Donor derived infections in transplantation

Epidemiology and surveillance

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Objectives

- To understand **rarer** contemporary scenarios in donor derived infections that may affect screening decisions
- To articulate steps in **epidemiologic investigation** that improve patient safety
- To elaborate what perioperative transplant professionals can do to **mitigate the risk** of disease transmission

Disclosures

None

Case: Something to fear?

The ugly

- Transplant recipient identified with post-transplant HCV and HIV infection with no obvious risk factors. Negative pre- transplant testing
- Reported to OPO, UNOS, and CDC
- Donor – Look-back Assessment
  - Negative serology for HIV & HCV
  - Appropriately labeled as “high risk” by PHS Guidelines
  - Subsequent testing of post-transfusion serum was + for HIV and HCV by PCR
- All other recipients tested + for HIV & HCV

Ison et al. Am J Transplant. 2011; 11: 1218–1225

Case: Something near?

The good

- Patient is a 56 year-old W male
- Underwent OLT
- CMV D+/R–
- Prophylaxis: Valganciclovir
- 9 days post-transplant
- Donor has + blood cultures drawn the day prior to donation
- Positive for Pseudomonas aeruginosa – generally easily treated

Case 1

- Male patient s/p deceased donor kidney transplant
- 17 months later: Presents to ED with R hip pain and radiation to the lower extremity
- 4 days later: Admitted with fever, diaphoresis, nausea, right lower extremity weakness, abdominal pain
- Eventually progressed to bilateral lower extremity weakness with ascending paresthesias

Case 1
Which is the culprit?

Case 1: Something rare?

The bad

- Patient eventually developed encephalopathy, excessive salivation, hemodynamic instability
- Died 22 days after admission
- Rabies virus RNA detected in saliva, nuchal skin biopsy, postmortem CNS tissues
- Donor: Admitted with upper extremity paresthesias, seizure, autonomic instability
- Donor brain tissue archived: Rabies virus antigen detected. Raccoon rabies variant
- 3 other recipients well (heart, kidney, liver)

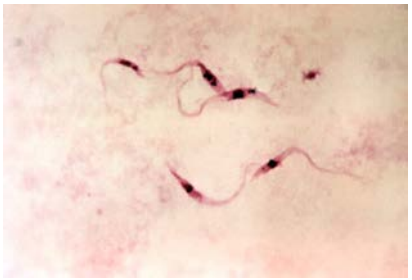
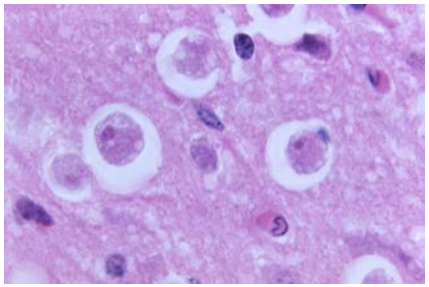
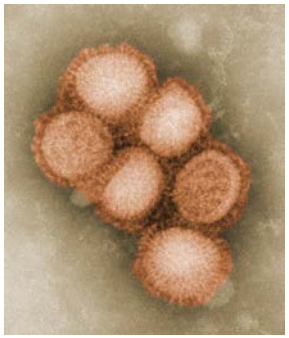
Vora et al, JAMA 2013; 310(4)

Questions to consider when accepting a potential donor with CNS process

- What is the potential donor's age and cause of brain death?
- Did the potential donor have a fever at presentation of illness?
- Were altered mental status and/or seizures part of the presentation that led to the donor's hospitalization?
- Was a CT of the head or MRI of the head or lumbar puncture consistent with an infectious process?
- Was the donor immunosuppressed?
- Did the donor have any unique environmental exposures?

http://optn.transplant.hrsa.gov/

Case
Which of these organisms are safe?


