SHOULD I ACCEPT THIS DONOR?

A Pediatric Transplant Infectious Diseases Learning Module

Using the Modules

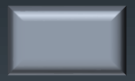
- The modules are case-based, with decision points (branches) containing questions
  - Many questions don't have right or wrong answers
  - Click on a response (e.g. a diagnostic test), and you will find out more about it
- Multiple "action buttons" help you navigate
- The basic modules are designed to take about 45 minutes to complete
- You might take longer, especially if you choose to investigate all of the informational links provided
- Take your time and enjoy!

Navigating the Modules

- DO NOT use your keyboard arrows or mouse click to advance slides
- Only use the navigation buttons on each slide – these will keep you from getting lost
  - If you do get lost, you can hit the "home" button any time to go back
- Unlabeled button types you might encounter:
  - Previous slide 
  - Next slide 
  - First slide 
  - More information 
  - Return to decision choices 

Navigating the Modules

DO NOT use your keyboard arrows or mouse click to advance slides
Only use the navigation buttons on each slide – these will keep you from getting lost

- **Click**  **to go back to the Case Slide**
- **Click on the**  **to go to the next slide**
- **Click on the**  **to go the previous slide**
- **Click on**  **to make your selection**
- **Click in**  **to learn more about a topic**

Overview

- Unanticipated transmission of infections from a donor to a transplant recipient is a rare occurrence, but may be associated with significant morbidity and mortality (and publicity!)

- Transplant ID clinicians play an important role in assessing risk and helping to determine what is acceptable vs. unacceptable

- Our approach to considering infectious risk must be balanced against the urgency with which an organ is needed for the recipient

Developing skills in assessing infectious risk

- The objectives of this exercise are to:
  - Learn the routine donor infectious screening vs. screening that varies based on geography or donor characteristics
  - Gain an understanding of the types of infectious screening tests available and the limitations of these tests
  - Recognize important components of the donor history – "red flags", need for additional information or testing
  - Understand the value of reporting and communication between providers and organ procurement organizations (OPOs)
  - Consider the approach to infectious risk in living donors compared to deceased donors

Developing skills in assessing infectious risk

- In the following slides, you will review the scenario and decide what path you would like to pursue
- Each path has resulting potential consequences for your patient
- Use the icons defined on the next slide to navigate your way through the clinical scenarios
- Summary slides and useful links will provide you with guidance on how to approach such cases in your practice
- You can go back to each of the scenarios and choose a different path to see where it takes you!

CASE

- A 5 year old male with biliary atresia is being listed for liver transplantation. His Father is being worked up as a potential donor.

Learn more about screening donors on the Organ Procurement and Transplantation Network website http://optn.transplant.hrsa.gov/resources/living-donation

CASE

- During the pre-transplant evaluation you ask parents about significant exposures. Dad is from Russia.

Learn more about screening donors

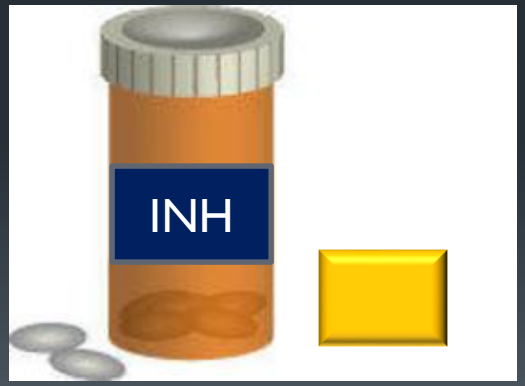
CASE

- As a part of your pre-transplant ID evaluation, you place a PPD on dad and it is positive 20 mm. A chest radiograph is negative. Dad is diagnosed with Latent Tuberculosis Infection (LTBI) . You ask the hepatology service if the transplant can be postponed while dad is being treated.

