51 Infections in Solid Organ Transplant Recipients

Speaker: Barbara Alexander, MD, MHS, FIDSA

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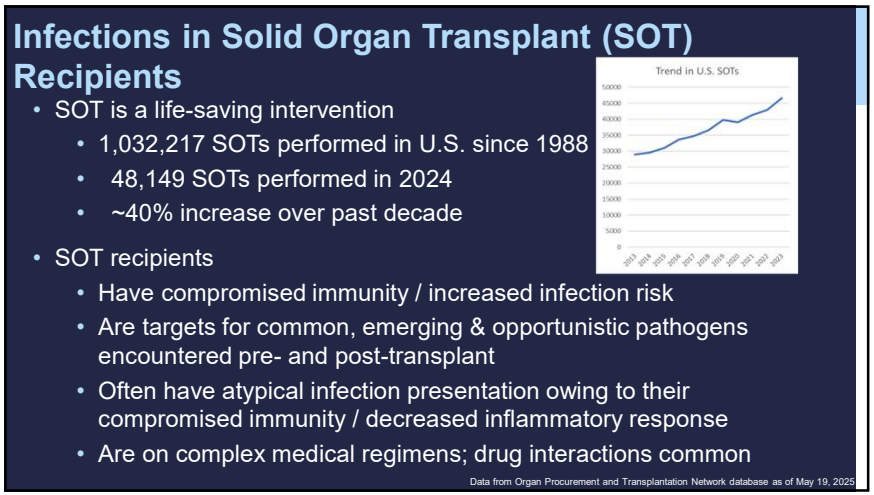

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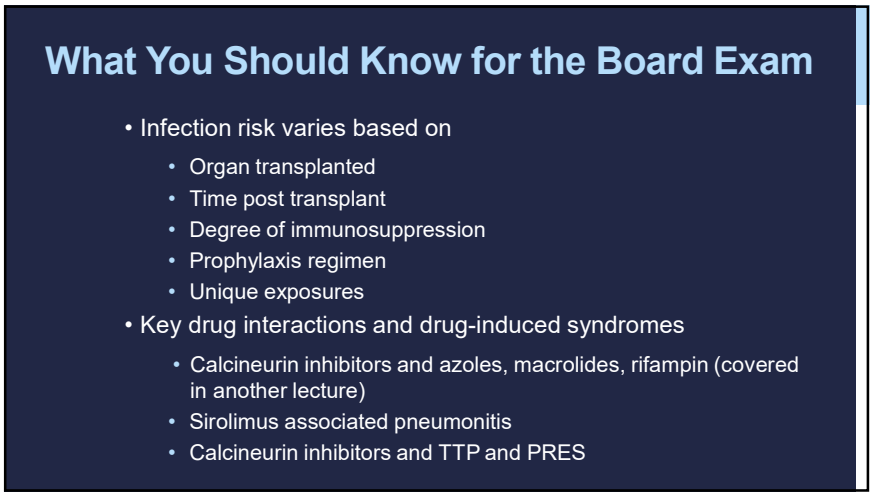

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51 Infections in Solid Organ Transplant Recipients

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What You Should Know for the Board Exam

- The following major clinical syndromes:
  - CMV syndrome & disease
  - EBV & Post Transplant Lymphoproliferative Disorder (PTLD)
  - BK virus nephropathy
  - Aspergillosis, Mucormycosis & Cryptococcosis
  - Tuberculosis
  - Toxoplasmosis
  - Donor-derived infections

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Play the Odds

The data in the stem let's you "play the odds" as to the most likely diagnosis

- Patient completing valganciclovir prophylaxis 6 weeks prior presenting with fatigue, low grade fever and leukopenia
  - CMV
- Donor died from skiing accident in freshwater lake in Florida and recipient presents 3 weeks post transplant with encephalitis
  - Naegleria
- Renal transplant recipient on valganciclovir prophylaxis presents with asymptomatic renal dysfunction
  - BK Virus
- Lung transplant recipient planted vegetable garden 2 weeks prior while on posaconazole prophylaxis and presents with productive cough and cavitary lung lesion
  - Nocardia

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Frequency, Type & Infection Source in the 1st Post Transplant Year

Transplant Type	Infection Episodes per Patient	Bacteremia	CMV Disease * (%)	Fungal Infections (%)	Most Common Source
Lung	3.19	8-25	39	8.6	Pulmonary
Liver	1.86	10-23	29	4.7	Abdomen & Biliary tract
Heart	1.36	8-11	25	3.4	Pulmonary
Kidney	0.98	5-10	8	1.3	Urinary tract