Case 2

- Organ donor: Hispanic female in early 40s with history of migraines
- Unresolving headache despite therapy
  - CT-angiogram of head: Right carotid cavernous fistula
  - Coiling and embolization
  - Intracranial bleed and craniotomy
  - Brain death
    - No autopsy performed

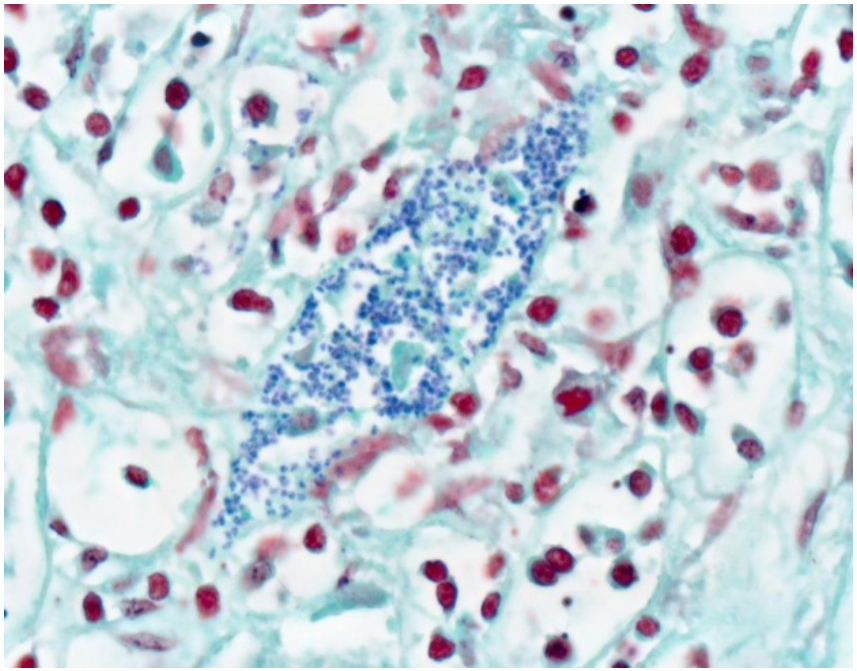
Case 2

Organ recipients

- Right Kidney
  - 6 weeks post-transplant: fever, myoclonus, abnormal gait, altered mental status
  - Died; autopsy performed
- Heart/Left kidney
  - 6 weeks post-transplant: fatigue, nausea, vomiting, confusion, myoclonus, fever, and mild aphasia.
- Liver
  - post-transplant diarrhea, tremor, and altered gait
- Transplant center testing
  - Only notable finding +measles IgG and IgM in heart/L kidney recipient (CSF)

