Chagas disease: a new worldwide challenge

Endemic Chagas disease began as a neglected disease of poor, rural and forgotten populations. Its spread from Latin America to non-endemic countries is a new worldwide challenge, say **José Rodrigues Coura** and **Pedro Albajar Viñas**.

Human American trypanosomiasis (Chagas disease), along with its causal agent *Trypanosoma* (*Schizotrypanum*) *cruzi*, which was discovered by Carlos Chagas[1] in Brazil in 1909, has existed in the Americas as an enzootic disease (that is, a disease of wild animals) for millions of years. Vectors mainly from the genera *Triatoma*, *Panstrongylus* and *Rhodnius* (Hemiptera; Reduviidae), but also from 12 other genera, have been transmitting the disease among animals for almost 10 million years. More than 150 species of triatomines (the disease vectors) and >100 species of mammals, mostly wild species, maintain *T. cruzi* infection in nature. The distribution of vectors and wild reservoirs of *T. cruzi* in the Americas extends from the United States to Argentina and Chile (latitudes 46°N to 46°S; see Who, how, what and where? on page S8). In total, 22 countries are endemic for enzootic disease in the Americas.

Humans arrived in the Americas between 26,000 and 12,000 years ago[2], either overland (via the Bering Strait) or across the oceans. An increase in agricultural activities and domestication of animals ~10,000 years ago will have encouraged infection, although for thousands of years it continued to be mainly an anthropozoonosis (that is, an accidental infection of humans). Nevertheless, *T. cruzi* DNA has been found in mummies from northern Chile and southern Peru that are almost 9,000 years old[3], and there is evidence of *Triatoma infestans* in human dwellings in pre-Columbian times, notably Inca and Chinchorro cultures, indicating gradual introduction of domestic transmission. Over the past 200–300 years, with progressive deforestation for agriculture and livestock rearing, and the opening of overland transportation routes (railroads and highways), triatomines gradually lost their primary food source of wild-animal blood, while at the same time having more opportunities to spread. They adapted to areas surrounding human dwellings and to the dwellings themselves, feeding on the blood of domestic animals and humans. In this manner, a new cycle of infection was established, and Chagas disease became a zoonosis[4] (that is, a disease that transmits between animals and humans endemically; see life-cycle image in Chagas disease 101 on page S4).

Chagas disease in Latin America

Endemic Chagas disease in Latin America began as a neglected disease of poor, rural and forgotten human populations. The wild triatomines progressively adapted to the domestic environment, living in cracks in the mud walls and roofs of huts. Some such dwellings can shelter up to 14,000 triatomines, feeding on human blood and transmitting *T. cruzi*. Millions of people have been infected, have developed the disease and have even died — without the possibility of getting a diagnosis, let alone medical assistance. Significant foci of domestic infestation might still be found, especially in areas of Bolivia, which has the highest prevalence rate of human infection (see Who, how, what and where? on page S8), and the 17 other Latin American countries that have not controlled vector transmission.

Progressive urbanization of the rural population in Latin America, mainly since the 1940s, has made Chagas disease an important urban medical and social problem. This has introduced new risks, such as the possibility of *T. cruzi* transmission through blood transfusion. In 1960, we estimated that as many as 6,000 and 10,000 cases of Chagas disease each year were caused by receiving an infected blood transfusion in Rio de Janeiro and São Paulo, respectively, which are the two largest cities in Brazil. In the same year, a World Health Organization (WHO) expert committee estimated 7 million cases per year due to blood transfusion in Latin America as a whole. To assess the scale of the problem, we performed a serological survey of two blood banks in Rio de Janeiro from 1961 to 1963, covering 4,595 blood donors. We found that 1.8% of samples were serologically positive for *T. cruzi* infection. We were able to trace 58 infected blood donors and 24 recipients of infected blood, and found that six of the recipients had acquired Chagas disease because of their transfusion. Such findings helped change policy and practice: now the blood banks are fully controlled in Brazil and in many — although not all — other Latin American countries. Infected blood is still a great problem in countries such as Bolivia, where, in cities like Santa Cruz de la Sierra and Cochabamba, up to one-half of blood donors can be infected with *T. cruzi*.

