

Guidance Document for Public Comment

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

OPTN Ad Hoc Disease Transmission Advisory Committee

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

Sponsoring Committee: Ad Hoc Disease Transmission Advisory
Public Comment Period: July 27, 2023-September 19, 2023

Executive Summary

The OPTN Ad Hoc Disease Transmission Advisory Committee (the Committee) is refreshing and combining existing guidance documents for endemic diseases for living and deceased donors. OPTN *Policy 14.4: Medical Evaluation Requirements for Living Donors* requires each living donor hospital to develop and follow a written protocol for identifying and testing donors at risk for transmissible seasonal or geographically defined endemic disease as part of its medical evaluation.¹ The purpose of this requirement is to minimize disease transmission through organ transplantation and promote living donor and transplant recipient safety. The Committee created four guidance documents to help living donor hospitals comply with this policy. The Committee reviewed these documents after the Centers for Disease Control and Prevention (CDC) representatives and the OPTN Membership and Professional Standards Committee (MPSC) requested the Committee provide clarity on endemic diseases. The Committee updated and condensed these documents while adding guidance for deceased donors as well.

The four guidance documents that will be updated and condensed are:

- *Recognizing Seasonal and Geographically Endemic Infections in Organ Donors: Considerations during Living Donor Evaluation*
- *Preventing Chagas disease in transplant recipients: Donor screening and recipient monitoring*
- *Identifying Risk Factors for West Nile Virus (WNV) During Evaluation of Potential Living Donors*
- *Guidance for Identifying Risk Factors for Mycobacterium tuberculosis (MTB) During Evaluation of Potential Living Kidney Donors*

These documents were implemented from 2012 to 2014 and need updates in nomenclature, testing, and potential donor-derived transmission events (PDDTE) data. These documents will incorporate guidance for screening for endemic diseases for deceased as well as living donors. They also warrant a refresh of current epidemiology and the addition of sections on testing turnaround time.

¹ OPTN Policy 14.4: Medical Evaluation Requirements for Living Donors (Accessed May 24, 2023)
https://optn.transplant.hrsa.gov/media/eavh5bf3/optn_policies.pdf.

The revision of these documents aims to maintain transplant recipient and living donor safety through infectious disease testing by minimizing disease transmission through organ transplantation. The Committee will evaluate the success of this guidance document through monitoring donor-derived transmission events.

Background

In 2022, the Endemic Diseases Subcommittee of the Committee reviewed the potential gaps in education and policy regarding certain endemic diseases that presented significant patient safety risks, and for which identification and treatment strategies exist but are not in common use. Diseases are endemic to a region when they are consistently prevalent in that specific area.² The Subcommittee included subject matter experts from the CDC and the Food and Drug Administration (FDA), along with Committee representatives from organ procurement organizations (OPOs). The MPSC wrote a memo to the Committee on opportunities to improve patient safety, noting concerns regarding a lack of standardized testing and reporting practices of OPOs for endemic diseases.³ The Committee received support from the OPTN OPO and Operations and Safety Committees for this guidance document.

The document provides guidance for six endemic diseases: Histoplasmosis, Coccidioidomycosis, Strongyloidiasis, Chagas disease, Tuberculosis, and West Nile Virus. It advises transplant hospitals and OPOs on how to screen, who to screen, and management of infected living donors and transplant recipients.

Histoplasmosis

Histoplasma capsulatum is a dimorphic fungus found throughout the world. It is endemic in the United States (U.S.) in the Ohio and Mississippi River Valley and into the Midwest and South-Central states.⁴ 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 histoplasmosis has only rarely been reported.⁵

Coccidioidomycosis

Coccidioides immitis and *Coccidioides posadasii* are dimorphic fungi endemic in arid and semi-arid climates in Washington state and the southwestern part of the U.S., Northern Mexico including areas along the U.S. border, and parts of Central and South America.⁶ 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 symptomatic

² Centers for Disease Control and Prevention. "Principles of Epidemiology." Lesson 1: Introduction to Epidemiology, May 18, 2012. <https://www.cdc.gov/csels/dsepd/ss1978/lesson1/section11.html>.

³ Ad Hoc Disease Transmission Advisory Committee, OPTN, meeting summary for February 14, 2022, accessed April 13, 2023, https://optn.transplant.hrsa.gov/media/jn4p42r3/2022_02_14_dtac_open_summary.pdf.

⁴ Akram SM, Koirala J. Histoplasmosis. [Updated 2023 Feb 25]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK448185/>

⁵ Ibid.

⁶ Chow NA, Kangiser D, Gade L, McCotter OZ, Hurst S, Salamone A, Wohrle R, Clifford W, Kim S, Salah Z, Oltean HN, Plumlee GS, Litvintseva AP. Factors Influencing Distribution of *Coccidioides immitis* in Soil, Washington State, 2016. *mSphere*. 2021 Dec 22;6(6):e0059821. doi: 10.1128/mSphere.00598-21. Epub 2021 Nov 3. PMID: 34730378; PMCID: PMC8565518.

pulmonary nodules, reticulonodular disease, or cavitary disease. Immunosuppressed individuals may develop disseminated infection.⁷ Multiple cases of donor-derived coccidioidomycosis have been reported, often with poor outcomes.

Strongyloidiasis

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. There are an estimated 370 million infected people worldwide.⁸

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, and the southeastern U.S.⁹ In the U.S., a prevalence of up to 6.1% has been reported in select populations, with a much higher prevalence of up to 46.1% in immigrant populations.¹⁰ Infection results primarily from exposed skin 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), unprotected skin contact with human waste or sewage, and occupations that increase contact with contaminated soil, such as farming and coal mining. Rural populations and those of a lower socioeconomic status are at higher risk.¹¹

Chagas Disease

Chagas disease is caused by infection with the protozoan parasite *Trypanosoma cruzi* (*T. cruzi*). It is estimated that eight million people are infected in the Americas, with over 300,000 infected individuals currently living in the U.S. Most infections were acquired in endemic regions of Mexico, South and Central America, where infection is transmitted by the bite of an infected triatomine bug. Infection can also be transmitted from an infected mother during the second and third trimester of pregnancy or rarely during childbirth, as well as through infected food or drink, and through blood transfusion and organ transplantation.¹²

⁷ Akram SM, Koirala J. Coccidioidomycosis. [Updated 2023 Feb 25]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK448161/>

⁸ Mora Carpio AL, Meseeha M. Strongyloides Stercoralis. [Updated 2023 Feb 7]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK436024/>

⁹ Schär F, Trostorf U, Giardina F, Khieu V, Muth S, Marti H, Vounatsou P, Odermatt P. Strongyloides stercoralis: Global Distribution and Risk Factors. PLoS Negl Trop Dis. 2013 Jul 11;7(7):e2288. doi: 10.1371/journal.pntd.0002288. PMID: 23875033; PMCID: PMC3708837.

¹⁰ Global Health, Division of Parasitic Diseases and Malaria. “CDC - Strongyloides - Epidemiology & Risk Factors.” Parasites-Strongyloides, December 31, 2018. <https://www.cdc.gov/parasites/strongyloides/epi.html>.

¹¹ Ibid.

¹² Global Health, Division of Parasitic Diseases and Malaria. “CDC - Chagas Disease - Epidemiology & Risk Factors.” Parasites- American Trypanosomiasis (also known as Chagas Disease), April 11, 2022. <https://www.cdc.gov/parasites/chagas/epi.html>.

¹² Bern C, Kjos S, Yabsley MJ, Montgomery SP. Trypanosoma cruzi and Chagas' Disease in the United States. Clin Microbiol Rev. 2011 Oct;24(4):655-81. doi: 10.1128/CMR.00005-11. PMID: 21976603; PMCID: PMC3194829. - American Trypanosomiasis (also known as Chagas Disease), April 11, 2022. <https://www.cdc.gov/parasites/chagas/epi.html>.

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.¹³ Parasitemia clears within eight to twelve 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 *T. cruzi* tests.¹⁴

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 Mexican, Central, and South American immigrant populations.¹⁵ 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 U.S. Two of 15 (13%) renal transplant recipients had donor-derived infection; none of these were living donor transplants. Living organ donor transmissions have been reported in Mexico and South America.¹⁶

Tuberculosis

Up to one-third of the world's population is infected with mycobacterium tuberculosis (MTB); however, infection in the U.S. is much less common.¹⁷ Reported cases of MTB disease have been declining in the U.S. since 1992 with most cases occurring in foreign born persons.¹⁸ After initial infection with MTB, most people do not develop MTB disease; the infection disseminates throughout the body and remains dormant. This condition is called tuberculosis infection (TBI) (previously referred to as "latent tuberculosis infection"). In 2022, there were 83,00 reported TB cases¹⁹ in the United States (a rate of 2.5 cases per 100,000 persons).²⁰ In patients with TBI, the highest risk of reactivation and the development of MTB disease occurs in the first two years after infection and then declines.²¹ Since initial infection

¹³ Bern C, Kjos S, Yabsley MJ, Montgomery SP. Trypanosoma cruzi and Chagas' Disease in the United States. Clin Microbiol Rev. 2011 Oct;24(4):655-81. doi: 10.1128/CMR.00005-11. PMID: 21976603; PMCID: PMC3194829.

¹⁴ Ibid.

¹⁵ Chin-Hong, P.V., B.S. Schwartz, C. Bern, S.P. Montgomery, S. Kontak, B. Kubak, M.I. Morris, M. Nowicki, C. Wright, and M.G. Ison. "Screening and Treatment of Chagas Disease in Organ Transplant Recipients in the United States: Recommendations from the Chagas in Transplant Working Group." American Journal of Transplantation 11, no. 4 (January 3, 2011): 672–80. <https://doi.org/10.1111/j.1600-6143.2011.03444.x>.

¹⁶ M.E. Levi, D. Kumar, M. Green, M.G. Ison, D. Kaul, M.G. Michaels, M.I. Morris, B.S. Schwartz, I.A. Echenique, E.A. Blumberg, Considerations for Screening Live Kidney Donors for Endemic Infections: A Viewpoint on the UNOS Policy, American Journal of Transplantation, Volume 14, Issue 5, 2014, Pages 1003-1011, ISSN 1600-6135, <https://doi.org/10.1111/ajt.12666>.

¹⁷ World Health Organization. "Tuberculosis." Tuberculosis . Accessed May 24, 2023. <https://www.who.int/news-room/questions-and-answers/item/tuberculosis#:~:text=About%20one%2Dthird%20of%20the,ill%20with%20TB%20of%2010%25>.

