and *pau-a-pique*) should not exclude innovations, but should be a means of allowing them to

be introduced as well as of permitting family involvement in the work to be carried out. This is important not only as an economic but also as an educational measure.

Housing improvement always requires certain materials that cannot be directly obtained from local sources, such as the necessary roofing materials and sanitary equipment. Small loans are therefore most important to enable families to obtain these materials.

In addition to financial assistance, an educational programme is required to provide information on the disease and on the conditions that favour its spread, and thereby to promote confidence in the population's ability to control it. However, the educational programme cannot be considered separately from the technological and operational aspects. The programme as a whole is educational, on both a formal and an informal level and, as such, should meet educational objectives.

A programme of this type can overcome the difficulties faced by a programme that is aimed exclusively at the control of Chagas disease and whose effects will therefore be seen only in the long term. A housing improvement programme such as the one carried out in Venezuela achieves both the aim of the ministry of health to control the disease and the desire of the *campesino* to have a better home. Furthermore, wider health objectives can be achieved as a result of the better protection offered to the poor rural population.

7.3.4 *Evaluation of vector control*

Every vector control programme should include components of entomological, serological, and clinical evaluation to determine the effectiveness of control activities and to measure the duration of their effect in order to be able to determine the required frequency of application of specific measures. It must be stressed that the interruption of transmission also depends upon the establishment of referral systems covering all medical and health care institutions and upon continuing educational activities.

Entomological evaluation

The entomological indicators recommended by a PAHO/WHO Study Group on Chagas disease control strategies (Washington, DC, 1984) are presented in Table 3.

Entomological evaluation methods may be either active (e.g., house inspections) or passive (sensor boxes).

House inspections. Usually one collector searches all possible refuges inside and outside the house for 1 hour or some other fixed time period. Solutions of pyrethrins (0.3-1.0%) or certain pyrethroids (e.g., tetramethrin/phenothrin 4:1, 0.125%) may be applied to potential hiding-places of the bugs to irritate them and flush them out. This active detection

Table 3
Entomological indicators for Chagas disease control

1. **Infestation index**	$\frac{\text{Number of houses infested by triatomines}}{\text{Number of houses examined}}$	$\times 100$
2. **Density index**	$\frac{\text{Number of triatomines captured}}{\text{Number of houses examined}}$	$\times 100$
3. **Crowding index**	$\frac{\text{Number of triatomines captured}}{\text{Number of houses with triatomines}}$	$\times 100$
4. **Dispersion index**	$\frac{\text{Number of localities infested with triatomines}}{\text{Number of localities examined}}$	$\times 100$
5. **Colonization index**	$\frac{\text{Number of houses with triatomine nymphs}}{\text{Number of houses positive for triatomines}}$	$\times 100$
6. **Natural infestation index**	$\frac{\text{Number of triatomines with } \textit{T. cruzi}}{\text{Number of triatomines examined}}$	$\times 100$

method has traditionally been done by trained personnel in vertical programmes, but more recently householders have been encouraged to do untimed searches. A small cardboard box or envelope, with a drawing of a triatomine and instructions to place bugs in an enclosed plastic bag or vial, is hung on the wall. The captured bugs are picked up by the primary health care worker or taken by the householder to the nearest health post, school or other reference centre.

Sensor boxes. Gomez-Nuñez boxes, developed in Venezuela, and Maria sensor boxes, developed in Argentina, are artificial refuges made of cardboard with holes in the sides for entry of the bugs and pleated paper inside for resting sites. Triatomines are attracted to these refuges and may enter or leave at will. The boxes, placed next to or on the interior walls of houses, are checked periodically for live or dead bugs and for signs of bugs, such as exuviae, faecal droppings, or eggs.

Wall bioassays. In order to determine the residual activity of insecticides, fifth-instar nymphs of a colony strain of the target species are exposed to the treated surfaces under Petri dishes for fixed time periods (1-24 hours

depending on species and insecticide) at intervals after treatment. Care must be taken to standardize the type of surface tested (mud, cement, thatch, etc.) according to the most common surfaces encountered in each area.

Serological evaluation

Despite the obvious value of entomological evaluation of control, it must be remembered that the final purpose of control is to reduce transmission, which may be measured by prevalence surveys that may in some cases be more practical and economical than entomological evaluation. Particular attention should be paid to young children in order to detect recent transmission. Selected cohorts (military personnel, schoolchildren, etc.) are usually utilized as a cross-sectional sample of an area or country, permitting an indirect evaluation of the interruption or reinstatement of transmission.

For proper quality control of serological tests a network of reference laboratories (see section 7.1.2), with wide coverage, should be utilized by any serological evaluation programme.

Clinical evaluation

Active and passive searches for acute symptomatic cases will also indicate whether transmission has been reduced or reinstated.

Impact of established control programmes

Control programmes were implemented in the early 1960s in Argentina and Brazil, resorting mainly to residual insecticide spraying, and in Venezuela, using a combination of insecticide spraying and housing improvement. In Argentina, the numbers of new acute cases have decreased since the 1970s and seropositivity in 18-year-old males has significantly decreased since 1980. In Brazil, vector transmission has been interrupted in the whole state of São Paulo since the mid-1970s and 74% of municipalities in the country have become negative for *T. infestans*. In Venezuela, entomological, serological and case-detection results have shown a steady decrease over the years in house infestation and seropositivity rates.

7.4 Prevention of transmission by blood transfusion

The problem of the transmission of *T. cruzi* by blood transfusion must not be considered in isolation but together with that of diseases that are also transmitted by contaminated blood, such as malaria, hepatitis, syphilis, and acquired immunodeficiency syndrome (AIDS). Preventing the transmission of these diseases in blood and blood products will only be possible when the governments, and in particular the public and private health sectors, of the countries of the region are made aware of the importance of transfusion as a risk factor. The risk increases with the number of transfusions received and the prevalence of these infections in the donor population.

Only five countries of the region (Argentina, Brazil, Honduras, Uruguay and Venezuela) have adopted laws that make serological testing of blood donors for *T. cruzi* mandatory. However, even in countries where the legislation exists, a government may not have the political will or the power to enforce it. Financial constraints may also hinder the full implementation of the law.

All the serological tests mentioned in section 7.1.2 are useful, but it may not always be possible to follow the recommendation there that two tests should be used to minimize the possibility of false-negative results. For routine screening of sera by, for example, the latex or IHA tests a single low serum dilution (1:8) would be acceptable, as mentioned in section 7.1.3. However, the true positives will be better identified if all the sera that are screened as positive are then assessed by two tests. Reliability, reproducibility, and comparability can be enhanced by the use of reference sera and standard antigens. This approach requires setting up a network of laboratories with a built-in system of quality control.

Migration from the rural endemic areas to the nonendemic urban areas increases the number of donors likely to transmit Chagas disease because the migrants are in the socioeconomically weakest groups of the population, who are inclined to sell their blood to raise money. Prohibiting the payment of donors would decrease the frequency of donation of seropositive blood. It is also important to make health professionals aware of the risks involved in transfusion of contaminated blood and of the need to restrict the number of transfusions, which may be unnecessarily high.

In areas where the proportion of seropositive donors is high, discarding all positive blood units might imperil the stock of blood available for emergencies. In these cases, blood positive for *T. cruzi* can be made safe by adding 125 mg of crystal violet per 500 ml of blood and storing it for 24 hours at 4 °C. There is no evidence that crystal violet at such doses produces any side-effects in humans except a transient blue staining of the skin and mucosa.

Attention should be called to the risk of introducing Chagas disease into nonendemic countries by blood banks that may unwittingly accept donors who have previously been exposed to *T. cruzi* infection.

7.5 Prevention of congenital transmission

Pregnant women who may have been exposed to risk should have their blood tested for antibodies. Since no measures can be taken to prevent congenital infection, infants of seropositive mothers need to be followed up for a year after birth: as soon as possible after birth by parasitological examination of their blood and search for specific IgM antibodies, followed by serological tests for specific IgG antibodies at 6 and 12 months of age. For practical purposes, a positive serological test at 6 and 12 months of age is an indication for treatment of the child.

7.6 Prevention of transmission by other routes

7.6.1 *Accidental laboratory infections*

The infective stages of *T. cruzi* constitute a source of high risk to people engaged in the laboratory manipulation of this parasite, and a number of accidental infections have been reported from endemic as well as nonendemic countries. Since recent infection may be readily curable, special attention should be given to any possibility of accidental laboratory infection. An accident involving a high concentration of parasites should be declared a "presumed infection" even before parasitological or serological confirmation.

The mechanism of infection is variable (see section 6.2.5) but infected blood from experimentally inoculated animals has been identified as the most frequent source of the disease.

Guidelines on safety precautions for laboratory work with *T. cruzi* have been prepared by the Scientific Working Group on Chagas Disease, of the UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases. The Expert Committee endorses these guidelines, which are given in Annex 5, and strongly recommends their implementation.

Many accidental laboratory infections have received conventional long-term treatment with benznidazole and nifurtimox. Recently, it has been demonstrated that short-term treatment (8-10 days) with either drug starting very early (preferably on the very day of the accident) usually aborts the presumptive infection.

7.6.2 *Organ transplants*

Prevention is by serological screening of the organ donor. As a rule seropositivity of the donor should be a contraindication to transplantation. However, if no compatible alternative donor is available, the risk of transmission can be reduced considerably by treatment of the donor with nifurtimox or benznidazole for 2 weeks before transplantation and of the recipient for 2 weeks after transplantation.

7.6.3 *Breast-feeding*

It has been suggested that *T. cruzi* may be transmitted by breast-feeding, though possibly owing to a traumatic lesion of the nipples (see section 6.2.4). However, no evidence has been adduced that incriminates milk as a vehicle of *T. cruzi*. Therefore breast-feeding by a woman infected with this parasite is not considered to constitute a risk for her infant and should not be discouraged.

7.7 Ethical and safety aspects

7.7.1 *Surveillance and treatment*

Seropositive persons

Blood donors who have been found to be seropositive by screening must be informed of the result and referred to a medical centre for clinical examination. The same is true of persons who are found to be seropositive during seroepidemiological surveys, the evaluation of control campaigns, or surveys of pregnant women.

Employment

So long as seropositivity is of limited value for predicting the duration of an asymptomatic period and the onset of clinical disease it cannot be considered justification for rejecting a person for employment. The policy adopted by some firms of permitting personnel whose medical examination reveals a realistic risk of incapacity to move to physically less demanding work is to be encouraged.

