



Editorial

Treat Chagas now!

Chagas disease is a silent killer. Every year it takes the lives of an estimated 14,000 people, many of whom did not even know that they were suffering from the disease. In the endemic countries of South and Central America, 8 to 15 million people are infected, primarily adults. As a result, Chagas has a significant socioeconomic impact. It is the most prevalent parasitic disease in the Americas.

The Brazilian physician Carlos Chagas first described the disease more than 100 years ago, and although much progress has been made in medical research since, there is still no effective treatment for Chagas.

It remains one of the most neglected and underfunded kinetoplastid diseases worldwide. Of the US\$ 139 million used in 2008 to fund research and development (R&D) of kinetoplastid diseases, 41.5% was for leishmaniasis, 24.8% for sleeping sickness, and only 11.2% for Chagas*. Due to a lack of funding, millions of people infected do not have access to adequate treatment.

It is time to take urgent measures to scale up diagnosis, treatment, and patient access to medical care and to boost research and development. It is time for policy makers and donors to grant Chagas the attention it deserves.

In 2009, DNDi and its partners launched a campaign called "Wake up! Time to Treat Chagas Disease!" with the following goals:

- to raise awareness
- to break the silence surrounding the disease
- to boost R&D of new tools for the disease

As part of this campaign, DNDi, Médecins Sans Frontières, and the University of California Los Angeles (UCLA) Program in Global Health convened a one-day symposium on Chagas disease in Los Angeles in October 2009. Participants agreed that urgent measures and concrete solutions are greatly needed. That same month, the Pan American Health Organization (PAHO) adopted a resolution for the elimination of neglected diseases, including Chagas. This is an important step, but it needs to be reinforced with measures such as adopting a resolution on Chagas disease at the World Health Assembly in May 2010 in Geneva, and including funding for Chagas programmes in the U.S. Government's Global Health Initiative.

Good efforts are undoubtedly underway. However, a lot more needs to be done for patients to finally have access to affordable, safe, and effective treatment. ■

Invest in R&D to deliver improved treatments

One of the objectives of the Drugs for Neglected Diseases *initiative* (DNDi) is to develop improved and new treatments for Chagas disease. DNDi is currently building its Chagas portfolio, which includes projects that yield near-term benefit to paediatric patients as well as long-term projects that will potentially benefit a large population of chronic-phase patients.

Although the disease was discovered more than 100 years ago by the Brazilian Carlos Chagas, very little investment has been made in research and development for an effective treatment. Currently available treatments are not effective and poorly tolerated. To address this serious unmet medical need, DNDi has raised funds from public and private donors, and formed R&D partnerships with a number of key institutions to develop Chagas treatments.

existing clinical research capacities through a regional platform of experts that supports high-standard clinical trials.

Drug discovery

Key elements in DNDi's drug discovery process include:

- **Focused approach to compounds sourcing:** DNDi has access to various chemical compounds, focused drug classes, and classes of



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wild-type *T. Cruzi*. This technology offers the possibility of more rapid identification of a hit and chemical series of interest to be progressed as drug candidates. The technology has already been successfully developed for the screening of compounds against the intracellular *Leishmania* parasite by DNDi at IPK.

- **Series to optimise (from screening to drug candidate):** at the end of 2008, a lead optimisation consortium was established to engage in a critical, interactive, and iterative process - Lead Optimisation - allowing a rapid turnaround and with the goal of optimising the antiparasitic efficacy of lead compounds while addressing their Distribution Metabolism Pharmacokinetics (DMPK) properties and improving their safety. This consortium consists of teams of analytical and medicinal chemists, pharmacologists, and parasitologists and includes institutions in Australia (Epichem, Murdoch, and Monash Universities) and in Brazil, the Universidade Federal de Ouro Preto (UFOP).

(CONTINUED ON PAGE 2)

CHAGAS DISEASE IN SHORT



The insect known as the 'kissing bug' transmits the parasite



Trypanosoma cruzi is the parasite that causes Chagas

Chagas disease is caused by the parasite *Trypanosoma cruzi* (*T. Cruzi*), transmitted primarily by insects known as "kissing bugs". The disease occurs in two phases.

- The first, acute stage is often asymptomatic or unrecognised due to non-specific symptoms such as fever, malaise, generalised lymphadenopathy (affecting the lymph nodes), and hepatosplenomegaly (enlargement of the liver and the spleen), which spontaneously resolve within weeks.
- The chronic phase may affect the heart and the gastrointestinal tract and, if left untreated, can lead to death. Over 8 million people across Central and South America are infected with Chagas disease. Chagas disease kills more people in this region than any other parasite-borne disease, including malaria.

Through migration, Chagas has spread to Australia, North America, Japan, and Europe.

Filling gaps in the pipeline

DNDi has adopted a balanced approach to build a Chagas disease portfolio and works to improve existing treatments through the development of new formulations that are better adapted to patients' needs. To address the short- and mid-term needs of patients, DNDi aims to find alternative drugs through therapeutic switching. In the long term, new chemical entities have to be developed that fit the target product profile. DNDi works with various investigators to overcome methodological constraints that limit the accurate diagnosis and clinical evaluation of responses to new treatments in the pipeline. Additionally, DNDi is involved in strengthening

inhibitors, as well as to data mining through a number of partnerships with various institutions and pharmaceutical companies.

- **Screening of compounds:** to ensure that screening results from different locations are comparable, reference screening centres with standard operating procedures in place are used for small set screening and hit confirmation. A key challenge to overcome has been the limited output of currently available screening methodologies and centres. In a partnership at the forefront of technology development, DNDi and Institute Pasteur Korea (IPK) have developed a visual-based high throughput screening (HTS) platform for

Target Product Profile for Chagas disease

- **A new treatment** for adults and children for acute and chronic disease
 - priority is a paediatric formulation
 - useful against parasite species in all regions
- **Better safety** profile than existing drugs
 - ideally requiring little or no monitoring
- **Equal or better efficacy** profile than existing drugs
- **Easy-to-use treatment**
 - ideally less than 30 days
 - oral
 - preferably once-a-day treatment, ideally outpatient
- **Affordable**
- **Stable** in tropical climates

* Neglected Diseases Research and Development: 'New Times, New Trends'; G-Finder 2009, The George Institute for International Health

Answering urgent needs

To minimise the risks and length of R&D, compounds already registered or in clinical development for other indications are evaluated. These compounds have a previously demonstrated *in vitro* and/or *in vivo* activity for Chagas disease. For almost 20 years, ergosterol biosynthesis has been recognised as a potential target for anti-*T. Cruzi* treatment but there is limited information and initially mixed results. A new generation of antifungal triazoles has appeared as promising alternative treatments as anti-trypanosomal agents. An agreement with the Japanese pharmaceutical company, Eisai, allows DNDi to assume responsibility for clinical development of one such compound, a pro-drug of ravuconazole, named E1224 (see page 3).

Since the 1990s, there has been consensus on the diagnosis and treatment of children and adolescents in the early chronic phase of Chagas disease. Despite decreasing vectorial transmission, young children continue to be an important target population for treatment, because congenital infection as a mode of transmission will remain a high risk for at least another generation. Current drugs, however, are formulated as tablets for adults only, and are not adapted to children's

bodyweights. To treat children, tablet fractionation and extemporaneous formulations are used, thus increasing the risk of improper dosages and raising safety concerns regarding efficacy and stability, particularly in very young and malnourished children.

A partnership agreement signed in 2008 between DNDi and the Pharmaceutical Laboratory of Pernambuco (Lafepe) will deliver at cost the first paediatric formulation of benznidazole, the most widely used drug for the treatment of Chagas disease (see page 3).

