Update on Infection Control Practices in Cancer Hospitals

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ABSTRACT: Therapies in oncology have evolved rapidly over the last years. At the same pace, supportive care for patients receiving cancer therapy has also evolved, allowing patients to safely receive the newest advances in treatment in both an inpatient and outpatient basis. The recognition of the role of infection control and prevention (ICP) in the outcomes of patients living with cancer has been such that it is now a requirement for hospitals and involves multidisciplinary groups. Some unique aspects of ICP for patients with cancer that have gained momentum over the past few decades include catheter-related infections, multidrug-resistant organisms, community-acquired viral infections, and the impact of the health care environment on the horizontal transmission of organisms. Furthermore, as the potential for infections to cross international borders has increased, alertness for outbreaks or new infections that occur outside the area have become constant. As the future approaches, ICP in immunocompromised hosts will continue to integrate emerging disciplines, such as antibiotic stewardship and the microbiome, and new techniques for environmental cleaning and for controlling the spread of infections, such as whole-genome sequencing. **CA: Cancer J Clin 2018;68:340-355. © 2018 American Cancer Society.**

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Introduction

Hippocrates (circa 460-377 BCE) originally recognized the effects of our surroundings on human diseases in his treatise *On Airs, Waters and Places*, attributing illness to characteristics of climate, water, modes of life, and nutrition.[1,2] Two thousand years later, in the 1800s, Ignaz Semmelweis (1818-1865 CE) documented the effects of environmental control through hand hygiene on clinical outcomes, achieving a dramatic decrease in puerperal mortality with the widespread use of aseptic techniques, in which practitioners cleaned their hands with chlorine solution in between patients.[3,4]

Although it took decades before the medical community accepted this discovery, infection control practices have changed the practice of medicine, have improved patients' outcomes, and have become the law of the land.[5,6] For immunocompromised patients, infection control strategies are a fundamental part of modern oncologic care and comprise a multilevel approach, including the patient, the health care environment, the community, and health care workers (Fig. 1).[7-9] Guidelines for infection control and prevention (ICP) in patients with hematologic or oncologic malignancies are centered on recommendations for hematopoietic cell transplant (HCT) recipients[10] and have typically been based on principles of hand hygiene, air quality, barrier isolation (eg, the use of gowns, gloves, masks, and eye protection, depending on the type of exposure), endogenous flora suppression by prophylactic antibiotics, and the prevention of device-related infections (eg, central venous catheters and urinary catheters).[11,12] An equally relevant aspect of ICP for patients with cancer is the recognition of higher rates of colonization and infections by multidrug-resistant organisms (MDROs), such as vancomycin-resistant *Enterococcus* (VRE), methicillin-resistant *Staphylococcus aureus* (MRSA), and multidrug-resistant Gram-negative bacilli (MDR-GNB), and *Clostridium difficile* compared

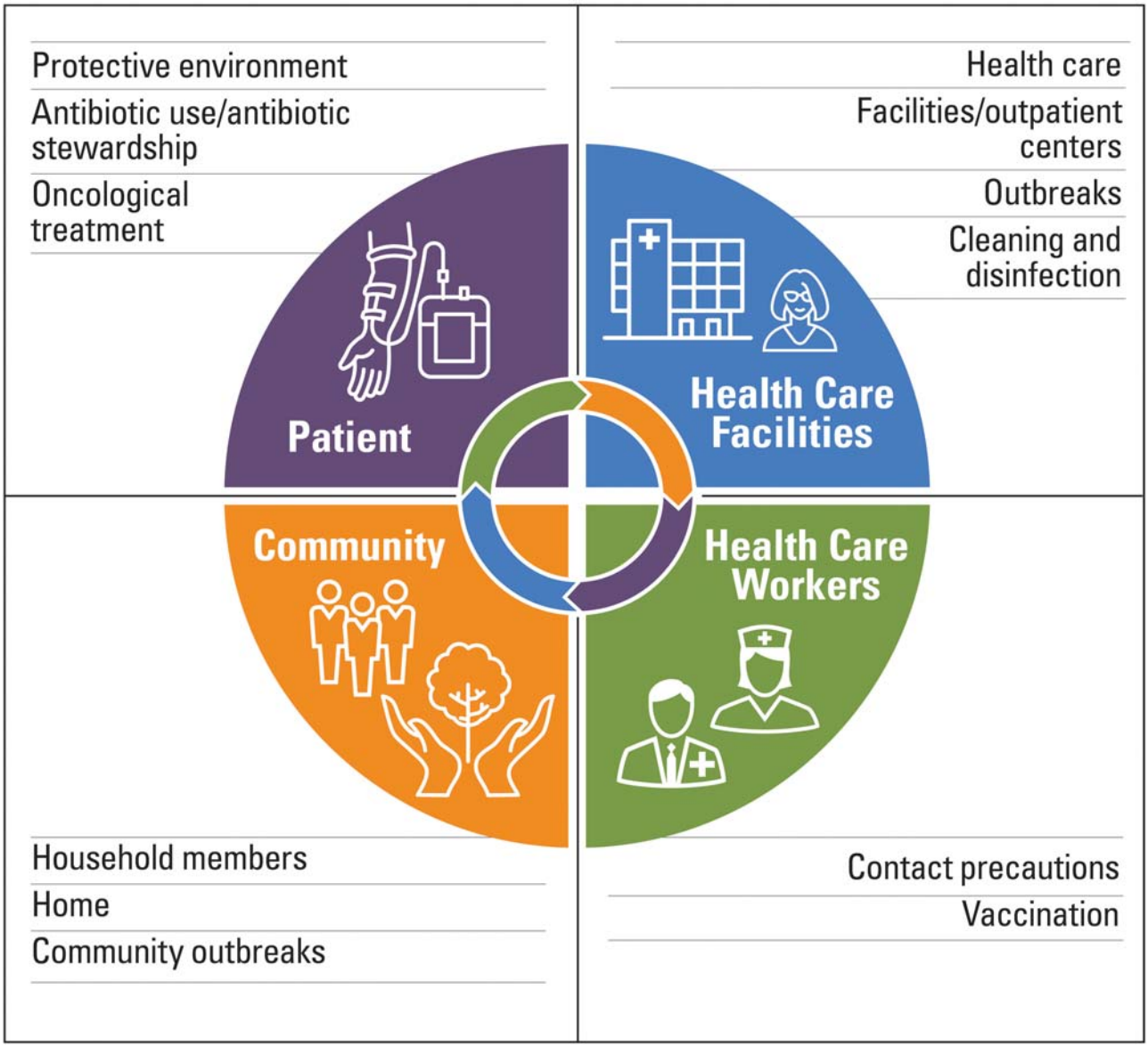


FIGURE 1. Important Aspects of Infection Control and Prevention in Patients Living With Cancer.