Treatment

Patients with a confirmed or suspected infection should be made aware of the risks and probable benefits of chemotherapy before treatment is started. In the clinical management of patients, special care must be taken to ensure that they are not submitted to unduly complex or costly clinical examinations or to ill-prepared clinical trials that, although possibly of great technical or scientific interest, may not be pertinent or beneficial to the improvement of their condition. Before any clinical trial is allowed to proceed, it should be approved by a national ethical committee after a thorough evaluation.

7.7.2 *Vector control*

The planning and implementation of a vector control programme raise a number of ethical, safety and related issues that should be addressed by each country in accordance with its local and sociocultural conditions. Issues of a general nature include:

- securing community involvement in programme planning;
- obtaining the informed consent of community members to the conduct of specific activities that affect them;
- ensuring equity in the distribution of materials and the delivery of services;
- proper evaluation and disclosure of the results of control activities;
- ensuring persistence of control activities through continuity in budget allocations.

Chemical control of vectors carried out by a specialized control programme, by the general health services, or through varying degrees of community participation requires consideration of some specific issues related to the method and the insecticide application procedures:

- avoidance of environmental contamination:
- attention to toxicological aspects as they relate to members of the target community, to members of the spraying team, and to nontarget organisms:
- preservation of privacy and avoidance of disruption and unnecessary nuisance.

In evaluation studies of new vector control methods, infested human dwellings should not be excluded from treatment in order to serve as controls.

7.7.3 *House improvement*

Considering the far-reaching implications of house modifications for the health status, welfare, and life-style of the population, careful analysis of the following issues is suggested:

- formulation and enforcement of rules for safe and sanitary construction appropriate to the local environmental conditions;
- use of autochthonous materials to the greatest extent possible;
- sociocultural adaptation of new houses;
- introduction in the programme of an educational element which, among other things, will aim to improve local construction skills;
- reinforcement of self-reliance.

8. Prevention and control strategies

8.1 Programme achievements

Chagas disease control is scientifically and technologically feasible. However, few countries have started a control programme despite the fact that the basic tools and strategies have been available for more than 30 years. The main reasons for this are political and economic constraints and the lack of epidemiological studies in some parts of the continent. As a result, many governments underestimate the prevalence of the disease and the social damage it causes. In few countries, therefore, is there an established policy for control.

A pioneer control programme against Chagas disease was undertaken in the late 1940s in Brazil, in the endemic areas of the state of Minas Gerais. Several approaches to the control of domestic *Triatoma infestans* were tried, including housing improvement, health education, and the application of insecticides. It was concluded that, for the programme to be successful, it had to be continuous over a long period and to operate in contiguous areas. Similar trials were successful in other endemic countries. Most programmes, however, are restricted to vector control at the domestic level. House-spraying with long-acting residual insecticides is at

present the common strategy in Argentina and Brazil, although Venezuela has developed a programme that combines insecticide application and house improvement.

Although transmission through blood transfusion has been considered of great importance, only Argentina, Brazil, Honduras, Uruguay, and Venezuela have introduced mandatory serological screening for *T. cruzi* infections in blood banks. The problem of transmission by blood transfusion of syphilis, Chagas disease, hepatitis B, and other diseases has long been recognized, but few concrete measures were taken in Latin America until recently, when, in the wake of the AIDS pandemic, a reorganization of blood transfusion systems was initiated.

The current status of the different control programmes can be summarized as follows:

- Only three of the endemic countries – Argentina, Brazil, and Venezuela – have established national programmes for control, chiefly through a vertical approach. The results have been satisfactory where the necessary degree of coverage has been attained and continuous operations have been assured.
- A few countries, Bolivia and Uruguay for example, have small vector control programmes with regular interventions using insecticides and small-scale housing improvement programmes, while a number of pilot control projects are being conducted in Chile and Paraguay. A structured national approach should be developed in these countries.
- In many other countries the problem of Chagas disease is still not well defined. In some of them, such as Guatemala and Mexico, the wide dispersion of the vectors and the suspected occurrence of human infection make it necessary to carry out a national survey to evaluate the health importance and social impact of the infection and disease.
- In countries such as Colombia, Costa Rica, and Panama, where there is considerable information suggesting that the disease is restricted to certain areas, national or local control programmes are needed.

8.2 Programme development

Preferably, the first step in programme development should be the appointment of a national coordinator for Chagas disease control, whose main responsibilities should be to facilitate the integration of activities at national level and to establish links with international technical centres and experts. Integration at national level will involve the establishment of links with directly related disciplines (e.g., biology, sociology, architecture, and engineering), with other sectors (e.g., agriculture), with municipal leaders, and with the different administrative departments. The national coordinator should initiate and coordinate each step of the programme development as broadly outlined below.

8.2.1 *Situation and resources analysis*

The demonstration of the social cost and economic implications of Chagas disease is a crucial prerequisite in order to arouse the interest of national planners and decision-makers and to mobilize national and international resources.

For the development of a national strategy and national programme the following preparatory steps need to be taken:

1. *Thorough review* of published and unpublished reports and all other sources of data (a) on the disease distribution, as available from blood banks, clinical records and municipal registries, (b) on housing standards and on sanitation, and (c) on the distribution of potential vectors.

2. *Spot surveillance* in the known endemic areas to obtain information on (a) disease distribution and prevalence, (b) vector distribution and infection rates, and (c) seropositivity rates in blood-bank samples.

3. *Estimate of disease control requirements* on the basis of information obtained in steps 1 and 2 above.

4. *Resources inventory* of (a) the health facilities, personnel, primary health care projects, laboratories, etc. and (b) the related facilities and programmes in other sectors such as malaria control programmes, universities, and research centres.

   Any proposal for programme development should include an inventory of the resources locally available for its implementation and the constraints on resources that hinder the full application of the strategy. An analysis of the social cost and economic implications of Chagas disease provides vital information permitting health planners to reach well-founded decisions on how best to allocate scarce resources. If lack of skilled human resources is identified as a constraint, then a programme of human resource development should be considered as the first step towards the realization of the programme.

5. *Possible additional resources* need to be explored where appropriate. For instance, for housing improvement programmes, the possibilities of resource sharing with other relevant sectors (housing, rural development) need to be investigated.

   The resources that can be contributed by the community with regard to vector monitoring, control, and housing improvement should not be underestimated and should be studied carefully.

   For programmes that require a heavy capital investment (principally housing improvement programmes), the possibility of attracting bilateral or multilateral external funds may be considered. Poverty relief allied to the concept of sustainable development is a major objective of most international aid agencies. Since Chagas disease

control programmes are directly relevant to these objectives, external support may be successfully negotiated.

For community-based activities it may be productive to seek support from appropriate nongovernmental organizations, which often concentrate their activities on field operations.

8.2.2 *Strategies*

Definition of an appropriate and affordable strategy for control will greatly strengthen the case for establishing a programme for the control of Chagas disease.

Control methods that meet the local needs in terms of effectiveness, economics, and social acceptability should form the basis for the design of a control strategy. Such a strategy should have sufficient flexibility to be able to respond adequately to new methodological developments and changing economic realities. An integrated control strategy contains one or more of the following components:

- vector control, combined with sanitation of the peridomicilium;
- medical surveillance and control of transmission by blood transfusion;
- housing improvement;
- health education and community involvement.

As part of strategy development, a vulnerability analysis that takes into consideration the epidemiology of the disease and the prevailing socioeconomic and cultural conditions can be very useful. It should aim at identifying the weak point in the transmission cycle that would be the most suitable for intervention. Usually vector transmission and transmission by blood transfusion form the most sensitive points for attack.

Since the epidemiology of Chagas disease is so heterogeneous, the balance between the components of an integrated approach must depend on the local circumstances. Three different situations may be distinguished.

Urban environment. The emphasis of an urban control strategy must be on preventing transmission by transfusion and on treating congenital cases, with due attention to providing medical care for the chronically infected. As urban house infestation rates are usually low, the establishment of a large-scale vector control programme would not be appropriate. A horizontal approach to health education linked with the promotion of vector control by fumigant canisters could be effective in eliminating urban foci of house infestation.

Rural agglomerations. Transmission by triatomine bugs is the most important factor, followed by congenital transmission. Therefore the control strategy should rely predominantly on vector control: through an intervention programme in the attack phase (see section 8.2.3), complemented as far as possible by community-based vector monitoring and control activities. When the proportion of infected triatomines and the

prevalence of chagasic infection in humans and domestic animals are high, special attention shoud be given to detecting and treating patients with the acute form of the disease. In some cases, measures to reduce the dispersal and spread of bugs and the infection to urban areas need to be considered.

Scattered rural populations. In spite of the difficulties that a control programme could meet trying to cover scattered populations (accessibility, logistics, etc.), the magnitude of the problem makes it necessary to introduce innovative and effective strategies to protect families by residual insectide spraying, followed by housing improvement and social measures to encourage community participation in entomological surveillance and housing maintenance. To be successful, control strategies in one area must take into account the coverage of control activities in contiguous areas and coordinate work with that being conducted in those areas.

8.2.3 *Operational phases*

The strategies for insecticide campaigns should provide for a preparatory phase (see section 8.2.1), an attack phase, and a surveillance phase.

The *attack phase* starts with a mass house-spraying operation, regardless of whether a particular house is infested or not. This is followed by a yearly "evaluation and attack phase" in which only the houses that are found infested at the time of evaluation are sprayed. This phase ends when the number of infested dwellings in a municipality is reduced to a given level (5% when the insecticide is a pyrethroid with long residual effect).

The *surveillance phase* relies upon intensive community participation, which must be sought from the start of the attack phase onwards. A triatomine monitoring and referral system operated by the populations themselves should be established, suited to the local sociocultural structures. Vector detection in individual houses can be done by house-owners, by volunteer community agents, by primary health care workers, or by other means. Specialized vector monitoring programmes may make use of local schools, health posts, etc. as well as of passive methods of vector detection such as sensor boxes or insect traps. In each town a second-line referral service should be established (attached to a suitable institution), which should be able (a) to confirm the identification of the insect, (b) to organize and carry out insecticide treatment of the infested houses identified, and (c) to organize insecticide supplies. Supervision must be regular and responsive to the local needs.

The impact of control programmes should be evaluated by entomological and/or serological surveys.

8.2.4 *Cost-effectiveness (see Annex 6)*

Cost-effectiveness analysis of disease control programmes should be made in order to ensure that a certain target can be reached at the lowest possible cost or maximum results achieved within a given budget. In analysing the

cost implications of the various options, the following aspects should be considered at the planning stage of control programmes.

Capital versus recurrent costs. Medical surveillance and insecticide spraying campaigns are long-term programmes, requiring a recurrent input of funds for operation, monitoring, and evaluation. Housing improvement, on the other hand, involves a high initial investment but lower recurrent costs. The percentage depreciation of money to be expended at a future point in time (represented by the prevailing discount rate) is a crucial parameter in the comparison of capital and recurrent costs.