*CMV, Cytomegalovirus; CMV disease rates in the absence of routine antiviral prophylaxis

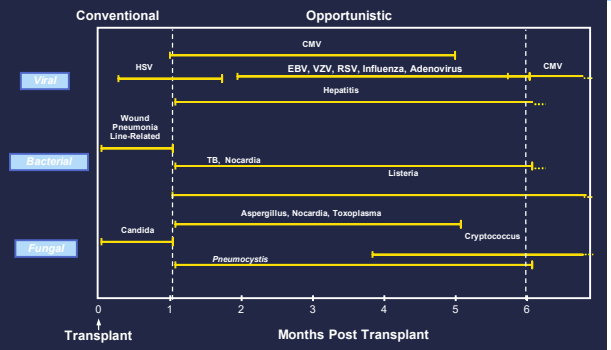
Table Modified from: Principles and Practices of Infectious Diseases, 8th Edition. Chapter 313: Infections in Solid-Organ Transplant Recipients by Nina Singh and Ajit Limaye. Editors: Bennett JE, Dolin R, and Blaser MJ. Elsevier Saunders, Philadelphia, PA, 2015.

Pappas P et al. CID 2010;50:1101-1111

7

Classic Timing of Infections Following Solid Organ Transplantation

Timing altered by:
- Enhanced immunosuppression
- Prophylaxis regimen
- Unique exposures



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"Early" Bacterial Infections Following SOT

Type & site of early bacterial infection varies based on organ transplanted, surgical approach/technique & transplant center

- Risk of peritoneal soilage/infection greater in liver transplantation with Roux-en-Y biliary drainage
- Recipient colonization with resistant organisms (e.g. MRSA, VRE, CRE) pre-transplant, confers risk of post-transplant infection
- Cluster with unusual pathogen - environmental problem? (e.g., *Legionella, M. abscessus* from hospital water distribution systems)

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"Late" Bacterial Infections Following SOT

80% of Late Bacterial Infections are Community Acquired

- *Streptococcus pneumoniae*
  - Incidence significantly > in SOT (146/100,000) vs general population (12/100,000)
  - Vaccination recommended
- *Listeria monocytogenes*
  - Bacteremia (Gram + Rods) / Diarrhea / Meningitis
  - Ampicillin treatment of choice
  - High relapse rate, treat for at least 3-6 wks

Kumar D et al., *Am J of Transplant* 2007;7:1209

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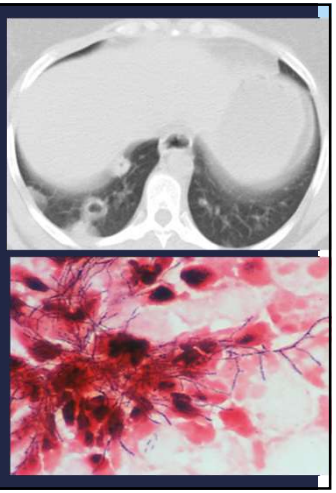
"Late" Bacterial Infections (Cont.)

- *Nocardia* species
  - 1%-6% of all SOT recipients
  - Presents most often as pulmonary nodules, CNS (15-20%), skin (15%), or bone (2-5%) lesions
  - Diagnosis: Culture and/or histopathology
    - Branching, filamentous Gram + Rods
    - Partially acid-fast by modified Kinyoun stain
    - *Nocardia* is *Neurotropic*; brain imaging critical
  - Treatment:
    - High dose TMP-SMX drug of choice
    - Otherwise, based on susceptibility data & site of infection
  - TMP-SMX dose used for PCP prophylaxis not protective



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CMV Disease After SOT Indirect and Direct Effects

INDIRECT Effects:

- Acute and Chronic Rejection
- Opportunistic Super-Infections (Gram negative bacteria & Molds)

DIRECT Effects:

- CMV Syndrome – most common presentation
  - CMV in blood + fever + malaise, leukopenia, atypical lymphocytosis, thrombocytopenia
- Tissue Invasive Disease
  - Evidence of CMV on biopsy + compatible signs/symptoms

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Risk of CMV Disease After SOT

CMV Serologic Status	Risk Category	Incidence of Disease (%)
D+/R-	High	50+
D+or D-/R+	Intermediate	10-15
D-/R-*	Low	0
ALA Therapy (R+)		
Induction	Intermediate	25-30
Rejection	High	65

D, Donor; R, Recipient; ALA, Antilymphocyte Antibody

*Should receive leukocyte depleted blood products

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CMV Disease After SOT
Prophylactic Approaches