Case 2

Microsporidium investigation slides



Case 2

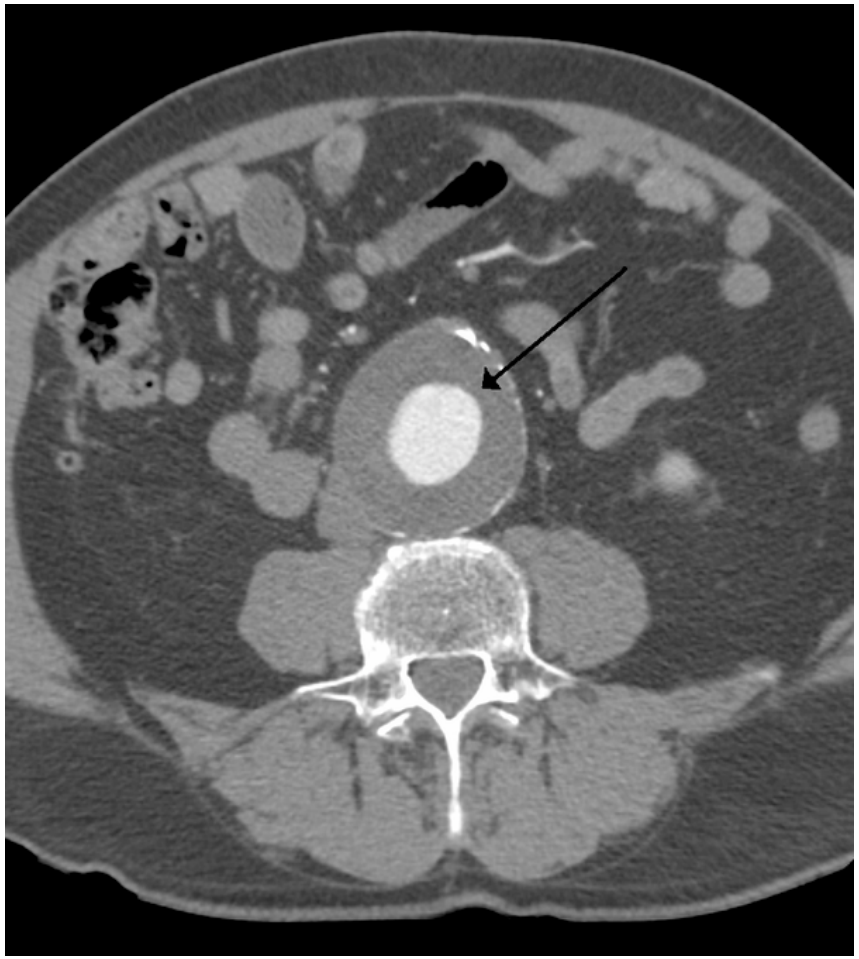
CDC Investigation

- Lymphocytic choriomeningitis virus and measles
  - Negative
- Right kidney recipient autopsy
  - Microsporidia by H & E and immunohistochemistry
- Heart/left kidney recipient and liver recipient
  - Urine PCR
- Organ donor
  - Investigational serology
- Evidence of Microsporidia infection identified in donor and all recipients

Case 2

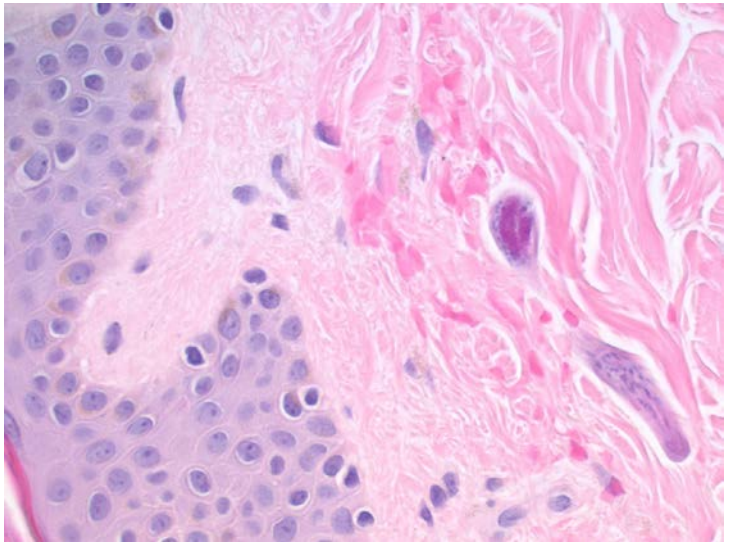
Back in San Francisco

- 64 year-old male with a history of HCV cirrhosis and HCC s/p liver transplantation 2/10/14
- 5/13/14 pt complains of tremor in clinic
- Call from CTDN (local OPO)
- CDC to the rescue
- 6/1/14 pt started on albendazole for potential disseminated microsporidium
- 6/18/14 pt admitted with abdominal pain, nausea, vomiting found to have 5cm abdominal aortic aneurysm
- True, true and unrelated?



Case 3

- 34 year-old W male with DM s/p kidney pancreas transplant 6 weeks prior
- Gram negative rod sepsis and abdominal rash
- U.S. born, no foreign travel. From Fresno, CA
- Donor was immigrant from Mexico. Immigrated 6 years ago. Farmer



Case 4

- 45 year-old kidney transplant recipient presents with abdominal pain, shortness of breath and this rash on his buttocks

Cases 3 & 4

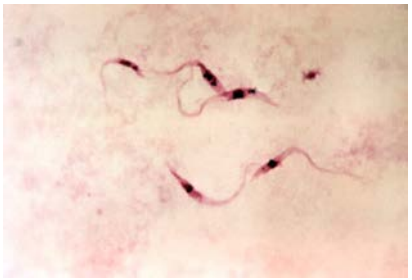
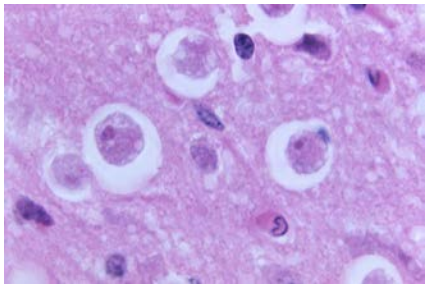
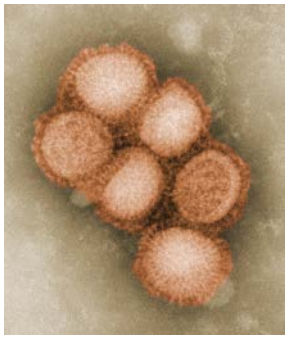
- **Strongyloides** rhabditiform larvae complete life cycle via peri-anal skin in IS hosts.
- Spread to lungs, skin, other areas
- Can cause bacteremia with GI bugs. Mortality rate is high
- Often no eosinophilia

