

GARCIA AND OTHERS

AUTOCHTHONOUS CHAGAS IN TEXAS

Case Report: Evidence of Autochthonous Chagas Disease in Southeastern Texas

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Abstract.

Autochthonous transmission of *Trypanosoma cruzi* in the United States is rarely reported. Here, we describe five newly identified patients with autochthonously acquired infections from a small pilot study of positive blood donors in southeast Texas. Case-patients 1–4 were possibly infected near their residences, which were all in the same region ~100 miles west of Houston. Case-patient 5 was a young male with considerable exposure from routine outdoor and camping activities associated with a youth civil organization. Only one of the five autochthonous case-patients received anti-parasitic treatment. Our findings suggest an unrecognized risk of human vector-borne transmission in southeast Texas. Education of physicians and public health officials is crucial for identifying the true disease burden and source of infection in Texas.

INTRODUCTION

Chagas disease (American trypanosomiasis) is a parasitic infection that affects up to 8 million people in Latin America.¹ Most people infected with the parasite *Trypanosoma cruzi* will not develop clinical manifestations. However, up to a third of those infected will develop cardiac disease characterized by conduction abnormalities, progressive dilated cardiomyopathy, ventricular aneurysm, and sudden cardiac death.² Without treatment, infection is lifelong.² Treatment with either benznidazole or nifurtimox can present a number of clinical and therapeutic challenges.^{3,4}

Vector-borne infection occurs when the *T. cruzi* parasite is transmitted from an infected *Triatoma* insect to a mammalian host during the blood meal defecation process. Transmission occurs in two cycles: sylvatic and domestic. Sylvatic transmission occurs in nature between competent *Triatoma* vectors and wildlife mammalian reservoirs.⁵ Domestic transmission occurs when vectors establish themselves near human residences where reservoirs of infection can include domestic mammals and humans. In endemic areas, domestic transmission correlates with human Chagas disease, which can go undetected for years.⁵

High composite risk for disease transmission, based on environmental factors and vector prevalence, has been suggested in Texas.⁶ Blood meals consisting of multiple mammalian hosts, particularly dogs, have been shown in four *Triatoma* species in Texas; dogs are thought to be a bridge vector between sylvatic and domestic transmission

cycles.⁷ Up to 82% of the *T. cruzi* positive vectors in a study by Kjos and others⁷ were collected near human residences and dog kennels, suggesting risk for establishment of domestic transmission cycles in Texas.

Locally acquired human cases along the Texas–Mexico border date back to 1955.⁸ In 2003, potential for domestic transmission along the Texas–Mexico border was described when nests of vectors and domestic dogs within close proximity to a human residence were found to be *T. cruzi* infected.⁹ Out of concern for blood-borne transmission, active blood donor screening began in 2008 in Texas. Since screening began, 1 in 6,500 Texas blood donors have confirmed positive for the parasite that causes Chagas disease.¹⁰ Because of the public health concern for this disease in Texas, Chagas disease was designated a reportable condition in 2013.¹¹

Although most human cases diagnosed in the United States originate in endemic foreign countries, recent studies have documented autochthonously acquired cases in the southern United States.^{12,13} To better understand transmission sources in southeast Texas, we performed a pilot study of infected blood donors assessing source of infection and cardiac outcomes.¹⁴ We present five cases of suspected autochthonous Chagas disease in Texas residents who do not have a significant history of travel to a foreign endemic country.

METHODS

Blood donors were identified by routine *T. cruzi* blood donor screening at Gulf Coast Regional Blood Center in Houston, TX. Testing by the blood center included the Ortho *T. cruzi* ELISA screening test and RIPA confirmation test. The Ortho *T. cruzi* enzyme-linked immunosorbant assay (ELISA) (Ortho Clinical Diagnostics Inc., Raritan, NJ) detected parasite-specific antibodies. A repeat reactive test result of signal-to-cutoff value (s/co) greater than or equal to one was considered positive, and the donor was deferred from future donation. Additional testing with the radio-immunoprecipitation assay (RIPA) for antibodies to parasite surface antigens was performed. Blood donors with positive Ortho *T. cruzi* ELISA and RIPA test results were considered Chagas disease case-patients (*T. cruzi* infection) and were invited to take part in our pilot study.

