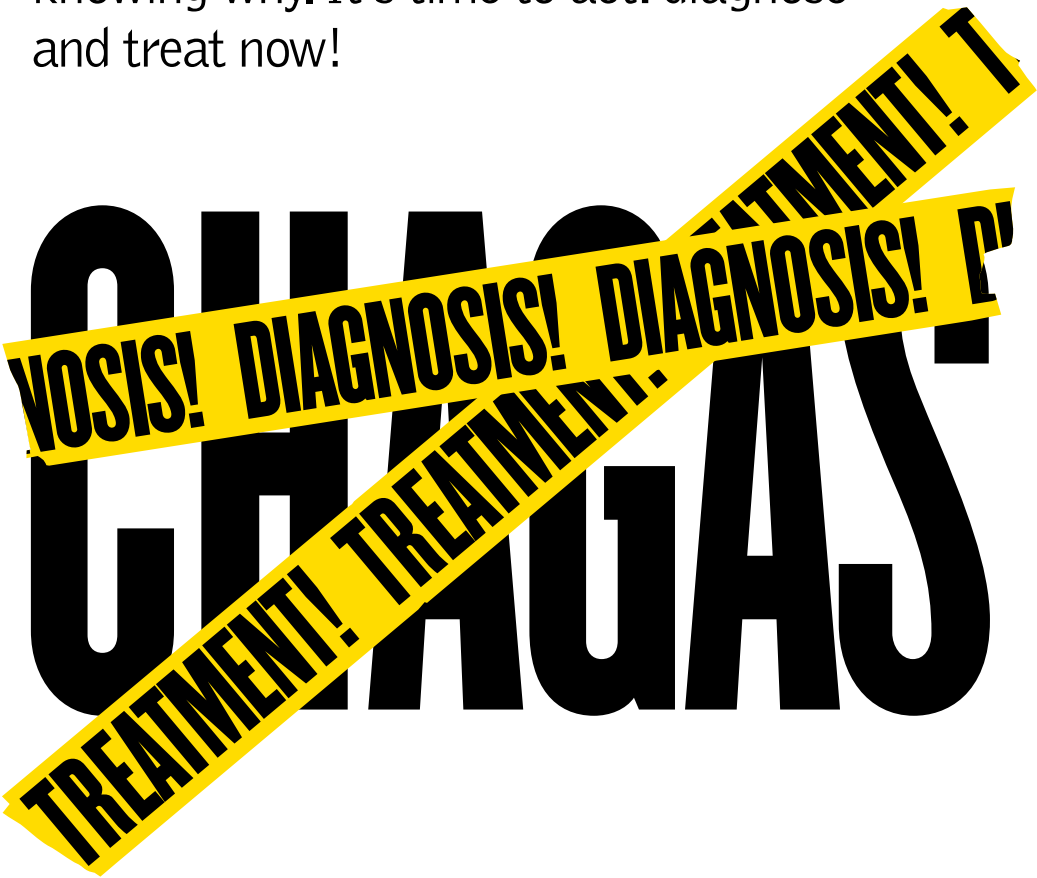
Chagas: it's time to break the silence

Millions of people are infected with Chagas disease yet they do not know. They can die in silence, without asking for help, without knowing why. It´s time to act: diagnose and treat now!



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MEDECINS SANS FRONTIERES

One hundred years of neglected patients

2009 marks the centenary of the discovery by the Brazilian doctor Carlos Chagas of the disease which bears his name. In 1909, Dr. Chagas announced to the world the existence of a new infectious disease. The previous year, he had discovered the parasite which causes it and the vector by which it is transmitted. His triple discovery is considered unique in the history of medicine.

One hundred years later, there is still a lack in the innovation of treatments and those that do exist are not available to the majority of sufferers. One hundred years later, many of those infected with Chagas disease are still unaware that they are sick. They are dying without knowing why and doing so in silence. Their voices do not reach the governments which should be responding to this public health problem, or the pharmaceutical companies which could be researching and developing new medicines. For one hundred years, Chagas disease has been a silent illness. The time has come to break the silence.

What is Chagas disease?
Chagas disease, or American human trypanosomiasis, is an infectious disease caused by the *Trypanosoma cruzi* parasite. Endemic in several Latin American countries, cases are found in rural areas, indigenous communities and the poorest suburbs from Mexico to Argentina, including the Caribbean. The disease causes 14,000 deaths each year. It is estimated that 10-15 million people suffer from the disease and 100 million more, 25 per cent of the population of Latin America, are at risk of contracting it. As a result of the increase global migration and mobility, an increasing number of cases are being reported in the United States, Europe, Australia and Japan.