UNIVERSAL

All SOT recipients receive therapy during highest risk periods

- Expensive
- May induce resistance
- Some pts exposed unnecessarily

PREEMPTIVE

Treatment based on asymptomatic viral replication in blood

- Optimal viral threshold for initiating therapy not well defined
- Requires serial weekly monitoring with detection assay

NOTE: Typically Valganciclovir or IV Ganciclovir used for prophylaxis
Letermovir now approved for use after Renal Transplant

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CMV Prophylaxis After SOT

Bottomline:

- D+/R- or ALA for rejection → Universal
  - First 3-6 months post-transplant
  - At least 1 month post-ALA for rejection
- R+ → Universal or Preemptive
  - First 3-6 months post-transplant

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CMV Disease After SOT

- Typically occurs 1-3 months post-transplant
  - Or after prophylaxis is stopped ("late onset")
- Disease of GI Tract and Eye may not have concurrent viremia
  - Diagnosis often requires biopsy/aspiration
- Viral load may continue to rise during first 2 weeks of Rx
  - Don't repeat PCR until Day 14 of treatment, then weekly until negative
- Treat for 2-3 weeks…
  - Resolution of symptoms AND clearance of CMV DNAemia
  - DO NOT STOP TIL VIREMIA CLEARs (high risk for relapse)

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CMV Disease After SOT
Ganciclovir Resistance

- **Suspect resistance if prolonged (> 6 weeks) (val)ganciclovir exposure AND:**
  - No reduction in viral load after 14 days of treatment
  - No clinical improvement after 14 days of treatment
- **Management of suspected ganciclovir resistance:**
  - Reduce immunosuppression
  - Switch to maribavir or foscarnet (± CMV hyperimmune globulin)

Lurain et al.JID 2002; Limaye et al Lancet 2000; Limaye et al JID 2002; Kotton et al Transplantation 2013.

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CMV Disease After SOT
Antiviral Resistance

Key mutations have been associated with resistance

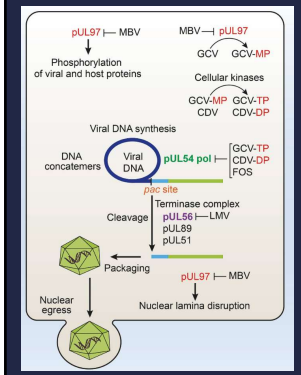
- •UL97 CMV Phosphotransferase gene mutations (most common)
  - Imply ganciclovir resistance

- •UL54 CMV DNA Polymerase gene mutations
  - May confer resistance to ganciclovir, foscarnet, & cidofovir

Lurain et al JID 2002; Limaye et al Lancet 2000; Limaye et al JID 2002;
Kotton et al. Transplantation 2018;102(6):900-931. Torre-Cisneros et al Transplantation Reviews 2016.

18

CMV Resistance: New Drug



Maribavir (MBV)

- Multi-modal CMV activity
  - Inhibits CMV DNA replication
  - Interferes with nuclear egress of viral capsid by inhibiting UL97 kinase
- UL97 kinase activates ganciclovir (GCV), thus MBV inhibits GCV activity
  - ⚠ MBV & GCV should not be used together
- MBV is active against many GCV resistant strains
  - Superior to SOC (Valgan/Gan, Foscarnet, or Cidofovir) in HSCT & SOT pts with refractory/resistant CMV infection
    - Cleared CMV viremia & resolved symptoms at 8 weeks
  - FDA approved Nov 2021 for "CMV (with or without genetic mutations that cause resistance) that does not respond to available antiviral treatment…"
  - ⚠ No activity against other herpes viruses (HSV/VZV)

Piret J, Boivin G. Antiviral Research 2019;163:91-105.
Avery RK, et al. Clin Infect Dis. 2021 Dec: Online ahead of print.

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Question #1

54-year-old male 60 days post-cardiac transplant was treated for rejection with steroids when fever and a non-tender anterior cervical mass appeared.

Biopsy showed nodal replacement by lymphocytes, many of which stained positively for Epstein-Barr virus as well as for the B cell marker, CD20.

His plasma EBV viral load was 10,000 copies /ml.

What is the most appropriate treatment for this condition?

