Emerging Infections in Transplantation

Michael Wong, MD

Emerging Infections

- Human infections that are emerging in immunocompromised patient populations:
  - MTB
  - CDAD
  - KPC
- Enzootic and Endemic conditions
  - LCMV
  - *T cruzi*
  - *Strongyloides*

Case 1

- 56 yr old, HCV with ESLD, s/p RFA for HCC, history of reactive PPD 30 yrs ago, and completed only 2 weeks of INH therapy for LTBI. MELD with points is 32.
- Sent to me for "ID clearance" for TXP.
  - "I didn't believe the doctor"
- Foreign born, left country of origin at age 22, family history positive for grandfather with active MTB when he was a child; told no problem since he received the BCG vaccine
- On CXR, he has a clear Gohn complex.

What do you do?

MTB following SOT

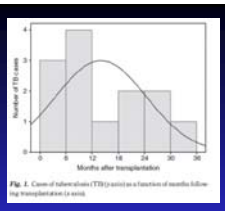
- Increasing migration patterns of populations with globalization from areas of high-endemicity (e.g., Haiti, South Africa, Eastern Europe) to the US
- Routine screening in primary health care settings lax including in immigrant populations
- Significant confusion and lack of understanding regarding the BCG, PPD and even the concept of LTBI exists among healthcare providers

- Singh and Paterson, Clin Infect Dis 1998
  - Large lit review, 511 cases of MTB following SOT with primary source being recipient reactivation of disease
  - Exception, Lung and heart/lung where donor was source (9%)
  - Risk factors were ALG therapy and non-US borne recipients
  - Outcomes poor if disease presented as dissemination
- Torres-Ciseneros et al. Clin Infect Dis 2009
  - REISTRA Experieince-4388 SOT
  - 21 active MTB infections post SOT
  - Incidence 255->2000/100,000 with highest rate in lung txp recipients
  - MV analysis revealed age of recipient and Lung TXP to be most consistent risk factors
- Lopez de Castilla et al, Transpl Infect Dis 2009
  - NYC/Columbia Med Ctr experience-4925 SOT from 1988-2005
  - 13 cases of MTB disease with case rate 264/100 000
  - Majority were reactivation in kidney recipients (largely non-US borne recipients)

NYC Experience

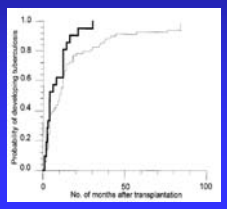
Lopez de Castilla et al, Transpl Infect Dis 2009

Median time to MTB disease post transplantation was 12 months



Singh and Paterson experience

Median time to disease post transplantation was 11.5 months



Back to our case

The recipient had no findings suggestive of active MTB disease on ealuation and sputa smears. He went forward with transplantation that was unremarkable, and was started on INH LTBI therapy rather than RIF at the end of Month +1 when his steroids were discontinued

•Chosen to minimize the drug-drug interactions of RIF and his IS, with the understanding he was at higher risk for LFT issues with INH.

He completed 9 months of INH therapy and had no untoward complications while on therapy

Case 2

- 55 yr old Cuban borne gentleman, presents with fevers to 103, 35# weight loss, and mental status changes and CHF
- Initial labs demonstrate WBC 110,000, 90% blasts; BMBx consistent with AML
- Exposure history: low risk employment (IT support), lives with family who are well, no MTB exposures, has pet parrot of 25 yrs at home. Had not travelled or returned to Cuba
  - *Let Cuba in the massive boat exodus in the 1980s. The immigres were all co-housed in Florida based detention and corrections centers.*

Numerous studies obtained; large effusion that was more evident on CT was sampled. MTB PCR was positive from the effusion, probe positive from sputum and AFB blood cultures all positive on the same day (hosp day 8)

Had prolonged course of antiMTB therapy, complicated by sterile abscesses that developed after his induction chemotherapy and counts returned (? IRIS equivalent).