How is it transmitted?
Certain insects of the *Triatominae* species, known as 'assassin bugs' or 'kissing bugs' depending on the geographical zone, transmit the parasite to humans. They live in cracks in the walls and ceilings of houses made from adobe bricks, sticks, straw, etc., and come out at night to feed on blood. When an assassin bug carrying the parasite bites a person, it deposits faeces on the skin. If the person scratches or rubs their eyes or mouth after touching the bite, the parasites can then pass into the blood stream. If an infected person is bitten by another assassin bug, the parasite infects the insect and the cycle goes on.

In many Latin American countries, prevention programmes are being developed with the aim of reducing the presence of the vector (the transmitting insect), but not all of them are as effective as they should be and they are never enough to eliminate the disease.

Chagas disease can also be transmitted through blood transfusions, from mothers to their children during pregnancy and, less frequently, through organ transplants or the ingestion of contaminated food. It is not transmitted through direct contact with infected individuals.

Diagnosis
The majority of people infected with *Trypanosoma cruzi*, the parasite which causes Chagas disease, show some sign or symptom at the time of infection. In a small number of cases acute Chagas disease causes death. For the majority, the symptoms go unnoticed and for years those infected have no further problems. It is estimated that approximately 70 per cent of these people live with the parasite without their health being affected.

Nevertheless, in the chronic phase of the disease, 30 per cent will develop problems in their heart, gastrointestinal tract and central nervous system which cause irreversible damage. Since it is impossible to predict who will develop the disease, treatment should be offered to all sufferers, with assessment of their clinical status and age.

As the disease often does not present symptoms, active detection of cases should be a priority in programmes to combat Chagas. Diagnosis currently requires confirmation through laboratory tests. In many cases, the endemic countries do not have the necessary facilities or staff available to carry out these tests. It is essential that communities living in endemic zones have access to diagnosis and can find out if they have been infected with *T. cruzi*. If not, thousands of people will die each year without knowing the cause.

Treatment

There are currently only two medicines to combat Chagas disease: benznidazole and nifurtimox. Both were developed over 35 years ago and in investigations not specifically aimed at Chagas disease. Nowadays, neither of these drugs is adapted for paediatric use and nor can they be used by pregnant women. The success rate reaches almost 100 per cent in newborns and infants. However, in older children, adolescents and adults treatment is only around 60 or 70 per cent effective and can have multiple side effects, and therefore has to be taken under medical supervision. This means having a weekly check-up with a trained healthcare worker.

Until a few years ago it was thought that the treatment was only effective in very young children and not in adults. However, recent studies demonstrate that it is possible to treat adults, even after the heart or the gastrointestinal tract are mildly affected (initial clinical forms of the chronic phase). As the side effects of the treatment are more common in older patients, doctors have been reluctant to administer the medicine out of fear of the consequences. We now know that the adverse effects are manageable.

Before starting treatment for Chagas disease, it is necessary to check that the parasite has not seriously affected the heart or other vital organs. In some very advanced cases, there is no evidence as yet that the treatment is beneficial because *T. cruzi* has already caused serious vital organ damage. On the other hand, adults aged 50 and above - probably infected by the parasite in their childhood or adolescence - who have not developed any pathology are most likely to fall within the 70 per cent who will not suffer organ damage. In such cases, and bearing in mind the toxicity of the treatment, the risks and the benefits for each individual have to be assessed before starting treatment.

Barriers to access

Millions of sufferers, especially in rural areas, have neither the opportunity to find out that they are infected nor the possibility of being treated. This is due to the numerous obstacles which could be avoided with greater political will and greater investment in research and development:

— **Confirming diagnosis** of Chagas disease requires laboratory tests, which means that the patient cannot get the result on the first visit to a health centre.

— As evidence regarding the effectiveness of **treatment in adults** is very recent, some doctors remain unconvinced as to the viability of treating adults and patients in the chronic phase with existing medicines.

— The possible **undesirable effects** are also an obstacle. Many doctors and nurses are reticent about beginning treatment for fear of causing unpleasant side effects.

— **Vector control is not integrated** with treatment of patients. Combined with ineffective efforts to combat the assassin bugs, this has caused the insect and the disease to reappear and patients to become re-infected.