¹⁸ Division of Tuberculosis Elimination, National Center for HIV, Viral Hepatitis, STD, and TB Prevention, Centers for Disease Control and Prevention. "Trends 2021." Tuberculosis (TB), November 9, 2022. <https://www.cdc.gov/tb/publications/factsheets/statistics/tbtrends.htm>.

¹⁹ provisional

²⁰ Division of Tuberculosis Elimination, National Center for HIV, Viral Hepatitis, STD, and TB Prevention, Centers for Disease Control and Prevention. "Trends 2021." Tuberculosis (TB), November 9, 2022. <https://www.cdc.gov/tb/publications/factsheets/statistics/tbtrends.htm>.

²¹ Petruccioli E, Petrone L, Chiacchio T, Farroni C, Cuzzi G, Navarra A, Vanini V, Massafra U, Lo Pizzo M, Guggino G, Caccamo N, Cantini F, Palmieri F, Goletti D. Mycobacterium tuberculosis Immune Response in Patients With Immune-Mediated Inflammatory Disease. Front Immunol. 2021 Aug 10;12:716857. doi: 10.3389/fimmu.2021.716857. PMID: 34447382; PMCID: PMC8382688.

does result in live MTB in many organs, tuberculosis can be transmitted via non-lung organs used for transplantation from donors who have never had clinical signs or symptoms of MTB disease.²²

West Nile Virus

West Nile Virus (WNV) is a ribonucleic acid virus that spreads to humans by mosquito bites. Birds serve as a reservoir for WNV, and humans are a dead-end host for the virus. The virus was first detected in North America in 1999, and since then, human infections have been reported in all U.S. states.²³ The number of human infections varies significantly based on the region and year, with most transmission occurring during the warmer months (July to October) when mosquitoes are most active.²⁴ While the majority of WNV infections are asymptomatic, about 20% of those infected may develop fever, and less than one percent develop neurological complications such as encephalitis or myelitis (involving the spinal cord).²⁵ This means that even donors who do not display symptoms could still transmit the virus to recipients. While several treatments have been explored, there is currently no established treatment for WNV.

Purpose

This guidance document aims to decrease donor-derived disease transmission from organ transplantation. Endemic diseases have high potential for morbidity and potential mortality if transmitted to recipients. As organ offer patterns continue to change, increased awareness and communication for potential endemic diseases across regions is necessary.

Recommendations

Histoplasmosis

The Committee recommends living and deceased donors with signs, symptoms, or radiological findings consistent with active histoplasmosis (cough, fever, sweats, weight loss, non-calcified pulmonary nodules/cavities, or lymphadenopathy)²⁶ have a thorough medical evaluation including serologic testing for histoplasmosis prior to organ donation. Living and deceased donors at higher risk of transmitting disease include those with recent infection or a prior history of known active histoplasmosis.²⁷ Screening should be considered for those donors. Potential donors with a history of pneumonia of an unknown

²² Abad CLR, Razonable RR. Donor derived Mycobacterium tuberculosis infection after solid-organ transplantation: A comprehensive review. *Transpl Infect Dis*. 2018 Oct;20(5):e12971. doi: 10.1111/tid.12971. Epub 2018 Aug 12. PMID: 30055041.

²³ Colpitts TM, Conway MJ, Montgomery RR, Fikrig E. West Nile Virus: biology, transmission, and human infection. *Clin Microbiol Rev*. 2012 Oct;25(4):635-48. doi: 10.1128/CMR.00045-12. PMID: 23034323; PMCID: PMC3485754.

²⁴ Shocket MS, Verwillow AB, Numazu MG, Slamani H, Cohen JM, El Moustaid F, Rohr J, Johnson LR, Mordecai EA. Transmission of West Nile and five other temperate mosquito-borne viruses peaks at temperatures between 23°C and 26°C. *Elife*. 2020 Sep 15;9:e58511. doi: 10.7554/eLife.58511. PMID: 32930091; PMCID: PMC7492091.

²⁵ L.D. Kramer, West Nile Virus, Editor(s): Brian W.J. Mahy, Marc H.V. Van Regenmortel, Encyclopedia of Virology (Third Edition), Academic Press, 2008, Pages 440-450, ISBN 9780123744104, <https://doi.org/10.1016/B978-012374410-4.00633-6>.

²⁶ Kauffman CA. Histoplasmosis: a clinical and laboratory update. *Clin Microbiol Rev*. 2007 Jan;20(1):115-32. doi: 10.1128/CMR.00027-06. PMID: 17223625; PMCID: PMC1797635.

²⁷ Kovacs CS Jr, Koval CE, van Duin D, de Morais AG, Gonzalez BE, Avery RK, Mawhorter SD, Brizendine KD, Cober ED, Miranda C, Shrestha RK, Teixeira L, Mossad SB. Selecting suitable solid organ transplant donors: Reducing the risk of donor-transmitted infections. *World J Transplant*. 2014 Jun 24;4(2):43-56. doi: 10.5500/wjt.v4.i2.43. PMID: 25032095; PMCID: PMC4094952.

type in the past two years should also be considered for screening.²⁸ Even in endemic areas, universal screening of living and deceased donors lacking any of the above characteristics is not likely to be productive.

The Committee advises potential living donors with clinical evidence of active histoplasmosis or a serological pattern suggestive of active disease receive treatment prior to organ donation. Recipients of donors with a history of histoplasmosis may not require specific prophylaxis. Clinical and laboratory monitoring for disease is a reasonable approach.²⁹

Coccidioidomycosis

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.³⁰ 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.³¹ Finally, it is reasonable to perform 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. Serological tests (enzyme immunoassay, complement fixation, or immunodiffusion) may be combined with chest imaging.³²

The Committee advises potential living donors with evidence of active infection require a thorough evaluation to determine the extent of the infection. Donation from actively infected living donors should be deferred until treatment is complete and evidence of active infection (based on clinical, radiographic, and serological factors) has resolved. Prophylaxis with antifungal medications active against *Coccidioides* species may be effective in preventing disease in recipients of infected donors.³³

Strongyloidiasis

Implementation of the *Improve Deceased Donor Evaluation of Endemic Diseases* proposal will require all deceased donors be screened for *Strongyloides*. Given the high mortality rate of donor-derived *Strongyloides* infection, and the efficacy, safety, simplicity and low cost of prophylactic therapy, universal screening for *Strongyloides* is recommended for all living donors. Serology is required for deceased donors and recommended for living donors. Serology should be completed using primarily an Immunoglobulin G assay for antibodies to *Strongyloides* pending implementation of *Improve Deceased Donor Evaluation of Endemic Diseases* and is recommended prior to implementation.

²⁸ N. Singh, S. Huprikar, S.D. Burdette, M.I. Morris, J.E. Blair, L.J. Wheat, Donor-Derived Fungal Infections in Organ Transplant Recipients: Guidelines of the American Society of Transplantation, Infectious Diseases Community of Practice[†], American Journal of Transplantation, Volume 12, Issue 9, 2012, Pages 2414-2428, ISSN 1600-6135, <https://doi.org/10.1111/j.1600-6143.2012.04100>.

²⁹ Ibid.

³⁰ Ibid.

³¹ Ibid.

³² Ibid.

³³ Ibid.

Donors infected with *Strongyloides* may still donate. Living donors can be treated with ivermectin, with no further delay in performing recovery and transplant. Recipients who receive organs from infected and untreated donors may be treated with ivermectin or albendazole.³⁴

Chagas Disease

Donors who were born in a country currently classified as endemic for Chagas disease by the CDC must be screened according to OPTN Policy 2.9 pending implementation of *Improve Deceased Donor Evaluation of Endemic Diseases* and is recommended prior to implementation.

Screening should be considered in the following circumstances for living and deceased donors:³⁵

- Children of women born in endemic regions if their birth mother's serology is positive or unknown
- Donors who have resided in an endemic region for more than three months
- Donors who received a blood transfusion in endemic regions and those who have a previous diagnosis of Chagas disease

Serologic testing using an FDA licensed, approved, or cleared assay should be performed on donors with risk factors for Chagas disease.

Living donors who test positive should be informed about the result and offered infectious disease consultation. Confirmatory testing through submission to the CDC or performance of at least two different FDA licensed, approved, or cleared antibody diagnostic tests should be performed.

Potential recipients of *T. cruzi* positive donor organs should be tested for the presence of *T. cruzi* antibody, particularly since they may share unrecognized risk factors with their potential donor. Once transplant has occurred, expert infectious disease consultation is recommended to coordinate post-transplant testing. In the United States, the CDC can assist with polymerase chain reaction (PCR) and parasitemia testing. 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.

Tuberculosis

The most easily identifiable risk factor for Tuberculosis (TB) is place of birth with estimated risk of TB infection (TBI) of 18.7% among foreign-born persons in the U.S. as compared to 1.8% among U.S. born persons.³⁶

³⁴ Fatehi Elzein, Hamad Albahili, Abdelkarim Bahloul, Thamer Alonazi, Adnan Alghamdi, Eid Alsufyani, Abdullatif Musa, Mohammed Alsaeed, Transplant-related strongyloidiasis in solid organ transplant recipients in Saudi Arabia and the Gulf Cooperation Council countries, *International Journal of Infectious Diseases*, Volume 93, 2020, Pages 133-138, ISSN 1201-9712, <https://doi.org/10.1016/j.ijid.2020.01.032>.

³⁵ Forsyth CJ, Manne-Goehler J, Bern C, Whitman J, Hochberg NS, Edwards M, Marcus R, Beatty NL, Castro-Sesquen YE, Coyle C, Stigler Granados P, Hamer D, Maguire JH, Gilman RH, Meymandi S. Recommendations for Screening and Diagnosis of Chagas Disease in the United States. *J Infect Dis*. 2022 May 4;225(9):1601-1610. doi: 10.1093/infdis/jiab513. PMID: 34623435; PMCID: PMC9071346.

³⁶ Vernon A. Treatment of latent tuberculosis infection. *Semin Respir Crit Care Med*. 2013 Feb;34(1):67-86. doi: 10.1055/s-0032-1333544. Epub 2013 Mar 4. PMID: 23460007.

The following factors would be expected to increase the risk of TBI³⁷:

- Close contacts of persons with infectious TB disease
- Those who spend significant time (greater than 3 months) in areas of the world with high rates of TB or those born in these regions including relief work in a country with high TB risk
 - The guidance document contains a map available on the CDC that outlines these regions
- History of injection of nonmedical injection drug use
- Persons who reside (or ever resided) or worked in institutional settings which resulted in increased risk of exposure to TB (hospitals, nursing homes, correctional facilities, other health care settings, homeless shelters)

Recipients of an organ from a donor who is tuberculosis skin test (TST) or Interferon Gamma Release Assay (IGRA)-positive, had recent exposure to active TB, or had radiographic evidence of untreated TB should be considered for TBI therapy, following CDC guidance for anti-tuberculosis agents and durations.

