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REVIEW ARTICLE

Chagas disease: Current perspectives on a forgotten disease

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Abstract Chagas disease is a parasitic zoonosis caused by *Trypanosoma cruzi*, a protozoan whose transmission to humans is primarily vector-borne. It is estimated that 6–8 million people worldwide are infected and that 65–100 million people are at risk of becoming infected. Its clinical spectrum is very broad. During the acute phase, non-specific manifestations develop that may go unnoticed. During the chronic phase, specific manifestations develop that are diagnosed late and increase the morbidity and mortality of those suffering from it. The drugs available to treat it are partially effective, and the efforts made to develop a vaccine remain insufficient. This article reviews the most significant aspects of Chagas disease, from the discovery of the disease to the development of a vaccine, to help train general practitioners and specialists to provide timely care to those suffering from the disease.

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PALABRAS CLAVE
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Enfermedades tropicales desatendidas;
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Enfermedad de Chagas: Perspectivas actuales sobre una enfermedad olvidada

Resumen La enfermedad de Chagas es una zoonosis parasitaria causada por *Trypanosoma cruzi*, un protozoario que se transmite principalmente de manera vectorial al ser humano. Se estima que entre 6-8 millones de personas alrededor del mundo se encuentran infectadas y que entre 65-100 millones están en riesgo de infectarse. Su espectro clínico es muy amplio, pudiendo desarrollar manifestaciones inespecíficas durante la fase aguda que pueden pasar desapercibidas y manifestaciones especificas durante la fase crónica que se diagnostican tardíamente e incrementan la morbimortalidad de quienes la padecen. Los medicamentos disponibles para su tratamiento son parcialmente eficaces y los esfuerzos para crear una vacuna aún continúan siendo insuficientes. En este artículo revisamos los aspectos más relevantes de la enfermedad de Chagas desde su descubrimiento hasta la vacuna, con el objetivo de contribuir en la preparación de médicos generales y especialistas para que proporcionen atención oportuna a quienes la padezcan.

Introduction

The World Health Organization (WHO) recognises American trypanosomiasis, or Chagas disease, as one of the 17 neglected tropical diseases, which have persisted in the poorest, most marginalised societies.[1] It is estimated that close to 6–8 million people worldwide are infected with *Trypanosoma cruzi* and that 65–100 million people are at risk of becoming infected.[2] The majority are in Latin America, where the disease represents a major problem with respect to the morbidity and mortality of the general population, and has become a burden that depletes the region's economic resources and affects the social and occupational environment of those suffering from it.[3] International migration has led to the influx of infected subjects from Latin America to the rest of the world, thus rendering the disease a problem for health systems on a global scale.[4]

Historical background

The first signs of Chagas disease date back almost 9000 years. Evidence of *T. cruzi* infection has been found in mummies from northern Chile and southern Peru. In the 18th and 19th centuries, explorers and naturalists such as Charles Darwin provided the first reliable descriptions of its existence and behaviour, without making any association between the parasite, vector, and disease. Only in 1909 did Dr Carlos Justiniano Ribeiro das Chagas make this association, thus giving the disease its eponym. Chagas had been sent to work on a campaign to eradicate malaria while new roads were being constructed in Minas Gerais, Brazil. At the same time, he became interested in studying the presence of insects that abounded in dwellings in precarious areas and fed on blood. When he dissected the insect and studied its gastrointestinal tract, he found protozoa which he identified as belonging to the genus *Schizotrypanum* (now *Trypanosoma*). He called them *T. cruzi* in homage to Dr Oswaldo Cruz, an epidemiologist and teacher. Later on, Dr Salvador Mazza managed to bring the disease to the interest of the scientific community, redefined the route of transmission, and described the signs and symptoms of the acute phase. Romaña, Jörg, Diaz, and Laranja described the signs and symptoms of the chronic phase.[5,6] Between the 1950s and the 1960s, migration from rural to urban areas brought about the ''urbanisation of the disease''.[7] The first programme to control and prevent the disease (Chagas Disease Control Programme) was created in 1960, while the amount of scientific research conducted was increased in the 1970s. The first and only antitrypanosomal drugs, nifurtimox and benznidazole, were developed in 1972 and 1980, respectively.[6,8]

The first cases in Mexico were reported in 1940 by Dr Luis Mazotti, who described its presence in two patients in Tejomulco, Oaxaca. In 1950, Perrín published the first case of chronic Chagas heart disease. In 1956, the Mexican National Campaign to Eradicate Malaria (CNEP) was launched. In this campaign, dichlorodiphenyltrichloroethane (DDT) was systematically sprayed on millions of dwellings located in malarious areas of Mexico that also corresponded with areas of endemic Chagas disease. Between 1966 and 1967, Biagi and Tay conducted seroepidemiological surveys in different Mexican states, reported the first cases of Chagas heart disease confirmed by parasitology, and used the indirect immunofluorescence (IIF) technique for the first time to diagnose the disease. Between 1972 and 1974, Zavala-Velásquez used nifurtimox for the first time for therapeutic purposes. In 1996, Guzmán-Bracho described the first case of congenital Chagas disease in Sahuayo, Michoacán, Mexico. In 1983, systematic treatment with nifurtimox and benznidazole was started at the cost of purchasing a small batch for the Clinical Unit of the Instituto de Salubridad y Enfermedades Tropicales (ISET).[9,10] Finally, in 2009, the Mexican national programme started to offer medicines to treat cases recorded at the state level.[4]

Epidemiology

According to WHO estimates, in the 1990s it was calculated that there were close to 16–18 million people infected, 100

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