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Screening and Treatment of Chagas Disease in Organ Transplant Recipients in the United States: Recommendations from the Chagas in Transplant Working Group

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Donor-derived transmission of *Trypanosoma cruzi,* the etiologic agent of Chagas disease, has emerged as an issue in the United States over the past 10 years. Acute *T. cruzi* infection causes substantial morbidity and mortality in the posttransplant setting if not recognized and treated early. We assembled a working group of transplant infectious disease specialists, laboratory medicine specialists, organ procurement organization representatives and epidemiologists with expertise in Chagas disease. Based on review of published and unpublished data, the working group prepared evidence-based recommendations for donor screening, and follow-up testing and treatment of recipients of organs from infected donors. We advise targeted *T. cruzi* screening of potential donors born in Mexico, Central America and South America. Programs can consider transplantation of kidneys and livers from *T. cruzi*-infected donors with informed consent from recipients. However, we recommend against heart transplantation from infected donors. For other organs, we recommend caution based on the anticipated degree of immunosuppression. Our recommendations stress the need for systematic monitoring of recipients by polymerase chain reaction, and microscopy of buffy coat and advance planning for immediate antitrypanosomal treatment if recipient infection is detected. Data on management and outcomes of all cases should be collected to inform future guidelines and to assist in coordination with public health authorities.

Key words: Chagas disease, donor-derived infection, nonendemic countries, *T. cruzi*, transplant infectious disease

Abbreviations: CDC, U.S. Centers for Disease Control and Prevention; EIA, enzyme immunoassay; FDA, U.S. Food and Drug Administration; IFA, immunofluorescent antibody test; OPO, organ procurement organization; PCR, polymerase chain reaction; RIPA, radioimmune precipitation assay; *T. cruzi*, *Trypanosoma cruzi*.

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Introduction

Chagas disease is caused by the protozoan parasite *Trypanosoma cruzi* and transmitted by infected triatomine bugs. An estimated 8–10 million people are living with *T. cruzi* infection in the Americas (1). In areas with endemic transmission, infection is most commonly acquired in childhood. In the absence of successful treatment, *T. cruzi* infection persists throughout life. Following the initial infection, individuals enter the acute phase, usually characterized by a mild febrile illness or nonspecific symptoms; most acute infections pass unrecognized. After 8–12 weeks, the parasitemia becomes undetectable by microscopy, the acute symptoms resolve without treatment, and infected persons enter the chronic phase. In the chronic phase, the diagnosis relies primarily on serologic tests for antibody to *T. cruzi*. Persons with chronic *T. cruzi* infection but without signs or symptoms are considered to have the indeterminate form of Chagas disease. However, 20–30% of infected persons progress over the course of years to decades to cardiac and/or gastrointestinal disease, which can cause substantial morbidity and mortality (2,3).

Table 1: Countries endemic for *T. cruzi* transmission

Vector-borne *T. cruzi* transmission occurs, or occurred until recently, in parts of these countries
• Mexico
• Belize
• Costa Rica
• El Salvador
• Honduras
• Guatemala
• Nicaragua
• Panama
• Argentina
• Bolivia
• Brazil
• Chile
• Colombia
• Ecuador
• Guyana
• Suriname
• French Guiana
• Paraguay
• Peru
• Uruguay
• Venezuela

As the proportion of United States organ donors born in endemic countries increases (Table 1), Chagas disease has become an increasingly important consideration for transplant professionals. An estimated 300 000 *T. cruzi*-infected individuals currently live in the United States (4), and these numbers will likely rise as immigration continues. Large Latin American immigrant populations now live in Spain, Italy, Switzerland, Canada, Japan and other countries, making this a relevant issue outside of the United States as well (5, 6). Unrecognized (usually indeterminate form) Chagas disease in organ donors can have unexpected consequences in immunosuppressed transplant recipients, particularly when diagnosis and treatment are delayed (7–9).

