INFECTION PREVENTION IN THE IMMUNOCOMPROMISED PATIENT POPULATION

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February 20, 2019
Outline

• Who is immune compromised?
• The effect of time post-transplant on infectious risk
• Preventing infection in immune compromised patients
• Specific healthcare-associated infections
Introduction

• How do we define “immune compromised”?
  – Solid organ transplant
  – Hematopoietic stem cell transplant
    • Autologous, allogeneic (at highest risk for infection)
  – Chemotherapy-induced neutropenia
    • Anticipated duration of neutropenia
  – Adverse drug reaction- or infection-related neutropenia

• How immune compromised must a patient be to have increased risk of infection?
  – From environmental mold
  – From mucosal barrier injury
Role of neutropenia

• Clinically significant neutropenia is defined as < 500 neutrophils

• Duration of neutropenia from hematologic malignancy and associated chemotherapy directly correlates with risk of environmental mold and mucosal barrier injury.

• Neutropenia from other causes does not confer the same risk, nor does neutropenia duration <7 days
Basic truths of transplant infections

• Type and frequency of infection vary with transplant type:
  – stem cell > lung > liver > heart > kidney
• More surgery → more infection
• More immunosuppression → more infection
• Donor can be a source of infection, especially early post-tx
• Transplant recipients also get “normal” infections
Infection prevention in the pre-transplant period

- Concerns:
  - Community-acquired organisms
  - Colonization with nosocomial pathogens due to healthcare exposure
  - Exposures to environmentally endemic pathogens
Strategies to prevent and control infection: recipient screening

• Assess for active infection
• Epidemiologic screening
• Vaccination history
• Screening labs:
  • HIV, CMV, HBV, HCV, syphilis, Quantiferon TB, EBV, HSV, VZV, Strongyloides, Toxoplasma, +/- Chagas
Strategies to prevent and control infection: **donor screening**

- Initial donor screening for infection is serologic antibody based
  - HIV, HBV, HCV, CMV, EBV, HSV, syphilis, Toxoplasma
- Cultures from donor are taken at time of organ donation
  - blood, urine, sputum, perfusion fluid
Strategies to prevent and control infection: **pharmacology**

- Prior to transplant:
  - vaccines
  - treat active and latent infections

- Peri-transplant:
  - prophylactic peri-op antibiotics

- Post-transplant:
  - prophylactic antiviral and antifungal medications
Vaccination of immunocompromised patients

- Vaccines should follow the CDC/ACIP recommended vaccine schedule
- Vaccines should be given prior to planned immunosuppression if possible
- Live vaccines should be avoided after SOT or allogeneic SCT or if significantly immune compromised.
- Inactivated vaccines should be given >2 weeks before immune suppression, if possible.
Strategies to prevent and control infection: **non-pharmacologic**

- Sterile insertion and maintenance of central lines and urinary catheters
- Standard precautions within the hospital
- Immunocompromised precautions for the highest risk patients

- Patients should avoid raw eggs, unpasteurized milk and juice, soft cheeses
- Zoonoses: avoid cat litter, bird cages
- Vaccinate family members against the flu.
Back to basics

• Standard hand hygiene
• Disinfection of mobile medical equipment and surfaces in patient rooms
• Isolation precautions per established guidelines.
  – Healthcare Infection Control Practices Advisory Committee, CDC
Timeline of infection after stem cell transplant

Timeline of infection after solid organ transplant

Common Infections in Solid-Organ Transplant Recipients

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

>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)
  - Hepatitis (HBV, HCV)
  - HSV encephalitis
- Community-acquired (SARS, West Nile virus infection)
- JC polyomavirus infection (PML)
- Skin cancer, lymphoma (PTLD)

Donor-Derived Infection
- <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
  - Recipient-derived infection (colonization):
    - Aspergillus, pseudomonas

Risk factors for early infection

- Intubation > 3 days
- Presence of central lines and urinary catheters
- Colonization (e.g., MRSA, CRE, VRE)
- History of *C. difficile*
- Latent viral or parasitic infection
- Exogenous immune suppression
<1 month post-SOT and pre-engraftment SCT

- Surgical complications
- Compromise of normal mucosal barriers
- Related to invasive devices (CVC)
- Environmental exposures within the hospital
- Ill healthcare workers or visitors

- Greatest concern:
  - Bacterial pathogens (MRSA, VRE, C. difficile)
  - Fungal species (Aspergillus, Candida)
  - Viral infections (reactivation of latent infection)
Infections during the first month post-transplant

- Infection carried by donor graft: bacterial, Candida
- Infection present in recipient prior to transplant
- Nosocomial:
  - Pneumonia: ~50% of infections
  - CLABSI, CAUTI
  - C. difficile infection
- Surgical site infections, including anastomotic sites
Infections from 1-6 months following transplant

- Classic opportunistic infections: toxoplasmosis, pneumocystis pneumonia
- Endemic pathogens: endemic mycoses, Strongyloides, *T. cruzi*
- Reactivation of latent viral infections: CMV, EBV, HSV, HBV, HCV, VZV
Infections from >6 to 12+ months post transplant

• Most patients have a gradual decrease in their immune suppression meds at this time, leading to fewer infections
  • Community-acquired pneumonia, UTI
• Subset of patients with chronic viral infection
  • BK nephropathy, HBV, CMV
• Subset of patient require more immune suppression for acute rejection, raising risk for recurrent OIs
Preventing infection after transplant: prophylaxis

• Use of prophylactic antimicrobials has led to reductions in:
  – All-cause mortality
  – Infection-related mortality
  – Risk of infections

• Despite this, infections remain a threat in this population
Preventing infection post-transplant

- **Candida:**
  - Occurs most commonly in the first 4 weeks post-transplant
  - Source: endogenous colonization, exogenous (poor healthcare worker hand hygiene)
  - Antifungal prophylaxis given in the immediate post-transplant period.
Aspergillus infection post-transplant

• Aspergillosis:
• Risk factors include: re-transplantation, pulse steroids, construction, elevator shafts.
• Diagnosis: chest imaging, sputum culture, galactomannan assay (blood or BAL), lung biopsy
• Treatment: amphotericin B, voriconazole
Role for Aspergillus prophylaxis

• Posaconazole or voriconazole prophylaxis for patients at high risk for invasive Aspergillus, plus inhaled AmB.

