Infection Prevention in the Cancer Center

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Cancer patients are frequently immunosuppressed and at risk for a wide range of opportunistic and healthcare-associated infections. A good infection prevention program is extremely important to reduce risk of infection. This review focuses on infection prevention measures specific to patients, healthcare personnel, and visitors in the cancer center.

Keywords. infection prevention; cancer center; immune suppressed.

PATIENT MEASURES

Hygiene
Proper hygiene is important in preventing infections in all patients, especially those with profound immunosuppression. Skin inspection should be done routinely with attention to sites at high risk for infection (eg, intravascular catheters, perineum); in our institution this is performed daily during nursing care with physician follow-up as needed. Expert recommendations include avoiding tampon use for menstruating hematopoietic stem cell transplant (HSCT) recipients as well as avoiding digital rectal examinations, rectal thermometers, enemas, and suppositories during periods of neutropenia to prevent mucosal breakdown [1]. There are increasing data to support the use of daily chlorhexidine bathing, particularly in critically ill patients, to prevent transmission of multidrug-resistant organisms (MDROs) and prevent infections [2, 3]. A recent randomized cluster trial in 9 intensive care units and 1 bone marrow transplant unit demonstrated a 23% reduction in MDRO acquisition and a 28% reduction in hospital-associated bloodstream infections with daily chlorhexidine bathing. Additional studies are needed to determine if this is an effective strategy in the general cancer center population.

Because the oral cavity is an important source of potentially pathogenic bacteria, stringent periodontal health is important. Complete periodontal examination followed by necessary treatment is recommended before management of head and neck cancers [4], high-dose
chemotherapy, HSCT and any cancer regimen that is expected to lead to significant immunosuppression [1]. Routine oral hygiene is important to minimize infections (eg, pneumonia) and may improve healing of mucositis. Oral rinses with sterile water or normal saline are recommended 4–6 times per day and neutropenic patients should routinely brush their teeth, taking care to minimize gingival trauma.

Low Microbial Diet
The Centers for Disease Control and Prevention (CDC) recommends a low microbial diet for HSCT recipients [1]. There are no guidelines for the use of a low microbial diet in other patients; however, many centers will prescribe one for patients with hematologic malignancies during periods of neutropenia. Theoretically, reducing exposure to microbes in foods such as unpasteurized cheeses or beverages, raw fruits and vegetables, and undercooked meats during periods of neutropenia may decrease the incidence of infection. To date, however, there is no scientific evidence to suggest the effectiveness of low microbial diets in any patient population. Many HSCT recipients choose to drink only bottled water; if so, they need to confirm that the water has been appropriately processed to remove Cryptosporidium [1, 5]. During hospital outbreaks of Legionella, HSCT recipients should be given sterile water instead of tap water for drinking, oral hygiene, and flushing of nasogastric tubes until water systems are disinfected [1].

Antibiotic Prophylaxis to Prevent Infection
Prophylactic antibiotics, most commonly fluoroquinolones, are often given to patients considered at high risk for serious infection. Use of prophylactic antibiotics is controversial. The largest randomized comparative trial failed to show benefit of fluoroquinolone prophylaxis in decreasing deaths due to infection among patients with chemotherapy-induced neutropenia [6]. Results from several metanalyses have reached conflicting conclusions [7–10]. A large meta-analysis of 17 randomized controlled trials comparing fluoroquinolones prophylaxis to no antibiotics primarily among patients with hematologic malignancies at high risk for infection demonstrated 48% reduction in risk for all-cause mortality for those patients who received prophylaxis (relative risk, 0.52 [95% confidence interval, .35–.77]) [9]. This study has led expert panels to recommend consideration of quinolone prophylaxis for patients at high risk such as patients with hematologic malignancies or HSCT recipients in whom profound neutropenia (absolute neutrophil count, <100 cells/mm³) is expected for a duration of >7 days [1, 11]. Decisions to implement prophylaxis should be balanced against the small expected potential benefit, particularly in cancer centers that achieve low rate of attributable mortality with traditional empirical treatment strategies for febrile neutropenia. In addition, surveillance strategies for monitoring fluoroquinolone resistance among gram-negative bacilli, staphylococci, and viridans streptococci, as well as rates of *Clostridium difficile* infection, should be considered [12, 13]. Prolonged antibiotic prophylaxis is recommended only in HSCT recipients with chronic, active graft-versus-host disease to prevent infection with *Streptococcus pneumoniae* [1]. Antibiotics with antistreptococcal activity, such as fluoroquinolones, trimethoprim-sulfamethoxazole, or penicillins, can be considered based on local epidemiologic patterns.