In 2008, a multidisciplinary working group was assembled to consider issues concerning screening for and treatment of Chagas disease in the setting of organ transplantation. Participants included transplant infectious disease specialists, laboratory medicine specialists and representatives from organ procurement organizations (OPOs) and the U.S. Centers for Disease Control and Prevention (CDC). The group's objectives were to: (1) review the epidemiology of *T. cruzi* infection in the United States; (2) review published and unpublished data on organ transplantation from *T. cruzi*-infected donors; (3) evaluate currently available tests for the diagnosis of chronic *T. cruzi* infection; (4) review data on efficacy, adverse effects and availability of antitrypanosomal treatment options and use this information to (5) make recommendations for screening of potential organ donors, and follow-up testing and treatment of transplant recipients when a transmission event is suspected or confirmed. Recommendations regarding the management of Chagas disease reactivation in seropositive recipients following transplantation will be addressed in a future document.

Recommendations of the Working Group

Which potential organ donors should be screened for Chagas disease?

Infected triatomine vectors and *T. cruzi*-infected domestic and wild animals are found in the southern half of the United States, and rare cases of autochthonous vector-borne transmission have been documented in Texas, California, Tennessee and Louisiana (10). Nevertheless, the vast majority of prevalent *T. cruzi* infections are found in immigrants who became infected in their countries of origin. Therefore, the epidemiology of Chagas disease in the United States predominantly reflects immigration patterns from Latin America. Since the 1970s, there has been a steady increase in immigrants, particularly from Mexico and Central America, but also from countries in South America (3, 11). Epidemiologic studies in the United States demonstrate *T. cruzi* infection in these populations. Among 205 Central American immigrants living in Washington DC, 4.5% had positive *T. cruzi* serology (12). A study of Latin American refugees and immigrants to Canada found that 1% of 102 participants had antibodies to *T. cruzi* (13).

Widespread blood bank screening for *T. cruzi* in the United States began in January 2007, offering a glimpse of geographic differences in prevalence of positive blood donors (14). During the first 16 months of screening, >14 million donations were tested. Of these, 1851 specimens had repeatedly reactive results on the screening enzyme immunoassay (EIA) and 519 donors (28%) had positive results by the confirmatory radioimmune precipitation assay (RIPA). Donors with confirmed *T. cruzi* infection were found in 37 states and Puerto Rico, but 253 (57%) came from just two states, California and Florida. The overall seroprevalence was 1:27 500 based on donations screened, with the highest rates in Florida (1:3800), followed by California (1:8300; Ref. 14). Since the beginning of blood screening in January 2007, there have been a total of 4236 donations repeatedly reactive by screening EIA, and 1208 with positive results by RIPA (Figure 1; Ref. 15).

Although blood bank data provide a unique opportunity to compare data from different regions in the United States, screening is not universal and some regions with large Latin American populations have been underrepresented (14). In addition, prior blood bank studies focusing on Southern California (before widespread screening was introduced) resulted in the removal of infected individuals from the donor pool, leading to a likely underestimate of *T. cruzi* infection prevalence in more recent data from California (4). Finally, blood donor data likely are not generalizable to other populations of interest such as organ donors.