NB: This was a treatment nightmare; while he was receiving induction and consolidation chemotherapy (IDA/ARA then HIDAC), his antiTB regimen as altered to Moxi/rifabutin/streptomycin (ETH and PZA were continued during induction chemo)

Ultimately went on to have a successful sibling matched allogeneic HSCT, and doing well now 4 years from HSCT.

Case 3

- 55 yr old s/p OLT for complications associated with Laennec's cirrhosis, complicated by failure to thrive only. Developed diarrhea on day +35 at rehab facility which was attributed to MMF
  - Neither he nor records acknowledged significant diarrhea though in retrospect he was having up to 10 watery bowel movements daily
- Admitted to our hospital with acute abdomen and fevers to 103.
- CT demonstrated toxic megacolon and stool markedly C diff tox + by EIA

- He was also GN septic, and went on to have a total colectomy with diverting ileostomy; at surgery, pseudomembranes were seen into the distal ileum.
- Course further complicated with non-albicans candida sepsis, but after combined tigecycline/micafungin/CDAD therapy, he survived and is doing well now 14 months post OLT.

CDAD following OLT

- Mayo experience- 487 consecutive OLT in 402 pts from 1998-2001
  - 32 pts developed CDAD (5-1999 days post OLT)
  - 30/32 (93.8%) developed CDAD within first year post OLT
  - Risk factors:
    - Early (< day 28)
      - major intraabdominal bleed, (P<0.001),
      - biliary complication (P=0,034)
      - Bile leak (P=0.026)
      - Concurrent systemic infection (P<0.001)
      - OLT redo (P=0.013)
      - Appears to be a relationship with MELD
    - Intermediate onset cases (days 29-365) were more likely to have similar risk factors that were clearly ongoing and more chronic technical issues
    - Late onset cases (>365 days)- only 3 cases; severe disease, multiple post-transplant complications (drug-related ITP, recurrent biliary stricture with stenting and prolonged systemic antimicrobial exposure

Albright et al. Transpl International 2007;20:856-66

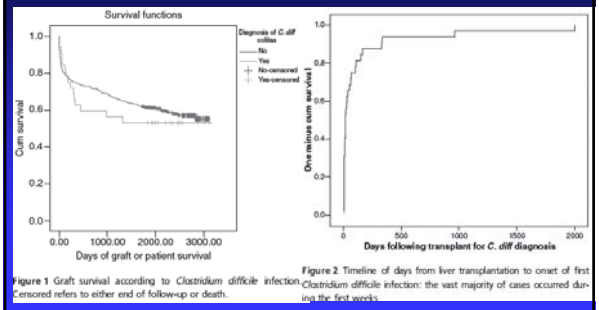


Figure 1 Graft survival according to *Clostridium difficile* infection. Censored refers to either end of follow-up or death.

Figure 2 Timeline of days from liver transplantation to onset of first *Clostridium difficile* infection: the vast majority of cases occurred during the first weeks.

Albright et al. Transpl International 2007;20:856-66

CDAD in HSCT

Bone Marrow Transplantation (2008) 42, 705–713

www.nature.com/bmt

REVIEW

***Clostridium difficile*-associated disease in human stem cell transplant recipients: coming epidemic or false alarm?**

D Bobak[1], LM Arfons[1,2], RJ Creger[1,2] and HM Lazarus[1,2]

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- 12 studies from 1994-2006
  - 1963 patients with CDAD; no denominator data provided,
    - Mix of allogeneic and autologous HSCT recipients
    - CDAD confirmed in 141 (7.18%)
    - 13 died from CDAD complications
      - Gorschluter et al, 2001
    - Median time to onset was between 4 to 45 dats
      - Arango, 2006; Yuen, 1998
    - Other major cause of diarrhea was GVHD (45%)

Clin Transplant 2009: DOI: 10.1111/j.1399-0012.2009.01035.x

Clinical Transplantation

Clostridium difficile-associated disease in allogeneic hematopoietic stem-cell transplant recipients: risk associations, protective associations, and outcomes