This pilot study was reviewed and approved by the institutional review boards at Baylor College of Medicine and Gulf Coast Regional Blood Center. Research participants provided a second blood sample for additional testing for *T. cruzi* and completed a questionnaire to assess transmission risk factors. At the time of enrollment in our study, research participants had an electrocardiogram performed and analyzed by a cardiologist. In the event of an abnormal electrocardiogram, the case-patient was asked to have an echocardiogram to assess structural damage and ejection fraction. Additional evaluations to rule out ischemic causes of cardiac abnormalities were not performed, as the primary focus of this investigation was to determine possible sources of infection.

Additional testing performed at the U.S. Centers for Disease Control and Prevention–Division of Parasitic Diseases and Malaria (CDC) included Chagatest recombinant v3.0 ELISA (Wiener, Rosario, Argentina), and trypomastigote excreted or secreted antigen immunoblot (TESA IB). Additional testing performed at our Baylor College of Medicine (BCM) laboratory included immunofluorescent antibody assay (IFA), immunochromatographic assay (Chagas Stat-Pak, Chembio, Medford, NY), and dual

path platform immunochromatographic confirmation assay (DPP Chagas Confirmation Assay, Chembio, Medford, NY).

Of the 17 donors that took part, we could not rule out evidence of autochthonously acquired infection in five donors. These five donors did not have a significant history of travel to an endemic country, did not have a mother born in an endemic country, and were born in the United States. For the purposes of this study, daytrips and vacations to Mexico lasting a week or less for tourist purposes in a non-rural area, were not considered an important risk for transmission. Duration of exposure in an endemic country associated with risk for infection is not known; however, trips < 2 weeks are not considered significant according to multiple published studies.^{12,15-18} Additionally, spending the night in a rural area is considered higher risk for transmission than daytrips when traveling in an endemic country. Finally, Mexico has a low *T. cruzi* seroprevalence, further supporting short travel to this country as an unlikely source of infection.¹³ We present these five donors' infection risk factor assessments, travel histories, medical histories, and *T. cruzi* testing information.

CASE-PATIENT REPORTS

Case-patient 1.

A 59-year-old Caucasian male with a 26-year history of controlled hypertension and diabetes took part in a routine blood donation in April 2007. The Ortho *T. cruzi* ELISA screening test values were consistently positive (1.98, 1.70, and 1.64). The RIPA confirmation was positive. Upon receiving the deferral letter from the blood bank with his testing results, the patient sought medical care from an infectious disease doctor. Treatment was deferred out of his physician's concern about false positive testing results. Results from a routine electrocardiogram performed in 2011 were normal.

In May 2013, he consented to participate in our research study. A blood sample collected in the same month yielded positive results on all tests except CDC's Weiner ELISA and Stat-Pak. The blood sample tested negative on two separate Weiner ELISA test runs. An electrocardiogram found a first degree atrioventricular block and left anterior fascicular block consistent minor Chagas cardiomyopathy.¹ An echocardiogram in June 2013 was normal.

Case-patient 1 was born in Matagorda County, 80 miles south of Houston, TX, where he resided for 29 years. He had since lived in a rural part of Ft. Bend County, 45 miles southwest of Houston, TX. His mother was born in Austin County, 33 miles southwest of Houston, TX. His maternal grandmother was born in a non-endemic country. He reported never seeing vector species at his house. Per request, his wife was tested and was negative for *T. cruzi* infection. Occupational exposures included 1) a 23-year history of farming in open fields and at night, 2) a 4-year history of maintenance for an electricity company working at night, and 3) a lifelong history of deer and bird hunting in tree and box stands. Hunting hygiene practices included "always" skinning the animal immediately post-mortem and "sometimes" wearing gloves during skinning.

In 2000, he started regularly spending time at one particular deer lease in Lavaca County, a rural county 113 miles west of Houston. In June 2013, three *Triatoma gerstaeckeri* bugs were collected from this deer lease. All three bugs were positive for *T.*

cruzi by polymerase chain reaction. Blood meal analysis showed that all three bugs had human blood meals. Additionally, cow and raccoon blood were detected in one of the bugs. We postulate lodging at this deer lease was the source of transmission for Case-patient 1; however, we cannot rule out his nightly occupational exposures and rural birth residence as potential sources.

Case-patient 2.

A 69-year-old Hispanic male with a 4-year history of Alzheimer's disease, a 3-year history of hypertension, and depression donated blood in May 2007. The Ortho *T. cruzi* ELISA screening test values were consistently positive (4.17, 4.36, and 4.00). The RIPA confirmation was positive. Upon receipt of test results, he sought care from his primary care physician who referred him to a cardiologist. Treatment was deferred caused by concern of minimal benefit for the patient. As a result of his profound bradycardia (HR < 40 bpm) a pacemaker was placed in 2011.

