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Donor-Derived *Trypanosoma cruzi* Infection in Solid Organ Recipients in the United States, 2001–2011

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Abstract

Although *Trypanosoma cruzi*, the parasite that causes Chagas disease, can be transmitted via organ transplantation, liver and kidney transplantation from infected donors may be feasible. We describe the outcomes of 32 transplant recipients who received organs from 14 *T. cruzi* seropositive donors in the United States from 2001 to 2011. Transmission was confirmed in 9 recipients from 6 donors, including 3 of 4 (75%) heart transplant recipients, 2 of 10 (20%) liver recipients and 2 of 15 (13%) kidney recipients. Recommended monitoring posttransplant consisted of regular testing by PCR, hemoculture, and serology. Thirteen recipients had no or incomplete monitoring; transmission was confirmed in five of these recipients. Four of the five recipients had symptomatic disease and all four died although death was directly related to Chagas disease in only one. Nineteen recipients had partial or complete monitoring for *T. cruzi* infection with weekly testing by PCR, hemoculture and serology; transmission was confirmed in 4 of 19 recipients with no cases of symptomatic disease. Our results suggest that liver and kidney transplantation from *T. cruzi* seropositive donors may be feasible when the recommended monitoring schedule for *T. cruzi* infection is followed and prompt therapy with benznidazole can be administered.

Keywords

Chagas; donor; transplantation; transmission

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Introduction

Chagas disease, caused by the protozoan parasite *Trypanosoma cruzi*, is endemic in many parts of Mexico, Central America and South America. The most common mode of *T. cruzi* transmission is vector-borne, via the feces of infected triatomine bugs. *T. cruzi* parasites can also be transmitted by congenital and foodborne routes, transfusion and transplantation. Chronic infection persists for life in the absence of treatment, and reactivation in immunosuppressed patients may result in severe disease with increased risk of mortality (1). Currently, two drugs are available to treat Chagas disease (2). Nifurtimox and benznidazole are not approved by the Food and Drug Administration (FDA) but are available in the United States through the Centers for Disease Control and Prevention (CDC) Drug Service under FDA-approved protocols.

An estimated eight million people in the Americas have Chagas disease (3) and Chagas disease is now found in previously nonendemic urban areas of Latin America and other regions of the world (4). In the United States, an estimated 300,000 Latin American immigrants have Chagas disease (5). In addition, at least 23 U.S. residents and possibly many more have become infected via domestic vector-borne transmission (6). Documented human cases of *T. cruzi* infection have been acquired in the United States by vector-borne, congenital, transfusion and transplant transmission (7).

Three investigations of donor-derived *T. cruzi* infection in U.S. organ transplant recipients were previously reported (1,8,9), and published recommendations for screening and treatment of Chagas disease in organ transplant recipients in the United States exist (10). The evidence to support these recommendations included results of several previously unpublished potential transplant-transmission investigations.

The first documented case of transplant transmission was reported in the United States in 2001 (8). This report describes the cumulative CDC experience identifying chronically infected organ donors and prospectively monitoring recipients of transplanted organs from those donors with comparisons based on adherence to the recommended monitoring strategy. We also describe details of four previously unpublished transplant-transmitted *T. cruzi* infections in organ recipients from three donors, including the first successful heart transplantation in the United States from a *T. cruzi* seropositive donor.

Materials and Methods

CDC was notified of potential transplant transmission of *T. cruzi* when either infected donors or recipients were identified. Donor infections were identified retrospectively when transplant-associated transmission was suspected in organ recipients or prospectively as a result of risk-based organ donor screening. Recipient infections were identified either after the development of symptomatic disease or after monitoring recipients for acute infection posttransplant.

CDC requested samples for confirmatory testing for any suspected infection. The international standard for confirming the diagnosis of chronic Chagas disease requires positive results on at least two different format serologic tests, preferably using different

antigen preparations. Acute Chagas disease is diagnosed by detection of *T. cruzi* parasite in blood smears or by polymerase chain reaction (PCR) testing of serial blood samples, documenting parasitemia. Serologic testing was performed on donor blood specimens to confirm *T. cruzi* infection status; most donors were tested with a CDC in-house immunofluorescence assay (IFA) based on fixed epimastigotes and the commercial Chagatest ELISA recombinante v.3.0 (Wiener Laboratorios, Argentina). Confirmation of chronic Chagas disease in the donor was determined by positive results on two or more serologic assays or, in cases with indeterminate serologic testing results, when transmission of *T. cruzi* was documented in recipients of organs from that donor. Recipients were tested for antibody to *T. cruzi* at or soon after transplantation to document baseline *T. cruzi* status.