Erik R. Dubberke, Kimberlay A. Reske, Anand Srivastava, Justin Sadhu, Robert Gatti, Rebecca M. Young, Lauren C. Rakes, Brian Dieckgraefe, John DiPersio and Victoria J. Fraser

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Table 2. Potential variables associated with CDAD on univariate analysis ($p \leq 0.10$)

Characteristic	Controls (n = 67)	Cases (n = 37)	OR (95% CI)
Diabetes[a]	10 (15)	13 (35)	3.1 (1.2–8.0)
Lung disease	1 (2)	4 (11)	8.0 (0.9–74.5)
Neutropenia	48 (72)	16 (43)	0.3 (0.1–0.7)
Receipt of a growth factor during admission	40 (60)	9 (24)	0.2 (0.1–0.5)
Receipt of a 3rd/4th generation cephalosporin during admission			
None	36 (54)	13 (35)	Reference
>0–7 d	27 (40)	12 (32)	1.2 (0.5–3.1)
>7 d	4 (6)	12 (32)	8.3 (2.3–30.4)
Receipt of carbepenems during admission	23 (34)	6 (16)	0.4 (0.1–1.0)

Table 3. Multivariable analysis of variables associated with CDAD on logistic regression

Variable	OR (95% CI)
Growth factor	0.1 (0.02, 0.3)
3rd/4th generation cephalosporin	4.6 (1.6, 13.1)
Diabetes	5.0 (1.5, 16.5)
Pre-engraftment period	4.0 (1.2, 13.1)

CDAD, *Clostridium difficile*-associated disease.

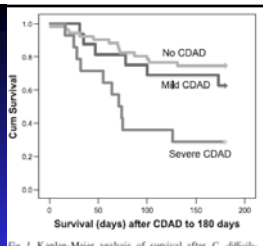

Fig. 1. Kaplan-Meier analysis of survival after *C. difficile*-associated disease (CDAD), stratified by CDAD severity.

Table 4. Variables associated with death at 180 d

Variable	Unadjusted HR	Adjusted HR
Age (continuous)	0.9 (0.9–1.0)	
Severe CDAD	3.7 (1.7, 8.1)	2.6 (1.1, 6.2)
Bloodstream infection[a]	2.6 (1.3, 5.6)	
Relapse/refractory disease	3.2 (1.6, 6.8)	3.7 (1.7, 7.8)
Late post-engraftment period	2.4 (1.2, 5.0)	
GVHD[a]	2.5 (1.2, 5.3)	
Severe GVHD[a]	3.4 (1.6, 7.1)	2.7 (1.2, 6.1)

GVHD, graft-vs.-host disease; CDAD, *Clostridium difficile*-associated disease.
[a]Onset after CDAD (after discharge from index hospitalization for controls).

CDAD

- Increasing frequency in both solid and liquid organ transplant recipients
- Infections associated with poorer outcomes including higher rates of graft loss, and death
- Risk factors appear to be diverse and variable

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Case report

Fatal cross infection by carbapenem-resistant *Klebsiella* in two liver transplant recipients

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A.J. Mathers, H.L. Cox, H. Bonatti, B. Kitchel, A.K.C. Brassinga, B. Wispelwey, R.G. Sawyer, T.L. Pruett, K.C. Hazen, J.B. Patel, C.D. Sifri. Fatal cross infection by carbapenem-resistant *Klebsiella* in two liver transplant recipients.
Transpl Infect Dis 2009: **11**: 257–265.

Abstract: Members of the family Enterobacteriaceae including *Klebsiella* have re-emerged as major pathogens in solid organ transplantation. The recent appearance and dissemination of carbapenemase-producing Enterobacteriaceae in Europe and the northeastern United States represents a major challenge to the treatment of enteric gram-negative bacterial infections in immunocompromised patients; however, few reports have detailed the outcomes of such infections. Here we report 2 cases of *Klebsiella pneumoniae* carbapenemase (KPC)-producing *Klebsiella* infections in orthotopic liver transplant recipients, which were the index case and initial secondary case for an outbreak of KPC-producing Enterobacteriaceae in our institution. In both instances, the pathogens were initially misidentified as being carbapenem sensitive, the infections recurred after cessation of directed therapy, and the patients ultimately succumbed to their infections.

