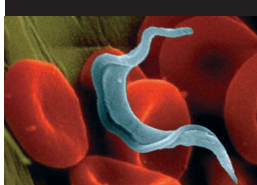


American Trypanosomiasis

CHAGAS DISEASE



WHAT IS THE IMPACT OF CHAGAS DISEASE?

Approximately 8 million cases^[1]
14,000 deaths^[2]
667,000 DALYs^[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 disease^[4].

WHERE DOES THE 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 "indeterminate" disease: patients can transmit the parasite, while showing no signs of the disease. This phase has a variable duration, and 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.

Chagas disease is a leading cause of infectious cardiomyopathy worldwide.

100 million people at risk

WHAT ARE THE CURRENT TREATMENTS AND THEIR LIMITATIONS?

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

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 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) and progressed through Chagas lead optimisation consortium

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

- 1 new paediatric formulation available
- 1 new drug registered

[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.