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Perspective Piece

Autochthonous Chagas Disease in the United States: How Are People Getting Infected?

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Abstract. In the United States, Chagas disease is diagnosed in less than 1% of the estimated > 300,000 people who have the disease. However, the actual prevalence remains unknown, and these estimates may be wide of the mark (too high or too low). The greater part of those living with the disease acquired the infection in an endemic region of Latin America, but autochthonous transmission in the United States is increasingly being described. These cases are considered rare, and the transmission routes are largely unknown. Although triatomines or "kissing bugs" harbor *Trypanosoma cruzi* in North America, most autochthonous cases are presumed rather than confirmed exposures to naturally infected kissing bugs. Public knowledge of Chagas is growing, and efforts are underway to provide greater awareness, but what are the risk factors for human transmission of Chagas disease in the United States?

Trypanosoma cruzi is a flagellated protozoan found among many mammals throughout the Americas. This parasite infects humans and other mammals usually through exposure to the feces of blood-sucking triatomines, known as kissing bugs in the United States.[1] Human infection can lead to the development of symptomatic Chagas disease in 30–40% of those infected, causing nonischemic cardiomyopathy, heart failure, cardiac arrhythmias, and sometimes, gastrointestinal disease.[2] The most common known risk for transmission is via direct contact with the fecal material of the kissing bug after a blood meal at which time the parasite can penetrate through exposed mucous membranes or a break in the skin. Other transmission routes include oral ingestion of contaminated food/drink products that contain the infected insect and/or fecal material, vertical transmission from an infected mother to a fetus while in utero, exposure to contaminated blood products such as a blood or platelet transfusion from an infected donor, and through organ transplantation from an infected donor.[1,2]

Here in the United States, autochthonous transmission has been described but is thought to be a rare occurrence.[1] However, multiple states have reported probable or confirmed autochthonous cases including Arizona, Arkansas, California, Louisiana, Mississippi, Missouri, Tennessee, and Texas.[3–11] One study from 2012 revealed another 15 cases among U.S. blood donors from undisclosed states which were believed to be acquired within the United States.[7] To date, it has been estimated that there are at least 78 well-documented cases, including a recent case reported in 2020 isolated from a blood donor in Missouri.[1,4,8] Eleven kissing bugs are found naturally in 29 states (10 species are known to harbor *T. cruzi*), but it appears that only four species (*Triatoma protracta*, *Triatoma rubida*, *Triatoma sanguisuga*, and *Triatoma gerstaekeri*) have been commonly associated with human dwellings.[1,12–15] Human blood is also found in triatomines either collected in the field or around the home.[16–18] Kissing bug bites can be allergenic, leading to significant cutaneous reactions, and sometimes, life-threatening anaphylaxis (at least one death in Arizona).[19,20] The manifestations of a bite can also mimic an actual chagoma (e.g., Romana's sign; when the parasite enters the mucous membranes after a bite on the face). Increasing exposure to triatomines in and around human dwellings has led many to seek medical advice with concerns about Chagas disease. So, who is at-risk for autochthonous Chagas here in the United States and does it correlate with a known exposure to a kissing bug such as a bite from this insect?

A study conducted in Arizona has shown that despite a high proportion of kissing bugs being infected with *T. cruzi* (> 50%) and residents frequently being bitten, none had confirmatory serologic evidence of Chagas disease.[21] Nonetheless, a likely autochthonous case was isolated from a young woman from southern Arizona who did not recall being bitten by kissing bugs but tested positive for *T. cruzi* infection at blood donation. Further investigation yielded *T. cruzi*–positive kissing bugs at her residence.[3] Another investigation in Texas of 885 outdoorsmen and hunters exposed to wildlife meat and blood, as well as native kissing bugs, demonstrated no serological evidence of Chagas disease.[22] Data obtained from 48 confirmed or presumed autochthonous cases of Chagas disease (from 2000 to 2018) revealed 15 (31.3%) had a vector sighting in and around their residence and only four individuals had a known bite from a kissing bug.[4] The most common risk factors reported were living in a rural setting in their lifetime (58.3%), a history of hunting or camping outdoors (47.9%), and a history of agriculture or outdoor employment (33.3%).[4] Among the four most recently presumed autochthonous cases reported from 2017 to 2020, one person from Arizona and one from Texas had seen kissing bugs in or around their home (one, suspected being bitten)[3–5]; one person from Missouri and one from California had no recollection of kissing bug exposure.[8,23] None of the four had sought testing for Chagas disease but tested positive for *T. cruzi* infection at blood donation. Three people were considered to be in the indeterminate phase of chronic Chagas,[3,5,23] and one person had electrocardiogram abnormalities consistent with Chagas heart disease.[8] With increasing awareness of Chagas disease and more testing being performed here in the United States, it appears unexpected cases are arising, and a possible new source of infection may need to be investigated.

