

## **Recognizing Seasonal and Geographically Endemic Infections in Organ Donors: Considerations during Living Donor Evaluation**

### **Background**

On November 13, 2014, the OPTN/UNOS Board of Directors approved modifications to existing policies related to the medical evaluation of living donors. These modifications removed specific donor testing requirements for Chagas disease, West Nile Virus, and Strongyloides from policy. Instead, policy will now require living donor recovery hospitals to develop a written protocol for identifying and testing potential donors at risk for transmissible seasonal or geographically defined endemic disease as part of the medical evaluation process.

### **Summary and Goals**

The OPTN/UNOS Disease Transmission Advisory Committee (DTAC) created this guidance document to assist living donor hospitals recognize potential living donors that may carry an increased risk of transmitting seasonal or geographically endemic disease to organ recipients.

This resource is not an OPTN policy, so it does not carry the monitoring or enforcement implications of policy. It is not an official guideline for clinical practice, nor is it intended to be clinically prescriptive or to define a standard of care. This is a resource tool intended to be of educational support for OPOs and transplant centers and is for voluntary use by members.

### **Developing a Written Protocol for Identifying and Testing Donors**

The DTAC reviews potential donor-derived disease transmission events reported to the OPTN for both deceased and living donors. A number of the potential donor-derived disease transmission events reported are seasonal and geographically associated. Some of the reported events resulted in recipient illness or death. Recognition of disease in these donors can be especially challenging, as risk factors may not be recognized and laboratory screening is typically not done.

This guidance document provides information the Committee believes will help living donor programs develop a written protocol for identifying and testing donors at risk for transmissible seasonal or geographically defined disease. This information is meant to assist the transplant community in performing organ donor infectious disease screening procedures as part of the overall medical evaluation process.

## Recognizing Risk Factors

There are a number of factors to consider when determining a donor's risk of transmissible infection. Recovery hospitals should consider the following when screening potential organ donors:

- Geographic risks (including duration of time spent in a location)
  - Where was the potential living donor born (outside versus inside U.S.)?
  - Home country/region? Prolonged residence outside home region, recent or distant?
  - Close family members countries of origin
  - Living donor recovery hospital region?
  - Occupational or recreational travel to other countries and/or regions?
- Occupational risks
  - Healthcare workers, vets/animal care workers
  - Landscapers, park rangers, and other outdoor workers
  - Peace Corps workers, international journalists
  - Current or previous military service, particularly outside the U.S.
  - Medical mission trips (consider a three month washout period prior to donation to allow identification of subclinical disease)
- Seasonal risks
  - Particularly with warm weather and insect exposure - local West Nile Virus, dengue, Chikungunya virus transmission, local Rickettsial infections, Lyme disease
- Hobbies
  - Hunting/dressing game, taxidermy
  - Time living outdoors including camping, swimming in lakes, drinking stream water, insect exposures
  - Adventure sports
  - Gardening
- Significant animal exposure (wild and/or domestic)
  - Large numbers of cats or dogs or any unusual pets
  - Laboratory/research animals
  - Veterinarian/vet assistant
- Family members and close contacts with potential risk factors
  - Geographic or seasonal infections previously diagnosed in close family members or other contacts may predict risk for subclinical infection in potential donor
- Personal history of seasonal or geographic infection in potential donor, even if remote

The organ donor population has become increasingly diverse geographically, reflecting the enhanced mobility and complex immigration patterns of the general population. Therefore, it is not practical to list all of the pathogens that have the potential for transmission through organ transplantation. Parasitic infections (such as amebiasis, babesiosis, leishmaniasis, schistosomiasis, microsporidiosis, echinococcosis) and malaria as well as bacterial infections (such as brucellosis and melioidosis) and fungal infections (such as paracoccidiomycosis and penicilliosis) have distinct areas of endemicity and may be transmitted through the organ allograft. In donors with a history of residence in developing countries or remote regions, unusual occupational exposure risks, or extensive travel, infectious disease (ID) consultation may be helpful as part of their pre-transplant evaluation. This guidance document does not replace expert ID evaluation. Table 1 covers a number of common seasonal and geographically endemic infections that may be transmitted from organ donor to recipient.