Long-term infection can have different health risks. One of the key problems is chagasic heart disease, which occurs with higher frequency in people aged 20–59 years — at the most productive time of their lives — and, in endemic areas, represents the main cause of disability and mortality. From the early 1960s to the late 1980s, we followed 510 Chagas disease patients in Rio de Janeiro who originated from 15 different Brazilian endemic states. Among them,

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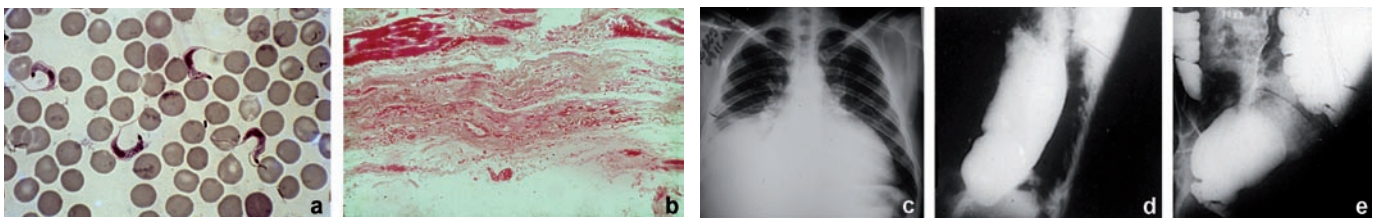

Fig. 1 | Acute and chronic phases of Chagas disease. **a**, *Trypanosoma cruzi* in the blood of an acute case. **b**, Scar in the cardiac tissue of a chronic case. **c–e**, Dilatation of the heart (**c**), oesophagus (**d**) and colon (**e**) in chronic cases of Chagas disease.

39.9% were asymptomatic, 52.1% had chagasic heart disease, and 14.3% had digestive forms of megaoesophagus and megacolon (including 6.3% who had both cardiac and digestive forms; Fig. 1). For the past 30 years, we have expanded our study, working in endemic areas across Brazil, in the southeast (Minas Gerais), northeast (Paraíba and Piauí), west (Mato Grosso do Sul) and Amazon regions, following hundreds of Chagas disease patients. We confirmed our previous hypothesis about the great regional diversity of Chagas disease morbidity. The disease is more severe in Minas Gerais and Piauí, and moderate in Paraíba, Mato Grosso do Sul and the Amazon region. Among other reasons, this is probably related to the type of *T. cruzi* and its infection burden. In the Amazon region, we did not find digestive forms, which were similarly absent in areas further north[4,5].

Regional variation in Chagas disease

As well as severity and nature of chronic infection, there are other regional differences in Chagas disease-transmission cycles, prevalence and control programmes, which can be arranged into four categories.

In Argentina, Bolivia, Brazil, Chile, Ecuador, Paraguay, Peru, Uruguay and Venezuela, Chagas disease is characterized by the presence of domestic, peridomestic and wild cycles, with zones of high prevalence of human infection, and the presence of myocardiopathy and digestive abnormalities (with the exception of Venezuela). Well-established vectorial and transfusional transmission controls exist (with 100% coverage of blood banks, except in Bolivia).

In Colombia, Costa Rica, Ecuador, El Salvador, Guatemala, Honduras, Nicaragua and Panama, Chagas disease similarly has domestic, peridomestic and wild cycles, and patients present with chronic Chagas disease cardiopathy but not digestive abnormalities. Vector and transfusional transmission controls exist, but are more recent.

In Belize, French Guiana, Guyana, Suriname, Mexico and even the United States, Chagas disease primarily has a wild cycle, and there is limited available information about acute and chronic clinical manifestations. Vectorial and transfusional transmission controls are at an incipient stage.

Finally, there are non-endemic countries that have significant population exchange with Latin America, mainly in the form of migration. Here, Chagas disease is a new challenge.