Clinical research - tackling the challenges

Outside of specific drug development projects, DNDi is working to address a number of key issues regarding clinical research:

- **Methodological issues for proof-of-concept evaluation in Chagas disease:** the long period for seroconversion after the elimination of the parasite has presented a challenge in the evaluation of response to treatment. Over recent years, an increasing body of data has pointed to a strong biological rationale in favour of the use of parasitological outcomes as surrogate markers of the therapeutic response in Chagas. A TDR-

sponsored study for standardisation and validation of qualitative polymerase chain reaction (PCR) testing for *T. Cruzi* has just been completed. This represents a valuable first step for implementation in future clinical trials. Further work is needed to validate quantitative PCR and to better define procedures for employment in drug studies.

- **Clinical site identification:** clinical trial sites must be identified to ensure adequate recruitment of patients who are suffering from different stages of the disease and who are infected with different strains of *T. Cruzi* to guarantee that clinical trials are implemented according to international standards.

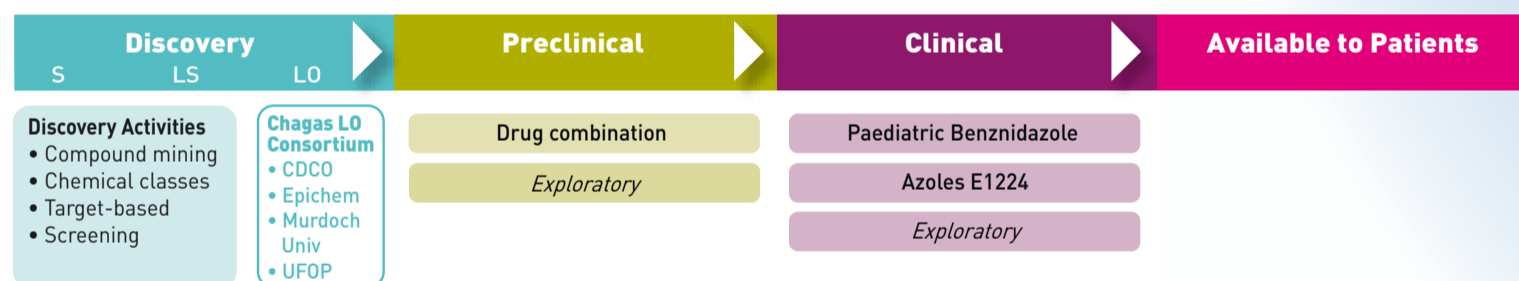
- **Strengthening clinical research:** the Chagas Platform was launched in 2009 with various partners, with the aim of strengthening clinical research capacity and creating an environment conducive to clinical trials. It also provides a forum for technical discussions, review of the Target Product Profile, and consensus-building, thus creating the potential to streamline clinical development processes and to facilitate access to new therapies. ■



According to the WHO, the number of diagnosed cases has been increasing over recent years



DNDi's Chagas Portfolio - 2010 Outlook



Promising treatment candidates: Triazole derivatives

To treat Chagas disease there are currently two drugs available – benznidazole and nifurtimox – which have limitations. There is a void of treatment options especially when it comes to treating the chronic stage of the disease. Existing antifungal drugs have shown promising activity against the Chagas pathogen. DNDi has been in negotiation with pharmaceutical companies to bring about change and hope for patients in need as quickly as possible. In recent years, the marketed antifungal drug posaconazole (Noxafil®, Schering-Plough) was one of the most desirable azoles. It has been shown to induce parasitological cure in mice with acute and chronic infections, including benznidazole-resistant strains. It is considered the leading azole candidate for proof-of-concept evaluation. The main drawbacks, however, are the complex nature of the molecule, with an expensive synthesis and formulation, as well as its current price. DNDi has been in negotiation with Schering Plough since 2006. Unfortunately, no agreement has been reached. Two other triazole derivatives, however, ravuconazole (with the pharmaceutical company Eisai, see page 3) and TAK-187 (with pharmaceutical company Takeda) have also shown encouraging *in vitro* and *in vivo* results. Both products have completed Phase I testing and are good candidates for further assessment as potential treatments. ■

Joining forces to combat Chagas

A new agreement signed in March 2010 in Barcelona, Spain, allows DNDi, the Barcelona Centre for International Health Research (CRESIB) and the Fundación Clínic para la Investigación Biomédica (FCRB) to join forces to enhance and advance the clinical research for Chagas.

DNDi, CRESIB and FCRB share a common interest in providing sustainable affordable treatments for neglected tropical diseases and Chagas disease in particular. The goal of this agreement is to establish and foster joint clinical research projects, to maximize the impact of the parties' resources and profit from the respective expertise, structure and contact to advance the efforts towards finding an effective treatment for Chagas disease. In its portfolio DNDi has recently added an agreement with the Japanese pharmaceutical company Eisai for the development of the promising drug candidate E1224 for Chagas. In a second step this compound will go into phase II clinical trial in Cochamamba in Bolivia. This collaboration with CRESIB will increase chances of success by strengthening the scientific capacities, first in Bolivia and potentially also in the Hospital Clínic de Barcelona. ■