with the general patient population.[11,13,14] Well known risk factors associated with the transmission of these MDROs include: hematologic malignancy; neutropenia; frequent contact with the health care environment; multiple and/or prolonged hospitalizations; devices, including urinary catheters and central lines; as well as changes in the microbiome driven by the use of antimicrobial agents and chemotherapy.[13-16] The reported colonization rates by MDROs in various populations of patients with cancer are from 4.7% to 36% for VRE,[15,16] from 5% to 10% for MRSA,[17] from 7% to 18% for *C. difficile*,[18,19] and from 3% to 29% for MDR GNB.[14,20-22] Moreover, intestinal colonization with VRE and extended-spectrum β-lactamases (ESBL) *Escherichia coli* has been associated with an increased risk ratio (RR) of developing bloodstream infection (BSI) with these organisms (ESBL BSI: RR, 4.5; VRE BSI, RR, 10.2).[22]

Emerging disciplines, such as outpatient cancer care and the entailed infection control practices (including up-to-date immunizations, community respiratory viruses, and prolonged shedding),[23] the role of antibiotic stewardship,[24] and the use of whole-genome sequencing (WGS) for outbreak investigations,[25] have great applications in ICP for patients living with cancer. However, there is no clear consensus or guidance on the variety of ICP strategies; recommendations for these practices are mainly center-adapted.[26,27] In this review, we discuss key aspects of robust, comprehensive ICP programs, not only for hospitals specialized in cancer but for all centers that care for oncological

patients, including practical algorithms and new approaches and technologies for enhancing these practices.

Preventing Infection

Hand Hygiene

Washing hands remains the main transmission-based precaution for preventing the spread of pathogens, and it has been the foundation of every ICP program.[28-30] Hand hygiene must be on the frontline in the care of patients living with cancer, because health care-associated pathogens can be recovered from infected or draining wounds,[31,32] from colonized areas of a patient's intact skin,[33] and from the patient's surrounding environment.[34,35] In 2006, the World Health Organization launched the "My Five Moments for Hand Hygiene" campaign, which defines key moments to perform hand hygiene based on known mechanisms of microbe cross-transmission between patients, the environment, and health care workers, including: 1) before touching a patient; 2) before cleaning/aseptic procedures; 3) after body fluid exposure/risk of such exposure; 4) after touching a patient; and 5) after touching a patient's surroundings.[36]

Simple hand washing with soap and water will remove almost all transient Gram-negative rods in 10 seconds, and most recent evidence does not support the use of antimicrobial soap over regular soap and water.[36] Alcohol-based products have shown superior activity over water and regular soap, both before and after contact with patients, except in the case of exposure to *C. difficile* or norovirus pathogens.[37] The use of alcohol-based products may be associated with increased compliance of approximately 25%.[38] Regardless of the product used, hand washing is an important modality for the prevention of infection and should be performed by patients, visitors, and health care workers.[39]

Average compliance with hand washing for health care workers in medical and surgical intensive care units of private tertiary care hospitals reportedly ranges from 40% to 50%.[40,41] Reports on compliance with hand washing in oncologic centers are scarce, with a few publications on self-reported rates between 80% to 90% in a pediatric oncology practice in Italy[42] and 90% at a hematology unit in Brazil.[43] Research and long-term quality-improvement projects are needed to develop reliable and sustainable methods to ensure compliance with hand hygiene.[43] A study by Pittet et al showed an association between improved hand washing compliance, increasing from 48% to 66%, and a 40% overall decrease in the rate of nosocomial infections.[31]

In addition to strict hand hygiene, health care workers in cancer centers should avoid wearing artificial nails or extenders, because these have been associated with the transmission of pathogens, including Gram-negative organisms.[20]

Dietary Principles

On the basis of current evidence, following standard principles (such as avoiding unwashed fruits and vegetables as well as undercooked meats, seafood, and eggs) is advised for patients undergoing cancer treatment.[44-46] The US Department of Agriculture recommendations for food safety for patients with cancer include: 1) consumption of only pasteurized juices and dairy products; 2) washing hands in warm, soapy water before handling, preparing, and eating food; 3) consuming food that has not passed the expiration date; and 4) storing raw meat, fish, and chicken carefully in wrapped containers to avoid spillage of juice onto other foods. Notably, these recommendations do not restrict fresh fruits and vegetables.[47] Stricter restrictions are usually applied for stem cell transplant (HCT) recipients and neutropenic patients with an absolute neutrophil count below 500 cells/mm^3 and include avoidance of raw fruits and vegetables, undercooked meats, unpasteurized milk and cheeses, and well water from private or public wells.[48] However, there is no clear evidence that strict dietary restrictions are associated with a lower risk for infectious complications. Two recent studies have questioned the value of a neutropenic diet. A randomized study in 150 pediatric patients who were receiving myelosuppressive chemotherapy in which groups were assigned to either a neutropenic diet or US Food and Drug Administration-approved food-safety guidelines found no difference in the prevention of infections.[49] In fact, a retrospective evaluation of 726 patients at Northwestern Memorial Hospital reported a higher rate of infections in HCT recipients who followed a neutropenic diet compared with those who consumed a general hospital diet.[50]

