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INFECTION PREVENTION IN THE IMMUNOCOMPROMISED PATIENT POPULATION

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Outline

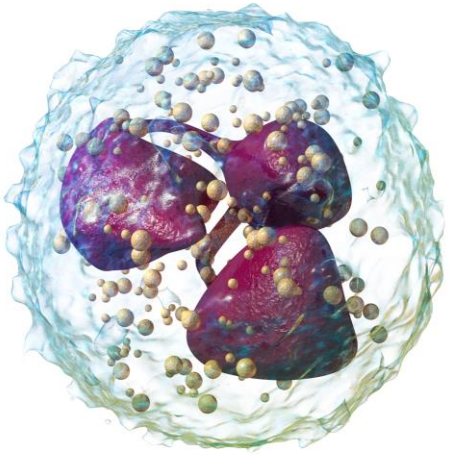
- Who is immune compromised?
- The effect of time post-transplant on infectious risk
- Preventing infection in immune compromised patients
- Specific healthcare-associated infections

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

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Infection prevention in the pre-transplant period

- Concerns:
  - Community-acquired organisms
  - Colonization with nosocomial pathogens due to healthcare exposure
  - Exposures to environmentally endemic pathogens

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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

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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.

Rubin LG, et al. 2013 IDSA clinical practice guidelines for vaccination of the immunocompromised host. Clin Infect Dis, 2014.

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

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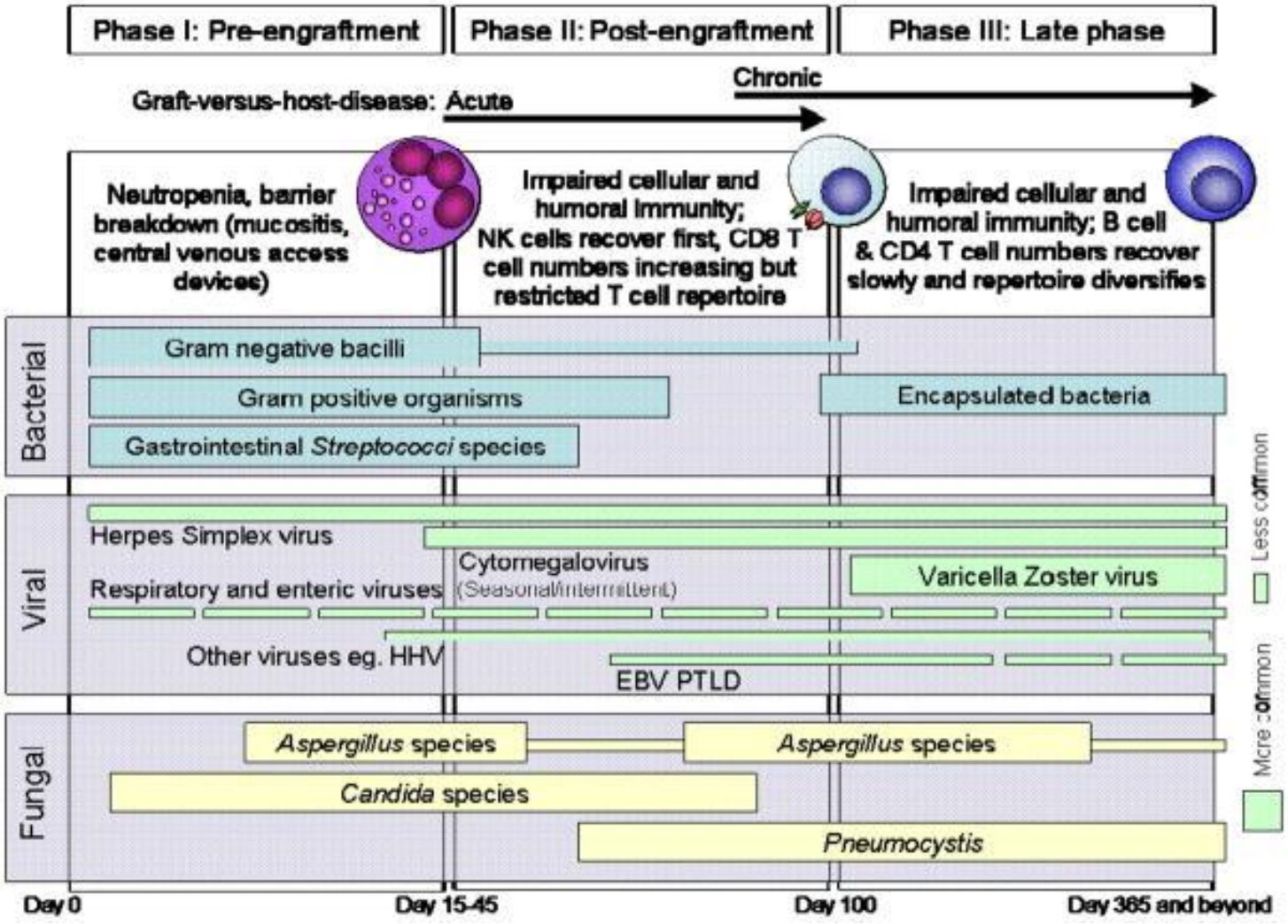
Timeline of infection after stem cell transplant



