Orally Acquired Chagas Disease: Lessons from an Urban School Outbreak

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(See the article by de Noya et al, on pages 1308–1315.)

The protozoan pathogen *Trypanosoma cruzi* causes Chagas disease, one of the most important parasitic infections in Latin America. Without effective treatment, infection is usually for life. A likely outcome of infection is heart disease, with electrocardiogram abnormalities and cardiomyopathy. In some geographical areas, this may be complicated by megasymph commercially, particularly megaesophagus and megacolon [1].

The insect vectors are blood-sucking triatomines. Transmission occurs when insects feed, but the route is precarious and indirect, by contamination of mucous membranes or abraded skin with *T. cruzi*-infected triatomine feces. The main culprit vectors are a few triatomine species that colonize poor rural dwellings and feed from the inhabitants and from their domestic animals. Despite the recent success of international programs to control such domestic triatomines (notably, *Triatoma infestans* in the Southern Cone countries of South America), wide regions of domestic transmission remain. Furthermore, *T. cruzi* is a zoonosis; there are many mammal reservoir hosts (such as opossums, armadillos, and rodents), and many triatomine species act as vectors in sylvatic habitats. Such sylvatic bugs pose a threat by replenishing household colonies or by new adaptations to domestic habitats, as well as by occasional incursion of adult insects that fly into houses and may cause sporadic cases of Chagas disease.

*T. cruzi* is not confined to transmission by contamination of the host as the vector feeds, and it has several secondary routes of dissemination. Potential transfusion of contaminated blood demands that all blood donors in areas of endemicity should be screened with serological testing. Similarly, transplant of organs and other tissues may require screening of both donors and recipients, who, if they carry *T. cruzi*, are liable to experience relapse to an acute infection when immunosuppressed. Ideally, the possibility of congenital transmission requires follow up of infants born to seropositive mothers. *T. cruzi* can travel with Latin American migrants, and these secondary routes allow transmission beyond the established regions of endemic Chagas disease. Thus, *T. cruzi* infection has been demonstrated among potential blood donors in North America and in Europe, where occasional autochthonous transmission has occurred.

As if that were not enough, there is at least 1 more increasingly apparent and important means of *T. cruzi* dissemination, and that is transmission by the oral route, which is the focus of the report by de Noya et al [2] that appears in this issue of the *Journal*. Consumption of infective forms of *T. cruzi* may occur as the result of eating raw or undercooked blood and meat of reservoir hosts or by contamination of food with the anal gland secretions of the common opossum, *Didelphis* (which, extraordinarily, may contain forms equivalent to the infective forms in the hindgut of the triatomine). However, by far the most likely source of orally acquired *T. cruzi* infection is food contaminated by an entire infected triatomine or by infected insect feces. Not only are the adult triatomine winged, but several species are attracted to artificial lights, bringing them into houses or to other sites where food is produced locally or commercially. In experimental animals, infection by ingestion and gastric invasion can readily occur and is believed to be an important mechanism of propagation among omnivorous or insectivorous mammal reservoirs of infection. *T. cruzi* is destroyed in dry triatomine feces and by high temperatures, so the food that is contaminated must remain...
moist or be partially liquid and be kept at not much more than ambient temperature. In such foods, T. cruzi may survive for hours or days and might even multiply in some foodstuffs. Cooling does not kill T. cruzi and may prolong survival, although freezing without chemical protection can destroy the organism. Palm, sugar cane, and fruit juices are therefore ideal contaminated sources for oral outbreaks, because they are often grown, harvested, and pressed locally, with the aid of artificial light, in rural or periurban areas where sylvatic triatomines may be abundant.

Orally acquired human infection with T. cruzi has been known since the 1930s but has risen to more recent prominence as a result of the series of outbreaks that has occurred in the Amazon region, which have been associated with preparation and consumption of popular juice from the fruit of the acai palm (Euterpe oleracea) [3]. These outbreaks are especially notable because, although T. cruzi is enzootic and abundant among Amazonian sylvatic vectors and reservoirs, there are as yet no commonly established domestic triatomine species, and orally acquired Chagas disease therefore accounts for approximately one-half of the known Amazonian cases. South of the Amazon region in Brazil, several outbreaks have been associated with consumption of sugar cane juice.