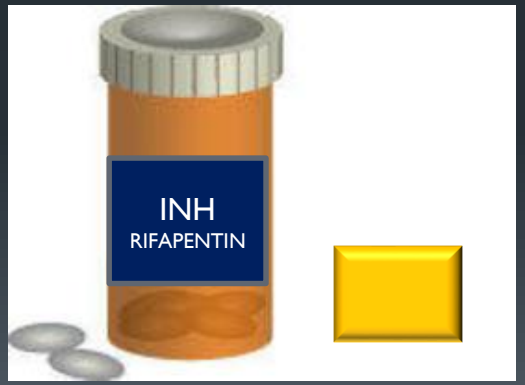
MAKE YOUR DECISION

CONTINUE WITH DAD AS THE DONOR SELECT A TREATMENT OPTION

TREAT DAD WITH ISONIAZID AND DEFER TRANSPLANT 9 MONTHS



TREAT DAD WITH ISONIAZID + RIFAPENTIN AND DEFER TRANSPLANT 3 MONTHS



4 WEEKS LATER WHILE PATIENT IS LISTED AND WAITING FOR AN ORGAN

- Patient deteriorates and is upgraded to status 1A

Learn more about liver status 1a at
http://www.unos.org/docs/Liver_patient.pdf

A liver becomes available. The donor is a 12 year-old who was in a motor vehicle accident. He is from **Brazil** and recently immigrated to the United States.

MAKE YOUR DECISION

Take the organ (12 year old from Brazil)

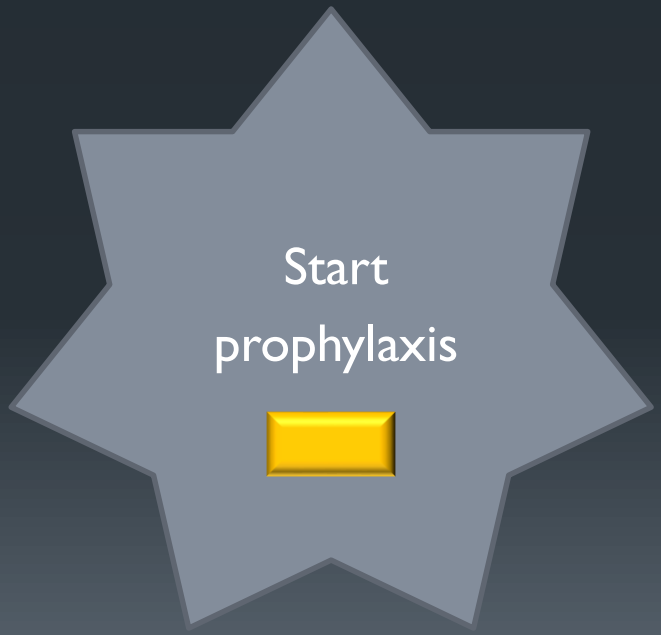
Use dad as donor

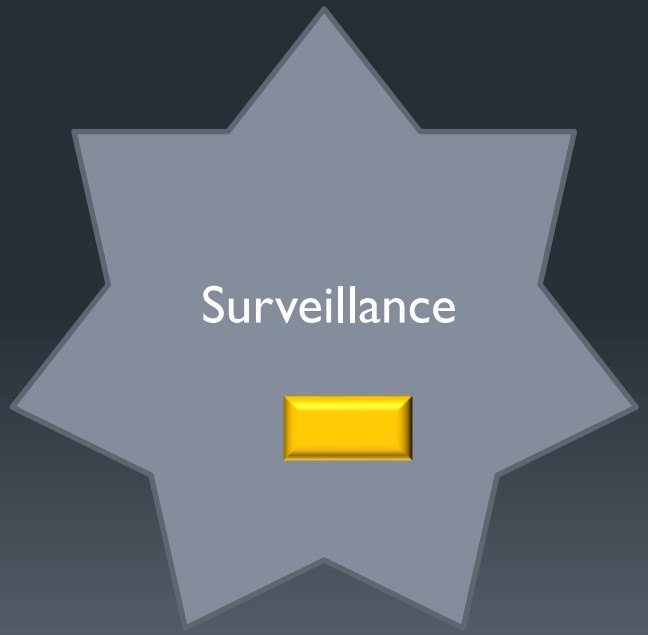
Wait for another donor

Click here to learn about selecting suitable donors to minimize donor derived infections

The OPO informs you that the donor has tested positive for Chagas disease, confirmation tests have been sent to the CDC

You took an organ potentially infected with *T. Cruzi* What is the appropriate next step?