The generally accepted dogma of Chagas disease transmission to humans is believed to be when a *T. cruzi*–infected kissing bug defecates on the host after feeding and the

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parasite enters into the blood stream through the mucosal membrane or a breach in the skin.[1,2] Given what we know about these reported cases, it seems that this traditional transmission route (vector bite and fecal contamination) is not to blame for most of these infections, and another transmission route may be occurring in the United States. Zeldón et al.[24] proposed a defecation index (DI) as a means to calculate the infectivity of triatomines (DI = percent of bugs defecating within 10 minutes × the average number of defecations/100), with a higher DI indicating the greater potential for infection. The DI has been used to predict whether a triatomine species is a risk for vector-borne transmission. Researchers have assessed whether North American kissing bugs defecate on or near the host while taking a blood meal, and results are suggestive this is less likely to be the case.[25–27] However, one study conducted with *T. rubida* under artificial conditions and feeding on heparinized blood showed most adult females defecated within 10 minutes of their blood meal.[28] Another study found that wild-caught *T. rubida* and *T. protracta* did not defecate on the host while feeding, with a majority defecating from 1.5 cm to 6 cm away from the host, and a third of these insects defecated 7 cm to 10 cm or up to the edge of the experimental housing.[25] The DI calculated for *T. protracta* was 0.26 and for *T. rubida* was 0.55, when taking into small differences between both sexes.[25] Known vectors of Chagas disease such as *T. dimidiata*, *T. infestans*, and *Rhodnius prolixus* have DIs ranging between 0.9, 1.3, and 2.5, respectively.[24] Accordingly, this implies that North American kissing bugs are behaving differently compared with their well-known counterparts from Mexico, and Central and South America, therefore less likely to be effective at transmitting *T. cruzi* to humans through fecal contamination of a mucous membrane or bite site.

Trypanosoma cruzi infection among sylvatic mammals and domestic pets is widespread in the United States. Raccoons, opossums, skunk, fox, coyote, wood rat and other rodents, white-tailed deer, and armadillo have all been shown to be infected, with varying rates depending on the region.[1,29–33] Even a zoo-housed red panda from northeastern Kansas was discovered to have lethal case of *T. cruzi* infection.[34] Recently, an assessment of working canines from across 41 states found 7.5% (N = 120/1,610) of dogs had serological evidence of infection, with four dogs having *T. cruzi* DNA found in the blood.[31] Nonhuman primates from research laboratories have also been shown to be infected from Louisiana and Texas, areas where kissing bugs naturally reside.[35–37] It has been long postulated that these animals are exposed to *T. cruzi* through oral ingestion, such as eating the actual kissing bugs, but this is still not well understood. With *T. cruzi* infection being demonstrated among wildlife, domestic mammals, and even humans, what other routes of transmission could we be overlooking here in the United States? Perhaps, oral contamination of food/drink with the parasite, such as ingestion of contaminated fecal material of kissing bugs or the insect themselves, is something that we need to consider in the United States.[37] In Latin American countries such as Colombia, Venezuela and Brazil, single cases and outbreaks associated with contaminated food/drink products have been well described.[38] This includes ingestion of wild animal meat, vegetables, sugar cane extract, açaí pulp, guava and bacaba juice, and vino de palma (palm wine).[38] Another potential way *T. cruzi* could contaminate our environment placing humans and other animals at-risk for transmission is through excretion of infected fluids from an infected animal. For example, opossum anal gland secretions are often expelled when the animal is marking territory, has become frightened, or during normal defecation.[39] Lenzi et al.[40] showed in one study that opossums infected with *T. cruzi* had anal gland secretions that may also contaminate their feces, thus adding to another possible source for *T. cruzi* to contaminate our environment. Recently, opossums surveyed in south Texas showed 17% were PCR positive in one or more tissue sample, with 80% of these infected opossums having *T. cruzi* DNA detected in the anal gland secretions.[39] These authors concluded that this presents a plausible source of transmission for humans and animals that would be exposed to these infected bodily fluids.[39,40] Experimental infections have shown that opossums are capable of allowing *T. cruzi* to colonize in the anal glands after infection.[41,42] One study conducted in Venezuela found that urbanized opossums that were naturally infected with *T. cruzi* were able to successfully transmit infection through exposure of anal gland secretions in known uninfected juvenile opossums and laboratory mice.[41] Interestingly, all the opossums survived as opposed to all the mice that did die from the infection. The complete life cycle of *T. cruzi* was also shown to occur within the opossum anal gland during these experiments.[41] Additional research is needed to assess if this is a transmission route that can indeed infect other mammals and humans.