**Table 1: Common Seasonal and Geographically Endemic Infections in Organ Donors**

<b>Disease</b>	<b>Signs/symptoms in potential donor</b>	<b>Known Risk Factors</b>	<b>Potential testing</b>	<b>Imaging that may be helpful</b>
Histoplasmosis	Fever, night sweats, lymphadenopathy, cough, non-calcified pulmonary nodules or cavities	Residence in Midwestern states Mississippi or Ohio river valleys	Serology -complement fixation -immunodiffusion -EIA -Urine or serum antigen testing	CXR or CT
Coccidioidomycosis	Fever, joint pains, cough, neck stiffness, headaches, pulmonary nodules or cavities, reticulonodular infiltrates	Residence in endemic areas of the southwestern United States and parts of South & Central America	Serology -enzyme immunoassay -complement fixation -immunodiffusion -Urine or serum antigen testing	CXR or CT
Chagas	Most asymptomatic; Symptomatic chronic infection may present with cardiomyopathy, cardiac conduction abnormalities, megaesophagus, megacolon	Born or resided in endemic areas of South & Central America, child of woman who lived in endemic area, received blood transfusion in endemic area	Serology testing (See Chagas Guideline, Table 3)	None unless symptomatic chronic Chagas disease
Strongyloides	Donors may have chronic abdominal pain, intestinal symptoms, and/or eosinophilia, or could be entirely asymptomatic.	Soil exposure in tropical/warm climates. Walking barefoot, or contact with human sewage, or contaminated soil. Exposure risk may persist for decades.	Donors could be tested by serology (preferable) and/or stool examination, specifically looking for <i>Strongyloides</i> .	None
Tuberculosis	Fever, night sweats, weight loss, cough, recurrent pneumonia, exudative pleural effusion of unknown etiology, lymphadenopathy, non-calcified pulmonary nodules or cavities	Born outside US, Prolonged residence outside US, Homeless, Alcohol or other substance abuse, Jail/Prison time, Health care worker, Known TB exposure	Positive tuberculin skin test (TST) or interferon gamma release assay (IGRA); Sputum/BAL AFB smear, culture, nucleic acid amplification, TB PCR; AFB smear, culture, PCR on tissue	CXR, CT thorax, CT abdomen/ pelvis (renal TB)
West Nile Virus	Often asymptomatic; 20% develop acute febrile illness; <1% encephalitis, myelitis	Mosquito exposure, blood transfusion; risk varies by season & location	Nucleic acid test (NAT) and IgM serology	None

West Nile Virus (WNV) and Mycobacterium Tuberculosis (MTB) are not covered in this guidance document, but are infections commonly reported as potential donor-derived infectious diseases. DTAC guidance documents on both are available on the OPTN website to assist the transplant community in considering these infections when developing an evaluation protocol:

- [Guidance for Identifying Risk Factors for West Nile Virus during Evaluation of Potential Living Donors](#)
- [Guidance for Identifying Risk Factors for Mycobacterium Tuberculosis During Evaluation of Potential Living Kidney Donors](#)

