Infectious Diseases After Transplant
Laura Ebel, MSN, RN, CCTC
Objectives

- Identify common pathogens that can cause infections after transplant and what time frame they may occur.
- Be aware of common infections depending on certain risk factors and organ transplanted.
- Recognize risk factors for developing infections after transplant.
- Understand appropriate pharmacological treatment of certain fungi, bacteria, and viruses common in transplant recipients.
- Understand side effects of pharmacological treatment of infections and interactions with immunosuppressive medications.
- Identify ways of preventing infection in the transplant patient.
Infections After Transplant

Infections are a leading cause of morbidity and mortality post transplant

- UTI's are responsible for 45-47% of complications of renal transplant
- 70% of renal transplant recipients have 1 infection by 3 years
- Infections are the most common cause of death in liver transplant recipients in the first year.
- Infections occur in 54-67% of liver transplant recipients
- 9.6% (30 days) and 35.6% (1 year) deaths from infection in lung transplant recipients
- 13% (30 days) and 30.8% (1 year) deaths from infection in heart transplant recipients.

Clauss, Heather E, et al; Clinical Microbiology Newsletter 35:7, 2013
International Society of Heart & Lung Transplantation
Infections After Transplant

- Organ Transplanted
- Intensity of Immunosuppression
- **Time After Transplant**
- Recipient Factors
- Donor Factors
- Rejection
- Surgical Complications
Infections and Risk Factors

- Type of organ
- Degree of immunosuppression
- Additional anti-rejection therapy
- Technical/surgical complications
- Concurrent infections
- Donor pathogens
- Rejection
- Older donor age
- Marginal graft
- Obesity
- Diabetes
- Prolonged warm ischemic time
Infections After Transplant

Good Graft Function – Decreased Risk of Infection

**Improvements**
- Better Surgical Technique
- Improved Immunosuppressive Therapy
- Improved Diagnostic Tools
- HLA Matching
- Prophylaxis

**Challenges**
- Antibiotic Resistance
- New Pathogens
- Sicker Recipients
- Marginal Donors
- Allograft Contamination
Donor Derived Infections

- Most are expected
  - CMV
  - HBV
  - EBV
  - HIV
- Bacterial Infections of respiratory tract, urinary tract or organ being transplanted
- Monitoring and preemptive therapy
Donor Derived Infections and Detection

- HIV serology
- Hepatitis serology
- History/Physical
- CMV IgG
- EBV Ab
- VZV Ab
- Cultures-urine, aspirate from trachea
Public Health Service and Increased Risk Donors

- Developed to reduce risk of HIV, HBV, and HCV transmission.
- Based on 12 criteria to assess donor risk for HIV, HBV, HCV infection.
- Addresses sexual contact – vaginal, anal, or oral.
- IV drug use for reasons other than medical.
- Individuals who have been in jail or prison in last 12 months.
- Newly diagnosed STD.
- Hemodialysis.
- Testing of recipients pre- and post transplant.
Pathogens Transmitted with Transplantation

<table>
<thead>
<tr>
<th>Bacteria</th>
<th>Fungi</th>
<th>Virus</th>
<th>Parasites</th>
<th>Mycobacteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staph aureus</td>
<td>Aspergillus</td>
<td>Cytomegalovirus</td>
<td>Toxoplasma</td>
<td>Mycobacterium tuberculosis</td>
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<tr>
<td>Klebsiella</td>
<td>Candida</td>
<td>Epstein Barr</td>
<td>Plasmodium</td>
<td>Non-tuberculosis mycobacterium</td>
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<td>Pseudomonas</td>
<td>Cryptococcus</td>
<td>Herpes Simplex</td>
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<td>Escherichia coli</td>
<td>Scedosporium</td>
<td>Varicella zoster</td>
<td>Trypanosoma cruzi</td>
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<td>Salmonella</td>
<td>Zygomycetes</td>
<td>Human Herpes Virus – 6</td>
<td>Strongyloides stercoalis</td>
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<tr>
<td>Enterobacter</td>
<td>Coccidioides immitis</td>
<td>Human Herpes Virus – 7</td>
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<tr>
<td>Acinetobacter</td>
<td>Histoplasma</td>
<td>Human Herpes Virus – 8</td>
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<td></td>
</tr>
<tr>
<td>Legionella</td>
<td>Prototheca</td>
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<tr>
<td>Nocardia</td>
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<tr>
<td>Listeria</td>
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<tr>
<td>Bacteroides fragilis</td>
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<td>Yersinia enterocolitica</td>
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<tr>
<td>Treponema pallidum</td>
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</tbody>
</table>