Testing for acute infection in recipients included microscopic examination of peripheral blood, hemoculture and PCR testing at CDC. Serologic testing was also performed to detect any developing antibody response to the parasite. Acute infection was confirmed by positive hemoculture or detection of trypomastigotes in peripheral blood; confirmation based on PCR testing was considered sufficient evidence of infection in many cases. CDC PCR testing approaches changed over time as advances in *T. cruzi* PCR methods became available. Prior to 2006, a PCR assay targeting the kinetoplast (minicircle DNA) was used (11). Cloning and sequencing of amplicons was performed on some specimens. A positive PCR result for one specimen was considered sufficient to presume transmission. From 2006 to 2008, a PCR assay targeting the TCZ minisatellite was also used (12). Amplicons from specimens only positive by minicircle PCR were cloned and sequenced for confirmation. Positive PCR results for both assays on a single specimen were considered sufficient to presume transmission. Since 2008 the PCR testing algorithm was changed to include three PCR assays targeting the kinetoplast, the TCZ mini-satellite and the small subunit ribosomal RNA gene, respectively (13). Positive PCR results with at least two of these assays on two consecutive specimens were required for an organ recipient to be considered infected.

Recommended monitoring involved PCR testing of whole blood specimens collected at weekly intervals posttransplant for 8–12 weeks with concurrent hemoculture and serological testing at CDC. Clinicians caring for recipients were advised to examine peripheral blood smears and buffy coat preparations at the local facility. After the first 2–3 months of intensive monitoring, monthly testing was performed for a total of 6 months posttransplant. More frequent testing was recommended if the recipient developed illness or immunosuppression was increased for treatment of rejection. After the initial 6 months, additional testing to monitor for infection was also based on development of illness or increase in immunosuppression.

Adherence to the posttransplant monitoring recommendations varied among investigations. To demonstrate the impact of monitoring, investigations were categorized by intensity of monitoring. Investigations with recommended monitoring were those where (1) PCR monitoring was initiated promptly with testing of specimens collected within 2 weeks of transplantation, (2) intensive weekly testing was performed for 2–3 months and (3) biweekly to monthly testing was performed for 6 or more months or until *T. cruzi* infection was diagnosed. We defined adherence to recommended monitoring as complete if all three criteria for recommended monitoring were met; partial if two of the three criteria were met;

and incomplete if only one criterion was met or no testing was performed prior to diagnosis at the time of symptom development in the recipient.

Donor histories were reviewed for potential risk factors for Chagas disease, including birth or residence in Latin America, mother's immigration status and previous transplantation or transfusion. Recipients were interviewed regarding risk factors and clinical information was extracted from medical records.

Results

From 2001 to 2011, CDC helped investigate potential transmission of *T. cruzi* from 14 seropositive organ donors to 34 solid organ transplant recipients who were seronegative at the time of transplantation (Tables 1 and 2). For 13 of 14 donors, birth country or mother's birth country was in Latin America; one donor and his mother were both born in the United States (Table 3). The organs from the 14 donors were procured in the following states: California (4), New York (4), Florida (2), Pennsylvania (1), Georgia (1), Tennessee (1) and Texas (1). The 34 transplant recipients received the following organs: isolated kidney (14), isolated liver (11), isolated heart (4), combined liver-kidney (1), combined kidney-pancreas (1) and bilateral lung (1). Three corneas from two donors and pancreatic islet cells from one donor were transplanted but information about those recipients is not included in this analysis. Two organ recipients were excluded from further analysis due to insufficient data (Table 1). The following results are based on analysis of the remaining 32 organ recipients.

Transplant transmission of *T. cruzi* was confirmed in 9 of the 19 recipients of organs from 6 donors (investigations 1, 4–6, 12, 14) and included three heart, two liver, two kidney, one combined kidney-pancreas, and one bilateral lung recipients. Infection was diagnosed only after the development of symptomatic disease in four recipients, all of whom had positive hemocultures (1,8,9) (Table 2). *T. cruzi* infection in one kidney recipient (Table 1, investigation 1) was diagnosed by hemoculture after the other recipients in the investigation developed symptomatic illness. Infection was diagnosed in the absence of symptoms by PCR monitoring in the other four recipients, two of whom also had a positive hemoculture (Table 2). The median interval from transplantation to diagnosis of infection was 8 weeks (range: 3–29 weeks). All recipients who developed evidence of infection were treated with either nifurtimox or benznidazole, obtained through the CDC Drug Service. The other ten organ recipients in these six investigations did not develop evidence of infection during the period they were monitored (median: 29 weeks, range: 7–42 weeks).

In seven investigations (investigations 2, 3, 7, 9–11, 13), none of the 13 recipients developed evidence of infection during the monitoring period. The median duration of follow-up was 37 weeks (range: 12–145 weeks). Although monitoring was not always performed on a weekly basis as recommended, most of these recipients were tested at least monthly for 5 or more months following transplantation (Table 2). In investigation 3, the only organ recipient received chemoprophylactic treatment and complete monitoring (for 145 weeks) with no evidence of infection during the follow-up period.