Prophylaxis is not indicated

Learn more about Chagas disease and Transplantation

Surveillance is indicated

Learn more about Chagas disease and Transplantation

CHAGAS DISEASE AND TRANSPLANTATION

- Approximately 300,000 Hispanic immigrants living in the United States are infected with *T cruzi*.
- Disease is endemic in Mexico, Central and South America.
- Most people with Chagas disease acquire it during childhood.
- Following the acute infection patients enter an indeterminate chronic phase where patients are asymptomatic
- 20-30% will develop symptomatic chronic form: Cardiac and gastrointestinal disease

CHAGAS DISEASE AND TRANSPLANTATION

- Any organ donor who has lived in an endemic area for a significant period (years) could potentially be infected with *T cruzi*.
- Treatment is effective soon after acute infection but less effective in chronic indeterminate phase and has no effect in the disease phase
- Transmission rates from seropositive donors to seronegative recipients are approximately 20% for kidney transplant recipients 30% for liver transplant recipients

CHAGAS DISEASE AND TRANSPLANTATION

- Two FDA tests have been approved for blood donor screening and these should be used also for Donor screening: Ortho EIA and Abbot Prism Chagas test

- For living donor, if the initial test is positive, a second confirmatory sample should be sent to the CDC for confirmatory radioimmunoprecipitation assay (RIPA)

- For the deceased donor, the test should be confirmed but the results may not be available by the time of the transplant

CHAGAS DISEASE AND TRANSPLANTATION

Donor	Advise	Additional consent	Additional donor Testing	Screening recipient	Treatment of Recipient
From Chagas Endemic country but no Serologies available or possible and no dilated cardiomyopathy or megacolon	Take all organs including heart	Consider discussing the small but possible risk for Chagas Disease	N/A	*Consider T cruzi* PCR and microscopy of fresh buffy coat and Giemsa-stained peripheral blood smears if febrile or rejection.	Treat if positive. Prophylaxis not indicated.
Donor died from Acute Chagas Disease	Reject all organs	N/A	N/A	N/A	N/A
Donor positive for Chagas serology or history of treated Chagas disease	Reject: heart and intestines Consider with discretion (based on urgency and immunosuppression) and appropriate consent: Lungs and Pancreas* Consider with appropriate consent: Kidney and Liver*	Obtain appropriate consent from the recipient of the risk of receiving an organ potentially infected with *T. cruzi*	Confirmatory RIPA to the CDC (results may not be available at time of transplant)	*T cruzi* PCR and microscopy of fresh buffy coat and Giemsa-stained peripheral blood smears: once weekly for 2 m; every 2 weeks on month 3 post transplant and every month on months 4-6	Treat if positive. Prophylaxis not indicated.

Learn more about Chagas Disease

Use a different donor

Chin-Hong, P.V., et al., Screening and treatment of Chagas disease in organ transplant recipients in the United States: recommendations from the Chagas in transplant working group. *Am J Transplant*. **11**(4): p. 672-80.

Use a different donor

DAD IS THE DONOR

- Father has completed 4 weeks of therapy

Does the recipient need prophylaxis?

Learn more about TB in living donors

TUBERCULOSIS AND TRANSPLANTATION

- In 2013, 9 million people in the world developed *M. tuberculosis* (TB) infection.
- In the United States, approximately 9,500 cases of TB were reported (rate: 3 cases/100,000 persons) mainly in foreign born emigrating from highly endemic areas.
- The majority of transplant cases occur post transplant secondary to reactivation in recipients with unrecognized or untreated LTBI following immunosuppressive therapy.
- Transmission of TB through the allograft can occur. (32 cases reported as of September 2012 (OPTN/UNOS data)

TUBERCULOSIS AND TRANSPLANTATION

- Diagnosis of TB may be challenging in the recipient:
  - Atypical presentations
  - May have low mycobacterial burden despite active disease resulting in negative sputum smears/gastric aspirates
  - Tuberculin skin testing (TST) and interferon gamma release assays (IGRA) may be falsely negative in the setting of immunosuppression

- Treatment of TB is difficult: drug toxicity (*Pediatr Infect Dis J* 2000 Jul;19(7):625-30), interactions with immunosuppressive medications

TUBERCULOSIS AND TRANSPLANTATION

- Assessment of the donor:
  - Identify country of birth
  - Obtain a ***thorough*** Past Medical History : focus on epidemiological TB risk factors (smoking, substance abuse, malnutrition, incarceration, HIV, close household contact with family member with tuberculosis) , history of prior positive TST/IGRA
  - Review any available radiographic imaging or obtain new images
  - In cases of prior active disease seek documentation of completed appropriate anti-tuberculosis treatment