A. Cidofovir
B. Ganciclovir
C. Acyclovir
D. Cyclophosphamide
E. Rituximab

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E. Rituximab *

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Epstein Barr Virus: Post Transplant Lymphoproliferative Disorder (PTLD)

- Virus establishes latency in B-lymphocytes which serve as lifelong reservoirs
- EBV transformed B-lymphocytes give rise to PTLD (a few cases may arise from T-lymphocytes)
- Risk factors:
  - 1° EBV infection
  - Donor seropositive, Recipient seronegative
  - Anti-lymphocytic antibody therapy (T-cell depletion)
  - Organ transplanted (Intestine > Lung > Heart > Liver > Kidney)

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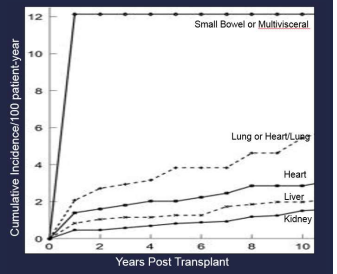
Epstein Barr Virus: Post Transplant Lymphoproliferative Disorder (PTLD)

- ~3% Cumulative 10-year incidence in SOT population
- Incidence varies based on organ transplanted
  - Small Bowel / Multivisceral – up to 32%
  - Lung / Heart / Liver - 3-12%
  - Kidney - 1-2%
- Biphasic pattern of disease after SOT:
  - First peak (20% cases) occurs 1st post-tx year
  - Second peak occurs 7-10 years post-tx



Olagne, J, et al. Am J Transplant. 2011 Jun;11(6):1260-9.

23

Epstein Barr Virus: Post Transplant Lymphoproliferative Disorder (PTLD)

Clinical manifestation - wide range
- Febrile mononucleosis-like illness with lymphadenopathy
- Solid tumors
  - Often involve transplanted graft
  - 50% are extranodal masses
  - 25% involve CNS

Definitive diagnosis requires tissue biopsy
- WHO Pathology Classification based is gold standard for diagnosis
- Molecular (PCR) tests available
  - WHO Standard for Assay Calibration available
  - Whole Blood vs Plasma controversial
  - Misses EBV-negative and some localized cases
  - Used as an aid for Diagnosis and Pre-emptive monitoring with stepwise reduction in immunosuppression to reduce PTLD rates

Petit B et al. Transplantation. 2002:73(2):265.
Peters AC et al. Transplantation. 2018; 102(9):1553.

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51 Infections in Solid Organ Transplant Recipients

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Epstein Barr Virus: Post Transplant Lymphoproliferative Disorder (PTLD)

Treatment:

- Antivirals not effective on latently infected lymphocytes (antivirals only work in lytic phase)
- Reduce Immunosuppression (Response ~ 45%)
- Rituximab: Anti-CD20 monoclonal antibody (Response ~ 55%)
- Cytotoxic Combination (CHOP, ACVBP) Chemotherapy
  - Reserved for non-responsive disease
  - High treatment associated mortality (13%-50%)
- Adoptive Immunotherapy (EBV cytotoxic T-cells)
  - Under study

Allen et al. Clin Transplant. 2019;33(9):e13652.

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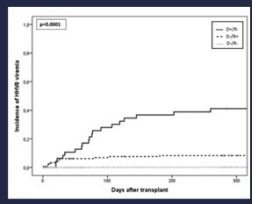
HHV-8 After Solid Organ Transplant

- Seroprevalence in U.S. considered low overall
- High seroprevalence among MSM in Southern United Status
  - 68% among MSM w/ HIV ; 37% among MSM
- Higher seroprevalence in Persons Who Inject Drugs
  - 36% among women who inject drugs
- U.S. OPTN DTAC 2018-2020 data:
  - 6 cases of HHV-8 transmission/KS from deceased organ donors
  - 6 donors -> 22 recipients -> 14 w/ post transplant HHV-8 infection
    - 6 developed KS; 4 died due to KS or associated complications
- Incidence of post-transplant KS 12.4 per 100,000 person years



Knights SM, et al. Open Forum Infect Dis. 2023 Mar 24;10(4):ofad160. Salyards M, et al. J Infect Dis. 2024 May 15;229(5):1387-1392. Cannon MJ, et al. N Engl J Med. 2001 Mar 1;344(9):637-43. Dollard, SC, et al. *American Journal of Transplantation*. 2021; 21(2). 681–688. Cahoon EK et al.. Int J Cancer. 2018 Dec 1;143(11):2741-2748. Mularoni A, et al. American Journal of Transplantation. 2025; 25(5):10070-1085.

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HHV-8 Oncovirus Presentations

- Kaposi Sarcoma
  - Skin, oral lesions
  - Visceral involvement
- Primary effusion lymphoma; other large cell lymphomas
  - Cytopathology alone may be insufficient for dx
  - Flow cytometry and special staining required
  - HHV-8 NAT from blood/fluid can be clue to dx
- Multicentric Castleman Disease (polyclonal B cell lymphoproliferative disorder)
- Kaposi Sarcoma Herpesvirus (KHSV) Inflammatory Cytokine Syndrome (KICS):
  - Systemic inflammatory syndrome, often severe with shock/ multiorgan failure
  - Most often occurs concurrently w/ KS
  - Poor prognosis

★ KICS could show up on the Boards!