With so much uncertainty on how both humans and other mammals are being infected with *T. cruzi* in the United States and possibly endemic areas of Latin America, more research is needed to better understand the complex nature of this neglected tropical disease. Potential areas of exploration include a better understanding of what factors are involved with peridomestic and domestic kissing bug and human exposures, revisiting North American kissing bug behavior and defecation patterns, infectivity of North American *T. cruzi* strains, enzootic transmission among wildlife reservoirs, and the potential for less commonly thought of transmission routes, such as exposure to infected kissing bug fecal material in the home or environment (not associated with a bite) and oral ingestion of the parasite through contaminated food or beverage products. Furthermore, clearly defining these risk factors will in turn support improvement in Chagas disease testing among at-risk populations, as one of our limitations in the United States is access to testing outside of those who are screened through blood donation. Until we investigate these key areas with scrutiny, our understanding of who is at-risk for autochthonous transmission for Chagas disease will remain limited.

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REFERENCES

1. Bern C, Messenger LA, Whitman JD, Maguire JH, 2019. Chagas disease in the United States: a public health approach. *Clin Microbiol Rev 33:* e00023–19.
2. Perez-Molina JA, Molina I, 2018. Chagas disease. *Lancet 391:* 82–94.
3. Beatty NL, Perez-Velez CM, Yaglom HD, Carson S, Liu E, Khalpey ZI, Klotz SA, Elliott SP, 2018. Evidence of likely autochthonous