Antibiotic and Antifungal Prophylaxis

Antibiotic prophylaxis is commonly followed in patients with hematologic malignancies and solid tumors who receive myeloablative therapy and develop profound neutropenia as well as in patients in the early post-transplant period. This approach has previously been shown to reduce the risk of all-cause mortality (RR, 0.52; 95% confidence interval [95% CI], 0.35-0.77) in earlier publications,[7,24,44,48] and there was an increased rate of GNB infections after quinolone prophylaxis was discontinued.[51] However, in a recent literature review from the European Conference on Infections in Leukemia, the authors concluded that, although quinolones were associated with a lower rate of Gram-negative bacteremia, they did not have an impact on mortality.[52] Therefore, the practice of quinolone prophylaxis needs to be constantly reevaluated, especially with regard to balancing antibiotic stewardship versus local susceptibilities to quinolones and an increased risk for drug-resistant infections, particularly with *E. coli* and *C. difficile*.[53,54]

Antifungal prophylaxis is used mostly in certain patients with high-risk cancer, such as patients with hematologic malignancies undergoing induction chemotherapy and high-risk transplant recipients, to decrease the incidence of *Candida* and *Aspergillus spp*. infections.[48,55] This practice has enabled the transfer of care from the inpatient to the outpatient setting for some chemotherapy regimens and low-risk transplant procedures.[56] The type of prophylaxis (eg, fluconazole vs broader triazoles with antimold properties) and the use of preemptive detection strategies (eg, galactomannan-β-D-glucan assays and chest-sinus computed tomography) are dictated by the host risk factors. High-risk patients for whom broader antifungal prophylaxis is indicated can include allogeneic stem cell transplant recipients with graft-versus-host disease, patients with acute myeloid leukemia who have prolonged neutropenia, or those receiving induction chemotherapy.[48,56,57]

Protective Environment

Protective hospital environments have been integral to preventing infection in patients with hematologic malignancies, especially patients with leukemia or those undergoing HCT, especially in recent decades.[58,59] A 2009 meta-analysis evaluated protective isolation measures and reported reductions in all-cause mortality and in infections linked to the use of antimicrobial prophylaxis (antifungals and antibiotics) in combination with barrier isolation and air-quality control (RR, 0.79; 95% CI, 0.72-0.87),[7] but not when isolation or air-quality control was the only prevention measured used.

Guidelines for health care facilities that house HCT recipients recommend specialized ventilation systems, including the use of laminar air flow units capable of 12 air exchanges per hour and high-efficiency particulate air (HEPA) filters. These filters maintain compliant indoor air quality by filtering 99.99% of particulates in the work area. Patient isolation units should use HEPA filtration with the capacity to remove particles greater than 0.3 μm, continuous pressure monitoring with positive air pressure between patients' rooms and the hallway, self-closing doors, and well sealed rooms.[10,20] A primary purpose of HEPA filters and laminar flow is reducing the risk of aspergillosis in high-risk patients (those with leukemia and those undergoing HCT); this reduction in risk has been shown in several studies.[60] Likewise, patients and health care workers should avoid construction areas because there is an increased risk for mold infections through an airborne route at these locations, and outbreaks of fungal infections because of construction have been reported.[61]

At our institution, we implement an ICP plan during construction, renovation, and structural repair activities that includes a barrier between construction and patients' areas with the aim of maintaining indoor air quality to prevent *Aspergillus* and other potentially pathogenic molds from being generated or released into the air. At our center, any activity that disturbs existing building features, possibly causing the release of harmful dust, warrants specific institutional precautions. All construction planning must comply with indoor air-quality requirements specified by an internal committee, and project contractors are required to provide personnel and equipment to contain and clean up dust and particulates in and around the work area, including dust mops, wet mops, adhesive walk-off mats, mop buckets, HEPA-filtered vacuums, and clean rags for removing dust inside and outside the construction site and from equipment.

Lastly, health care facilities are required to perform routine environmental (water) controls to prevent HAIs from water sources as hospital water systems are frequently identified as sources of health care-associated infections (HAIs), especially in immunocompromised individuals. These controls include the upkeep of a quality-managed water system, routine sampling and testing of water and surveillance for HAIs from water sources, and actions required in health care facilities if HAIs from water sources (eg, *Pseudomonas* infections, legionellosis, cryptosporidiosis, and atypical mycobacterial infections) are suspected.[62,63]

Isolation Precautions

Other contact precautions include the use of gowns or gloves, placing patients in a private room, or cohorting patients, which have been used within health care facilities to help contain pathogens to a restricted location. Contact precautions are recommended for patients who have viral infections and MDROs identified either by screening or from evidence of active infection.[11,20,64] The appropriate use of a mask and/or eye and face protection varies by type of pathogen, exposure, and other risks.

Because these interventions come with financial and social costs,[65,66] each center must delineate their own policies and periodically analyze the risks and benefits. There is growing knowledge regarding the role of the hospital environment and risk for nosocomial infections, which are discussed below.

Multidrug-Resistant Organisms and *Clostridium difficile*

The main risk factors for the acquisition of MDROs in patients with cancer are admission to an intensive care unit in the past 3 months, previous receipt of antibiotic therapy, and the use of a urinary catheter.[67] Patients with hematologic malignancies (acute leukemia in particular) or HCT recipients, who experience extended periods of neutropenia, are at the highest risk for complications because of MDROs