Device-Associated Infections
Because of the unique needs of cancer patients, intravascular catheters, particularly tunneled or implantable catheters, are used more often and for longer durations in these compared to other hospitalized patients as catheters provide long-term access for frequent blood draws and infusion of chemotherapy and blood products. Thus, these patients are at particular risk for catheter-related complications including infections.

Catheter-related infections are more common with the use of nontunneled central venous catheters (CVCs) [14]. No catheters, however, are without risk. In a recent prospective observational cohort study of all adult patients requiring a CVC in a cancer unit, the rate of central line–associated bloodstream infection (CLABSI) per 1000 line-days was 2.50 [14]. CVC type was a risk factor, greatest for nontunneled lines (hazard ratio [HR], 3.50; *P* < .0001) and tunneled lines (HR, 1.77; *P* ≤ .011) compared to peripherally inserted central venous catheter lines. In theory, the best way to prevent catheter-related complications is to minimize catheter use; however, this is often not feasible. Regardless, the need for catheters should be reassessed regularly and catheters removed when no longer needed. “Bundled” strategies aimed at CLABSI prevention, such as insertion by experienced personnel with full barrier precautions, rigorous exit site care with daily assessment, and patient/caregiver training, should be employed for cancer patients as they are for other patients [15].

There are few published data regarding the frequency of use of urinary catheters or the incidence of catheter-associated urinary tract infections (CAUTI) in the cancer center population. Regardless, implementation of strategies aimed at reducing CAUTI is prudent for those patients requiring urinary catheterization. These strategies include ensuring appropriate catheter use, including removal when no longer necessary, use of aseptic technique during insertion, and maintaining a closed-drainage system with unobstructed flow [16].

Community Respiratory Viruses
Infection with common community respiratory viruses can lead to serious disease and significant morbidity and mortality among patients with cancer, especially HSCT recipients. Given the potential adverse outcomes and the relative ease of spread
of infection, healthcare-associated and household transmission is a serious concern. Significant effort to prevent and control the spread of these infections should be made.

Acute viral respiratory infections are most commonly due to respiratory syncytial virus, influenza viruses, rhinoviruses, parainfluenza viruses, human metapneumoviruses, coronaviruses, and adenoviruses and typically reflect disease activity in the community [17, 18]. Rhinoviruses, coronaviruses, and adenoviruses are the most commonly encountered [17]. However, immunosuppressed patients may present with atypical lower respiratory tract disease (in addition to typical upper tract disease), and the incidence of lower respiratory tract infection is higher with respiratory syncytial virus, influenza viruses, parainfluenza viruses, human metapneumoviruses, and adenoviruses [17]. Early studies suggested that nearly half of cancer patients (HSCT recipients and leukemia patients) infected with these viruses progress to viral pneumonia with a mortality rate of >50%; however, our experience in outpatient populations of HSCT recipients using polymerase chain reaction (PCR)–based testing of all upper respiratory infections demonstrated that most respiratory viral infections resolve without the need for inpatient hospitalization [18–20]. Due to limited effective treatments for most of these viruses, prevention is essential particularly during periods of greatest immune suppression.

An effective infection prevention strategy includes vaccination (influenza); community outbreak surveillance; hospital surveillance for nosocomial transmission outbreaks; patient and personnel education regarding disease recognition, prevention strategies, and modes of transmission; rapid diagnosis with early isolation for suspected and confirmed cases; and restriction of potentially infected visitors and healthcare personnel from the cancer center.

Awareness of local disease activity can be accomplished through both community surveillance (eg, communicable disease reporting and syndromic surveillance through a local health department) and hospital surveillance (eg, syndromic surveillance and virology reports within individual facilities). Ongoing hospital surveillance, particularly during times of high disease activity, is also necessary to identify cases or outbreaks and interrupt transmission.

Prompt diagnosis and implementation of appropriate prevention measures are essential in controlling spread. Whenever possible, all patients presenting with acute respiratory symptoms (rhinorrhea, nasal congestion, pharyngitis, cough and fever) during winter months should be placed on contact and droplet precautions until a diagnosis is made. Diagnosis should be attempted and we recommend the use of molecular testing by multiplex PCR whenever possible, which has improved sensitivity, specificity, and turnaround time compared to alternative diagnostic approaches. If a particular etiology is determined, isolation precautions can be geared to each specific virus [21–25] (Table 1).