Fischer. American Journal of Transplantation. 6 March 2013
Timeline Infection After Transplant
(Time most infections occur)

- **0 – 30 days:** **surgical**, candida, HSV, common bacteria, pneumonia, urinary tract, catheter sepsis, C. diff, donor derived, ischemia, reperfusion injury
  - Renal/Pancreas – peri-graft hematoma
  - Liver – portal vein thrombosis, hepatic vein occlusion, hepatic artery thrombosis, biliary stricture/leaks
  - Heart – mediastinitis, mycotic aneurysm, infection aortic suture line
  - Lung – bronchial anastomotic infection, reactivation of previous infection
- **1 – 6 months:** CMV, pneumocystis, norcardia, aspergillus, opportunistic pathogens, mycobacterium, viral hepatitis, candida, EBV, BK
- **> 6 months:** community acquired infections (influenza, pneumococcal), endemic fungi, urinary tract

Changing timeline of infection after organ transplantation

Donor Derived Infection

- Nosocomial, technical (door or recipient)
- Activation of latent infection (relapsed, residual, opportunistic)
- Community Acquired

Transplantation

Recipient-Derived Infection

Common Infections in Solid-Organ Transplant Recipients

<1 Month
- Infection with antimicrobial-resistant species:
  - MRSA
  - VRE
  - Candida species (non-albicans)
- Aspiration
- Catheter infection
- Wound infection
- Anastomotic leaks and ischemia
- *Clostridium difficile* colitis
- Donor-derived infection (uncommon)
  - HSV, LCMV, rhabdovirus (rabies), West Nile virus, HIV, *Trypanosoma cruzi*
- Recipient-derived infection (colonization):
  - Aspergillus, pseudomonas

Infections

Fungal/Yeast
- *candida, aspergillus, cryptococcus*

Viral
- Coronavirus, CMV, BK virus, metapneumovirus, influenza, RSV, parainfluenza, ehrlichia

Bacterial
- Pseudomonas, MRSA, C. diff, VRE, mycobacteria, nocardia, staph

Parasites
- Giardia, cryptosporidium, toxoplasma
Time After Transplant

- 1<sup>st</sup> month: “surgical complications”
  - Antibiotic resistant organisms
  - Catheter sepsis
  - HSV
  - Bacterial
  - Candida
  - Pneumonia
  - C. diff
Common Infections After Transplant

<table>
<thead>
<tr>
<th>Kidney</th>
<th>Liver</th>
<th>Heart</th>
<th>Lung</th>
</tr>
</thead>
<tbody>
<tr>
<td>• UTI</td>
<td>• Bacterial/ fungal infection of abdomen and GI Tract</td>
<td>• Community and nosocomial pulmonary infections</td>
<td>• Colonization of native lung</td>
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<tr>
<td>• Candida</td>
<td>• Candida</td>
<td>• Mediastinitis</td>
<td>• Mediastinitis</td>
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<tr>
<td>• Gram negative</td>
<td>• CMV</td>
<td>• Fungal infections</td>
<td>• Fungal infections</td>
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<tr>
<td>• BK virus</td>
<td>• Hepatitis B &amp; C</td>
<td>• Toxoplasmosis</td>
<td>• Bacterial</td>
</tr>
<tr>
<td>• CMV</td>
<td></td>
<td></td>
<td>• CMV</td>
</tr>
<tr>
<td>• Herpes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Surgical site</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>
Nosocomial Infections