NEW PAEDIATRIC

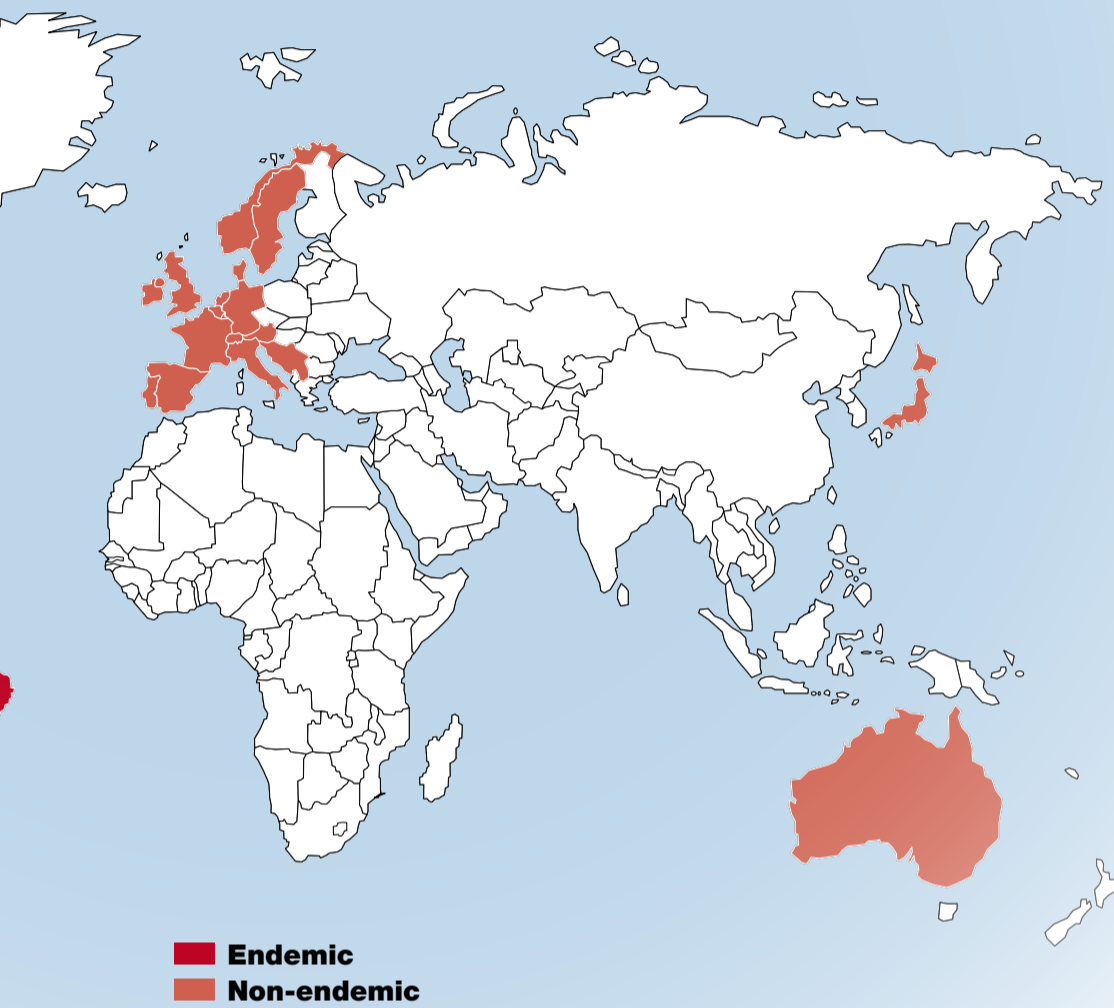


100 Million People at Risk Worldwide



The lack of effective, rapid diagnostic tests in Bolivia reduces access, since diagnosis can only be done where specialised laboratory tests are available

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ABOUT CHAGAS DISEASE

Chagas disease is primarily transmitted by reduviid insects widely known as “the kissing bugs”, which are endemic in 21 countries across Latin America. An average of **14,000 people die of Chagas disease every year** and approximately 8 million people are believed to carry the disease. Without treatment, one third will develop serious and potentially fatal heart or intestinal complications.

What are the symptoms of Chagas?

The disease has two clinical stages:

- The acute stage often remains **unrecognised because it manifests through non-specific symptoms** such as fever, malaise, generalised lymphadenopathy (affecting the lymph nodes), and hepatosplenomegaly (enlarged spleen and liver). These symptoms spontaneously resolve in four to six weeks. **In this stage, the disease is especially dangerous for children; 2% to 8% of infected children die.**
- The second, **chronic stage** happens in two phases: **the chronic asymptomatic “indeterminate” phase**, during which patients can transmit the parasite to others (e.g. through blood transfusion, mother-to-child transmission) while showing no signs of the disease. This stage may last for decades after the infection has taken place. **The chronic symptomatic phase affects 10% to 30% of these patients**, who go on to develop **heart or gastrointestinal complications.**

What is the impact of Chagas?

Chagas disease is a leading cause of infectious cardiomyopathy worldwide, killing more people in Latin America each year than any other parasite-borne disease, including malaria. It affects mostly poor people living in rural areas or on the outskirts of larger urban centres.

What are the current treatments and their limitations?

Two treatments are **currently available**: nifurtimox and benznidazole. Both were discovered decades ago and **have limited efficacy** in the chronic phase of the disease, and a poor tolerability profile in adults. The development of a new treatment that is effective in the chronic phase of the disease is an urgent need.

Often, chronic patients will require pacemakers, implantable defibrillators and, in some cases, heart transplants. Many patients also die suddenly, sometimes without ever realising that they have been infected with Chagas disease. According to WHO, the number of **diagnosed cases has been increasing over recent years**. This is due to increasing migration. Chagas today surfaces in countries and regions classified as non-endemic, such as **Australia, Canada, Europe, Japan, and the United States**. In these countries, there is a high risk of transmission of the disease through blood transfusion, congenital infection, and organ transplantation. ■

THE WAY FORWARD

PAEDIATRIC FORMULATION ABOUT TO BE LAUNCHED



A paediatric formulation of benznidazole is underway and will be launched in the coming months

Benznidazole, one of the two products registered for Chagas disease, can be highly efficacious in children. However, no paediatric formulation exists. Numerous approaches have been examined to best meet the need of developing a new paediatric formulation that is affordable, age-adapted, and easy to comply with. With the goal of developing an adapted dispersible tablet of benznidazole, DNDi and the Brazilian Pharmaceutical Laboratory of Pernambuco (Lafepe) signed a development deal in July 2008 for the first paediatric formulation of benznidazole. While Lafepe is taking the lead on the production of the paediatric formulation of benznidazole, DNDi is involved in assisting Lafepe for registering the drug with government authorities, developing distribution strategies, and providing assistance for the pre-qualification of the product by the Pan American Health Organization (PAHO). Since 2008, the project team has been engaged in pre-formulation and analytical development activities. Using current benznidazole dose recommendations, dosing practices, and patient age and weight profiles from 10 centres that treat children with *T. Cruzi* infections as a guide, the team has determined the most appropriate paediatric tablet formulation, strength and associated dosing regimen. Work is progressing, with batch production and stability testing planned for 2010. The treatment will be sold to countries in need at no profit. ■



© Lafepe

DNDi and Eisai are developing the first new compound in nearly 40 years to treat Chagas disease



In an agreement with the Japanese pharmaceutical company Eisai, DNDi will take full responsibility for the clinical development of the compound E1224, a prodrug of the antifungal ravuconazole. E1224 has shown potent activity against the infection *in vitro* and in animal models.

Ravuconazole has a very long half life, which will allow dosing once a week. The initial proof-of-concept trial will aim to achieve maximum clearance of the parasite in chronic cases, in which current drugs are effective in 60-70% of cases. DNDi anticipates initiating the first clinical trials in 2010, with confirmation of activity by early 2011. Regulatory approval could come as early as 2014. ■

Brazil: Tackling a complex disease

By Paulo Gadelba, President of Fiocruz & Tania Araujo-Jorge, Director of the Institute Oswaldo Cruz.

Since its discovery in 1909, progress in fighting Chagas disease has been made. But many challenges still lie ahead.

In Brazil, an estimated four million people suffer from chronic Chagas; 600,000 people have developed heart or gastrointestinal complications; and each year 5,000 people succumb to the disease. In absolute values, the number of deaths caused by Chagas disease in Brazil is on a par with those caused by tuberculosis, and is ten times higher than the combined number of fatalities resulting from schistosomiasis (a parasitic disease caused by trematode flatworms of the genus *Schistosoma*), malaria, leprosy, and leishmaniasis. The disease mainly affects people between 30 and 60 years of age. Because this is the working population, the loss of earnings and the inability to work have a major social and economic impact. Moreover, the disease afflicts mostly the poor and, given its serious impact, leads to a vicious circle in which poverty is perpetuated and aggravated.

The discovery and the consequences

In the early 20th century, Carlos Chagas travelled inland to Minas Gerais in Brazil. Chagas had been appointed by Oswaldo Cruz, then director of the Federal Department of Public Health, to carry out an investigation into an outbreak of malaria that was jeopardising the completion of the national central railway extension. The investigation resulted in the identification of a new vector, a blood-sucking bug commonly known as the "kissing bug", a new species of parasite, *Trypanosoma cruzi*, named after Oswaldo Cruz, as well as the finding of a new disease, called after the discoverer himself. Carlos Chagas announced the triple discovery in 1909. This was an unprecedented breakthrough in the history of medicine, encompassing the whole cycle of the disease: etiologic agent, insect vector, and human infection. Oswaldo Cruz described it as follows: "The discovery of this disease is the most beautiful illustration of the power of logic at the service of science. Never before, in the field of biological research, has such a fully researched and brilliant discovery been made in such a short time and, what is more, by a single researcher." The scientific discov-



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Vector control in Brazil was on the forefront of the agenda. In 2006, Brazil was certified by WHO as having interrupted the transmission of the disease

ery bolstered the country's international prestige, and among other acknowledgments from national and international institutions, Carlos Chagas was nominated for the Nobel Prize twice – in 1913 and 1921.