— With the methods currently available, **confirming the cure** of adolescents and adults can take years, making the research and development of new medicines difficult, and dissuading many sufferers from starting treatment.

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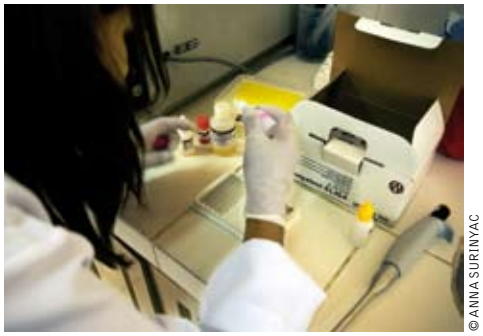

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“Many people think that nobody gets sick or dies from Chagas and fortunately, in many cases, that’s true. But in many other cases they get very sick, mostly with heart problems, but also intestinal, and they can die. And these are very sensitive cases, which hit communities hard because it is young people, of working age, with families who die.”

Víctor Conde, field doctor with the MSF project in Cochabamba

Alejandra Barón lives with her husband and two sons, aged 5 and 2, in one of the poorest districts of Cochabamba in Bolivia. When she was pregnant with her second son she was told she had Chagas. She took her oldest son Kevin to the health centre and he also tested positive. He was the first to be started on medication. “He remembered the pills himself and asked me for the treatment,” explains his mother. Alejandra had to wait to give birth and to finish breastfeeding her baby before the two could start treatment. She had some difficulties giving the treatment to her young daughter as it was hard to dissolve the tablets.

“I knew nothing about Chagas disease until I got pregnant and they told me. I asked, “What’s that?” and they told me that it came from the assassin bug and I remembered that there were many assassin bugs when I lived with my mother. That must be it, I don’t see any assassin bugs here, only in my village,” explains Alejandra and she adds: “We poor people who come from villages in the country are the ones who get Chagas. Yes, I felt like going from house to house and explaining it to them, especially in the countryside.”

Laura (not her real name) is 39 and lives in the city of Cochabamba. She has suffered a great deal with Chagas disease and, although she tells her story so that others don’t have to go through what she did, she doesn’t want to speak in front of the camera. “I found out seven years ago. I couldn’t even walk a block without feeling tired. I went to the doctor and he told me that it was too late to start treatment, that I would have to get a pacemaker. I ignored it and then I went to MSF, where they told me the same. I think I became infected 19 years ago and I only found out seven years ago!”