## I. FUNGAL INFECTIONS

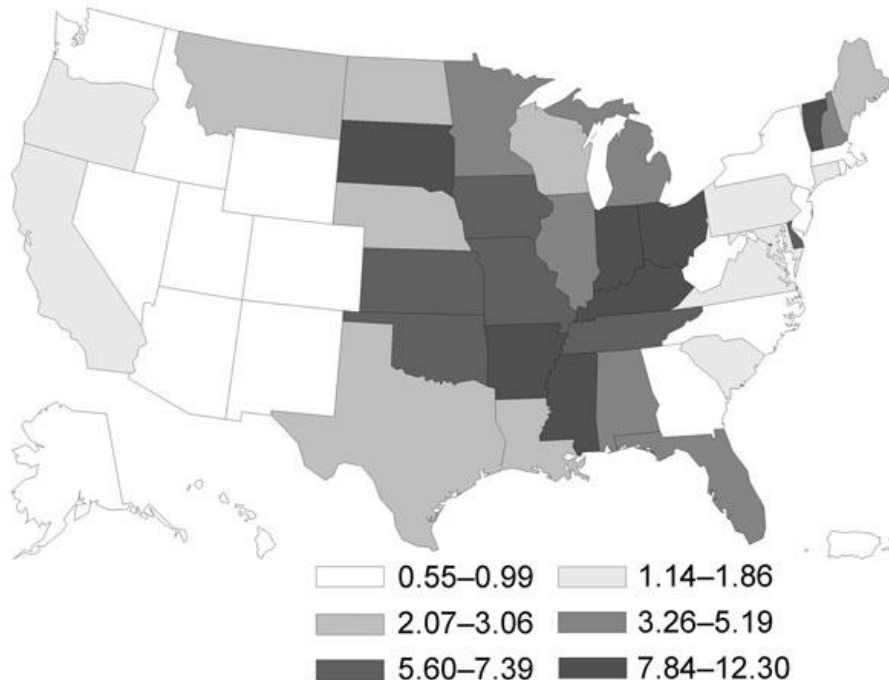
### Histoplasmosis Guidance

#### **Background**

*Histoplasma capsulatum* is a dimorphic fungus found throughout the world. It is endemic in the U.S. in the Ohio and Mississippi river valleys (see Figure 1). In most cases, clinical signs of infection in immunocompetent patients are limited to the lungs, though many patients are asymptomatic. Immunocompromised patients may develop severe disseminated disease that is fatal without prompt diagnosis and treatment. Donor-derived *Histoplasma capsulatum* has only rarely been reported<sup>i, ii</sup>.

#### **Who Should be Screened?**

In endemic areas, up to 75% of the population is infected with *Histoplasma capsulatum*, therefore no further exposure risk factors need be elicited in residents of these areas. Donors at higher risk of transmitting disease include those with recent infection or a prior history of known active histoplasmosis. Screening tests should be considered for those donors<sup>iii</sup>. Potential donors with a history of pneumonia of unknown type in the past 2 years should also be considered for screening<sup>iii</sup>. Donors with signs, symptoms, or radiological findings consistent with active histoplasmosis (fevers, sweats, weight loss, non-calcified pulmonary nodules/cavities or lymphadenopathy) need a thorough medical evaluation including testing for histoplasmosis prior to organ donation. Even in endemic areas, universal screening of donors lacking any of the above characteristics is not likely to be productive. Potential donors with the sole finding of a calcified granuloma on chest imaging do not require further testing.



**Figure 1.** Geographic distribution of histoplasmosis in persons  $\geq 65$  years of age, United States, 1999–2008. Values are no. cases/100,000 person-years.

Downloaded from <http://wwwnc.cdc.gov/eid/article/17/9/10-1987-f1.htm> on July 8, 2014.

### How to Screen

In asymptomatic potential donors, serological tests should be used to screen at risk potential donors. Complement fixation and immunodiffusion testing are the most commonly performed tests. Complement fixation titers of 1:8 and 1:16 may just indicate previous infection at low risk for transmission. Positive immunodiffusion testing is more concerning for the presence of viable organisms, particularly if an H band is present<sup>iii</sup>.

### Management of Infected Living Donors

Potential living donors with clinical evidence of active histoplasmosis (or a serological pattern suggestive of active disease) require treatment prior to organ donation. For patients with histoplasmosis limited to the lungs, a reasonable approach would include 3-6 months of treatment, usually with itraconazole, and resolution of clinical signs and symptoms of histoplasmosis as well as resolution of antigenuria/antigenemia (if present at diagnosis). After treatment and resolution of antigenuria/antigenemia, the risk of donor-derived infection is likely low. Given that disseminated histoplasmosis is typically associated with other significant medical conditions, it is unlikely that a patient with a history of disseminated histoplasmosis would qualify for living organ donation.

### Management of Recipients

Recipients of donors with a history of histoplasmosis may not require specific prophylaxis if the donor has been treated. Clinical and laboratory monitoring for disease is a reasonable approach. Serial urine or serum antigen testing (every 1-3 months) for 1 year might identify donor-derived histoplasmosis prior to the development of clinical symptoms. Serological tests have low sensitivity after organ transplantation, and most SOT recipients with histoplasmosis have negative serological studies. Over 80% of transplant patients with histoplasmosis present with

disseminated disease, typically with fever, weight loss, cytopenia, and pulmonary symptoms, often with progression to sepsis. Urine and/or serum antigen testing are the most sensitive diagnostic tests. Treatment in patients with severe disease typically consists of liposomal amphotericin followed by itraconazole. Patients with mild disease can be treated with itraconazole alone.