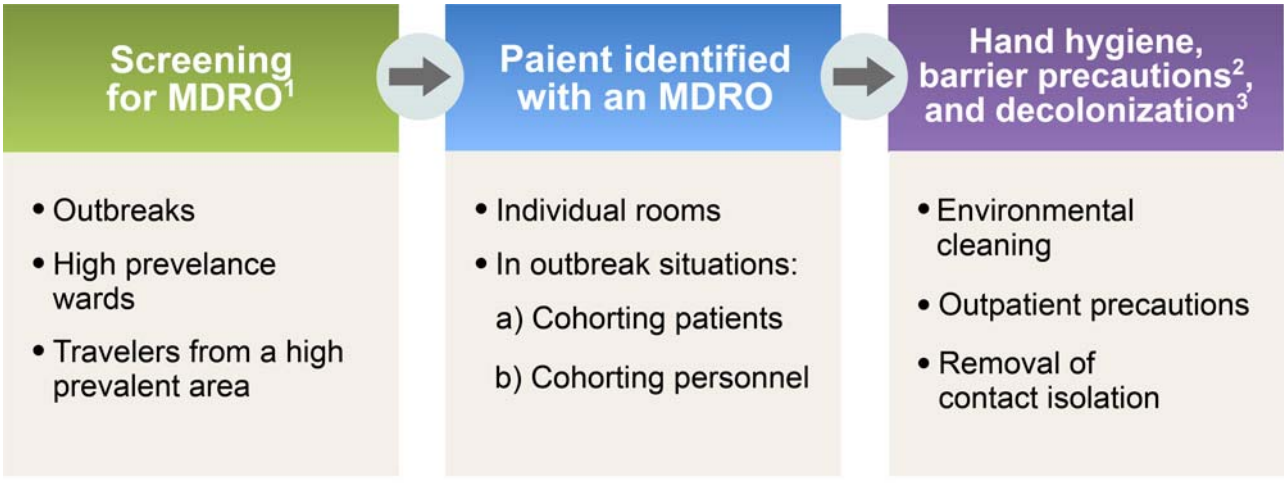
and have a high subsequent mortality rate of up to 80%.[68] Outbreaks because of MDROs in cancer centers have been reported, mainly from *Enterococci* and drug-resistant Gram-negative organisms.[69] Surveillance studies have demonstrated how being admitted to a hospital room that has been occupied by a preceding patient colonized with antibiotic-resistant bacteria could be a risk factor for acquisition of such organisms,[70] including MRSA,[71] VRE,[72] and *C. difficile*.[73]

Currently, there are not clear guidelines for the detection of MDRO colonization during hospitalization. The type and frequency of screening MDROs and the audience to which screening is directed varies among institutions owing to differences in patient populations, including high-risk inpatient groups, prevalence, and these measures also can change in an outbreak setting.[13,74] How often patients need to be screened is a matter of debate and depends on the type of organism and the center (Fig. 2). Other unanswered questions include the screening modality and the target organisms. The recent Society for Health Care Epidemiology of America (SHEA) guidelines highlight the benefits of screening for VRE colonization[75]; consequently, several institutions such as ours perform rectal screening for VRE in the hematologic services and intensive care units, both on admission and once a week.[11] Data are less clear between ESBL carriage and subsequent infections or outcomes, or the benefit of screening for MDR Gram-negative bacilli (MDR-GNB).[76] Recent publications suggest the need to screen patients or travelers from regions with high endemicity of MDR-GNB, such as the Middle East and Asia, or regions with recent outbreaks.[68] Recommendations are clear, however, that, once MDROs are detected, hospitalized patients should be on contact precautions to prevent horizontal transmission or hospital spread.[11,20] Most recommendations to reduce the transmission of MDROs in hospitalized patients involve a bundle of best practices, including hand hygiene, active screening of patients with swabs for cultures, contact barrier precautions, enhanced environmental cleaning, decolonization in the case of MRSA, and antimicrobial stewardship.[20,68]

Some practices, such as antiseptic whole-body washing or bathing of patients, have been shown by some researchers to reduce VRE and MRSA colonization and infections in hematologic units[77-79] and have been proposed by some for selected patients with recurrent MRSA soft tissue infections.[80] However, this impact has not been reproduced in other studies.[81] Interestingly, in a recent report, the use of a chlorhexidine wash was associated with an increased risk of infections caused by MDR-GNB, including carbapenem-resistant Enterobacteriaceae,[79] as well as the development of reduced susceptibility to chlorhexidine and the presence of efflux-mediated resistance genes in staphylococci.[82]

Multidrug-resistant gram-negative bacteria

Gram-negative organisms can develop resistance to β-lactams or carbapenems and many other antimicrobials, including quinolones, aminoglycosides, and polymyxins. The most common MDR-GNBs are ESBL-producing organisms, MDR-*Pseudomonas aeruginosa*, MDR-*Acinetobacter* spp., and carbapenem-resistant Enterobacteriaceae. A recent systematic review on the transmission of MDR-GNB



1. MDROs include: methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant enterococcus (VRE), and multidrug-resistant gram-negative (MDR-GNB).
2. Barrier precautions include gowns, and gloves.
3. Decolonization: may be consider in selected cases of recurrent soft tissue infection with MRSA, including mupirocin nasal ointment, and some data using full body wash with chlorhexidine soap.

FIGURE 2. Suggested Infection-Control Practices for Multidrug-Resistant Organisms (MDROs) in Cancer Centers.

showed that the hospital water environment was a key factor for transmission of MDR-GNB and for nosocomial infections, including clonal spread of MDR-*Klebsiella* spp.,[83] which has been linked to several nosocomial outbreaks.[35,84]

Active surveillance for MDR-GNB in patients without signs or symptoms of such infections is not recommended, except in the situation of an outbreak or infections with high prevalence at a specific ward or unit. However, in cases of outbreaks or a high prevalence of MDR-GNB, the application of bundle interventions can be effective as part of infection control measures in intensive care units.[85] A multifaceted intervention in an oncological intensive care unit, including hand hygiene, contact precautions, and patient screening upon intensive care unit admission and weekly thereafter, along with environmental cleaning, resulting in a sustained decrease of MDR-*Pseudomonas* infection and colonization[86]; however, the effectiveness and sustainability of these best practices in the long term are still undetermined.[86]

Vancomycin-resistant enterococci

VREs usually are not highly pathogenic and tend to cause more colonization than infection. However, in a recent meta-analysis that included adult and pediatric patients diagnosed with VRE infection, VRE was associated with an increase in hospital mortality, even in a nonimmunocompromised population.[87] VRE colonization rates in HCT recipients are 6% to 40% at admission, and VRE colonization has been associated with an increased risk for VRE BSIs.[88,89] In patients with hematologic malignancies, active surveillance for VRE by rectal swabs on admission and weekly thereafter, with subsequent isolation if the patient is VRE-positive, has been shown to decrease the incidence of VRE nosocomial infections by decreasing rates of nosocomial transmission.[15,16,75,89]