Chagas disease abroad: a new challenge

Non-infected triatomine vector species have been found along the coastal regions of Africa, the Middle East, Southeast Asia and the western Pacific regions, having spread via maritime trade from Latin America from as early as the sixteenth century. In fact, the first entomological description of the vector was made by the Swedish scientist De Geer (1773). The vector might also be spread along air transportation routes in passengers' baggage, thereby increasing the risk of transmission outside of Latin America[6]. The first triatomine, described by De Geer as *Cimex rubrofasciatus* and today known as *Triatoma rubrofasciata*, transmits *Trypanosoma lewisi* among rats, and is not currently a risk to humans.

The *T. cruzi* parasite can travel with population movements from endemic to non-endemic countries such as North America (United States and Canada), the western Pacific region (particularly Japan and Australia) and, more recently, Europe (mainly Belgium, Spain, France, Italy, the United Kingdom and Switzerland, and to a lesser extent Germany, Austria, Croatia, Denmark, the Netherlands, Luxemburg, Norway, Portugal, Romania and Sweden). It has been estimated that there are now >300,000 individuals infected with *T. cruzi* in the United States, >5,500 in Canada, >80,000 in Europe and in the western Pacific region, >3,000 in Japan and >1,500 in Australia[7–9] (Fig. 2).

These population movements have started to create new epidemiological, economic, social and political challenges, as *T. cruzi* has spread worldwide. With the absence of natural vectors, the main threats are from infected blood transfusions and vertical transmission from mother to child, with organ transplantation and laboratory accidents making up a lower risk pool. The number of cases of infection among people travelling to Latin America for tourism or work reasons, and even among adopted children, is also significant. All this shows the need to improve information and surveillance systems at national and supranational levels, implement medical care for patients with Chagas disease in non-endemic countries, intercept vertical transmission, implement additional controls for blood banks and organ transplantation, and include the differential diagnosis for Chagas disease within travel medicine[10]. In addition to the medical, social and economic factors, the spread of Chagas disease poses a political problem: many developed countries rely on migrants to form part of the labour force, yet are not prepared for the challenges they bring, notably the need to organize infrastructure, prepare blood banks to screen millions of blood donors, perform donor and recipient screening for organ transplantation, screen women of child-bearing age who are at risk of being infected and their children, organize out-patient clinics to care for these patients, and train personnel to diagnose and treat Chagas disease.

Chagas disease has become more than simply a zoonotic disease that mainly affects the rural poor in Latin America: it is a worldwide concern that can have severe consequences for human health over the long term. If it is not taken seriously, it could become a major threat to global health. ■

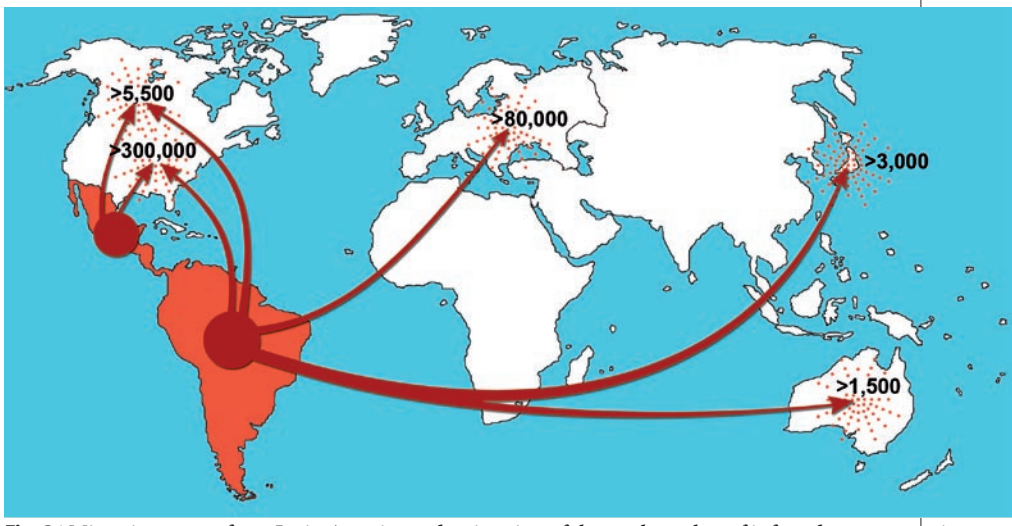

Fig. 2 | **Migration routes from Latin America and estimation of the total number of infected individuals in non-endemic countries.**

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