### **Infection Avoidance between Testing and Transplant**

In endemic areas, exposure to histoplasmosis may occur with many daily activities and is difficult to entirely avoid. Nonetheless, in the pre-donation period certain activities (cave exploration, significant time in construction sites, exposure to bird droppings or bat guano) should be avoided.

### **Coccidioidomycosis Guidance**

#### **Background**

*Coccidioides immitis* and *Coccidioides posadasii* are dimorphic fungi endemic in arid climates in the southwestern part of the United States and parts of Central and South America. The most common clinical syndrome is pneumonia often accompanied by joint pains, fatigue, and weight loss. Chronic fibrocavitary pulmonary disease may follow primary infection, and some infected persons have persistent asymptomatic pulmonary nodules, reticulonodular disease, or cavitary disease. Immunosuppressed individuals may develop disseminated infection. Multiple cases of donor-derived coccidioidomycosis have been reported, often with poor outcomes.

#### **Who Should be Screened**

One study indicated that 2.1% of persons evaluated for living donation in an endemic region were seropositive, suggesting recent or active disease<sup>iv</sup>. Since many patients with transmissible coccidioidomycosis are asymptomatic and infection is widespread in endemic areas, some experts recommend screening as part of the routine evaluation of all potential donors who reside in endemic areas or who have recently resided or had prolonged stays in such areas. Persons with symptoms consistent with coccidioidomycosis (fevers, weight loss, poorly responding pneumonia) or those with unexplained chest imaging findings (cavities, nodules, lymphadenopathy, reticulonodular infiltrates) require screening as well. Finally, it is reasonable to do further screening on donors with a known history of coccidioidomycosis as potential donors with persistently positive serologic studies are more likely to harbor viable organisms.

#### **How to Screen**

In asymptomatic potential donors, serological tests (enzyme immunoassay, complement fixation, or immunodiffusion) may be combined with chest imaging. Patients with suggestive findings on imaging (non-calcified nodules, cavities, lymphadenopathy, reticulonodular infiltrates) may require sputum cultures or bronchoscopy with culture of lavage fluid, although sensitivity of cultures may be low. While negative serologies do not entirely rule out the possibility of transmissible infection, prospective donors with normal imaging and negative serologies require no further evaluation.

#### **Management of Infected Living Donors**

Potential donors with evidence of active infection require a thorough evaluation to determine the extent of the infection. Donation from actively infected donors should be deferred until treatment is complete and all evidence of active infection (based on clinical, radiographic, and serological factors) has resolved.

## Management of Recipients

Prophylaxis with antifungal medications active against *Coccidioides* species may be effective in preventing disease in recipients of infected donors. Fluconazole or itraconazole can be used as prophylaxis; fluconazole is more reliably absorbed and interactions with calcineurin inhibitors are less significant. Posaconazole and voriconazole are second line options. Echinocandins or inhaled polyenes are not effective. The recommended duration and dose of prophylactic agents has not been well defined but would typically consist of 400 mg of fluconazole daily for at least 3 months, although in some circumstances lifelong prophylaxis is recommended<sup>iii</sup>. Whether or not additional prophylaxis is needed for recipients of donors who received adequate treatment for coccidioidomycosis in the past is unknown. While periodic post-transplant serological monitoring could be considered, the sensitivity of serological testing in immunosuppressed patients is likely low. Recipients should be closely monitored when prophylaxis is discontinued, with periodic clinical, radiologic, and serologic assessments, especially in the first 6-12 months after cessation of prophylaxis<sup>iii</sup>.

## Infection Avoidance between Testing and Transplant

For people living in endemic areas, completely avoiding exposure to *Coccidioides* is difficult to impossible. Highest risk activities include those that result in heavy inhalation of desert soil, particularly in the dry periods following the rainy season. Potential donors that develop pulmonary infection or illness characterized by fatigue, cough, and/or joint pain after initial screening may require repeat evaluation.