Recent outbreaks reported to CDC and DTAC

- Three donors from Strongyloides endemic areas
- Transmission 1
  - 5 organs transplanted; 1 recipient affected (CTDN)
- Transmission 2
  - 5 organs; 2 recipients dead. Results known but not reported to TC
- Transmission 3
  - 4 organs; donor tested prior to transplantation; all recipients treated. No disease (NYODN)
- CDC
  - Since 2009, 7 other clusters; 20 recipients; 2 deaths
- NYODN
  - Screening since 2010
  - 10 positive donors
  - 355 screened

Abanyie F et al, 2014

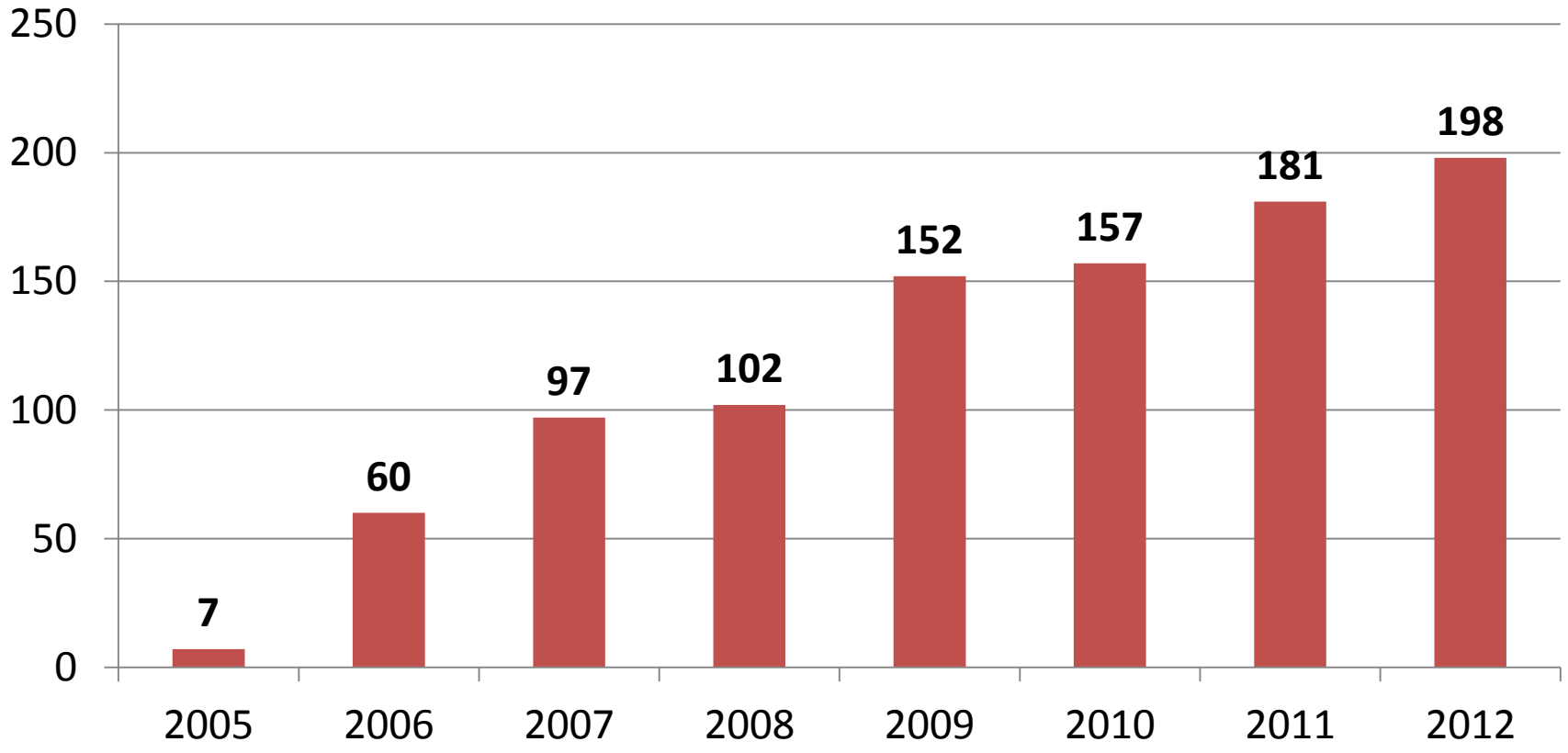
Case
Which of these organisms are safe?