- Pneumonia (most common)
  - Streptococcus, MRSA, aspergillus, pseudomonas, klebsiella, enterobacter, acinetobacter
- UTI
- Bacteremia
- Surgical site
- Leading cause of morbidity/mortality
- Occurs in first month
  - Donor derived
  - Recipient derived
Risk Factors for Nosocomial Infections

- Pulmonary Complications
- Surgery
- Hospitalization
- Other Recipient Factors
- Rejection
- Donor Factors
Nosocomial Infections

- Kidney – UTI
- Lung/Heart – lung infections
- Liver – highest rate of surgical site infections

Dorschner, P. Transplant Infectious Disease 2014:16:171-187
Post Operative Infections

- Thrombosis of hepatic artery post liver transplant
- Vesicouretal reflux post kidney transplant
- Mediastinal bleeding post lung or heart transplant
- Prolonged use of indwelling catheters
- Ventilator
- Nosocomial infections
  - RSV
  - Rotavirus
  - VRE
**Clostridium Difficile Infection**

“Higher incidence post transplant than general population”

**Signs/Symptoms:**
- Diarrhea
- Abdominal pain
- Fever
- Elevated WBC

**Risk:**
- Prior antibiotic use (1st/2nd generation cephalosporin)
- Steroids
- Hypogammaglobulinemia
- Ganciclovir prophylaxis
- Use of PPI/H2 blocker

**Onset:** 18 – 31.5 days

**Treatment:**
- Metronidazole 500 mg every 8 hours (mild – mod)
- Vancomycin (oral) 125 mg every 6 hours (severe)

Dorschner, P. Transplant Infectious Disease 2014:16:171-187
Clostridium Difficile Infection Rates

- Kidney: 2.2%
- Heart: 2.7%
- Lung: 3.7%
- Liver: 3.8%

Dorschner, P. Transplant Infectious Disease 2014:16:171-187
Changing timeline of infection after organ transplantation

Donor Derived Infection

- Nosocomial, technical (door or recipient)
- Activation of latent infection (relapsed, residual, opportunistic)
- Community Acquired

Transplantation

Recipient-Derived Infection

Dynamic assessment of risk of infection

Common Infections in Solid-Organ Transplant Recipients

1-6 Months
With PCP and antiviral (MCV, HBV) prophylaxis:
- Polyomavirus BK infection, nephropathy
- C. difficile colitis
- HCV infection
- Adenovirus infection, influenza
- Cryptococcus neoformans infection
- Mycobacterium tuberculosis infection
- Anastomotic complications

Without prophylaxis:
- Pneumocystis
- Infection with herpes viruses (HSV, VZV, CMV, EBV)
- HBV Infection
- Infection with listeria, nocardia, toxoplasma, strongyloides, leishmania, T. cruzi

>6 Months
Community-acquired pneumonia, urinary tract infection
Infection with aspergillus, atypical molds, mucor species
Infection with nocardia, rhodococcus species
Late viral infections:
- CMV infection (colitis and retinitis)
- HSV encephalitis
- Community-acquired (SARS, West Nile virus infection)
- JC polyomavirus infection (PML)
- Skin cancer, lymphoma (PTLD)
Time After Transplant

- **2nd – 6th month:**
  - CMV
  - Pneumocystis
  - Aspirgillus
  - Nocardia
  - Mycobacterium
  - Histoplasma
  - Candida
  - HBV
  - HCV
Time After Transplant

- **Beyond 6th months**: Same infections as general community
  - Influenza
  - UTI
  - Pneumococcal pneumonia
  - Herpes zoster
  - Mucor streptococcus
  - Haemophilus influenza
  - BK virus

Syndman. Clinical Infectious Diseases, 2001; 33 (Suppl 1)
Infections Beyond 6 months

- Transplant outcome
- Chronic/progressive infections
- Recurrent or chronic rejection
- Community Acquired
Viruses After Transplant