Death within 1 year of transplantation was observed in six of the 32 recipients. All four of the recipients who developed symptomatic Chagas disease died; however, Chagas disease was reported as the cause of death for only one recipient (Table 1). Two recipients who were monitored by PCR died within 1 year. One was infected and her infection was detected by complete PCR monitoring. Chagas disease was not listed as the cause of death. The other recipient died without evidence of *T. cruzi* infection after partial monitoring. An additional death occurred more than 4 years after transplant, leading to a total of eight deaths reported in this case series (Table 1).

Three investigations involving four previously unreported cases of transplant-transmitted *T. cruzi* infection associated are described below. In all cases, donor infection status was recognized at the time of transplant and prospective monitoring led to prompt recognition of *T. cruzi* transmission with successful intervention of antitrypanosomal treatment to prevent clinical disease, including the first description of a successful outcome in a heart transplant recipient with donor-derived *T. cruzi* infection in the United States. The outcomes of the other investigations are summarized in Table 1.

Investigation 6

The donor was a 60-year-old Bolivian woman who had lived in the United States for 15 years before her death from stroke in 2006. A pre-mortem serum sample from the donor was tested at CDC with positive results on IFA (titer 1:256). The liver was transplanted into one recipient and both kidneys were transplanted into another recipient the following day. Both recipients developed evidence of *T. cruzi* infection.

Liver recipient

The liver recipient was a 56-year-old U.S.-born man who had hepatitis C virus (HCV) cirrhosis. Immunosuppression included induction therapy with daclizumab followed by maintenance therapy with tacrolimus, mycophenolate, and prednisone. Based on diagnosis of infection in the organ donor, *T. cruzi* PCR testing was performed at CDC. The results were negative at weeks 1 and 3 but positive 8 weeks after transplant although the recipient did not have signs or symptoms of Chagas disease. No *T. cruzi* parasites were seen on stained peripheral blood smears examined at CDC. Antitrypanosomal therapy with nifurtimox was initiated at this time. Infection was confirmed 15 weeks posttransplant by positive hemoculture of a pretreatment sample. Over the next 2 months the patient developed hallucinations, tremors, ataxia, pain, anorexia and weight loss. Nifurtimox was discontinued after approximately 8 weeks of therapy and all symptoms resolved. Benznidazole was obtained from the CDC Drug Service at that time; however, the patient did not take the medication and was lost to follow-up for over 1 year. In late 2007, he returned to care and was asymptomatic with stable liver function. He was lost to follow-up again until the middle of 2008. At that time *T. cruzi* PCR and serologic results were negative. Over the next year, he was hospitalized several times due to chronic kidney disease and eventually required hemodialysis. *T. cruzi* PCR and serologic testing were negative when last performed in June 2010. Later that year he died at another hospital from complications unrelated to Chagas disease.

Right and left kidney recipient

The recipient of both kidneys was a 73-year-old woman. She was monitored weekly after transplantation for evidence of *T. cruzi* transmission by PCR, serologic testing, hemoculture and blood smear examination. The results of all testing were negative until 5 weeks posttransplant. The sample collected at that time tested positive by PCR but negative by hemoculture and serology. Nifurtimox therapy was initiated 1 week after the positive PCR result but was discontinued after the patient developed tremors; benznidazole was obtained from CDC but the patient died from kidney failure before benznidazole treatment was initiated.

Investigation 12

The donor was a 22-year-old man from Puebla, Mexico who had moved to New York City in 2004. In 2010, he was declared brain dead from head trauma. Six days later, heart and liver transplantations were performed. A post-mortem serum specimen had been submitted for *T. cruzi* testing but results were not available until after transplantation. The donor serum tested positive for antibodies to *T. cruzi* by the Ortho® *T. cruzi* ELISA Test System (Ortho Clinical Diagnostics, Raritan, NJ); additional serologic testing was performed at two other laboratories with reported positive results. CDC was notified regarding the testing results and confirmed the donor infection serologically. The results of PCR testing and hemoculture of donor blood were negative. Kidney transplantation was subsequently performed on two recipients after the additional results were reported. Baseline samples from all four recipients had negative results by serological testing at CDC. Only the heart recipient developed evidence of *T. cruzi* infection.

Heart recipient

The heart recipient was a 20-year-old woman from Israel living in New York City who had familial restrictive cardiomyopathy. After obtaining informed consent regarding the potential for Chagas disease transmission because of donor risk factors, she underwent heart transplant and tricuspid valve annuloplasty. Immunosuppression included mycophenolate, tacrolimus, and prednisone without induction therapy. The recipient was monitored weekly by PCR and serologic testing starting the day of surgery. Three weeks after transplant, PCR results were weakly positive and benznidazole therapy was started. Eight weeks after transplantation, the patient returned to Israel where she completed a 60-day course of benznidazole and continued to be monitored weekly by PCR, hemoculture and serologic testing until week 12 posttransplantation and less frequently thereafter. All test results were negative during an 8-month monitoring period. The recipient remains asymptomatic with stable graft function at least 24 months after transplantation.