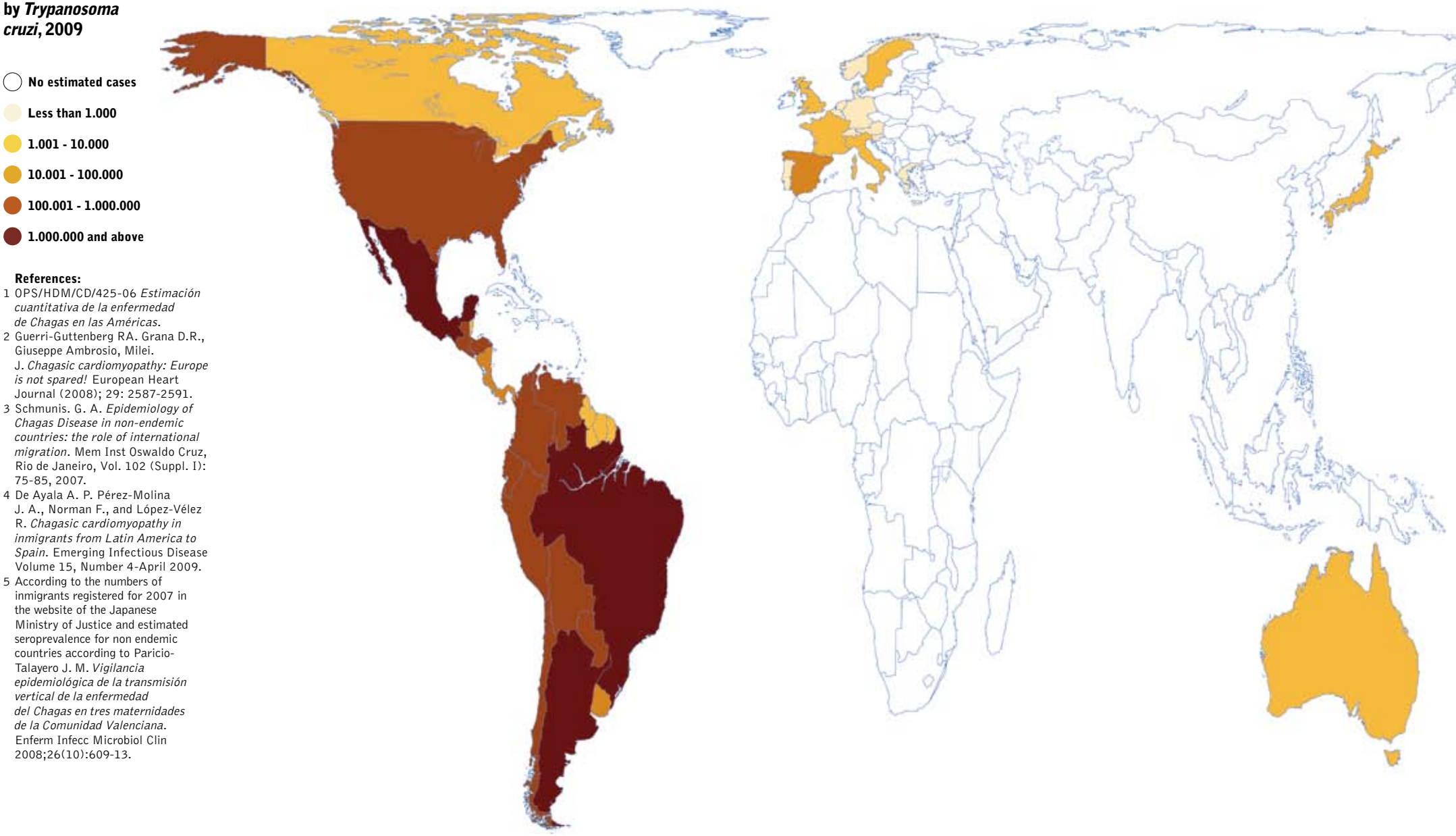
When they told her that she needed a pacemaker, Laura’s husband insisted on taking out a loan to pay for it. But Laura refused. She didn’t want to owe money and was very afraid about the surgery, despite the fact that it could save her life. MSF arranged for an American organization to insert the pacemaker for free, but even then she didn’t want it. Her cousin and her uncle died, probably from Chagas disease, after they had had pacemakers inserted.

“It hurts when you find out and they tell you there’s no treatment. I had been married for four years then. I have tried to work and I have managed to get this house, I had to do it for my daughters,” explains Laura. She adds: “My family has suffered, my mother, my brothers, because they said that my heart was very inflamed. My youngest daughter would ask me why I was crying. Later I made myself become calmer because I didn’t want my family to suffer”.

A few months ago, Gualberto Paniagua, 33, was diagnosed with Chagas and he is now taking medication for the disease. “Up until now I haven’t felt anything, so I could have said ‘why should I take treatment?’ But in the future I could have problems, so if I have the chance I have to try it. If there is a chance, I have to take advantage of it and get treatment because you never know. I’ve seen family members, who were healthy, die. If there is a treatment, you should take it.”

Gualberto is from the rural part of Cochabamba and believes that he became infected when he lived in his parents’ house because there were a lot of assassin bugs. “I’m 33. Why didn’t they treat me when I was 15?” he asks. “In my town several people have died, adults and young people. It was said that it was from Chagas, but we never knew where the disease came from. We now know that the assassin bug is the carrier.” Gualberto is married and has two daughters. His whole family has taken the test for Chagas disease. He and his older daughter are the only ones infected. His daughter will start treatment in the coming months.

Estimated global population infected by *Trypanosoma cruzi*, 2009



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Research and Development: 100 years of procrastination

A recent G-Finder study reveals that less than 0.5 per cent of all worldwide Research and Development (R&D) into neglected diseases in 2007 was aimed at Chagas disease.

With the limited resources currently available to treat Chagas disease, medical teams have to deal with many shortfalls and sometimes they don't have any treatment options. New diagnostic tests, better medicines and cure tests urgently need to be developed to deal with this illness.

Better diagnostic tests

Currently, MSF uses a rapid diagnostic test to detect cases. Following the recommendations of the World Health Organization (WHO), all positive cases are confirmed with two conventional laboratory serological assays. If there is any discrepancy between the two tests, a third laboratory test must be used to obtain a reliable result.