Clostridium difficile

Collateral damage from antimicrobial use includes alterations in the normal intestinal microbiota, creating the right environment for *C. difficile* infection (CDI).[41,42] Several studies have demonstrated that the risk for *C. difficile* is higher in HCT and solid organ transplant recipients than for other hospitalized or surgical patients, particularly in the setting of graft-versus-host disease, given the potential for damage to the gut luminal mucosa and the need for additional immunosuppression.[14,18] Incidence has been estimated between 5% and 27%, with higher rates in patient after HCT.[14] Environmental contamination by *C. difficile* spores plays a major role in horizontal transmission to patients and subsequent infections.[90] Certain strains of *C. difficile* that are known to hypersporulate have been linked to several outbreaks.[91] Therefore, patients with *C. difficile* should be placed under contact precautions; all personnel should wear gowns and gloves, whether or not they anticipate touching the patient's environment. Hand washing with soap and water and thorough cleaning of all potentially contaminated surfaces with a 1:10 dilution of concentrated sodium hypochlorite are recommended and may reduce the environmental burden of *C. difficile*.[92] A multicenter survey to determine the rates of CDI in patients with cancer and in HCT recipients assessed isolation practices and found great variations across all centers. Most centers kept patients on isolation until the resolution of gastrointestinal symptoms, but few centers did so for the entire duration of hospitalization.[93]

Viral Infections

Respiratory viruses

Respiratory viral infections can cause high morbidity and mortality in patients with cancer. Respiratory viruses spread primarily through exposure to respiratory droplets expelled during coughing or sneezing from infectious individuals. Droplet transmission is associated with particles greater than 5 μm in diameter that do not remain suspended in the air, and airborne transmission is associated with particles 5 μm or less in diameter that remain suspended in the air for a long time.[94] Current ICP measures for respiratory viruses are intended to prevent droplet, contact and, for some viruses, airborne transmission.[95] Furthermore, outbreak of respiratory viral infections can be fatal in some patients receiving cancer therapy.[96-98] Therefore, preventing the exposure and spread of respiratory viruses is of utmost importance and involves not only patients but also visitors and hospital personnel. Health care workers and visitors with respiratory viral infections should abstain from direct contact with immunocompromised patients until symptoms of infection resolve.

A lack of data precludes recommendations regarding the routine testing of asymptomatic patients for respiratory virus infections. However, active surveillance of patients living with cancer who have signs and symptoms of respiratory viral infection is strongly indicated.[23,99] Some respiratory viruses, including respiratory syncytial virus, influenza viruses, and human metapneumovirus, are seasonal and occur most commonly in winter; however, perennial infections have been reported with other viruses, such as parainfluenza viruses, adenovirus, rhinovirus, and coronavirus.[99,100] Patients who have symptoms compatible with respiratory viral infection should be placed on contact precautions while diagnosis is underway.[99,101-103]

A recent meta-analysis by Cochrane showed that the spread of respiratory viruses can be prevented by hygienic measures, such as barrier precautions and hand washing.[101] Different modalities of isolation by viruses are portrayed in Table 1,[94,102,104-123] including current recommendations by

TABLE 1. Recommendations for Contact Precautions for Respiratory Viral Infections

VIRUS	MODE OF TRANSMISSION	PRECAUTIONS RECOMMENDED		REPORTS OF OUTBREAKS IN HEMATO-ONCOLOGY UNITS
		ASBMT	MD ANDERSON CANCER CENTER	
Respiratory syncytial virus	Small and large droplets and fomites[102]	Contact	Droplet and contact	Stem cell transplant units[104-106]
Parainfluenza viruses	Large droplets and fomites[107]	Contact	Droplet and contact	Pediatric[108] and adult hematology[109]
Influenza viruses	Large and small droplets and fomites[94,110]	Droplet	Droplet and contact	Pediatric hematologic unit[111] and pediatric oncology[112]
Adenovirus	Large and small droplets and fomites[113]	Droplet and contact	Droplet and contact	Stem cell transplant units[114,115]
Coronavirus	Large droplets and fomites[116,117,a]	Contact	Droplet and contact	No reports in patients with cancer[a]
Rhinovirus	Large droplets and fomites, with recent data indicating small droplets[117,118]	Contact	Droplet and contact	Hemato-oncology wards[119]
Human metapneumovirus	Small droplets, close contacts, and fomites[120]	No recommendation	Droplet and contact	Hematology unit[121]

Abbreviation: ASBMT, American Society of Bone Marrow Transplantation. [a]Reports on Middle East respiratory syndrome in the nonimmunocompromised population indicate that the virus can be transmitted on large droplets and fomites, and there is potential for animal-to-human transmission. Adapted from: Ho KY, Singh KS, Habib AG, et al. Mild illness associated with severe acute respiratory syndrome coronavirus infection: lessons from a prospective seroepidemiologic study of health-care workers in a teaching hospital in Singapore. *J Infect Dis*. 2004;189:642-647[122]; and Patrick DM, Petric M, Skowronski DM, et al. An outbreak of human coronavirus OC43 infection and serological cross-reactivity with SARS coronavirus. *Can J Infect Dis Med Microbiol*. 2006;17:330-336.[123]

the American Society of Blood and Marrow Transplantation guidelines and standard practices at our own institution. Emerging data regarding enhanced isolation precautions, including contact and droplet precautions for all respiratory viruses, showed a 39% reduction in nosocomial infections.[124] Furthermore, the importance of health care workers' compliance with masking was evident in a recent study from Duke University Medical Center, in which universal masking was associated with a reduction in respiratory viral infections.[125] While this practice has several drawbacks, including long-term compliance and the possible perception of a barrier between patient and provider, it does bring up the importance of health care workers' compliance with ICP, especially during the active respiratory season and during outbreaks.