Key words: carbapenem; resistance; *Klebsiella*; β-lactam; liver transplantation; carbapenemase; KPC; Enterobacteriaceae

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Transpl Infect Dis 2009: **11**: 257–265

Brief Report: Lymphocytic Choriomeningitis Virus Transmitted Through Solid Organ Transplantation --- Massachusetts, 2008

MMWR

July 25, 2008 / 57(29);799-801

- 45 yr old Domincan Republic borne recipient, HIV, HBV and HCV negative, ESRD presumed from HTN received one of a pair of kidneys in mid February 2008
- Course uncomplicated; in follow up at 1 month, complained of some fevers, fatigue and nausea
- Admission labs at end of March demonstrated leukopenia, profound transaminitis, and some blood and protein in his urine

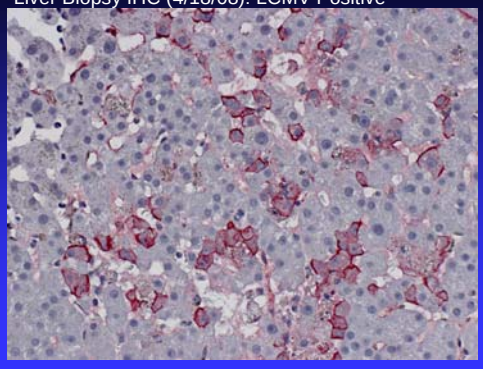
- Extensive initial work up was unrevealing; liver and kidney biopsies were unremarkable except for inflammatory changes in the liver
- At same time, report from NEOB that the paired recipient was in the ICU at another local hospital

Donor Review

- Donor packet revealed the donor was living in a local shelter, and was found down outside the shelter
- In ED, he was febrile to 102 and had a witnessed seizure;
  - BAC was elevated and assumed to be the cause of the seizure;
  - CXR demonstrated infiltrate and assumed aspiration PNA cause of the fever
- In ICU, he remained unresponsive. Head imaging was unremarkable except for some atrophy
  - LP- demonstrated protein >100, glucose 30, and CSF pleocytosis at 150, mononuclear cell predominance
  - Routine cultures and studies negative
  - Assumed by local ID and Neurologist to be consistent with seizure

- Serologies of the paired recipient returned LCMV positive, prompting the notification to us, MDPH and CDC
- CDC proved the Donor had acute LCMV and transmission was to both recipients with positive evolving serologies and plasma PCR detection in prior stored and serial specimens
- Both recipients died from complications of LCMV
  - Our recipient rapidly developed acute renal failure not related to IS modification or AR;
    - in spite of this we treated with IV RBV per emergent IND
    - Minimal hemolysis was experienced
    - At post, his liver was necrosing; his kidney was completely necrotic
    - In surveillance, LCM viremia cleared

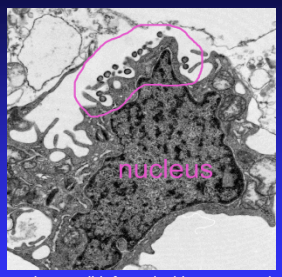
Liver Biopsy IHC (4/18/08): LCMV Positive



Courtesy, Pierre Rollins, CDC

Arenaviruses

- Generally associated with rodent-transmitted disease
- First arenavirus to be isolated was **LCMV** in 1933
- LCMV 110-130 nm



Vero E6 tissue culture cell infected with an arenavirus
Image shows extracellular virus particles budding from the cell surface.

www.cdc.gov/ncidod/dvrd/spb/mnpages/dispages/arena.htm

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Transmission of Lymphocytic Choriomeningitis Virus by Organ Transplantation