Table 1-1 outlines the management of living donors with a history of active TBI and the treatment of recipients of these organs.

TABLE 1-1: Management of latent or history of active TB in living donors and recipients of these organs

Clinical Scenario: Living Donor	Risk for Transmission	Recommendation
History of TBI-treated appropriately	Lower	Monitor recipient clinically
History of TBI-treated insufficiently or not treated or treatment details not clear OR new diagnosis of TBI-positive TST or Interferon gamma release assay found during pre-transplant evaluation; evaluation finds no evidence of active TB	Moderate	Consider deferring transplant if possible until donor has taken some/all of chemoprophylaxis and consider chemoprophylaxis of recipient; monitor clinically
Unexplained pulmonary apical fibrosis in donor without cavitation and without additional testing	Variable	Defer donation pending further evaluation
History of MTB disease treated appropriately over two years ago	Lower to moderate	Monitor recipient clinically; consider cultures of previous TB

³⁷ Division of Tuberculosis Elimination, National Center for HIV, Viral Hepatitis, STD, and TB Prevention, Centers for Disease Control and Prevention. "Who Should Be Tested for TB Infection." Tuberculosis (TB), April 14, 2016. <https://www.cdc.gov/tb/topic/testing/whobetested.htm>.

		sites if possible. Consider TB prophylaxis of recipient.
History of MTB disease-site remote from transplant treated appropriately within two years	Lower to moderate	Monitor recipient clinically; consider cultures of previous TB sites if possible. Suggest chemoprophylaxis of recipient.
History of MTB disease-site remote from transplant treated insufficiently and/or with other than standard regimen Excluding disseminated or CNS TB.	Higher Increased risk if less than two years since active TB diagnosis.	Defer live donors until adequately treated; consider consult with infectious disease specialist; recommend cultures of previous TB sites prior to transplant if possible
History of renal MTB disease treated appropriately. (If not treated appropriately donation should be deferred until after appropriate treatment)	Moderate	Verify treatment; monitor clinically; recommend chemoprophylaxis for recipient; recommend cultures of previous TB site(s); consider consult with infectious diseases specialist.

West Nile Virus

Screening strategies for WNV in living and deceased donors include universal year-round testing of all donors versus targeted testing during periods of human WNV activity. As the yield of testing during the winter months is likely of low yield and given the potential for Immunoglobulin M (IgM) to remain positive after resolution of the illness, year-round testing is discouraged unless programs are unable to manage the complexity of more targeted testing strategies. Targeted testing strategies could include testing during a pre-determined timeframe, or testing donors only during times of human WNV activity in the area where the donor lives or has traveled.³⁸

It is advisable to screen deceased donors during months of regional WNV activity. WNV nucleic acid test (NAT) testing is a viable option, but the results may not be available before transplantation. It is important to note that WNV transmission has occurred in donors who tested negative on NAT, and that there is potential for false positive NAT test results if protocols are not in place to improve specificity, as are used by blood collection organizations, or if testing is performed outside of the WNV transmission season, decreasing the pretest probability.

In cases involving deceased donors, the feasibility of conducting WNV testing within a required timeframe is uncertain. As such, the Committee advises against recovering organs from donors who satisfy any of the following criteria: (1) a confirmed WNV infection, (2) a positive WNV NAT test result, ideally meeting a threshold signal-to-cutoff ratio or verified by repeat testing as recommended by the

³⁸ Soto RA, McDonald E, Annambhotla P, Velez JO, Laven J, Panella AJ, Machesky KD, White JL, Hyun J, Freuck E, Habel J, Oh D, Levi M, Hasz R, Eidbo E, Staples JE, Basavaraju SV, Gould CV. West Nile Virus Transmission by Solid Organ Transplantation and Considerations for Organ Donor Screening Practices, United States. *Emerg Infect Dis.* 2022 Feb;28(2):403-406. doi: 10.3201/eid2802.211697. Epub 2021 Nov 29. PMID: 34843660; PMCID: PMC8798677.

manufacturer, or (3) clinical manifestations of meningitis, encephalitis, or flaccid paralysis of indeterminate origin, particularly if they originate from regions with documented WNV activity.

Living donors should be screened with WNV NAT within seven to 14 days of donation. Although no studies have examined organ donation after WNV infection, the Committee suggests postponing donation for a minimum of 28 days in living donors, after which NAT and IgM testing should be performed. If both tests are negative, it is likely that the initial NAT was a false positive, and organ donation can be considered.

Development of symptoms compatible with WNV infection within the first several weeks of transplant should prompt testing in the recipient. There are currently no specific medications available for the treatment of WNV infection.

NOTA and Final Rule Analysis

The Committee submits this guidance document under the authority of the National Organ Transplantation Act (NOTA), which states that the OPTN shall, "adopt and use standards of quality for the acquisition and transportation of donated organs"³⁹ and under the authority of the OPTN Final Rule, which states, "An OPTN member procuring an organ shall assure that laboratory tests and clinical examinations of potential organ donors are performed to determine any contraindications for donor acceptance, in accordance with policies established by the OPTN."⁴⁰ This guidance document will assist living donors in complying with OPTN *Policy 14.4: Medical Evaluation Requirements for Living Donors* and allow OPOs to use standards of quality when allocating organs.

Conclusion

This guidance document aims to decrease donor-derived disease transmission from organ transplantation and provide appropriate recommendations for living donor hospitals and OPOs when screening donors for endemic diseases. The document advises transplant hospitals on recipient management after transplanting organs from donors with endemic diseases. The Committee will assess the success of this guidance document through decreased endemic disease transmissions in organ recipients.

Considerations for the Community

The Committee requests feedback on the following questions:

- How can we promote communication between transplant programs and OPOs who may now need to share information about screening for endemic diseases?
- How can transplant programs communicate with patients on screening practices for endemic diseases?
- Are there any additional screening practices that should be incorporated for these diseases?

³⁹ 42 USC §274(b)(2)(E).

⁴⁰ 8 42 CFR §121.6(a)

Guidance Document

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

Background

Both deceased and living donors are at risk for transmitting endemic diseases that are either geographically or seasonally defined. Since 2014, Organ Procurement and Transplantation Network (OPTN) policy has required living donor hospitals to develop a written protocol for identification and testing potential donors at risk for these endemic infections as part of the medical evaluation process. More recently on June 26, 2023, the OPTN Board of Directors approved additional policies to address screening of deceased donors for endemic diseases to further reduce the risk for potential donor-derived infectious events.

Summary and Goals

The OPTN Ad Hoc Disease Transmission Advisory Committee (DTAC) created this guidance document to assist programs in identification of potential living and deceased donors who may carry an increased risk of transmitting seasonal or geographically endemic disease to organ recipients. This document will also help programs manage recipients that receive organs from donors with endemic diseases. This resource is not 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 organ procurement organizations (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 (PDDTE) reported to the OPTN for both deceased and living donors. A number of the PDDTE reported are seasonally 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 not generally universally performed. This guidance document provides information the DTAC believes will help programs and OPOs identify and test donors at risk for transmissible seasonally or geographically defined disease. This information is meant to assist the transplant community in performing organ donor and recipient infectious disease screening procedures as part of the overall medical evaluation and recipient management process.

Recognizing Risk Factors

There are several factors to consider in determining a donor's risk of transmissible infection. OPOs and living donor recovery hospitals should consider the following when screening potential organ donors:

- Geographic risks (including duration of time spent in a location)
 - Birthplace of the potential donor

- 44 ○ Home country/region of the U.S., and prolonged residence outside home region, either
- 45 recent or remote
- 46 ○ Close family members' countries of origin
- 47 ○ Donor hospital region
- 48 ○ Occupational or recreational travel to other countries and/or regions
- 49 • Occupational risks
 - 50 ○ Healthcare workers, veterinarian/animal care workers
 - 51 ○ Construction workers, landscapers, park rangers, and other outdoor workers
 - 52 ○ Peace Corps workers, international journalists
 - 53 ○ Current or previous military service, particularly outside the U.S.
 - 54 ○ Medical mission trips
- 55 • Seasonal risks
 - 56 ○ Residence in/travel to warm weather climates with potential insect exposures
- 57 • Hobbies
 - 58 ○ Hunting/dressing game, taxidermy
 - 59 ○ Time living outdoors including camping, swimming in lakes, drinking stream water,
 - 60 insect exposures
 - 61 ○ Adventure sports
 - 62 ○ Gardening
- 63 • Significant animal exposure (wild and/or domestic)
 - 64 ○ Large numbers of cats or dogs or any unusual pets
 - 65 ○ Laboratory/research animals
 - 66 ○ Veterinarian/vet assistant
- 67 • Family members and close contacts with potential risk factors
 - 68 ○ Geographic or seasonal infections previously diagnosed in close family members or
 - 69 other contacts may predict risk for subclinical infection in the potential donor
- 70 • Personal history of seasonal or geographic infection in the potential donor, even if remote

71

72 The organ donor population has become increasingly geographically diverse, reflecting the enhanced

73 mobility and complex migration patterns of the general population. Therefore, it is not practical to list all

74 the pathogens that have the potential for transmission through organ transplantation. Parasitic

75 infections such as amebiasis, babesiosis, leishmaniasis, schistosomiasis, echinococcosis, and malaria,

76 bacterial infections such as brucellosis and melioidosis, fungal infections such as paracoccidiomycosis

77 and talaromycosis, and viral infections such as Eastern Equine Encephalitis Virus have distinct areas of

78 endemism and may be transmitted through the organ allograft. In donors with a history of residence in

79 developing countries or remote regions, unusual occupational exposure risks, or extensive travel,

80 infectious disease (ID) consultation may be helpful as part of the pre-transplant evaluation for living

81 donors or prior to organ acceptance for deceased donors. This guidance document does not replace

82 expert ID evaluation. Table 1 covers a number of common seasonal and geographically endemic

83 infections that may be transmitted from organ donor to recipient.