During periods of disease activity, visitors and healthcare personnel should be screened for signs and symptoms of acute viral respiratory infection. Persons with viral symptoms should be restricted from the cancer center and any contact with immunosuppressed patients [1]. The CDC recommends restriction of healthcare personnel in the acute stages of an acute respiratory infection from the care of immunosuppressed patients [26, 27].

**Fungal Pneumonia**

Invasive pulmonary aspergillosis and other fungal pneumonias are a serious concern, particularly in patients with prolonged neutropenia or HSCT recipients [28, 29]. *Aspergillus* species are responsible for a majority of invasive fungal infections among cancer patients; and, although decreased in recent years, mortality remains high [30–34]. *Aspergillus* is ubiquitous in the
environment, including hospital water supplies; infection occurs primarily through inhalation of conidia [27].

The CDC recommends establishing a surveillance program to alert infection prevention teams to the identification of Aspergillus from a pulmonary source using microbiologic, histologic, and postmortem data [27]. An increase in positive clinical cultures above the baseline should elicit an epidemiologic investigation to determine and eliminate the source [27].

High-efficiency particulate air (HEPA) filters have been used to maintain ultraclean air in areas where patients may be at high risk for aspergillosis, and HEPA filtration has been associated with a decrease in Aspergillus conidia air counts [35, 36]. HEPA filtration has been shown to decrease nosocomial infection with Aspergillus in HSCT recipients by 19%, and current guidelines recommend this practice for all HSCT patients [11, 27, 35]. HEPA filtration has been shown to decrease infection during outbreaks in patients with hematologic malignancies, but there is no official recommendation in the endemic setting [27, 37]. In addition to HEPA filtration, HSCT recipient rooms should also have directed air flow and positive air pressure relative to the corridor, be properly ventilated (≥12 air changes per hour) and well sealed, and be designed to minimize dust (ie, avoid carpets and upholstery) [25]. Transplantation protocols have changed significantly in the last 20 years, and current practices have moved many treatments to the outpatient setting. Therefore, HEPA filtration is likely less important currently for preventing aspergillosis and is being supplanted by anti-Aspergillus-azole prophylaxis and preemptive detection strategies (antigen monitoring, chest computed tomography).

Aspergillus outbreaks have been linked to hospital construction or renovation [38]. A hospital plan should be made during all times of construction to prevent exposures, including the temporary erection of an impermeable barrier between construction and patient care areas [27].

Aspergillus species have been isolated from dried and fresh flowers as well as potted plants. Although exposure has not been directly linked to fungal pneumonia, there remains a theoretical risk of transmission and the CDC recommends that HSCT recipients and other severely immunosuppressed cancer patients should not be exposed to these items [1, 27]. Furthermore, immunosuppressed cancer patients should be discouraged strongly for smoking marijuana because of risk of inhaling Aspergillus spores from contaminated marijuana [39, 40].

Multidrug-Resistant Organisms
Historically, cancer centers used surveillance cultures of the skin or perirectal areas to guide empiric antibiotic therapy for patients with neutropenic fevers. Many centers discontinued this practice due to the lack of supporting data and cost. The role of surveillance culture for MDROs (eg, vancomycin-resistant enterococci, methicillin-resistant Staphylococcus aureus, and multidrug-resistant gram-negative organisms) has yet to be well defined in the cancer center [1, 11]. Yet, many advocate for the use of MDRO surveillance, particularly in high-risk patients (eg, HSCT or acute leukemia). Local epidemiology should help guide decisions to perform active surveillance and for what organisms. Multidrug-resistant gram-negative organisms, such as carbapenem-resistant Enterobacteriaceae (CRE), are particularly concerning, and the CDC has recently updated guidelines for preventing CRE transmission, which include contact precautions and screening of epidemiologically linked patients [41].

HEALTHCARE PERSONNEL AND VISITORS

Immunizations for Healthcare Personnel
Healthcare personnel are at unique risk for both exposure to and transmission of many infectious diseases, including vaccine-preventable diseases. A lengthy discussion regarding all vaccinations recommended by the US Public Health Service’s Advisory Committee on Immunization Practices is beyond the scope of this review; for specific recommendations, refer to the CDC Guideline for Immunization of Healthcare Personnel [42].