Foreign exchange substitution. Insecticides are usually not locally produced and will require the use of often scarce foreign currency. Housing improvement (provided it is based on traditional construction methods using locally available materials), the development of local insecticides manufacture, or other methods may offer an attractive alternative. However, this poses an economic dilemma between immediate high capital investments in local currency or lower but long-term investments in foreign exchange, which must be taken into account when strategies are being designed.

Opportunity costs. Control programmes that are implemented with the help of the community may appear financially preferable to vertical programmes because of the reduced labour-cost component. However, the opportunity cost[1] of the contribution by the community has to be taken into account. Similarly, at national level, the alternative use for other important purposes of resources tentatively assigned for Chagas disease control should also be considered.

Incidental benefits. Chemical control of Chagas disease vectors has a very narrow immediate objective: reduction of the incidence and prevalence of the disease. Housing improvement programmes may be initiated with the same narrow objectives in mind, but they will have other benefits for health and the quality of life at no extra cost.

8.2.5 *Programme definition and budget*

As a guide for the programming and budgeting process, possible components of the budget are listed in Table 4.

8.3 Programme implementation in the context of primary health care approaches

Primary health care (PHC) is based on the use of feasible and acceptable means for offering health assistance to a community. Community participation is necessary if actions are to be undertaken in the most

[1] The cost that corresponds to the time spent on housing improvement that could otherwise have been used for different activities in economic demand.

Table 4
Budget frame for a Chagas disease control programme

Item		Cost
1. **Programme development and evaluation**		
National coordinator[a] (coordination of relevant sectors, disciplines and different administrative levels)	___ person-months	_____
Office staff[a] (secretary, administrative assistant)	___ person-months	_____
Training (national seminars, information circulars, books, periodicals, manuals)		_____
Supplies and equipment (office materials)		_____
Transport (liaison vehicle, maintenance, fuel)		_____
Travel (national/international)		_____
Trials or demonstration projects[b]		_____
2. **Vector control**		
Personnel[a] (entomologists, spray operators, technicians and other laboratory auxiliaries, drivers)	___ person-months	_____
Supplies and equipment (spraying equipment and its maintenance, insecticides, outdoor equipment, monitoring equipment and supplies)		_____
Training (application techniques, safe use of pesticides)		_____
Laboratory support (supplies and equipment, insectary,[c] insecticide resistance kits)		_____
Transport (vehicles, maintenance, fuel)		_____
3. **Medical surveillance and treatment**		
Personnel[a] (medical officers, biologists, immunologists, nurses, auxiliaries, laboratory and field staff)	___ person-months	_____
Supplies and equipment (diagnostic equipment, materials and reagents, other laboratory equipment)		_____
Strengthening of blood-bank laboratory network (serological equipment, materials and reagents, sampling, sample transport and storage)		_____
Training		_____
Drugs		_____
Transport (vehicles, maintenance, fuel)		_____
4. **Housing improvement**		
Personnel[a] (architects, engineers, sociologists, biologists)	___ person-months	_____

[a] Charged as programme costs but could be already existing post(s) of the health department.
[b] Optional components.
[c] Insectary and entomological services also to be made available to medical surveillance for xenodiagnosis.

Table 4 (continued)
Budget frame for a Chagas disease control programme

Item		Cost
Construction equipment and materials		_____
Training		_____
Transport and storage		_____
Accounting/administrative support		_____
Evaluation surveys on house maintenance[a]		
5. **Community mobilization**		
Personnel[b] (health educators, social workers)	___ person-months	_____
Sociological surveys		_____
Strengthening the infrastructure for primary health care		_____
Health education equipment and materials (projectors, blackboards, printed materials, training packages)		_____
Transport (vehicles, maintenance, fuel)		_____
6. **Miscellaneous and contingencies**		_____

[a] Optional components.
[b] Charged as programme costs but could be already existing post(s) of the health department.

cost-effective manner according to the resource potential of the country. PHC brings solutions to the community through coordinated activities in different health fields undertaken by the community as a whole rather than by separate efforts by individuals. So far, most Chagas disease control activities have been carried out by specialized services. To incorporate control activities within the current work of the PHC workers has several advantages since those workers belong to the community, they are trained by the regular local health personnel, and part of their normal tasks is to make regular visits to houses. They are therefore in an ideal position to act as agents of liaison and to promote the participation of the rural inhabitants in control activities.

8.3.1 *Intersectoral collaboration*

Effective collaboration between the health sector and other public sectors, as well as with the private sectors, is of vital importance for the long-term success of a Chagas disease control programme. Two main features of intersectoral collaboration are resource sharing and policy adjustment.

Resource sharing

Intersectoral collaboration implies coordination with other relevant sectors in the planning and implementation of interventions, with a view to identifying each sector's resources and constraints, so that the jointly available resources can be used for the maximum benefit.

Policy adjustment

In a dialogue with other relevant sectors, the possibility should be explored of mutually adjusting policies in order to accommodate, where possible, the improvement of human health as an integral part of other sectoral goals. In the case of Chagas disease control, other relevant public sectors, with their respective areas for collaborative activities, include:

- *Housing and rural development:* joint implementation of housing improvement programmes; establishing specific construction specifications; granting of agricultural credits; crop – and thereby income – improvement.
- *Education:* development of health education modules for use at community level; establishing or strengthening a Chagas disease programme within universities, comprising research and postgraduate training; creating specific training facilities to meet the human resource requirements of a control programme.
- *Environment:* safe and environmentally sound application of insecticides.

8.3.2 *Integrated approach within the health services and task distribution at different levels*

Integration of various health services into the PHC structure can be achieved provided it is done gradually and with appropriate training at all levels. This integration, if successful, can offer solutions to problems identified by the community and, in addition to helping to improve the quality of life, it can provide effective control of an endemic disease such as Chagas disease.

For the purpose of Chagas disease control, it is less important to debate whether the programme should be organized through vertical or horizontal services than it is to identify the health staff, irrespective of how their service may be organized, who can best deal with the local circumstances and requirements. For example, one approach is to centralize all spraying and entomological surveillance activities; another is to make the PHC worker responsible for entomological surveillance, insecticide spraying, and the taking of blood samples for serological tests.

In both instances, a network of laboratory services with different facilities and at different technical levels should be made available for diagnosis. Similarly, patient care should be ensured by clinical services of different levels, from health posts to tertiary health care centres for the treatment of those with Chagas disease.

An interesting experiment using PHC workers in control activities is being carried out in Argentina. Sensor boxes are fixed in the houses by the inhabitants and the PHC worker monitors them. If vectors are detected in a house, the PHC worker can take on-the-spot action to apply an insecticide with a portable spray-can or with fumigant canisters. The feasibility of this approach in different settings needs to be investigated.

8.3.3 *Community participation*

Community participation is essential if control of the vectors of *T. cruzi* is to show permanent results. The community should predominate in identifying the problems, searching for the solutions, evaluating the action taken, and assessing the needs. A first step towards achieving such participation is for the spraying of insecticides to be done on a voluntary basis by the communities themselves.

Another approach is to have the entomological surveillance largely done with the participation of the community. This approach is based on detection of triatomine bugs by community members, who report their findings to a coordinating centre within the municipality that is responsible for subsequent spraying and treatment of positive dwellings. Teachers in rural areas are usually found effective in liaison between the community and the local health authorities.

Use is also made of what is called a "minimum surveillance unit", which is composed of posters with instructions that are distributed in a community, together with plastic bags in which bugs are placed when collected and with special papers to be placed in appropriate situations where the bugs may leave their characteristic faecal smears upon them, thus permitting confirmation of their presence. The numbers of insects and faecal smears are reported to the coordinating centre, and insecticides are then applied by the leaders of the community as required. Yet another approach to community participation in surveillance activities is the use of sensor boxes mentioned in the preceding section. Special attention should also be given to the participation of families and communities in the process of housing improvement, not just to save expense, but as a means of stimulating the responsibility and confidence of the population in the control of the disease and ensuring that house maintenance is done in good time.

8.4 Health education

Although health education is a fundamental instrument of all public health protection programmes, it is often neglected in the budget and in personnel allocations. It is also important to note that health education activities should not be restricted to a department designed for this purpose alone, but that all activities under a control programme should be analysed and oriented to the relevant educational activities.

The control programme personnel should be able to contribute continuously, through their daily routine, to the educational objectives for the population at risk – especially in the following contexts:

- the meaning and objectives of the house-spraying activities;
- the importance of good housing conditions to lessen the risk of infestation;

- the various ways of modifying houses to make them "unpropitious" for vectors, and appropriate sanitary and housing maintenance measures;
- the promotion, through dialogue, of community participation in entomological surveillance and early reporting.

Educational objectives and training for the surveillance phase should incorporate the information about the various risk factors for reinfestation and about its prevention. The educational strategy should always remain compatible with the overall objective of general health protection.

The media to be used in educational strategies should be selected in accordance with the local social and geographical conditions of the target population and easily adaptable to application by unskilled people. The approach and timing for imparting the requisite knowledge to the population at risk should be planned in such a way that they correspond with the habits of that population, in order to guarantee the maximum audience.

8.5 Technical cooperation among developing countries and international collaboration

Technical cooperation among developing countries is an important mechanism for initiating, designing, organizing, and supporting public health programmes. It is also a tool for acquiring, transferring, and sharing knowledge and experience of mutual benefit in order to build up national and subregional capabilities for social and economic development. Technical cooperation among developing countries involves an agreement between two or more countries to cooperate in the conduct of common enterprises for public health protection and promotion; requirements, constraints, priority areas, and specific lines of action are jointly defined by parties involved. There are several examples of close and effective collaboration between neighbouring countries in the implementation of Chagas disease control measures in their frontier areas.

9. Human resources development

9.1 Training for control of Chagas disease

Among the many aspects of training for Chagas disease control programmes, the following should be included:

- Identification of the staff to be trained when a situation and resources analysis has been made but prior to strategy and programme development.
- Organization of training courses, workshops, and seminars on PHC strategy and programming for personnel at all levels.
- Provision of the technical documentation and literature covering the above activities; this should include a control manual for Chagas disease.

- Establishment and strengthening of a programme to promote the development of special skills and practical knowledge related to Chagas disease control.

9.2 Postgraduate research training

Biomedical training capabilities have been greatly improved in the past few years in Latin America as a result of organized scientific communities pressing for priority to be given to national and international recognition of Chagas disease research. Great progress in basic and applied research has been made in biology, immunology, and diagnostic techniques. The past decade has also witnessed the development of systematic techniques for housing modifications, through the development of construction methods designed to use local materials and skills.