In addition, in immunocompromised patients, shedding of respiratory viruses can be prolonged to more than 30 days and, in some instances, up to 160 days[117,126,127] or even a period of years, especially in transplant recipients on steroids.[126] Prolonged shedding of respiratory viruses in an immunocompromised host needs to be considered when establishing ICP in the inpatient and outpatient setting to limit horizontal transmissions.[126]

Gastrointestinal Viruses

Gastrointestinal viruses are most commonly transmitted by the fecal-oral route, but reports of airborne transmission also have been established.[128] Several nosocomial outbreaks have been linked to norovirus and rotavirus in pediatric oncology units in association with shared toys.[129-131] These organisms can survive on nonporous surfaces for several days and require strict infection control precautions, including contact precautions and environmental cleaning.[131] In the case of norovirus, soap and water are needed for hand washing, and sodium hypochlorite is required for environmental cleaning.[132] As with respiratory viruses, prolonged shedding from the gastrointestinal tract is common and has been linked to nosocomial infections.[133]

Catheter-Related Infections

Important risk factors associated with hospital-acquired infections in patients living with cancer are the use of invasive medical devices, especially central lines, indwelling urinary catheters, and intratracheal tubes. In this section, we discuss central line-associated BSIs (CLABSIs).

In patients receiving oncological treatments, central venous catheters are commonly used for venous access for chemotherapy, blood transfusions, and intravenous fluid administration. The presence of these catheters is associated with increased risk for BSIs.[134] CLABSI is a surveillance definition used by the Centers for Disease Control and Prevention (CDC) and the National Health Safety Network as follows: recovery of a pathogen from a blood culture (a single blood culture for an organism not commonly present on the skin and 2 or more blood cultures for an organism commonly present on the skin) in a patient who had a central line at the time of infection or within 48 hours before the

development of infection. CLABSIs also must meet the following criteria: 1) the patient has a recognized pathogen culture from one or more blood cultures, and the organisms cultured are not related to an infection at another site; and 2) the patient has at least one of the following signs or symptoms within 24 hours: fever, chills, and hypotension.[135] Furthermore, in 2013, the National Health Safety Network and the CDC added a definition for CLABSI that applies to patients with hematologic malignancies and/or HCT recipients: mucosal barrier injury laboratory-confirmed BSI, which is defined by either only an intestinal organism or only viridans group streptococcus; by allogeneic transplant within the past year with grade 3 or 4 graft-versus-host disease, or more than a single liter of diarrhea, or neutropenia with an absolute neutrophil count below 500 cells/mm^3 within 7 days of the positive cultures.[136,137]

In recent studies, the reported catheter-related infection rate in adults with cancers was from 0.02 to 3 per 1000 catheter-days,[138] and the incidence of exit-site infection ranged from 1.9% to 60.9%.[139,140] Risk factors reported for CLABSI in patients with cancer include thrombosis, difficulty during the insertion procedure, total parenteral nutrition, neutropenia, age, hematologic malignancies, and HCT.[138,141,142]

The central venous port has grown in importance in cancer centers because of its advantages over central venous catheters, including the reduction of contamination of the device by external or skin pathogens, with an incidence of port-related infection that varies between 0.9% and 5.4%.[143,144] Compared with the incidence of CLABSI for tunneled lines (hazard ratio, 1.77; $P \leq .011$), nontunneled central venous catheters have a higher incidence of infection (hazard ratio, 3.50; $P < .0001$),[142,145,146] with the exception of peripherally inserted central catheters, in which the incidence rate of infection has been low, between 0.5 and 0.95 per 1000 catheter-days.[147,148]

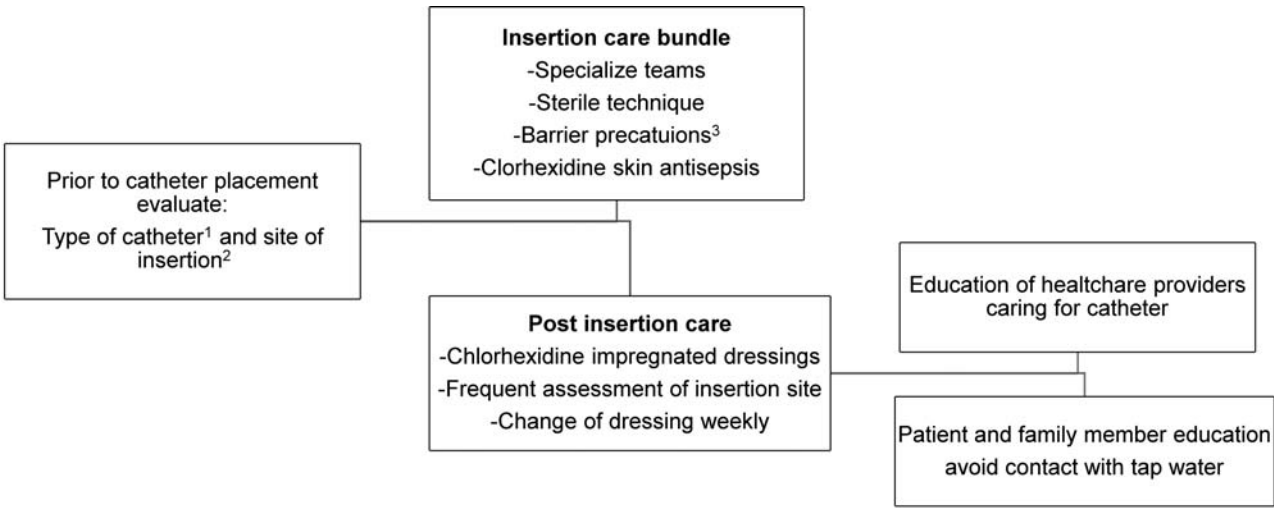
In terms of site, CLABSI is generally more common when catheters are inserted in the femoral veins and, probably to a lesser degree, in the internal jugular veins compared with the subclavian veins.[149,150]