84

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

<u>Disease</u>	<u>Signs/Symptoms in Potential Donor</u>	<u>Known Risk Factors</u>	<u>Potential Testing for Deceased Donors</u>	<u>Potential Testing For Living Donors</u>	<u>Imaging that may be helpful</u>
<u>Histoplasmosis</u>	<u>Fever, night sweats, lymphadenopathy, cough, non-calcified pulmonary nodules or cavities</u>	<u>Residence in Midwestern or South-Central states along the Mississippi or Ohio river valleys</u>	<u>Serology</u> <u>-complement fixation</u> <u>-immunodiffusion</u> <u>-EIA -Urine or serum antigen testing</u>	<u>-Serology</u> <u>-complement fixation</u> <u>-immunodiffusion</u> <u>-EIA -Urine or serum antigen testing</u>	<u>Chest X-ray (CXR) or CT</u>
<u>Coccidioidomycosis</u>	<u>Fever, joint pains, cough, neck stiffness, headaches, pulmonary nodules or cavities, reticulonodular infiltrates</u>	<u>Residence in endemic areas of Washington state, the southwestern United States, Northern Mexico, and parts of South & Central America</u>	<u>Serology</u> <u>-enzyme immunoassay (preferred)</u> <u>-complement fixation</u> <u>-immunodiffusion</u> <u>-Urine or serum antigen testing</u>	<u>Serology</u> <u>-enzyme immunoassay (preferred)</u> <u>-complement fixation</u> <u>-immunodiffusion</u> <u>-Urine or serum antigen testing</u>	<u>CXR or CT</u>
<u>Strongyloidiasis</u>	<u>Donors may have chronic abdominal pain, bloating, heartburn, intermittent diarrhea and constipation, dry cough, skin rashes, and/or eosinophilia, or could be entirely asymptomatic.</u>	<u>Soil exposure in tropical/warm climates. Walking barefoot or unprotected skin contact with human sewage or contaminated soil. Infection may persist for decades.</u>	<u>Serologic testing is required for all*</u> <u>*pending policy implementation of <i>Improve Deceased Donor Evaluation of Endemic Diseases</i></u>	<u>Donors could be tested by serology (preferred) and/or stool ova and parasite examination, specifically looking for <i>Strongyloides</i>.</u>	<u>None</u>
<u>Chagas disease</u>	<u>Most asymptomatic; symptomatic chronic infection may present with cardiomyopathy, cardiac conduction abnormalities, megaesophagus, megacolon</u>	<u>Born or resided in endemic areas of Mexico, South & Central America, child of woman who lived in endemic area, received blood transfusion in endemic area</u>	<u>Required by OPTN policy if donor is born in endemic country*:</u> <u>Serology testing (See Chagas Guideline, Table 3)</u> <u>*pending policy implementation of <i>Improve Deceased Donor Evaluation of Endemic Diseases</i></u>	<u>Serology testing (See Chagas Guideline, Table 3)</u>	<u>None unless symptomatic with chronic Chagas disease</u>

<u>Tuberculosis</u>	<u>Fever, night sweats, weight loss, cough, recurrent pneumonia, exudative pleural effusion of unknown etiology, lymphadenopathy, non-calcified pulmonary nodules or cavities</u>	<u>Born outside U.S., Prolonged residence outside U.S., Homeless, Alcohol or other substance abuse, Jail/Prison time, Health care worker, Known TB exposure</u>	<u>Positive tuberculin skin test (TST) or interferon gamma release assay (IGRA)**; Sputum/BAL AFB smear, culture, nucleic acid amplification, TB PCR; tissue AFB smear, culture, TB PCR</u> <u>**Deceased donors on high-dose steroids may have false-negative IGRA/TST</u>	<u>Positive tuberculin skin test (TST) or interferon gamma release assay (IGRA); Sputum/BAL AFB smear, culture, nucleic acid amplification, TB PCR; tissue AFB smear, culture, TB PCR</u> <u>*refer to OPTN Policy 14</u>	<u>CXR, CT thorax, CT abdomen/pelvis (renal TB)</u>
<u>West Nile Virus</u>	<u>Often asymptomatic; 20% develop acute febrile illness; <1% encephalitis, myelitis</u>	<u>Mosquito exposure, blood transfusion; risk varies by season & location</u>	<u>Nucleic acid test (NAT)</u>	<u>Nucleic acid test (NAT)</u>	<u>None</u>

86

87 **I. FUNGAL INFECTIONS**

88

89 **Histoplasmosis Guidance**

90

91 **Background**

92 *Histoplasma capsulatum* is a dimorphic fungus found throughout the world. It is endemic in the
 93 U.S. in the Ohio and Mississippi River Valleys and into the Midwest and South-Central states
 94 (Figure 1). In most cases, clinical signs of infection in immunocompetent patients are limited to
 95 the lungs, though many patients are asymptomatic. Immunocompromised patients may
 96 develop severe disseminated disease that is fatal without prompt diagnosis and treatment.
 97 Donor-derived histoplasmosis has only rarely been reported. In endemic areas, up to 75% of the
 98 population is infected with *Histoplasma capsulatum*; therefore, no further exposure risk factors
 99 need be elicited in residents of these areas.

100

101 **Who Should be Screened**

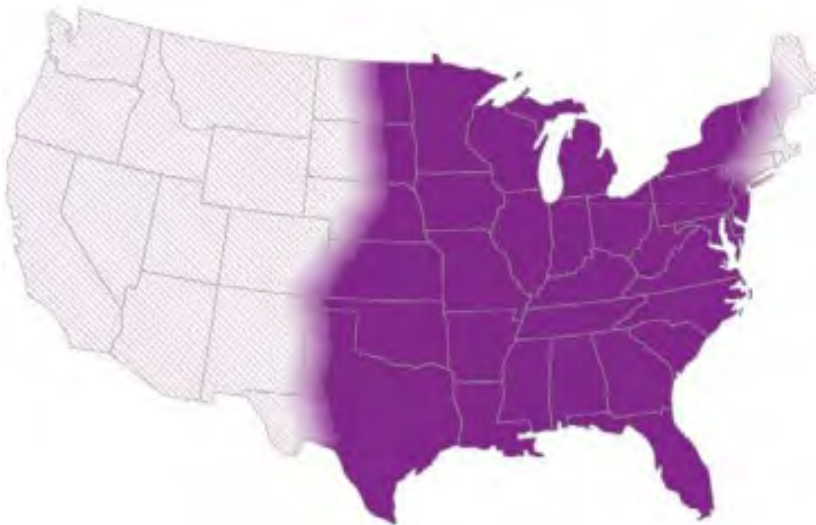
102 **Living and Deceased Donors**

103 Donors at higher risk of transmitting disease include those with recent infection or a prior
 104 history of known active histoplasmosis and should be screened. Potential donors with a history
 105 of pneumonia of unknown type in the past two years should also be considered for screening.
 106 Donors with signs, symptoms, or radiological findings consistent with active histoplasmosis
 107 (cough, fever, sweats, weight loss, non-calcified pulmonary nodules/cavities, or
 108 lymphadenopathy) need a thorough medical evaluation including testing for histoplasmosis

109 prior to organ donation. Even in endemic areas, universal screening of donors lacking any of the
 110 above characteristics is not likely to be productive. Potential donors with the sole finding of a
 111 calcified granuloma on chest imaging do not require further testing.

112

113 **Figure 1: Centers for Disease Control and Prevention’s (CDC) current estimate of *Histoplasma***
 114 **endemicity in the United States⁴¹**



115

116 Darker shading indicates areas where *Histoplasma* is more prevalent. Diagonal shading shows
 117 the potential geographic range of *Histoplasma*.

118

119 **How to screen**

120 **Living and Deceased Donors**

121 In asymptomatic potential donors, serological testing can be used to screen those at risk for the
 122 infection. Complement fixation and immunodiffusion testing are the most commonly performed
 123 tests. Complement fixation titers of 1:8 and 1:16 may just indicate previous infection at low risk
 124 for transmission. Positive immunodiffusion testing is more concerning for the presence of viable
 125 organisms, particularly if a H band is present.

126

127 **Management of infected living donors**

128 Potential living donors with clinical evidence of active histoplasmosis (fever, night sweats,
 129 lymphadenopathy, cough, non-calcified pulmonary nodules or cavities) or a serological pattern
 130 suggestive of active disease should receive treatment prior to organ donation. For patients with
 131 histoplasmosis limited to the lungs, a reasonable approach would include six to 12 weeks of
 132 treatment, with resolution of clinical signs and symptoms of histoplasmosis. After treatment and
 133 resolution of antigenuria/antigenemia, the risk of donor-derived infection is likely low. Given
 134 that disseminated histoplasmosis is typically associated with other significant medical

⁴¹ CDC. “More Information about the Estimated Areas with Blastomycosis ...” More information about the estimated areas with blastomycosis, coccidioidomycosis (Valley fever), and histoplasmosis in the United States. Accessed June 23, 2023. <https://www.cdc.gov/fungal/pdf/more-information-about-fungal-maps-508.pdf>.

135 conditions, it is unlikely that a patient with a history of disseminated histoplasmosis would
136 qualify for living organ donation.

137

138 **Management of Recipients**

139 Recipients of donors with a history of histoplasmosis may not require specific prophylaxis.
140 Clinical and laboratory monitoring for disease is a reasonable approach. Serial urine or serum
141 antigen testing (every one to three months) for one year might identify donor-derived
142 histoplasmosis prior to the development of clinical symptoms. Serological tests have low
143 sensitivity after organ transplantation, and most solid organ transplant recipients with
144 histoplasmosis have negative serological studies.

145

146 **Infection Avoidance Between Testing and Transplant**

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

151

152 **Coccidioidomycosis Guidance**

153

154 **Background**

155 *Coccidioides immitis* and *Coccidioides posadasii* are dimorphic fungi endemic in arid and semi-
156 arid climates in Washington state and the southwestern part of the U.S. (Figure 2), Northern
157 Mexico including areas along the U.S. border, and parts of Central and South America. The most
158 common clinical syndrome is pneumonia often accompanied by joint pains, fatigue, and weight
159 loss. Chronic fibrocavitary pulmonary disease may follow primary infection, and some infected
160 persons have persistent symptomatic pulmonary nodules, reticulonodular disease, or cavitary
161 disease. Immunosuppressed individuals may develop disseminated infection. Multiple cases of
162 donor-derived coccidioidomycosis have been reported, often with poor outcomes.

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164

Figure 2: CDC's current estimate of *Coccidioides* endemicity in the United States⁴²

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Darker shading shows areas where *Coccidioides* is more likely to be present. Diagonal shading shows the potential geographic range of *Coccidioides*.

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Who Should be Screened

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Living and Deceased Donors

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One study indicated that 2.1% of persons evaluated for living donation in an endemic region were seropositive, suggesting recent or active disease. 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 perform 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.

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How to Screen

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Living and Deceased Donors

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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. For prospective donors with normal imaging and negative serologies, the risk of donor-derived infection is likely low.

⁴² CDC. "More Information about the Estimated Areas with Blastomycosis ..." More information about the estimated areas with blastomycosis, coccidioidomycosis (Valley fever), and histoplasmosis in the United States. Accessed June 23, 2023. <https://www.cdc.gov/fungal/pdf/more-information-about-fungal-maps-508.pdf>.