Staci A. Fischer, M.D., Mary Beth Graham, M.D., Matthew J. Kuehnert, M.D., Camille N. Kotton, M.D., Arjun Srinivasan, M.D., Francisco M. Marty, M.D., James A. Comer, Ph.D., Jeannette Guarner, M.D., Christopher D. Paddock, M.D., M.P.H.T.M., Dawn L. DeMeo, M.D., M.P.H., Wun-Ju Shieh, M.D., Ph.D., M.P.H., Bobbie R. Erickson, B.S., Utpala Bandy, M.D., M.P.H., Alfred DeMaria, Jr., M.D., Jeffrey P. Davis, M.D., Francis L. Delmonico, M.D., Boris Pavlin, M.D., Anna Likos, M.D., M.P.H., Martin J. Vincent, Ph.D., Tara K. Sealy, B.S., Cynthia S. Goldsmith, M.S., Daniel B. Jernigan, M.D., M.P.H., Pierre E. Rollin, M.D., Michelle M. Packard, M.P.H., Mitesh Patel, B.S., Courtney Rowland, B.S., Rita F. Helfand, M.D., Stuart T. Nichol, Ph.D., Jay A. Fishman, M.D., Thomas Ksiazek, D.V.M., Ph.D., Sherif R. Zaki, M.D., Ph.D., and the LCMV in Transplant Recipients Investigation Team*

N ENGL J MED 354;21 WWW.NEJM.ORG MAY 25, 2006

The NEW ENGLAND JOURNAL of MEDICINE

March 6, 2008

A New Arenavirus in a Cluster of Fatal Transplant-Associated Diseases

Gustavo Palacios, Ph.D., Julian Druce, Ph.D., Lei Du, Ph.D., Thomas Tran, Ph.D., Chris Birch, Ph.D., Thomas Briese, Ph.D., Sean Conlan, Ph.D., Phenix-Lan Quan, Ph.D., Jeffrey Hui, B.Sc., John Marshall, Ph.D., Jan Fredrik Simons, Ph.D., Michael Egholm, Ph.D., Christopher D. Paddock, M.D., M.P.H.T.M., Wun-Ju Shieh, M.D., Ph.D., M.P.H., Cynthia S. Goldsmith, M.G.S., Sherif R. Zaki, M.D., Ph.D., Mike Catton, M.D., and W. Ian Lipkin, M.D.

- Australia
- 3 organ recipients died
- A new arenavirus was detected - **Unbiased High-Throughput Sequencing**
- Donor with no symptoms, no virus detected, IgM+ and IgG+

Subsequent sequence analysis at CDC revealed this to be LCMV. Personal communications, P Rollin

T cruzi (Chaga's disease)

- Endemic in Latin America
- Transmitted by the Triatome or "kissing" bug which defecates the eggs as it feeds; we scratch the eggs into the wound
- Causes smooth muscle paralysis (megacolon, myocarditis, heart blocks, distal esophagitis)
- Transmission reported in SOT and HSCT by donors and blood transfusions

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- WHO estimates
  - 16-18 million persons infected with *T cruzi*
  - Incidence of 300,000 persons/year
  - Mortality >50,000 per year
  - Distribution is in South and Central America, but seropositivity through blood bank screening ranges from 1.7% in Sao Paolo Brazil, to 53% in Santa Cruz, Bolivia
- The risk to the recipient population is dependent upon the geographic location of the center, and the donor history.
  - 404 deceased donors in So Cal
    - 25% donors are Hispanic
    - 6 (1.5%) were EIA+ for *T cruzi*
    - 1 had active disease

Chagas disease. Interruption of transmission. Wkly Epidemiol Rec 1997; 72:1.

Control of Chagas disease. Report of a WHO Expert Committee. World Health Organ Tech Rep Ser 1991; 811:1.