The most commonly reported causative pathogens in catheter-related infections remain coagulase-negative staphylococci, *S. aureus*, *Enterococcus* spp., and *Candida* spp. Gram-negative organisms accounted for 19% of CLABSIs reported to the CDC and for 21% of CLABSIs reported to the Prevention's National Healthcare Safety Network (NHSN).[151,152] Because bacteria can enter the catheter through migration of skin organisms, the most common etiology of CLABSI is the contamination of the hub by hand manipulation or blood products.[134,153,154] Thus aseptic techniques during catheter insertion, specialized "intravenous teams," and postinsertion care bundles are best practices that have been shown to decrease the rates of CLABSI, especially for short-term catheters.[155-157] In addition, recognized postinsertion practices that reduce the rates of CLABSI include the use of chlorhexidine gluconate-impregnated dressings,[158] assessment of the insertion site, change of dressings weekly or as needed, scrubbing the hub for 15 seconds or more before access, clot prevention strategies, continuous reevaluation of the need for the catheter,[134,159,160] and the use of an antiseptic barrier cap using alcohol-impregnated port protectors. Regarding the barrier cap, 2 recent studies demonstrated a 34% reduction in hospital-wide CLABSI rates.[161,162]

Further modalities for the prevention of CLABSI, especially for long-term catheters, include: 1) catheters impregnated with minocycline-rifampin[134,163]; and other antimicrobial and antiseptic preparations[164] and 2) lock solutions containing minocycline and ethylene diamine tetraacetate (M-EDTA),[165] or ethanol locks.[166] The use of ethanol locks lessens concern for antibiotic resistance compared with antibiotic-coated catheters or antibiotic-based lock solutions[165,167]; however, concerns about protein precipitation with ethanol locks warrant further studies before these locks can be routinely recommended. Continuous education and training of health care workers, regular audits of bundle implementation, and engagement of patients and caregivers are key for the long-term prevention of CLABSI (Fig. 3).

Surgical Site Infections

The incidence of surgical site infections (SSIs) in patients with oncological diagnosis has been reported to be between 3.2% and 7.9%[168] and is similar to that of patients without malignancies. The most frequent organisms found at surgical sites in patients with malignancies are Gram-positive bacteria, specifically *S. aureus*, as in the general population. However, the rates of MRSA infections can be higher in patients with cancer than in those without cancer (up to 40%),[169] and, more recently, different authors have reported higher rates of GNB, *P. aeruginosa*, ESBL-producing organisms, and other MDROs, such as VRE.[169-171] In general, however, the isolated organisms depend on the type of surgery, as shown in a retrospective review from The University of Texas MD Anderson Cancer Center (MD Anderson), where *S. aureus* was the predominant organism in SSIs after breast cancer surgery, thoracotomy, craniotomy, and abdominal/pelvic surgery; however, 42% of SSIs were polymicrobial, with *P. aeruginosa* and *E. coli* being the predominant organisms among the GNBs.[169] Prevention strategies for SSIs include enhanced nutritional support; preoperative bathing; decolonization with mupirocin ointment with or without chlorhexidine body wash for MRSA nasal carriers;



1. Infection rates lower with non-tunneled catheters and peripheral inserted catheters. Consider antibiotic impregnated catheter
2. Risk of infection is highest for femoral , second highest for internal jugular and lowest for subclavian site.
3. These precautions include a large sterile drape, gown, mask, cap, and sterile gloves during insertion

FIGURE 3. Algorithm for the Prevention of Central Line-Associated Blood Stream Infection (CLABSI).

surgical site preparation with alcohol-based, antiseptic solutions that contain chlorhexidine gluconate; and, mainly, timing and stopping at 24 hours of the appropriate perioperative antimicrobial prophylaxis.[169,172]

Environmental Cleaning

There is growing knowledge about the role of the health care environment as a reservoir of and vehicle for the transmission of various pathogens and how environmental cleaning and sterilization practices can help decrease the transmission of HAIs.[35] For patients with cancer who are in constant contact with the health care environment, this role is of paramount importance. Survival times of organisms on dry, inanimate objects vary according to temperature, humidity, and surface type[173,174] and have been reported to be several days (>12 days) for viruses,[175] 2 months for MRSA, and up to 36 months for VRE.[84,176] These organisms can thereby be a continuous source of hospital-associated transmission of infections.

Environmental cleaning is typically performed manually using disinfectant agents, including hypochlorous acid, hydrogen peroxide, and paracetic acid; however, studies have shown that manual cleaning is not predictable and depends on the education of cleaning personnel and nurses and the appropriate amounts of disinfectant solutions,[177] with reports indicating that only about 47% of surfaces are appropriately disinfected.[41,178]

Environmental cleaning also can be supplemented by using automated technologies (also known as no-touch disinfection methods), including aerosol and hydrogen peroxide vapor systems such as microcondensation systems, which have shown effectiveness in cleaning MRSA, *C. difficile*, and *Mycobacterium tuberculosis*; and, although several studies have shown that these are effective decontamination methods (especially microcondensation systems), the costs and room turn-around times have hampered adoption of this technology in health care settings,[41] and mobile devices that emit continuous ultraviolet (UV-C) light have become more popular. In particular, a portable UV light germicidal device using pulsed xenon lamps (PX-UV) has been shown to be a safe, easy-to-operate, and effective system for decreasing the number of pathogens in the environment. PX-UV uses a xenon flash lamp to generate broad-spectrum, high-intensity UV light to deactivate and kill bacteria, spores, and viruses on high-touch surfaces in 5 minutes or less.[179] PX-UV was evaluated in clinical hematologic and bone marrow units, and it provided an overall reduction of 90% in total aerobic colony counts compared with a 76% reduction with manual cleaning.[180] At MD Anderson, we observed that PX-UV light was noninferior compared with bleach for decreasing *C. difficile* spores from patients' rooms,[181] as described in a recent systematic review of over 20 studies in which the use of automated UV-C light devices achieved a significant reduction in *C. difficile* infections (RR, 0.64; 95% CI, 0.49-0.84) and VRE infections (RR, 0.42; 95% CI, 0.28-0.65); however, there was no significant impact on the rates of infection with MRSA or MDR-GNB.[182] In a recent cluster-randomized, multicenter, crossover study, there was a decrease in the target organisms (mainly *C. difficile*) in exposed patients after adding UV-C light (using mercury devices) to standard cleaning, but this decreased rate was not associated with a change in

TABLE 2. Recommendations for Infection-Control Practices in an Outpatient Settings[a]