192 **Management of Infected Living Donors**

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

197
 198 **Management of Recipients**

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

212
 213 **Infection Avoidance between Testing and Transplant**

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

219

220 **II. PARASITIC INFECTIONS**

221

222 ***Strongyloidiasis* Guidance**

223

224 **Background**

225 *Strongyloides stercoralis* is a nematode (roundworm). Unlike other parasites, *Strongyloides* can
 226 replicate for decades within humans via an autoinfection cycle, resulting in chronic symptomatic
 227 or asymptomatic infections that can flourish in the setting of immunosuppression. There are an
 228 estimated 370 million infected people worldwide.

229

230 *Strongyloides* is most common in tropical, subtropical, or warm temperate climates, including
 231 the Caribbean, Mexico, South and Central America, Africa, Southeast Asia, Southern and Eastern
 232 Europe, and the southeastern U.S. In the U.S., a prevalence of up to 6.1% has been reported in
 233 select populations, with a much higher prevalence of up to 46.1% in immigrant populations.
 234 Infection results primarily from exposed skin contact with soil that is contaminated with
 235 *Strongyloides* larvae. Activities that increase the risk of becoming infected include direct contact
 236 with contaminated soil (i.e. walking barefoot), unprotected skin contact with human waste or

237 sewage, and occupations that increase contact with contaminated soil, such as farming and coal
 238 mining. Rural populations and those of a lower socioeconomic status are at higher risk.

239
 240 Hyperinfection occurs in immunocompromised hosts and can lead to disseminated infection,
 241 with mortality as high as 85%. From 2009 to 2013, the CDC assisted in investigations of donor-
 242 derived strongyloidiasis in 11 recipients from seven organ donors and found 86% of the donors
 243 to originate from *Strongyloides* endemic areas. Prophylaxis with ivermectin was noted to be
 244 highly effective in preventing disease transmission in the CDC series and in another series
 245 reported by an OPO.

246 247 **Who Should Be Screened**

248 Given the high mortality rate of donor-derived *Strongyloides* infection, and the efficacy, safety,
 249 simplicity and low cost of prophylactic therapy, universal screening for *Strongyloides* is
 250 recommended for all living donors and is required for deceased donors by OPTN Policy 2.9
 251 pending implementation of *Improve Deceased Donor Evaluation of Endemic Diseases*, and is
 252 recommended prior to implementation.

253
 254 Donors with a personal history of previously treated *Strongyloides* infection should be at low risk
 255 for transmission, although repeat (new) infection after treatment can occur, and the
 256 autoinfection cycle could allow for subclinical persistence. Although transmission within families
 257 is unlikely, a family history should trigger screening given the likelihood of similar exposures.

258 259 **How to Screen**

260 **Living and Deceased Donors**

261 Screening is by serology or stool examination. Serology is required for deceased donors pending
 262 implementation of *Improve Deceased Donor Evaluation of Endemic Diseases*, and recommended
 263 for living donors. Serology is primarily an Immunoglobulin G (IgG) assay for antibodies to
 264 *Strongyloides*. The enzyme-linked immunosorbent assay (ELISA) is preferable because of its
 265 greater sensitivity (90%) and specificity (99%), compared with indirect fluorescent antibody (IFA)
 266 and indirect hemagglutination (IHA) tests. Antibody testing cannot differentiate between
 267 current and prior or treated infections; titers do not reliably decrease rapidly after treatment.
 268 The assays may produce false positive results in patients with filariasis and other nematode
 269 infections. Serology testing is commercially available, often with turnaround times of one to five
 270 days.

271
 272 Stool testing is less sensitive than serology, as stools are positive only during larval shedding
 273 which can be intermittent and would be indicated when serological testing is unavailable or
 274 when serological findings are negative but clinical suspicion of disease is high. A single stool
 275 specimen has a sensitivity of only 15%–30%, although sensitivity increases to nearly 100% if
 276 seven consecutive daily stool specimens are examined in an expert laboratory, which may not
 277 be practical in the transplant setting. Intestinal endoscopy with biopsies may also diagnose
 278 *Strongyloides* infection, although it would not be used for routine screening.

279
 280 For living donors, screening should be done with initial testing to allow time for subsequent
 281 treatment if necessary.

282

283 **Management of Infected Donors**

284 Donors infected with *Strongyloides* may still donate. Living donors can be treated with
 285 ivermectin, with no further delay in organ transplant. Additional serologic or stool testing after
 286 treatment is not likely to be helpful.

287
 288 **Management of Recipients**

289 Recipients who receive organs from infected and untreated donors may be treated with
 290 ivermectin or albendazole. Ivermectin is well tolerated and is preferred (when available) due to
 291 superior efficacy. Ivermectin is usually administered as two single microgram/kg doses either on
 292 two consecutive days or two weeks apart (allowing for one autoinfection cycle). Only oral
 293 ivermectin is available in the U.S. There may be a drug interaction between ivermectin and the
 294 calcineurin inhibitors (tacrolimus and cyclosporine), therefore monitoring of drug levels is
 295 recommended.

296
 297 Transplant centers should follow up on such pre-transplant test results and give prophylaxis to
 298 recipients if their donors were not previously treated. Prophylaxis and treatment doses of anti-
 299 parasitic medications in this setting are probably the same, although they have not been
 300 studied. Most cases of donor-derived strongyloidiasis occur several weeks to months after
 301 transplant, so centers should have adequate time to treat recipients before infection occurs. In
 302 cases in which there is insufficient time for test results to return and treatment to be given to
 303 donors, centers should plan for post-transplant treatment of the recipient. Informed consent
 304 should be considered in both situations.

305
 306 People dually infected with Human T-Cell Lymphotropic Virus-1 (HTLV-1) and *Strongyloides* are
 307 more likely to develop severe cases of strongyloidiasis and are at higher risk for recurrence. It
 308 may be worthwhile to screen patients with *Strongyloides* infection for HTLV-1, so the treating
 309 clinicians are aware of the risk of increased disease severity and recurrence.

310
 311 Patients from areas of Africa endemic for loiasis (primarily central and western sub-Saharan
 312 Africa) should be screened for *L. loa* microfilaremia, as administration of ivermectin to those
 313 with microfilaremia can precipitate life-threatening encephalopathy, known as the Mazzotti
 314 reaction.

315
 316 **Infection Avoidance between Testing and Transplant**

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

321
 322 **Chagas Disease Guidance**

323
 324 **Background**

325 Chagas disease is caused by infection with the protozoan parasite *Trypanosoma cruzi* (*T. cruzi*). It
 326 is estimated that eight million people are infected in the Americas, with over 300,000 infected
 327 individuals currently living in the U.S. Most infections were acquired in endemic regions of
 328 Mexico, South and Central America, where infection is transmitted by the bite of an infected

329 triatomine bug. Infection can also be transmitted from an infected mother during the second
 330 and third trimester of pregnancy or rarely during childbirth, as well as through infected food or
 331 drink, and through blood transfusion and organ transplantation.

332
 333 Most infections are acquired in childhood during residence in an endemic area. The acute phase
 334 of infection may be associated with a mild febrile illness and is often unrecognized. Parasitemia
 335 clears within eight to 12 weeks without treatment, but individuals remain chronically infected.
 336 Infection persists for the individual's life, with chronic disease developing in 20-30%, usually
 337 manifesting as cardiac or gastrointestinal disease. Chronic infection can be diagnosed through
 338 serologic tests for antibody to *T. cruzi*.

339
 340 Blood donor screening in the U.S. beginning in 2007 identified confirmed infections in donors
 341 from 37 states and Puerto Rico, with 57% of all positive tests from California and Florida, areas
 342 with significant Mexican, Central and South American immigrant populations. Latent infection
 343 with *T. cruzi* can persist for decades, therefore organ donor screening of high-risk individuals
 344 using serology testing is utilized at some centers. Transmission of Chagas disease has been
 345 studied in 32 organ transplant recipients from 14 seropositive donors in the United States. Two
 346 of 15 (13%) renal transplant recipients had donor-derived infection; none of these were living
 347 donor transplants. Living organ donor transmissions have been reported in Mexico and South
 348 America.

349 **Who Should Be Screened**

350 Living and Deceased Donors

351 Deceased donors who were born in a country currently classified as endemic for Chagas disease
 352 by the CDC must be screened according to OPTN Policy 2.9 pending implementation of *Improve*
 353 *Deceased Donor Evaluation of Endemic Diseases* and is recommended until then. Screening is
 354 recommended for living donors as well.

355
 356
 357 Screening should be considered in the following circumstances:

- 358 • Children of women born in endemic regions if their birth mother's serology is positive or
 359 unknown
- 360 • Donors who have resided in an endemic region for more than three months
- 361 • Donors who received a blood transfusion in endemic regions and those who have a
 362 previous diagnosis of Chagas disease

363
 364 Countries currently classified as endemic for Chagas disease by the CDC:

365
 366 Argentina

367 Belize

368 Bolivia

369 Brazil

370 Chile

371 Colombia

372 Costa Rica

373 Ecuador

374 El Salvador

375 French Guiana

376 Guatemala

- 377 [Guyana](#)
- 378 [Honduras](#)
- 379 [Mexico](#)
- 380 [Nicaragua](#)
- 381 [Panama](#)
- 382 [Paraguay](#)
- 383 [Peru](#)
- 384 [Suriname](#)
- 385 [Uruguay](#)
- 386 [Venezuela](#)

How to Screen

Deceased and Living Donors

Serology testing using an FDA licensed, approved, or cleared assay (see Table 2) should be performed on donors with risk factors for Chagas disease. Turnaround time for serology tests ranges from one to 10 days. 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 throughout the individual's life.

Table 2: Serological Tests Available for *T. cruzi* Infection

<u>Test name, Manufacturer</u>	<u>Target Antigen</u>	<u>Test Format</u>	<u>Sample Type</u>	<u>FDA-cleared/approved use</u>
<u>Abbott Prism Chagas (T. cruzi [E. coli, recombinant] antigen)⁴³, Abbott Laboratories, Abbott Park, IL</u>	<u><i>T. cruzi</i> recombinant antigens (FP10, FP6, FP3, TcF)</u>	<u>ChLIA⁴⁴</u>	<u>Serum/plasma</u>	<u>Donor screening</u>
<u>ORTHO T. cruzi ELISA Test System Ortho-Clinical Diagnostics, Inc. Raritan, NJ</u>	<u>Whole cell lysate</u>	<u>EIA⁴⁵</u>	<u>Serum/plasma</u>	<u>Donor screening, individual diagnostics</u>
<u>Chagatest ELISA recombinant v.3.0⁴⁶Wiener Laboratories S.A.I.C., Rosario, Argentina</u>	<u>Recombinant epimastigote and trypomastigote Proteins</u>	<u>EIA</u>	<u>Serum/plasma</u>	<u>Diagnosis, NOT donor screening test</u>

⁴³ This test may only be available through local blood bank.

