- Chagas disease, also known as American trypanosomiasis, is a potentially life-threatening disease the by caused parasite Trypanosoma cruzi. It is most commonly transmitted by biting insects known as 'kissing bugs' that are infected with the parasite. As people typically show no symptoms for many years, most are unaware they have Chagas.
- Up to a third of people with Chagas will suffer heart damage that becomes evident only many years later and can lead to progressive heart failure or sudden death. Chagas kills more people in Latin America each year than any other parasitic disease, including malaria.

What is the impact of Chagas disease?

- •Over 6 million people estimated to have Chagas in the world
- •Over 75 million people at risk
- •173,000 new cases per year
- •9,490 deaths in 2019
- •Fewer than **10%** of those infected have been diagnosed
- •Endemic in **21** countries across Latin America
- •Also present in North America, Europe, Japan, and Australia

Chagas's Disease: Endemic in 21 Latin America Countries



How do you get Chagas disease?

- **1. Insect bites:** triatomine bugs, commonly known as kissing bugs, transmit the *T. cruzi* parasites by biting people and defecating or urinating close by; the parasites enter the body when people unintentionally scratch the area, allowing the parasites in the faeces or urine to enter the bite
- **2. Mother-to-child:** transmission from mother to child during pregnancy or childbirth
- **3. Blood transfusion or organ transplant:** this type of transmission has decreased in the last decade because of improved control in blood banks and hospitals
- 4. Food: eating food contaminated with infected kissing bugs or their feces

What are the symptoms of Chagas disease?

The disease has two clinical phases:

Acute phase:

- Lasts for about 2-8 weeks after infection
- Can occasionally cause severe symptoms or deaths, especially in infants
- In most cases, symptoms are absent or mild and unspecific
- Possible skin lesions or a purplish swelling of the lids of one eye
- Possible fever, headache, enlarged lymph glands, pallor, muscle pain, difficulty in breathing, swelling, and abdominal or chest pain
- **Chronic phase,** which can be divided into two stages:
- The chronic, indeterminate stage is when people have no symptoms. This stage lasts for the rest of the infected person's life unless they are treated. During this stage, the parasite is hidden deep in organ tissue (especially the heart).
- The advanced chronic stage is when 30-40% of people with Chagas experience symptoms. This stage develops years after infection and most often results in damage to the heart, while others may experience abnormal enlargement of the colon or esophagus.
- People in both chronic stages are at risk for severe symptoms if their immune system is suppressed due to medical treatment or immune disorders such as HIV.

How is Chagas disease diagnosed?

Suspected cases of acute Chagas are confirmed by detecting parasites in the blood through a microscope. In the chronic phase, when the vast majority of people are tested, the parasite is difficult to detect. Healthcare providers instead test blood for antibodies, which are produced by the body to fight the disease. Because no test is sufficiently accurate to work as a stand-alone, two or three different tests must be used. A lack of easy, straightforward testing in most settings is one of the major barriers that prevents people from starting treatment. After treatment, it takes many years for current tests to show as "negative". A better test of cure is another important need.

There is no single reliable test of cure that can be used to monitor the efficacy of a treatment in chronic Chagas disease patients in a timely manner. The lack of validated early markers of serological cure poses a significant hurdle for the development and regulatory approval of new drugs. Current work is focused on raising awareness among Chagas stakeholders about the need for biomarkers, with particular emphasis on regulatory aspects and the biomarker development process. The potential of the MultiCruzi assay is being further refined and assessed in adults for its ability to predict cure quicker than conventional serology. The analysis of a multicentre study carried out by NHEPACHA, an Ibero-American network of researchers working on Chagas, highlighted the need for further studies to identify more appropriate tools for early assessment of therapeutic outcomes in Chagas disease.

Project updates 2020

- Following more than a year's consultation with experts in Chagas disease, a Target Product Profile (TPP) was published in April 2020 for a test to determine if a Chagas disease patient has been cured after treatment.
- The development of a prototype assay using a host marker (ApoA1 fragment) and a new *T. cruzi* parasite antibody (Ab3 from InfYnity Biomarkers) was put on hold while discrepancies between results from different platforms are being investigated.
- DND*i* began testing the diagnostic performance of a Multiplex assay, MultiCruzi, which appears to predict seroconversion earlier than conventional serology in children; further refinement of the algorithm continued.

What are current treatments for Chagas disease?

- The two current treatments, **benznidazole and nifurtimox**, were both discovered half a century ago.
- They are effective against the disease if given soon after infection and appear to be effective in the chronic asymptomatic phase of the disease. However, they have significant drawbacks, including:
- long treatment periods (60-90 days)
- serious side effects
- a high drop-out rate of patients due to side effects
- they have not been proven effective in people with severe chronic symptoms
- To improve treatment in the short and medium-term, research's are investigating new regimens of benznidazole to reduce side effects, and, together with partners, we have helped develop the first form of benznidazole specifically for children.

What new treatments for Chagas disease are needed?

- Chagas disease has been targeted by the World Health Organization (WHO) for elimination but fewer than 10% of people with Chagas have been diagnosed and even fewer have been treated. To eliminate the disease, we need a new drug for both chronic stages of the disease that is safe, efficacious, and adapted to the field. Access to treatment and diagnostics also needs to be greatly expanded. We also need to identify better biomarkers, to measure the impact of treatment and predict who is at risk for developing severe symptoms.
- What Chagas disease medicines are we working on?
- We aim to deliver new, safer, more affordable and effective treatments for people affected by Chagas disease. We are also focused on improving access to diagnosis and treatment using existing tools.
- Find out about our work developing treatments for Chagas disease

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