The report by de Noya et al [2] in this issue is unique and extraordinary in several respects. First, it describes by far the largest known outbreak of orally acquired Chagas disease. Second, it is urban and occurred in a school. Third, it indicates a new type of contaminated food, guava fruit juice. Furthermore, the study incorporates considerable detail on the clinical presentation and uses an interesting combination of epidemiological methods. Several important conclusions are derived from or reinforced by the investigation.

A crucial initial observation was the detection by microscopy of trypomastigotes in blood smears obtained from the 9-year-old index case patient, which triggered follow-up in other students who were hospitalized with fever of unknown origin. A combination of parasitology, serological testing, and polymerase chain reaction amplification of T. cruzi kinetoplast DNA led to the confirmation of 103 cases among the 1000 individuals exposed. As expected, cardiovascular symptoms were commonplace, whereas some clinical features were considered to be unusual and possibly related to the oral transmission route. Because the school was in a relatively well-developed urban area with no evidence of vector infestation, it was presumed that contaminated food must be the source.

A traditional investigative epidemiological approach was then used, with a within-cohort, case-control approach for all students, staff, at-risk contacts, and external food producers. Questionnaires, odds ratios, and multivariate analysis revealed that guava juice, prepared and cooled over night in a Caracas suburb, was the likely source. Infection was most common among the morning shift of children, who were the first to consume the juice. Peridomestic rodents and T. cruzi–infected Panstrongylus geniculatus were found in the suburb where the juice was prepared; P. geniculatus has previously shown signs of adapting to peridomestic habitats in both Brazil and Venezuela [4]. Commendably, de Noya et al [2] then married this traditional approach with molecular characterization of the T. cruzi genetic lineage that was involved in the outbreak. A provisional comparison of 3 isolates from patients with 1 isolate from P. geniculatus found no differences, which supported the identification of the source.

T. cruzi is not a single entity but a complex of at least 6 genetic lineages or discrete typing units. Until recently, these were divided into TcI and TcIIa-c, but they have now, more logically, been redesignated as 6 distinct groups—TcI, TcII, TcIII, TcIV, TcV, and TcVI—with differences between ecologies, hosts, vectors, and geographical and disease distributions [1, 5]. North of the Amazon, the principal agent of Chagas disease is TcI, which, consistent with the Caracas outbreak, causes severe and fatal cardiomyopathy. In contrast, in the Southern Cone countries, where megaoesophagus and megacolon are common, Chagas disease is predominantly caused by TcII, TcV, and TcVI. It is of considerable epidemiological interest that TcV and TcVI are natural TcII/TcIII hybrids, which have spread rapidly through the Gran Chaco and adjacent regions of South America.

Robust and relatively straightforward methods are now available to identify all 6 T. cruzi genetic lineages [6], and multilocus microsatellite typing (MLMT) provides additional high-resolution analysis for molecular epidemiological tracking [1]. It would be of great value to deploy these methods far more widely and routinely to research groups in areas of endemicity, to allow more-detailed epidemiological investigations. Although investigation of the Caracas outbreak benefited from the limited molecular comparisons, under ideal circumstances, far more isolates would have been available and characterized in detail by molecular methods. Both multilocus sequence typing and MLMT can also be applied to resolve population structures of closely related and morphologically similar triatomine species, clarifying the risk of reinvasion from sylvatic cycles after vector-control programs [1].

Several important messages might be drawn from the landmark study of de Noya et al [2]. First, the importance of awareness among clinicians of the presentation of Chagas disease beyond the usual epidemiological circumstances, and even among populations far from areas of vector-borne transmission. Second, the need for a rapid response, including standardized, proven diagnostic procedures and easy access to chemotherapy. Third, the importance of the traditional epidemiological approach and the added value of molecular methods, which allow precise epidemiological tracking and should be
more widely deployed. Fourth, the need for health education to diminish the risk of orally acquired Chagas disease. Vigilance or cleaning of crops might exclude insects. Presses should ideally be covered to protect against triatomines and should not be operated directly beneath or adjacent to artificial light. Commercial açai production can be made safe by pasteurization. Vulnerable juice preparations should not be left uncovered and open to contamination. Finally, despite the novelty and undeniable importance of orally acquired Chagas disease, it is well to remember that domestic vectors still colonize houses across wide areas, and efforts to eliminate them must be sustained.

References