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KICS: Working Definition

1. At least 2 **Clinical Manifestations** from at least 2 categories
   - **Symptoms**: Fever, Fatigue, Edema, Cachexia, Respiratory Symptoms, GI disturbance, Arthralgia/myalgia, Altered mental state, Neuropathy
   - **Laboratory**: Anemia, Thrombocytopenia, Hypoalbuminemia, Hyponatremia
   - **Radiographic**: Lymphadenopathy, Splenomegaly, Hepatomegaly, Body Cavity, Effusions
2. **Systemic Inflammation**: CRP (≥ 3g/dL)
3. **Elevated KSHV plasma viral load**: HHV-8 ≥ 1000 copies/mL
4. No **pathologic evidence of MCD or PEL**
   (Requires biopsy of any lymphadenopathy if present)

Polizzotto, M. N., et al. Clinical Features and Outcomes of Patients With Symptomatic Kaposi Sarcoma Herpesvirus (KSHV)-associated Inflammation: Prospective Characterization of KSHV Inflammatory Cytokine Syndrome (KICS). *Clinical Infectious Diseases. 2016;*62(6):730–738.

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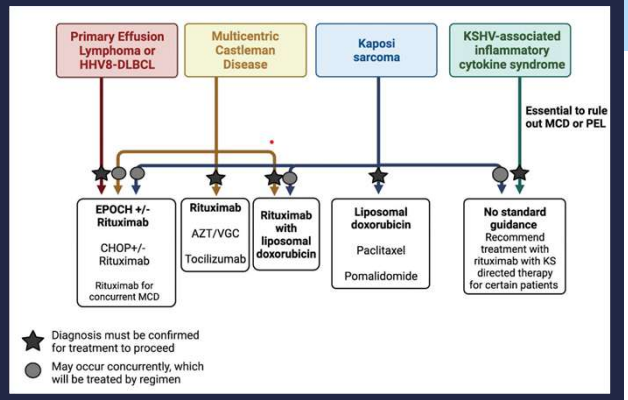
Management of HHV8-Associated Diseases

- Consider KICS in SOT presenting with sepsis/multi-organ failure
- May be donor-derived or primary infection
- Management differs based on disease presentation



Patel R, Lurain K, Yarchoan R, Ramaswami R. Clinical management of Kaposi sarcoma herpesvirus-associated diseases: an update on disease manifestations and treatment strategies. Expert Rev Anti Infect Ther. 2023 Jul-Dec;21(9):929-941.

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Question #2

- 52-year-old female S/P cadaveric renal transplant receiving tacrolimus, prednisone and mycophenolate
- Week 30 post transplant serum creatinine rose from 1.5 to 2.3 mg/dl
- Tacrolimus levels were in therapeutic range
- Urinalysis revealed one plus protein and no cells or casts

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Question #2

Which would be most helpful in understanding if BK virus was causing her renal failure?

A. Presence of decoy cells in urine cytology
B. Urine BK viral load
C. Urine culture for BK virus
D. Plasma BK viral load
E. Demonstration of BK inclusions in renal tubular epithelium on renal biopsy

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Question #2

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Polyomavirus
BK Virus Nephropathy

- Ubiquitous, DNA virus
  - 1° infxn – URI during early childhood
  - 80% worldwide population sero+
  - Renal & uroepithelial cells, site of latency
- Cause of nephropathy post renal transplant
  - Up to 15% of renal recipients effected
  - Time to onset 28-40 weeks (majority within 1st yr post tx)
  - Manifests as unexplained renal dysfunction (as does rejection)

Hayashi RY et al. UNOS Database: Abstract 76, 2006 World Transplant Congress; Ramos et al. *J Am Soc Nephrol* 2002;13:2145; Hirsch et al. Transplantation 2005;79:1277-1286

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BK Virus Nephropathy
Diagnosis

- Replication in urine precedes replication in blood precedes nephropathy
- Renal Bx - "Gold Standard" for diagnosis
- Blood PCR
  - Sensitive (100%) but less specific (88%)
  - Cannot rule out rejection
  - Useful as indicator for biopsy
- Urine Cytology, Electron microscopy, & PCR
  - Detection in urine: Low PPV but High NPV

Hirsch et al, Transplantation 2005;79:1277-1286; Nickeleit et al, NEJM 2000;342 (18):1309-1315; Ramos et al. *J Am Soc Nephrol* 2002;13:2145

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BK Virus Nephropathy Treatment

- Reduce immunosuppression
- Case series with variable success using:
  - Low-dose cidofovir
  - Leflunomide
- New drugs & randomized controlled trials needed
- Preemptive monitoring key to prevention

Hirsch et al. Transplantation 2005;79:1277-1286; Farasati et al. Transplantation 2004;79:116; Vats et al. Transplantation 2003;75:105; Kabambi et al. Am J Transplant 2003;3:186; Williams et al N Engl J Med 2005;352:1157-58.