Primary vs Reactivation

Cytomegalovirus
- Fever, aches
- Bone marrow suppression – decreased WBC
- Pneumonia
- Hepatitis
- Retinitis
- CMV PCR

Treatment
- Ganciclovir, valganciclovir, cytogam
Viruses After Transplant

Primary vs Reactivation

BK Virus - polyoma
- Colonizes renourinary tract
- Seroprevalence 90%
- Effects graft function / loss
- Risks include recipient older age, male gender, higher immunosuppressive levels

Treatment
- Reduction in immunosuppression, IVIG, fluoroquinolones, cidofovir, leflunamide
- Screen every 3 months x 2 years with urine and blood

Hirsch. American Journal of Transplantation. 6March2013
Viruses

Hepatitis C (recurrence 30%)
- Most common indicator for liver transplant (>50%)
- Higher rate of decompensation after transplant
- Liver biopsy is gold standard for diagnosing
- HCV viral loads monitored
- Lack of suitable agents for treatment

Treatment
- interferon, ribavirin
- bocepravir, telaprevir
- daclatasvir, sofosbuvir, simeprevir

RNA Respiratory Viruses

- Influenza
- RSV
- Parainfluenza
- Rhinovirus
- Metapneumovirus
- Coronavirus
## Treatment

<table>
<thead>
<tr>
<th>Influenza</th>
<th>RSV</th>
<th>Parainfluenza</th>
<th>Metapneumovirus (severe cases only)</th>
<th>Rhinovirus (common cold)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Oseltamivir (Tamiflu)</td>
<td>• Ribavirin</td>
<td>• Ribavirin</td>
<td>• Ribavirin</td>
<td>• No treatment</td>
</tr>
<tr>
<td>• Inhaled zanamivir (Relenza)</td>
<td>• IGIV</td>
<td></td>
<td>• Immunoglobulin</td>
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<tr>
<td></td>
<td>• RSVIG</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Palivizumab</td>
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</tbody>
</table>

Manuel. American Journal of Transplantation. 6 March 2013
# Anti-Viral Drug Interactions

<table>
<thead>
<tr>
<th>Antiviral</th>
<th>Immunosuppressant</th>
<th>Severity</th>
<th>Interaction</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acyclovir</td>
<td>MMF</td>
<td>+/-</td>
<td>↑ ACV, ↓ MPA</td>
<td>None</td>
</tr>
<tr>
<td>Valacyclovir</td>
<td>MMF</td>
<td>+/-</td>
<td>↓ MPA</td>
<td>None</td>
</tr>
<tr>
<td>Ganciclovir</td>
<td>MMF, AZA</td>
<td>+/-</td>
<td>Neutropenia</td>
<td>Monitor WBC</td>
</tr>
<tr>
<td>Valganciclovir</td>
<td>MMF, AZA</td>
<td>++</td>
<td>Neutropenia</td>
<td>Monitor WBC</td>
</tr>
<tr>
<td>Foscarnet</td>
<td>CSA / TAC</td>
<td>+++</td>
<td>Nephrotoxicity ↓ Ca, ↓ Mg</td>
<td>Monitor renal, Ca, Mg, CNI levels</td>
</tr>
<tr>
<td>Cidofovir</td>
<td>CSA, TAC</td>
<td>+++</td>
<td>Nephrotoxicity</td>
<td>Monitor renal</td>
</tr>
<tr>
<td>Boceprevir</td>
<td>CSA, TAC, SRL, EVR</td>
<td>+++</td>
<td>↑ levels</td>
<td>↓ dose Imm</td>
</tr>
<tr>
<td>Telaprevir</td>
<td>CSA, TAC, SRL, EVR, Prednisone</td>
<td>+++</td>
<td>↑ levels</td>
<td>↓ dose Imm</td>
</tr>
<tr>
<td>Leflunomide</td>
<td>MMF, AZA, SLR, EVR</td>
<td>+++</td>
<td>Myelosuppression</td>
<td>HOLD MMF, AZA Monitor WBC, HCT, PLT</td>
</tr>
<tr>
<td>Oseltamivir</td>
<td>CSA, TAC, MMF SRL</td>
<td>+/-</td>
<td>13% ↑ TAC None</td>
<td>Monitor Imm level None</td>
</tr>
</tbody>
</table>