Liver recipient

The liver recipient was a 46-year-old man originally from Ecuador who had sclerosing cholangitis. He was living in New York City with no reported travel back to Ecuador since 1983. Serologic testing of saved serum was negative prior to transplantation. Immunosuppression included mycophenolate, tacrolimus and prednisone without induction therapy. The recipient was monitored by PCR and serologic testing for the first 12

weeks posttransplant and monthly for an additional 2 months. All results were negative including a blood specimen collected 9 months (42 weeks) posttransplant. He has remained asymptomatic with stable graft function at least 30 months after transplantation.

Kidney recipient A

One kidney recipient was a 56-year-old man born in Jamaica and residing in New York City for 30 years. He had end stage renal disease secondary to diabetes mellitus and hypertension and history of prior failed kidney transplantation. The risk of *T. cruzi* transmission was weighed against high recipient panel reactive antibody (PRA 97%) and negative cross match with the donor, and kidney transplantation was performed with informed consent. Immunosuppression included thymoglobulin, corticosteroids, mycophenolate and tacrolimus. Two weeks later the recipient was diagnosed with grade IIA acute cellular rejection (C4d positive) and was treated with high-dose corticosteroids, thymoglobulin and intravenous immunoglobulin without any subsequent episodes of rejection. He was monitored weekly by PCR and serologic testing for the first 3 months posttransplant. All results were negative, including testing of blood specimens collected 5 and 8 months posttransplant. He has remained asymptomatic with stable graft function at least 30 months after transplantation.

Kidney recipient B

The second kidney transplant recipient was a 66-year-old woman from Maryland without prior travel to Mexico or Central or South America. The patient had a complex medical history, including hypertension and end stage renal disease. Immunosuppression included basiliximab, corticosteroids, tacrolimus and mycophenolate. She was monitored weekly by PCR and serologic testing for the first 3 months posttransplant and monthly for an additional 4 months. All testing was negative, including a blood specimen collected 8 months posttransplant. She has remained asymptomatic with stable graft function at least 30 months after transplantation.

Investigation 14

The donor was a 48-year-old woman, originally from El Salvador, who had lived in the United States for 6 years before her death from stroke in 2011. Prior to her death, the donor had been treated for arrhythmias and reduced ejection fraction (25%). Based on the donor's birth country and clinical presentation, Chagas disease serologic testing was performed at a reference laboratory, and the results were positive. A donor serum sample was also tested at CDC and found to be positive by both IFA and ELISA. Donor infection status was known at the time of liver and lung transplantation and no other organs or tissues were transplanted. The bilateral lung recipient developed *T. cruzi* infection.

Bilateral lung recipient

The lung recipient was a 36-year-old man from North Dakota who had cystic fibrosis. Immunosuppression included prednisone, mycophenolate and tacrolimus. Monitoring began 1 week posttransplant and continued at weekly intervals for 9 weeks posttransplant then at biweekly intervals up to 17 weeks posttransplant; serologic and PCR test results were

negative. Following 12 weeks of no further testing, specimens received at 29 and 30 weeks posttransplant tested positive by PCR, hemoculture and/or serology (TESA immunoblot). The patient was asymptomatic. Treatment with benznidazole began 31 weeks posttransplant. The patient developed tacrolimus toxicity at week 8 with nausea that resolved after adjustment of tacrolimus dosing, and he completed the benznidazole course. PCR testing results from a sample collected at week 34 were negative although serology remained positive. By week 43, the results of serologic and PCR testing were negative. Routine follow-up testing at 61 and 63 weeks posttransplant were again positive by PCR, and a second course of treatment was initiated. The patient was asymptomatic but the outcome remains undefined.

Liver recipient

The liver recipient was a 42-year-old woman from Tennessee with hepatic sarcoidosis and prior liver transplantation but no travel outside the United States. She developed autoimmune hepatitis and underwent a second liver transplant from the *T. cruzi* infected donor. However, due to primary nonfunction of the second liver, a third liver transplantation was performed 2 days later. Her course was complicated by kidney failure, multiple intra-abdominal surgeries for hepatic artery repair, kidney failure and multiple episodes of sepsis; she died 11 weeks after the third transplant due to septic shock. Monitoring for possible *T. cruzi* transmission began 4 days after the transplant from the infected donor. Weekly specimens were tested for 1 month. No specimens were submitted for the next 3 weeks, until the patient was admitted for nausea and vomiting 7 weeks posttransplant. Serologic and PCR results were negative for evidence of *T. cruzi* infection.