In May 2013, he was consented by his power of attorney and enrolled into our study. A blood sample collected in the same month was positive on all subsequent diagnostic tests. On electrocardiogram, we found atrial pacing with right bundle branch block and isolated left anterior fascicular block consistent with Chagas cardiac disease. An echocardiogram was normal.

Case-patient 2 was born in Nueces County, a rural county 211 miles southwest of Houston, where he lived for 29 years. He then lived for 2 years in St. Charles Parish, Louisiana; 35 years in Harris County, TX; and moved to his current residence in 2004 in Fayette County, TX, a rural county 95 miles northwest of Houston. His mother was born in a Webb County, TX, a Texas–Mexico border town. His maternal grandmother was born in an endemic country. He reported never having seen vector species at any of his residences. Travel history included 1) a 1-week trip to Monterrey, Mexico in 1962; 2) a one-night trip to Nuevo Laredo, Mexico; 3) a 4-day trip to Mexico City, Mexico in 1984; and 4) a 1-week trip to Guadalajara, Mexico in 1997. None of these trips were in a rural area, nor did he report staying the night in a rural area.

No occupational exposures were reported. Recreational exposures included a 13-year history of gardening, a 12-year history of daily walking in his property's pastureland, and a 10-year history of tent, camper, and lean-to camping in Texas and Florida. Case-patient 2 was most likely exposed at his current residence with a high composite risk locally⁶; however, we cannot rule out his travel and camping exposure, and his 2-year residential history in Louisiana. It is possible that his infection came from his maternal grandmother (two series of congenital infection), but unlikely given the low risk of congenital transmission, estimated at 1–5%.¹³ His transmission risk from camping is thought to be low as a result of the use of lodging structures (no tarps or open exposure sleeping), and staying in designated campgrounds close to a main road (not in thick forested areas).

Case-patient 3.

A 47-year-old healthy Caucasian female donated blood in September 2007. The Ortho *T. cruzi* ELISA screening test values were consistently positive (3.43, 3.11, and 3.25). The RIPA confirmation was positive. Upon receipt of her test results, she consulted an infectious disease doctor who performed a cardiac evaluation. Her doctor

recommended deferral of treatment because of her healthy status and lack of related clinical findings. In May 2013, she was enrolled in our current research study. A blood sample collected in the same month was positive on all diagnostic tests; however, the first run on Weiner ELISA was negative and the subsequent second run was positive. An electrocardiogram was normal.

Case-patient 3 was born in Lavaca County, a rural county 113 miles west of Houston (the same county as Case-patient 1's deer lease). Residence history included 2 years in Louisiana and the remainder of the time at her current residence in a suburban area of Ft. Bend County, 29 miles west of Houston. Her mother was born in the United States. Her maternal grandmother was born in a non-endemic country. She did not have any occupational exposures and never saw vectors around her residence. Her only recreational exposure was gardening in a 500 square foot non-wooded backyard; however, as a result of it being an unsuitable habitat for the vector, we considered it a low risk exposure. She was most likely exposed in her birth county or during her 2 years living in Louisiana.

Case-patient 4.

A 72-year-old Caucasian male with history of a triple bypass without blood transfusion in 1998 and 15-year history of controlled hypertension donated blood in December 2010. The Ortho *T. cruzi* ELISA screening test values were consistently positive (5.71, 5.73, and 6.30). The RIPA confirmation was positive. Upon receipt of his test results, he sought care from his primary care physician. His doctor told him that his test results were "likely a false positive" caused by his lack of Hispanic ethnicity and deferred further work-up and treatment.

In May 2013, he was enrolled into our research study. A blood sample from the same month was positive on all diagnostic tests. An electrocardiogram found sinus rhythm with first degree atrioventricular block with inferior-posterior myocardial infarction. These changes could be caused by Chagas heart disease or this patient's ischemic heart disease. An echocardiogram 1 month later was normal.