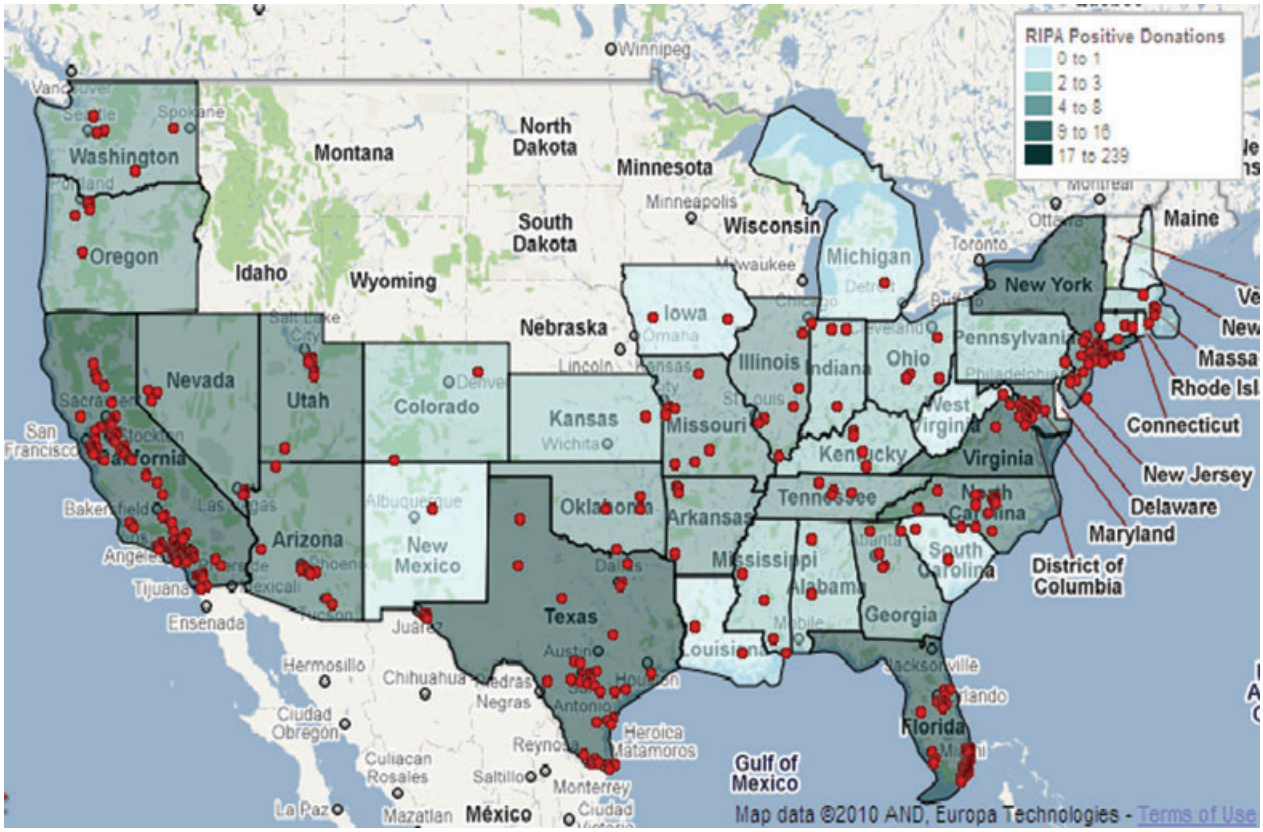

Figure 1: Continental U.S. map showing *T. cruzi* confirmatory test RIPA positives (most recent 24 months to date; Ref. 15) [reprinted by permission of the American Association of Blood Banks (AABB)].

In a case-control study performed by American Red Cross investigators in Los Angeles and Miami in the mid 1990s, at-risk donors (defined by birth/residence in a *T. cruzi*-endemic country) were compared to controls. Of 23 978 at-risk donors, 33 had positive *T. cruzi* serology, compared to 1 of 25 587 controls (16). In a follow-up paper that included a higher number of donors in Los Angeles and Miami, the same authors showed similar findings (17). Following the introduction of widespread blood bank screening, investigators from the Blood Centers for the Pacific interviewed a sample of donors chosen based on confirmatory RIPA results. Compared to those whose donations were negative by RIPA, those with RIPA-confirmed infection were significantly more likely to have lived in a rural area of Latin America, lived in a house with a thatched roof, lived in a house made of mud or earth, seen the vector, had a mother born in Latin America, and a grandmother born in Latin America (personal communication, Brian Custer PhD, MPH, San Francisco, CA, 2010).

Data measuring *T. cruzi* seroprevalence among organ donors in the United States are sparse. Nowicki and colleagues tested 404 archived serum samples from deceased organ donors in southern California between May 2002 and April 2004 (18). Of these, six had initially reactive EIA, three were repeatedly positive by the immunofluorescent antibody test (IFA) and one (0.25%) was confirmed positive by IFA at the CDC. In more recent data, of 187 organ donors tested in Miami in a universal testing strategy, 2 (1%) had positive screening EIA for *T. cruzi* antibodies (personal communication, Michele Morris, MD, Miami, FL, 2010). Current data from the Los Angeles area show 0.5% seropositivity for *T. cruzi* antibodies from 1395 donors tested since routine screening was implemented (personal communication, Marek Nowicki PhD, Los Angeles, CA, 2010).