The magnitude of Carlos Chagas' discovery can be appreciated in light of the success achieved in the interruption of the transmission of Chagas disease through vector control. In 2006, Brazil was certified by WHO as having interrupted the transmission of the disease by *Triatoma infestans*, the main Chagas vector in the country. Other challenges, however, still need to be addressed: ensuring the sustainability of the vector control, to prevent transmission by other insects or mechanisms (e.g. via dietary exposure), and making quality care available to millions of patients suffering from both, acute and chronic Chagas disease.

Major challenges ahead to tackle a complex disease

To prevent and identify acute infection, it

is still necessary to improve diagnostic tools, test drug combinations, and gain a better understanding of patients' responses to treatment protocols. Rapid and low-cost tests are essential to ensure proper care is given to chronic patients, for whom it is necessary to define reliable markers to monitor disease evolution and manifestation. The relationship between the immune system and the nutritional profile of patients also requires further investigation and clarification, especially in terms of ingestion of selenium and vitamins.

One important epidemiological challenge is the emergence of the disease in the Amazon – and as in the rest of country, it is necessary to improve the tools for monitoring and controlling vectors in wild environments and habitats. In the past century, little progress has been made in terms of specific awareness-raising activities to address the challenges of this national disease. Overall, there is a lack of initiatives and resources targeting the population at risk, health and education pro-

Voices from the field: Helping the affected: Chagas patients' association in Brazil



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Manoel do Nascimento
President of the first officially registered Chagas disease patients' association in the world

Manoel do Nascimento is the President of the first officially registered Chagas disease patients' association in the world. He, himself, suffers from Chagas disease. But he only came to know about it when the disease

began to affect his heart about a decade ago. As a result of serious complications, he has recently undergone surgery to implant his sixth pacemaker. He is leading a patients' association that was founded in 1987 in the Chagas disease clinic of the Oswaldo Cruz University Hospital (HUOC) at the University of Pernambuco, in Recife. The association offers legal, social and psychological assistance to more than 2,800 Chagas patients. The work is conducted with help from volunteers and receives very little assistance from the government, the medical community, the public, or the press. Most of the association's resources come from donations, which allows it to distribute food assistance and medication that is not available through the public healthcare system.

More info: www.chagas.org.br
e-mail: chagas.icc@chagas.org.br

fessionals, and patients. Yet undoubtedly the biggest gap concerns the development of new drugs. Brazil remains as committed to playing a responsible and leading role as Carlos Chagas and his collaborators did in the first decade of the 20th century. ■

Bolivia: Breaking the Silence



Dr Tom Ellman
Head of mission, Médecins Sans Frontières (MSF) in Bolivia

Médecins Sans Frontières (MSF) has been treating people with Chagas disease in Bolivia since 2002. Despite considerable challenges and difficulties in the field, the four projects MSF has been involved in since then have demonstrated the importance and

the feasibility of providing diagnosis and treatment even in the remotest areas. These experiences have been instrumental in helping to change attitudes toward the disease and promoting access to treatment. Of the many countries where Chagas disease is endemic, Bolivia is hit the hardest. Over 1 million of the country's 9 million inhabitants are infected with the disease, and 4 million are at risk. The disease is most frequent among those who live in poverty or in rural areas, but, through migration, urban populations are heavily affected too.

Treating is compelling

More than 10% of Bolivians are believed to carry the parasite – the vast majority unaware that they are infected. If they are not treated, one-third will develop serious heart or intestinal damage that could debilitate or kill them. And 10, 20, 30 or 40 years after having been infected, they may suddenly die.

The challenges are vast: how to explain to people who seem healthy that they have a deadly disease and need to take a drug that makes them feel unwell for 60 days? How to encourage health workers to prescribe a treatment that they are scared to use? MSF, in collaboration with partners at government, municipal, and community levels, is develop-

ing and researching innovative approaches related to prevention, diagnosis, and treatment – approaches that are appropriate and potentially sustainable in the socio-economic and cultural contexts where the disease is most common.

While in 2006 the National Chagas Programme started diagnosing and treating patients under 15 years of age in various parts of the country, access to treatment remains unavailable for the great majority. Moreover, the lack of effective, rapid diagnostic tests

MSF PROVES: TREATMENT IMPLEMENTATION IN RURAL AREAS IS POSSIBLE

The outcome of MSF's field experience in two Chagas programmes in Bolivia demonstrates the feasibility of implementing Chagas disease diagnosis and treatment programmes in poor, remote, rural areas, as well as in the urban environment. While side effects were frequent, only three children required hospital stays to manage these, and there were no deaths due to side effects.

Entre Rios, Bolivia, 2002-2006. The MSF programme aimed to treat all children younger than 15 years of age in a rural area of Southern Bolivia. A total of 7,613 children were screened, of whom 1,475 were confirmed with *T. Cruzi* infection, giving a seroprevalence rate of 19.4%. Seroprevalence by age group was 5.0% in younger than 5 years old; 14.8% in the 5-9 year-old-age group; 31.0% in the 10-14 year-old-age group; and 51.7% for 15-16 year olds. Of these, 1,409 patients began treatment – 1,363 completed at least 30 days of treatment and 1,276 completed at least 55 days (defined as a complete standard course of treatment). A total of 28 (2%) children stopped treatment due to adverse events.

Sucre, Bolivia, 2005-2008. In 2005, MSF started Chagas disease diagnosis and treatment in two districts of Sucre – a peri-urban environment in Bolivia. The age group for treatment was expanded up to 18 years old and rapid diagnostic tests were introduced as a diagnostic screening tool, based on Bolivian national protocol (diagnosis with Chagas Stat-Pak RDT and confirmation with ELISA).

A total of 19,400 children were tested in two districts of Sucre, of whom 1,145 were positive for *T. Cruzi*, resulting in a seroprevalence rate of 5.9%. Seroprevalence by age group was 1.9% in up to 5 years old; 4.1% in 5-9 years old; 8.6% in 10-14 years old; and 14.2% in 15-18 years old. Of these, 1,040 patients started benznidazole treatment. A total of 912 (87.7%) patients completed a full course of treatment, 18 of whom completed it after switching to nifurtimox (second-line treatment) due to adverse events. A total of 61 (5.8%) patients (0% in younger than 5 years old; 8.6% in the 15-18 year old age group) stopped treatment due to adverse events.

Argentina: More Action Needed

By Hector Freilij, paediatrician, Children's hospital Ricardo Gutierrez, Buenos Aires.

The Gran Chaco covers an eco-region of 1.3 million km², extending over Argentina, Bolivia, and Paraguay. Chagas disease is prevalent in this region, with incidences rising since 2001 especially in Argentina, despite major control efforts. Currently, it is believed that 1.5 to 2 million Argentines carry the disease. Every week, 15 Argentines die of Chagas disease. Most of the infected live in the provinces of Santiago del Estero, Chaco, Formosa, the areas to the east of Salta and Tucuman, and northern Santa Fe.

Actions taken to address Chagas disease in the region have largely been limited to vector control. Little has been done in providing treatment and healthcare to infected children, adolescents, and young adults. Nevertheless some progress is being made. The implementation of active screening and treatment campaign for children has just started in schools in Argentina and neighbouring countries, and advances have also been made in training doctors to better detect the disease.