Discussion

Due to the increasing disparity between the number of organ transplant candidates on the waiting list and available organs, intense pressure exists to safely expand the donor pool. The use of organs from infected donors is considered acceptable when transmission can be easily monitored, detected and treated without compromising patient and graft survival. For example, organs from cytomegalovirus (CMV)-seropositive donors have been successfully transplanted in CMV-seronegative recipients with effective prophylaxis or preemptive strategies that that can minimize risk of disease in the recipient. *T. cruzi* seropositive donors are a potential source for organs. Although uninfected recipients who receive an organ from a *T. cruzi*-infected donor may develop acute *T. cruzi* infection, transmission under these circumstances is not universal. In the investigations summarized here, nine *T. cruzi* infections were diagnosed. Five infections were only diagnosed after development of symptomatic Chagas disease in four recipients in the absence of monitoring. The other four infections were identified by either complete or partial PCR monitoring. None of the 19 patients with complete or partial monitoring developed symptomatic Chagas disease (Figure 1). Our experience suggests that intensive monitoring and prompt *T. cruzi* therapy when transmission occurs may be a safe and effective management strategy for recipients of livers and kidneys from seropositive donors.

In 2011, published recommendations from the Chagas in Transplant Working Group advised targeted screening of donors from Mexico, Central America and South America and consideration of transplantation of liver and kidneys from infected donors with prospective monitoring for infection and prompt treatment. The data presented here provide further evidence to support the recommendations for donor screening and prospective recipient monitoring when organs from infected donors are transplanted. The prospective monitoring strategy is also recommended by the Chagas Disease Argentine Collaborative Transplant Consortium (14).

Although advocated by some authors (15,16,17), we agree with previously published guidelines that do not recommend chemoprophylaxis in transplant recipients from *T. cruzi*-seropositive donors. Our data suggest that preemptive monitoring identifies infection that can be treated before disease occurs. Although limited by sample size, preemptive monitoring appears to be a safe strategy. The rationale for recommending against prophylaxis also includes avoidance of potential drug toxicity and interactions. Furthermore, the efficacy of chemoprophylaxis remains undefined; parasitologic and molecular methods are not sufficiently sensitive to confirm that the recipients remain uninfected posttreatment and, as demonstrated by our data, immunosuppressed patients who become infected are unlikely to seroconvert. In this setting, the lack of detectable antibody to *T. cruzi* does not exclude infection.

Heart transplantation from *T. cruzi* seropositive donors is currently not recommended. In Argentina, hearts from *T. cruzi*-infected donors are discarded (14). The Chagas in Transplant Working Group also advises against heart transplantation from *T. cruzi* seropositive donors. In our investigations, four heart recipients were from seropositive donors. (Table 2) Of the three infected recipients, two were previously reported (1,9) and one is described here. The fourth recipient of a heart from a seropositive donor (investigation 10) has not developed detectable infection, but the donor was not an immigrant from Latin America and he was suspected to have acquired *T. cruzi* infection domestically. The donor was seropositive when tested at two commercial laboratories and was positive on ELISA but not IFA at CDC. The heart recipient in investigation 12 is one of two reports of a good outcome associated with heart transplantation from a confirmed *T. cruzi* seropositive donor with implementation of a prospective monitoring and treatment strategy (18). Infection was detected by PCR testing and clinical disease was prevented by a full course of benznidazole treatment. The results of follow-up testing have been negative to date. Although this case illustrates the potential efficacy of this strategy in heart transplantation, transmission did occur and we still favor avoiding this organ type. Furthermore, infection in the lung recipient from a *T. cruzi* seropositive donor (investigation 14) demonstrates that transmission may occur via lung transplantation as well. To our knowledge, this is the first reported transmission of *T. cruzi* via lung transplantation.

Before the publication of the guidelines from the Chagas in Transplant Working Group, a survey of all 58 U.S. organ procurement organizations (OPOs) revealed that only 11 (19%) OPOs performed any donor screening for Chagas disease (19). If the donor is known to be infected, transplant centers can make informed decisions and appropriately monitor recipients of organs from seropositive donors. Based on our investigations, the likelihood

of transmission appears to vary by organ type. Transplanted organ types associated with infection included heart (3/4; 75%), liver (2/10; 20%), kidney (2/15; 13%), combined liver-kidney (0/1; 0%), combined kidney–pancreas (1/1; 100%) and bilateral lung (1/1; 100%). In the reported investigations, intensive monitoring of recipients led to prompt recognition and treatment of transplant-associated *T. cruzi* infection. This evidence supports the recommendation that the liver and kidneys from seropositive donors may be transplanted provided the transplant center and recipients are committed to appropriate prospective monitoring and advance planning for potential therapy (10,20). Further investigation is needed to understand the risk for transmission and the factors that affect outcomes associated with transplantation of organs from *T. cruzi* infected donors, by organ type and recipient characteristics.