transmission of Chagas disease in Arizona. *Am J Trop Med Hyg 99:* 1534–1536.
4. Lynn MK, Bossak BH, Sandifer PA, Watson A, Nolan MS, 2020. Contemporary autochthonous human Chagas disease in the USA. *Acta Trop 205:* 105361.
5. Hernandez S, Flores CA, Viana GM, Sanchez DR, Traina MI, Meymandi SK, 2016. Autochthonous transmission of *Trypanosoma cruzi* in southern California. *Open Forum Infect Dis 3:* ofw227.
6. Dorn PL, Perniciaro L, Yabsley MJ, Roellig DM, Balsamo G, Diaz J, Wesson D, 2007. Autochthonous transmission of *Trypanosoma cruzi*, Louisiana. *Emerg Infect Dis 13:* 605–607.
7. Cantey PT et al., 2012. The United States *Trypanosoma cruzi* infection study: evidence for vector-borne transmission of the parasite that causes Chagas disease among United States blood donors. *Transfusion 52:* 1922–1930.
8. Turabelidze G, Vasudevan A, Rojas-Moreno C, Montgomery SP, Baker M, Pratt D, Enyeart S, 2020. Autochthonous Chagas disease — Missouri, 2018. *MMWR Morb Mortal Wkly Rep 69:* 193–195.
9. Herwaldt BL, Grijalva MJ, Newsome AL, McGhee CR, Powell MR, Nemec DG, Steurer FJ, Eberhard ML, 2000. Use of polymerase chain reaction to diagnose the fifth reported US case of autochthonous transmission of *Trypanosoma cruzi*, in Tennessee, 1998. *J Infect Dis 181:* 395–399.
10. Garcia MN, Aguilar D, Gorchakov R, Rossmann SN, Montgomery SP, Rivera H, Woc-Colburn L, Hotez PJ, Murray KO, 2015. Evidence of autochthonous Chagas disease in southeastern Texas. *Am J Trop Med Hyg 92:* 325–330.
11. Gunter SM et al., 2017. Likely autochthonous transmission of *Trypanosoma cruzi* to humans, south central Texas, USA. *Emerg Infect Dis 23:* 500–503.
12. Klotz SA, Shirazi FM, Boesen K, Beatty NL, Dorn PL, Smith S, Schmidt JO, 2016. Kissing bug (*Triatoma* spp.) intrusion into homes: troublesome bites and domiciliation. *Environ Health Insights 10:* 45–49.
13. Klotz S, Schmidt J, Dorn PL, 2013. *Trypanosoma cruzi* carriage by *Triatoma rubida* and *Triatoma protracta* in a zoological park near Tucson, Arizona. *J Kans Entomol Soc 86:* 373–374.
14. Curtis-Robles R, Meyers AC, Auckland LD, Zecca IB, Skiles R, Hamer SA, 2018. Parasitic interactions among *Trypansoma cruzi*, triatomine vectors, domestic animals, and wildlife in Big Bend National Park along the Texas-Mexico border. *Acta Trop 188:* 225–233.
15. Curtis-Robles R, Hamer SA, Lane S, Levy MZ, Hamer GL, 2018. Bionomics and spatial distribution of triatomine vectors of *Trypanosoma cruzi* in Texas and other southern states, USA. *Am J Trop Med Hyg 98:* 113–121.
16. Beatty NL, Behren-Bradley N, Love M, McCants F, Smith S, Schmidt JO, Hamer SA, Dorn PL, Ahmad N, Klotz SA, 2019. Rapid detection of human blood in triatomines (kissing bugs) utilizing a lateral flow immunochromoatographic assay – a pilot study. *Mem Inst Oswaldo Cruz 114:* e190047.
17. Waleckx E, Suarez J, Richards B, Dorn PL, 2014. *Triatoma sanguisuga* blood meals and potential for Chagas disease, Louisiana, USA. *Emerg Infect Dis 20:* 2141–2143.
18. Klotz SA, Schmidt JO, Dorn PL, Ivanyi C, Sullivan KR, Stevens L, 2014. Freeroaming kissing bugs, vectors of Chagas disease, feed often on humans in the Southwest. *Am J Med 127:* 421–426.
19. Beatty NL, Klotz SA, 2018. The midnight bite! A kissing bug nightmare. *Am J Med 131:* 343–344.
20. Lo Vecchio F, Tran TV, 2004. Allergic reactions from insect bites. *Am J Merg Med 22:* 631.
21. Behrens-Bradley N, Smith S, Beatty NL, Love M, Ahmad N, Dorn PL, Schmidt JO, Klotz SA, 2020. Kissing bugs harboring *Trypanosoma cruzi*, frequently bite residents of the US southwest but do not cause Chagas disease. *Am J Med 133:* 108–114e13.
22. Gunter SM, Ronca SE, Sandoval M, Coffman K, Leining L, Gorchakov R, Murray KO, Nolan MS, 2020. Chagas disease infection prevalence and vector exposure in a high-risk population of Texas hunters. *Am J Trop Med Hyg 102:* 294–297.
23. Harris N, Woc-Colburn L, Gunter SM, Gorchakov R, Murray KO, Rossmann S, Garcia MN, 2017. Autochthonous Chagas disease in the southern United States: a case report of suspected residential and military exposures. *Zoonoses Public Health 64:* 491–493.
24. Zeledón R, Alvarado R, Jirón L, 1977 Observations on the feeding and defecation patterns of three triatomine species (Hemiptera: Reduviidae). *Acta Tropica 34:* 65–77.