## II. Parasitic Infection Guidance

### Strongyloides Guidance

#### Background

*Strongyloides stercoralis* is a nematode (roundworm). Unlike other parasites, *Strongyloides* can replicate for decades within humans via an autoinfection cycle, resulting in chronic symptomatic or asymptomatic infections that can flourish in the setting of immunosuppression. The larvae are small, up to 1.5mm, and enter through exposed skin, such as bare feet. There are an estimated 30 – 100 million infected people worldwide<sup>v,vi</sup>.

Donor-derived *Strongyloides* infection is rare, but in a recent review, roughly half of donor-derived infection cases succumbed to *Strongyloides* or related complications. Hyperinfection occurs in immunocompromised hosts and can lead to disseminated infection, with mortality as high as 85%<sup>vii</sup>. From 2009 to 2012, the CDC assisted in seven investigations of organ donors and associated recipients with strongyloidiasis determined to be donor derived. The incidence of transmission remains unknown<sup>viii</sup>.

#### Who Should Be Screened

*Strongyloides* is most common in tropical, subtropical, or warm temperate climates, including the Caribbean, Mexico, South and Central America, Africa, Southeast Asia, southern and Eastern Europe, the United Kingdom and the southeastern United States<sup>v,ix</sup>. Infection results primarily from contact with soil that is contaminated with *Strongyloides* larvae. Activities that increase the risk of becoming infected include direct contact with contaminated soil (i.e. walking barefoot), contact with human waste or sewage, and occupations that increase contact with contaminated soil, such as farming and coal mining<sup>v</sup>. Rural populations and those of a lower socioeconomic

status are at higher risk.

Donors and recipients who have spent significant time in endemic regions should be screened for *Strongyloides* by serology, especially those who have unexplained eosinophilia, chronic abdominal pain, or diarrhea. The majority of donors involved in transmission cases had significant geographic exposures, but did not have clinical symptoms, so limited screening based on symptoms is likely to result in many missed cases.

Those donors with a personal history of prior treated *Strongyloides* infection should be at low risk for transmission, although repeat (new) infection after treatment can occur, and the autoinfection cycle could allow for subclinical persistence. Although transmission within families is unlikely, a family history should trigger screening given the likelihood of similar exposures.

### **How to Screen**

Screening is by serology or stool examination. Serology is primarily an IgG assay for antibodies to *Strongyloides*. The enzyme-linked immunosorbent assay (ELISA) is preferable because of its greater sensitivity (90%) and specificity (99%), compared with indirect fluorescent antibody (IFA) and indirect hemagglutination (IHA) tests<sup>vii, viii, ix</sup>. Antibody testing cannot differentiate between current and prior or treated infections; titers do not reliably decrease rapidly after treatment. The assays may produce false positive results in patients with filariasis and other nematode infections. Serology testing is commercially available, often with turn-around times of a week or more.

Stool testing is less sensitive than serology, as stools are positive only during larval shedding, and would be indicated when serological testing is unavailable or when serological findings are negative but clinical suspicion of disease is high. A single stool specimen has a sensitivity of only 15%–30%, although sensitivity increases to nearly 100% if 7 consecutive daily stool specimens are examined in an expert laboratory, which may not be practical in the transplant setting<sup>vii</sup>. Intestinal endoscopy with biopsies may also diagnose *Strongyloides* infection, although it would not be used for routine screening.

For living donors, screening should be done with initial testing to allow time for subsequent treatment if necessary. Transplant centers should follow-up on such pre-transplant test results and give prophylaxis to recipients if their donors were not previously treated. Prophylaxis and treatment doses of anti-parasitic medications in this setting are probably the same, although they have not been studied. The majority of cases of donor-derived strongyloidiasis occur several weeks to months after transplant, so centers should have adequate time to treat recipients before infection occurs<sup>x</sup>.

### **Management of Infected Donors**

Donors infected with *Strongyloides* can be used, and should not be deferred. Living donors can be treated with two doses of ivermectin (see below), with no further delay in performing the organ transplant. Additional serologic or stool testing after treatment is not likely to be helpful. In cases in which there is insufficient time for test results to return and treatment to be given to donors, centers should plan for post-transplant treatment of the recipient. Informed consent should be considered in both situations.