Given the current state of advancement of the biomedical disciplines, an integrated approach to the public health problem is now needed. Postgraduate training in research on Chagas disease should be reoriented towards a multidisciplinary approach to the application of the new knowledge, as well as to new approaches to transmission control with a broader concept of public health care in mind. The promotion of social betterment and of measures to bring about lasting improvements in living conditions should become integral elements of control. This reorientation could be achieved by strengthening and supporting postgraduate training in epidemiological methods, social sciences and entomology. In the present economic situation, funds for research training have had to be drastically reduced in Latin America, and these are the disciplines on which they should now be concentrated. Innovative mechanisms for exchange training programmes should be promoted in order to take the greatest advantage of the existing centres of excellence in Latin America.

10. Research

Outstanding advances in basic and applied research on *Trypanosoma cruzi* have been made since the beginning of the century, and institutions in endemic countries such as Argentina, Brazil, Chile, Colombia, and Venezuela have built up remarkable research capabilities. Nevertheless, although national research coordinating and financing bodies have accorded priority to Chagas disease for many years, this research policy has not always been matched by adequate funding in some countries nor has it always followed a goal-oriented course.

Over the past decade, in addition to the efforts of national research councils and universities, the UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases (TDR) has played a crucial role in financing and coordinating basic and applied research, not only in the endemic countries (75% of the TDR operational programme on Chagas disease), but also in laboratories in nonendemic

countries of the northern hemisphere. Moreover, linkages between institutions in the endemic and nonendemic countries have been developed through the TDR programme and have been built up through concrete research projects. As a consequence, knowledge of Chagas disease, *T. cruzi,* its vectors, and the means of controlling them has progressed greatly in the past 10 years.

Prevalence studies have been supported by TDR in order to provide accurate information on the numbers of human *T. cruzi* infections and on the disease rate in most of the endemic countries in which such information was partial or lacking. These studies were carried out during the 1980s through the ministries of health of Chile, Colombia, Ecuador, Honduras, Mexico, Paraguay, and Uruguay. It is now estimated that the overall prevalence of human infection in the continent amounts to 16-18 million cases. The accurate information obtained by individual countries has also permitted a better planning and evaluation of the national control programmes.

For vector control, new methods for delivery of insecticides have been developed and small pilot trials conducted in the field. New serological reagents, like synthetic or recombinant peptides, have become available for testing, while a modified polymerase chain reaction for amplification and detection of kDNA in serum or plasma samples is being evaluated.

In chemotherapy, three lines of research have been pursued: studies on parasite biochemistry to identify potential drug targets, *in vitro* and *in vivo* screening of compounds, and studies on modes of action of drugs active against *T. cruzi* to identify leads to more effective and safer compounds.

In immunopathology, attempts to unveil the intricate mechanisms involved in the pathogenesis of chronic lesions have included the development of suitable animal models, T-cell cloning, and molecular definition of relevant parasite and host antigens that may cross-react. In relation to vaccine research, parasite antigens with immunogenic potential have been identified, characterized, and produced. Surface-membrane glycoproteins have been purified and tested as immunogenic agents. Synthetic peptides binding to the parasite's fibronectin attachment-site may interfere with the penetration of host cells by *T. cruzi.*

There are, however, still wide gaps in knowledge in several areas. To fill these gaps the following research priorities have been identified.

10.1 Epidemiology, clinical pathology, and field research

10.1.1 *Course of infection and clinical pathology*

Accurate data on the course of infection and clinical pathology are scarce, just as they are on the parasite, the host, and the environmental factors that affect the transmission rates and geographical distribution of the different clinical forms. A more precise description and quantification of the various clinical and geographical forms of the disease is a matter of high priority.

At the same time, analytical epidemiological case-control studies should be carried out in different countries to identify factors related to the parasite, host or environment that might be responsible for the varied clinical forms of the disease. These must be followed by multicentre clinical studies. Standardized methods for a better characterization of strains are needed.

10.1.2 *Prevalence studies*

The undertaking of prevalence studies in countries where such information is lacking should be encouraged.

10.1.3 *Diagnostic tests*

Research should be aimed at the development and evaluation of improved tests for clinical diagnosis, blood-donor screening, monitoring of therapy, and evaluation of control activities. Reagents using defined molecules encoded by cloned parasite genes that are being obtained by synthesis or recombination techniques should be developed and evaluated. Assays for circulating antigens and methods to detect parasite kDNA, such as the polymerase chain reaction, should be further developed. Predictive values of available and newly developed diagnostic tests should be determined.

10.1.4 *New tools for vector control*

Innovative approaches in vector control operations need to be pursued and improvements sought to increase the efficacy and efficiency of control programmes. For this purpose field studies should be undertaken to compare different complementary intervention strategies, such as the domestic use of slow-release formulations of insecticides incorporated in paints and the application of insecticides by means of fumigant canisters.

Research should also include investigations in operational and health economics to optimize the use of resources and studies to develop improved vector control agents, formulations, and methods. At the same time, studies aimed at a better understanding of the mechanisms of vector resistance to insecticides should be pursued.

Special attention should be given in research and control to the peridomicilium as a distinct ecotope for the vectors and to its importance as a link between the sylvatic and domiciliary infection cycles, as well as to the role of peridomiciliary animals as blood sources and reservoir hosts for secondary vector species.

10.2 Biochemistry and drug development

Basic studies on the metabolism of the parasite should continue to be a high priority. Studies on the mode of action of substances that kill parasites present in transfusion blood should also continue. Screening of available compounds for activity against *T. cruzi* infection should be pursued.

10.3 Pathogenesis, immunopathology and vaccine development

Future research should include studies on structural and functional factors involved in the host-parasite interactions, including the immune system and the processes responsible for the pathogenesis of chronic lesions. The extent of the role of autoimmune mechanisms should also be clarified. The identification of protective antigens encoded by cloned parasite genes should be pursued with a view to developing a vaccine.

10.4 Social and economic research

10.4.1 *Health education*

Communication techniques have not been adequate to bring about the degree of community participation required for primary health care strategies. Promotion of research should be aimed at developing health education procedures to improve the transfer of information to populations in such a way as to achieve behavioural changes. Educational strategies should aim at reinforcing self-reliance.

10.4.2 *Housing improvement*

Research on traditional construction techniques and autochthonous materials is required for housing improvement. Innovative approaches are also needed to introduce cheaper and easier alternatives for roofing and wall plastering. Such approaches require creative combinations of new and traditional technologies.

10.4.3 *Community participation*

Special attention should be given to studying the various areas of cooperation possible between communities, local authorities, and control personnel as well as to devising alternative strategies for the interventions that are required to ensure the active participation of the population at risk in such control activities as spraying, housing improvement, and surveillance. The basic factors that predispose people to participate, individually or collectively, need to be defined and put to use in control strategies.

10.4.4 *Programme organization*

Future research should be aimed at the development of improved operational methods for the design and evaluation of national control programmes in the context of primary health care and community participation.

Operational research on the organizational structure of control programmes, and particularly on the functioning of control programme offices, is needed in order to improve their administrative efficacy and the acceptability by the community of their approaches and methods.

10.4.5 *Cost-effectiveness*

Future research should include the economic analysis of control strategies and tools so as to help health authorities in the assessment and selection of optimal programmes in terms of cost and the protection provided.

10.4.6 *Social and cultural risk factors*

Accurate data on the social and cultural factors that contribute to the risk of contracting the disease are needed. Future research should define those factors and identify the interventions required, so that they may be incorporated in control programme strategies.

11. Recommendations

In addition to the recommendations contained in the body of the report, and notably in section 10, the Expert Committee recommends that:

1. In each Member State in which epidemiological data indicate that there is a considerable risk of transmission of *T. cruzi,* a national programme for the control and prevention of Chagas disease should be formulated and implemented.
2. National programmes for control and prevention should focus on vector control, prevention of transmission by blood transfusion and of congenital Chagas disease, and surveillance. Priority should be given to high-transmission areas, where the attack phase should consist of the wide-scale application of insecticides.
3. A permanent surveillance system – through institutionalized services, primary health care workers, and/or the communities themselves – should be the essential basis of any approach to control.
4. Strong and continuous efforts should be made to ensure that the work of control programmes is closely associated with that of other sectors and disciplines. This is particularly important in programme activities concerning housing improvement and health education.
5. As a part of national control and prevention programmes a network of laboratories should be established for the diagnosis of *T. cruzi* infections and the identification of triatomine vectors.
6. Since blood transfusion has become an important route of transmission within and outside the endemic areas, (a) the Member States concerned should make serological screening of blood donors legally mandatory when and where the risk of infected donors exists; (b) the opportunity should be taken to combine such screening with the systematic testing of blood for human immunodeficiency virus infections and hepatitis B; (c) blood donors should be selected on an unpaid basis; and (d) clinicians should critically review the indications for transfusion with a view to restricting the number of transfusions.

7. *T. cruzi* infection in mothers should not be a contraindication to breast-feeding.

8. Persons found seropositive during seroepidemiological surveys, by blood transfusion services, or during pregnancy should be systematically referred to a medical centre for a complete clinical examination for possible lesions due to Chagas disease.

9. Each Member State in which Chagas disease occurs should compile and regularly update national information on the geographical distribution and prevalence of *T. cruzi* infections, and acute cases should be notifiable at national and international level.

10. The research activities stimulated as part of the UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases should continue to follow the adopted priorities, which have proved very effective in the development of strategies for control intervention, in the standardization of measures, techniques and criteria, in initiating epidemiological studies, and in providing training opportunities.

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Annex 1

Labelling of *Trypanosoma cruzi* isolates, identification centres, and standard strains

1. Labelling of isolates

In accordance with the recommendations of a meeting (Panama, 1985) organized by the UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases on standardization of methods for *T. cruzi* classification,[1] the code for the designation of isolates should consist of four elements, separated by oblique strokes:

1. *The type of host animal or vector from which the strain was isolated.* A four-letter code should be used, the first indicating the class to which the animal or vector belongs (M for Mammalia, I for Insecta) followed by three letters indicating the generic name of the host or 000 if the host has not yet been identified. Table A1.1 gives the code letters to be used for mammalian genera.
2. *The country in which the isolation was made.* The country of isolation is indicated by the two-letter codes shown in Table A1.2.
3. *The year of isolation.* This is indicated by the last two digits or 00 if unknown.
4. *The laboratory designation* (e.g., laboratory code and serial number).

Examples of the four-element code are given in Table A1.3, listing reference strains.