⁴⁴ ChLIA, chemiluminescence immunoassay

⁴⁵ EIA, enzyme immunoassay

⁴⁶ Preferred tests for initial donor screening

<u>Test name, Manufacturer</u>	<u>Target Antigen</u>	<u>Test Format</u>	<u>Sample Type</u>	<u>FDA-cleared/approved use</u>
<u>Hemagen Chagas' Kit, Hemagen Diagnostics, Inc., Columbia, MD</u>	<u>Purified antigens from cultured <i>T. cruzi</i></u>	<u>EIA</u>	<u>Serum</u>	<u>Diagnosis, NOT donor screening test</u>
<u>Abbott ESA Chagas Assay, Abbott Laboratories, Abbott Park, IL</u>	<u><i>T. cruzi</i> recombinant antigens (FP10, FP6, FP3, TcF)</u>	<u>Enzyme Strip Assay</u>	<u>Serum/plasma</u>	<u>Supplemental test in donors who test positive with first-line assays, not approved for individual diagnosis</u>

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*Serologic testing may also be available through the CDC

Management of Infected Living Donors

Living donors who test positive should be informed about the result and offered ID consultation. Confirmatory testing through a submission to the CDC or performance of at least two different FDA licensed, approved, or cleared antibody diagnostic tests should be performed. 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 organs from *T. cruzi* positive donors on an individual basis with informed consent and close monitoring of the recipient. Potential recipients of a *T. cruzi* positive donor organ 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 anti-parasitic therapy that is FDA approved but may lead to side effects that may be difficult to tolerate.

Once transplant has occurred, expert ID consultation is recommended to coordinate post-transplant testing. In the U.S., the CDC can assist with PCR and parasitemia testing. 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.

426 PCR and parasitemia tests of peripheral blood should be performed using the following
 427 schedule:

- 428 • Weekly for the first three months post-transplant
- 429 • Every two weeks for the fourth post-transplant month
- 430 • Monthly thereafter until a minimum of six months post-transplant AND until net state of
 431 immunosuppression is at optimal post-transplant baseline with no evidence of infection
 432 or rejection
- 433 • More frequent monitoring is recommended any time the patient requires antirejection
 434 therapy

435
 436 For access to testing of transplant recipients at risk for reactivation of Chagas, contact the CDC
 437 Division of Parasitic Diseases and Malaria at 404-718-4745 (business hours) or 770-488-7100
 438 (nights and weekends) or via e-mail at parasites@CDC.gov.

439
 440 Current therapy for Chagas disease is limited to benznidazole and nifurtimox (Lampit®, Bayer),
 441 both of which are partially metabolized via cytochrome P450 reductase and may increase
 442 tacrolimus and cyclosporine blood levels. Both drugs have potential adverse effects, but
 443 benznidazole is generally better tolerated and is given twice a day while nifurtimox is given
 444 three times a day.

445 **Infection Avoidance between Testing and Transplant**

446 Potential living donors should avoid prolonged travel to endemic regions, particularly rural areas
 447 with primitive housing or significant insect exposure. Consumption of uncooked food or drink
 448 from endemic regions should also be avoided.

449 **III. BACTERIAL INFECTIONS**

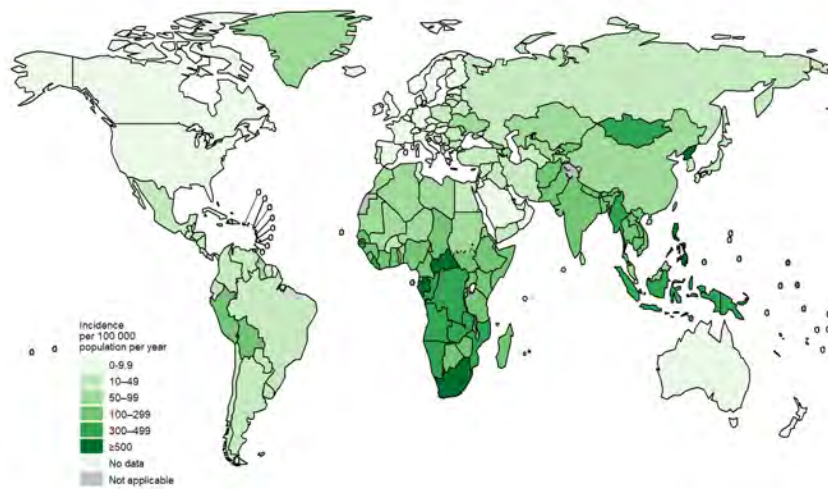
450 **Mycobacterium Tuberculosis (MTB) Guidance**

451 **Background**

452 Up to one-third of the world's population is infected with MTB; however, infection in the United
 453 States is much less common. Reported cases of MTB disease have been declining in the United
 454 States since 1992 with the majority of cases occurring in foreign born persons. After initial
 455 infection with MTB, most people do not develop MTB disease; the infection disseminates
 456 throughout the body and remains dormant. This condition is called tuberculosis infection (TBI)
 457 (previously referred to as "latent tuberculosis infection"). In 2022, there were 83,00 reported TB
 458 cases⁴⁷ in the United States (a rate of 2.5 cases per 100,000 persons). Since initial infection does
 459 result in live MTB in many organs, tuberculosis can be transmitted via non-lung organs used for
 460 transplantation from donors who have never had clinical signs or symptoms of MTB disease.

⁴⁷ provisional

466

Figure 3. World Health Organization Estimated Global TB Incidence Rates, 2021⁴⁸

467

Who Should Be Screened**Living and Deceased Donors**

Since TBI precedes the development of MTB disease, similar risk factors would be expected to be present. One difference is that since the rate of reactivation decreases with time from infection, donors with distant infection would still be at risk for transmission but at a lower risk for MTB disease. The most powerful easily identifiable risk factor is place of birth with estimated risk of TBI of 18.7% among foreign-born persons in the U.S. as compared to 1.8% among U.S. born persons. Higher risk countries are identified by incidence per 100,000 population per year in Figure 3.

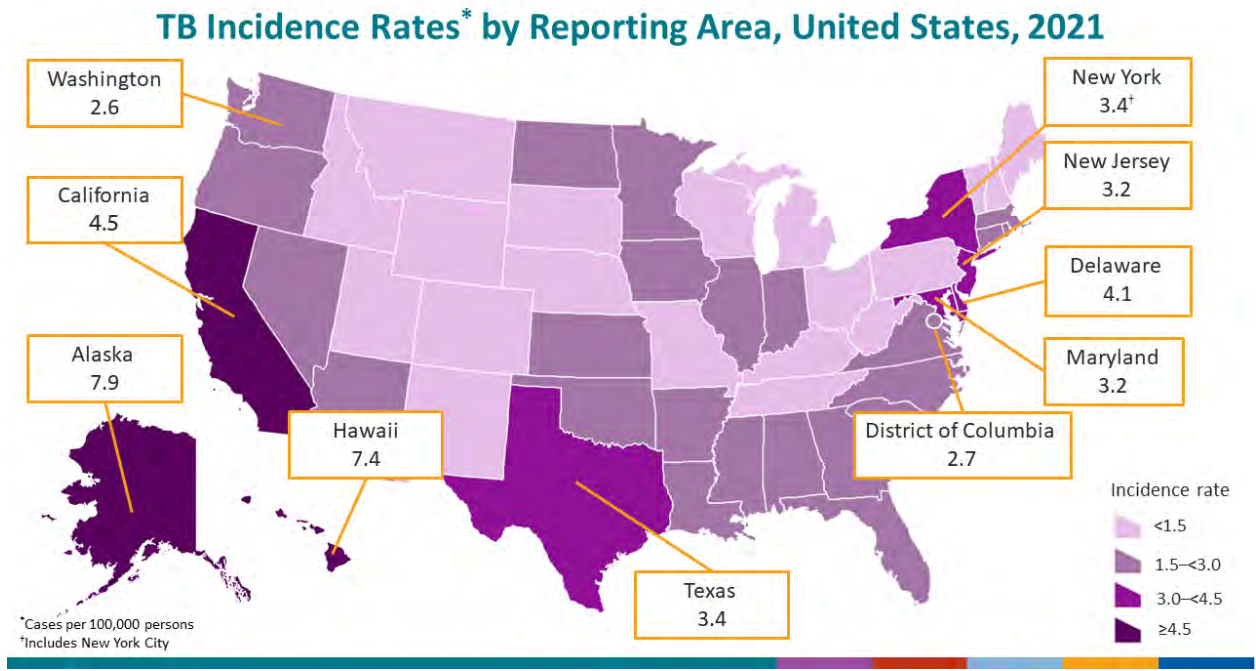
For individuals from lower risk regions, including the United States, the following factors would be expected to increase the risk of TBI:

- Close contacts of persons with infectious TB disease
- Those who spend significant time (greater than 3 months) in areas of the world with high rates of TB or those born in these regions (all but the lightest shaded area of Figure 4) including relief work in a country with high TB risk.
- History of injection drug use
- Persons who reside (or ever resided) or worked in institutional settings which resulted in increased risk of exposure to TB (hospitals, nursing homes, correctional facilities, other health care settings, homeless shelters)

⁴⁸ WHO. "2.1 TB Incidence." World Health Organization, October 27, 2022. <https://www.who.int/teams/global-tuberculosis-programme/tb-reports/global-tuberculosis-report-2022/tb-disease-burden/2-1-tb-incidence>.
<https://www.who.int/teams/global-tuberculosis-programme/tb-reports/global-tuberculosis-report-2022/tb-disease-burden/2-1-tb-incidence>

- 487 • The percentage of TB cases that occur in Hispanic or Latino, Black or African American,
488 and Asian persons is higher than expected based on the percentage of these
489 populations in the U.S. population.
- 490 • Radiographic evidence of prior tuberculosis on chest radiograph

491 **Figure 4: TB Incidence Rates by Reporting Area, United States, 2021⁴⁹**



492

493 **How to Screen**

494 Living and Deceased Donors

495

496 While MTB disease can involve almost any organ and cause many syndromes (e.g., meningitis), a
 497 careful medical history and examination will likely identify most patients with MTB disease. TBI,
 498 by definition, is asymptomatic and specific testing is required to identify patients with TBI. The
 499 current FDA-approved screening methods for TBI in the US include the tuberculin skin test (TST)
 500 and the interferon gamma release assays (IGRAs): QuantiFERON-TB gold in tube (QFT), and T-
 501 SPOT.TB. These tests do not differentiate TBI from MTB disease and may be negative during
 502 times of MTB disease. The TST test requires injection into the skin and a return visit in 48-72
 503 hours to interpret the test. The IGRAs are blood tests and may show positive, negative, or
 504 indeterminate results.

