

Infections in Transplant Recipients of International Origin

Buckeye Chapter 9 of the International Transplant
Nurses Society Annual Focus on Transplantation

“The Modern Era: **Travel**, Transition,
Technology and **Transplantation**.”

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*PI on studies sponsored by Roche, Chimerix & GSK





THANK YOU!



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Outline

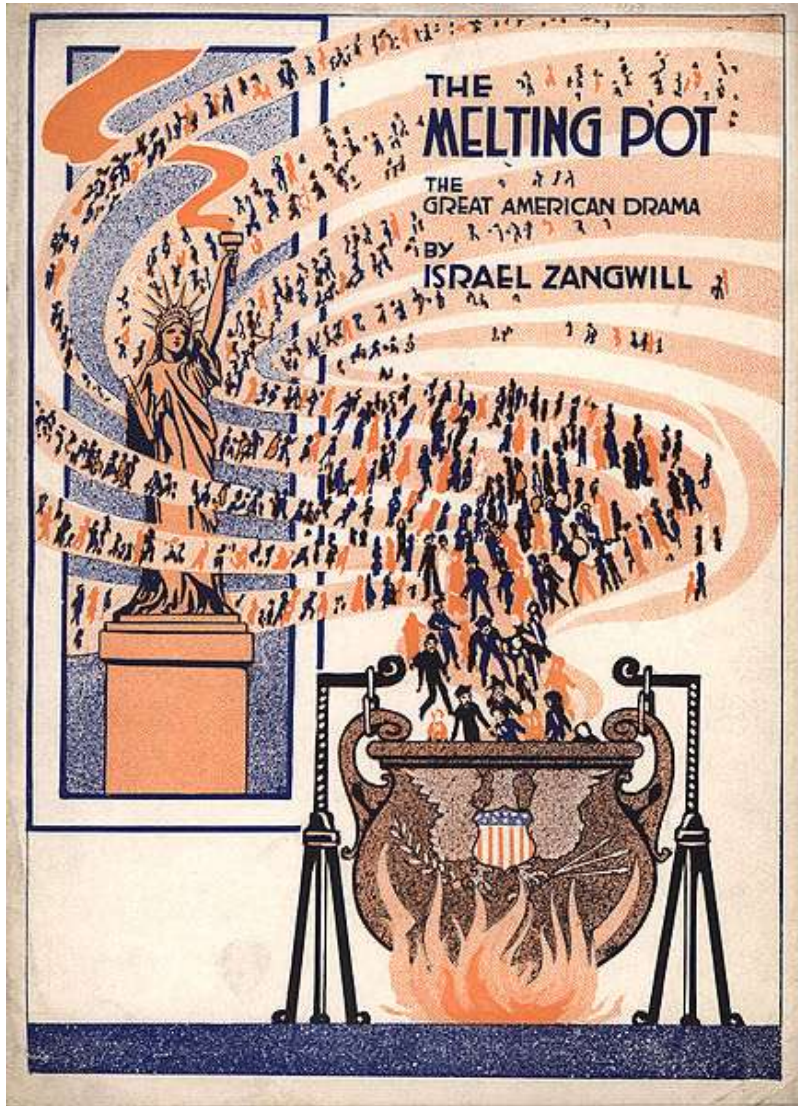
- Timeline of infections
- Infections pertinent to transplant recipients of international origin:
 - Data from Cleveland Clinic
 - TB, Strongyloidiasis, schistosomiasis, Chagas
 - Vaccinations:
 - SOT
 - HSCT
- Travel precautions

Timeline of Infections Following Solid Organ Transplantation

First month	Months 1-6	> 6 Months
<ul style="list-style-type: none">-Nosocomial & surgical site infections-Donor derived infections-Reactivation of prior recipient infections	<ul style="list-style-type: none">-Opportunistic infections: e.g. CMV, PJP, toxo	<ul style="list-style-type: none">-Community acquired infections



