

## Perspective Piece

### What Do We Know about Chagas Disease in the United States?

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**Abstract.** Chagas disease, caused by the parasite *Trypanosoma cruzi*, affects more than 5 million people worldwide leading to serious heart and gastrointestinal disease in a proportion of chronically infected patients. Important modes of transmission include vector-borne, congenital, and via blood transfusion or organ transplant from an infected donor. Vector-borne transmission of Chagas disease occurs in the Americas, including the southern half of North America, where the specific vector insects (triatomines), *T. cruzi*, and infected reservoir mammalian hosts are found. In the United States, there are estimated to be at least 300,000 cases of chronic Chagas disease among people originally from countries of Latin America where Chagas disease is endemic. Fewer than 30 cases of locally acquired infection have been documented in the United States, although a sylvatic transmission cycle has been known to exist in this country for at least a century. Studies defining risks for locally acquired infection and effective prevention strategies are needed to help prevent domestic transmission of *T. cruzi*. To help address Chagas disease in the United States, improved health-care provider awareness and knowledge, better tools for screening and diagnosing patients, and wider availability of treatment drugs are needed.

#### BACKGROUND

Chagas disease is caused by a protozoan parasite, *Trypanosoma cruzi*. *Trypanosoma cruzi* is transmitted by insect vectors called triatomines; vector-borne transmission occurs only in the Americas. The parasite is passed in the feces of infected triatomine bugs and enters the body when breaks in the skin or the conjunctiva are contaminated with infected bug fecal matter. Vector-borne transmission occurs primarily in parts of Mexico, Central, and South America, where triatomine species are adapted to domiciliary and peridomestic settings. In some parts of Latin America, transmission via contaminated food or beverages has been documented. Although vector-borne transmission of *T. cruzi* only occurs in the Americas, congenital transmission and transmission by blood transfusion or organ transplant from infected donors can occur wherever infected people are found. Infection with *T. cruzi* is characterized by an acute phase lasting several weeks to months, when parasitemia can be detected, and a chronic phase when the parasite is primarily present in various tissues and organs in the body. In the absence of treatment, infection persists for the lifetime of the individual and causes serious cardiac and/or gastrointestinal disease in about 30% of those chronically infected. Acute infection is rarely identified when it occurs; in vector-borne acute infection, symptoms are typically mild and often subclinical. In congenital acute infection, a small proportion of acutely infected babies can have serious disease at birth or shortly after.<sup>1</sup>

More than 5 million people worldwide have Chagas disease.<sup>2</sup> In the United States, there are estimated to be at least 300,000 cases of chronic Chagas disease among people originally from countries of Latin America where Chagas disease is endemic.<sup>3</sup> Chagas disease is one of five neglected parasitic infections in the United States, targeted for public health action because it causes serious illness in a large number of

people, but many U.S. health-care providers are not familiar with identifying those at risk or managing the disease.<sup>4,5</sup>

Triatomines and *T. cruzi* are not new to the United States. The triatomine species *Triatoma protracta* was reported as a human pest in California in the 1860s because of the allergic reactions associated with the triatomine bites. The parasite *T. cruzi* was first identified in a *T. protracta* bug collected in California in 1916.<sup>6</sup> Another vector, *Triatoma sanguisuga*, is widely distributed in the southern and eastern United States as far north as Pennsylvania and was first reported to cause allergic reactions in people in the mid-1800s. Since these early reports, 11 species of triatomine bugs have been documented in the United States and all but one (*Triatoma incassata*) have had demonstrated infection with *T. cruzi*. Mammals, including woodrats, infected with *T. cruzi* were first reported in 1934, also from California. At least 24 U.S. species of wildlife mammals have been identified as hosts for the parasite, including woodrats, raccoons, and opossums. Domestic dogs have also been found to carry the infection, although their importance as a reservoir has not been determined. More recent reports of infections in vectors and reservoir hosts demonstrate the continued existence of a well-established zoonotic cycle of *T. cruzi* in the southern half of the United States, dating back at least 150 years.<sup>7</sup>

**What we do not know about triatomines in the United states.** In contrast to triatomine species such as *Rhodnius prolixus* and *Triatoma infestans* that are adapted to domiciliary and peridomestic settings in Central and South America, U.S. triatomine species are primarily sylvatic and not found colonizing human dwellings. Research studies on the feeding and defecating patterns of triatomine species have yielded variable results. The important Latin American vector species tended to defecate while feeding on the host or within 1–2 minutes of completing a blood meal, which would promote transmission, more often than sylvatic species.<sup>8–10</sup> Among the U.S. vectors, *Triatoma rubida* occasionally defecated during a blood meal or soon after feeding, but the other species studied, *Triatoma gerstaeckeri*, *T. protracta*, and *T. sanguisuga*, rarely or never defecated on the host, and a low percentage within 1–2 minutes of completing the blood meal.<sup>11–14</sup> Triatomines have been reported in many states

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throughout the southern half of the United States but field studies have been focal; triatomines typically have been found in their preferred ecological niche, which may or may not be widely distributed in a given state. The converse is also true: lack of a report of triatomines in a given area with suitable ecological characteristics does not mean the insects are not present. It may simply mean that no effort has been made to identify them there. This is an important consideration when assessing potential geographic spread of triatomines and attempting to determine whether a new introduction or new identification has occurred in an area where no previous attempt has been made to identify triatomines there in the past.