25. Klotz SA, Dorn PL, Klotz JH, Pinnas JL, Weirauch C, Kurtz JR, Schmidt J, 2009. Feeding behavior of triatomines from the southwestern United States: an update on potential risk for transmission of Chagas disease. *Acta Trop 111:* 114–118.
26. Pippin WF, 1970. The biology and vector capability of *Triatoma sanguisuga* texana Usinger and *Triatoma gerstaeckeri* (Stal) compared with *Rhodnius prolixus* (Stal) (Hemiptera: Triatominae). *J Med Entomol 7:* 30–45.
27. Martínez-Ibarra JA, Alejandre-Aguilar R, Paredes-González E, Martínez-Silva MA, Solorio-Cibrián M, Nogueda-Torres B, Trujillo-Contreras F, Novelo-López M, 2007. Biology of three species of North American triatominae (Hemiptera: Reduviidae: Triatominae) fed on rabbits. *Mem Inst Oswaldo Cruz 102:* 925–930.
28. Reisenman CE, Gregory T, Guerenstein PG, Hildebrand JG, 2011. Feeding and defecation behavior of *Triatoma rubida* (Uhler, 1894) (Hemiptera: Reduviidae) under laboratory conditions, and its potential role as a vector of Chagas disease in Arizona, USA. *Am J Trop Med Hyg 85:* 648–656.
29. Brown EL, Roellig DM, Gompper ME, Monello RJ, Wenning KM, GabrielMW, Yabsley MJ, 2010. Seroprevalence of *Trypanosoma cruzi* amongeleven potential reservoir species from six states across the southern United States. *Vector Borne Zoonotic Dis 10:* 757–763.
30. Curtis-Robles R, Lewis BC, Hamer SA, 2016. HighTrypanosoma cruziinfection prevalence associated with minimal cardiac pathology among wild carnivores in central Texas. *Int J Parasitol Parasites Wildl 5:* 117–123.
31. Meyers AC, Purnell JC, Ellis MM, Auckland LD, Meinders M, Hamer SA, 2020. Nationwide exposure of U.S. Working dogs to the Chagas disease parasite, *Trypanosoma cruzi*. *Am J Trop Med Hyg 102:* 1078–1085.
32. Zecca IB, Hodo CL, Slack S, Auckland L, Rodgers S, Killets KC, Saunders AB, Hamer SA, 2020. Prevalence of *Trypanosoma cruzi* infection and associated histologic findings in domesic cate (*Felis catus*). *Vet Parasitol 278:* 109014.
33. Gunter SM, Cordray C, Gorchakov R, Du I, Dittmar B, Brown EL, Murray KO, Nolan MS, 2018. Identification of white-tailed deer (*Odocoileus virginianus*) as a novel reservoir species for *Trypanosoma cruzi* in Texas, USA. *J Wildl Dis 54:* 814–818.
34. Huckins GL, David E, Schwartz D, Morton M, Herrin BH, Cerezo A, Yabsley MJ, Schneider SM, 2019. *Trypanosoma cruzi* infection in a zoo-housed red panda in Kansas. *J Vet Diagn Invest 31:* 752–755.
35. Hodo CL, Wilkerson GK, Birkner EC, Gray SB, Hame SA, 2018. *Trypanosoma cruzi* transmission among captive nonhuman primates, wildlife, and vectors. *EcoHealth 15:* 426–436.
36. Dorn PL, Daigle ME, Combe CL, Tate AH, Stevens L, Phillippi-Falkenstein KM, 2016. Low prevalence of Chagas parasite infection in a nonhuman primate colony in Louisiana. *J Am Assoc Lab Anim Sci 51:* 443–447.
37. Robertson LJ, Devleesschauwer B, Alarcón de Noya B, Noya González O, Torgerson PR, 2016. *Trypanosoma cruzi*: time for international recognition as a foodborne parasite. *PLoS Negl Trop Dis 10:* e0004656.
38. Paredes CF, Villamil-Gomez WE, Schultz J, Henao-Martinez AF, Parra-Henao G, Rassi A Jr., Rodriguez-Morales AJ, Suarez JA, 2020. A deadly feast: elucidating the burden of orally acquired acute Chagas disease in Latin America- Public health and travel medicine importance. *Travel Med Infect Dis* (In press). https://doi.org/10.1016/j.tmaid.2020.101565.
39. Zecca IB, Hodo CL, Slack S, Auckland L, Hamer SA, 2020. *Trypanosoma cruzi* infections and associated pathology in urban-dwelling *Virginia opossums* (*Didelphis virginiana*). *Int J Parasitol Parasites Wildl 11:* 287–293.
40. Lenzi HL, Jansen AM, Deane MP, 1984. The recent discovery of what might be a primordial escape mechanism for *Trypanosoma cruzi*. *Mem Inst Oswaldo Cruz 79:* 13–18.
41. Urdaneta-Morales S, Nironi I, 1996. *Trypanosoma cruzi* in the anal glands of urban opossums. I-Isolation and Experimental Infections. *Mem Inst Oswaldo Cruz 91:* 399–403.
42. Jansen AM, Madeira F, Carreira JC, Medina-Acosta E, Deane MP, 1997. *Trypanosoma cruzi* in the opossum *Didelphis marsupialis*: a study of the correlations and kinetics of the systemic and scent gland infections in naturally and experimentally infected animals. *Exp Parasitol 86:* 37–44.