American Journal of Transplantation 2013; 13: 318-326
RNA Respiratory Viruses

**Symptoms**
- Seasonal
- Signs/symptoms mild congestion, rhinorrhea, tracheobronchitis, broncholitis, pneumonia
- Viral shedding prolonged in transplant patient
- Risk factor for rejection
- Diagnose by viral culture – NVS or BAL if clinical evidence of lower tract involvement
Fungal Infections

- Occur 1 – 6 months post transplant
- Aspirgillus common pathogen
  - Fumigatus
  - Flavus
  - Niger
- Candida – most common
  - Albicans
  - Tropicalis

Rubin, R. Clinical Syndromes and Organ Systems
Fungal Infections and Risk Factors

Risks:
- Neutropenia
- Malnutrition
- Viral infection (CMV)
- High level of immunosuppression
- Donor derived
- Sinus disease
- Invasive
- Diabetes
- Surgical anastomotic issues
- > 6 months post transplant with poor outcome
- Environmental
  - Endemic
  - Hospital
  - Occupational
- Previous colonization
- Use of broad spectrum antibiotics

Rubin, R. Clinical Syndromes and Organ Systems
Aspergillosis

Risk factors – Invasive 15%

Liver
- Transplant for fulminant hepatic failure
- Reoperation

Lung
- Single lung
- Airway ischemia
- Rejection – augmented immunosuppression
- Low IgG
- CMV

Heart
- Reoperation
- CMV
- Post transplant hemodialysis

Kidney
- Graft failure
- High and prolonged steroid use

Treatment – ampho, voriconazole* Singh. American Journal of Transplantation. 30 May 2013
Rare Fungus

Zygomycete
Fusariom
Scedosporium
Trichosporan
Malessezia
Rhodotorula

- Liver and lung at greatest risk
- Rare
- From direct contact or inhalation
- Found in soil, vegetation, water, sewage and air
- Most start in respiratory tract or skin
- May be contributed to use of azoles and other antifungals for prophylaxis
- Recipient may be colonized
- Treatment is dependent on organism and ranges from Ampho-B to azole
- Diagnose by bronchoalveolar lavage, biopsy, culture

Candida Infections

- Most invasive in all transplant
- Risk with use of broad spectrum antibiotics
- Risk with catheters
- Risk with prolonged neutropenia
- Risk factor with diabetes
- Most susceptible to “azole” treatment
# Treatment of Candida

<table>
<thead>
<tr>
<th>Candida</th>
<th>Fluconazole</th>
<th>Itraconazole</th>
<th>Voriconazole</th>
<th>Posaconazole</th>
<th>AmB</th>
<th>Echinocandins</th>
</tr>
</thead>
<tbody>
<tr>
<td>C. albicans</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
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<td>C. tropicalis</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
</tr>
<tr>
<td>C. parapsilosis</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S to R</td>
</tr>
<tr>
<td>C. glabrata</td>
<td>S-DD to R</td>
<td>S-DD to R</td>
<td>S-DD to R</td>
<td>S-DD to R</td>
<td>S to I</td>
<td>S</td>
</tr>
<tr>
<td>C. krusei</td>
<td>R</td>
<td>S-DD to R</td>
<td>S</td>
<td>S</td>
<td>S to I</td>
<td>S</td>
</tr>
<tr>
<td>C. lusitaniae</td>
<td>S</td>
<td>R</td>
<td>S</td>
<td>S</td>
<td>S to R</td>
<td>S</td>
</tr>
</tbody>
</table>

*S = sensitive  
R = resistant  
I = intermediate  
S-DD = susceptible dose dependent*
Endemic Infections