Case-patient 4 was born in Bell County, a rural county 154 miles northwest of Houston, where he resided for 18 years. He then spent 2 years on Navy bases in California, Nevada, Oklahoma, and Florida. He had since lived in a suburban part of Ft. Bend County, 36 miles southwest of Houston. His mother was born in the Czech Republic. His maternal grandmother was born in a non-endemic country. Travel history included one daytrip to Cancun during a cruise. Neither occupational exposure nor seeing vector around his residence was reported. Recreational exposure included a life-long history of hunting; however, his outdoor and vector exposure was minimal with this activity. He only hunted birds, never skinned animals, never used hunting stands, and never stayed the night at hunting locations (camping, deer leases, etc.). Case-patient 4 was most likely infected from a residential source, either from his rural hometown or from his moderately rural suburban home.

Case-patient 5.

A 21-year-old healthy Caucasian male donated blood in 2011. The Ortho *T. cruzi* ELISA screening test and RIPA confirmation were positive. Upon receiving his test

results from the blood center, he saw his primary care physician, an infectious disease doctor and a consulting infectious disease researcher from an academic institution. His electrocardiogram was normal. He received treatment with benznidazole in 2011. Yearly follow-ups have been normal. In August 2013, he was enrolled into our research study. A blood sample from the same month was positive on all diagnostic tests. As expected, his electrocardiogram was normal.

Case-patient 5 was born and resided in the same suburb in Harris County, TX despite moving once. His mother was born and had lived in the same county for the duration of her life. His mother did not report any symptoms consistent with cardiac disease. To our knowledge, his mother has never been tested for *T. cruzi* infection. His maternal grandmother was born in a non-endemic country. Occupational history included 1 week in 2003 performing landscaping for a charity organization in Cameron County, a Texas–Mexico border town. During this trip, he slept in a gym in good condition. He reported that other travel companions on this trip tested negative for *T. cruzi* infection; however, specific testing information was not available. Case-patient 5 reported never seeing the vector around his residence. Recreational exposure included a 15-year history in a civic youth organization, which involved monthly camping and outdoor activities in Texas and Missouri. While camping he slept in tents, lean-tos, and “rarely” without shelter. He recalled waking up 5 years ago with a “chagoma”-like lesion that he considered a spider bite at the time and did not treat. As a result of the lack of evidence for congenital transmission, we considered regular camping and outdoor activities the highest probability of transmission exposure for Case-patient 5.

DISCUSSION

This report adds an additional five autochthonous Chagas disease cases in the United States to the literature. All case-patients had lived in rural counties and/or had high levels of outdoor exposure, possibly leading to autochthonous infection. Figure 1 displays the geographic areas of importance, Table 1 summarizes the exposure risk for disease transmission, and Table 2 summarizes the testing results for our five case-patients. Despite our small sample size, our findings suggest supporting evidence of an ongoing domestic cycle occurring in southeast Texas resulting in locally acquired cases.⁹

The United States is considered a non-endemic country for transmission, with rare reports of locally acquired human cases occurring.¹² Since active blood donor screening began in 2007; we have begun to learn more about the burden and source of infection in this country. The US CDC recently reported rare cases of domestically acquired infection from a large nationwide follow-up study of infected blood donors.¹² In contrast, our pilot study of 17 RIPA-positive blood donors in the Houston area found 35% (6 of 17) with evidence of locally acquired infection.¹⁴ Five of those six with evidence of autochthonous infection are reported here. One person was not described in this case report caused by the inability to rule out the source of infection from their urban Mexican birth city, despite a report of seeing the vector around their Houston residence and poor living conditions.

Our case reports showed non-traditional exposures. The primary exposure in endemic countries where the vector species are adapted to peridomestic settings is *Triatoma*-infested homes with substandard housing structures.¹ With higher standards of living in

the United States, it is not surprising that vector exposure is more likely occurring by increased outdoor exposure. Camping and hunting are two outdoor exposure activities shown by our case reports as probable sources of infection. These two exposure activities have also been previously described in United States domestically acquired case reports.¹² Inadequate temporary lodging and/or increased exposure to the vector during these activities may be important contributing factors for transmission associated with these outdoor activities.¹⁹ Exposure to infectious blood while skinning a dead animal without gloves is another possible important transmission route.¹⁹

Congenital transmission is a possible source of infection in the United States, given the number of Latin American immigrant women in this country. None of the five case-patients reported here were children of mothers who had immigrated to the United States from Latin America. However, without testing the mothers as well we cannot rule out possible congenital transmission completely because their mothers may have acquired Chagas disease from autochthonous transmission, blood transfusion before 2007, or congenitally from their respective mothers. All potential sources of infection should be considered when evaluating *T. cruzi*-infected patients in the United States. Additionally, children born to mothers who are diagnosed with Chagas disease should be evaluated.