Because of the paucity of relevant data, the current recommendations are provisional. Well-designed studies to address gaps in the data are urgently needed to guide screening. In populations with a high prevalence of individuals at risk of *T. cruzi* infection, such as those born in endemic areas, universal testing may be a reasonable approach, as is currently being performed in Los Angeles and Miami. In populations with lower prevalence of at-risk individuals, a rational approach may be to screen only if risk factors are reported for the potential donor. One potential screening question is: Was the donor born in Latin America (South America, Central America or Mexico)? Two other questions that could prompt additional testing are:

Was the donor born in, or did s/he spend significant time in Latin America? Was the donor's mother born in Latin America? Additional considerations regarding confirmatory tests, utilization of organs and management of recipients are addressed in the remainder of this document.

Summary: The working group felt that there was insufficient evidence to guide a recommendation for universal screening based on a specific threshold of at-risk population in a particular geographic area. However, OPOs may make this decision based on local epidemiology. The working group advises that all OPOs consider at a minimum targeted screening in all populations (including living donors) with the question 'Was the potential donor born in Latin America (South America, Central America or Mexico)?' We recommend serologic testing for donors with an affirmative answer.

Which tests should be used for screening for Chagas disease?

Because chronic *T. cruzi* infection is often asymptomatic, most infected organ donors will not have a known history of the disease and laboratory screening is essential. Screening for chronic Chagas disease relies on detection of antibodies to *T. cruzi* antigens, most commonly by the EIA or IFA test. There are two EIA kits approved by the U.S. Food and Drug Administration (FDA) for blood and organ donor screening in the United States, the Ortho *T. cruzi* EIA test system (Ortho Clinical Diagnostics, Raritan, NJ, USA; approved December 2006) and Abbott Prism Chagas (Abbott Laboratories, Abbott Park, IL, USA; approved May 2010). From January 2007 to May 2010, the Ortho EIA was the sole Chagas disease screening test used by blood banks in the United States; confirmatory testing of repeatedly EIA-reactive units used the radio-immune precipitation assay (RIPA). The Ortho EIA is reported to have 100% sensitivity and 99% specificity in clinical trial data (19). However, the predictive value of a positive test will vary depending on the *T. cruzi* prevalence in the tested population. In U.S. blood donor screening from 2007 to 2008, comprising a very low prevalence population, the positive predictive value was 28%; this estimate is comparable to the 25% positive predictive value for the HIV blood donor screening EIA (14). The Abbott test has not yet been widely implemented. There are limited data for screening by any test on serum or plasma from deceased donors.

The Ortho EIA has FDA approval for clinical diagnostic testing. Whereas FDA approval requires demonstration of effectiveness of a test or device, FDA clearance only requires the demonstration of equivalence with a previously cleared test. Two EIA test kits are FDA-cleared for diagnostic testing. These are the Hemagen Chagas Kit (Hemagen Diagnostics, Inc., Columbia, MD, USA) and Chagatest EIA Recombinante v. 3.0 (Laboratorios Weiner, Rosario, Argentina). There are multiple other serologic assays available in Latin America for testing donor and clinical specimens with variable performance in laboratory evaluations (20). For the purpose of clinical diagnosis (in contrast to screening), no single assay has sufficient sensitivity and specificity to be relied on alone; two serological tests based on different antigens (e.g. whole parasite lysate and recombinant antigens) and/or techniques (e.g. EIA and IFA, or EIA and RIPA) are used in parallel to increase the accuracy of the diagnosis (2, 21).

For *T. cruzi* screening of living donors, the working group recommends use of one of the FDA-approved blood donor screening tests, the Ortho or the Abbott Prism Chagas. An FDA-cleared test with good performance characteristics in published data could be used as an alternative. Although relevant data are sparse, the working group also recommends using these tests to screen deceased donors. If a donor is found positive by serologic screening, we recommend consultation with the local transplant infectious diseases specialist and the CDC (see below) for additional testing. This testing will take additional time, but may not preclude the use of certain organs.

Summary: The Ortho EIA and Abbott Prism Chagas test systems are FDA-approved for blood donor screening. The working group recommends use of one of these tests for screening of living and deceased donors. An FDA-cleared test with documented good performance characteristics could be used as an alternative.

Should organs from a potential donor with known or suspected Chagas disease be used?

