Chagas disease in Nicaragua

Implementation of Chagas disease diagnostics for screening and management

July 2010

PATH

This document is part of a larger case study on Nicaragua's health system and diagnostic needs. The health system case study employed two main methodological approaches. The first was a review of official Ministry of Health (MINSA) data and epidemiological reports, as well as publications in peer-reviewed journals. The second was a concurrent series of field visits in 2008 to provide firsthand evidence of diagnostic needs and difficulties. A more detailed account of these methodological approaches can be found in the methodology section of the health system case study.

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About PATH

PATH is an international nonprofit organization that creates sustainable, culturally relevant solutions, enabling communities worldwide to break longstanding cycles of poor health. By collaborating with diverse public- and private-sector partners, PATH helps provide appropriate health technologies and vital strategies that change the way people think and act. PATH's work improves global health and well-being.

Cover photo: PATH/Mike Wang

Contents

Glossary

Brigadistas	Independent health volunteers trained by MINSA to serve rural areas
CNDR	Centro Nacional de Diagnóstico y Referencia (National Diagnostic and Reference Center)
ELISA	Enzyme-linked immunosorbent assay
MINSA	Ministerio de Salud (Ministry of Health)
MSF-B	Médecins Sans Frontières—Belgium
PAHO	Pan American Health Organization
PATH	Program for Appropriate Technology in Health
RAAN	Región Autónoma del Atlántico Norte (North Atlantic Autonomous Region)
RAAS	Región Autónoma del Atlántico Sur (South Atlantic Autonomous Region)
SILAIS	Sistemas Locales de Atención Integral de Salud (Local Comprehensive Health Care Systems, which are the Nicaraguan health system's 17 administrative units corresponding to the country's departments and autonomous regions)
WHO	World Health Organization

Introduction

Chagas disease, or American trypanosomiasis, is a chronic parasitic disease caused by the Trypanosoma cruzi parasite that exclusively affects the Americas. It is most common in the poorest, marginalized populations in remote rural areas and has not been prioritized like other diseases. The Pan American Health Organization (PAHO) estimates that around 8 million people are currently infected in the 21 countries where the disease is endemic and that almost 14,000 people die from Chagas disease every year.[1]

In about 80% of cases, insect vectors (hematophagous triatomines) transmit *T. cruzi* directly. PAHO estimates that every year approximately 41,200 people are infected by vectors, and almost 14,000 infants are born with congenital Chagas disease. About 1% of all infections are transmitted via blood transfusions and transplants.[1]

Although Chagas disease is present in almost all Central American and South American countries, there is great complexity in terms of the main mode of transmission, the clinical symptoms, the vectors involved, the characteristics of the parasite, and the pathology it produces. One common feature, related to economics and social development, is that it mainly affects poor people living in rural and peri-urban areas. In terms of culture, prevalence is related to certain customs, such as keeping domestic animals inside the house, and the types of housing (e.g., brick houses with many cracks). A lack of knowledge about Chagas disease among communities and health care workers also facilitates its transmission and prevalence.

Developing comprehensive public health strategies for Chagas disease requires the enhancement of laboratory capabilities. The disease is difficult for most clinicians to diagnose as it usually develops with very unspecific symptoms, such as fever. The infection then remains dormant for a number of years in a small proportion of patients, who later develop major and lethal complications. Because they may be too expensive or involve specifications not always suitable for low-resource countries, new diagnostic technologies are often unknown or unavailable, Without appropriate tests, Chagas disease remains undetected by most clinicians.

In addition to supporting the work of doctors at the point of care, laboratories conduct studies and maintain accurate epidemiological surveillance. Information from clinical/epidemiological studies determines the number of infected people at different stages of the disease, establishes the geographic concentration of cases, and identifies sources of infection. Knowing the level of Chagas disease endemicity among specific groups is essential to monitoring the implementation of vector control and assessing progress towards eliminating disease transmission.

In Nicaragua, certain geographical zones bear a higher disease burden of Chagas disease.[2] Despite efforts aimed at controlling and eliminating the disease, Nicaragua lacks reliable data on morbidity and mortality, largely due to the nature of the disease, limited diagnostic capabilities, and the prioritization of other health problems. These and other factors will be further examined in this paper.

Recent trends

Background

First discovered in 1909, Chagas disease exists throughout Latin America. El Salvador reported the first human case of Chagas disease in Central America in 1913. Panama reported its first case in 1931, Guatemala in 1933, and Costa Rica in 1941. Nicaragua documented its first case in 1949, and the insects *Rhodnius prolixus* and *Triatoma dimidiata* were confirmed as the country's main disease vectors in 1965.[3] According to unpublished MINSA reports, it became obligatory to report Chagas disease in 1985, making it subject to epidemiological surveillance, although it only became part of the national epidemiological surveillance system in 1992. Also in 1992, MINSA initated the National Chagas Disease Control Program.[4]

Over the last ten years, a series of initiatives have been implemented to reduce Chagas disease in Nicaragua, although a comprehensive and coordinated national strategy to eliminate Chagas is not yet developed. MINSA currently offers diagnostic tests and free treatment to all people affected by *T. cruzi*. While vector control and eventual disease elimination are still considered attainable goals, several challenges remain. These include improving housing, promoting behavioral change, increasing diagnostic capabilities, ensuring adequate budgeting, and training health personnel. In 2010, Nicaragua will implement the new Chagas Control Program in partnership with Japan International Cooperation Agency (JICA). The program will focus on vector control, with no planned diagnostics component.

Most successful interventions have targeted specific regions where studies have reported high levels of disease transmission. These interventions have primarily resulted in improved epidemiological data, decentralized health care for Chagas disease, and sustained vector-control activities.[4]

With the exception of a few region-specific prevalence studies, Nicaragua has no reliable data on Chagas-related morbidity and mortality and huge discrepancies exist between the prevalence data gathered from studies and from routine reports. Because official statistics only include actual clinical cases attended to at the MINSA health facilities, they exclude data from serological studies and donated blood screenings (see the Data and Surveillance section for statistics).

Prevalence studies

Serological tests are important tools for estimating levels of exposure to *T. cruzi* in endemic regions and can potentially evaluate program impact. The following studies employed such tests:

- In 1989, a clinical and serological survey was conducted using indirect immunofluorescence (IIF) and indirect hemagglutination (IHA), with 13% of samples testing positive in the Santa Rosa community of the northern Nicaraguan department of Madriz.[5] The same group of researchers (Rivera, T. et al.) also reported on triatomine household infestation rates based on a survey conducted in three rural settlements in Nicaragua.[6]
- An unpublished 1989 MINSA study of military service recruits in the northern departments of Estelí, Nueva Segovia, and Madriz revealed 4% positivity.[4]
- In 1989, Palacios, X. et al. used enzyme-linked immunosorbent assay (ELISA) and IIF tests in a serological survey of eight rural communities in Somoto municipality, department of Madriz. The ELISA test revealed *T. cruzi* antibodies among 11% of those examined, with fewer cases among the younger age groups. Like Rivera, T. et al., they discovered that the older the group the higher the rate of infection—the same pattern found in other endemic regions.[5,6]
- A series of serological surveys funded by PAHO/WHO from 1992 to1993 revealed Madriz and

Nueva Segovia as the departments with the highest seroprevalence of Chagas infection among blood donors (See Annex 1).[7]