**Human Chagas disease in the United States due to autochthonous vector-borne infection.** A small number of domestically acquired *T. cruzi* infections have been reported in the United States. The first reports of human autochthonous *T. cruzi* infection were two cases reported separately in 1955, in two infants in Texas. One was identified as an acute infection, diagnosed on the basis of circulating parasite in a blood smear; no details were provided for the second case. The next report was from California in 1982 of an acute infection in an adult woman. Over the following 34 years, another four cases were reported, three of which were acute infections. In five of the total seven cases, triatomines were found in or near the patient's dwelling, including the one case of chronic Chagas disease diagnosed in a woman living in Louisiana.<sup>7</sup> The introduction of blood donor screening for *T. cruzi* infection in the United States in 2007 led to increased awareness of Chagas disease as a result of the identification of chronic infections among asymptomatic blood donors. Two studies conducted in collaboration with blood collection agencies investigated blood donors who had tested positive by the screening and supplemental tests. These studies were designed to exclude positive blood donors whose suspected infection had likely been acquired outside the United States or congenitally from a mother whose infection had been acquired outside the United States. Another 21 cases of likely autochthonous *T. cruzi* infection were identified in these two studies, bringing the total number of documented infections acquired in the United States to 28 during 1955–2015.<sup>15,16</sup>

Blood donor screening has opened a window into understanding the geographic distribution of chronically infected people in the United States, and may help to direct public health efforts to improve diagnosis and management for those at risk for the manifestations of chronic Chagas disease. Although blood donors can be a relatively easily accessed study population, blood donor studies have important limitations. Chagas disease donor screening is designed to detect existing chronic infection but does not indicate when that infection occurred, and thus, these data cannot be used to derive an annual incidence of *T. cruzi* infection. An antibody-positive blood donor might have been infected months to decades earlier. Blood donor screening is by design sensitive, to avoid missing any potential infections in blood donors. Confirmation of potential cases identified by screening conducted as part of the blood donation process is required. When diagnostic testing is performed, a percentage of donors who initially tested positive are found not to have Chagas disease. The published blood donor studies results have led to hypotheses about the risks for acquisition of *T. cruzi* infection in the United States. These hypothesized risk factors are behaviors that bring individuals into contact more often with vector

bugs in sylvatic settings including outdoor activities such as hunting, gardening, and camping.<sup>15,17</sup> Any putative risk factor should be investigated through epidemiologic studies to understand its role, if any, in *T. cruzi* infection in the United States. Identifying exposures associated with infection is challenging because past activities that led to infection may be subject to recall bias. In addition, the distribution of vectors, infected reservoir hosts, and the parasite may also have changed significantly since the time of infection.

**What needs to be done.** Public awareness of triatomines has grown over the last several years, and concerns for acquisition of autochthonous vector-borne *T. cruzi* infection have also increased. More data are needed to define risk and then to recommend prevention strategies. One way to assess incidence and define risks for *T. cruzi* infection is to conduct prospective studies of people living in areas where vector insects, infected reservoir hosts, and the parasite coexist. In these studies, data should be collected on the number of new infections occurring over a given time period. Exposures reported by people who acquired the infection should be compared with those reported by people who did not become infected. Other gaps include assessment of the cardiac disease burden associated with infection with *T. cruzi* strains circulating in the United States; a small study in several Houston hospitals started in 2015 to address this question. The information from studies of U.S. blood donors can identify geographic areas to target for more detailed study of autochthonous vector-borne risk.

Although locally acquired infection can occur in the United States and evidence-based prevention strategies are needed to address that risk, Chagas disease mostly impacts people who came to the United States from endemic areas of Latin America and are unaware of their infection. US Centers for Disease Control and Prevention (CDC) estimated more than 300,000 people from Latin America have Chagas disease; this estimate was derived from immigration estimates by country and reported seroprevalence in endemic countries.<sup>3</sup> Further refinement of these estimates are needed. This is the population most heavily affected by the burden of cardiac disease due to Chagas disease in the United States. Babies born to infected women from Latin America are at risk for congenital transmission, and strategies to identify mothers at risk and protect their children's health are needed.

Most U.S. health-care providers are not familiar with Chagas disease,<sup>4,5</sup> and increasing provider awareness can lead to better patient diagnosis and management for all patients, regardless of where the infection was acquired. As health-care provider knowledge and awareness increase, other barriers to Chagas disease control become more acute. Better diagnostic modalities for Chagas disease are needed in the United States so effective screening can be performed outside of formal laboratory settings. For example, a US Food and Drug Administration (FDA)-approved rapid test would allow for screening of pregnant women at risk for Chagas disease during visits to antenatal care clinics. Currently, neither of the drugs that are accepted treatments for Chagas disease, nifurtimox and benznidazole, are FDA approved. Both are available under investigational protocols at CDC, but the administrative requirements for participation under the protocols are a barrier for the typical busy clinician. Approved drugs would allow clinicians and patients easier access to these critically needed drugs.

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