T. cruzi screening of potential organ donors and recipients is performed in many transplant centers in Latin America. Based on the high *T. cruzi* infection prevalence in potential donors, scarcity of available organs and small studies showing that not all transplants resulted in transmission, some centers perform kidney transplantation from known *T. cruzi*-infected donors (22). The only two studies that report interpretable denominator data come from Argentina. A small retrospective study detected no donor-derived *T. cruzi* infections based on serology 1–24 months posttransplant in seven kidney recipients (23). The only published prospective study demonstrated transmission to 3 (19%) of 16 seronegative recipients of kidneys from *T. cruzi*-infected donors (22). In this study, patients were systematically monitored by serological and parasitological methods weekly for the first 2 months, every 15 days during the third month, then monthly afterwards (22). Recipients found to have parasitemia were treated with nifurtimox or benznidazole. None of the infected patients died; one eventually lost his graft secondary to rejection. The authors noted that infected recipients did not necessarily develop positive serology, and that previously positive serology sometimes became negative with immunosuppression; they recommended reliance on parasitological methods for monitoring. In total, studies and case reports

from Latin America document *T. cruzi* transmission to 12 kidney and 2 liver recipients (22,24–29).

Published literature from the United States documents 11 recipients of organs from three *T. cruzi*-infected donors (7–9) (Table 2). Five of 11 recipients became infected with *T. cruzi* and 4 infected patients died (only one directly attributable to Chagas disease). Fourteen additional unpublished instances of organ transplantation (one heart-kidney, six kidneys, six livers and one pancreatic islet cells) from seven infected donors are known to have occurred in the United States (CDC, unpublished data). Two of the liver recipients were treated prophylactically with antiparasitic drugs and their ultimate infection status is unknown. One kidney recipient and one liver recipient were diagnosed with *T. cruzi* infection. There are therefore a total of 21 organ recipients who did not receive prophylaxis and for whom sufficient data are available to assess outcome. Of these, 2/3 (67%) heart, 2/11 (18%) kidney and 2/7 (29%) liver recipients became infected (7–9) (and CDC unpublished data).

In the Argentine kidney transplant cohort, the serologic status of donors was known prior to transplant, close post-transplant monitoring of recipients for parasitemia was performed and clinical outcomes were generally good (22). The published U.S. transmission events only came to attention after the infected recipients were already ill, and diagnosis and treatment were delayed, likely contributing to morbidity and mortality (7–9). In contrast, there are some limited data from the United States demonstrating that early recognition of donor infection led to monitoring of recipients, early initiation of antitrypanosomal therapy and good clinical outcomes (9).

Given existing evidence from Latin America and the United States, the working committee believes that with prompt detection of donor infection and careful monitoring of the recipient, kidneys and livers from *T. cruzi*-infected donors may be considered for transplant. We recommend against transplanting hearts from *T. cruzi*-infected donors, based on sparse data suggesting higher transmission risk and the known tropism of the parasite. Transplantation of other organs should be approached with caution, based on the anticipated degree of immunosuppression in the recipient. Potential recipients should undergo informed consent, and local transplant infectious diseases specialists should be closely involved.

Summary: Not all organ transplantations from *T. cruzi*-infected donors result in transmission to the recipient. If the donor status is known and appropriate posttransplant monitoring ensured, clinical outcomes can be good in transplant recipients. Transplant centers can consider transplanting kidneys and livers from *T. cruzi*-infected donors. The working group advises against transplanting hearts from *T. cruzi*-infected donors, based on sparse data suggesting higher transmission risk and the known tropism of the parasite. Other organs (lung, pancreas and intestines) can be considered with caution based on the anticipated degree of immunosuppression in the potential recipient and the urgency of the need for transplantation. All patients should provide appropriate informed consent concerning risks and benefits.

How should the recipient of an organ from a T. cruzi*-infected donor be managed?*

The best recipient outcomes are seen when the donor infection status is known prior to or shortly after transplantation, allowing prospective recipient monitoring and immediate antitrypanosomal therapy if donor-derived *T. cruzi* infection occurs (30). The symptoms of acute *T. cruzi* infection in a transplant recipient are generally nonspecific, including fever, malaise and anorexia. In the case of cardiac transplantation, acute Chagas disease may mimic transplant rejection. Acute myocarditis and decreased cardiac function can also occur. In the published U.S. transplant clusters, the donor infection status was unknown until recipients presented with symptoms and were subsequently diagnosed with acute *T. cruzi* infection. Four of five infected recipients died; while only one death was directly attributed to Chagas disease, the infection likely contributed to the poor outcomes (9). In contrast, four subsequent recipients of organs from known *T. cruzi*-infected donors underwent prospective monitoring, were asymptomatic at the time of diagnosis, and had prompt successful treatment of their infections (9).