The use of live-attenuated vaccines in persons who care for or are in close contact with immunosuppressed patients deserves special mention due to the theoretical risk of transmission of the vaccine strain pathogens. Vaccine-strain polio virus in oral polio vaccine has the potential for person-to-person transmission and is absolutely contraindicated in healthcare personnel, family members, and other caregivers of immunocompromised patients [43]. On the opposite spectrum, there is no evidence that the live-attenuated vaccine-strain viruses in the measles-mumps-rubella vaccine are transmitted from person to person, and this vaccine is generally considered safe for all immunocompetent healthcare workers [44].

Of particular interest in the cancer center is the risk of transmission of vaccine virus due to the live-attenuated influenza and varicella vaccines. The live-attenuated influenza vaccine (LAIV) may shed vaccine virus at very low levels for some time after administration, and person-to-person transmission of the vaccine strain virus is theoretically possible [45, 46]. Thus, the CDC does not recommend the use of LAIV in persons who may have close contact with “severely” immunosuppressed patients (ie, recent HSCT recipients who require a protected environment); these persons should receive the killed vaccine instead [42]. Transmissibility of vaccine virus is rare [47], and no cases of person-to-person transmission of LAIV have been documented in the healthcare setting. At this time, no recommendations exist to exclude LAIV in populations other than those described above.

Transmission of varicella vaccine virus from the varicella vaccine, but not the zoster vaccine, has been documented, although transmission is uncommon [48]. Recommendations
state that personnel who, within the first 42 days of receiving the varicella vaccine, develop a rash that cannot be covered should avoid any contact with immunosuppressed patients until the rash is crusted [26]. We believe a similar policy should be followed for zoster vaccine.

Transmissible Diseases From Visitors and Healthcare Personnel
Leukemia patients and HSCT recipients often have prolonged hospitalizations. They may have a large number of visitors both in the hospital and at home while still profoundly immunosuppressed. All visitors should be instructed on basic infection prevention including hand hygiene techniques and isolation procedures. In the hospital, a system should be established whereby all visitors can be screened for potential transmissible diseases [1]. The CDC recommends that any visitor with an upper respiratory tract infection, a flu-like illness, a herpes zoster rash (whether covered or not), or recent known exposure to any transmittable disease should not be allowed access to the unit or should at least be restricted from visiting severely immunosuppressed patients [1]. Likewise, visitors should be asked about recent vaccinations, and any with a recent history of oral polio vaccination or those who develop a rash within 6 weeks of live-attenuated varicella-zoster virus vaccination should also be restricted [43, 48]. Healthcare personnel with a disease transmitted by air, droplet, or direct contact should be restricted from direct patient contact [1].

CONTINUED INFECTION PREVENTION OUTSIDE THE CANCER CENTER
At times, the cancer center patient, even those with severely depressed immune systems, may be cared for in healthcare settings outside the cancer center. Whenever possible, these patients should be cared for in single-patient rooms and the infection prevention measures outlined above should be followed. Although there are no specific neutropenic precautions per se,
many hospitals create their own isolation category to educate noncancer center staff on the prevention of infection in profoundly neutropenic patients, addressing a variety of issues, such as specialized diets and viral respiratory precautions.

A majority of cancer treatment is delivered in the outpatient setting [49]. Many patients receive all of their treatment in the outpatient setting whereas others, particularly HSCT recipients, remain immunosuppressed and at risk for developing infections after discharge from the inpatient cancer center. The CDC recommends that all outpatient oncology centers have a formal infection prevention program; detailed guidelines for infection control after hospital discharge are available from the CDC [1, 50]. Patients and their families should be educated regarding ways to decrease risk of transmission and infection with microorganisms outside the healthcare setting (Table 2).

In summary, we focused on infection prevention measures specific to patients, healthcare personnel, and visitors in the cancer center, highlighting unique issues of surveillance and prevention in this population (Figure 1). Special care should be given to educate patients and healthcare workers regarding measures to reduce risk of exposure to infectious pathogens, such as common bacteria, community respiratory viruses, and fungi. In addition, clinicians and infection prevention experts should be aware of the local epidemiology and important antibiotic-resistant pathogens prevalent in the cancer center population as well as potential strategies to reduce exposure to and infection by these organisms. Finally, infection prevention experts should be aware of unique issues regarding HAI prevention in the cancer center.

Note

Potential conflicts of interest. All authors: No reported conflicts. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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