ASPECT OF CARE	RECOMMENDATIONS MUST INCLUDE GUIDANCE ON
Standard precautions	Hand hygiene, use of personal protective equipment (including gloves, masks, and gowns)
Respiratory hygiene and cough etiquette	Identification of potential respiratory infections, including asking about and separation of persons with respiratory symptoms
Injection safety and central venous catheter care	Safe practices for procedures
Cleaning and disinfection of devices and environmental surfaces	Patient areas, bathrooms, waste disposal, and cleaning spills of blood and body substances
Transmission precautions	Contact, droplet, and airborne transmission precautions according to facility protocol
Medication storage and handling	Both outpatient centers and patients at home
Dietary recommendations	In general, avoid nonpasteurized milk products; cheese with molds; raw or undercooked meat, poultry, fish, seafood, game, and tofu; undercooked eggs; unwashed fruits and vegetables; fresh store bought salsa or salads; unroasted nuts
Immunizations	Follow recommendations by the CDC, the IDSA on immunizations, the risk for transmission, and receipt of live-attenuated vaccines

Abbreviations: CDC, Centers for Disease Control and Prevention; IDSA, Infectious Diseases Society of America. [a]Adapted from: Division of Healthcare Quality Promotion, National Center for Emerging and Zoonotic Infectious Diseases, Centers for Disease Control and Prevention (CDC). Basic Infection Control and Prevention Plan for Outpatient Oncology Settings. Atlanta, GA: CDC; 2011. cdc.gov/hai/pdfs/guidelines/basic-infection-control-prevention-plan-2011.pdf. Accessed October 17, 2017[23]; Ariza-Heredia EJ, Kontoyiannis DP. Our recommendations for avoiding exposure to fungi outside the hospital for patients with haematological cancers. *Mycoses*. 2014;57:336-341[46]; and Sipsas NV, Kontoyiannis DP. Occupation, lifestyle, diet, and invasive fungal infections. *Infection*. 2008;36:515-525.[190]

the incidence of *C. difficile* infection.[183] Therefore, further data are needed to clearly determine the benefits of UV light, but enhanced terminal cleaning may be part of the solution. Some of the drawbacks for the use of automated methods has been cost-effectiveness and logistical problems, including the ability of the systems to reach certain areas, the need for furniture rearrangement in the rooms for its use, and longer cleaning times of an average 1 hour per room.[184] More recently, we were able to demonstrate equivalent efficiency in reduction of colony counts (approximately 73%) on high-touch surface areas between cycles of 2 and 8 minutes using the PX-UV system at a single position in the operating rooms.[185]

Outbreak Management

The future of outbreak investigation will include the integration of WGS, which allows strain characterization and epidemiologic investigation and will likely replace traditional methods of identification, such as pulsed-field gradient electrophoresis and other sequence-based methods.[186] WGS has yielded important insights into transmission pathways for several significant pathogens and has revealed outbreaks in situations in which standard infection control surveillance and definitions showed no indications of causative pathogens.[104,186] In a recent study at MD Anderson using WGS of VRE isolates, we demonstrated potential transmission networks between the patient and the environment within and between rooms as well as between patients within and between floors.[25] The limitations of WGS include the need for effective semiautomated pipelines, standardized quality control and data interpretation, bioinformatics expertise, and the infrastructure's cost.[187]

Outpatient Infection Control

Because cancer centers deliver most of their care on an outpatient basis,[188] ICP programs for this setting are of particular importance. Guidance for prevention in outpatient oncology settings has been published by the CDC. Key recommendations comprise the development of an outpatient infection prevention program that includes at least one individual with training in infection prevention, the establishment of infection prevention policies and procedures (ie, hand hygiene and standard precautions, use of personal protective equipment, injection safety, and environmental cleaning), as well as provision of the appropriate supplies necessary for adherence to standard precautions.[23]

Other important considerations beyond those of the CDC guidance include recommendations regarding diet; outdoor activities; hobbies; pet care; and immunizations of patients, family members, and health care personnel (Table 2).[8,23,46,189,190] In addition, managing the access of visitors during the respiratory viral season (usually during winter time) by screening for respiratory illnesses at the point of entrance, alerting about hand and cough hygiene, and

encouraging influenza vaccination are of utmost importance.[23] Similar practices should be upheld for health care workers,[125] particularly the receipt of influenza vaccination, because we recently demonstrated the relation between health care workers' vaccination and decreased rates of nosocomial influenza infection.[191]

Antibiotic Stewardship

The main goal of antimicrobial stewardship is to help optimize the use of antibiotic therapy through several strategies (including education and the development of guidelines), to increase drug safety, and to avoid antibiotic overuse and consequent antimicrobial resistance.[24,192] Because of the high risk of infectious complications in patients receiving cancer care, as well as the increased risk for MDROs and *C. diff*, there is increased interest in the role and importance of antimicrobial stewardship in cancer centers.[192] Several strategies used by different centers include antimicrobial cycling, antimicrobial restrictions, and computer-based programs.[24,192] According to a recent survey in US transplant centers, some of the tests perceived as useful for guiding antibiotic therapy include respiratory viral panels, testing for azole levels, and serum/bronchoalveolar lavage galactomannan.[27,193]

Future

The future of ICP practices in centers caring for patients with cancer will involve further work on environmental control, modern technologies that improve and facilitate cleaning of hospital surfaces, the role of microbiota-fecal transplant in the control of MDROs, and the use of lytic bacteriophages as part of controlling antibiotic-resistant bacteria not only in the clinical setting but also in applications to control bacterial food contamination.

Conclusions

The growth of the infection control discipline has played a vital role in the progress of cancer treatments, allowing patients to safely undergo new therapies. The application of current recommendations to cancer care and other health care environments must follow local patterns of infections; must continuously be reevaluated; and requires a multidisciplinary team, including infection control practitioners, physicians, nurses, and administrators, as well as a space for patients to voice their concerns. A good ICP program depends on current and open communication within the institution to ensure constant guidance on evolving infection control ICP practices, especially those that cover the needs of the immunosuppressed patient. ■

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