- Coccidioidomycosis
- Blastomycosis
- Histoplasmosis
Endemic Infections - Fungal

Histoplasmosis
- Ohio and Mississippi River Valley
- Febrile illness – multi organ failure
- Excavated soil, avian or bat droppings, caves, construction, agricultural areas
- Primary or reactivation
- Febrile, hepatosplenomegaly, pneumonia, pancytopenia, weight loss, hepatic enzyme elevations, increased LDH
- 1-2 years after transplant

Treatment
- Amphotericin, intraconazole – 12 months

Figure 1. Geographic distribution of histoplasmosis in persons ≥65 years of age, United States, 1999–2008. Values are no. cases/100,000 person-years.

Main Article

1This research was presented in part at the 74th American College of Rheumatology Annual Meeting, November 7–11, 2010, Atlanta, Georgia, USA.

The opinions expressed by authors contributing to this journal do not necessarily reflect the opinions of the U.S. Department of Health and Human Services, the Public Health Service, the Centers for Disease Control and Prevention, or the authors’ affiliated institutions. Use of trade names is for identification only and does not imply endorsement by any of the groups named above.
Endemic Infections - Fungal

Blastomycosis
- Common in mid-western, southeastern, south central, particularly along Ohio-Mississippi River Valley
- Men who are outdoors involving soil exposure

In immunosuppressed
- Severe pneumonia, disseminated disease (36-50%)
- Onset 1 week – 20 years post transplant
- Can be reactivation or primary infection
- Fever, chills, arthralgias, cough, infiltrate – bilateral (78%)
- Respiratory failure

Treatment:
- Amphotericin B – oral intraconazole, voriconazole (12 months)

Figure 3  Geographic distribution of blastomycosis in persons ≥65 years of age, United States, 1999–2008. Values are no. cases/100,000 person-years.

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Endemic Infections - Fungal

Coccidioidomycosis
- Desert soil of southwestern U.S., particularly San Joaquin Valley, Sonoran desert, Arizona, Northern Mexico, New Mexico, Western Texas
- From travel to endemic area or from spores on surfaces of objects/produce from endemic area
- Rainy areas or area with earthquake – soil disrupted
- Primary or reactivation
- Dissemination – multi organ failure, severe pneumonia
- Fever, chills, night sweats, cough, dyspnea, lobar consolidation, nodules, mass like lesions, or cavitary disease

Risk Factors
- Male, African, Filipino, or Native American

Treatment
- Mild – fluconazole or intraconazole
- Severe – amphotericin
- Anti-fungal prophylaxis if live in endemic area – up to 12 months

Figure 2. Geographic distribution of coccidioidomycosis in persons ≥65 years of age, United States, 1999–2008. Values are no. cases/100,000 person-years.

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# Antifungal Therapy

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<thead>
<tr>
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<th>Fluconazole</th>
<th>Itraconazole</th>
<th>Voriconazole</th>
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<th>Amphotericin</th>
<th>Echinocandin</th>
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<tbody>
<tr>
<td><strong>Histoplasmosis</strong></td>
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<tr>
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<tr>
<td><strong>Coccidioidomycosis</strong></td>
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<tr>
<td><strong>Aspergillus</strong></td>
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<tr>
<td><strong>Scedosporium</strong></td>
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<tr>
<td><strong>Fusarium</strong></td>
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<td>++</td>
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<td>+</td>
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</tr>
<tr>
<td><strong>Zygomycetes</strong></td>
<td>-----</td>
<td>-----</td>
<td>-----</td>
<td>++</td>
<td>+</td>
<td>+/-</td>
</tr>
</tbody>
</table>

+/- = good in vitro data, clinical experience is lacking
## Anti-Fungal Drug Interactions

