

Current global situation of Chagas disease

Trypanosoma cruzi has existed in humans for >9000 years¹. Parasite, vector and human disease were described by Carlos Chagas in 1909². Vectorial and congenital transmissions account for ~70% and 26% of new infections, respectively. The clinical course of Chagas Disease (CD) is generally presented with acute parasitemic phase, clinically asymptomatic indeterminate phase, and chronic phase when patients develop cardiac, colon, or neurological disorders. Heart failure is recognized as the major cause of death in CD patients. The global productivity gain by treating acute or chronic CD and preventing heart failure and death is estimated to be \$8 billion US dollars in 2021-2030³. Thus, just the economic benefits make a strong case for new investments in controlling this disease.

Our first challenge is to really address the under diagnosis of *T. cruzi* infection and CD. World Health Organization estimate *T. cruzi* causes ~30000 cases/year, and CD affects 6-10-million people and result in ~12,000 deaths per year⁴. However, these old estimates are based on incomplete and unavailable data. There is no doubt detection of CD in itself is not easy. Several studies indicate <10% of the infected individuals know their disease, and a majority living in endemic areas do not want to know their infection status or seek healthcare because of concerns for social exclusion and stigmatization and adverse treatment experiences of the family members or others^{5,6}. Growing mobility of the populations has also modified epidemiologic characteristics as 2/3rd of the infected people now live in urban areas in endemic countries and also inhabit other continents⁷. I believe increased diagnosis of infection in endemic rural areas and coordination and collaboration among various agencies within and between countries where shared experience can offer the accurate data on the rate of infection and

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disease burden is needed. Yet, there is practically no investment and multi-country collaboration on collection of accurate data on the size and scope of the problem. One can envision that availability of accurate data on CD would incentivize the in-country and international healthcare system and public health officials to acknowledge and address the problem. Once we know the scope of the problem, transformative and innovative approaches, and their implementation in the area of information, education and communication would be needed to increase access to healthcare, positive experience, and social integration (discussed in ⁶).

There is a need to maintain and strengthen the vector control programs because when implemented with rigor, these programs are successful in reducing the acute transmission rate in several countries in Latin America ⁸. However, very limited efforts are made to detect, diagnose, and treat congenital infection. This is despite the fact that clinical studies have repeatedly shown that benznidazole is effective in curing > 90% of infections in children and international guidelines recommend that children up to 14 years old should be treated with anti-parasitic drug therapies (reviewed in ⁹). I propose that a standardized diagnostic algorithm as we proposed in Rios et al ⁹ should be adopted by all countries for identifying congenital infection and then follow up and treat the infected infants. This is a win that does not require new drugs and large financial investments. All we need is the willingness of the governments and public health officials to implement strong policies and procedures for following up the infected mothers and infants to halt congenital infection.

Underfunding of the academic research and limited to no interest of the private sector has further contributed to unacceptable progress in control of CD. While heart is the primary target organ, mega-colon and neurological disorders are also noted in CD. We still do not know what host factors contribute to the development of cardiac, digestive, and neurological abnormalities (individually or in combination) in infected individuals. Chagas disease is underfunded and ignored to such an extent that

very few research labs work on vaccines or drug development and none of these labs have succeeded in getting the experimental vaccines and drugs approved for human use. Increased collaboration and funding for high quality research where experimental vaccines and drugs are completely vetted in in vitro and in vivo systems before they are taken to clinical trial stage would certainly increase the success rate in identifying new therapies. All we need is one new, effective, anti-parasite drug as the induced drug resistance in humans is low. There remains a need for prophylactic vaccine. However, in my humble opinion vaccines or immune therapies capable of reducing the parasite persistence along with pathological oxidative and inflammatory stress would be more advantageous ^{9, 10}. Such therapies could be offered to target infected population only, and reasonable markers of cure are already available. Immune therapies (or therapeutic vaccines) could also be safely given to pregnant women to halt the congenital infection and to the infants born with *T. cruzi* infection ^{9, 10}.

In summary, I believe, that dedication, commitment, and collaboration between scientific communities and public and private sectors, and investments from high-income countries and philanthropies can provide solutions for eliminating human CD burden.

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