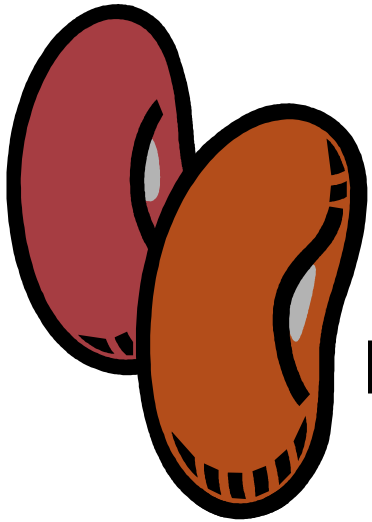
The “Melting Pot”



- 35 million US residents are foreign born
- 52 million speak a language other than English at home
- 1 in 12 are classified as “limited English proficient”

Wikipedia. 1908 play “*The Melting Pot*”

How do transplant recipients acquire endemic infections?



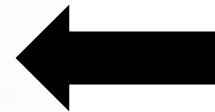
Transmission with the graft



Reactivation of latent infection due to immunosuppression



De novo exposure



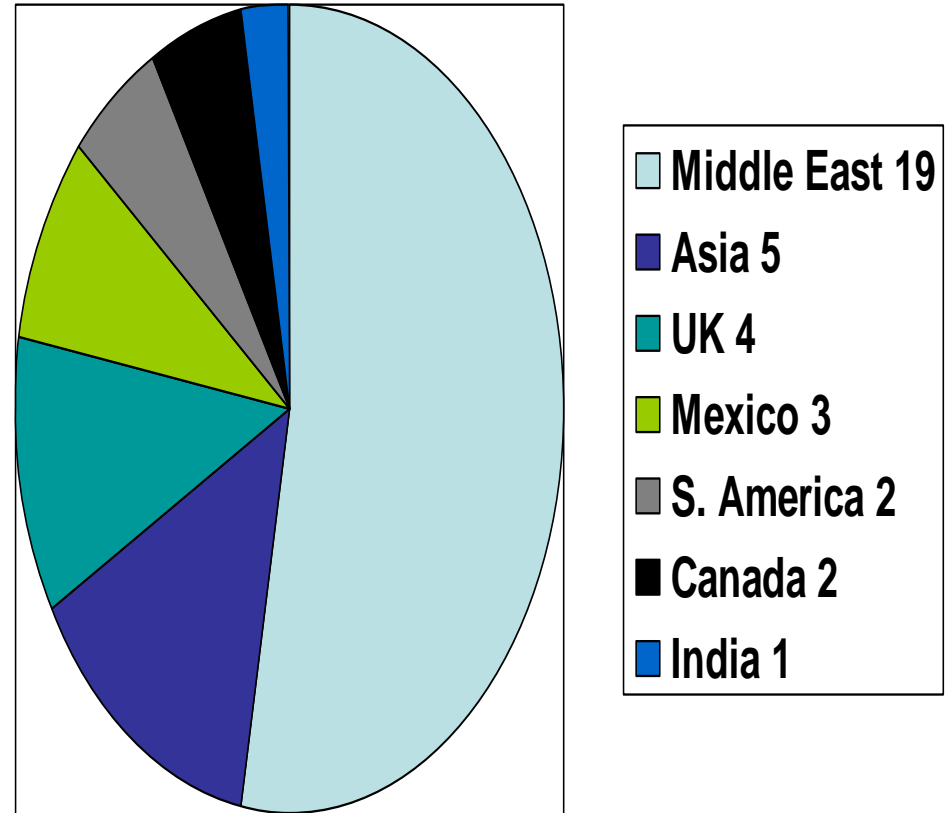
Are infectious complications more common in foreign born transplant recipients than in US born transplant recipients?

- Language barrier may lead to suboptimal communication between international transplant recipients and their health care providers:
 - Less able to clearly relay symptoms
 - May misunderstand instructions about diagnostic tests or treatments prescribed.