### **Management of Recipients from Infected Donors**

Recipients who receive organs from infected and untreated donors may be treated with ivermectin, thiabendazole or albendazole. Ivermectin is well tolerated, and is preferred (where available) due to superior efficacy<sup>vi</sup>. Ivermectin is usually administered as two single 200



microgram/kg doses either on two consecutive days or two weeks apart (allowing for one autoinfection cycle), unless there is hyperinfection or disseminated disease for which daily therapy would be recommended. Only oral ivermectin is available in the USA. Intravenous therapy is available for veterinary use, but can be used in humans subcutaneously in emergency situations (with regulatory approval). There may be a drug interaction between ivermectin and the calcineurin inhibitors (tacrolimus and cyclosporine), therefore monitoring of drug levels is recommended.

People dually infected with Human T-Cell Lymphotropic Virus-1 (HTLV-1) and *Strongyloides* are more likely to develop severe cases of strongyloidiasis, and are at higher risk for reoccurrence. It may be worthwhile to screen patients with *Strongyloides* infection for HTLV-1 so the treating clinicians are aware of the risk of increased disease severity and reoccurrence<sup>vii, ix</sup>.

Patients from areas of Africa endemic for loiasis (primarily central and western sub-Saharan Africa) should be screened for *L. loa* microfilaremia, as administration of ivermectin to those with microfilaremia can precipitate life-threatening encephalopathy, known as the Mazzotti reaction.

### **Infection Avoidance between Testing and Transplant**

In the absence of exposure, acquisition of acute infection would generally be rare in the several months between testing and transplant for most living donors, unless they travel to endemic regions and have significant soil exposure. Shoes should be worn in endemic areas to avoid contact with infected soil.

## **Chagas Guidance**

### **Background**

Chagas disease is caused by infection with the protozoan parasite *Trypanosoma cruzi*. It is estimated that 8-10 million people are infected in the Americas, with over 300,000 infected individuals currently living in the United States. The majority of infections were acquired in endemic regions of South and Central America, where infection is transmitted by the bite of an infected triatome bug. Infection can also be transmitted from an infected mother at the time of childbirth, as well as through infected food or drink, and through blood transfusion and organ transplantation.

Most infections are acquired in childhood during residence in an endemic area. The acute phase of infection may be associated with a mild febrile illness, and is often unrecognized. Parasitemia clears within 8-12 weeks without treatment, but individuals remain chronically infected. Infection persists for the individual's life, with chronic disease developing in 20-30%, usually manifesting as cardiac or gastrointestinal disease. Chronic infection can be diagnosed through serologic tests for antibody to *T. cruzi*.

Blood donor screening in the United States beginning in 2007 identified confirmed infections in donors from 37 states and Puerto Rico, with 57% of all positive tests from California and Florida, areas with significant Central and South American immigrant populations. Latent infection with *T. cruzi* can persist for decades, therefore organ donor screening of high-risk individuals using serology testing is utilized at some centers. Transmission of Chagas disease has been studied in 32 organ transplant recipients from 14 seropositive donors in the United States. Two of 15 (13%) renal transplant recipients had donor-derived infection; none of these were living donor transplants<sup>x</sup>. Living organ donor transmissions have been reported in Mexico and South America.

## Who Should Be Screened

Donors born or who live/have lived in an endemic region (see Table 2) should be screened. Children of women born in endemic regions if their birth mother's serology is positive or unknown. In addition, donors who received a blood transfusion in endemic regions and those who have a previous diagnosis of Chagas disease should be screened<sup>xi</sup>. Persons from an endemic region with cardiac or gastrointestinal diseases that might be due to *T. cruzi* infection should also be carefully screened.

**Table 2: Countries endemic for *T. cruzi* transmission<sup>xi</sup>**

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

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## How to Screen

Serology testing using one of three FDA-cleared assays (see Table 3) should be performed on donors with risk factors for Chagas disease. Tests for parasitemia are not sensitive enough to detect chronic *T. cruzi* infection. Detectable antibody is usually present within a month of infection and remains present through the individual's life.