Abbreviations:

CDC	Centers for Disease Control and Prevention
CMV	cytomegalovirus
FDA	Food and Drug Administration
HCV	hepatitis C virus
IFA	immunofluorescence assay
OPO	organ procurement organization
PCR	polymerase chain reaction

References

1. Kun H, Moore A, Mascola L, et al. Transmission of *Trypanosoma cruzi* by heart transplantation. Clin Infect Dis 2009; 48: 1534–1540. [PubMed: 19400748]
2. Bern C, Montgomery SP, Herwaldt BL, et al. Evaluation and treatment of Chagas disease in the United States: A systematic review. JAMA 2007; 298: 2171–2181. [PubMed: 18000201]
3. Organizacion Panamericana de la Salud. Estimacion cuantitativa de la enfermedad de Chagas en las Americas. Montevideo, Uruguay: Organizacion Panamericana de la Salud, 2006.
4. Dias JC, Silveira AC, Schofield CJ. The impact of Chagas disease control in Latin America: A review. Mem Inst Oswaldo Cruz 2002; 97: 603–612. [PubMed: 12219120]
5. Bern C, Montgomery SP. An estimate of the burden of Chagas disease in the United States. Clin Infect Dis 2009; 49: e52–e54. [PubMed: 19640226]
6. Cantey PT, Stramer SL, Townsend RL, et al. 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 2012; 52: 1922–1930. [PubMed: 22404755]
7. Bern C, Kjos S, Yabsley MJ, Montgomery SP. *Trypanosoma cruzi* and Chagas' disease in the United States. Clin Microbiol Rev 2011; 24: 655–681. [PubMed: 21976603]
8. Centers for Disease Control and Prevention (CDC). Chagas disease after organ transplantation—United States, 2001. MMWR 2002; 51: 210–212. [PubMed: 11922190]
9. Centers for Disease Control and Prevention (CDC). Chagas disease after organ transplantation—Los Angeles, California, 2006. MMWR 2006; 55: 798–800. [PubMed: 16874295]
10. Chin-Hong PV, Schwartz BS, Bern C, et al. Screening and treatment of Chagas disease in organ transplant recipients in the United States: Recommendations from the Chagas in transplant working group. Am J Transplant 2011; 11: 672–680. [PubMed: 21401868]

11. Sturm NR, Degrave W, Morel C, Simpson L. Sensitive detection and schizodeme classification of *Trypanosoma cruzi* cells by amplification of kinetoplast minicircle DNA sequences: Use in diagnosis of Chagas' disease. Mol Biochem Parasitol 1989; 33: 205–214. [PubMed: 2565018]
12. Virreira M, Torrico F, Truyens C, et al. Comparison of polymerase chain reaction methods for reliable and easy detection of congenital *Trypanosoma cruzi* infection. Am J Trop Med Hyg 2003; 68: 574–582. [PubMed: 12812349]
13. Qvarnstrom Y, Schijman AG, Veron V, Aznar C, Steurer F, da Silva AJ. Sensitive and specific detection of *Trypanosoma cruzi* DNA in clinical specimens using a multi-target real-time PCR approach. PLoS Negl Trop Dis 2012; 6: e1689. [PubMed: 22802973]
14. Chagas' Disease Argentine Collaborative Transplant Consortium, Casadei D. Chagas' disease and solid organ transplantation. Transplant Proc 2010; 42: 3354–3359. [PubMed: 21094779]
15. D'Albuquerque LA, Gonzalez AM, Filho HL, et al. Liver transplantation from deceased donors serologically positive for Chagas disease. Am J Transplant 2007; 7: 680–684. [PubMed: 17217440]
16. Ortiz AM, Troncoso P, Sainz M, Vilches S. Prophylaxis and treatment of Chagas disease in renal transplant donor and recipient: Case report. Transplant Proc 2010; 42: 393–394. [PubMed: 20172356]
17. Salvador F, Len O, Molina I, et al. Safety of liver transplantation with Chagas disease-seropositive donors for seronegative recipients. Liver Transpl 2011; 17: 1304–1308. [PubMed: 21618698]
18. Amato Neto V [Heart transplantation: donor with Chagas' disease and clinical course of the receptor]. Rev Hosp Clin Fac Med Sao Paulo 1992; 47: 92. [PubMed: 1340020]
19. Schwartz BS, Paster M, Ison MG, Chin-Hong PV. Organ donor screening practices for *Trypanosoma cruzi* infection among US organ procurement organizations. Am J Transplant 2011; 11: 848–851. [PubMed: 21426487]
20. McCormack L, Quinonez E, Goldaracena N, et al. Liver transplantation using Chagas-infected donors in uninfected recipients: A single-center experience without prophylactic therapy. Am J Transplant 2012; 12: 2832–2837. [PubMed: 22813351]