505 Indeterminate results indicate that the controls did not work in that patient, and this result is
 506 more common in immunosuppressed patients. One advantage of the IGRAs is that patients who
 507 received a childhood BCG vaccine (very common outside of North America and Western Europe)

⁴⁹ CDC. "Health Disparities." Centers for Disease Control and Prevention, November 10, 2022.
<https://www.cdc.gov/tb/topic/populations/healthdisparities/default.htm>.

508 are less likely to have a false-positive test with IGRAs than with the TST test, due to enhanced
509 specificity of the *Mycobacterium tuberculosis* antigens used in the IGRA assays.

510

511

512 **Management of Infected Living Donors**

513 Table 3 outlines management of living donors with a history of active TBI and treatment of
 514 recipients of these organs.

515 **TABLE 3: Management of latent or history of active TB in living donors and recipients of these organs**

<u>Clinical Scenario: Living Donor</u>	<u>Risk for Transmission</u>	<u>Recommendation</u>
<u>History of TBI-treated appropriately</u>	<u>Lower</u>	<u>Monitor recipient clinically</u>
<u>History of TBI-treated insufficiently or not treated or treatment details not clear OR new diagnosis of TBI-positive TST or Interferon gamma release assay found during pre-transplant evaluation; evaluation finds no evidence of active TB</u>	<u>Moderate</u>	<u>Consider deferring transplant if possible until donor has taken some/all of chemoprophylaxis and consider chemoprophylaxis of recipient; monitor clinically</u>
<u>Unexplained pulmonary apical fibrosis in donor without cavitation and without additional testing</u>	<u>Variable</u>	<u>Defer donation pending further evaluation</u>
<u>History of MTB disease treated appropriately over two years ago</u>	<u>Lower to moderate</u>	<u>Monitor recipient clinically; consider cultures of previous TB sites if possible. Consider TB prophylaxis of recipient.</u>
<u>History of MTB disease-site remote from transplant treated appropriately within two years.</u>	<u>Lower to moderate</u>	<u>Monitor recipient clinically; consider cultures of previous TB sites if possible. Suggest chemoprophylaxis of recipient.</u>
<u>History of MTB disease-site remote from transplant treated insufficiently and/or with other than standard regimen Excluding disseminated or CNS TB.</u>	<u>Higher Increased risk if less than two years since active TB diagnosis.</u>	<u>Defer live donors until adequately treated; consider consult with infectious disease specialist; recommend cultures of previous TB sites prior to transplant if possible</u>
<u>History of renal MTB disease treated appropriately. (If not treated appropriately donation should be deferred until after appropriate treatment)</u>	<u>Moderate</u>	<u>Verify treatment; monitor clinically; recommend chemoprophylaxis for recipient; recommend cultures of previous TB site(s); consider consult with infectious diseases specialist.</u>

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Management of Recipients

For recipients of an organ from a donor who is TST or IGRA-positive, had recent exposure to active TB, or had radiographic evidence of untreated TB should be considered for TBI therapy, following CDC guidance for anti-tuberculosis agents and durations. Specific attention should be given to potential drug-drug interactions of TBI agents and immunosuppressive medications with careful monitoring of calcineurin inhibitors.

Infection Avoidance between Testing and Transplant

Potential living donors should avoid prolonged travel to endemic regions and behavioral exposures that increase risk if possible, including institutional settings which may result in increased risk of exposure to TB (hospitals, nursing homes, correctional facilities, other health care settings, and homeless shelters).

IV. VIRAL INFECTIONS

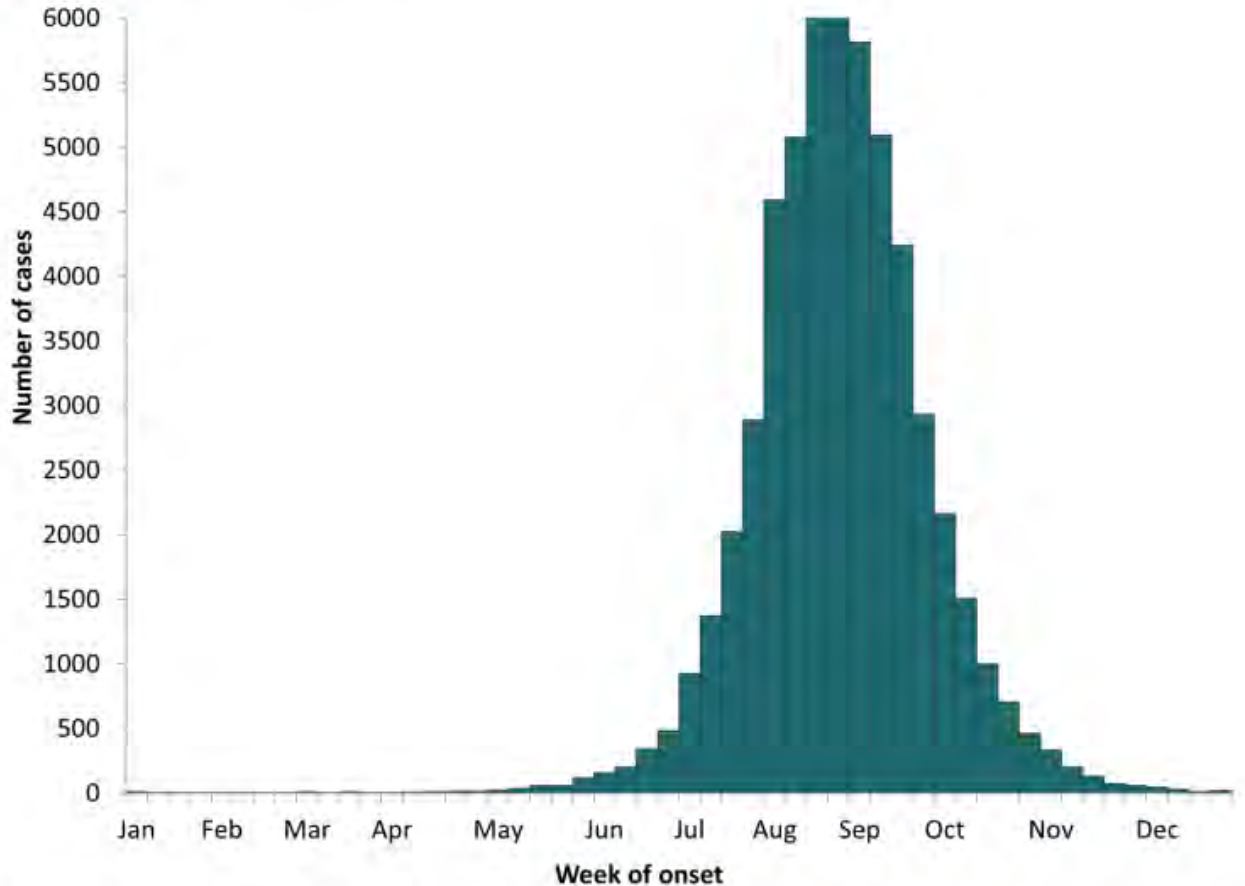
West Nile Virus (WNV) Guidance

Background

Epidemiology and pathophysiology

WNV is an RNA virus that spreads to humans primarily by the bite of infected mosquitoes, although multiple non-vector modes of transmission have been described, including blood transfusion, organ transplantation, breastfeeding, intrauterine, and laboratory exposure. Birds serve as a reservoir for WNV, and humans are a dead-end host for the virus. The virus was first detected in North America in 1999, and since then, has spread to all 48 contiguous U.S. states. The number of human infections varies significantly based on the region and year, with most transmission occurring during the warmer months (July to October) when mosquitoes are most active, although warmer regions can have a longer season (as shown in Figure 5). While the majority of WNV infections are asymptomatic, about 20% of those infected may develop fever, and less than one percent develop neurological complications such as encephalitis or acute flaccid myelitis (involving the spinal cord). This means that even donors who don't display symptoms could still transmit the virus to recipients. While several treatments have been explored, there is currently no established treatment for WNV.

553

Figure 5: Months of typical WNV activity in the United States⁵⁰**West Nile virus disease cases reported to CDC by week of illness onset, 1999-2021**

Source: ArboNET, Arboviral Diseases Branch, Centers for Disease Control and Prevention

554

Who Should Be Screened**Living and Deceased Donors**

Since the transmission of WNV is limited by geography and season, OPOs and transplant programs should consider certain factors when determining whether to perform laboratory testing on a potential living donor. A positive test result obtained during a period of WNV inactivity is more likely to represent a false positive than when the test was performed during periods of higher activity. Any false positive result could result in unnecessary delays to the transplant.

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⁵⁰ CDC. "West Nile Virus Disease Cases Reported to CDC by Week of Illness Onset ..." West Nile virus cases reported to CDC by week of illness onset, 1999-2021. Accessed June 23, 2023. <https://www.cdc.gov/westnile/resources/pdfs/data/WNV-Week-Onset-1999-2021-P.pdf>.

564 Factors to consider in evaluating donors for possible WNV infection:

- 565 • Has human infection with WNV virus been recognized locally this WNV season?
- 566 • Has the donor travelled to an area with human WNV activity this WNV season?
- 567 • Has the donor ever been diagnosed with WNV fever or WNV neuroinvasive disease?
- 568 • Has the donor had an undifferentiated febrile illness within the current WNV season?
- 569 • Has the donor had significant mosquito exposure this WNV season?

570 **Geographic and seasonal factors to consider.**

571 Screening strategies for WNV in donors include universal year-round testing of all donors versus
 572 targeted testing during periods of human WNV activity. As the yield of testing during the winter
 573 months is likely low and given the potential for IgM to remain positive after resolution of the
 574 illness, year-round testing is discouraged unless programs are unable to manage the complexity
 575 of more targeted testing strategies. Targeted testing strategies could include testing during a
 576 pre-determined timeframe, or testing donors only during times of human WNV activity in the
 577 area where the donor lives or has traveled (i.e., triggered strategy).

578 Triggering strategies can involve communicating with local blood collection organizations and
 579 determining whether they have shifted from minipool to individual donation (ID)-NAT screening,
 580 indicating that a WNV-reactive donor has been identified within a 50-mile radius of the
 581 triggering zip code. Another method involves using WNV human and non-human surveillance
 582 data collected by state and local health departments. Alternatively, testing could begin each
 583 year during the local WNV transmission season as determined by historical data (typically July
 584 through October, or longer intervals in warmer regions).