Nowicki et al. Transplantation 2006;81:477-9

Chaga's Disease

- Acute phase:
  - incubation period of 7 to 10 days.
  - Local skin swelling: chagomas.
  - Romana's sign: unilateral periorbital edema and swelling of the eyelid if conjunctival inoculation
  - Other symptoms include: fever, myalgias, sweating, hepatosplenomegaly.
  - Cardiac involvement is present in over 90 percent of those in whom the diagnosis is made.
    - variable signs of cardiac failure secondary to myocarditis
    - frequency and severity of myocarditis are inversely proportional to age
  - Very rarely, can present as meningoencephalitis.
  - Recovery is spontaneous in over 95% of those acutely infected with normalization of ECGs

- Indeterminant form:
  - Persons who are asymptomatic but are seropositive for the disease
  - 2% per year will have slowly developing evidence of end organ involvement (GI, cardiac)
  - In one report, 38.3% of persons who were seropositive but asymptomatic at time of diagnosis developed signs and symptoms of cardiac involvement within 10 years.

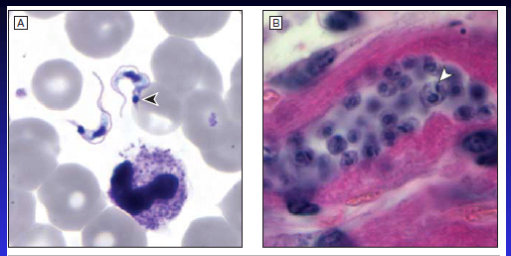
Dias, JC. Rev Soc Bras Med Trop 1989; 22:147.
Coura, JR,et al. Minas Gerais. Mem Inst Oswaldo Cruz 1985; 80:73.

- Chronic disease (cardiac)
  - Biventricular failure
  - High rate of sustained and nonsustained dysrythmias with sudden death reported in up to 55% of persons with cardiac disease
  - Ventricular aneurysms may be found
  - Mural thromboembolism reported in 44% of autopsy pts with embolic CVA complications reported in up to 56% of pts with chronic cardiac disease

Diagnostics

- FOCUS IFA: highly reliable with results >1:256 with sensitivity >93% at this level
- CDC IFA and EIA: essentially confirmatory with sensitivities and specificities >95%
- PCR appears to be the new gold standard in endemic regions.
  - 194 patients at high risk for chronic Chagas' disease
    - Serology negative in 80 pts (41%)
    - 12 of the 80 (15%) were positive by PCR.
    - 3 of the 12 (25%) had clinical signs and symptoms that suggested Chagas' heart disease.
- It is available through the CDC.

Salomone, OA et al. Emerg Infect Dis 2003; 9:1558.



A, The trypomastigote forms of *Trypanosoma cruzi* in a peripheral blood smear from a patient with acute Chagas disease. Arrowhead indicates the kinetoplast (Giemsa stain, original magnification ×1000). B, Nest of *T cruzi* amastigotes within a cardiac myocyte in a patient with chronic Chagas disease. Arrowhead indicates the kinetoplast (hematoxylin-eosin, original magnification ×1000). Courtesy of the Division of Parasitic Diseases, US Centers for Disease Control and Prevention.

Bern et al. JAMA 2007:298:2171-81

As pertains to Transplantation

- Reactivation reported in:
  - 9-16% of KT[1]
  - 50-100% hearts[2]
  - 17% autologous HSCT[3]
  - 40% allogeneic HSCT[4]
  - Surveillance recommended to include at minimum the direct Strout test (assessment for parasitemia)
  - PCR is being suggested as a suitable surveillance tool
  - Suggestion in endemic areas to pre-emptively treat with a positive result

1. Riarte et al. Clin Infect Dis 1999;29:561-7. 2. Diez et al. Am J Transplant 2007:7:1633-40. 3. Altclas et al. Bone Marrow Transpl 2005;36:123-9. 4. Viotti et al. Ann Intern med 2006;144:724-34.

- Inspite of potential transmission through HSCT or with SOT, or reactivation occurring post-transplant, outcomes can be reasonably good with recognition pre-transplantation, good surveillance (PCR vs smear for parasitemia), and treatment

  Riarte et al. Clin Infect Dis 1999;29:561-7

- ? Reactivation or disease mitigation with use of azoles (fluconazole, voriconazole) as these are structural similar to benznidazole.