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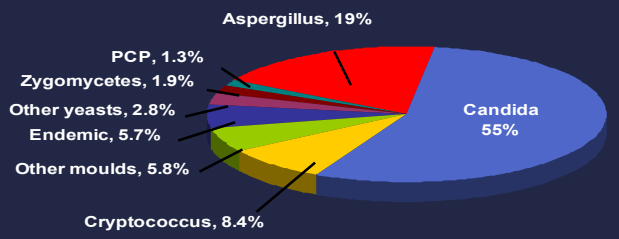
Invasive Fungal Infections in Solid Organ Transplant Recipients



Type of fungal infection varies depending on organ transplanted

Pappas P et al. CID. 2010:50:1101-1111.

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Invasive Fungal Infections According to Organ Transplanted

N=16,808

	Kidney	Heart	Pancreas	Liver	Lung	Small Bowel
12 Month IFI Incidence (%)	1.3	3.4	4.0	4.7	8.6	11.6
IFI Type (%)					70% Molds	
Candidiasis	49	49	76	68	23	85
Aspergillosis	14	23	5	11	44	0
Other molds	7	10	3	6	26	0
Cryptococcosis	15	10	5	6	2	5
Endemic	10	3	6	5	1	0
Pneumocystosis	1	3	1	0	2	0
Other	4	2	4	4	2	10

Pappas P, Alexander B, Andes D, et al. CID 2010:50:1101-1111

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Invasive Fungal Infections *Risk Factors After SOT*

Each solid organ group will have unique risks for IFIs

Strongly influenced by medical & surgical factors including technical complexity

Liver
- Re-transplantation
- Pre-tx fulminant hepatic or renal failure
- Heavy *Candida* colonization peri-tx
- Large volume intra-operative transfusions
- Bleeding complications requiring re-operation
- Choledochojejunostomy

CANDIDA

Lung
- Vulnerable anastomotic site
- Continuous environmental exposure
- *Aspergillus* colonization of airways
- CMV pneumonitis
- Acute rejection
- Obliterative bronchiolitis

ASPERGILLUS

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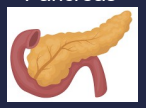
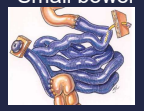
Antifungal Prophylaxis for Solid Organ Transplant Recipients

Lung	Liver	Pancreas	Small bowel
			
• All recipients • *Candida* & Molds	• High-risk recipients • *Candida*	• High-risk recipients • *Candida*	• All recipients • *Candida*
Per ISHLT Guidelines	Per AST Guidelines		

Husain S, et al. *J Heart Lung Transpl.* 2016;35:261-82.
Aslam S, Rotstein C. AST ID COP. *Am J Transpl.* 2019;33:e13623.
Husain S, Camargo J. AST ID COP. *Am J Transpl.* 2019;33:213544

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Tuberculosis

- 34-74 fold higher risk of active disease in SOT recipients than general population
- Incidence 1% - 6% (up to 15% in endemic areas)
- Median onset 9 months post-tx (0.5-144 months)
- 33% of infections are disseminated at diagnosis
- Treatment
  - Rifampin-based regimens associated with graft loss/rejection in 25%
- Mortality ~30%
- Treat latent TB prior to transplant when possible

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Question #3

- 35-year-old female s/p heart transplant in France 90 days prior presented with fever, dyspnea and a diffuse pneumonia on chest CT.
- She was receiving prednisone, tacrolimus & mycophenolate.
- Both recipient & donor were CMV negative; she was not on CMV prophylaxis.
- She was on inhaled pentamidine for PCP prophylaxis.