- In 1999, MINSA conducted the first national serological survey among seven- to 14-year-old schoolchildren in 15 Local Comprehensive Health Care Systems (SILAIS); 408 of 12,040 filter paper samples tested positive for Chagas disease, an overall positivity of 3.3%.[11] In this national survey, Matagalpa showed the highest infection rates, with 15% prevalence in Esquipulas and La Dalia. Two years later, Médecins Sans Frontières—Belgium (MSF-B) conducted more serological surveys in northern Nicaragua, finding an infection rate of just 1% at the project baseline.[9]
- The vast under-registration of Chagas disease has led MINSA to conduct larger-scale studies that provide a more accurate picture of the disease's prevalence, including screening blood bank donors. These studies resulted in 2,050 positive results from 359,625 samples between 1999 and 2007, giving a positive case rate of 0.57% for the total number of donors (419,300).[8] (See Annex 2).
- In 2003, a serological survey of children under the age 15 was conducted in areas infested with Rhodnius prolixus; 187 (5.5%) of the 3,407 children tested positive (Annex 3).
- A MINSA study with pregnant women living in Madriz, Nueva Segovia, and Matagalpa departments (2005–2006) revealed seroprevalences of 15.6% in Mozonte municipality (Nueva Segovia), 21.1% in San José de Cusmapa (Madriz), and 25.5% in Totogalpa (Madriz). An active transmission rate of 6% was discovered for congenital Chagas disease in the same departments.[7] MSF-B also conducted a serological survey with pregnant women in the north Nicaragua, revealing an infection rate of just 1.7% at the project baseline.[9]

Although serological surveys continue to be carried out periodically to further examine the prevalence of Chagas disease, given its under-registration in the country, the only national-level survey took place in 1999. There is a need for another national survey to evaluate behavior changes among the vector and human populations.

Data and surveillance

Clinics rarely run serological confirmation tests on patients with cardiac or suspected intestinal problems. As a result, MINSA has no precise mortality figures for Chagas disease. In Nicaragua, autopsies are generally conducted for accidental and incidental causes of death, and less often for more natural causes of mortality, such as disease-related death.

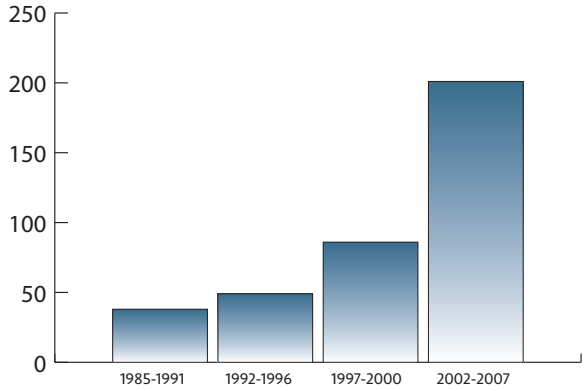
Regarding morbidity, there are huge discrepancies between the prevalence data reported in studies and what is routinely reported by official statistics. The sporadic nature of these studies, the different methodologies used, and the fact that the study sites have been limited to certain regions have made it difficult to extrapolate or generalize results. Official statistics only count actual clinical cases identified at health facilities. According to data from MINSA epidemiological surveillance system, around ten new cases of Chagas disease have been reported annually over the last five years, with 12 cases reported in 2007 for an incidence rate of 0.02 per 10,000 inhabitants.10 These surveillance reports show that the most affected age groups are one- to four-year-old children and adults over 49. There are no significant gender differences.10

The epidemiological surveillance data show that Chagas cases occur throughout the year, providing no evidence of seasonal specificity for the disease. Between 1985 and 2007, 374 cases tested serologically positive for Chagas, of which only 245 (65%) were statistically registered with MINSA's statistics department. These data, however, do not classify cases according to the phase of the illness (acute, latent, or chronic).[4] Controlling *T. cruzi* transmission through blood transfusions has increased slightly, although 100% coverage has not been achieved.[3] Specific serological studies conducted between 2005 and 2007 revealed prevalence rates of 0.57% in blood donors and 3.3% in seven- to 14-year-old schoolchildren.

Recent trends

Analysis of epidemiology reports shows an increase in the detection rate in recent years. This increase coincides with projects designed to strengthen the control program, including epidemiological surveillance, serological surveys, and access to diagnostic techniques in hospitals. Although Figure 1, below, shows a huge increase in positive cases, it should not necessarily be interpreted as an increase in infection rates, but rather as the result of specific interventions. The period between 1997 and 2000, for example, included the first national serological survey, while MSF-B implemented an intervention in northern Nicaraguan communities between 2002 and 2007.[9] According to MINSA data, MSF-B captured 60% of all notified cases within those five years.[4] It should be stressed, however, that there is still no systematic case detection.

FIGURE 1: **Serologically positive cases of Chagas disease, 1985–2007**



Geographic distribution

Data from National Epidemiological Program reports and other published studies show that Chagas disease is most endemic in northern and central Nicaragua, particularly the departments of Madriz, Nueva Segovia, and Matagalpa. This may reflect the fact that most studies have focused on these areas. Although epidemiological surveillance is being improved nationwide, poor living conditions are common and the main vectors (*Rhodnius prolixus* and *Triatoma dimidiata*) are widely distributed across Nicaragua. The full magnitude of this problem may not yet be realized. (For more details on vector distribution and infection, see the section of this paper on "Chagas disease vectors in Nicaragua.")

The first national serological survey of schoolchildren classified three SILAIS as high prevalence: Matagalpa (9.4%), Managua (8.8%), the capital city of Nicaragua, and Chontales (7.4%). The prevalence in five municipalities— Esquipulas and La Dalia (department of Matagalpa), Muelle de los Bueyes (RAAS), and Tipitapa and San Rafael del Sur (Managua)—was greater than 15%.[11] Figures 2 and 3 show a corresponding the results of a serological survey of schoolchildren performed in 2000–2001.

Chagas disease in the Madriz SILAIS

Somoto municipality first confirmed the presence of Chagas disease in 1965, and is now known as a high prevalence zone. Located on the border with Honduras at an altitude of 600 meters, Somoto is a mountainous and wooded area with a tropical climate. It has poor socioeconomic indicators and its population is mainly comprised of agriculturists. Most of Somoto's houses are made of mud, wood, and palm leaves with earthen floors. Domestic animals (especially cats and dogs) often live with or near residents, acting as reservoir hosts of *T. cruzi* and contributing to the transmission of the disease.

FIGURE 2: **Schoolchildren seropositive for Chagas disease, 2001**

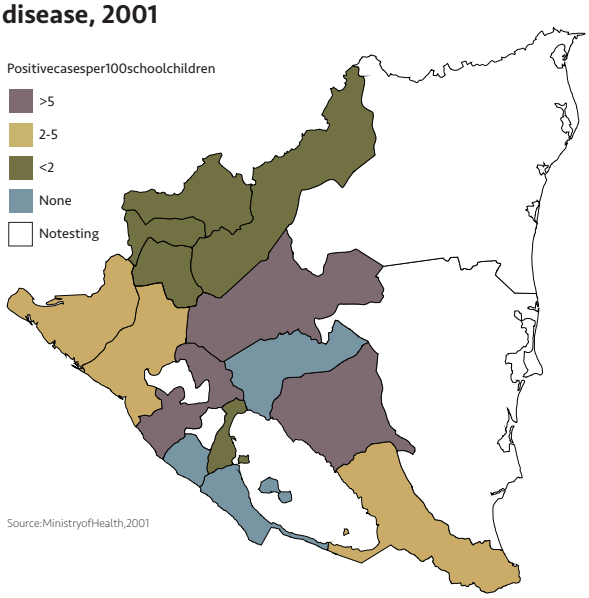
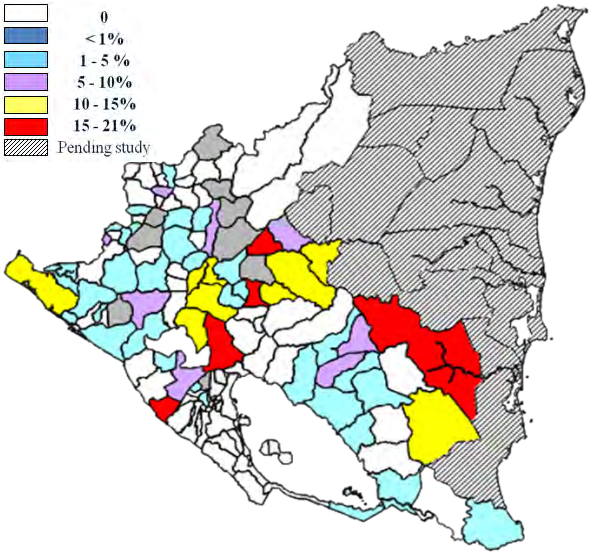