Chin-Hong et al, Am J Transplant. 2011; (11)4
Roy et al, Am J Transplant. 2014; (14)1
Kumar et al, Am J Transplant. 2010; (10)1
Chin-Hong et al, ATC 2013

Potential donor derived transmission events

DTAC 2005=2012



Reported cases to DTAC

2005-2012

Disease Types	# of Donor Reports	# of Recipients w/ Confirmed Tx	# of DDD-Attributable Recipients Deaths
Malignancies	282	69	25
Viruses	205	58	17
Bacteria	152	42	12
Fungi	106	37	13
Mycobacteria	63	11	3
Parasites	47	34	10
Other Diseases	47	1	0
Total	**902**	**252**	**80**

Lessons learned: DTAC data

- Bacterial Transmissions
  - Likely under-recognized & under-reported
  - Often involves resistant bacteria
  - Follow-up of outstanding culture data
- Fungal Transmissions
  - Endemic mycoses & Cryptococcus increasing
  - High morbidity and mortality
- Mycobacteria Transmissions
- Parasite Transmissions
  - Increase in Strongyloides, Chagas, & Amoeba
- Viral Transmissions
  - Increased recognition of PB19, LCMV
  - Need to use NAT to diagnose transmission, esp for HCV

Lessons learned: DTAC data

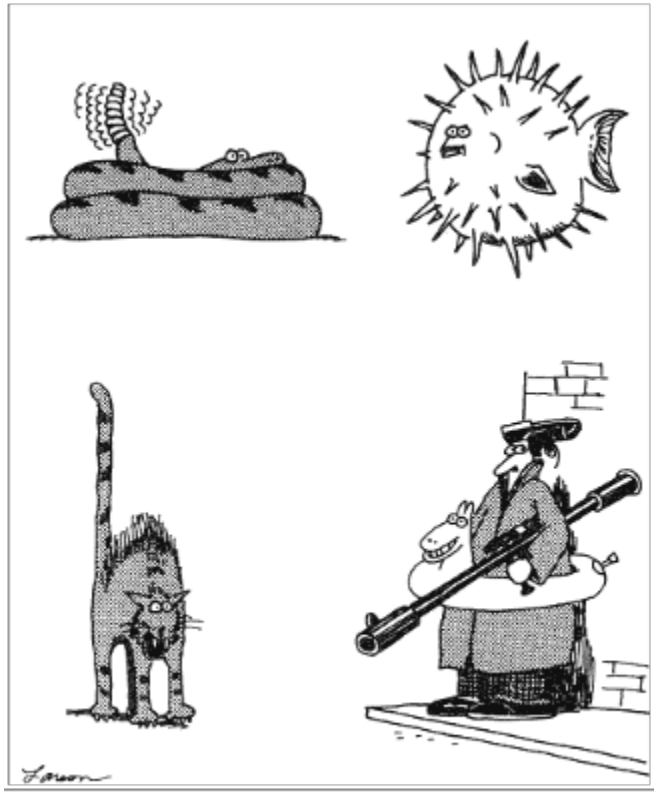
- Communications
  - Inefficient system currently in place in the US
- Poor systems for recognizing donor-derived disease transmissions
  - No cluster analysis
  - Severe outcomes not recognized by all recipient teams
  - Variable recognition and report
  - Management of positive cultures/result information locally
- Increased risk donors
  - Variable definitions used across US
  - Variable understanding of risk by clinicians and patients
  - Variable follow-up of recipients
- Human errors
- Living donors are not spared

What transplant professionals can do peri-operatively

- Ensure **donor screening** performed
  - Review medical & social history
  - Physical examination
  - Screening of blood samples of donor and recipient
  - Serology
  - Nucleic Acid Testing (NAT)
- Define the **increased risk** donor
  - OPTN-defined increased risk donor
  - New definitions
  - Increased risk of transmission of other infections may affect peri-transplant antimicrobials
- Screen high-risk recipients **post-transplant**