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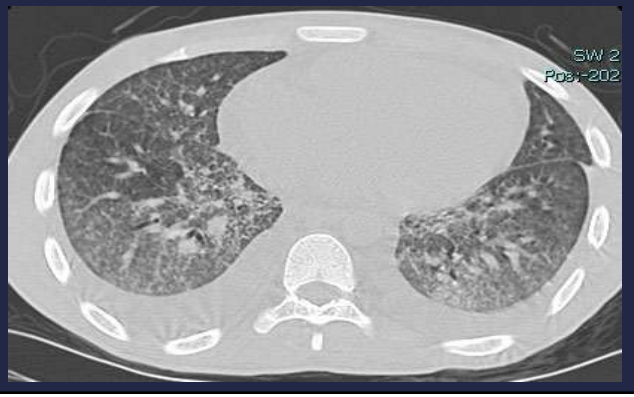
Question #3: Chest CT



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Question #3

Trimethoprim-sulfamethoxazole was started empirically, and she began improving.

Bronchoalveolar lavage (BAL) was negative for:

- Pneumocystis by direct fluorescent antibody stain & PCR,
- Fungi by calcifour white / potassium hydroxide stain,
- Mycobacteria by AFB smear,
- Bacteria by gram stain, and
- Respiratory viruses by multiplex PCR

Routine bacterial BAL and blood cultures were negative.

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Question #3

Assuming trimethoprim-sulfamethoxazole was causing her improvement, which additional test on the BAL might have explained her improvement?

A. PCR for CMV
B. PCR for toxoplasmosis
C. PCR for tuberculosis
D. Galactomannan
E. Cold enrichment culture for Listeria

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C. PCR for tuberculosis
D. Galactomannan
E. Cold enrichment culture for Listeria

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Toxoplasmosis

- After SOT, acute toxoplasmosis can develop from reactivation, acquisition via blood transfusion or ingestion of contaminated food or water, or from the donated organ
- Donor seropositive/Recipient seronegative at high risk
- HEART > LIVER > KIDNEY TRANSPLANT
- Presents with myocarditis, pneumonitis & meningitis
- DIAGNOSIS:
  - PCR
  - Giemsa smear of BAL
  - Brain aspirate for tachyzoites
  - Immunoperoxidase stain of endocardial biopsy or other tissue
- TREATMENT: sulfadiazine-pyrimethamine-leucovorin

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Question #4

Liver transplant recipient on Bactrim & valganciclovir prophylaxis

presented 21 days post transplant with confusion, tremors, lethargy, anorexia

- Rapid progressive neurologic decline → agitation & delirium →intubation
- Brain MRI: non-revealing
- Blood & urine cultures: negative
- CSF: lymphocytic pleocytosis (25 WBCs/mm^3) & elevated protein
  - Gram stain, bacterial, fungal cultures negative for organisms
- Empiric intravenous ganciclovir, vancomycin, ceftriaxone & ampicillin
- Day 6 Repeat MRI: diffuse encephalitis
- Expired 13 days after neurologic symptom onset
- Donor was previously healthy presenting with subarachnoid hemorrhage
  - Toxicology screen: + cocaine & marijuana
  - Brain CT: expanding subarachnoid hemorrhage
  - Recently on camping trip

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Question #4

What is this presentation is most consistent with?

A. CMV encephalitis
B. HHV6 encephalitis
C. VZV encephalitis
D. Rabies encephalitis
E. Cryptococcal meningitis

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Question #4

What is this presentation is most consistent with?

A. CMV encephalitis
B. HHV6 encephalitis
C. VZV encephalitis
D. **Rabies encephalitis ***
E. Cryptococcal meningitis

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"Expected" Donor Derived Infections

- **Expected = known before tx or for which there are recognized standard prevention guidelines**
  - Cytomegalovirus (CMV)
  - Epstein–Barr virus (EBV)
  - Toxoplasmosis

*United Network for Organ Sharing / Organ Procurement and Transplant Network

Ison M et al. Am J Transplant. 2009;9:1929-1935.

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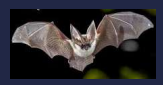
"Unexpected" Donor Derived Infections

Viruses, Viruses, & Parasites, Oh My…

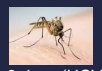
- Lymphocytic choriomeningitis virus (LCMV)
  - Hamsters and rodents
  - 4 outbreaks (3 USA, 1 Australia); 9 deaths

- Rabies virus
  - Unreported bat bite in donor
  - 3 outbreaks (2 USA, 1 Germany); 8 deaths



- Chagas' Disease (Trypanosoma cruzi)
  - Reduviid bug (Latin America)
  - Screening tests lack sensitivity
  - Multiple transmissions reported

- HIV, Hep C, Hep B, West Nile Virus (WNV)
  - Remember the "Window" prior to development of antibodies
  - Nucleic Acid Tests decrease "window" to ~5-10 days (HIV), 6-9 days (HCV)



Fisher SA et al. N Engl J Med. 2006;354:2235-2249. MMWR Morb Mortal Wkly Rep. 2008;57:799-801. Kusne S et al.Transpl. 2005;11:1295-1297. Maier T et al. CID 2010;50:1112-1119 Mattner F et al Infection. 2007;35(4):219-24. Grossi PA, et al. Am J Transpl. 2009;9:S19-S26.