FIGURE 3: **Serological survey of Chagas disease among rural schoolchildren aged 7–14 living in endemic areas, 2000-2001**



Between 2000 and 2007, surveys in Madriz SILAIS detected the following: 109 positive cases in the latent and chronic stages (no acute cases) through blood bank screening, ten cases in the serological survey of pregnant women (the follow-up also revealed four cases of congenital Chagas disease among their children), 156 positive cases in the serological survey of schoolchildren, and 157 positive cases revealed by an active search by the MSF-B project.[9]

Chagas disease in the Matagalpa SILAIS

A serological survey with schoolchildren in Matagalpa SILAIS[11] revealed a seroprevalence in seven municipalities greater than that in the department of Matagalpa as a whole, which has a seroprevalence of 9.4%. The municipalities and their seroprevalence rates are: Esquípulas (20%), La Dalia (15%), San Isidro (15%), Sébaco (13%), Muy Muy (13%), Ciudad Darío (12%), and Río Blanco (11%).

From 1999 to 2008 the following cases were detected in Matagalpa department: 16 acute cases through medical consultations, 68 cases through blood bank screening, 146 positive cases in the serological survey of schoolchildren, and 78 cases diagnosed through MSF-B interventions.[9]

Eight people with acute Chagas disease lived in the Ciudad Darío municipality. Six acute cases occurred among one- to four-year-olds, while four cases occurred among five- to 14-year-olds and four among 30- to 49-year-olds. In terms of gender, six cases corresponded to women and ten to men.

Chagas disease vectors in Nicaragua

According to the *Handbook for Zoonotic Diseases of Companion Animals*,[13] "Chagas disease is vector-borne, transmitted primarily by triatomine insects, which are also called reduviid insects, 'kissing beetles,' or 'assassin bugs.' Approximately 100 insect species in three genera—*Triatoma*, *Rhodnius*, and *Panstrongylus*—are capable of transmitting *T. cruzi*. The parasite usually completes its life cycle by cycling between an insect species and a mammal species with which the insect lives in close association. The mammalian hosts include wildlife, domestic animals, and humans. In the United States, Chagas disease is mainly transmitted by triatomine insects that live in sylvatic environments and are associated with wildlife.

In Nicaragua, the two most epidemiologically important vectors are *R. prolixus* and *T. dimidiata*. In 2000, the country identified 13 municipalities in eight departments infested with R. prolixus. Following insecticide spraying, entomological surveillance reported this vector in only one municipality of Madriz department, which borders Honduras. *T. dimidiata*, on the other hand, has been reported in all of the country's departments.[3]

Meanwhile, the discovery of *R. pallescens* in southern Nicaraguan municipalities on the border with Costa Rica raises the need to initiate vector surveillance and the investigation of other species, in addition to humans, which could be epidemiologically important in the future.[3]

An insect spray trial from August to September 1998 compared three operational strategies for controlling *Triatoma dimidiata*. An evaluation conducted after one year indicated that all three strategies were similarly effective, and all sprayed

houses remained free of infestation. Although this study reports three interesting approaches to the entomological survey, there are a number of problems with the experiment's design. First, it compares municipalities with different levels of prior infestation and sample sizes. There was also no clear definition of how effectiveness would be assessed.[2,14]

In 1998, MINSA conducted the first national study of triatomine insects[15] in 5% of houses across Nicaragua, with the exception of the two Caribbean coast autonomous regions (RAAS and RAAN). Researchers visited 3,430 communities and found triatomines in 649, for a dispersion index of 18.9%. They discovered *Triatoma dimidiata* in all 649 communities, *Rhodnius prolixus* in 20 communities (0.6%), and *Triatoma ryckmani* in three communities (0.08%). The study reported the highest infestation rates in the departments of Madriz (13%), Masaya (10.6%), Estelí (6.3%), Boaco (6.2%), Granada (5.7%), Jinotega (4.5%), Matagalpa (3.6%), and Nueva Segovia (3.4%, and the highest percentages of vectors infected with the *T. cruzi* parasite in Granada (37%), Chinandega (25%), Managua (21%), Matagalpa (21%), Rivas (21%), Estelí (17%), Madriz (12%), Carazo (11%), and Jinotega (10.1%).

Current diagnostic practices in Nicaragua

Chagas disease has three clinical stages or phases (acute, latent, and chronic), which are important for diagnostic purposes. Around 6,260 Chagas samples analyses are conducted in Nicaragua each year at the *Centro Nacional de Diagnóstico y Referencia* (CNDR) Parasitology division, regardless of the clinical phase and/or diagnostic method involved, nor the source of sample (donated blood, antenatal care, clinics, hospitals, etc.).

According to the organization Médecins Sans Frontières, the acute stage "begins when the parasite *Trypanosoma cruzi* enters the body and the bloodstream. Most patients do not have any symptoms at this moment, but some feel malaise and have a fever, the shivers, tiredness, and present hepatomegaly and splenomegaly. When the parasite enters the body through an area near the eyes, or the conjunctiva, patients have an edema or swelling of the eyes, a characteristic sign of the acute infection, called the Romaña sign. The acute stage can also elapse with no signs or symptoms. After four to eight weeks, these clinical manifestations disappear and the patient enters the 'silent' period, which can last five to 20 years (latent stage). Between 20% and 30% of the infected persons will pass on to the chronic stage with clinical manifestations, principally causing cardiac and/or digestive dysfunction."[16]

Acute stage. Can be detected in fresh blood examinations, whether in thick smear microscopy (most widespread technique), isolation of the parasite in a culture medium, or xenodiagnosis. The Strout method is recommended for detecting parasites in a microscopic sample, but requires centrifugation and special training, which is not yet provided in Nicaragua. **Latent and chronic stages**. Can be detected through serological tests (IIF, IHA, and ELISA) or xenodiagnosis.