TUBERCULOSIS AND TRANSPLANTATION

DONOR WITH LATENT TB INFECTION (LTBI)

LTBI	RISK OF TRANSMISSION	RECOMMENDATION
Appropriately treated LTBI	Lower	Clinical monitoring
LTBI inadequately treated, not treated or unclear if treated; positive IGRA/TST during pre TX evaluation . Work up **shows no evidence of disease**	Moderate	Consider deferring transplant until donor has taken some/all the prophylaxis. Consider prophylaxis in the recipient. Monitor clinically
CXR with unexplained fibrosis in apices without cavitations and no additional testing available	Variable	Defer donation until evaluation is complete

http://optn.transplant.hrsa.gov/resources/living-donation

TUBERCULOSIS AND TRANSPLANTATION

DONOR WITH HISTORY OF ACTIVE TB

HISTORY OF ACTIVE TB	RISK OF TRANSMISSION	RECOMMENDATION
History of active TB treated appropriately > 2 years ago	Lower-Moderate	Consider culture of previous TB sites, consider prophylaxis for the recipient. Monitor recipient clinically
History of active TB at a remote site from transplanted treated adequately within 2 years	Lower-Moderate	Consider culture of previous TB sites, suggest prophylaxis for the recipient. Monitor recipient clinically
History of TB-site remote not appropriately treated and/or treated with non-standard regimen; excluding CNS/disseminated disease	Higher especially if < 2 years from treatment	Defer transplant until donor treated; consider culture of previous TB sites

READ THE CONSENSUS GUIDELINES: *American Journal of Transplantation 2012; 12: 2288–2300*

Use a different donor

NEW DONOR

- Donor is a 6 year old with meningitis. Blood cultures are positive for non-typeable *H influenza*. The donor has been on antibiotics for 72 hours

- Repeat cultures are pending

- LP done after brain death: CSF shows abundant WBCs, low glucose, negative gram stain, cultures are pending. Influenza, enterovirus, adenovirus, parainfluenza PCRs negative. HSV and enteroviral PCR from CSF are negative

NEW DONOR

NEW DONOR

- **Bacterial meningitis in a donor is not usually a contraindication to accepting organs**

Does the recipient need treatment?

Learn more about donors with meningitis

DONOR WITH MENINGITIS

- Because of the paucity of available organs meningitis is no longer deemed an absolute contraindication for organ donation

- Successful allograft procurement from donors with microbiologically proven bacterial meningitis has been reported

- Guidelines now recommend accepting an organ if the etiology of the meningitis is *Streptococcus pneumoniae, Neisseria meningitidis, Haemophilus influenzae, Escherichia coli, or* group B streptococcus

DONOR WITH MENINGITIS

- Meningitis must be confirmed as the only site of infection in the donor
- Preferably the donor should have received appropriate therapy for 48 h prior to procurement with signs of clinical improvement
- Additional consent from the recipient and/or family should be obtained
- The recipient should receive pathogen-directed therapy of the
  for at least 2 wk after transplantation
- Grafts from patients infected with highly virulent organisms (*Listeria*) should not be accepted

Use a different donor

Routine Donor Screening

- Deceased donor evaluation must occur within a few hours, includes donor medical and social history
- Testing typically performed through the Organ Procurement Organizations (OPO)
- Typical tests for all donors
  - Cytomegalovirus (CMV) IgG
  - Epstein-Barr virus (EBV) IgG
  - Human Immunodeficiency Virus (HIV) antibody
  - Hepatitis C antibody
  - Hepatitis B surface antigen, core antibody
  - Blood, sputum, urine cultures
  - HSV IgG, VZV IgG – many OPOs no longer performing routinely

REDUCING THE RISK OF DONOR TRANSMITTED INFECTIONS – SELECTING SUITABLE DONORS

NAT vs. Standard Screening

- Nucleic acid amplification tests (NAT) allow rapid identification of recent acquisition of certain infections, before serologic tests may become positive
  - HIV, HBV, HCV

Table 1: Window periods by assay type (3–6)

Virus	Serology	NAT[1]
HIV	22 days	5–9 days
HBV	44 days	22 days
HCV	66 days	3–7 days

[1]Based on individual blood donor data.