Malinis M. Outcomes of infections in International Solid Organ Transplant Recipients: 9 years experience at a major U.S. transplant center

Demographics

- 36 of 3739 SOT recipients (1%) from 1/1/2001 to 12/31/2009 were identified as foreign nationals (born and raised in countries other than the US)
- Age: 52 (10 - 74) years [median (range)]
- Organ type: 13 liver, 12 kidney, 6 heart, 4 lung & 1 kidney + liver



Malinis M. Outcomes of infections in International Solid Organ Transplant Recipients: 9 years experience at a major U.S. transplant center

Additional Pretransplant Screening Tests

- Schistosoma IgG in 36%: all -ve
- Strongyloides IgG in 22%: all -ve
- TB screening:
 - PPD: 6 tested, 1 +ve
 - Quantiferon TB blood: 5 tested, 1 +ve
 - 1 previously treated latent TB

Malinis M. Outcomes of infections in International Solid Organ Transplant Recipients: 9 years experience at a major U.S. transplant center

Posttransplant Infections

- Timing: 36 (0 – 2,035) [median (range)] days
- 19 patients (53%) had 37 infection episodes:
 - 10 CMV
 - 5 bacterial pneumonia
 - 5 intraabdominal infection
 - 5 skin & soft tissue infection
 - 5 UTI
 - 2 clostridium difficile
 - 2 CLABSI
 - 1 each histoplasmosis, aspergillosis & influenza
- Gram +ve bacteremia: 26/1000 patient f/u years
- Gram -ve bacteremia: 28/ 1000 patient f/u years
- *No TB, schistosomiasis, strongyloidiasis, or Chagas*

Infections Pertinent to Transplant Recipients of International Origin

- Tuberculosis
- Strongyloidiasis
- Schistosomiasis
- Chagas

Tuberculosis

- Global burden:
 - 1/3 world population is infected with TB
 - Prevalence: 16 million active TB cases
 - Incidence: 7 million new cases annually
- Role of prior BCG vaccine
- Screening transplant **candidates** for latent TB:
 - TST/PPD vs IGRA
 - Manuel O. Comparison of quantiferon-TB gold with tuberculin skin test for detecting latent tuberculosis infection prior to liver transplantation. American Journal of Transplantation, 2007, 7, 12, 2797-2801:
 - 24% +ve TST
 - 22% +ve QFT-G
 - Agreement 85%.
 - No discordance due to prior BCG.
 - Indeterminate QFT-G due to lymphopenia & high MELD score.

Tuberculosis

- Theodoropoulos N. Use of the QuantiFERON-TB Gold interferon-gamma release assay for screening transplant **candidates**: a single-center retrospective study. Transplant Infectious Disease, 2011; 26 AUG 2011

- 10% +ve: foreign born (43%) or known prior TB exposure
 - 8% indeterminate: majority in liver transplant candidates
 - 9 (0.43%) developed active TB posttransplant:
 - 2 had +ve screening QFT
 - 3 US born

Tuberculosis

- Screening organ **donors** for latent TB:
 - Hernandez-Hernandez E. Screening for tuberculosis in the study of the living renal donor in a developing country. *Transplantation*, 2006, 81, 2, 290-292:
 - 222 Mexican living kidney donors
 - 36% had +ve PPD, but –ve CXR, excretory urogram, UA & UC for TB
 - INH prophylaxis in donors did not alter transmission of TB to recipients

Strongyloidiasis

- *Strongyloides stercoralis*
- Global burden:
 - Tropical & subtropical regions, including southeastern US & the Caribbean
 - 30-100 million infected worldwide
- Autoinfection possible → May be chronic
 - 50% asymptomatic
 - Rash “Larva currens”
 - Hyperinfection syndrome → Gram negative bacteremia

- Roxby AC. Strongyloidiasis in Transplant Patients. *Clinical Infectious Diseases*, 2009, 49, 9, 1411-1423:
 - True incidence in transplant recipients unknown
 - Usually first 3 months after transplant
 - Progression of chronic infection
 - 50% mortality
 - Role of transmission from donor

- Roxby AC. Strongyloidiasis in Transplant Patients. *Clinical Infectious Diseases*, 2009, 49, 9, 1411-1423:
 - Who to screen: Patients from endemic areas, unexplained GI sx, eosinophilia
 - How to screen: strongyloides IgG, stool microscopic exam
 - Role of empiric prophylactic treatment