If the donor is known to have a past medical history of Chagas disease, the diagnosis should be confirmed. In the case of a living donor, there may be time to obtain documentation of diagnosis. If the diagnosis is not clearly documented, at least two serologic tests based on different antigens and/or techniques should be performed (2,21). There are three FDA-approved or -cleared EIAs for clinical diagnosis of Chagas (Ortho *T. cruzi* EIA test system, Hemagen Chagas Kit (Hemagen Diagnostics, Inc., Columbia, MD, USA) and Chagatest EIA Recombinante v. 3.0 (Laboratorios Weiner, Rosario, Argentina). Commercial laboratories may offer these tests. The CDC offers diagnostic consultations and performs several serologic tests and polymerase chain reaction (PCR) assays for Chagas disease (contact information below). PCR may also be available at research laboratories that specialize in Chagas disease.

In the case of targeted or universal donor screening, diagnostic results for a potential donor may become known shortly before or soon after transplantation. We recommend concurrent (1) serologic confirmation of the diagnosis in the donor and (2) initiation of prospective clinical and laboratory monitoring in the recipient. Seroconversion may be delayed or never occur in immunocompromised individuals. Recipient monitoring therefore relies primarily on microscopy of fresh buffy coat preparations, Giemsa-stained peripheral blood smears, and PCR. PCR

Table 2: Published instances of organ transplantation from *T. cruzi*-infected donors in the United States

Donor	Organ	Date transplanted	Date recipient diagnosed	Recipient age and clinical presentation	Treatment of recipient	Outcome of recipient
Male immigrant from Central America	Kidney and pancreas	March 5, 2001	April 23, 2001	37-year-old female with fever. *T. cruzi* on peripheral blood smear	Nifurtimox × 4 months, 1 course completed and taking second course	Dead (October 8, 2001). Chagas myocarditis
	Kidney	March 5, 2001	>April 23, 2001	69-year-old female. No symptoms. *T. cruzi* blood culture positive	Nifurtimox × 4 months	Alive
	Liver	March 5, 2001	>April 23, 2001	32-year-old. No symptoms. *T. cruzi* blood culture positive	Nifurtimox × several weeks (died during therapy)	Dead (July 8, 2001). Sepsis and hepatic and renal failure. Thought unrelated to Chagas disease
Male traveler to Mexico. Patient's mother born in Mexico	Heart	December 2005	February 2006	64-year-old male. Organ rejection diagnosed January 2006. Anorexia, fever and diarrhea. *T. cruzi* PCR positive	Nifurtimox	Dead (April 2006). Rejection. Thought unrelated to Chagas disease.
	Liver	December 2005	NA	Negative by *T. cruzi* serology and PCR	No treatment	Alive
	Kidney	December 2005	NA	Negative by *T. cruzi* serology and PCR	No treatment	Alive
	Kidney	December 2005	NA	Negative by *T. cruzi* serology and PCR	No treatment	Alive
Male immigrant from El Salvador	Heart	January 2006	February 2006	73-year-old with fever, fatigue, abdominal rash. *T. cruzi* on blood smear	Nifurtimox	Dead (June 2006). Cardiac failure. Thought unrelated to Chagas disease
	Liver	January 2006	NA	Negative by *T. cruzi* serology and PCR	No treatment	Alive
	Kidney	January 2006	NA	Negative by *T. cruzi* serology and PCR	No treatment	Alive
	Kidney	January 2006	NA	Negative by *T. cruzi* serology and PCR	No treatment	Alive

techniques provide the most sensitive diagnostic tool and usually show positive results days to weeks before circulating trypomastigotes are detectable by microscopy of peripheral blood smears and buffy coat preparations (31). Hemoculture may used as an additional technique in experienced laboratories but its clinical utility is limited by the 2–8 week delay in the availability of results. Transplant-transmitted *T. cruzi* infection may have a longer incubation than classical vector-borne infection; parasitemia is usually detected within 2–3 months of transplantation, but the delay can be as long as 6 months (2,9,21,22,24).