[1] *Report of a meeting on the standardization of methods for* Trypanosoma cruzi *classification.* Geneva, World Health Organization, 1985 (unpublished document TDR/EPICHA-TCC/85.3; available, on request, from UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases, World Health Organization, 1211 Geneva 27, Switzerland).

Table A1.1

Generic codes for labelling *T. cruzi* isolates from mammals[a] according to the proposed international code

AKO	*Akodon* (ROD)	LAS	*Lasiurus* (CHT)
ALO	*Alouatta* (PMT)	LUT	*Lutreolina* (MSP)
ANO	*Anoura* (CHT)	MAR	*Marmosa* (MSP)
AOT	*Aotus* (PMT)	MEP	*Mephitis* (CAR)
ART	*Artibeus* (CHT)	MET	*Metachirus* (MSP)
ATE	*Ateles* (PMT)	MIM	*Mimon* (CHT)
BAS	*Bassaricyon* (CAR)	MIN	*Micronycteris* (CHT)
BRA	*Bradypus* (EDE)	MOL	*Molossops* (CHT)
CAA	*Capra* (ARD)	MON	*Monodelphis* (MSP)
CAB	*Cabassous* (EDE)	MOR	*Mormoops* (CHT)
CAI	*Carollia* (CHT)	MOS	*Molossus* (CHT)
CAL	*Caluromys* (MSP)	MUS	*Mus* (ROD)
CAN	*Canis* (CAR)	MYO	*Myotis* (CHT)
CAO	*Calomys* (ROD)	NAS	*Nasua* (CAR)
CAV	*Cavia* (ROD)	NEC	*Nectomys* (ROD)
CBL	*Cebuella* (PMT)	NEO	*Neotoma* (ROD)
CEB	*Cebus* (PMT)	NOC	*Noctilio* (CHT)
CEM	*Cercomys* (ROD)	OCT	*Octodon* (ROD)
CER	*Cerdocyon* (CAR)	ORT	*Oryctolagus* (LGM)
CHO	*Choloepus* (EDE)	ORY	*Oryzomys* (ROD)
CHP	*Chaetophractus* (EDE)	OXY	*Oxymycterus* (ROD)
CIT	*Citellus* (ROD)	PER	*Peromyscus* (ROD)
CLC	*Callicebus* (PMT)	PET	*Peroteryx* (CHT)
CLX	*Callithrix* (PMT)	PHI	*Philander* (MSP)
COE	*Coendou* (ROD)	PHS	*Phyllostomus* (CHT)
CON	*Conepatus* (CAR)	PHT	*Phyllotis* (ROD)
CUN	*Cuniculus* (ROD)	POT	*Potos* (CAR)
DAP	*Dasyprocta* (ROD)	PRC	*Procyon* (CAR)
DAS	*Dasypus* (ROD)	PRO	*Proechimys* (ROD)
DES	*Desmodus* (CHT)	RAT	*Rattus* (ROD)
DIA	*Diaemus* (CHT)	RHN	*Rhynophylla* (CHT)
DID	*Didelphis* (MSP)	RHT	*Rhynchonycteris* (CHT)
DPM	*Diplomys* (ROD)	SAC	*Saccopteryx* (CHT)
DUS	*Dusicyon* (CAR)	SAG	*Saguinus* (PMT)
ECH	*Echimys* (ROD)	SAI	*Saimiri* (PMT)
EIR	*Eira* (CAR)	SCI	*Sciurus* (ROD)
EPT	*Eptesicus* (CHT)	SIG	*Sigmodon* (ROD)
EUM	*Eumops* (CHT)	STU	*Sturnira* (CHT)
EUP	*Euphractus* (EDE)	SUS	*Sus* (ARD)
FEL	*Felis* (CAR)	SYL	*Sylvilagus* (LGM)
GAL	*Galea* (ROD)	TAD	*Tadarida* (CHT)
GAT	*Galictis* (CAR)	TAM	*Tamandua* (EDE)
GLO	*Glossophaga* (CHT)	THO	*Thomasomys* (ROD)
HET	*Heteromys* (ROD)	TOL	*Tolypeutes* (EDE)
HIS	*Histiotus* (CHT)	TRA	*Trachops* (CHT)
HOM	*Homo* (PMT)	TYL	*Tylomys* (ROD)

[a] ARD = Artiodactyla; CAR = Carnivora; CHT = Chiroptera; EDE = Edentata; LGM = Lagomorpha; MSP = Marsupiala; PMT = Primates; ROD = Rodentia.

Table A1.1 (continued)
Generic codes for labelling *T. cruzi* isolates from mammals[a] according to the proposed international code

URD	*Uroderma* (CHT)	VAR	*Vampyrum* (CHT)
URO	*Urocyon* (CAR)	WIE	*Wiedomys* (ROD)
VAM	*Vampyrodes* (CHT)	ZAE	*Zaedyus* (EDE)
VAP	*Vampyrops* (CHT)	ZYG	*Zygodontomys* (ROD)

[a] CAR = Carnivora; CHT = Chiroptera; EDE = Edentata; ROD = Rodentia.

Table A1.2
Designation of endemic countries or territories according to the codes developed by the International Organization for Standardization (ISO)

Argentina	AR	Guyana	GY
Bahamas	BS	French Guiana	GF
Barbados	BB	Honduras	HN
Brazil	BR	Mexico	MX
Bolivia	BO	Nicaragua	NI
Chile	CL	Panama	PA
Colombia	CO	Paraguay	PY
Costa Rica	CR	Peru	PE
El Salvador	SV	Suriname	SR
Ecuador	EC	Uruguay	UY
Guatemala	GT	Venezuela	VE

Table A1.3
Standard reference strains of *T. cruzi*

MHOM/PE/00/Peru	MHOM/BR/82/Dm-28c[a]
MHOM/BR/00/12-SF	MHOM/BR/78?/Sylvio-X10-CL1[a]
MHOM/CO/00/Colombia	MHOM/BR/78/Sylvio-X10-CL4[a]
MHOM/BR/00/Y	MHOM/BR/77/Esmeraldo-CL3[a]
MHOM/CL/00/Tulahuen	MHOM/BR/68/CAN-III-CL1[a]
MHOM/AR/74/CA-I[a]	MHOM/BR/68/CAN-III-CL2[a]
MHOM/AR/74/CA-I-72[a]	MHOM/BO/80/CNT-92: 80-CL1[a]
MHOM/AR/00/CA-I-78[a]	IINF/BO/80/Sc43-CL1[a]
MHOM/AR/00/Miranda-83[a]	IINF/PY/81/P63-CL[a]
MHOM/AR/00/Miranda-88[a]	MHOM/AR/78/RA (low virulence strain)

[a] Derived from clonal populations.

2. Identification centres

Identification techniques are carried out at the following centres, which can accept material for identification. The institutions are listed in alphabetical order and the techniques of identification are available and given in brackets.[1]

- Centro de Pesquisas "Gonçalo Möniz", rua Valdemar Falcao 121, Brotas, 41945 Salvador, Bahia, Brazil (BIO).
- Centro de Pesquisas "René Rachou", Avenida Augusto de Lima 1715, C.P. 1743, 30190 Belo Horizonte MG, Brazil (ISO).
- Instituto Oswaldo Cruz (FIOCRUZ), Avenida Brasil 4365, C.P. 926, Rio de Janeiro RJ, Brazil (DNA).
- Instituto de Biofísica, Centro de Ciencias da Saude - Bloco G, Universidade Federal do Rio de Janeiro, Cidade Universitaria, Rio de Janeiro, RJ 21941, Brazil (ULT).
- Instituto Nacional de Diagnóstico e Investigación de la Enfermedad de Chagas "Dr Mario Fatala Chabén", Avenida Paseo Colón 568, 1063 Buenos Aires, Argentina (SER).

The minimal data that should be supplied with any isolate sent for identification are:

1. Host
   (*i*) Scientific name
   (*ii*) Clinical form
   (*iii*) Organ or tissue
2. Geographical origin
   (*i*) Country
   (*ii*) State
   (*iii*) Locality
   (*iv*) Map coordinates
3. Date of isolation
   Day/Month/Year
4. Name of laboratory
   Name (and initials) of research worker
5. Laboratory number of isolate
6. Mode of conservation
7. Identification methods used
   (*i*) Method(s)
   (*ii*) Result
8. Other observations

[1] Key to identification techniques: BIO, biological methods; ISO, isoenzymes; SER, serology; ULT, ultrastructural studies; DNA, DNA restriction.

3. Standard strains

The standard reference strains listed in Table A1.3 may be obtained on request from the following collaborating centres:

- Department of Parasitology, University of Panama, Estafeta Universitaria, Panama City, Panama.
- Centro de Pesquisas "René Rachou", Avenida Augusto de Lima 1715, C.P. 1743, 30190 Belo Horizonte MG, Brazil.

Annex 2

Alphabetical list of the Triatominae of the Americas[1]

There are 117 recognized species of Triatominae grouped in 5 tribes with 14 genera. Of these, 13 genera and 105 species occur in the Americas. Over half have been reported naturally infected with *Trypanosoma cruzi*; these are indicated in the following list by an asterisk (*) preceding the name.

Order	HEMIPTERA	
Family	REDUVIIDAE	
Subfamily	TRIATOMINAE	
Tribe Alberprosenini Martínez & Carcavallo, 1977		
Genus *Alberprosenia* Martínez & Carcavallo, 1977		
	Alberprosenia goyovargasi Martínez & Carcavallo, 1977	Venezuela.
	Alberprosenia malheiroi Serra, Atzingen & Serra, 1980	Brazil.
Tribe Bolboderini Usinger, 1944		
Genus *Belminus* Stål, 1859 (= *Marlianus* Distant, 1902)		
	Belminus costaricensis Herrer, Lent & Wygodzinsky, 1954	Costa Rica, Mexico.
	Belminus herreri Lent & Wygodzinsky, 1979	Brazil, Panama.
	Belminus peruvianus Herrer, Lent & Wygodzinsky, 1954	Peru.
	Belminus rugulosus Stål, 1859 (= *Conorhinus diminutus* Walker, 1873; = *Marlianus diminutus* Distant, 1902)	Colombia, Venezuela.
Genus *Bolbodera* Valdés, 1914 (= *Callotriatoma* Usinger, 1939)		
	Bolbodera scabrosa Valdés, 1914	Cuba.
Genus *Microtriatoma* Prosen & Martínez, 1952		
*	*Microtriatoma borbai* Lent & Wygodzinsky, 1979	Brazil.
	Microtriatoma trinidadensis (Lent, 1951) (= *Bolbodera trinidadensis* Lent, 1951; = *Microtriatoma mansotoi* Prosen & Martínez, 1952)	Bolivia, Brazil, Colombia, Panama, Peru, Suriname, Trinidad, Venezuela.
Genus *Parabelminus* Lent, 1943		
*	*Parabelminus carioca* Lent, 1943	Brazil.
	Parabelminus yurupucu Lent & Wygodzinsky, 1979	Brazil.
Tribe Cavernicolini Usinger, 1944		
Genus *Cavernicola* Barber, 1937		
	Cavernicola lenti Barrett & Arias, 1985	Brazil.
	Cavernicola pilosa Barber, 1937	Brazil, Colombia, Ecuador, Panama, Venezuela.