As pertains to Renal transplantation

- Renal Transplant experience, Argentina
  - 23 seropositive recipients
    - 5 reactivated between day 35 to month 29
    - Reactivation defined by parasitemia (3), cutaneous disease (2)
    - All treated with benznidazole for 21-30 days and repeated with parasitemia recurrence
    - 10 became seronegative over time
  - 16 seronegative recipients received organs from seropositive donors
    - Transmission occurred in 3 pts (18.755)
    - All had parasitemia
    - Nifurtimox was used until day 20 in 1 pt; benznidazole in the other 2

Riarte et al. Clin Infect Dis 1999;29:561-7

Table 1. Reactivation of *Trypanosoma cruzi* infection in chronic chagasic recipients of kidney transplants.

Patient	Age (y)/sex	Donor	Serology: Before transplantation	Serology: After transplantation	Diagnostic indicator	Onset (time)	Treatment	Outcome
1	57/M	Cadaveric	Positive	Decreased	Patent parasitemia*	35 d	Benznidazole for 21 d; discontinued because of leukopenia	Died at 60 d from surgical complication
2	47/M	Cadaveric	Positive	Unchanged	Cutaneous lesions positive for *T. cruzi*	60 d	Benznidazole	Recovered; follow-up for 3 y
3	32/F	Cadaveric	Positive	Unchanged	Cutaneous lesions positive for *T. cruzi*	2 y, 5 mo	Benznidazole	Recovered; follow-up for 2 y, 9 mo
4	17/F	Living related donor, chagasic	Positive	Unchanged	Patent parasitemia	97 d	Self-limited	Spontaneously recovered; follow-up for 4 y, 3 mo
5	46/F	Cadaveric	Positive	Unchanged	Patent parasitemia	63 d	Benznidazole	Recovered; follow-up for 1 y

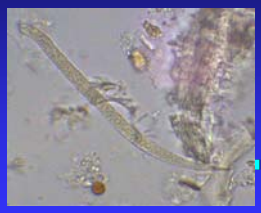
Riarte et al. Clin Infect Dis 1999;29:561-7

Table 2. Transmission of *Trypanosoma cruzi* infection by infected kidneys in recipients of kidney transplants.

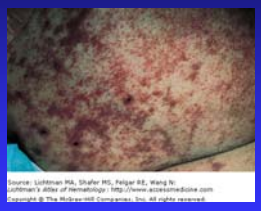
Patient	Age (y)/sex	Donor	Serology: Before transplantation	Serology: After transplantation	Diagnostic indicator	Onset (time)	Treatment	Outcome
1	52/F	Cadaveric, chagasic	Negative	Positive	Patent parasitemia* and serological conversion	60 d	Benznidazole: suspended at day 20 because of leukopenia	Recovered from acute infection; nephrectomy done at 2 y, returning to hemodialysis; follow-up for 5 y
2	23/F	Living related donor, chagasic	Negative	Negative until 1 y after transplantation; at 1 year, serologic conversion	Fever, patent fluctuating and persisting parasitemia	37 d	Benznidazole: suspended because of side effects; nifurtimox for 2 mo	Recovered from acute infection; associated cytomegalovirus infection and osteomyelitis
					Relapses of patent parasitemia	3 y, 20 d	Benznidazole for 30 d	Reactivation of chronic chagasic infection during a chronic rejection episode; follow-up for 4 y
3	27/M	Cadaveric, chagasic	Negative	Negative; no serologic conversion	Fever and patent parasitemia	165 d	Benznidazole	Recovered from acute episode; remains without signs of Chagas' disease; follow-up for 1 y, 5 mo

Riarte et al. Clin Infect Dis 1999;29:561-7

Strongyloides



- *Strongyloides stercoralis*- very small threadlike roundworm that is found throughout the tropic and subtropical regions of the world
- Typical infestation is from very few parasites