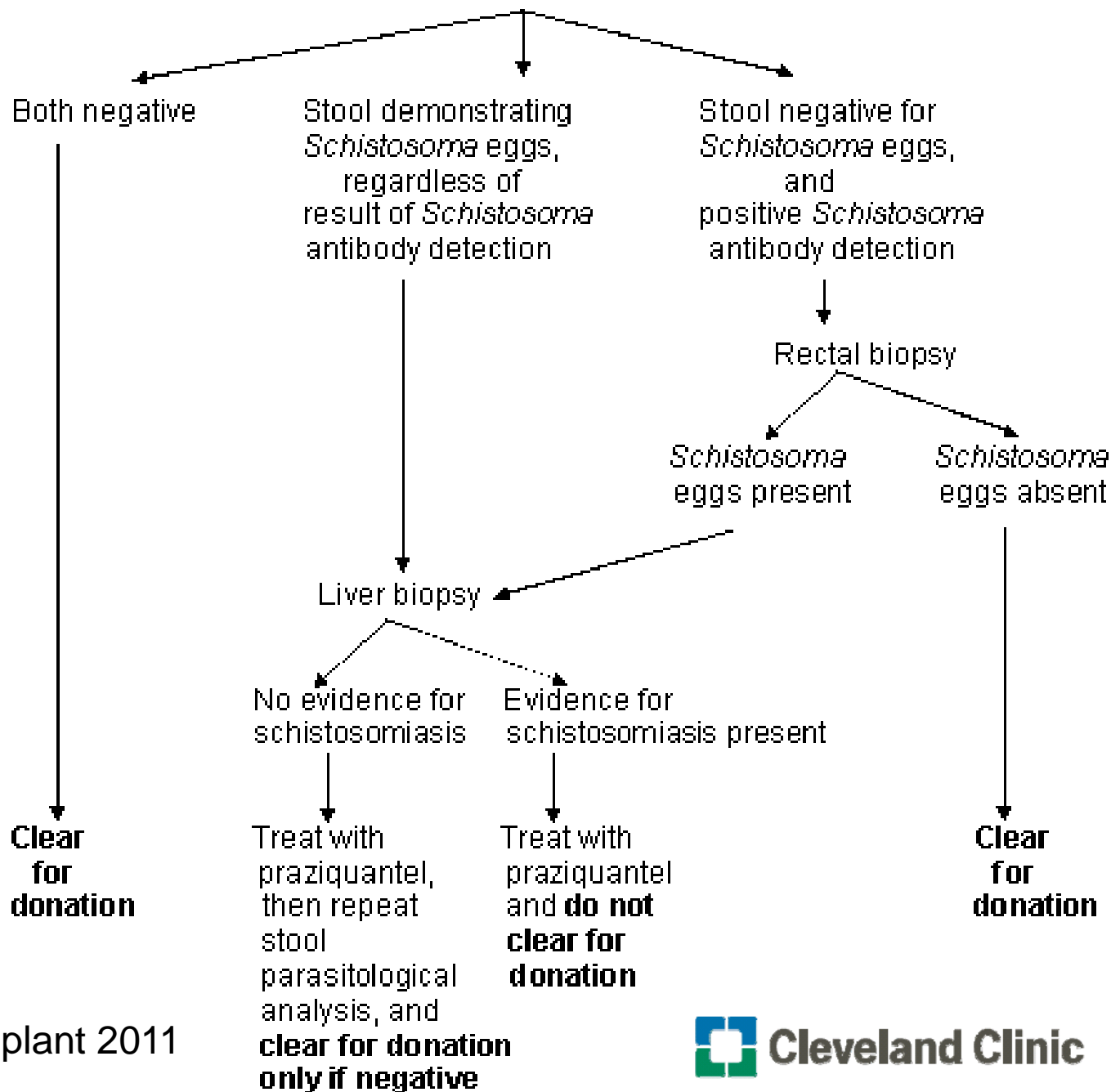
Schistosomiasis

- 5 species: mansoni, hematobium, japonicum, mecongi & intercalatum
- Global burden:
 - 700 million worldwide at risk
 - 200 million infected → 400,000 live in US
- Case reports of reactivation of latent infection & donor derived infection
 - Vincenzi R. Schistosoma mansoni infection in the liver graft: impact on donor and recipient outcome. Liver Transplantation 2011; in press
 - Ahmed K. Intestinal schistosomiasis following orthotopic liver transplantation: a case report. Transplantation Proceedings. 39(10):3502-4, 2007