[1] The Expert Committee accepted the taxonomic classification of the Triatominae proposed by one of its members, recognizing that there may be differences of opinion with respect to some details. These differences, however, have no immediate implications for the control strategies proposed in the Expert Committee's report.

Tribe RHODNIINI Pinto, 1926	
Genus *Psammolestes* Bergroth, 1911	
* *Psammolestes arthuri* (Pinto, 1926) (= *Eutriatoma arthuri* Pinto, 1926)	Colombia, Venezuela.
Psammolestes coreodes Bergroth, 1911	Argentina, Bolivia, Paraguay.
Psammolestes tertius Lent & Jurberg, 1965	Brazil.
Genus *Rhodnius* Stål, 1859[1]	
Rhodnius brethesi Matta, 1919	Brazil, Colombia, Venezuela.
Rhodnius dalessandroi Carcavallo & Barreto, 1976 [of uncertain validity]	Colombia.
* *Rhodnius domesticus* Neiva & Pinto, 1923	Brazil.
* *Rhodnius ecuadoriensis* Lent & Leon, 1958	Ecuador, Peru.
Rhodnius nasutus Stål, 1859 (= *Rhodnius brumpti* Pinto, 1925)	Brazil.
* *Rhodnius neglectus* Lent, 1954	Brazil, Venezuela.
Rhodnius neivai Lent, 1953	Colombia, Venezuela.
Rhodnius pallescens Barber, 1932 (= *Rhodnius dunni* Pinto, 1932)	Central America, Colombia, Panama.
* *Rhodnius paraensis* Sherlock, Guitton & Miles, 1977	Brazil.
* *Rhodnius pictipes* Stål, 1872 (= *Conorhinus limosus* Walker, 1873; = *Rhodnius amazonicus* Almeida, Santos & Sposina, 1973)	Belize, Bolivia, Brazil, Colombia, Ecuador, French Guiana, Guyana, Peru, Suriname, Trinidad, Venezuela.
* *Rhodnius prolixus* Stål, 1859 (= *Conorhinus limosus* Walker, 1873)	Brazil, Colombia, Costa Rica, El Salvador, French Guiana, Guatemala, Guyana, Honduras, Mexico, Nicaragua, Suriname, Venezuela.
* *Rhodnius robustus* Larrousse, 1927	Bolivia, Brazil, Colombia, Ecuador, French Guiana, Peru, Venezuela.

[1] Some species of *Rhodnius*, such as *neglectus, prolixus,* and *robustus,* can be very difficult to determine accurately on morphological characters. For this reason, many distribution records for these species are considered uncertain (especially those published before 1954), and those given here may not fully reflect the actual distribution of these species.

Tribe TRIATOMINI Jeannel, 1919	
Genus *Dipetalogaster* Usinger, 1939	
* *Dipetalogaster maxima* (Uhler, 1894)	Mexico.
Genus *Eratyrus* Stål, 1859	
* *Eratyrus cuspidatus* Stål, 1859	Colombia, Ecuador, Guatemala, Panama, Venezuela.
* *Eratyrus mucronatus* Stål, 1859	Bolivia, Brazil, Colombia, French Guiana, Guyana, Peru, Suriname, Trinidad, Venezuela.
Genus *Panstrongylus* Berg, 1879 (= *Lamus* Stål, 1859; = *Mestor* Kirkaldy, 1904)	
Panstrongylus chinai (Del Ponte, 1929) (= *Triatoma chinai* Del Ponte, 1929)	Ecuador, Peru.
Panstrongylus diasi Pinto & Lent, 1946	Bolivia, Brazil.
* *Panstrongylus geniculatus* (Latreille, 1811) (= *Conorhinus lutulentus* Erichson, 1848; = *Conorhinus corticalis* Walker, 1873; = *Triatoma tenuis* Neiva, 1914; = *Triatoma fluminensis* Neiva & Pinto, 1922; = *Panstrongylus parageniculatus* Ortíz, 1971)	Argentina, Bolivia, Brazil, Colombia, Costa Rica, Ecuador, French Guiana, Guyana, Nicaragua, Panama, Paraguay Peru, Suriname, Trinidad, Uruguay, Venezuela.
* *Panstrongylus guentheri* Berg, 1879 (= *Triatoma larroussei* Pinto, 1925; = *Triatoma seai* Del Ponte, 1929)	Argentina, Bolivia, Paraguay.
* *Panstrongylus herreri* Wygodzinsky, 1948	Peru.
* *Panstrongylus howardi* (Neiva, 1911)	Ecuador.
Panstrongylus humeralis (Usinger, 1939) (= *Mestor humeralis* Usinger, 1939)	Panama.
Panstrongylus lenti Galvão & Palma, 1968	Brazil.
* *Panstrongylus lignarius* (Walker, 1873)	Brazil, Guyana, Peru, Suriname, Venezuela.
* *Panstrongylus lutzi* Neiva & Pinto, 1923	Brazil.
* *Panstrongylus megistus* (Burmeister, 1835) (= *Conorhinus gigas* Burmeister, 1861; = *Conorhinus porrigens* Walker, 1873; = *Triatoma africana* Neiva, 1911; = *Triatoma wernickei* Del Ponte, 1923)	Argentina, Brazil, Paraguay.
* *Panstrongylus rufotuberculatus* (Champion, 1899) (= *Triatoma coxo-rufa* Campos, 1932)	Bolivia, Brazil, Colombia, Costa Rica, Ecuador, Mexico, Panama, Peru, Venezuela.
* *Panstrongylus tupynambai* Lent, 1942	Brazil, Uruguay.

Genus *Paratriatoma* Barber, 1938	
Paratriatoma hirsuta Barber, 1938	Mexico, USA.
Paratriatoma hirsuta kamiensis Ryckman, 1967	
Paratriatoma hirsuta papagoensis Ryckman, 1967	
Paratriatoma hirsuta primae Ryckman, 1967	
Paratriatoma hirsuta yumanensis Ryckman, 1967	
Genus *Triatoma* Laporte, 1832 (= *Conorhinus* Laporte, 1833)	
Triatoma arthurneivai Lent & Martins, 1940	Brazil.
* *Triatoma barberi* Usinger, 1939	USA.
Triatoma bolivari Carcavallo, Martínez & Peláez, 1987	Mexico.
Triatoma brailovskyi Martínez, Carcavallo & Peláez, 1984	Mexico.
* *Triatoma brasiliensis* Neiva, 1911	Brazil.
Triatoma brasiliensis melanica Neiva & Lent, 1941	
Triatoma brasiliensis macromelasoma Galvão, 1956	
Triatoma breyeri Del Ponte, 1929 (= *Triatoma breyeri dallasi* Del Ponte, 1930)	Argentina.
Triatoma bruneri (Usinger, 1944)	Cuba.
* *Triatoma carrioni* Larrousse, 1926	Ecuador, Peru.
Triatoma circummaculata (Stål, 1859)	Argentina, Brazil, Uruguay.
* *Triatoma costalimai* Verano & Galvão, 1958	Brazil.
Triatoma deanei Galvão, Souza & Lima, 1967	Brazil.
* *Triatoma delpontei* Romana & Abalos, 1947	Argentina, Paraguay.
* *Triatoma dimidiata* (Latreille, 1811) (= *Triatoma capitata* Usinger, 1941)	Belize, Colombia, Costa Rica, Ecuador, El Salvador, Guatemala, Honduras, Mexico, Nicaragua, Panama, Peru, Venezuela.
Triatoma dimidiata maculipennis (Stål, 1859)	
* *Triatoma dispar* Lent, 1950	Ecuador, Panama.
* *Triatoma eratyrusiformis* Del Ponte, 1929 (= *Triatoma ninoi* Carcavallo et al., 1964)	Argentina.
* *Triatoma flavida* Neiva, 1911	Cuba.
* *Triatoma gerstaeckeri* (Stål, 1859)	Mexico, USA.
* *Triatoma guasayana* Wygodzinsky & Abalos, 1949	Argentina, Bolivia, Paraguay.
Triatoma guazu Lent & Wygodzinsky, 1979	Paraguay.
* *Triatoma hegneri* Mazzotti, 1940	Mexico.
Triatoma incrassata Usinger, 1939	Mexico, USA.
Triatoma incrassata apachaensis Ryckman, 1962	
Triatoma indictiva Neiva, 1912	Mexico, USA.
* *Triatoma infestans* (Klug, 1834) (= *Conorhinus renggeri* Herrich-Schaeffer, 1848; = *Conorhinus sex-tuberculatus* Spinola, 1852; = *Conorhinus gracilipes* Philippi, 1860; = *Conorhinus octotuberculatus* Philippi, 1860; = *Conorhinus paulseni* Philippi, 1860; = *Conorhinus gigas* Burmeister, 1861; = *Conorhinus nigrovarius* Blanchard, 1890; = *Triatoma oswaldoi* Neiva & Pinto, 1923; = *Triatoma sordelli* Dios & Zuccarini, 1926; = *Triatoma mazzae* Jorg, 1937; = *Triatoma infestans erythrophthalmus* Noe & Silva, 1949)	Argentina, Bolivia, Brazil, Chile, Paraguay, Peru, Uruguay.