**Table 3: Serological Tests Available for *T. cruzi* Infection<sup>xii</sup>.**

Test name, manufacturer	Target antigen	Test Format	Sample Type	FDA-cleared/approved use
Abbott Prism Chagas ( <i>T. cruzi</i> [ <i>E. coli</i> , recombinant] antigen), <sup>2</sup> Abbott Laboratories, Abbott Park, IL	Recombinant antigens	ChLIA	Serum/plasma	Donor screening
ORTHO <i>T. cruzi</i> ELISA Test System <sup>3</sup> Ortho-Clinical Diagnostics, Inc. Raritan NJ	Whole cell lysate	EIA	Serum/plasma	Donor screening, individual diagnosis
Chagatest ELISA recombinant v.3.0 <sup>3</sup> Wiener Laboratories S.A.I.C., Rosario, Argentina	Recombinant epimastigote and trypomastigote Proteins	EIA	Serum/plasma	Diagnosis, NOT donor screening test
Hemagen Chagas' Kit, Hemagen Diagnostics, Inc., Columbia, MD	Purified antigens from cultured <i>T. cruzi</i>	EIA	Serum	Diagnosis, NOT donor screening test
Abbott ESA Chagas Assay, Abbott Laboratories, Abbott Park, IL	4 <i>T. cruzi</i> recombinant antigens (FP10, FP6, FP3, TcF)	Enzyme Strip Assay	Serum/plasma	Supplemental test in donors who test positive with first-line assays, not approved for individual diagnosis

Adapted from <http://www.fda.gov/BiologicsBloodVaccines/BloodBloodProducts/APprovedProducts/LicenseProducts>.

<sup>1</sup>Serological testing also available via CDC.

<sup>2</sup>This test may only be available through local blood bank.

<sup>3</sup>Preferred tests for initial donor screening.

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### Management of Infected Living Donors

Living donors who test positive should be informed about the result and offered infectious disease consultation. A second serologic assay based on a different diagnostic method may be recommended for confirmation. Infected donors may require further evaluation for chronic Chagas disease, and may ultimately require specific treatment. Evaluation and treatment of these individuals should proceed in accordance with local guidelines, as the availability of confirmatory diagnostics and anti-parasitic therapy varies.

### Management of Recipients

The risk of transmission of *T. cruzi* infection from an infected donor to an uninfected deceased kidney donor recipient has been reported to be between 13 and 18%. There are no data regarding living donor transmissions. It is reasonable to consider accepting donor kidneys from *T. cruzi* positive donors on an individual basis with informed consent and close monitoring of the recipient. Potential recipients of Chagas positive donor organs should themselves be tested for the presence of *T. cruzi* antibody, particularly since they may share unrecognized risk factors with their potential living donor. If the recipient tests negative and the decision is made to proceed with the transplant, recipients must be counseled specifically about the transmission risk and the need for close monitoring post-transplant, with the potential need for toxic anti-parasitic therapy that is not FDA approved or readily available<sup>xii</sup>.

Once transplant has occurred, expert infectious disease consultation is recommended to coordinate post-transplant testing. In the United States, the Centers for Disease Control (CDC) can assist with PCR and parasitemia testing. Practitioners outside the U.S. should develop a testing strategy using available reference laboratories pre-transplant. Incorporating a PCR testing

platform into the post-transplant testing program is recommended, as molecular testing may be positive weeks before parasitemia is detected using standard screening.

PCR and parasitemia tests of peripheral blood should be performed using the following schedule<sup>xi</sup>:

- Weekly for the first 2 months post-transplant
- Every 2 weeks for the third post-transplant month
- Monthly thereafter until a minimum of 6 months post-transplant AND until net state of immunosuppression is at optimal post-transplant baseline with no evidence of infection or rejection
- More frequent monitoring is recommended any time the patient requires antirejection therapy

For access to testing and treatment of transplant recipients at risk for reactivation of Chagas, contact the CDC Division of Parasitic Diseases and Malaria at 770-488-7775 (business hours) or 770-488-7100 (nights and weekends) or via e-mail at [parasites@CDC.gov](mailto:parasites@CDC.gov)<sup>xiii</sup>.

### **Infection Avoidance between Testing and Transplant**

Potential living donors should avoid prolonged travel to endemic regions, particularly rural areas with primitive housing or significant insect exposure.