<table>
<thead>
<tr>
<th>Antifungal</th>
<th>Immunosuppressant</th>
<th>Severity</th>
<th>Interaction</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Azoles:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ketoconazole</td>
<td>CSA, TAC, SRL, EVR</td>
<td>+++</td>
<td>↑ level</td>
<td>↓ Imm dose by 1/2</td>
</tr>
<tr>
<td>Voriconazole</td>
<td>CSA, TAC, SRL, EVR</td>
<td>+++</td>
<td>↑ level</td>
<td>↓ CSA by 1/2, ↓ TAC by 2/3</td>
</tr>
<tr>
<td>Itraconazole</td>
<td>CSA, TAC, SRL, EVR</td>
<td>++</td>
<td>↑ level</td>
<td>↓ CSA/TAC by 1/2</td>
</tr>
<tr>
<td>Posaconazole</td>
<td>CSA, TAC, SRL, EVR</td>
<td>+++</td>
<td>↑ level</td>
<td>↓ CSA by 1/4, ↓ TAC by 2/3</td>
</tr>
<tr>
<td>Fluconazole</td>
<td>CSA, TAC, SRL, EVR</td>
<td>++</td>
<td>↑ level</td>
<td>Monitor Imm levels</td>
</tr>
<tr>
<td><strong>Echinocandins:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caspofungin</td>
<td>TAC CSA</td>
<td>+/-</td>
<td>↓ level</td>
<td>None Monitor AST/ALT</td>
</tr>
<tr>
<td></td>
<td></td>
<td>++/+</td>
<td>↑ Caspofungin level</td>
<td></td>
</tr>
<tr>
<td><strong>Polyenes:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amphotericin</td>
<td>CSA/TAC</td>
<td>++</td>
<td>Nephrotoxicity</td>
<td>Monitor renal function</td>
</tr>
<tr>
<td>Liposomal Amphotericin</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*American Journal of Transplantation 2013; 13: 318-326*
Screening Donors & Recipients

Screening Donors
- Serological testing - UNOS/CDC
- Cultures – blood, urine sputum
- History – medical, social

Screening Recipients
- Serological – before and after
- Immunity
- Current infections – lines, VAD, catheters
- History – medical, social
Evaluation for Infections

- UA – culture
- Chest x-ray
- Blood cultures
- CMV PCR
- BC PCR
- Sputum culture
- Nasal viral swab
- Bronchoscopy
- Lumbar puncture
- Biopsy of lesion
- Stool culture
- CT scan
Treating Infection After Transplant

- Differentiating infection/rejection
- Early recognition
- Prevention
- Prophylaxis
- Change immunosuppressive regimen
Prophylaxis and Infection

- TMP/SMX
  - PCP
- Acyclovir
  - HSV
- Fluconazole or Nystatin
  - Candida
## Anti-infective Drug Interactions

<table>
<thead>
<tr>
<th>Antimicrobial</th>
<th>Immunosuppressant</th>
<th>Severity</th>
<th>Interaction</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antibacterial:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ofloxacin</td>
<td>CSA, TAC</td>
<td>++</td>
<td>↑ level</td>
<td>Chose alternate</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>CSA, TAC</td>
<td>+/-</td>
<td>May ↑ level</td>
<td>None</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>CSA</td>
<td>+/-</td>
<td>May ↑ level</td>
<td>None</td>
</tr>
<tr>
<td>Moxifloxacin</td>
<td>CSA, TAC, SRL, EVR</td>
<td>-</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td><strong>Macrolides:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Erythromycin</td>
<td>CSA, TAC, SRL, EVR</td>
<td>+++</td>
<td>↑ level</td>
<td>Avoid</td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>CSA, TAC, SRL, EVR</td>
<td>+++</td>
<td>↑ level</td>
<td>Avoid</td>
</tr>
<tr>
<td>Azithromycin</td>
<td>CSA, TAC, SRL, EVR</td>
<td>+/-</td>
<td>↑ level</td>
<td>None</td>
</tr>
<tr>
<td><strong>Other:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Linezolid</td>
<td>MMF, AZA</td>
<td>++</td>
<td>Myelosuppression</td>
<td>Monitor WBC, PLT</td>
</tr>
<tr>
<td>Sulfonamides</td>
<td>MMF, AZA, CSA, TAC</td>
<td>++</td>
<td>Myelosuppression</td>
<td>Monitor WBC, HCT, PLT, Renal</td>
</tr>
<tr>
<td>Tetracycline</td>
<td>CSA, TAC, SRL, EVR</td>
<td>+</td>
<td>↑ level</td>
<td>Monitor level</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>CSA, TAC, SRL, EVR</td>
<td>+/-</td>
<td>May ↑</td>
<td>None</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>CSA, TAC, SRL, EVR</td>
<td>+/-</td>
<td>May ↓</td>
<td>None</td>
</tr>
</tbody>
</table>