- Females tend to burrow into the small bowel or colon wall and either encyst or every couple of weeks release an egg that may or may not hatch in the gut
- Transmission is rarely through the fecal-oral route, but more often by the adolescent worm burrowing through the skin

- In most cases, SHS is from recipient specific hyperparasitism following exposure to immunosuppressive or cytoreductive therapies
- Donor associated infections include:
  - Recipient SHS following intestinal transplant[1]
    - Recipient survived the infection
  - Recipient SHS following heart transplantation[2]
    - Recipient died from the infection

1. Patel et al. Transpl Infect Dis 2008;10:137-42;
2. Schaeffer et al. J Heart Lung Transpl 2004;23:905-11.

- While transmission through SOT is rare, if the recipient is infected, exposure to steroids and IS can result in hyperparasitism which is life-threatening
  - Some suggestion that there may be a steroid dependent promotor region that is upregulated on the female nematode.[1]
    - Results in the female becoming hypergravid
    - Gravid females become highly active, migrating through tissue planes
    - Can present with GN sepsis, 'sterile' sepsis, and cyclic hypereosinophilia[2] (improved with steroids; exacerbated with steroid withdrawl)
  - Other agents also implicated including ALG, biologics including rituximab, and cytoreductive chemotherapy

1. Genta. Clin Mocriobiol Rev 1992:345-355. 2. Huston et al. Transpl Infect Dis 2009;11:277-80

Conclusions

Syndromic Approaches to donor/recipient evals

- CNS disease-
  - Arboviruses, rabies, LCMV, leptospirosis, NIPAH virus, toxoplasma
- Sepsis Syndromes
  - Acute hepatitis E, brucella, coxiella, leptospirosis, tularemia, Chaga's disease, strongyloidiasis, toxoplasma
- Unexplained hepatitis
  - Hepatitis C, leptospirosis, Bartonella, Brucella, Coxiella, LCMV, Nipah, leishmaniasis, Babesia, anaplasma
- Eosinophilia
  - Strongyloidiasis, acute viral infections, endemic mycoses.

- In all cases, need:
  1) GOOD social history for both donor and recipient.
     - A good history should be done by the Donor site as part of the organ procurement process
       - Rabies case in 2004,
       - The New England LCMV case in 2006
       - Our LCMV in 2008
  2) careful review of the labs and radiographic studies; while not specific, there may be enough circumstantial information to clear or not clear a potential donor
       - GESITRA, European ID Society recommendations now to forego any lung harvest if granuloma present.

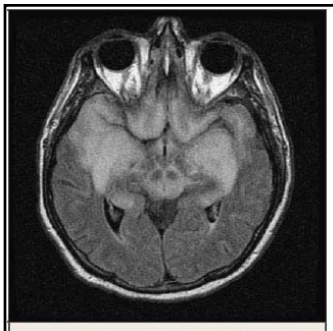


Figure 2. Axial Fluid-Attenuated Inversion Recovery MRI Scan Showing Profound Signal Abnormalities within the Bilateral Frontal and Temporal Lobes, Hippocampi, Basal Ganglia, and Medulla in Patient 2.

Srinivasan et al, 2005 (NEJM 2005, 352, 1103-11)

Rarely associated with SOT, but in 2004, 4 recipients became infected when the organs of donor were transplanted into them.

The donor presented 4 days prior to harvesting to the local ED where he complained of headache and difficulty swallowing; no exposure history was provided at that time. Toxicology screen revealed cocaine.

He decompensated rapidly, developing seizures and requiring intubation. Head CT demonstrated intracranial hemorrhage.

- 3 organ recipients and 1 iliac artery recipient died from rabies
- Prior reports include infection from corneal transplantation.
- Rabid bat rate in NE
  - In 2006, 4% (34/756) of the bats submitted to the Rabies Laboratory at the State Laboratory Institute (SLI) were positive.
  - This past summer, we saw a patient from Quincy who caught a bat in her home that was rabid.