In contexts with limited resources, such as rural areas in Bolivia, where the incidence of the disease is high, the ideal would be to have a highly sensitive and highly specific rapid diagnostic test which would reveal whether the patient was infected or not in a short space of time and would not require specialized laboratories. If a single test is not possible, a combination of two rapid tests could be another option.

More effective and less toxic treatments

There are only two medicines for treating Chagas disease (benznidazole and nifurtimox). The possible side effects from the treatment mean that some patients are unable to complete it and that it is impossible for sufferers to take it without supervision by trained healthcare workers. This all results in restricted access to the treatment, above all in rural areas or where there are no specialised human resources. The problem is particularly serious in adult patients and at the moment, there are still no paediatric versions of the treatment.

The Drugs for Neglected Diseases initiative (DNDi), of which MSF is one of the founding members, is working on a paediatric formula of benznidazole which will probably be available at the end of 2009. DNDi is also working on possible alternative treatments such as posaconazole. Regretfully, these drugs are a long way off from being available in the market, and at low cost, and their effectiveness is still far from being demonstrated.

There is an urgent need to develop new less toxic medicines which require a shorter course of treatment, are effective in the acute and chronic phases of the disease in both adults and children, and are safe for pregnant women.

Testing for cure

The current serological methods can take decades to confirm the effectiveness of treatment in adolescents and adults. PCR (polymerase chain reaction) techniques, based on genetic information, have a low sensitivity and specificity for parasites, and they are only available in some research centres. Development of rapid treatment tests which allow for the effectiveness of treatment to be measured and cure to be confirmed in the first two years after treatment for all age groups is essential.

Better prevention strategies

Treatment for Chagas disease does not mean that a person cannot become infected again by a bite from an assassin bug. Vector control strategies, which are fundamental to limit the spread of the disease, depend on detecting the vector and spraying with insecticides. Nevertheless, the assassin bugs have now been found to be resistant to certain products. In addition, to eliminate the insect, spraying must be continuous and housing must be improved.

Furthermore, greater effort must be made to ensure the quality of blood banks to avoid contamination from transfusions or transplants, and to continue to implement prenatal detection control strategies for pregnant women to avoid transmission from mother to child.

Helping governments to find alternative sources of R&D funding for Chagas disease

The lack of commercial incentives has relegated Chagas disease to be forgotten. In 2007, only $10.1 million dollars were spent on R&D for this disease. Less than half of this was spent on treatment, vaccines, diagnostic tools and vector control products[1]. In 2006 the WHO Commission for Intellectual Property Rights, Innovation and Health (CIPIH) recognised the failure of current incentives and financing mechanisms for neglected diseases. There is a need to identify new incentives for R&D, including those which de-link the costs of R&D and the final price of health products to obtain better and new diagnostics and treatments.

1. *Neglected diseases Research & Development: how much are we really spending?* by Mary Moran, Javier Guzman, Anne-Laure Ropars, Alina McDonald, Nicole Jameson, Brenda Omune, Sam Ryan, Lindsey Wu, published by *PLoS Medicine*, February 2009, Volume 6, Number 2

MSF experience in the field


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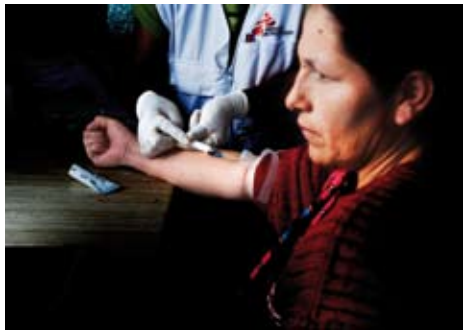
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In 1999, Médecins Sans Frontières (MSF) set up its first diagnosis and treatment project for sufferers of Chagas disease in Yoro, Honduras. Since then, the organization has developed several programmes in Nicaragua, Guatemala and Bolivia.

In 2002, MSF began its first Chagas disease project in Bolivia, the country with the highest incidence of the disease in the world. For four years, the organization worked in the rural area of Entre Ríos, in the province of O'Connor, in the Tarija region, treating patients up to the age of 15. Following this, MSF increased treatment up to the age of 18 in a new project, this time in suburban zones in two districts of Sucre, also in Bolivia.

Based on the experience acquired in their projects and the results of recent studies into the effectiveness of the treatment in adults, MSF is now working in three suburban districts in the city of Cochabamba. The activities are being carried out in collaboration with the Bolivian Ministry of Health in an integrated way in five primary care centres, where children and adults up to the age of 50 are treated and diagnosed. Using the same approach, the organization is currently setting up a new project in the rural zone of Cochabamba region, where it is working to involve the communities in all aspects of the strategy (prevention, diagnosis and treatment), in an area where the vector is much more prevalent.