• High risk:
  – Hematologic disorders with poorly functioning neutrophils
  – Acute leukemia with prolonged neutropenia
  – History of invasive Aspergillus prior to transplant
  – SCT with graft vs host disease
  – Lung transplant recipients
Protected environment rooms

- Prevents exposure to mold
- HEPA filtration
- Positive pressure
- Sealed windows, doors and electrical outlets
- High rates of room air exchange (>12 / hour)
- Sealed barriers between patient care areas and areas of construction
Who should be in a protected environment room?

- Hospitalized allogeneic SCT recipients
- Other patients with anticipated prolonged neutropenia
  - acute leukemia undergoing induction or consolidation chemotherapy
  - Certain autologous SCT patients
- Lung transplant recipients

- What if there is no P.E. room?
  - Single patient rooms, no plants or cut flowers
  - Environmental mold sampling
  - Mold remediation
  - Surveillance system for invasive mold infections.
Safe water

- Opportunistic molds and Legionella can be present in hospital water systems

- Use reverse osmosis water for drinking

- Use filters on sinks, shower heads and ice machines to reduce Legionella exposure

- Surveillance systems to monitor water supply and to identify potential hospital-onset pneumonia cases.
Healthcare workers and hospital exposures

- Important to target potentially preventable infections

- Hospitals should have a comprehensive vaccination policy adherent to national guidelines to decrease risk of transmission from HCWs to patients.

- HCWs should receive inactivated vaccine rather than live virus vaccine to minimize risk of transmission of vaccine virus to immune compromised recipients.
  - Live attenuated influenza vaccine, oral polio vaccine, varicella vaccine
Screening of staff and visitors

• Strong effort to restrict direct patient contact between HCWs with potentially transmissible infections and transplant recipients.

• Hospitals should develop screening policies for visitors to transplant units
  – e.g., screening for respiratory symptoms during winter months

• Symptomatic visitors and HCWs or those with recent exposure to communicable infection should avoid contact with transplant candidates/recipient

• Some transplant centers place all transplant recipients on droplet isolation precautions during respiratory viral season.
Screening for asymptomatic bacterial colonization

• Universal *Staph aureus* decolonization in ICUs more effective than targeted decolonization or screening/isolation in preventing MRSA or any bloodstream infection.
  – Unknown benefit for other inpatient settings.

• Liver transplant candidates and recipients colonized with MRSA or VRE were at higher risk for subsequent invasive infection.

• Implementation of MRSA screening, cohorting and decolonization led to decreased colonization and rates of invasive MRSA infection
Multidrug-resistant gram negative infections

- Increased rates of quinolone-resistant and ESBL-phenotype gram negative bacteria seen in transplant cohorts
- Significantly decreased survival of patients infected with MDR bacteria
- Asymptomatic carriage is associated with subsequent infection with these organisms
- Transplant recipients colonized with MDR bacteria may introduce these organisms into hospital settings.

- Consider active surveillance, although no guidelines currently support this.
**Clostridium difficile**

- CDI is more frequently seen in SOT recipients than other hospitalized populations.
  - Estimated prevalence: 3-31%
  - Estimated prevalence in hospitalized overall: 1.3%

- Severe CDI is more frequent in SOT:
  - Fulminant colitis in 13% of SOT with CDI, compared with 8% in other patients.

- CDI occurs frequently early after allo-SCT (17%) but disease is typically mild.
Infection control related to C. difficile

- Strict hand hygiene
  - ABHR vs soap and water
- Appropriate contact precautions
  - Duration?
- Environmental disinfection
  - Dilute bleach, hydrogen peroxide, UV light
CLABSI

- Risk of mucosal barrier injury (MBI) related bloodstream infections in prolonged neutropenia from hematologic malignancy and stem cell transplant
  - Basic oral care: prevent infection, control pain, maintain oral function
  - rinses, chlorhexidine, soft brushing, saliva substitutes, photobiomodulation

- Educations for providers is needed regarding the newer, non-culture-based diagnostics and the effect of these results on CLABSI definition
  - Concern for false positive results
Infection control related to CLABSIs

- All CVCs should be inserted using maximal sterile barrier precautions
- Use a CLABSI prevention bundle for maintenance
- Use alcohol-impregnated caps
- Antimicrobial-impregnated catheters should be considered
- Patients and families should receive education re: CVCs
Conclusions

• “Immune compromised” is a broad term that is interpreted widely, but it is key to identify our highest risk patients and use measures beyond standard precautions to protect them
  – Identify those at risk for environmental mold exposure and use protected environments

• Transplant recipients are at highest risk for infection in the first months after transplant

• Similarly, patients with hematologic malignancies risk of infection correlates with duration of neutropenia.

• Immune compromised patients are at higher risk for common healthcare associated infections, such as CLABSI and C. difficile.