Parasite detection

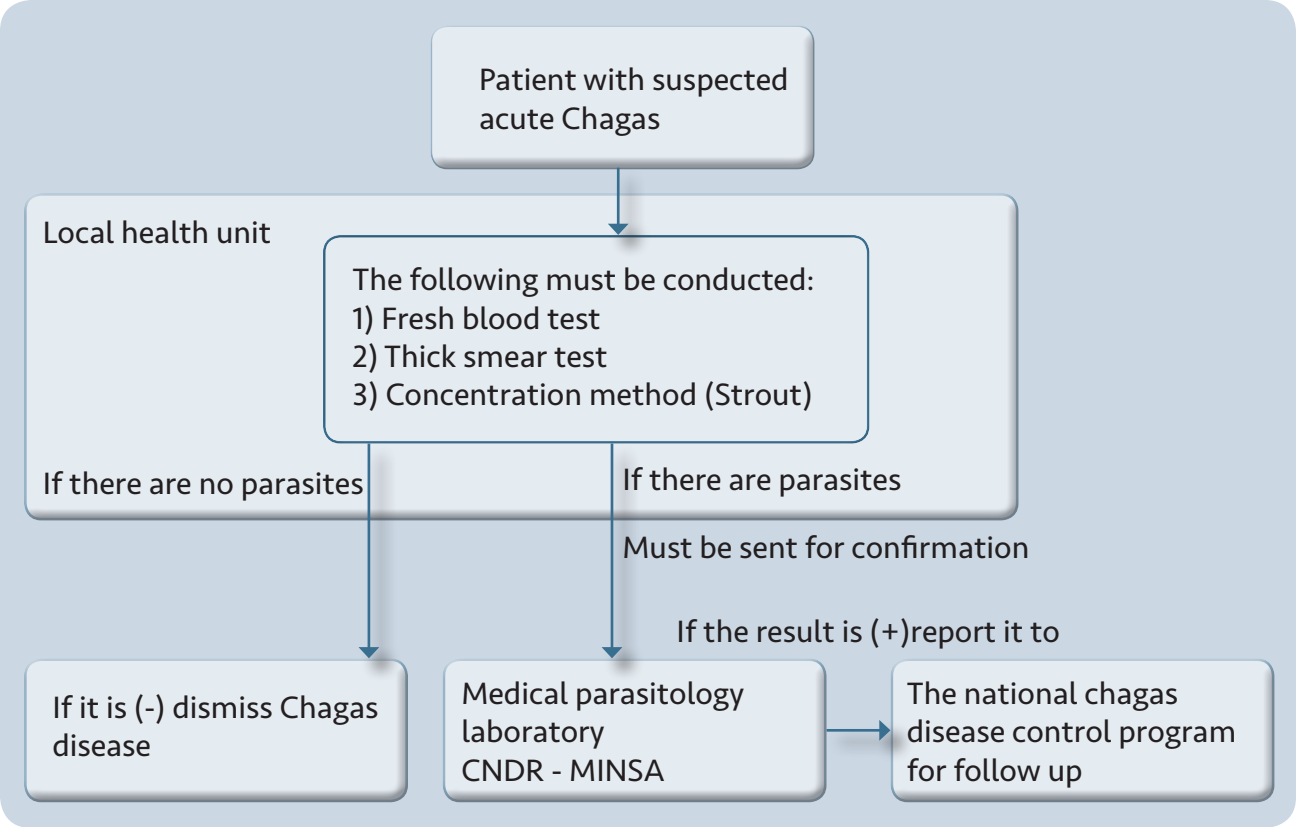
In Nicaragua, *T. cruzi* is only detected in blood samples in the CNDR and in the Matagalpa laboratories in Estelí and Granada. Figure 4 shows the diagnostic algorithm for parasitic confirmation of Chagas disease.

The detection of acute cases requires early suspicion from the clinical personnel and transport of the appropriate sample (fresh blood test or Strout's concentration), but there is limited local-level training for this. The disease cannot be confirmed in its initial acute stage through serology.

Xenodiagnosis, which consists of detecting *T. cruzi* in uninfected triatomines that fed on blood samples with suspected infection, is no longer used at the CNDR, following the advances made with the ELISA and IIF techniques.

The technique of isolating the parasite in a culture medium is only conducted in the CNDR.

FIGURE 4. **Parasitological confirmation of Chagas disease**



Serology

In 1999, the CNDR's parasitology division created and standardized a reactive "Chagas kit," which consists of an ELISA test that employs a locally produced antigen reagent, has 98% sensitivity and 100% specificity.[17] Figure 5 shows the diagnostic algorithm for serological confirmation.

The CNDR aimed to increase diagnosis and establish a highly technical and sensitive test that would allow many samples to be tested simultaneously, reducing expenses as compared to commercial tests. Each locally produced Chagas kit costs approximately US$0.20,[a] although no systematic cost analysis has been conducted. Hospitals use the Chagas kit for the serological detection of *T. cruzi* antigens in donated blood and blood derivatives. The Red Cross, which concentrates all donated blood, does not use the kits.

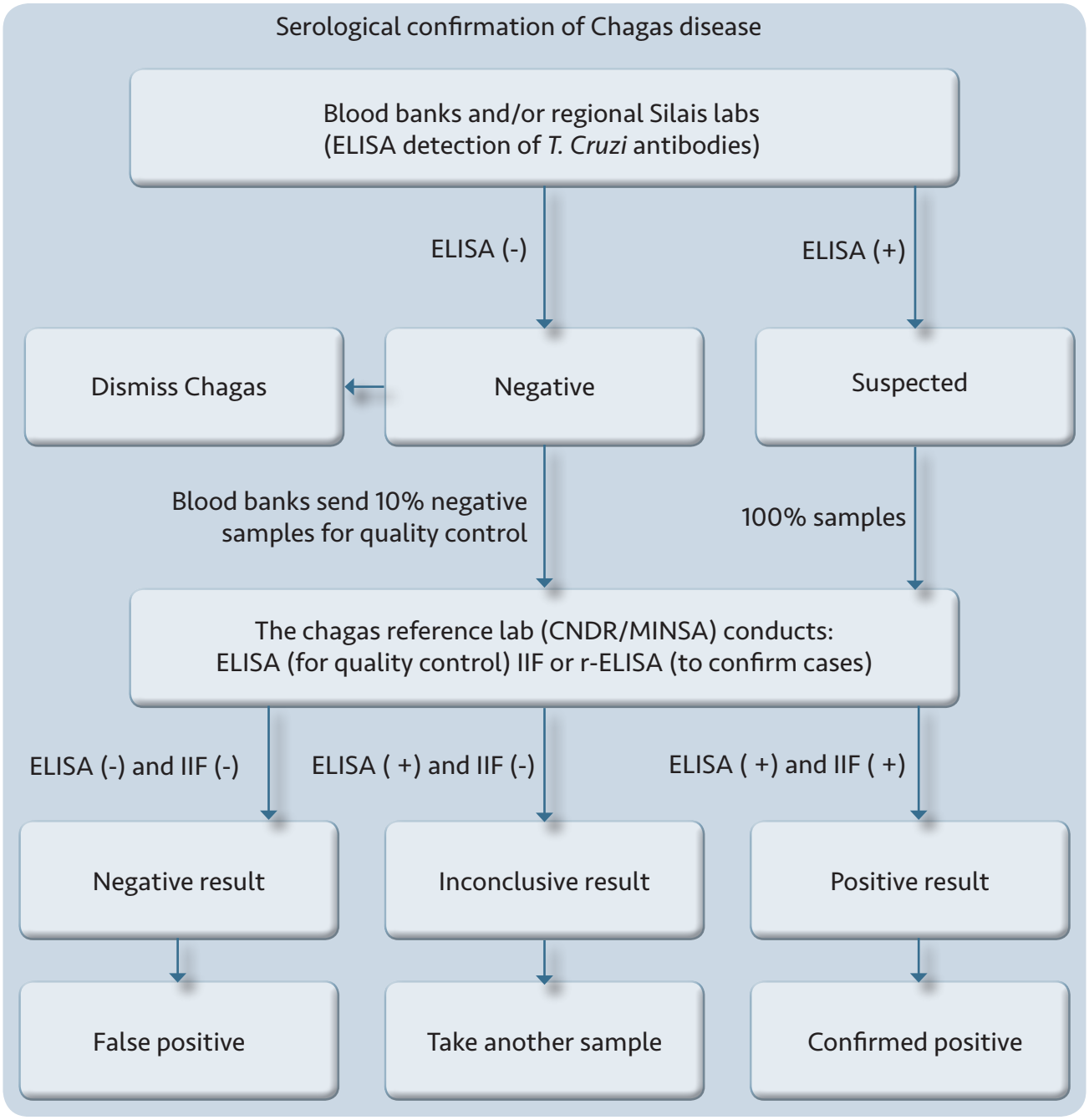
The reasons behind the decision to produce the Chagas test locally included:

- The high cost of commercial tests.
- The lower cost of the locally produced test, which facilitated decentralization and its transfer to more local levels.
- Increased sensitivity using local antigens.
- The difficulty of ensuring the timely supply of imported reagents, mainly due to long bidding processes.