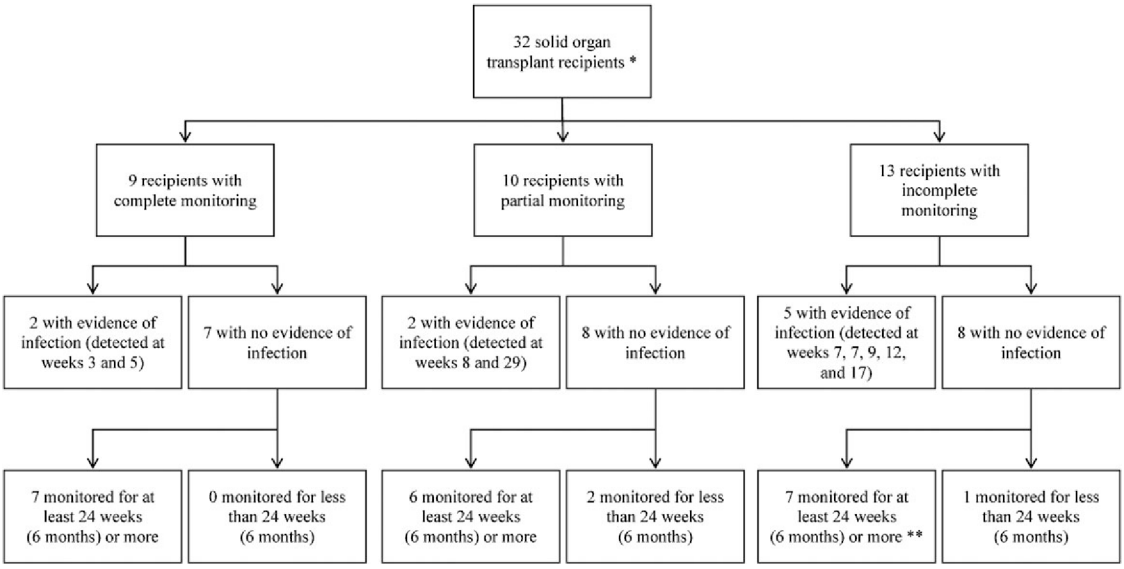

Figure 1: Solid organ recipient outcomes by PCR monitoring category.

* The kidney recipient from investigation 13, who died 4 days post-transplantation, and the liver recipient from investigation 8, whose pretransplant infection status could not be confirmed (Table 1), were not included in the figure or in the analyses. ** Frequency of follow-up monitoring varied by recipient. Some patients who were monitored for at least 6 months were classified as having incomplete monitoring because the other two criteria (prompt and intensive weekly testing) were not met.

Table 1:

Solid organ recipients monitored for donor-derived *T. cruzi* infection in the United States, 2001–2011

Investigation #	Year	State of donation	Organ	Age/Sex	State of transplantation	Monitoring level	Acute Chagas disease diagnosis	Transplant to diagnosis of infection (weeks)	Length of monitoring (weeks)	Outcome of recipient	Transplant to death (weeks)	Reported cause of death
1	2001	GA	Liver	32 yo female	GA	Incomplete	After symptomatic	12	12	Died	17	Rejection
			Kidney and pancreas	37 yo female	GA	Incomplete	After symptomatic	7	7	Died	31	Chagas myocarditis
			Kidney	69 yo female	AZ	Incomplete	After other recipients became symptomatic	17	57	Alive		
2	2005	TX	Liver and kidney	48 yo male	TX	Incomplete			12	Alive		
			Kidney	32 yo female	NY	Incomplete			31	Alive		
3	2005	CA	Liver	53 yo male	CA	Complete *			145	Alive		
4	2006	CA	Heart	64 yo male	CA	Incomplete	After symptomatic	9	10	Died	20	Rejection
			Liver	56 yo female	CA	Partial			28	Alive		
			Kidney	17 yo female	CA	Incomplete			27	Alive		
			Kidney	20 yo female	CA	Incomplete			30	Alive		
5	2006	CA	Heart	73 yo male	CA	Incomplete	After symptomatic	7	7	Died	25	Cardiac failure
			Liver	46 yo male	CA	Partial			36	Alive		
			Kidney	67 yo female	MO	Partial			28	Alive		
			Kidney	52 yo female	CA	Incomplete			24	Alive		
6	2006	PA	Liver	56 yo male	NY	Partial	By PCR monitoring	8	224	Died	244	Gl bleed
			Bilateral kidneys	73 yo female	PA	Complete	By PCR monitoring	5	15	Died	15	Kidney failure