A frequently recommended monitoring schedule consists of weekly specimens for 2 months, every 2 weeks for the third month, then monthly afterwards for a period to be determined by the specific clinical scenario. For example, if rejection is being treated with more intensive immunosuppression, a decision to continue monitoring for a longer period can be made. Antirejection therapy has been associated with *T. cruzi* reactivation in transplant recipients with preexisting chronic infection (32). In the absence of other indications and assuming no evidence of infection has been detected, the monitoring interval can be lengthened after 6 months posttransplantation. Systematic data on the efficacy of prophylactic treatment are lacking and its use may mask signs of transmission. Confirmation of infection (or its absence) has important implications for the long-term management of the patient. Taking these considerations and the potential for drug toxicity into account, we prefer the approach of careful monitoring for evidence of infection over the use of prophylactic treatment.

T. cruzi infection should be treated with benznidazole or nifurtimox. Neither drug is FDA-approved in the United States; both are available for use under Investigation New Drug protocols from the CDC. Early contact and advance coordination with CDC is recommended to expedite the release of treatment drug if transmission is detected. We recommend benznidazole as the first line drug. Both drugs can have significant adverse effects (Table 3) but benznidazole is better tolerated among transplant recipients and has fewer meaningful drug interactions compared to nifurtimox. Nevertheless, nifurtimox may be indicated if a patient fails to respond to or cannot tolerate benznidazole. The development of peripheral neuropathy with either drug is a cause for cessation of therapy and may take months to resolve. Other agents such as posaconazole are reported to have *T. cruzi* activity but have not been systematically evaluated.

Summary: If a potential organ donor is known or suspected to have *T. cruzi* infection, we recommend serologic confirmation. When transplantation of an organ from an infected donor has occurred, we recommend close monitoring of the recipient and advance planning to coordinate release of antitrypanosomal treatment if recipient infection is detected. Monitoring consists of *T. cruzi* PCR and microscopy of blood specimens weekly for the first 2 months, every 2 weeks during the third month, then monthly until at least 6 months posttransplantation. Additional specimens should be examined in case of fever or symptoms of rejection. We do not recommend prophylactic antitrypanosomal treatment. Detection of recipient *T. cruzi* infection should prompt treatment with benznidazole (first line) or nifurtimox (second line). If a transmission event is suspected or confirmed, we recommend close coordination with the local OPO, UNOS, local transplant infectious diseases specialists, state health authorities and the CDC.

Conclusions

Chagas disease is an emerging infection in transplant recipients, particularly due to donor-derived transmission, as donor demographics increasingly include persons with origins in or travel to *T. cruzi*-endemic countries. Increased awareness by transplant professionals has led to screening in the United States but with varying approaches. Use of kidneys and livers from *T. cruzi*-infected donors can be considered based on the cumulative experience to date; hearts should not be used. Use of other organs can be considered with caution based on the anticipated degree of immunosuppression in the potential recipient. All patients should provide appropriate informed consent concerning the risk of receiving a potentially *T. cruzi*-infected organ. When donor-derived *T. cruzi* transmission is suspected or confirmed, local infectious disease specialists and the CDC should be contacted (see below). State health authorities should be notified. Providers should collect baseline donor specimens, and specimens for monitoring by *T. cruzi* PCR, culture and microscopy at regular intervals posttransplant. If *T. cruzi* is confirmed in the recipient, antiparasitic therapy is available from CDC.

More research is needed, including assessment of local disease prevalence by geographic area, in order to give more specific recommendations to OPOs regarding universal or targeted screening. Current confirmatory testing is limited in its availability and is time consuming; the availability of more rapid confirmatory testing for *T. cruzi* would reduce organ wastage. Likewise, systematic collection of outcome data for recipients of organs from *T. cruzi*-infected donors is needed to inform future policy and practice. Currently, used antitrypanosomal drugs have significant limitations and newer agents should be developed and evaluated in transplant patients.