All positive ELISA tests are sent to the CNDR for quality control, where the same technique is repeated and then confirmed using either an IgG assay based on recombinant antigens, with 100% sensitivity and 96% specificity, or the IIF assay.[17,18] After t year 2000, hospitals in ten SILAIS adopted the Chagas kit for the serological detection of the *T. cruzi* parasite in donated blood, as legally established in the country's transfusion safety and hemotherapy law.

[a] Interview with Dr. Alberto Montoya, current Director of Parasitology at the CNDR in Managua, Nicaragua.

FIGURE 5. **Diagnostics algorithm for serological confirmation of Chagas disease**



The process of taking the sample, sending it, and receiving the result takes four to seven days in regional laboratories and ten to 15 days in the CNDR, depending on the priority given to sending the samples at the local level. Confirmation of a positive result can take up to three weeks. Between 2002 and 2006, the CNDR serologically analyzed 4,911 samples for quality control of Chagas testing; 4% of the cases tested positive.

Rapid tests

Nicaragua acquires about 150 to 200 CHEMBIO tests annually, which cost approximately US$1.60 each. They are used only in the Nueva Segovia, Madriz, and Matagalpa SILAIS for blood screening, investigating suspected cases, and helping to evaluate other available tests. These tests are then confirmed through ELISA and IIF in the CNDR.

The Nicaraguan health system considers the increased use of rapid tests an important priority to ensure quick interventions and the control of epidemic foci in Chagas-positive communities.[b]

Current control methods

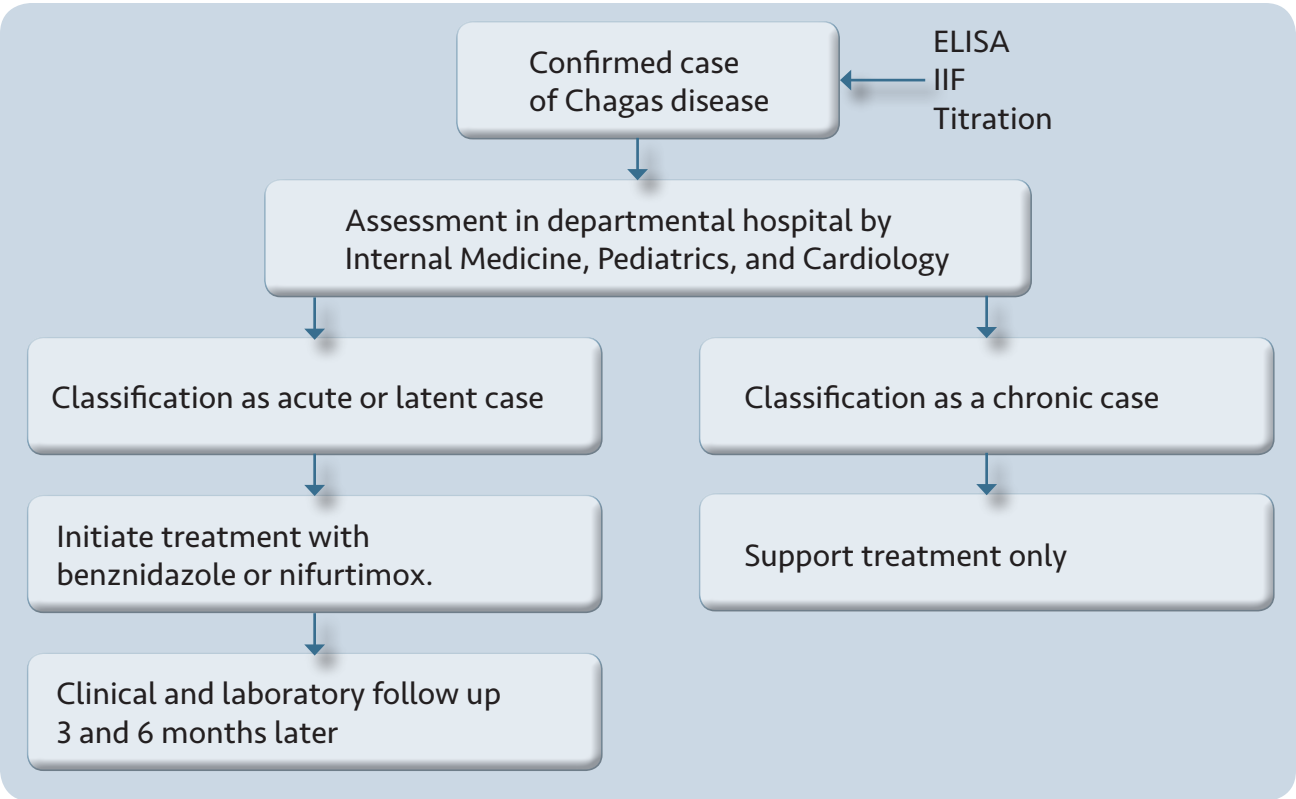
Treatment

Treating Chagas disease is more efficacious during the acute phase. Treatment is recommended for people of all ages with acute infection, including cases of congenital infection and for people with suppressed immune systems. It is also recommended for children with chronic infection. Adults with chronic infection may also benefit from treatment. Benznidazole and nifurtimox are the only drugs with proven efficacy against Chagas disease. Both are known to reduce symptom severity and shorten the clinical course and duration of detectable parasitemia. Parasitological cure is thought to occur in 60% to 85% of patients in the acute phase and in more than 90% of congenitally infected infants treated in the first year of life. Nifurtimox and benznidazole do not work well for chronic patients as they are largely ineffective against parasites in the bloodstream at this clinical stage.[19]

In Nicaragua, Chagas disease has mainly been treated with benznidazole in 100-mg doses. The country initially obtained this drug in 2001 with funds donated for the treatment of acute cases detected in the 1999 serological survey. Infected people detected in previous years were clinically assessed, and etiological treatment and follow-up were provided using this medicine. Those treated include children under age 15 detected in the survey of schoolchildren, people detected through the serological samples, and acute cases detected in the malaria thick smear quality control.

The epidemiological surveillance system and the Vector-Transmitted Disease Program record each confirmed case. This confirmation initiates treatment (either nifurtimox or benznidazole), and the start of outbreak control activities, including

FIGURE 6. **Treatment algorithm**



[b] ibid

the investigation of contacts, the search for vectors, education activities, and selective vector control measures (spraying in and around the house with a chemical insecticide betacyfluthrin at recommended doses).