Tomblyn M, et al. Guidelines for preventing infectious complications among hematopoietic cell transplant recipients: a global perspective. Biol Blood Marrow Transplant, 2009.

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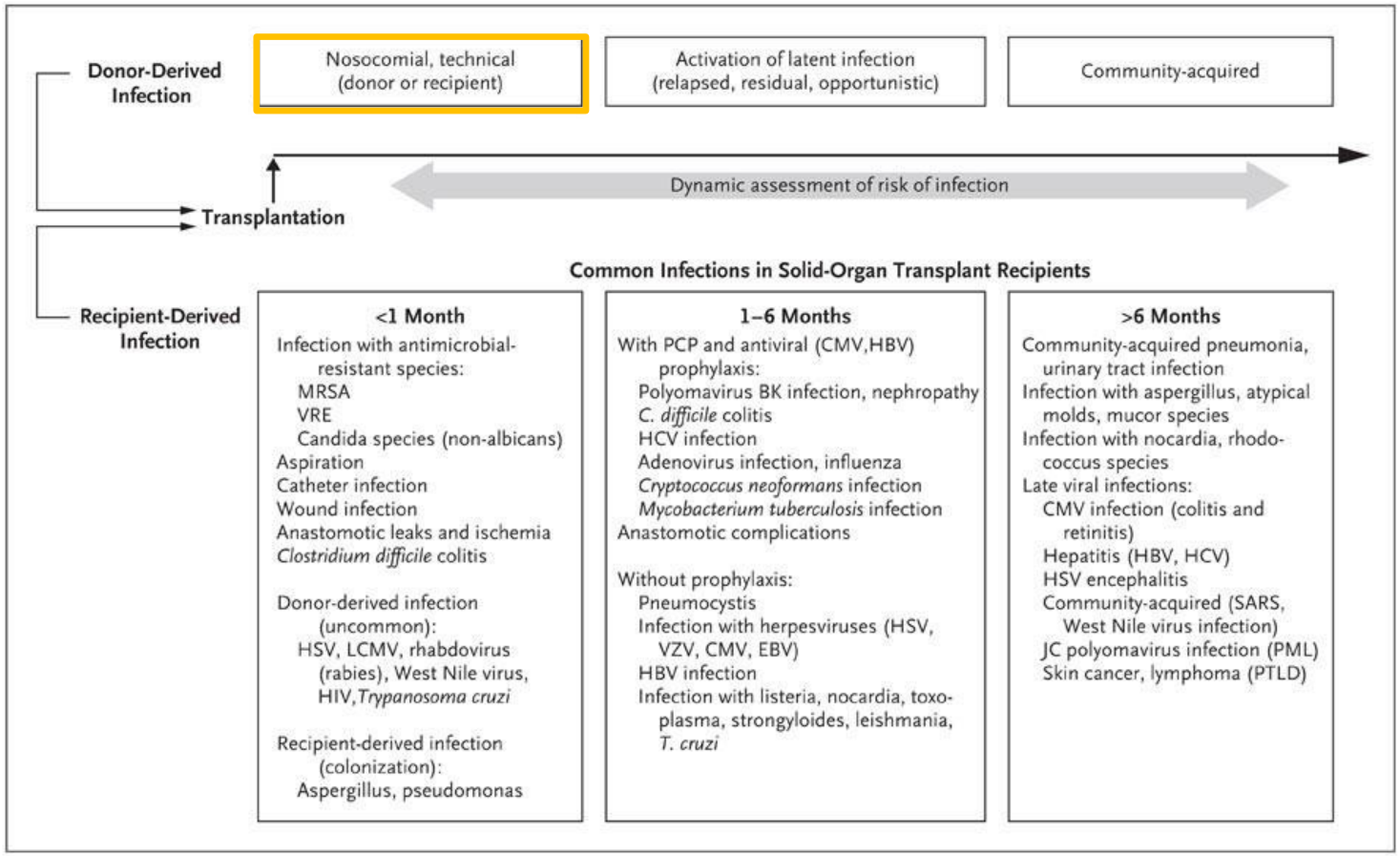
Timeline of infection after solid organ transplant



Fishman JA. N Engl J Med 2007;357:2601-2614.