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Investigation #	Year	State of donation	Organ	Age/Sex	State of transplantation	Monitoring level	Acute Chagas disease diagnosis	Transplant to diagnosis of infection (weeks)	Length of monitoring (weeks)	Outcome of recipient	Transplant to death (weeks)	Reported cause of death
7	2006	NY	Kidney	56 yo female	NY	Incomplete			56	Alive		
			Kidney	61 yo male	NY	Incomplete			53	Alive		
8	2007	NY	Liver	28 yo female	NY	Not applicable **			8	Alive		
9	2008	FL	Liver	55 yo female	FL	Partial			35	Alive		
			Kidney	63 yo male	FL	Complete			48	Alive		
			Kidney	62 yo female	FL	Partial			43	Alive		
10	2008	FL	Heart	14 yo female	FL	Partial			22	Alive		
			Liver	48 yo male	FL	Complete			38	Alive		
11	2010	CA	Kidney	19 yo female	CA	Incomplete			37	Alive		
12	2010	NY (NYC)	Heart	20 yo female	NY (NYC)	Complete	By PCR monitoring	3	35	Alive		
			Liver	46 yo male	NY (NYC)	Complete			42	Alive		
			Kidney	66 yo female	MD	Complete			37	Alive		
			Kidney	56 yo male	NY (NYC)	Complete			37	Alive		
13	2010	NY (NYC)	Liver	65 yo female	WI	Complete			24	Alive		
			Kidney	43 yo female	NY (NYC)	Not applicable ***				Died	0	Information not available
			Kidney	46 yo male	NY (NYC)	Partial			25	Alive		
14	2011	TN	Bilateral lung	36 yo male	WI	Partial	By PCR monitoring	29	61	Alive		
			Liver	42 yo female	TN	Partial			7	Died	11	Septic shock

*Although not in line with the recommended guidelines, the recipient received chemoprophylactic treatment. The recipient received complete monitoring with no evidence of infection during the follow up period.

**Recipient had serologic evidence of *T. cruzi* infection at 7 days post transplant. No pre-transplant specimens were available. This recipient was excluded from the analysis because pre-transplant infection status and Chagas disease risk history could not be determined.

*** Recipient died 4 days after transplantation and was excluded from the analysis because no post-transplant sample was available for testing and infection status post-transplant could not be determined.

Table 2:

Diagnostic testing results for recipients in investigations with transmission

Investigation #	Organ	Transplant to diagnosis of infection (weeks)	Acute Chagas disease diagnosis	PCR	Hemoculture	Serology	Total length of follow-up (weeks)
1	Liver	12	After symptomatic	Not done	**Positive**	Negative	12
	Kidney and pancreas	7	After symptomatic	Not done	**Positive**	**Indeterminate (IFA)**	7
	Kidney	17	After other recipients became symptomatic	Not done	**Positive**	Negative	57
4	Heart	9	After symptomatic	**Positive**	**Positive**	Negative	10
	Liver			Negative	Negative	Negative	29
	Kidney			Negative	Negative	Negative	28
	Kidney			Negative	Negative	Negative	30
5	Heart	7	After symptomatic	**Positive**	**Positive**	Negative	8
	Liver			Negative	Negative	Negative	37
	Kidney			Negative	Negative	Negative	29
	Kidney			Negative	Negative	Negative	24
6	Liver	8	By PCR monitoring	**Positive**	**Positive**	Negative	224
	Bilateral kidneys	5	By PCR monitoring	**Positive**	Negative	Negative	12
12	Heart	3	By PCR monitoring	**Positive**	Negative	Negative	35
	Liver			Negative	Negative	Negative	42
	Kidney			Negative	Negative	Negative	37
	Kidney			Negative	Negative	Negative	37
14	Liver			Negative	Negative	Negative	7
	Bilateral lung	29	By PCR monitoring	**Positive**	**Positive**	**Positive**	29

For recipients not included in this table, all testing results were negative.

Table 3:

Donor demographics and characteristics in *T. cruzi* infection investigations in the United States, 2001–2011

Investigation #	Age/sex	Birth country	Duration of US residence (years)	Cause of death
1	35 yo male	El Salvador	5	Trauma
2	52 yo male	El Salvador	Unknown	Myocardial infarction
3	34 yo female	Mexico	Unknown	Collapsed; h/o cardiac disease
4	23 yo male	US; mother from Mexico	23	Trauma
5	25 yo male	El Salvador	3	Trauma
6	60 yo female	Bolivia	15	Cerebrovascular accident
7	57 yo male	El Salvador	Unknown	Cerebrovascular accident
8	26 yo male	El Salvador	Unknown	Cerebrovascular accident
9	63 yo female	Argentina	37	Cerebrovascular accident
10	21 yo male	US; mother from US	21	Trauma
11	25 yo female	Mexico	9	Not applicable (living donor)
12	22 yo male	Mexico	6	Trauma
13	21 yo male	Mexico	1.5	Trauma
14	48 yo female	El Salvador	6	Cerebrovascular accident