More recently, Nicaragua obtained nifurtimox, which is currently being used to treat acute cases previously classified and assessed by a clinical team. This involves two doses of 8 to 10 mg/kg per day for 60 to 90 days. It is a less expensive product, but has more adverse reactions. Initiating the treatment with either medicine requires diagnostic confirmation from the CNDR and a specialized medical assessment from the departmental hospital. The national program requests treatment and health personnel at the nearest health post administer it.. Despite the existence of these two alternatives, treatment for Chagas disease is not consistently available.

Vector control

Following the national triatomine survey, MINSA launched a project to eliminate *Rhodnius prolixus*. The program has been a great success, surpassing its original goal of elimination to include eradicating the insect through two cycles of chemical spraying in 142 infested communities. MINSA reported that no communities were found positive in 2007.[4]

MINSA has also made progress in controlling *Triatoma dimidiata* in infested communities where CNDR confirmed acute cases. This involves selective interventions using recommended doses of a chemical insecticide in and around suspected households as well as educational and promotional activities.

Education

Education produces important behavioral changes that reduce the risk of contracting Chagas disease. For example, in the Madriz Urban and Rural Housing Institute project, education about animal husbandry, wood storage, and house construction and expansion helps prevent re-infestation of homes. Another community-level promotion and education campaign implemented by MINSA, in parallel with intensive anti-vector spraying, involved producing, printing, and distributing educational and promotional materials (leaflets, posters, calendars, laminated posters, and booklets), and training community health promoters to recognize vectors and symptoms of the illness in areas with the highest infestation rates.[4]

Role of hospitals, health centers, health posts, and volunteers

Hospitals diagnose patients and manage inpatient and outpatient cases.

Health centers diagnose and manage outpatient cases, follow up on positive cases and epidemic focus controls, implement vector-control activities through the Vector-Borne Disease Program, and educate the population.

Health posts identify and refer outpatient cases and educate the population.

Health volunteers refer suspected cases and educate the population.

Surveillance system

Chagas disease requires immediate notification in Nicaragua and is one of the pathologies included in the national surveillance system, which has a notification network consisting of MINSA's health units, laboratories, private clinics, and community promoters. It is based around the community or local health post, with health volunteers or personnel reporting cases at the municipal level. Information is then consolidated, sent to the SILAIS, and passed to the central level. In reality, however, at the health unit and community levels, surveillance of Chagas disease is less consistent than the surveillance of other diseases. Doctors tend to not consider Chagas as a possible diagnosis for febrile cases. In contrast, more systematic notification of Chagas disease occurs in the SILAIS of Matagalpa, Madriz, and Nueva Segovia, where a specific project strengthened surveillance. The surveillance system defines a suspected case of Chagas disease as any case that complies with the following clinical definitions.[20]

Acute phase. Main signs and symptoms include general discomfort, high fever with shivering, migraine, painless inflammation of only one eye (Romaña's sign), weight loss, fatigue, and adenopathy. These appear one to two weeks after the triatomine bites and persist for four to eight weeks.

Latent phase. The latent phase follows the acute phase and is characterized by the absence of symptoms. It can last for many years or indefinitely. If serological tests (ELISA and IIF) turn out to be positive, the infection can be detected by xenodiagnosis in 20% to 60% of cases.

Chronic phase. Characterized by complications that reflect severe cardiac and digestive damage and irreversible neurological damage. This phase appears ten to 20 years after the illness is contracted.

All cases with laboratory confirmation are defined as confirmed cases.

Funding mechanisms

There is no defined institutional funding for the Chagas program. As a result, research and control actions have been sporadic rather than ongoing and have relied on the support of foreign cooperation. Both national entomological and serological surveys and specific control interventions receive PAHO cooperation funds.

At the SILAIS level, the Nicaraguan government only earmarks a small percentage of the funds for fighting epidemics to Chagas disease.[c]

Nongovernmental agencies and other groups

Médecins sans Frontières—Belgium

Joint design, coordination, and implementation of the MINSA/MSF-B Chagas disease project in three municipalities corresponding to the Matagalpa SILAIS (Esquipulas, Ciudad Darío, and Matagalpa) and the Totogalpa municipality in the Madriz SILAIS. MSF-B also supported the national program's promotion and education campaign on Chagas disease, and strengthened the program's management capacity by distributing forms for recording case follow-up and control actions.

Urban and Rural Housing Institute

A project to improve housing in an area with endemic Chagas disease in the municipality of Totogalpa in the Madriz SILAIS.

Government of Taiwan

Production and distribution of educational and promotional materials on parasitosis (including leaflets, posters, calendars, laminated posters and booklets). The Government of Taiwan also supports strengthening the laboratory network for blood bank activities.

The Pan American Health Organization

Provides technical and financial assistance for training and evaluating control strategies.

The Japanese International Cooperation Agency

Supports regional research, training, and exchange of experiences.

[c] Interview with Dr. Francisco Acevedo, Director of Applied Epidemiology, MINSA.

Regional examples of control strategies

Madriz

A housing improvement project implemented in the municipality of Totogalpa and strengthened community-level epidemiological and entomological surveillance resulted in the improved physical infrastructure of nearly 600 rural houses in the Cuje and Cayantú sectors. The houses had been highly infested with *Rhodnius prolixus* and *Triatoma dimidiata*.

The follow-up system for determining the efficacy of treating acute cases is also being strengthened. The MSF-B project trained Madriz SILAIS health personnel on the clinical approach for patients with Chagas disease (diagnosis, treatment, and follow-up). It also included community-level awareness-raising campaigns as part of its extensive educational efforts to ensure the population knew about the illness, how it is transmitted, and how to prevent it.

PAHO/WHO funded and provided technical support to a communication for behavioral impact (COMBI) plan for Chagas disease in Totogalpa municipality's Cujilica community. MSF-B identified this community because it had one of the highest seroprevalence rates. The plan accounts for local cultural factors, which is especially relevant in some of Totogalpa's communities, like San José de Cusmapa which have indigenous origins and crucial for any project hoping to produce behavioral changes. The plan has not yet been implemented due to staff changes in the SILAIS headquarters and the target municipality.

"One of the best results in terms of Chagas disease control has been the housing improvement project.... The COMBI strategy directly involves the community in solving the problem of Chagas disease, taking cultural factors into account..." Dr. Doribel Tercero, Epidemiologist at the Madriz SILAIS.

Matagalpa

MINSA and MSF-B implemented a project in Esquipulas, Ciudad Darío, and Matagalpa municipalities, including training activities for health personnel and members of the community on recognizing the vector and the illness, investigating cases, strengthening the diagnostic network, and following up with patients. The follow-up system is being strengthened to determine the efficacy of treating acute cases.

Nueva Segovia

As in Matagalpa and Madriz, the follow-up system is being strengthened to determine the efficacy of treating acute cases. This includes a hospital multidisciplinary team indicating the right therapy, while a network of health volunteers and health post personnel administer treatments in the community and provide appropriate follow-up.

"We have made a lot of progress in appropriate assessment by hospital doctors and the follow-up in the community by the health volunteers and health post personnel in order to guarantee the patients are cured...." Juan Vega, head of VTD at the Nueva Segovia SILAIS.

Unmet clinical needs

The following information largely comes from the individual interviews and group discussions described in the methodology section. It is limited to what health care personnel considered applicable to Chagas disease.

Primary health care

Diagnosis is the access point to medical care without which Chagas patients cannot receive comprehensive medication and health program directors cannot develop appropriate public health interventions. The Nicaraguan Chagas Disease Control Program has at least two clear unmet needs on this level: 1) Rapid tests for acute-phase diagnosis, so that treatment can be started as early as possible, particularly for children, and 2) systematic testing for all pregnant women and newborns, not just those living in high prevalence areas.