*American Journal of Transplantation 2013; 13: 318-326*
# Vaccines

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Frequency</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Influenza</td>
<td>Yearly</td>
<td>No intranasal</td>
</tr>
<tr>
<td>Measles</td>
<td>MMR – live attenuated</td>
<td>Contraindicated</td>
</tr>
<tr>
<td>Varicella/Zoster</td>
<td>Live attenuated</td>
<td>Contraindicated</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>3 doses</td>
<td>? If seroconvert</td>
</tr>
<tr>
<td>Hepatitis A</td>
<td>2 doses</td>
<td>? If seroconvert</td>
</tr>
<tr>
<td>Salmonella enterica</td>
<td>Typhim V</td>
<td>OK</td>
</tr>
<tr>
<td>Live typhoid vaccine</td>
<td>NA</td>
<td>Contraindicated</td>
</tr>
<tr>
<td>Polio OPV</td>
<td>Live attenuated</td>
<td>Contraindicated</td>
</tr>
<tr>
<td>Polio IPV</td>
<td></td>
<td>OK</td>
</tr>
<tr>
<td>Meningococcus</td>
<td>If indicated</td>
<td>OK</td>
</tr>
<tr>
<td>Yellow Fever</td>
<td>Live attenuated</td>
<td>Contraindicated</td>
</tr>
<tr>
<td>Rabies</td>
<td>If indicated</td>
<td>OK</td>
</tr>
<tr>
<td>Japanese encephalitis</td>
<td>If indicated</td>
<td>OK</td>
</tr>
<tr>
<td>Human papilloma virus</td>
<td>If indicated</td>
<td>OK</td>
</tr>
<tr>
<td>Tetanus/diphtheria</td>
<td>Every 10 years</td>
<td>OK</td>
</tr>
<tr>
<td>Pertussis</td>
<td></td>
<td>OK</td>
</tr>
<tr>
<td>Pneumococcal</td>
<td>Every 5 years</td>
<td>OK</td>
</tr>
<tr>
<td>Cholera</td>
<td>If indicated</td>
<td>OK</td>
</tr>
</tbody>
</table>

*American Journal of Transplantation 2013; 13:337-347*
Preventing Infections After Transplant

- Hand washing
- Gloves when working in soil
- Care when working in wooded areas – long pants, long sleeved shirts
- Avoid body piercings, tattoos
- Avoid close contact with infected persons
- Mask during influenza season
- Avoid tobacco smoke
- Occupational risks – farming, animal care
- Avoid construction sites
- Avoid well water

- Don’t drink water from rivers or lakes
- Avoid hot tubs
- Avoid unpasteurized milk or fruit/vegetable juices
- Avoid eating raw or undercooked eggs
- Avoid eating raw or undercooked meat
- Wash vegetable products
- Avoid cleaning bird cages, cat boxes, or handling animal feces
- Safe sexual practices
- Travel safety
- Mosquito repellant with DEET
- Vaccines

Summary

- Transplant patients are at higher risk of developing infections related to immunosuppression.
- Certain infections are more common depending on time after transplant.
- Pharmacologic treatment of infections in transplant patients can be done successfully and safely with adequate monitoring and judicious prescribing.
- Prophylaxis in transplant patients is important.
- Prevention and early detection of infections is imperative to survival.