585 Given that human WNV disease incidence varies greatly from year to year and even county to
 586 county, targeted testing based on real-time measurement of local WNV activity at local blood
 587 banks might be the most cost-effective strategy and will reduce the number of false positives.
 588 This strategy is, however, more complex and time-consuming than a fixed seasonal strategy.
 589 Some institutions may already be using a local or regional blood bank testing lab to test other
 590 material (e.g., peripheral stem cells used in stem cell transplantation). In contrast, the strategy
 591 of testing during a defined time period regardless of local WNV activity would be simpler to
 592 implement, but both costs and false positive rates would be expected to be higher. Table 4
 593 describes the advantages and disadvantages of different testing strategies.

594 **Table 4: Advantages and Disadvantages of Different Testing Strategies**

	<u>Year-round testing (1)</u>	<u>Seasonal testing (2)</u>	<u>Triggered testing (3)</u>
<u>Ease of implementation</u>	<u>Easy</u>	<u>Intermediate</u>	<u>Difficult</u>
<u>Positive predictive value</u>	<u>Lower during periods of human WNV inactivity</u>	<u>Intermediate depending on level of human WNV activity</u>	<u>High</u>
<u>Cost effectiveness</u>	<u>Least</u>	<u>Intermediate</u>	<u>Most</u>

- 595 1. This strategy is not recommended.

- 596 2. Typically July through October, but time period should be guided by local historical WNV data, in
 597 consultation with state and local health departments
 598 3. Testing triggered by switch from minipool to individual blood donation-NAT testing in zip codes
 599 of residence of donors. Testing stops when WNV activity no longer noted and blood banks
 600 switch back to minipools. Routine communication with local blood bank is required.

601 **How to Screen**

602 Living and Deceased Donors

603 To screen for WNV, healthcare professionals use NAT and IgM serologic tests. Currently, there
 604 are two FDA-licensed NAT donor screening assays; these are routinely performed at blood banks
 605 or some reference labs, but are not commonly available in hospital laboratories. Serologic tests
 606 which rely on the response of the immune system to infection with WNV, particularly the IgM
 607 assay performed on serum and cerebrospinal fluid, are commonly used to diagnose
 608 neuroinvasive WNV. IgM is detectable for a median of about five months after infection but may
 609 persist longer, even years after infection, and is not used in blood donors to screen for WNV,
 610 although it may be performed for use in donor counseling. IgG typically remains positive for life
 611 and would not be useful to routinely screen for WNV. Table 5 describes the characteristics of
 612 NAT and IgM testing.

613 **Table 5: Tests that could be used to screen for WNV infection**

	<u>Nucleic Acid Tests (NAT)(1)</u>	<u>IgM (serology)(2)</u>
<u>Available Tests</u>	<u>Procleix West Nile Virus Assay COBAS</u> <u>TagScreen West Nile Virus Test</u>	<u>Various</u>
<u>FDA licensed for organ screening</u>	<u>Yes</u>	<u>No</u>
<u>Availability</u>	<u>Blood bank testing labs</u> <u>Reference labs</u>	<u>Reference labs</u> <u>Commercial labs</u> <u>State public health labs</u>
<u>False positive rate</u>	<u>Low</u>	<u>Likely higher than NAT, but not</u> <u>evaluated for donor screening</u>
<u>Indicates active infection</u>	<u>Yes</u>	<u>Remains positive for median of five</u> <u>months (up to seven years</u> <u>documented); active infection may</u> <u>have cleared</u>
<u>Required for blood donor screening</u>	<u>Yes</u>	<u>No</u>

- 614 1. Should be used as part of any testing strategy
 615 2. Consider in combination with NAT testing but will increase false positive rate

616 **Deceased donors**

617 It is advisable to screen deceased donors during months of regional WNV activity. WNV NAT
 618 testing is a viable option, but the results may not be available before transplantation. It is
 619 important to note that WNV transmission has occurred in donors who tested negative on NAT,
 620 and that there is potential for false positive NAT test results if protocols are not in place to

621 improve specificity, as are used by blood collection organizations, or if testing is performed
622 outside of the WNV transmission season, decreasing the pretest probability.

623 In cases involving deceased donors, the feasibility of conducting WNV testing within a required
624 timeframe is uncertain. As such, the Committee advises against proceeding with donors who
625 satisfy any of the following criteria: (1) a confirmed WNV infection, (2) a positive WNV NAT test
626 result, ideally meeting a threshold signal-to-cutoff ratio or verified by repeat testing as
627 recommended by the manufacturer, or (3) clinical manifestations of meningitis, encephalitis, or
628 flaccid paralysis of indeterminate origin, particularly if they originate from regions with
629 documented WNV activity.

630 **Living donors**

631 Living donors should be screened with WNV NAT within seven to 14 days of donation.

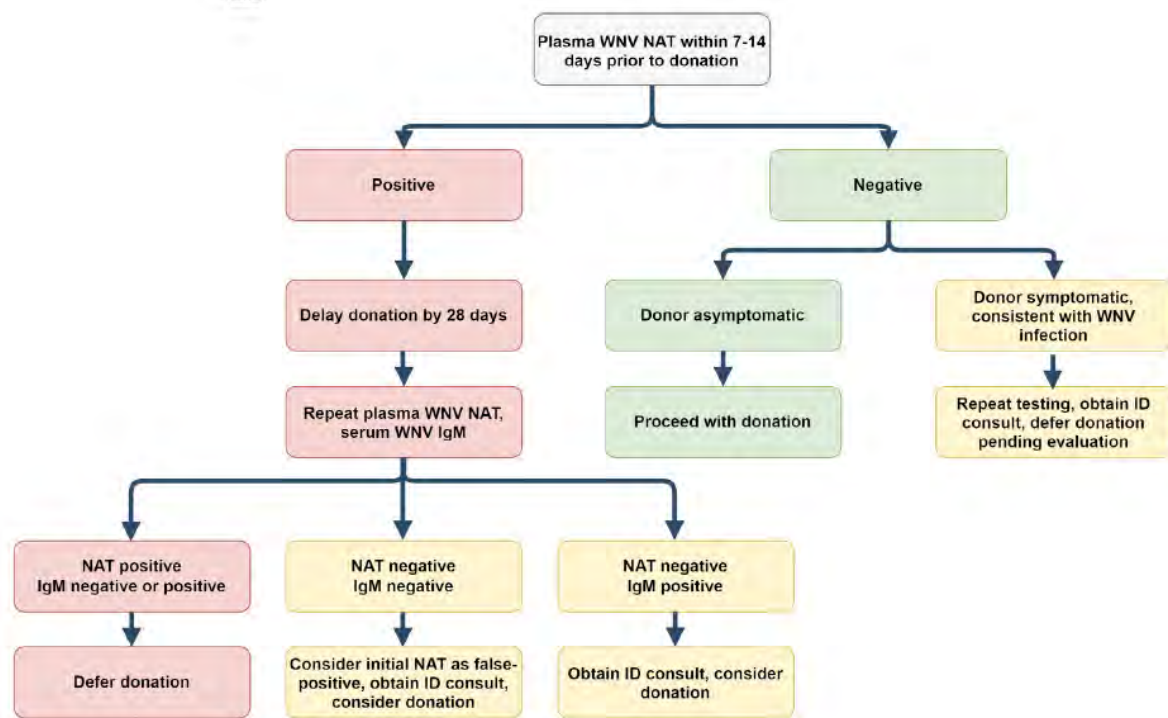
632 **Management of Infected Living Donors**

633 Although no studies have examined organ donation after WNV infection, we suggest postponing
634 donation for a minimum of 28 days in living donors, after which NAT and IgM testing should be
635 performed. If negative, it is likely that the initial NAT test was a false positive, and organ
636 donation can be considered. If the NAT is negative but IgM is positive, this likely reflects viral
637 clearance and organ donation can be considered. However, if the NAT remains positive, organ
638 donation should be postponed. (Refer to Figure 6 for additional information).

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640

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Figure 6: Living donor screening recommendations for WNV⁵¹

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643

Management of Recipients

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Development of symptoms compatible with WNV disease within the first several weeks of transplant (and up to six weeks, since transplant recipients can have prolonged incubation periods with WNV infection) should prompt testing in the recipient. There are currently no specific medications available for the treatment of WNV infection.

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Infection Avoidance Between Screening and Transplant

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We advise potential living donors to take measures to prevent mosquito exposure during periods of mosquito activity, such as wearing loose-fitting, long sleeve shirts and pants, using EPA-registered insect repellent, and avoiding outdoor activities during dawn and dusk when mosquitoes are most active. Further, a potential living donor should report febrile illnesses to his or her transplant center. WNV diagnostic testing should be performed if clinical evaluation suggests the possibility of WNV infection in the potential living donor.

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V. SHARING INFORMATION

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Recommendations for Sites Participating in Paired Organ Exchanges

⁵¹ Anesi, JA, Silveira, FP; the AST Infectious Diseases Community of Practice. Arenaviruses and West Nile Virus in solid organ transplant recipients: Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. *Clin Transplant*. 2019; 33:e13576. <https://doi.org/10.1111/ctr.13576>

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

664
665 **When to Report a Potential Donor-Derived Transmission Event**

666 If the recipient is suspected to be at risk for disease transmission either by the OPO or a
667 transplant center, a potential donor-derived disease transmission event should be reported to
668 the OPTN Improving Patient Safety Portal per OPTN Policies *15.4 Host OPO Requirements for*
669 *Reporting Post-Procurement Test Results and Discovery of Potential Disease Transmissions* and
670 *15.5 Transplant Program Requirements for Communicating Post Transplant Discovery of Disease*
671 *or Malignancy*. This promotes prompt intervention for other recipients of the same donor's
672 organs.

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Appendix*

Table 6: OPTN Ad Hoc Disease Transmission Advisory Committee Data on PDDTE

<u>Endemic Disease</u>	<u>Number of Proven or Probable Transmissions since 2008</u>
<u>Histoplasmosis</u>	<u>19</u>
<u>Coccidioidomycosis</u>	<u>10</u>
<u>Chagas disease</u>	<u>7</u>
<u>Strongyloidiasis</u>	<u>39</u>
<u>Tuberculosis</u>	<u>21</u>
<u>West Nile Virus</u>	<u>0</u>

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***Updated biennially by the DTAC**

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 699 [assays#AntiT.%20Cruzi%20Assays%20\(Detect%20antibodies%20to%20Trypanosome%20cruzi\)](https://www.fda.gov/vaccines-blood-biologics/complete-list-donor-screening-assays-infectious-agents-and-hiv-diagnostic-assays#AntiT.%20Cruzi%20Assays%20(Detect%20antibodies%20to%20Trypanosome%20cruzi)).

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