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Typical Presentations Of Unexpected Donor Derived Infections

- Most present in the first 3 months post transplant
- Look for epidemiologic clues for potential donor exposure in the stem (e.g. possible bat bites, new pet hamsters, tap water nasal irrigations, recent travel to a region endemic for certain pathogens)

PATHOGEN	PRESENTATION
LYMPHOCYTIC CHORIOMENINGITIS VIRUS	ENCEPHALITIS
RABIES	ENCEPHALITIS
TOXOPLASMOSIS	DIFFUSE PNEUMONIA MYOCARDITIS RETINITIS ENCEPHALITIS
WEST NILE VIRUS	MENINGITIS ENCEPHALITIS POLIOMYELITIS-LIKE FLACCID PARALYSIS
CHAGAS' DISEASE	FEVER MYOCARDITIS
ACANTHAMOEBA	SKIN LESION ENCEPHALITIS
BALAMUTHIA MANDRILLARIS	ENCEPHALITIS
VISCERAL LEISHMANIASIS	PANCYTOPENIA HEPATOSPLENOMEGALY
MALARIA	FEVER

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51 Infections in Solid Organ Transplant Recipients

Speaker: Barbara Alexander, MD, MHS, FIDSA

Vaccination Recommendations for SOT

Update vaccinations pre-SOT:

- COVID
- Hepatitis A, Hepatitis B, Flu, TDaP, Pneumococcal
- Live Varicella, MMR vaccines (≥4 wks pre-tx)
- HIB, Meningococcal if planned splenectomy (e.g. Multivisceral Tx)

Recommended post-SOT:

(Delay 1 month post-tx; 3–6 months to maximize response)

- COVID
- Pneumococcal
- Tetanus-diphtheria toxoid
- Inactivated Influenza

Live vaccines are NOT recommended after SOT including:

- Measles Mumps Rubella
- Varicella
- Inhaled influenza
- Oral polio
- Yellow fever
- BCG
- Small pox
- Salmonella typhi (oral)

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Solid Organ Transplant *Patient Travel*

- **REGIONAL EXPOSURES**
  - **COCCIDIOIDOMYCOSIS: Southwest U.S.**
  - **HISTOPLASMOSIS: Central/Mid-Atlantic U.S.**
  - **VISCERAL LEISHMANIASIS: Spain, Mediterranean Basin**
  - **MALARIA: Tropics**
  - **BABESIA MICROTI: Northeast & Upper Midwest U.S.**
- **AND ALL THE "NORMAL" RISKS TO TRAVELERS**
  - **DIARRHEA**
  - **STIs**
  - **MDR-TB**
  - **BLOOD SUPPLY (need for TRANSFUSIONS), etc…**
- **AVOID LIVE VACCINES: Yellow Fever, Oral typhoid, etc.**
- **DRUG INTERACTIONS →Transplant meds + travel related prophylactic agents**

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Key Drug Toxicities / Syndromes

- Calcineurin inhibitors and TTP and PRES (RPLS)
- Sirolimus-induced pneumonitis
  - Progressive interstitial pneumonitis (22% in one study)
  - Risk factors: late switch to sirolimus & impaired renal function
  - Symptoms: dyspnea, dry cough, fever, and fatigue
    - Radiographic & bronchoalveolar lavage consistent with bronchiolitis obliterans organizing pneumonia & lymphocytic alveolitis
  - Recovery with sirolimus withdrawal

Euvrard S et al. N Engl J Med. 2012;367(4):329. Champion L et al. Ann Intern Med 2006;144:505. Weiner SM et al. Nephrol Dial Transplant. 2007;22(12):3631.

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Other Pearls for Boards…

If you're thinking PCP but its not → think TOXO

Patient presenting atypically during first month post transplant → think donor transmitted infection

- Rabies, WNV, Coccidioides, Chagas, LCMV (look for epidemiologic clues in stem)

Remember drug interactions and syndromes

- Addition of mold active azole leading to acute kidney injury from elevated CNI
- TTP and PRES induced by calcineurin inhibitors
- Sirolimus-induced pneumonitis

Remember *Strongyloides* hyperinfection syndrome

TB- Don't miss a case!

BKV, CMV and EBV/PTLD – know how to diagnose and manage

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