Treatment of adults and children

According to a 1998 WHO/PAHO technical report on treatment guidelines, any infected individual may receive treatment, regardless of age – adults can therefore receive etiological treatment. Furthermore, the study clearly demonstrated that adults receiving parasiticidal treatment may have lower incidence of cardiopathy. Fortunately, the definition of the indeterminate – or chronic asymptomatic – phase has changed.



Field of treatment needs to be reinvented

Sergio Sosa-Estani, Chief of Epidemiological Service at the National Centre for Research in Endemic Diseases of the Ministry of Health (Argentina) says about Chagas: "Research into the disease is so dated and so oriented towards prevention that the field of treatment has to be practically reinvented. The clinical trials for a new compound E1224, a prodrug of ravuconazole, will help to reinvigorate the field. The traditional method of monitoring treatment measures antibodies to *T. cruzi*. Although useful, this method is not very accurate, and antibodies can persist for years after the parasite has been eradicated. Researchers have developed two standardised polymerase chain reaction tests that detect *T. cruzi* in blood with qualitative or quantitative results. It can be used to identify infection in individual patients. The quantitative test will help give a better understanding of the course and staging of the disease and response to treatment. Evidence indicates an association between *T. cruzi* levels, inflammation, and organ damage. That test is in the process of being validated."

Extract from http://www.bmj.com/cgi/content/full/339/oct06_1/b4084

In regard to children, doctors and investigators have demonstrated that 9 out of 10 children infected with Chagas disease receiving treatment are completely cured. Furthermore, the experience at the Ricardo Gutiérrez Pediatric hospital in Buenos Aires has shown that if a child begins treatment before the age of one, the likelihood of cure is almost 100%. The cure rate is about 85–90% if we take into account all children treated in the department below the age of 16. Researchers recommend that children born to mothers serologically reactive for Chagas disease receive early

diagnostic screening for congenital Chagas disease.

One of the main limitations faced is that the only drug currently available is an adult formulation – 100mg and 120mg tablets. Working with paediatric patients, including infants who weigh less than 4kg, it is very difficult to administer an appropriate dosage that corresponds to their weight and age from a 100mg tablet. This is where the development of a paediatric formulation is badly needed, especially for paediatricians responsible for treating newborns, infants, and children.



© National Chagas and Leishmaniasis Control Program of Honduras
Because there is currently no paediatric formula available, administering appropriate dosage to children becomes a challenge. Often tablets are fractioned

Treatment is also prevention

Treating children with Chagas has several advantages: it can avoid the development of cardiac and gastrointestinal diseases later on in their life; treating little girls now can avoid the transmission of Chagas during pregnancy in their adult life, thus avoiding congenital Chagas disease. Furthermore, it allows for a greater number of blood and organ donors.

As Chagas affects a poor region – it does not reach Buenos Aires – there is little economic interest for big pharmas and others who could make a real difference, and so the disease remains neglected. We know that it can be treated and cured – but knowing is not enough...what we need is action. ■

A PLATFORM OF EXPERTS TO SUPPORT DEVELOPMENT OF NEW TREATMENTS

The **Chagas Clinical Research Platform** was launched in 2009 at Uberaba in Brazil, and brings together partners, experts, and stakeholders in a network, which will provide support to the successful evaluation and development of new treatments for Chagas disease. The main objectives of the platform are to facilitate clinical research by creating a forum for technical discussions, **to develop a critical mass of expertise and to strengthen institutional research capacities**. In addition, the platform will continuously identify and review priority needs, work towards standardisation of methodology to assess drugs

efficacy to treat *T. Cruzi* infection, review alternatives for using current drugs approved (new schemes, doses, combination), special scenarios (resistance), and link investigators and groups of experts on Chagas disease in a collaborative network.

Three clinical trials are planned to start in the first semester of 2010. The first is a population pharmacokinetics study of paediatric benznidazole and will be conducted in Argentina at sites in Buenos Aires as well as in the north of the country where the disease is highly prevalent. The second one is an

evaluation of the polymerase chain reaction (PCR) blood test or assessment of therapeutic response in patients with chronic indeterminate Chagas disease, and the third study, conducted in Bolivia, is to evaluate the safety and efficacy of E1224, a prodrug of ravuconazole.

The Chagas Platform will **meet for the first time in early 2010** to review the target product profile for Chagas disease, to **update DNDi's strategy** for the disease, and to provide training for investigators involved in the planned clinical trials.

for the disease further reduces access, as it means diagnosis can only be done where specialised laboratory tests are available. MSF projects have focused on reversing this situation, both by demonstrating simple and effective strategies for increasing access, and by advocating for treatment within Bolivia and internationally. MSF also supports the idea of creating a price fund to stimulate research and development (R&D) into better diagnostics for Chagas disease.

Overcoming treatment fears

There are, however, still several basic barriers to treatment: the lack of interest in researching drugs for diseases of poverty; the difficulties inherent in proving efficacy of treatment in the absence of a reliable test of cure; and persistent myths that exaggerate the dangers of treatment. The perception of risk is not matched by the reality. While there is no doubt that side effects of treatment are a major problem and that they are more frequent in older children and adults, research from MSF projects has shown that the vast majority are mild and safely manageable.

The 60 or 90 days required for treatment, and the cost of the drugs also increase the difficulty of ensuring effective treatment. Local medical personnel often tell adult patients

- incorrectly - that there is no treatment for Chagas. In fact, evidence clearly shows that chronically infected adults, as well as children, benefit from treatment, even when there is already evidence of cardiac damage. Better, safer, faster-acting drugs are urgently needed, but in the meantime the existing drugs must be provided for all those who need them. MSF's first project opened in October 2002, treating children in O'Connor province – a rural area of South-Eastern Bolivia. Since 2007, MSF has been building new approaches in its response to Chagas, based on experiences from this first project, and a second, in the outskirts of the city of Sucre. Between them, these projects screened about 30,000 children, and treated 2,500.

Working with DNDi

MSF is working with DNDi and others, to increase funding for research and to find potential new drugs to treat this disease, circumventing the lack of interest shown by the pharmaceutical industry.

For more information on the Chagas campaign please consult:
www.chagas-break-the-silence.com
www.treatchagas.com ■



Treatment is a priority

Faustino Torrico, Professor of Parasitology and Infectiology, Universidad Mayor de San Simon, Cochabamba, Bolivia and member

of the Scientific Advisory Committee of DNDi: "In Bolivia, where one million (12%) of the total population is infected with *T. Cruzi*, the need for an effective treatment is now a priority. Until the year 2000, more than 60% of the country was virtually infested with vinchucas (Kissing bugs). In several places, we found that up to 100% of the adult population was infected. Since 2000, the national Chagas control programme has carried out systematic and comprehensive vector control programmes in the six Chagas-endemic departments. Today the risk of infection is low in 50% of the municipalities, but there are still areas of resistance, where infestation is higher than 20%. Many challenges lie ahead, but the results are promising. The actions were made possible by grants received from the Inter-American Development Bank (IADB). Unfortunately, the funding finished in 2007 and currently there is a transfer of roles and responsibilities from the central level of the Ministry of Health to local municipalities, whose contributions differ depending on their circumstances – which explains, in part, the difference in our response activities to the disease at the municipal level."



RESEARCH ON NEGLECTED DISEASES
TIME TO TREAT
CHAGAS DISEASE!