Interestingly, Case-patient 3 did not have significant outdoor exposure. Her only probable source of infection was being born in a rural county, as her current suburban residence was not conducive to the vector's habitat. Because she was in the indeterminate form of chronic infection, it is likely that she could have been exposed at any point in her life. Of note, Case-patient 3 did have three pregnancies resulting in four daughters. One child was tested for *T. cruzi* infection after discovering her mother's disease status. The one child was negative, but no other children have been tested. These children are all of childbearing potential with two grandchildren having been born. Previous studies of Latin American immigrant women in Houston, TX assessing seroprevalence of maternal infection during pregnancy found low rates; however, they remained consistent over a 10-year time point.^{20,21} Screening women of childbearing potential from rural counties in southeast Texas might be beneficial for prevention of congenital transmission.

These case-patient reports have evident limitations. Given the manner of disease diagnosis, we were unable to know the exact origin or duration of infection. The site of potential acquisition of infection was based on self-reported histories that were potentially inaccurate. The likely sites where infection occurred were hypothesized based on interviews assessing specific exposure variables. As most of these case-patients were elderly, there is a chance of recall bias. It is possible that we missed important exposures; however, the questionnaire was developed based on expert opinion and previously used questionnaires in a similar population. In addition to the questionnaire, exposure investigations included visiting residences, performing environmental assessments, and testing of available *Triatoma* insects. The environmental assessments included analyzing the housing structure for possible vector infestation, determine location of possible vector nests near residence, and rural influence on supporting vector habitats. Given the thorough nature of the investigations, we feel confident that all data presented in these case-patient reports are accurate.

Of additional interest is the finding that for two of the patients reported here, their primary care physician assumed that positive serology for *T. cruzi* infections represented

“false positives.” Such findings are consistent with previous CDC observations of low awareness about Chagas disease among practicing physicians in the United States.²² It is important that physicians are aware that blood donors testing positive for *T. cruzi* infection can be true positives, despite a lack of history to an endemic country.

With the onset of active blood donor screening, more *T. cruzi* cases have been reported since 2007. Some of these cases are suspected locally acquired infections, although exact origin of transmission will likely never be known. Inasmuch as history of travel and/or being born in an endemic country is typically used in the differential diagnosis, these patients are at risk for being undiagnosed with potential Chagas cardiac disease. At this current juncture, the exact risks associated with United States blood donors screening positive for the parasite that causes Chagas disease are unknown. Accordingly, it is imperative that additional testing be performed to ascertain the true disease status of these individuals. Finally, three of these five case-patient reports had electrocardiogram abnormalities consistent with Chagas cardiac disease. Although we do not know all the potential other underlying causes of these case-patients’ cardiac disease, they highlight the importance of physician awareness and accurate diagnosis. With Chagas cardiac disease being progressive, it is imperative that persons at high risk be screened for *T. cruzi* infection. Additional studies are needed to better understand the risk of autochthonous transmission in southeast Texas.

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FIGURE 1. County of birth, county of current residence, and county of additional locations of importance by case-patient report numbers.

TABLE 1

Exposure risk for multiple transmission sources for all five case-patient reports

	Birthplace	Area surrounding current residence	Congenital	Occupational	Recreational-camping	Recreational-hunting
Case-Patient 1	++	+	0	++	0	+++
Case-Patient 2	++	+++	0	0	+	0
Case-Patient 3	+++	+	0	0	0	0
Case-Patient 4	+++	++	0	0	0	+
Case-	0	0	+	+	+++	0

Patient 5						
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High risk: +++; Moderate risk: ++; Low risk: +; No risk: 0.

TABLE 2

Serologic diagnostic tests performed at Gulf Coast Regional Blood Center, Baylor College of Medicine, and the Centers for Disease Control

	Gulf Coast Regional Blood Center		Centers for Disease Control and Prevention-Parasitic Division		Baylor College of Medicine		
	Ortho <i>T. cruzi</i> ELISA	RIPA	Weiner ELISA	Tesa IB	IFA	Stat-Pak	DPP
Case-Patient 1	+	+	-/-*	+	+	-	+
Case-Patient 2	+	+	+	+	+	+	+
Case-Patient 3	+	+	-/+*	+	+	+	+
Case-Patient 4	+	+	+	+	+	+	+
Case-Patient 5	+	+	+	+	+	+	+

* Two tests were performed as the first test was negative.

Figure 1