## **III. Sharing Information**

### **Recommendations for Sites Participating in Paired Organ Exchanges**

Transplant hospitals participating in organ exchanges should consider sharing their protocols for screening living donors for seasonal and geographically endemic infections in addition to related testing results. This will provide recipient centers more information about the living donor screening process at the donor organ center.

### **When to Report a Potential Donor-Derived Transmission Event**

If the recipient is suspected to be at risk for disease transmission either by the OPO or a transplant center, a potential donor-derived disease transmission event should be reported to the OPTN's Improving Patient Safety portal per [Policies 15.4 \(Reporting of Potential and Proven Disease Transmissions\)](#) and [15.5 \(Requirements for Post-Transplant Discovery of Donor Disease or Malignancy\)](#). This promotes prompt intervention for other recipients of the same donor's organs.

Additional guidance on reporting potential donor derived disease transmission events may be found at:

[http://optn.transplant.hrsa.gov/SharedContentDocuments/Guidance\\_DTAC\\_PDDTE.pdf](http://optn.transplant.hrsa.gov/SharedContentDocuments/Guidance_DTAC_PDDTE.pdf)

## References

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- <sup>i</sup> Assi M, Martin S, Wheat LJ, et al. Histoplasmosis after solid organ transplant. *Clin Infect Dis* 2013; 57 (11): 1542.
- <sup>ii</sup> Limaye AP, Connolly PA, Sagar M, et al. Transmission of *Histoplasma capsulatum* by Organ Transplantation. *New England Journal of Medicine* 2000; 343 (16): 1163.
- <sup>iii</sup> Singh N, Huprikar S, Burdette SD, et al. Donor-derived fungal infections in organ transplant recipients: guidelines of the American Society of Transplantation, infectious diseases community of practice. *Am J Transplant* 2012; 12 (9): 2414.
- <sup>iv</sup> Blair JE, Mulligan DC. Coccidioidomycosis in healthy persons evaluated for liver or kidney donation. *Transpl Infect Dis* 2007; 9 (1): 78.
- <sup>v</sup> Parasites - Strongyloides. Centers for Disease Control and Prevention, 2014. (Accessed April 24, 2014, at [http://www.cdc.gov/parasites/strongyloides/.](http://www.cdc.gov/parasites/strongyloides/))
- <sup>vi</sup> Neglected Tropical Diseases, Strongyloides. World Health Organization, 2014. (Accessed April 24, 2014, at [http://www.who.int/neglected\\_diseases/diseases/strongyloidiasis/en/.](http://www.who.int/neglected_diseases/diseases/strongyloidiasis/en/))
- <sup>vii</sup> Roxby AC, Gottlieb GS, Limaye AP. Strongyloidiasis in transplant patients. *Clin Infect Dis* 2009;49:1411-23.
- <sup>viii</sup> Centers for Disease C, Prevention. Transmission of *Strongyloides stercoralis* through transplantation of solid organs--Pennsylvania, 2012. *MMWR* 2013;62:264-6.
- <sup>ix</sup> Le M, Ravin K, Hasan A, et al. Single donor-derived strongyloidiasis in three solid organ transplant recipients: case series and review of the literature. *Am J Transplant* 2014;14:1199-206.
- <sup>x</sup> Huprikar S, Bosserman E, Patel G, Morre A, et al. Donor-derived *Trypanosoma cruzi* infection in solid organ recipients in the United States, 2001-2011. *Am J Transplant* 2013 Sep;13(9):2418-25.
- <sup>xi</sup> Chin-Hong PV, Schwartz BS, Bern C, Montgomery SP, Kontak S, Kubak B, Morris MI, Nowicki M, Wright C, Ison MG. 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 Apr;11(4):672-80.
- <sup>xii</sup> Levi ME, Kumar D, Green M, Ison MG, Kaul D, Michaels MG, Morris MI, Schwartz BS, Echenique IA, Blumberg E, et al. Considerations for screening live kidney donors for endemic infections: a viewpoint on the UNOS policy. *Am J Transplant* 2014 May;14(5):1003-11.
- <sup>xiii</sup> Schwartz BS, Mawhorter SD. Parasitic infections in solid organ transplantation. *Am J Transplant* 2013 Mar;13 Suppl 4:280-303