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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

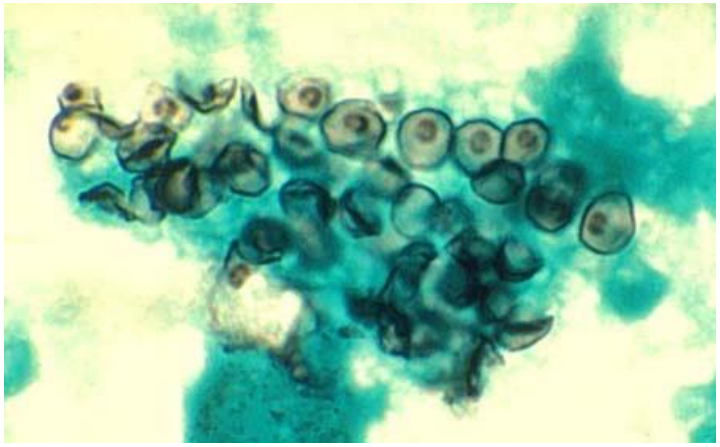
- Greatest concern:
  - Bacterial pathogens (MRSA, VRE, C. difficile)
  - Fungal species (Aspergillus, Candida)
  - Viral infections (reactivation of latent infection)

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

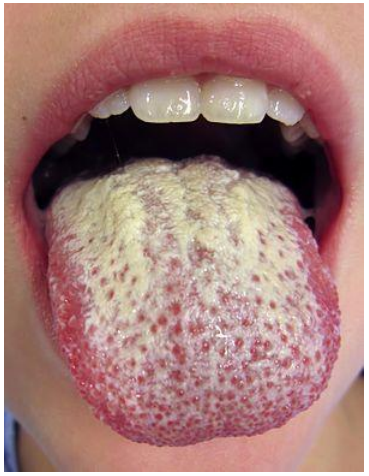
Preventing infection after transplant: prophylaxis

- 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

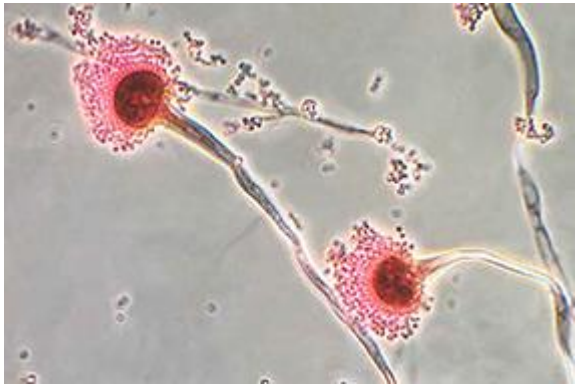
Preventing infection post-transplant

- 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

Patterson TF, et al. Practice guidelines for the diagnosis and management of aspergillosis: 2016 update by the Infectious Diseases Society of America. Clin Infect Dis, 2016.

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.

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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/recipients

- Some transplant centers place all transplant recipients on droplet isolation precautions during respiratory viral season.

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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

Huang SS, et al. Targeted versus universal decolonization to prevent ICU infection. NEJM, 2013.
Russell DL, et al. Outcomes of colonization with MRSA and VRE among liver transplant candidates and recipients. Am J Transplant, 2008.
Singh N, et al. Impact of an aggressive infection control strategy on endemic Staphylococcus aureus infection in liver transplant recipients. ICHE, 2006.

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.

D. Van Duin, et al. Multidrug-resistant gram-negative bacteria infections in solid organ transplantation. Am J Transplant 2013; 13:31-41.

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.

ER Dubberke, et al. Clostridium difficile infections in solid organ transplantation. Am J Transplant 2013; 13:42-49
MA Kinnebrew, et al. Early Clostridium difficile infection during allogeneic hematopoietic stem cell transplantation. PLoS One, 2014.

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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

ER Dubberke, et al. Clostridium difficile infections in solid organ transplantation. Am J Transplant 2013; 13:42-49

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.

THANK YOU

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