Rapid tests

Rapid tests are only available in three of Nicaragua's departments. Developing cheaper, easy-to-use rapid tests for Chagas disease would provide health posts and health centers with diagnostic tools, encourage the search for cases, and enhance epidemiological surveillance, providing quicker results and strengthening field work.

There is an urgent need for a high quality, easy-to-use rapid test to identify Chagas disease during its acute stage. Although the ELISA test works better for chronic cases, treatment is more effective the earlier it is given.

"The rapid tests have excellent antigen detection in the acute stage and also work for the chronic stage. We think they should be used to first carry out a rapid test and then provide treatment." Dr. Alberto Montoya, Director of Parasitology, CNDR.

Systematic testing for all pregnant women and newborns

Mother-to-child vertical transmission is the second most important means of infection. Pregnant women in the latent or chronic stages are asymptomatic and unaware of their infection. The study of pregnant women carried out in the departments of Madriz, Nueva Segovia, and Matagalpa in 2005 revealed high seroprevalence rates ranging from 15.6% to 25% (see section on prevalence studie"). In addition, four children of the ten pregnant women who tested positive in the Madriz SILAIS had congenital Chagas disease.

Pregnant women and newborns provide an excellent opportunity for Chagas surveillance and intervention impact measurement at both the primary health center and hospital levels. Routine care includes a series of diagnostics for pregnant women and newborns that represent a window of opportunity for introducing systematic Chagas screening in a country with an endemic profile.

Testing for other neglected tropical diseases

Developing a rapid test should improve the capacity to develop and administer other rapid tests, such as leptospirosis or dengue. A multiplex diagnostic test would help to address other neglected diseases endemic in Nicaragua, such as leishmaniasis and malaria.

Hospital care

Chronic patients

Although anti-parasitic treatment is not very effective for chronic patients, identifying Chagas as the underlying cause of the chronic ailment contributes greatly to treatment. Once infection is confirmed, health care providers can test cardiac and liver functions for signs of the common consequences of chronic Chagas infection. This evaluation allows health care providers to adjust treatment to the patient's condition.

Blood examination

Because Chagas disease is endemic in Nicaragua, blood screening tests exist, but limited funding and/or reagents still stymie the breadth of their effectiveness. Many Chagas ELISA kits are still needed for blood bank screening and algorithm confirmation. To temporarily resolve this shortage, the Red Cross is now responsible for the blood banks and for screening for the five pathogens, including T. cruzi.

National administration and the CNDR

At the central administrative level, program directors and technical staff concur about the great need to study cases involving high fever to identify pathogens that generate high morbidity and significantly contribute to infant and overall mortality. More accurate data would provide a firmer basis for launching programs and strengthening disease surveillance and awareness.

User requirements

Sensitivity and specificity

Nicaraguan health authorities want a rapid test with high sensitivity and specificity to detect patients in the acute stage of the disease. If an adequate supply of the rapid tests cannot be ensured, then use of the local ELISA Chagas test should be considered as an alternative. This local test has been validated, with 100% sensibility and 98% specificity.[17,18]

Improving the features of the locally produced test

With appropriate equipment and technical staff well trained in diagnostic techniques, the CNDR in Managua is currently the only national institution capable of serological testing and confirming Chagas disease The CNDR needs to increase diagnostic capabilities throughout Nicaragua's laboratory network.

The standardized CNDR ELISA test for detecting *T. cruzi* antibodies should be simplified. Adapting it into a test strip would make the test easier to read, and make it available to most laboratories, even local-level health posts. For example, the test could be converted into an easy-to-read color strip that changes with antigen reactions, avoiding the need to send samples to the ELISA reading device in the CNDR.

A multiplex test is also needed to simultaneously test for several fever-related diseases and should have high sensitivity and specificity. Being a new test, a review of protocols, algorithms, and quality control would be required. The introduction of such a test should be accompanied by several other processes, such as providing staff with appropriate training, adjusting and implementing central-level quality control, strengthening the information system, and guaranteeing treatment for the diseases being tested.

Affordability and sustainability

The main problem with incorporating a multiplex test is the cost, particularly considering the current Nicaraguan health budget, which is the lowest in the Central American region. In this respect, producing ELISA kits is still a good idea, as they are estimated to be less expensive, although no thorough cost analysis has yet been carried out.

Several other considerations should also be made in relation to a rapid test. These include producing packets containing fewer determinations, which would allow health units to carry out the tests with just a few patients. Waiting for more patients forces health personnel to waste tests that have already been opened. Improving the Chagas kits could also involve automated production and antigen purification, although this may require greater investment in laboratories. Chagas

disease diagnostic kits are currently produced manually. Automating kit production could reduce production time and costs, increasing availability and access. In this respect, it would be useful to conduct a thorough cost analysis.

Barriers and Facilitating Factors

Barriers

Costly investment

While it is possible to automate the production of ELISA tests, this may require an investment that is beyond the reach of the Nicaraguan government and probably most laboratories in Central America. Therefore, a regional strategy may be needed to secure funding to further develop diagnostic tools for detecting Chagas infection.

Information system

Testing for *T. cruzi* in blood banks, health centers, and hospitals, and during specific serum studies, generates a large amount of data that is not currently integrated. This contributes to the fragmented nature of the laboratory network's information system, which is characterized by weak monitoring and supervision and the delayed return of results to patients.

Facilitating factors

Network of community health volunteers

As MSF-B demonstrated, community involvement is a key to controlling both the transmission of the vector and the parasite.[9] One of Nicaragua's strengths in terms of health promotion and prevention is the existence of an extensive network of community health volunteers consisting of brigadistas (health volunteers), traditional midwives, and community leaders.

If an appropriate test is available at the community level, a considerable number of very poor women living in remote areas could have access to it. In another similar experience with a vector-borne disease at the primary health care level, community brigadistas and volunteer collaborators used rapid tests to manage malaria.

CNDR monitoring

The CNDR has more than 20 years of experience supporting and supervising the laboratory network across the country, as well as day-to-day epidemiological surveillance and rapid responses to outbreaks, and more than 100 differentiated diagnostics. Two regional laboratories perform a list of specific confirmatory tests to support clinical work and epidemiological surveillance. Decentralizing the ELISA test to hospitals and main health centers requires the CNDR to plan and train health care workers in these facilities.

The CNDR also collaborates with several international research institutions working to combat tropical diseases. Its strengths could be of great value to ensuring calibration and gold standard measurement as well as to monitoring progress in the implementation and acceptance of new point-of-care diagnostic tests.

Global strategies

In the framework of the Millennium Development Goals, two important strategies are relevant for addressing Chagas disease: its inclusion in the list of neglected tropical diseases and in the Drugs for Neglected Diseases Initiative. Both of these strategies provide opportunities for more funding and research in this field. Additionally, Nicaragua must comply with international and regional commitments toward the elimination of Chagas disease by 2010.[21] Nicaragua is scheduled to start a Chagas vector elimination project funded by the JICA, which comprises several actions that would synergize with what has been accomplished in

neighboring countries, including strengthening epidemiological surveillance and information systems and promoting behavioral changes towards disease prevention and vector-control activities.

Conclusions

Despite documentation in Nicaragua for almost half a century, Chagas disease is still an endemic, highly un-registered illness. As it goes undetected, the disease continues to cause high mortality among the adult population and is a problem for maternal and child health. Most information about the incidence and prevalence of Chagas disease in Nicaragua comes from studies conducted in the last ten years, including one national study. Although these studies have produced varying results, they all reveal higher prevalence in Matagalpa, Madriz, and Nueva Segovia, followed by Chontales and Managua.