	Triatoma lecticularia (Stål, 1859)	Mexico, USA.
	Triatoma lecticularia occulta (Neiva, 1911)	
	Triatoma lecticularia floridana (Usinger, 1944)	
	Triatoma lenti Sherlock & Serafim, 1967 (= *Triatoma bahiensis* Sherlock & Serafim, 1967; = *Triatoma pessoai* Sherlock & Serafim, 1967)	
	Triatoma limai Del Ponte, 1929 (= *Triatoma circummaculata limai* Carcavallo & Martínez, 1968)	Argentina.
	Triatoma longipennis Usinger, 1939	Mexico.
*	*Triatoma maculata* (Erichson, 1848) (= *Conorhinus immaculata* Patton & Cragg, 1913)	Colombia, Guyana, Netherlands Antilles (Aruba, Bonaire), Suriname, Venezuela.
*	*Triatoma matogrossensis* Leite & Barbosa, 1953	Brazil.
*	*Triatoma melanocephala* Neiva & Pinto, 1923	Brazil.
	Triatoma mexicana (Herrich-Schaeffer, 1848)	Mexico.
*	*Triatoma neotomae* Neiva, 1911	USA.
*	*Triatoma nigromaculata* (Stål, 1872)	Colombia, Venezuela.
*	*Triatoma nitida* Usinger, 1939	Costa Rica, Guatemala, Honduras, Mexico.
	Triatoma obscura (Maldonado & Farr, 1962)	Jamaica.
	Triatoma oliveirai (Neiva, Pinto & Lent, 1939)	Brazil.
*	*Triatoma pallidipennis* (Stål, 1872)	Mexico.
*	*Triatoma patagonica* Del Ponte, 1929	Argentina.
*	*Triatoma peninsularis* Usinger, 1940	Mexico.
	Triatoma petrochii Pinto & Barreto, 1925	Brazil.
*	*Triatoma phyllosoma* Burmeister, 1835	Mexico.
	Triatoma phyllosoma intermedia Usinger, 1944	
	Triatoma phyllosoma longipennis Usinger, 1939	
	Triatoma phyllosoma mazzotti Usinger, 1939	
	Triatoma phyllosoma paltidipennis (Stål, 1872)	
	Triatoma phyllosoma picturata Usinger, 1939	
	Triatoma phyllosoma usingeri Mazzotti, 1943	
*	*Triatoma picturata* Usinger 1939	Mexico.
*	*Triatoma platensis* Neiva, 1913 (= *Triatoma rosenbuschi* Mazza, 1936)	Argentina, Bolivia, Brazil, Paraguay, Uruguay.
*	*Triatoma protracta* (Uhler, 1894)	Mexico, USA.
	Triatoma protracta nahuatlae Ryckman, 1962	
	Triatoma protracta navajoensis Ryckman, 1962	
	Triatoma protracta woodi Usinger, 1939	
	Triatoma protracta zacatecensis Ryckman, 1962	
*	*Triatoma pseudomaculata* Correa & Espinola, 1964	Brazil.
*	*Triatoma recurva* (Stål, 1868)	Mexico, USA.
	Triatoma recurva nigricollis Usinger, 1944	
*	*Triatoma rubida* (Uhler, 1894)	Mexico, USA.
	Triatoma rubida cochimiensis Ryckman, 1967	
	Triatoma rubida jaegeri Ryckman, 1967	
	Triatoma rubida sonoriana Del Ponte, 1930	

Triatoma rubida uhleri Neiva, 1911	
* *Triatoma rubrofasciata* (De Geer, 1773) (= *Cimex rubrofasciatus* De Geer, 1773; = *Cimex variegatus* Drury, 1773; = *Reduvius gigas* Fabricius, 1775; = *Cimex gigas* Gmelin, 1788; = *Cimex claviger* Gmelin, 1788; = *Cimex erythrozonias* Gmelin, 1788; = *Nabis gigas* Latreille, 1804; = *Conorhinus gigas* Laporte, 1832; = *Triatoma gigas* Laporte, 1833; = *Reduvius giganti* Klug, 1834, in Meyen; = *Reduvius variegatus* Westwood, 1837; = *Conorhinus rubrofasciatus* Amyot & Serville 1843; = *Conorhinus stalii* Signoret, 1860; = *Conorhinus variegatus* Stål, 1872; = *Triatoma rubrofasciata* Breddin, 1905; = *Triatoma variegata* Neiva, 1914; = *Triatoma rubrofasciata* Neiva, 1914; = *Triatoma rufofasciata* Van Duzee, 1916; = *Triatoma rubrofasciata* Neiva & Lent, 1936; = *Triatoma evandroi* Figueiredo, 1938; = *Triatoma rubrofasciata* Usinger, 1944; = *Triatoma rubrofasciata* Lent & Wygodzinsky, 1979; = *Triatoma rubrofasciata* Ryckman & Archbold, 1981)	Antigua, Argentina, Bahamas, Brazil, Cuba, Dominican Republic, French Guiana, Grenada, Guadeloupe, Haiti, Jamaica, Martinique, St Croix, St Vincent, Trinidad, Venezuela Virgin Is., USA. (Also reported from several port areas of Asia, Africa, and the Eastern Mediterranean, and from some rural areas of India and southeastern Asia.)
* *Triatoma rubrovaria* (Blanchard, 1843) (= *Conorhinus rubroniger* Stål, 1859; = *Triatoma gomesi* Neiva & Pinto, 1923; = *Triatoma bruchi* Mazza & Jorg, 1944)	Argentina, Brazil, Uruguay.
Triatoma ryckmani Zeledon & Ponce, 1972	Guatemala, Honduras.
* *Triatoma sanguisuga* (Leconte, 1855)	USA.
Triatoma sanguisuga ambigua Neiva, 1911	
Triatoma sanguisuga texana Usinger, 1944	
* *Triatoma sinaloensis* Ryckman, 1962	Mexico.
* *Triatoma sordida* (Stål, 1859) (= *Triatoma garciabesi* Carcavallo et al., 1967).	Bolivia, Brazil, Paraguay, Uruguay.
* *Triatoma spinolai* Porter, 1934 (= *Triatoma chilena* Usinger, 1939; = *Triatomaptera porteri* Neiva & Lent, 1940)	Chile.
* *Triatoma tibiamaculata* (Pinto, 1926)	Brazil.
* *Triatoma venosa* (Stål, 1872)	Colombia, Costa Rica.
* *Triatoma vitticeps* (Stål, 1859) (= *Triatoma chagasi* Brumpt & Gomes, 1914; = *Triatoma holmbergi* Del Ponte, 1923; = *Triatoma nevai* Del Ponte, 1923; = *Triatoma chagasi nevai* Del Ponte, 1930)	Brazil.
* *Triatoma williami* Galvão, Souza & Lima, 1965	Brazil.
Triatoma wygodzinskyii Lent, 1951	Brazil.

Annex 3

Standard data required for identification and incrimination of animal hosts and characterization of *Trypanosoma cruzi* strains

I. General

1. Survey title and number
2. State (department or province)
3. Municipality (indicate whether urban or rural)
4. Locality (e.g., *aldea, vereda, partido, parroquia*)
5. Date (day/month/year)

II. Ecology

1. Altitude (metres above sea level)
2. Relative humidity (%)
3. Holdridge life zone (enter appropriate descriptive name)[1]
4. Species of animal (indicate scientific and common names)
5. Sex
6. Age
7. Size:
   overall length
   length of tail
   length of ear
   length of front leg
   length of back leg
8. Weight
9. Number of other animals of same species captured

III. Laboratory

1. Date of direct examination (day/month/year)
2. Result of direct examination
3. Date of xenodiagnosis (day/month/year)
4. Result of xenodiagnosis:
   negative
   positive *T. cruzi*
   positive *T. rangeli*
   positive *T. cruzi* and *T. rangeli*
   positive other trypanosomes
5. Serological result whenever possible

[1] A convenient summary of Holdridge's zones is contained in *McGraw-Hill encyclopedia of science and technology*, 6th ed. New York, McGraw-Hill, 1987, vol. 10, pp. 49-50.

6. Characterization of *T. cruzi* strains:
   morphology
   isoenzyme analysis
   other biochemical analysis
   antigenic structure
   development in laboratory animals
   development in vectors
   development in tissue cultures

Annex 4

List of sylvatic and domestic or peridomestic animal reservoir hosts of *Trypanosoma cruzi* and countries in which they have been found infected[1, 2]

I. Sylvatic Mammals

Order MARSUPIALIA

Family DIDELPHIDAE

Caluromys derbianus, Costa Rica, Panama.

Caluromys lanatus, Brazil (Minas Gerais), Venezuela.

Caluromys philander, French Guiana, Venezuela.

Didelphis albiventris (= *D. paraguayensis*; = *D. azarae*) Argentina, Bolivia, Brazil (Ceará, Minas Gerais, São Paulo, Santa Carina), Uruguay.

Didelphis marsupialis, Brazil, Colombia, Costa Rica, Ecuador, French Guiana, Guatemala, Honduras, Mexico, Panama, USA, Venezuela.

Lutreolina crassicaudata, Argentina, Brazil (São Paulo).

Marmosa agilis, Brazil.

Marmosa alstoni, Costa Rica.

Marmosa elegans, Argentina, Brazil.

Marmosa microtarsus, Brazil.

Marmosa murina, Colombia.

Marmosa pusilia, Argentina.

Marmosa robinsoni, Venezuela.

Metachirus nudicaudatus, Brazil.

Monodelphis brevicaudata, Venezuela.

Monodelphis domestica, Brazil.

Philander opossum, Brazil, Colombia, Costa Rica, Panama.

Order EDENTATA

Family MYRMECOPHAGIDAE

Tamandua tetradactyla, Brazil, Colombia, Panama, Venezuela.

Family BRADYPODIDAE

Bradypus infuscatus, Columbia, Panama.

Choloepus hoffmanni, Panama.

Family DASYPODIDAE

Cabassous tatouay, Argentina.

Cabassous unicinctus, Argentina, Brazil, French Guiana, Venezuela.

Chaetophractus vellerosus, Argentina.

Chaetophractus villosus, Argentina.

Dasypus kapleri, Colombia, Venezuela.

Dasypus novemcinctus, Argentina, Brazil, Colombia, Costa Rica, French Guiana, Guatemala, Mexico, USA, Venezuela.

Euphractus sexcinctus, Brazil, Venezuela.

Tolypeutes matacus, Argentina.

Zaedyus pichiy, Argentina.

Order CHIROPTERA

Family EMBALLONURIDAE

Rhynchonycteris naso, Colombia.

Peroteryx macrotis, Colombia.

Saccopteryx bilineata, Colombia, Venezuela.

Family NOCTILIONIDAE

Noctilio albiventris, Brazil, Colombia.

Noctilio leporinus, Colombia.

Family PHYLLOSTOMIDAE

Anoura caudifera, Brazil.

Artibeus jamaicensis, Brazil.

Artibeus lituratus, Colombia, French Guiana, Venezuela.

Carollia castanea, Colombia.

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[1] For some species *T. cruzi* was not formally identified.

[2] Largely following the systematics for Central and South American mammals of Cabrera, A. Catálogo de los mamíferos de America del Sur. *Revista del Museo Argentino de Ciencias Naturales "Bernadino Rivadavia"*..., 4: 1–732 (1957–61); and for North American mammals of Hall, E.R. & Kelson, K.R. *The mammals of North America.* New York, Ronald, 1959 (rev. 1981 by Hall).