U.S.: Increasing Prevalence, Continued Neglect



Michelle French
Former Regional
Communications
Manager,
DNDi North America



Catherine Lalonde
Consultant DNDi

Chagas disease has traditionally been characterised as a Latin American phenomenon, endemic only to the 21 countries south of the United States border. However, recent studies have shown that the prevalence of Chagas disease outside of Latin America is increasing, in large part due to population flows, and Chagas disease is becoming an important global health issue.^[1] Caryn Bern and Sue Montgomery of Centres for Disease Control (CDC) estimate that in 2005 there were 300,167 individuals infected with Chagas disease living in the U.S.^[2] This is more than six times the estimated prevalence of Chagas in Spain (47,743)^[3] – the country with the next highest population of Latin American immigrants.

Modes of transmission in the U.S.

According to Bern and Montgomery, “the U.S. cannot be classified as an area of non-endemicity for Chagas in the same sense as Europe or Asia” due to the fact that eleven Chagas-carrying triatomine species live in the U.S. Although the likelihood of vector-borne transmission is rare, due to modern housing conditions and lower efficiency of vectors, there have been seven reported cases of autochthonous Chagas disease in the U.S.^[4]

In January 2007, the U.S. began routinely screening blood donations for Chagas disease, and organ donation screening has now begun in some areas. According to the American Red Cross, 1 in 30,000 blood donations nationwide – and roughly 1 in 300 donations from Latin Americans in Southern California – continue to test positive for Chagas disease, even though donations from individuals with a known history of Chagas disease are not accepted.^[5]

A case of neglect

CDC estimates of the prevalence of Chagas disease is based on demographic data, not actual diagnoses. This raises the question: of

the 300,000 plus people who are estimated to be infected with Chagas disease in the U.S., how many have been – or will be – diagnosed? Testing for Chagas disease is not routine in the U.S., and the populations most at risk often do not have access to healthcare.

Health practitioners unfamiliar with Chagas disease

Even when patients are diagnosed, health-care providers in the U.S. are largely unaware of Chagas disease and are unfamiliar with treatment protocols. Dr Meymandi, director of the Centre of Excellence for Chagas Disease, regularly sees patients who have been referred to her from around the country because of a lack of knowledge in the wider medical community.

In 2007, CDC published practical recommendations for the evaluation and treatment of Chagas disease in the U.S.^[7] in an effort to address the lack of knowledge and standardisation in this area, but more education and training in the healthcare community is needed to ensure adequate surveillance, diagnosis and treatment of Chagas disease in the U.S.

Bern and Montgomery also estimate that every year, 63 to 315 babies may be born with Chagas disease. Despite the fact that these levels are in the range of other congenital conditions that appear in the American College of Genetics’ recommended newborn screening panel, screening for congenital transmission of Chagas disease is rarely conducted, suggesting a lack of awareness among obstetricians and gynecologists. To date, no congenital cases have been recorded in the U.S.

Furthermore, Bern and Montgomery conservatively project that up to 45,000 cases of heart disease could be attributed to the disease – in many cases, without the patients or their healthcare providers ever realising the cause.^[8] The healthcare community’s lack of awareness may contribute to an increased burden on the healthcare system from patients with serious heart complications caused by Chagas, who may require aggressive treatments, such as defibrillators or heart transplants. These complications are, in large part, preventable if the disease is treated early.

U.S. global health policies neglect Chagas

Though more than 100 million people are at risk from Chagas in the Americas, the disease is often neglected in U.S. global health and neglected disease policies and



Raise awareness with prominent support: Mia Maestro (left) is an award-winning actress from Argentina and is supporting DNDi in a mobile outreach clinic to screen for Chagas disease in Los Angeles

programmes for disease control. For example, neglected disease programmes such as the President’s NTD Initiative and the Food and Drugs Administrations’ priority review voucher system do not include Chagas. In 2007, less than US\$ 2.5 million of the federal^[9] budget was spent on research and development (R&D) for new Chagas drugs and diagnostics – a negligible amount for a disease affecting more than 8 million people.^[10]

President Obama’s five-year Global Health Initiative could change this by including Chagas disease programmes in its efforts to control NTDs, including: support for increasing surveillance, diagnosis, and treatment programmes; investment in R&D for new drugs and diagnostics; regulatory agency support; and measures to strengthen research capacity in disease-endemic countries. Increased attention is also needed to improve the situation for those living with Chagas disease in the U.S.. Public leadership is needed to ensure Chagas disease is appropriately addressed in international policies (i.e. WHO and PAHO), which should reflect the urgent needs for prevention, treatment, and development of new diagnostics and medicines. Over the long term, the emphasis must be on working with our Latin American neighbours to control the disease.

With the Chagas disease burden concentrated in marginalised populations, Chagas patients do not have the political clout necessary to move this silent disease out of the shadows. DNDi’s Chagas campaign aims to raise awareness about this important public health issue, push for policy changes, and encourage R&D investments that will make a difference for Chagas patients in the future. ■

Voices
from
the field

Treatment access in the U.S.



Dr Sheba Meymandi
Director of the Centre
of Excellence for
Chagas Disease

In the U.S., nifurtimox is available to physicians through special Centres for Disease Control (CDC) protocols, but benznidazole is more difficult to obtain and is rarely used.

According to Dr Sheba Meymandi, director of the Centre of Excellence for Chagas Disease, “We can get [benznidazole], but it is a very laborious process through the FDA. Hopefully the CDC will have access to benznidazole soon.” Dr. Meymandi adds, “The difference, in terms of the treatments, is that benznidazole is a shorter course – two months – with a better side effect profile. Nifurtimox, which we have easier access to in the U.S., is a three-month course, and the side effect profile is pretty abysmal. It is like giving chemotherapy. Major side effects are nausea, vomiting, memory loss, neuropathies, and the list goes on.”

[1] Tarleton RL, Reithinger R, Urbina JA, Kitron U, Gürtler RE. 2007 The Challenges of Chagas Disease - Grim Outlook or Glimmer of Hope?. PLoS Med 4(12): e332. doi:10.1371/journal.pmed.0040332. [2] Bern C, Montgomery SP. An Estimate of the Burden of Chagas Disease in the United States, CID 2009; 49 e52-54 DOI: 10.1086/609509. [3] Gascon, J., et al., Chagas disease in Spain, the United States and other non-endemic countries. Acta Trop. (2009), doi:10.1016/j.actatropica.2009.07.019. [4] Bern & Montgomery, 2009. [5] Based on 147 confirmed positives since screening began in 2007 divided by the total estimated number of Latino Blood donors (40 000 – 50 000) in that period. Information provided by Cliff Numark and Ross Herron of the American Red Cross Blood Services. [6] Centres for Disease Control and Prevention (CDC). (2007). Blood donor screening for Chagas disease-United States, 2006-2007. Morbidity and Mortality Weekly Report, 56, 141-143. [7] Bern C, Montgomery SP, Herwaldt BL, Rassi A, Jr, Marin-Neto JA, et al. Evaluation and treatment of Chagas disease in the United States: A systematic review. JAMA. 2007;298:2171-81. [PubMed]. [8] Bern & Montgomery, 2009. [9] This includes Centre for Disease Control, Department of Defense, National Institutes of Health and United States Agency for International Development. [10] Families USA, “The World Can’t Wait: More Funding Needed for Research on Neglected Infectious Diseases.” December 2008.