Contacting the CDC

Consultations about known or suspected *T. cruzi* infections, confirmatory testing, and monitoring and treatment of transplant recipients should be directed to the Division of Parasitic Diseases and Malaria, CDC. Phone: 770–488-7775. E-mail: parasites@cdc.gov. CDC Emergency

Table 3: Summary of properties of benznidazole and nifurtimox

	Benznidazole	Nifurtimox
Formulation	100 mg tablets	30 mg, 120 mg tablets
Adult dosing	5—7 mg/kg/day in 2 divided doses	8–10 mg/kg/day in 3 divided doses
Renal dosing	No adjustment	No adjustment
Hepatic dosing	No adjustment	No adjustment
Duration of treatment (anticipated)	60 days	90 days
Adverse effects	Rash [photosensitivity to exfoliative dermatitis] (30%), dose-dependent peripheral neuropathy (30%)	Gastrointestinal [anorexia, weight loss, nausea, vomiting, pain] (30–70%), central nervous system [irritability, insomnia, tremors]
	Less common: Bone marrow suppression, anorexia, weight loss, nausea, vomiting, dysgeusia, insomnia	Less common: paresthesias, dose-dependent polyneuropathy, peripheral neuritis, dizziness, mood changes, myalgias
Monitoring	Baseline complete blood cell count, hepatic enzymes, bilirubin, serum creatinine, blood urea nitrogen. Repeat complete blood cell count every 2–3 weeks while on therapy. Monitor for dermatitis beginning 9–10 days after therapy begins	Baseline complete blood cell count, hepatic enzymes, bilirubin, serum creatinine, blood urea nitrogen. Repeat 4–6 weeks into the course of therapy and at the end of therapy
		Monitor for signs of peripheral neuropathy every two weeks, particularly during months 2 and 3
Drug interactions	Alcohol (disulfiram-like effects with concomitant use) should be avoided	Alcohol (increases risk of adverse effects) should be avoided
		Can increase tacrolimus levels (metabolized via cytochrome P450 reductase) and tremors if both agents used in combination

Operator (after business hours and on weekends): 770–488-7100.

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Disclosure

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Executive Summary of Recommendations

Screening: There is insufficient evidence to guide a recommendation for universal screening based on a certain threshold of at-risk population in a particular geographic area. However, OPOs may make this decision based on local epidemiology. All OPOs should consider at a minimum targeted screening in all populations (including living donors) with the question 'Was the potential donor born in Latin America (South America, Central America or Mexico)?' We recommend serologic testing for donors with an affirmative answer.

Screening tests: The Ortho EIA and Abbott Prism Chagas test systems are FDA-approved for blood donor screening. The working group recommends use of one of these tests for screening of living and deceased donors. An FDA-cleared test with good performance characteristics in published data could be used as an alternative.

Utilization of organs: Not all organ transplantations from *T. cruzi*-infected donors result in transmission to the recipient. If the donor status is known and proper posttransplant monitoring ensured, clinical outcomes can be good in transplant recipients. Transplant centers can consider transplanting kidneys and livers from *T. cruzi*-infected donors. The working group advises against transplanting hearts from *T. cruzi*-infected donors. Other organs (lung, pancreas and intestines) can be considered with caution based on the anticipated degree of immunosuppression in the potential recipient. All patients should provide appropriate informed consent.

Management of recipients: If a potential organ donor is known or suspected to have *T. cruzi* infection, we recommend serologic confirmation. When transplantation of an organ from an infected donor has occurred, we recommend close monitoring of the recipient and advance planning to coordinate release of antitrypanosomal treatment if recipient infection is detected. Monitoring consists of *T. cruzi* PCR and microscopy of blood specimens weekly for the first 2 months, every 2 weeks during the third month, then monthly until at least 6 months posttransplantation. Additional

specimens should be examined in case of fever or symptoms of rejection. We do not recommend prophylactic antitrypanosomal treatment. Detection of *T. cruzi* infection should prompt treatment with benznidazole (first line) or nifurtimox (second line). If a transmission event is suspected or confirmed, we recommend close coordination among the local organ procurement organization, UNOS, local transplant infectious diseases specialists, state health authorities and the CDC. The transmission event should be reported to OPTN as required by policy (33).

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