At the end of 2008, MSF had tested over 60,000 people for Chagas disease and treated 3,100 patients, of whom around 2,800 successfully completed the treatment. This shows that, although current resources are not ideal, the diagnosis and treatment of Chagas disease is viable in environments with limited resources and remote areas if various coordinated activities are carried out:

— **Informing and educating the population** about possible means of transmission, symptoms, treatment and the basic hygiene and prevention measures for the disease. This includes educating local authorities, health workers, community leaders and the families of sufferers.

— **Integrating vector control with diagnosis and treatment programmes** to avoid new infections. Houses where sick people are living must be checked for the presence of the vector and fumigated when necessary, but the importance of prevention should not mean that treatment is relegated to second place.

— **Actively detecting and diagnosing infection.** The lack of symptoms and the problem of access to diagnosis for a large section of the at-risk population continue to be a serious problem. It is for this reason that MSF recommends the detection of Chagas in endemic areas; the availability of rapid tests makes this much easier.

— **Treating the sick.** The treatment of Chagas disease has to be supervised weekly by qualified healthcare workers, as it can cause side effects. With good supervision, these effects are manageable and a high percentage of patients complete the treatment, with a low incidence of adverse effects requiring hospitalisation (0.07 per cent in MSF projects) and no deaths.

— **Training healthcare workers** in the diagnosis, treatment and supervision of patients.

There is a need for doctors for controlling serious side effects, nurses for early detection, monitoring and adherence to treatment, and laboratory technicians for the tests to confirm infection.

— **Ensuring supply and logistics** to attend to rural communities (the most affected). For this, it is of the utmost importance to have a strong supply chain of medicines and laboratory reagents, as well as the capacity to store serological samples in optimal refrigeration conditions for future treatment tests.

In addition to these six components, the motivation and commitment of the healthcare workers and the patients themselves in tackling the disease, as well as government support, are essential if the programme is to be a success.

The time has come to act!

Historically, Chagas disease programmes have focused on prevention of the disease and on vector control. Now, knowing that the majority of those infected by the parasite can be treated, this focus, which excluded treatment, is no longer acceptable. In its ten years of experience in the field, MSF has proved that the diagnosis and treatment of Chagas disease, even in remote rural environments, is viable, necessary and ethically beyond question.

It is time for the governments of endemic countries to fight on all fronts against Chagas disease:

DIAGNOSIS! DIAGN

Diagnosis of the sick at the primary care level: Integrating the diagnosis of Chagas disease at the primary care level with available resources. Carrying out routine analysis to find those infected with the parasite, especially in areas where vector transmission is active, in rural zones and zones which receive immigrants from endemic areas.

T! TREATMENT! TR

Treatment for children and, wherever possible, for adults, in the primary care system: Free treatment for children and adults, with monitoring of possible side effects. All children should be treated. Adults should always be assessed to see whether or not it is possible to start treatment. Treating adults with mild heart problems may prevent these from progressing. There is no evidence regarding the effectiveness of the treatment when damage is very advanced. In those over 50 who were probably infected in their childhood or adolescence, the risks and benefits of treatment should be assessed.

CE! PREVALENCE! PR

Determining the prevalence of Chagas: Systemising the collection of data on Chagas disease to establish the number of infected in an area and using this information to calculate the real requirements for medicines and laboratory reagents, to be able to ensure the availability of diagnosis and treatment.

SUPPLY! SUPP

Reinforcing the supply chains: In order for medicines and diagnostic tests to reach the primary care centres in the remotest zones, strong supply chains are needed. In addition, doctors should ask for the medicines they need.

TROL! CONTROL! C

Vector control activities: When treating a patient, their house and environment need to be assessed for the presence of the vector, and fumigated if necessary. In addition, systematic fumigations should be carried out in risk areas to control the spread of the insect, and at the same time investment should be made in improving housing.

This year is the centenary of the discovery of Chagas disease. Based on our experience, MSF appeals to the governments of endemic countries to increase the use of existing diagnostic tools and treatments, as well as access for patients to the care they need. Likewise, MSF underlines the urgent need for improved rapid diagnostic tests, new less toxic and more effective medicines, paediatric formulas and treatment tests.

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