Carollia perspicillata, Brazil, Colombia, Panama, Venezuela.

Carollia subrufa, Colombia.

Carollia villosum, Colombia.

Glossophaga soricina, Brazil, Colombia, Panama.

Micronycteris branchyotis, Colombia.

Micronycteris minuta, Colombia.

Mimon bennettii, Colombia.

Mormoops megalophylla, Colombia.

Phyllostomus discolor, Colombia.

Phyllostomus elongatus, Brazil, Venezuela.

Phylllostomus hastatus, Argentina, Colombia, French Guiana, Panama, Venezuela.

Rhinophylla pumilio, Colombia.

Sturnira lilium, Colombia.

Sturnira tildae, Colombia.

Trachops cirrhosus, Brazil.

Uroderma bilobatum, Colombia, Panama.

Vampyrodes caraccioloi, Colombia.

Vampyrops helleri, Colombia.

Vampyrum spectrum, Colombia.

Family Desmodontidae

Desmodus rotundus, Brazil, Colombia, Panama, Venezuela.

Diaemus youngi, Colombia.

Family Vespertilionidae

Myotis nigricans, Colombia.

Eptesicus brasiliensis, Argentina, Brazil.

Eptesicus furinalis, Argentina.

Histiotus montanus, Argentina.

Lasiurus borealis, Argentina.

Lasiurus cinereus, Brazil.

Lasiurus ega, Brazil.

Family Molossidae

Tadarida laticaudata, Brazil.

Eumops auripendulus, Brazil.

Eumops bonariensis, Argentina.

Eumops glaucinus, Brazil.

Eumops perotis, Brazil.

Eumops trumbulli, Colombia.

Molossops temminckii, Colombia.

Molossus bondae, Colombia.

Molossus molossus, Brazil, Colombia, Venezuela.

Order CARNIVORA

Family Canidae

Cerdocyon thous, Argentina, Brazil.

Dusicyon culpaeus, Argentina, Chile.

Dusicyon griseus, Argentina, Chile.

Dusicyon vetulus, Brazil.

Urocyon cinereoargenteus, USA.

Family Procyonidae

Bassaricyon gabbii, Panama.

Nasua nasua, Argentina, Brazil.

Nasua narica, Belize, Costa Rica, Panama.

Potos flavus, Panama.

Procyon cancrivorus, Brazil, Venezuela.

Procyon lotor, Costa Rica, Guatemala, USA.

Family Mustelidae

Mephitis mephitis, USA.

Conepatus semistriatus, Costa Rica.

Eira barbara, Argentina, Brazil, Colombia.

Galictis cuja, Argentina and Brazil.

Galictis vittata, Brazil.

Family Felidae

Felis yaguaroundi, Argentina.

Order LAGOMORPHA

Family Leporidae

Sylvilagus orinoci

Sylvilagus floridanus

Order RODENTIA

Family Sciuridae

Citellus leucurus, USA.

Sciurus aestuans, Brazil, Venezuela.

Sciurus ignitus, Argentina.

Sciurus igniventris, Colombia.

Sciurus granatensis, Panama, Venezuela.

Family Heteromyidae

Heteromys anomalus, Venezuela.

Family Cricetidae

Akodon arviculoides, Brazil.

Akodon lasiotis, Brazil.

Akodon nigritus, Brazil.

Calomys expulsus, Brazil.
Calomys laucha, Argentina.
Calomys toner, Brazil.
Nectomys squamipes, Brazil.
Neotoma albigula, USA.
Neotoma fuscipes, USA.
Neotoma micropus, USA.
Oryzomys capito, Brazil.
Oryzomys concolor, Venezuela.
Oryzomys nigripes, Brazil.
Oryzomys subflavus, Brazil.
Oxymycterus hispidus, Brazil.
Peromyscus boylii, USA.
Peromyscus truei, USA.
Phyllotis griseoflavus, Argentina.
Sigmodon hispidus, Colombia, El Salvador.
Thomasomys dorsalis, Brazil.
Tylomys panamensis, Panama.
Wieodmys pirrhorhinus, Brazil.
Zygodontomys lasiurus, Brazil.
Family Octodontidae
Octodon degus, Chile.
Family Echimyidae
Cercomys cunicularius, Brazil.
Diplomys labilis, Panama.
Echimys semivillosus, Venezuela.
Proechimys guayanensis, Colombia.
Proechimys semispinosus, Panama, Venezuela.
Family Caviidae
Cavia sp, Argentina.
Cavia aperea, Brazil.
Galea spixii, Brazil.
Family Dasyproctidae
Dasyprocta aguti, Brazil, Venezuela.
Dasyprocta azarae, Brazil.
Dasyprocta fuliginosa, Colombia.
Dasyprocta punctata, Ecuador, Panama.
Family Agoutidae
Cuniculus paca, Venezuela.
Family Erethizontidae
Coendou insidiosus, Brazil.
Coendou mexicanus, Costa Rica.
Coendou prehensilis, Venezuela.
Coendou rothschildi, Colombia.
Coendou vestitus, Venezuela.

Order PRIMATES
Family Cebidae
Alouatta caraya, Brazil.
Alouatta senicula, Colombia, Venezuela.
Aotus trivirgatus, Panama.
Ateles belzebuth, Colombia.
Ateles fuscipes, Panama.
Ateles geoffroyi, Colombia.
Callicebus nigrifrons, Brazil.
Callicebus ornatus, Colombia.
Cebus albifrons, Colombia.
Cebus apella, Brazil, Colombia, French Guiana, Venezuela.
Cebus capucinus, Colombia, Panama, Venezuela.
Saimiri oerstedii, Panama.
Saimiri sciureus, Brazil, Colombia, Panama, Peru.
Family Callithricidae
Callithrix argentata, Brazil.
Callithrix geoffroyi, Brazil.
Callithrix jacchus, Brazil.
Callithrix penicillata, Brazil.
Cebuella pygmaea, Colombia.
Saguinus geoffroyi, Panama.
Saguinus nigricollis, Colombia.
Saguinus leucopus, Colombia.

II. Domestic and Peridomestic Mammals

Canis familiaris
Capra hyrcus
Cavia porcellus
Felis domesticus
Mus musculus
Oryctolagus cuniculus
Rattus norvegicus
Rattus rattus
Sus scrofa

Annex 5

Safety precautions for laboratory work with *Trypanosoma cruzi*[1]

All personnel handling either *Trypanosoma cruzi, in vitro* or *in vivo,* or infected triatomines must, first, be expert in general laboratory procedures, second, know the techniques specially related to *T. cruzi* and, third, have a good background knowledge of the parasite. Initially they must also work under close supervision. The following must be considered as additional precautions essential to the safety of competent research workers and their technicians:

1. Restrict access to laboratory, animal rooms and insectary to those people actually working on the organism. Make sure these areas are well marked.
2. Provide secure barriers to prevent the escape of infected animals or insects.
3. Provide a suitable protocol for the disposal of dead infected animals and insects (e.g., autoclaving or incineration).
4. Wear protective clothing:
   face mask
   back-fastening gown
   gloves
   shoes (not sandals)
5. Do not pipette by mouth.
6. Modify apparatus and procedures to reduce hazards (e.g., provide safety boxes for homogenizers, caps for centrifuge tubes, safety hoods for subculturing).
7. Provide a suitable protocol for the decontamination of glassware, etc. (e.g., disinfectant autoclaving).
8. Inform maintenance staff, fire brigade, etc., of the nature of the work being carried out.
9. Inform the medical staff of the organization of the nature of the work being carried out so that suitable procedures are established for the monitoring of accidents and treatment of the personnel involved.
10. Monitor all staff periodically (e.g., every 6 months) for *T. cruzi* antibodies.
11. Provide a protocol to be followed in the event of a suspected accident:
    (a) clean the skin immediately with ethanol or a disinfectant;
    (b) report accident to appropriate medical person;
    (c) if there is only a slight risk of infection, monitor blood for next few months;
    (d) if risk of infection is high, treat with nifurtimox or benznidazole;
    (e) report accident, if required, to public health authority.

[1] Prepared by the Scientific Working Group on Chagas Disease, UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases, World Health Organization.

12. Provide all staff with a copy of the accident protocol and give them proper instruction in how to carry it out. It is important that they should be aware of possible dangers so they will avoid a casual approach. It is equally important that they should not be frightened of working with the organism.

Recommendation: When a confirmed accident does occur, start treatment with nifurtimox or benznidazole immediately, without waiting for evidence of infection.

Annex 6

Sequential steps for cost-effectiveness analysis

1. Monitoring the extent of Chagas disease in the population

This is done through quick local surveys, studies in neighbouring villages, and general assessment (Delphi method). The following indices should be established:

- house infestation index, dispersion index, colonization index (see Table 3, page 52);
- triatomine infection rate;
- human infection rate (especially in children under 5 years old);
- prevalence of infection seen in blood banks and transfusion services;
- morbidity rate of neonatal Chagas disease.

2. Vulnerability analysis

For this purpose, all available knowledge of the epidemiology of Chagas disease and of the prevailing socioeconomic and local cultural conditions must be taken into consideration in order to identify the points of weakness through which it may be possible to mount a successful attack. To date, the most sensitive points of attack have proved to be those directed against vector transmission and transmission by transfusion.

3. Objectives

Determination of the objectives of morbidity and mortality reduction in Chagas disease control programmes can be made by applying different models, which have to be validated for a given geographical area.

4. Indicators of effectiveness

Based on available information, the effectiveness of different forms of control should be considered. For instance, while residual insecticide spraying inside houses has succeeded in reducing transmission in several regions, its effectiveness increases every year for about 5 years and then tends gradually to decline.

Modification of the house is an effective way of reducing triatomine infestation; nevertheless, the life-styles and family and community motivations, together with the socioeconomic development pattern of Latin American countries have so far limited its applicability.

It should be noted that it may be difficult to evaluate the outcome of action taken during the first and second years, but that as from the third year, it does become possible to characterize the effectiveness of definite results. Control activities must be defined so as to be equitable for the population concerned. Therefore, technical solutions must be discussed with the community in the light of local resources and finances; these are basic

questions for which the answers cannot be imposed by a centralist structure. A programme operation and administration structure is required at the local level so as to be able to draw upon resources near to where Chagas disease is present – i.e., the community.

5. Calculation of effectiveness and costs and selection of alternative methods

Once the theoretical and practical aspects have been considered and costs calculated according to local conditions, the effectiveness coefficient must be determined in order to select the best of the alternative methods considered.

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