



RESEARCH ON NEGLECTED DISEASES
TIME TO TREAT
CHAGAS DISEASE!

JOIN THE GLOBAL CHAGAS CAMPAIGN

COMING SOON

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DNDi

Drugs for Neglected Diseases *initiative*

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More about DNDi

The Drugs for Neglected Diseases initiative (DNDi) is an independent, not-for-profit drug development initiative that aims to develop new, improved, and field-relevant drugs for neglected diseases such as Chagas disease, leishmaniasis, human African trypanosomiasis, and malaria. DNDi's partners include Médecins Sans Frontières (MSF), Institute Pasteur, and public sector research institutions from Brazil, Kenya, Malaysia, and India; along with the UNICEF/UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases (TDR) acting as a permanent observer. DNDi's present portfolio includes projects in various stages of drug research and development. DNDi is the only current PDP with product pipeline for Chagas.

For further information, please visit: <http://www.dndi.org>

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2009 is the 100th anniversary of the discovery of Chagas disease. 100 million people are at risk. Progress in treating patients is too little and too slow. Better treatments are urgently needed.



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American Trypanosomiasis **Chagas Disease** 100 million people at risk

WHAT IS THE IMPACT OF CHAGAS DISEASE?

Approximately 8 million cases¹
14,000 deaths²
667,000 DALYs^{2,3}

Chronic Chagas disease results in significant disability with great social and economic impact including unemployment and decreased earning ability. In Brazil alone, losses of over US\$ 1.3 billion in wages and industrial productivity were due to workers with Chagas disease⁴.

WHERE DOES CHAGAS DISEASE OCCUR?

Endemic in 21 countries across Latin America, Chagas disease kills more people in the region each year than any other parasite-born disease, including malaria. Patient numbers are growing in non-endemic, developed countries (eg. Australia, Canada, Japan, Spain, Italy, France and the United States), due to increased population movements.

HOW IS CHAGAS DISEASE TRANSMITTED?

Caused by the kinetoplastid protozoan parasite *Trypanosoma cruzi*, Chagas disease is primarily transmitted by large, blood-sucking reduviid insects widely known as "the kissing bugs" in endemic countries. Other ways of transmission are blood transfusion, organ transplantation, as well as congenital and oral transmissions.

WHAT ARE THE SYMPTOMS/PRESENTATIONS?

The disease has two clinical phases:

- Acute (in which 2-8% of children may die) – often asymptomatic, or unrecognized due to non-specific symptoms such as fever, malaise, generalised lymphadenopathy, and hepatosplenomegaly – which spontaneously resolve in four to six weeks.
- Chronic disease, with different clinical forms:
 - chronic asymptomatic "indeterminate" disease, during which patients can transmit the parasite to others while showing no signs of the disease. This initial phase has a variable duration, may last decades after infection.
 - chronic symptomatic disease develops in 10% to 30% of infected patients and most often involves the heart and/or gastrointestinal tract, depending on geographical location or parasite strain. Chagas disease is a leading cause of infectious cardiomyopathy worldwide.

WHAT ARE THE CURRENT TREATMENTS AND THEIR LIMITATIONS?

Current treatments can cure infected patients, but highest efficacy is seen early in infection.

- Benznidazole, nifurtimox to treat acute & early chronic disease:
 - Long treatment period (30-60 days)
 - Dose-dependent toxicity
 - High rate of patient non-compliance
 - No paediatric formulations
- No treatment for chronic disease with target organ involvement.

1 PAHO. <http://www.paho.org/English/AD/DPC/CD/psit-nd-poster.htm>. Accessed August 18, 2008.

2 WHO. The World Health Report. Geneva; 2004. Available from <http://www.who.int/whr/2004>.

3 DALYs are a measure of societal impact, being the sum of years of potential life lost due to premature mortality and the years of productive life lost due to disability.

4 Moncayo A, Ortiz Yanine M. Ann Trop Med Parasitol. 2006;100:1-15.

WHAT ARE THE CURRENT PATIENT TREATMENT NEEDS?

Improved treatment options are needed for all clinical forms of Chagas disease:

- A paediatric formulation which is affordable, age-adapted, safe, and efficacious would cure patients with early disease.
- A new drug for chronic disease that is safe, efficacious, and adapted to the field, and ideally would work in both phases of the disease.

WHAT IS DNDi DOING TO ADDRESS UNMET TREATMENT NEEDS?

DNDi's Chagas-specific portfolio balances short- and long-term objectives.

Short term: better use of existing treatments through new formulations, therapeutic switching, and combination therapy

- **Paediatric formulation of benznidazole:** first treatment designed specifically for children
- **Azoles:** clinical development of a well-known compounds already used against fungal infections

Long term: new drugs and improved research & treatment capacity

- New drugs developed from promising compounds identified in discovery activities (such as GSK library of **pyridones and cysteine protease inhibitors** – see page 18) and progressed through Chagas **Lead optimisation consortium**

By 2014, DNDi aims to deliver from its Chagas-specific portfolio:

- 1 new paediatric strength available
- 1 new drug registered



DNDi campaign in 2009/2010

WE AIM TO:

- 1) Prioritize Chagas in the agenda of policy makers and donors. It is time for effective political willingness.
- 2) Raise awareness on the disease and its reality. Silence of the disease must be broken.
- 3) Boost R+D for new tools for the disease. New tools and sustainable mechanisms are urgently needed to allow new diagnostics and treatment.