Public Health Reports July-August 2013, Volume 128

Donor Screening in Special Circumstances

- Other donor testing is based on OPO, geographic location, donor characteristics:
  - *T. cruzi* (Chagas disease)
  - West Nile virus
  - Endemic mycoses
  - Donor bronchoscopy for lung donation
  - *Toxoplasma* IgG, especially for heart transplant recipients
  - *Strongyloides* IgG
  - Respiratory virus testing
  - Histopathological tests on donor tissues

Limitations of Infectious Screening Tests

- Donors may have asymptomatic but transmissible infections at the time of death
- Difficult to diagnose tuberculosis, non-tuberculous mycobacterial infections, many viral infections, tropical/parasitic diseases
- CNS disease of unknown etiology may be infectious but may not be – testing can be difficult and may take too long, but some infections are contraindications to transplantation

Red Flags in Donor Assessment

- CNS infections: organs from donors with non-bacterial meningitis/encephalitis should generally be rejected
  - Concern for transmission of non-treatable infections including *Naegleria fowleri*, rabies, prion disease
- Sepsis of unknown etiology
- Donor with neurologic disorders such as Guillain-Barre
- Donor history: illicit drug use, sexual history
  - High-risk donors may require informed consent for recipients

Management of Potentially Treatable Infections

- Bacterial meningitis, bacteremia – do not exclude organs, treat Donor (D)/Recipient (R)
- Bacterial pneumonia or other bacterial infections in potential donor organs – often exclude donation of infected organ
- Influenza infection – typically exclude lungs, intestine, treat D/R
- Other respiratory viral infections (e.g. RSV) – exclude lungs
- Fungal infections – if untreated candidemia or other disseminated fungal infection, typically exclude all organs; may consider if donor treated for candidemia with evidence of resolution; treat D/R
- *T. cruzi* – exclude all organs if donor died of Chagas disease; if donor seropositive only exclude heart and intestine, consider other organs
- Syphilis – do not exclude organs, treat R
- *Strongyloides* seropositivity – do not exclude organs, treat R

Communication and Reporting with OPOs

- OPOs communicate donor cause of death and infectious testing results through donor online networks
- OPOs can facilitate history-taking from donor's care providers
- Communicate with OPO when recipients develop unexpected infections, if the post-transplant course is atypical, when there is an unanticipated severe complication or death – OPO can investigate clinical symptoms in other organ recipients from same donor, follow-up on additional clinical information from donor center

Living Donors

- Able to obtain detailed medical and social history
- More time for testing and follow-up testing
- Opportunity to treat an infection before organ is harvested for donation

Summary and Take Home Points

- Donor testing enables risk mitigation, but we cannot eliminate risk
- Red flag cases – consider each individually, ID consult when possible for both donor and recipient
- Important to consider the risk of postponing transplantation vs. risk of infection

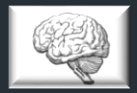
References

- Fischer SA, Lu K and the AST Infectious Diseases Community of Practice. Screening of donor and recipient in solid organ transplantation. *American Journal of Transplantation* 2013; 13:9-21.

- Seem DL, Lee I, Umscheid CA, Kuehnert MJ. PHS guideline for reducing human immunodeficiency virus, hepatitis B virus, and hepatitis C virus transmission through organ transplantation. *Public Health Reports* July-August 2013, Volume 128.

- Kovacs CS, Koval CE, van Duin D, de Morais AG et al. Selecting suitable solid organ transplant donors: Reducing the risk of donor-transmitted infections. *World J Transplant* 2014 Jun 24;4(2):43-56.

Click on the icon to Review

- CASE  SLIDE 6
- CHAGAS DISEASE AND TRANSPLANTATION  SLIDE 19
- LATENT TUBERCULOSIS AND TRANSPLANTATION  SLIDE 25
- MENINGITIS AND TRANSPLANTATION  SLIDE 33
- REDUCING THE RISK OF DONOR TRANSMITTED INFECTIONS  SLIDE 36
- ROUTINE DONOR SCREENING  SLIDE 35

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Original version date: 7/22/2015

Revised on: 1/31/2020

Part of an educational effort through the PIDS Transplant Infectious Diseases working group and the AST ID Community of Practice

Feedback on the Modules

- **PLEASE help to provide us with feedback on the content of these modules!**
  - **Let us know what you learned and what we can do better**
  - **Your feedback will help us to improve this work and design future modules**

- **For any questions or concerns, please contact Tanvi Sharma tanvi.sharma@childrens.harvard.edu**