The Chagas program faces a number of very important challenges. First, it has no national database to classify patients and monitor follow up on treatment, and there is no regular institutional funding for vector control and active case detection. In addition, human resources are insufficient, and those that do work on Chagas disease also work in many other areas and lack sensitivity to and knowledge about the particular approach to this problem. The control actions have been more directed at areas with an infestation of Rhodnius prolixus, although this has not been done systematically. Meanwhile, Triatoma dimidiata is widely dispersed across the country.

Several lessons from the MSF-B's Chagas disease intervention should be considered when developing a national strategic approach. At the intervention's start, health care personnel and community volunteers had little accurate knowledge on Chagas disease and also lacked methods and tools for identifying the disease. Although MSF-B deliberately focused on certain communities believed to be hardest hit by Chagas disease, the findings of the national seroprevalence study and the MSF-B study used to identify these communities revealed differences in their findings. These variations could be accounted for through different methodologies or other unexplored events and demonstrate the need for reliable information.

Important advances have been made in the serological diagnosis of this disease, which is now included in blood bank screening. The diagnosis of acute cases, however, still needs to grow so that timely and more effective treatments can be administered. The National Control Program must increase the use of rapid tests, especially in remote communities with high vector prevalence and a history of positive cases. Developing rapid tests in Nicaragua would help to ensure sustainability. These tests could be relatively inexpensive because of locally available reagents.. Adequate monitoring and evaluation are also necessary.

One important finding revealed by the field visits and interviews for this case study is that clinicians and program administrators often mentioned the importance of identifying Chagas disease as a cause of fever. This finding is very promising in terms of future actions, demonstrating that health personnel are concerned about and aware of the problem of Chagas disease

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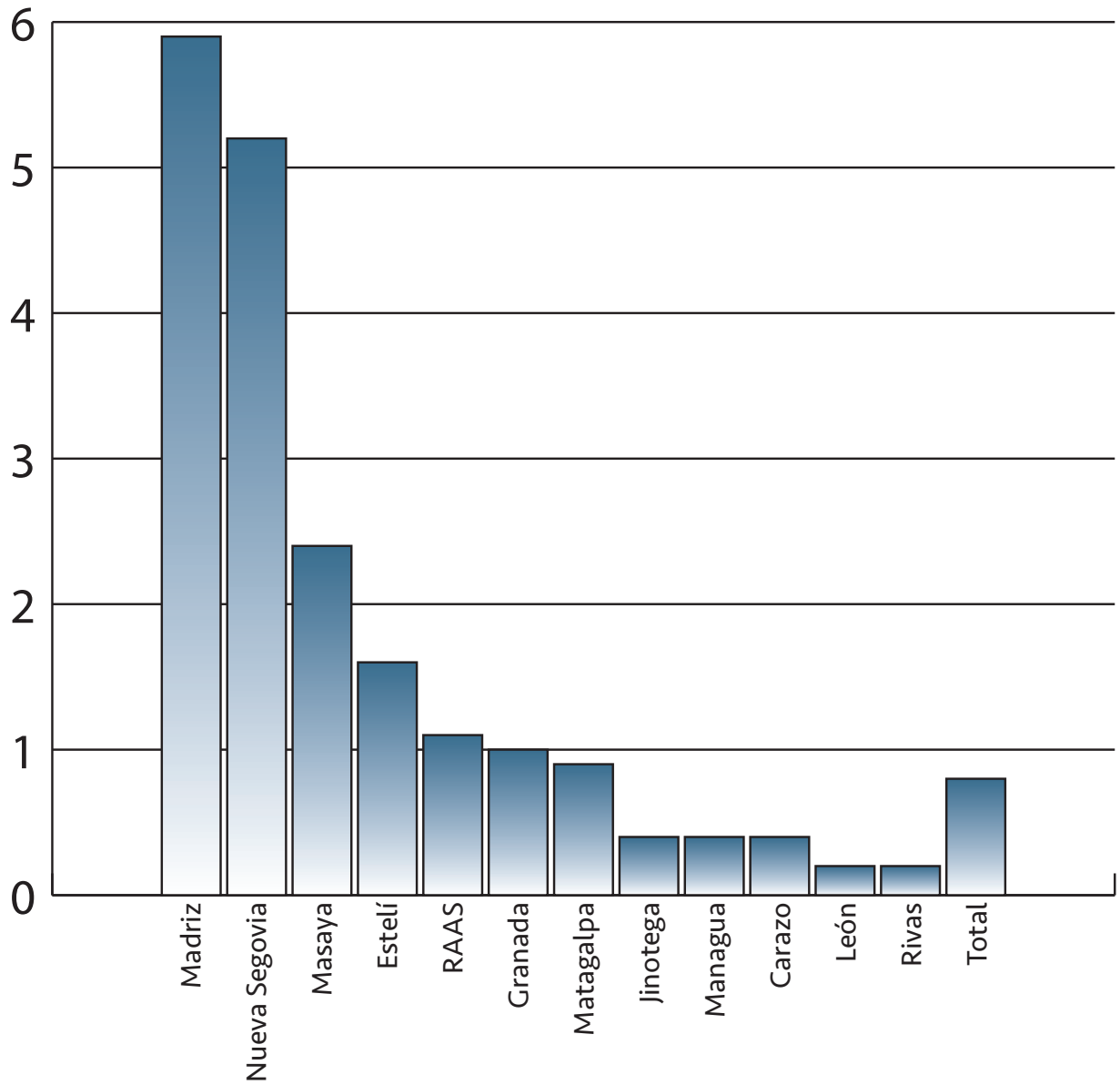
Appendix

FIGURE A-1: **Seroprevalance of *T. cruzi* among blood donors in Nicaragua, 1992–1993.**



Source: MINSA Reports. Parasitology Division at the CNDR.

TABLE A-1: **Blood bank screening for *Trypanosoma cruzi* Nicaragua, 1999-2007.**

Year	Donors	Samples screened	Positive samples	Positivity (%)
1999	47,606	32,078	112	0.3
2000	50,581	37,515	122	0.3
2001	52,764	46,250	276	0.6
2002	50,994	42,205	185	0.4
2003	54,078	44,041	277	0.6
2004	49,764	49,764	228	0.4
2005	54,117	48,376	399	0.9
2006	48,549	48,549	430	0.9
2007	10,847	10,847	21	0.1
Total	419,300	359,625	2,050	0.57

Source: MINSA/CNDR annual blood bank reports, 1999-2007 (the report for 2007 was preliminary).

TABLE A-2: **Seroprevalence of Chagas disease among under 15s in SILAIS and municipalities where *R. prolixus* is present. Nicaragua, 2003.**

SILAIS	Municipalities	Total children sampled	# of children positive	% positive in the municipality	% positive in the
Madriz	Totogalpa	910	128	14.1%	10.8%
	Cusmapa	466	21	4.5%	
Nueva Segovia	Mozonte	132	26	19.7%	4.5%
	Ciudad Antigua	364	8	2.2%	
	Jícaro	96	1	1.0%	
	Macuelizo	188	0	0%	
Granada	Diriá	162	1	0.6%	0.6%
Masaya	Niquinohomo	977	2 (2p)	0.2%	0.2%
Carazo	San Marcos	112	0	0%	0%
TOTAL		3407	187	5.5%	5.5%

Source: Baseline study of Chagas disease among under 15s living in areas infested with R. prolixus. Nicaragua, August 2003.

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