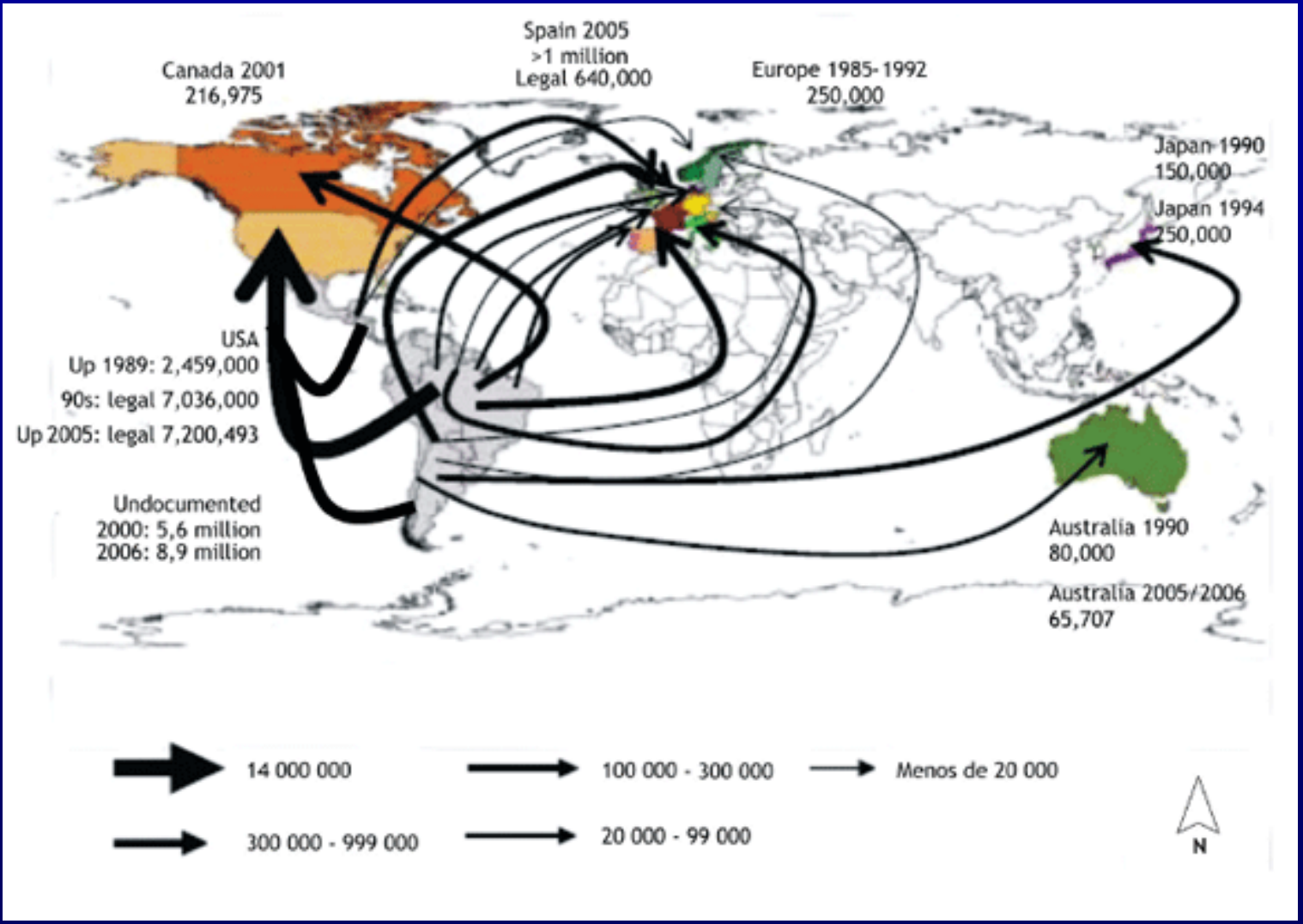
Screening 123

1. The "**Big 3**": HIV, Hep B, Hep C
2. The **givens**: CMV, EBV, HSV, VZV, toxoplasma, syphilis, bacteria
3. The "**Next 3**": TB, Chagas, endemic mycoses
4. More **a la carte**: Strongyloides, West Nile
5. The **impossibles**: LCMV, microsporidia



How nature says, "Do not touch."

Hocevar S et al, Ann Intern Med; 2014; 160(4)
Kotton C, Ann Intern Med; 2014; 160(4)



Schmunis GA. Mem Inst Oswaldo Cruz. 2007 Oct 30;102 Suppl 1:75-85

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