Maira Gutierrez, an El Salvador native and an U.S. resident of 29 years, was diagnosed with Chagas disease by the Red Cross in 1997 after donating blood. At the time, the Red Cross was conducting exploratory screening of the disease (routine blood screening for Chagas was not implemented in the U.S. until 2007).^[6] In the following years, Gutierrez repeatedly sought treatment without success – the doctors she contacted either did not know of Chagas disease or did not know how to treat it. Despite suffering

from heart palpitations, Gutierrez gave up her search. In 2007, a decade later, her sister called to tell her that there was a story on the evening news about the opening of the Centre of Excellence for Chagas Disease, at Olive View-UCLA Medical Centre in Los Angeles County. Gutierrez subsequently underwent treatment for Chagas disease at the Centre, but she still doesn’t know if she’s cured, because no definitive “test of cure” currently exists. The American Red Cross now refers blood donors who test positive for Chagas to the Olive View-UCLA Centre of Excellence for Chagas Disease for treatment – still the only centre of its kind in the US. The Centre has implemented one of the only programmes in the country that proactively screens at-risk individuals for Chagas disease through outreach programmes in Hispanic communities in the Los Angeles area.

Voices
from
the field

Chagas Disease: an emerging health problem in Europe



Dr. François Chappuis

Physician Assistant from the International and Humanitarian Medicine Division of the Geneva University Hospitals

Dr. François Chappuis, Assistant Physician from the International and Humanitarian Medicine Division of the Geneva University Hospitals, describes the current situation in regards to Chagas in the U.S. and Europe: "There has been a sharp increase in the number of patients diagnosed with Chagas disease in non-endemic countries. The U.S. and Europe are now hosts to the disease. In Geneva, 50% of Latin American undocumented migrants are Bolivians from Santa Cruz and Cochabamba, which are the most endemic and poor regions of their country. Over the past five years, we have noticed an increase in the number of patients diagnosed with the chronic (or indeterminate) phase of the disease or with cardiac complications, and we have recorded two cases of congenital Chagas. In 2008, the Geneva University Hospitals, in partnership with the WHO, set up a large study in the local Latin American community: out of the 1,012 individuals tested, 130 were diagnosed with Chagas. Among Bolivians, 26% carried the parasite. These results have prompted us to expand Chagas screening programmes and to improve case management."

WAKE UP! JOIN THE CAMPAIGN!

By Eric Stobbaerts, Head of DNDi Latin America

In July 2009, DNDi launched its campaign to increase research & development (R&D) for Chagas disease, aimed at finding new and better treatments for patients. The launch of the campaign – with the theme: 'Wake up now: time to treat Chagas disease' – took place at the International Symposium organised by Oswaldo Cruz Foundation (Fiocruz) in Rio de Janeiro to mark the 100th anniversary of the discovery of Chagas disease. At a public event on Copacabana beach, researchers and students attending the symposium and Chagas disease patients' associations pledged their support to the campaign. Brazilian actress, Vera Holtz, volunteered to join the cause as goodwill ambassador for Chagas. After the launch event in Rio de Janeiro, the campaign gained an international dimension with a series of events in Amsterdam, Buenos Aires, London, Los Angeles, Mexico City and other cities. More information about the campaign can be found at: www.treatchagas.org.



In July 2009, DNDi launched its campaign 'Wake up now: time to treat Chagas disease' in Rio de Janeiro

A Call for Action

Chagas disease remains the leading parasitic killer in the Americas. Considering the unmet needs of millions, it is time for a variety of actors to mobilise to push forward urgent measures and concrete solutions. This could include, for example, implementation of the recently adopted resolution for elimination of neglected diseases, including Chagas, by the Pan American Health Organization (PAHO) Directing Council; adopting a resolution on Chagas disease at the World Health Assembly (WHA) in 2010; and including funding for Chagas programmes in the U.S. government's Global Health Initiative. Participants of the Los Angeles symposium called on governments, intergovernmental agencies, researchers, drug and diagnostic developers, nongovernmental organisations, patient groups, and funders to take action in two key areas:

1 Scale up diagnosis, treatment, and patient access to care

Millions of people infected with Chagas are not tested and do not receive treatment in both endemic and non-endemic countries. Urgent actions and measures to increase the medical response to Chagas must be taken to:

- Implement routine testing, diagnosis, and treatment of Chagas in health care systems, treating all children and offering treatment to adults.
- Obtain regulatory approval of benznidazole and nifurtimox, as well as the future new paediatric formulation of benznidazole, in both endemic countries and non-endemic countries. This will require coordination and harmonisation of regional regulatory efforts and the inclusion of neglected tropical diseases, specifically Chagas, in the WHO/PAHO prequalification process.
- Secure availability of benznidazole and nifurtimox as well as diagnostic tests by:
 - reinforcing diagnostics and drug procurement systems, forecasting needs, and supply chains
 - implementing the Strategic Fund (revolving fund) to secure long-term affordability of existing drugs in endemic countries rather than relying on a system based on donations
 - exploring approaches, like differential pricing systems, for non-endemic countries

On October 2nd, 2009 in Los Angeles, DNDi, MSF and the University of California Los Angeles (UCLA) Program in Global Health convened a one-day symposium on Chagas disease, bringing together clinical researchers, drug developers, health professionals, policymakers, donors, and activists. Conference participants agreed that there is an urgent need for specific actions to scale up diagnosis and treatment of the disease and to increase research and development for new and better medical tools.



Participants of a Los Angeles symposium on Chagas disease called on governments to take action

- ensuring access and affordability of future new formulations, including paediatric benznidazole.
- Formalise and promote international clinical guidelines for the use of the existing drugs for all stages of the disease.
- Ensure monitoring and evaluation systems for better epidemiologic data collection to determine the prevalence of Chagas disease.
- Support research into appropriate models for the delivery of prevention, diagnosis, and treatment of Chagas within health systems in endemic settings.
- Increase political commitments, funding, and human resources for Chagas patient care programmes.

2 Boost research and development for new tools

Existing tools available to health staff and national programmes are lacking or inadequate, while research and development (R&D) for Chagas is virtually non-existent.

A recent study showed that less than 0.5% (US\$ 10M) of all worldwide neglected disease R&D funds was devoted to Chagas disease in 2007, and over half was spent on basic research. There is an urgent need to develop new treatments and diagnostics that are safer, more effective, affordable, and adapted to patient needs. Actions and measures to boost and sustain innovation must be taken to:

- Foster innovation for new tools for Chagas disease that include:
 - continued development of new treatment regimens or combinations that shorten treatment duration
 - developing new diagnostic tools, including a definitive test for cure and a better rapid diagnostic test
 - facilitating access to knowledge for new classes of compounds and existing drugs marketed for other indications.
- Increase capacity for clinical research to evaluate and guide the development of new tools and facilitate their use.
- Support new approaches for the regulation and approval of new treatment tools, including fast-track mechanisms and use of existing biomarkers, to speed up access to new discoveries.
- Increase public and private funding for Chagas-related R&D including:
 - Push mechanisms that include investments for all stages of R&D for new diagnostics and drugs in both the public and private sectors, including in endemic countries
 - Pull mechanisms like securing the market through the Strategic Fund (revolving fund) for endemic countries and differential pricing for developed countries, and exploring innovative incentives to catalyse R&D (e.g. price funds, FDA priority review vouchers, etc.).
- Commit political leadership
 - Adopt a WHO resolution on Chagas disease that addresses the need of more R&D
 - Implement PAHO resolution for elimination of neglected diseases and other poverty related infections.