Schistosomiasis

- Screening methods:
 - Stool analysis
 - Serology
 - Rectal biopsy
 - Liver biopsy

Algorithm for identifying schistosomiasis in liver donors from endemic areas



Chagas Disease

- *Trypanosoma cruzi*
- 8-10 million infected in the Americas
 - 100,000 in US
- Blood donor screening in US since 12/06
- Targeted organ donors screening: born in Mexico, Central America and South America
- Heart transplantation from infected donors is not recommended

Bern C. Evaluation and Treatment of Chagas Disease in the United States: A Systematic Review. *JAMA*, 2007, 298, 18, 2171-2181

Chagas Disease

- Organs other than heart considered with informed consent
- Systematic monitoring of recipients by polymerase chain reaction, and microscopy of buffy coat
- Advance planning for immediate antitrypanosomal treatment if recipient infection is detected

Chin-Hong PV. Screening and Treatment of Chagas Disease in Organ Transplant Recipients in the United States: Recommendations from the Chagas in Transplant Working Group. Am J Transplant 2011; 11(4): 672-680.

Vaccination (adults)

- Vaccinate transplant candidates as early as possible before transplant
- Inactivated vaccines vs live-attenuated vaccines
- Vaccinating close contacts “herd immunity”
- Limited immunogenicity is better than no vaccination
- Fear of rejection is not evidence-based

Influenza Vaccination in Transplant Recipients

- Vaccinate all SOT & BMT recipients
- No risk of rejection
- Inactivated, not live-attenuated vaccine
- > 3 months (SOT), 4-6 months (BMT)
 - Except during pandemics: 1 month
- Role of within season revaccination?
- Insufficient data: high dose, adjuvant, intradermal

Influenza Vaccination in Transplant Recipients

- Inactivated vaccine *preferred* over live-attenuated vaccine in contacts & HCW
- Patients with history of hives to eggs may receive the inactivated vaccine by a HCW who is familiar with the potential manifestations of egg allergy, and should be observed for at least 30 minutes for signs of a reaction
- A previous severe allergic reaction to influenza vaccine, regardless of the component suspected to be responsible for the reaction, is a contraindication to receipt of influenza vaccine.

Vaccination in SOT candidates & recipients

Vaccine	Candidates	Recipients
Influenza		✓
HBV		✓
HAV		✓
Tdap		✓
Pneumovax		✓
Meningococcal		✓
HPV		✓
VZV (Chicken pox)	✓	X
VZV (shingles)	✓	X

Vaccinations in HSCT recipients

	Time post HSCT (months)	Number of doses
Influenza	4-6	1 annually
Pneumococcal	3-6	3-4
Haemophilus influenzae	6-12	3
Hepatitis B (& A)	6-12	3
Tdap	6-12	3
Polio	6-12	3
Meningococcal	6-12	1 (college, asplenia)
MMR	24 (off all IS rx)	1



Travel Precautions for transplant recipients

- Visit travel clinic several weeks ahead of travel
- Vaccinations:
 - Update standard vaccines
 - Travel vaccines: HAV, salmonella typhi, polio, meningococcal, rabies, Japanese encephalitis
 - Contraindicated vaccines: live attenuated nasal flu, oral polio, yellow fever, BCG, typhoid
- Food & water precautions
- On demand cipro or azithromycin for diarrhea, fever or bloody stools

Other travel precautions

- Malaria prophylaxis
- Insect repellents (malaria, dengue, others)
- Safe sexual practices
- Drug interactions with immunosuppressants

Summary

- Transplant recipients of international origin have additional risks of infections
- Donors from endemic areas should be carefully screened
- Follow vaccination guidelines
- Visit Travel Clinic several weeks ahead of travel



America