Recent Scientific Publications on Chagas Disease

- 1: Ribeiro I, Sevcik AM, Alves F, Diap G, Don R, Harhay MO, Chang S, Pecoul B., New, Improved Treatments for Chagas Disease: From the R&D Pipeline to the Patients. *PLoS Negl Trop Dis* 3(7): e484.
- 2: Franco-Paredes C, Bottazzi ME, Hotez PJ (2009). The Unfinished Public Health Agenda of Chagas Disease in the Era of Globalization. *PLoS Negl Trop Dis* 3(7): e470.
- 3: Yun O, Lima MA, Ellman T, Chambi W, Castillo S, et al. (2009). Feasibility, Drug Safety, and Effectiveness of Etiological Treatment Programs for Chagas Disease in Honduras, Guatemala and Bolivia: 10-Year Experience of Médecins Sans Frontières. *PLoS Negl Trop Dis* 3(7): e488.
- 4: Chatelain E, Don R., Drug discovery for neglected diseases: View of a public-private partnership in Antiparasitic Antibacterial Drug Discovery. *Paul M. Selzer (Ed); 2009 Apr: Wiley-Blackwell.*
- 5: Ioset JR, Natural Products for Neglected Diseases: A Review. *Current Organic Chemistry* 2008 May; 12 (8): 643-666.
- 6: Tarleton RL, Reithinger R, Urbina JA, Kitron U, Gürtler RE. The Challenges of Chagas Disease - Grim Outlook or Glimmer of Hope? *Plos Med* 2007 Dec; 4 (12): 1852-1857.



NECT was officially made available in September 2009 at the International Scientific Council for Trypanosomiasis Research and Control meeting in Kampala, Uganda

Sleeping Sickness: WHO has made an improved treatment



NECT (Nifurtimox-Eflornithine Combination Therapy), has recently been made available to patients and is the first new treatment against human African trypanosomiasis (HAT) or sleeping sickness in 25 years. NECT combination therapy consists of a simplified co-administration of oral nifurtimox and intravenous eflornithine. Developed by DNDi, Epicentre, Médecins Sans Frontières (MSF), the Swiss Tropical and Public Health Institute, and the National Trypanosomiasis Control Programmes of the Republic of Congo and the Democratic Republic of the Congo (DRC), NECT cuts the cost of treatment by half, reduces the total number of infusions of eflornithine from 56 to 14, and shortens hospitalisation from 14 days to 10. This makes the treatment more convenient for patients.

NECT only requires two infusions a day administered during daytime, which puts less burden on the health staff and makes the treatment far more suitable for remote and resource-poor settings where HAT is being treated. Endemic countries have now begun with the process of ordering the new combination treatment through the World Health Organization (WHO). Until February 2010, the Democratic Republic of Congo, Central African Republic, Chad, Uganda, and South Sudan have accepted NECT as a treatment against HAT in their territories. DRC has received their first 1,000 treatments. More information on www.dndi.org. ■

New compound in development for sleeping sickness

Development of a new compound by DNDi, which has the potential for simplified treatment of human African trypanosomiasis, was announced at the 58th annual meeting of the American Society of Tropical Medicine and Hygiene in Washington DC in November 2009. The drug candidate was developed from chemical technology for new anti-infective drugs licensed by DNDi from the San Diego based biotechnology company, Anacor, in 2007. This novel technology has been the focus of a DNDi-sponsored drug discovery team at Scynexis Inc. in North Carolina and Pace University in New York and has culminated in the production of the new clinical candidate, SCYX-7158, which will undergo pre-clinical safety testing during 2010. It is anticipated that SCYX-7158 will enter clinical trials as a short-course, oral treatment for second stage sleeping sickness in early 2011. ■

Pfizer and DNDi advance international research efforts in the fight against neglected tropical diseases

Pfizer Inc. and Drugs for Neglected Diseases *initiative* (DNDi) have signed an agreement that is designed to facilitate advancements in the battle against human African trypanosomiasis (HAT), visceral leishmaniasis (VL) and Chagas disease, which afflict vulnerable populations in the developing world. Under the agreement, DNDi will have access to the Pfizer library of novel chemical entities in order to screen it for compounds that have the potential to be developed into new treatments. The screening will be undertaken at the Eskitis Institute for Cell and Molecular Therapies, Griffith University in Brisbane, Australia for HAT and the Institut Pasteur Korea, for VL and Chagas disease. Press release on www.dndi.org. ■

DNDi receives \$15M from the Bill and Melinda Gates Foundation. The grant will help develop a promising new medicine against sleeping sickness

The Drugs for Neglected Diseases *initiative* (DNDi) has received a \$US15 million grant from the Bill and Melinda Gates Foundation to undertake clinical development of a new medicine to treat human African trypanosomiasis (HAT), also known as sleeping sickness, a fatal disease that threatens 60 million people in sub-Saharan Africa. The grant to be disbursed to DNDi over five years, will provide critical funding for the development of fexinidazole, currently the only new drug candidate in clinical development for sleeping sickness. Press release on www.dndi.org. ■

DNDi publishes "Registering New Drugs: The African Context"



The report was commissioned by DNDi to the George Institute for International Health and recommends measures to facilitate regulatory authorisation for medicines against Neglected Tropical Diseases (NTDs) in Africa. These measures would include a closer collaboration between developing and developed countries, and the World Health Organization (WHO) taking on a key role in regards to regulatory processes for Neglected Tropical Diseases (NTDs). Download the report from www.dndi.org. ■

India and Brazil are among the Top 5 of government funders for neglected diseases

Key findings of the second G-FINDER report show that nearly US\$ 3billion was spent on making new products for neglected diseases in 2008, but less than 5% was spent on kinetoplastid diseases. Brazil and India ranked in the Top 5 government funders globally, investing US\$ 36.8m and US\$ 32.5m (1.7%) respectively. The U.S. was the largest government funder (US\$ 1.3bn), followed by the European Commission (US\$ 129.9m,) and the UK (US\$ 103.3m). Although R&D almost came to a standstill in 2008, with funding cuts or stagnancy everywhere, significant contributions led to a net increase of US\$ 100.1m (3.9%).

More information on www.thegeorgeinstitute.org. ■

ASTMH 2009 in Washington DC, U.S.

In November 2009 DNDi attended the American Society of Tropical Medicine and Hygiene (ASTMH) meeting in Washington DC. A joint symposium with sanofi-aventis took place on pharmacovigilance of new anti-malarial treatments. Furthermore DNDi organised a symposium on ASMQ, the fixed-dose combination treatment of artesunate and mefloquine for malaria, and was highly represented in the Kinetoplastida session with several presentations and Isabela Ribeiro, DNDi Senior Project Manager, co-chairing the session. More details on www.dndi.org. ■



More information on www.dndi.org. ■

On the Calendar

→ 31 March - 2 April 2010
4th East African Health Sciences Congress (EAHSC), Nairobi, Kenya

→ 14-18 June 2010
37th Annual International Conference on Global Health (Global Health Council) Washington, DC, USA

www.globalhealth.org/conference_2010/

→ 15-20 August 2010
XIIth International Congress of Parasitology (ICOPA) Melbourne, Australia

www.icopaxii.org/

→ 3-7 November 2010
59th Annual Meeting of the American Society of Tropical Medicine and Hygiene (ASTMH) Atlanta, GA, USA

www.astmh.org

→ 3 December 2010
DNDi Stakeholder Meeting, New Delhi, India

NEW people at DNDi

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- **Patient representative:** Prof. Md. Abul Faiz, Professor of Medicine at Sir Salimullah Medical College Mitford, Dhaka, Bangladesh

Scientific Advisory Committee

- Dr. Federico Gómez de las Heras, retired, former Research Director and Director of Diseases of the Developing World Drug Discovery at GlaxoSmithKline, Madrid, Spain
- Dr. Faustino Torrico, Professor of Parasitology and Infectiology, Universidad Mayor de San Simon, Cochabamba, Bolivia

DNDi

Drugs for Neglected Diseases *initiative*

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