Management of Health-Care–Associated Infections in the Oncology Patient

By Peter C. Nowell, MD [2]

Each year, 2.4 million patients in the United States develop healthcare–associated infections (HAIs), requiring treatment at an annual cost of approximately $4.5 billion. HAI is the primary cause of death in approximately 30,000 patients and contributes to the death of 70,000 annually. Oncology patients are more susceptible than other patients to HAIs due to compromised immune systems, surgery (drains), invasive technology (catheters), and environmental factors. This paper will review each of these risk factors and discuss preventive steps such as a predictive index, antibiotic therapy, and infection control practices.

ABSTRACT: Each year, 2.4 million patients in the United States develop healthcare–associated infections (HAIs), requiring treatment at an annual cost of approximately $4.5 billion. HAI is the primary cause of death in approximately 30,000 patients and contributes to the death of 70,000 annually. Oncology patients are more susceptible than other patients to HAIs due to compromised immune systems, surgery (drains), invasive technology (catheters), and environmental factors. This paper will review each of these risk factors and discuss preventive steps such as a predictive index, antibiotic therapy, and infection control practices.

Health-care-associated infections (HAIs) pose a major public health problem for patients, their families, and society. According to the Centers for Disease Control and Prevention (CDC), 2.4 million patients in the United States developed an HAI in 1998. Among these patients, HAI was the primary cause of death in 30,000, and contributed to the deaths of an additional 70,000.[1] By contrast, 17,171 Americans died of the acquired immunodeficiency syndrome (AIDS) in 1998, and 44,190 died of breast cancer in 1997. These infections cost approximately $4.5 billion to treat. HAIs are defined as infections that develop within a health-care facility or are produced by microorganisms acquired during hospitalization.[2] They usually occur within 48 to 72 hours after admission to a healthcare facility. In most cases, HAIs become clinically apparent while the patient is still hospitalized, but they can develop after discharge for diseases with long incubation periods (such as hepatitis B) or as a result of early discharge or same-day surgery.

Most Common HAIs

The most frequent HAIs are urinary tract infections, pneumonia, surgical site infections, and bloodstream infections. Although urinary tract infections are the most common, they are not associated with high morbidity rates in otherwise healthy patients. However, they do present a problem in immunosuppressed cancer patients and can lead to bacteremia as a result of long-term catheter use.[3]

Pneumonia is the second most common HAI in the United States. Most health-care-associated pneumonia is caused by aspiration of bacteria colonizing the patient's oropharynx or upper gastrointestinal tract. Seventy different underlying diseases are considered strong predictors of death in patients with pneumonia.[4-6] The CDC guidelines for the prevention of health-care-associated pneumonia have identified a variety of risk factors, including immunosuppression in the presence of underlying diseases such as Legionnaire's disease, aspergillosis, respiratory syncytial virus, and influenza.

Surgical site infections are the third most frequent HAI and are associated with high morbidity and mortality rates. Cancer patients often receive drains after their surgery, and this puts them at high risk for an HAI.[5]

Finally, bloodstream infections (bacteremia) account for about 200,000 HAIs each year and are related to the use of some intravascular catheter devices.[6] Cancer patients frequently receive treatment via Hickman catheters or intra-arterial devices that remain in place long-term, and thus, carry a risk of infecting the blood with bacteria. Mortality from bacteremia can be as high as 20%.[7]
This paper will review specific risk factors for HAIs in oncology patients, reported outbreaks of HAI, and preventive programs.

**HAI Risk Factors in Oncology Patients**

Oncology patients are more susceptible than other patients to acquiring an HAI because of compromised immune systems, surgery, the use of invasive technology (ie, catheters), and environmental factors. Each of these risk factors are discussed in light of current research in infection control.

**Compromised Immune System**

The susceptibility of oncology patients to HAIs is related to the underlying malignancy, treatment, and the immune response. Any malignant process will diminish host defense capabilities to some degree. For example, patients receiving stem cell transplants are at higher risk of developing an HAI than are patients with solid tumors because of prolonged neutropenia and the graft response. Alternatively, patients with impaired humoral immunity are at greater risk for HAIs with encapsulated organisms such as *Streptococcus pneumoniae* or *Cryptococcus neoformans*. Increased use of indwelling tubes, transplanted tubes, and potent drugs also diminish the host's immune response and make patients more susceptible to bacteremia, pneumonia, or urinary tract infection.

Antineoplastic chemotherapies have improved survival rates but are also associated with more severe, prolonged immunosuppression, and in turn, a higher susceptibility to HAIs. A few studies have shown that adult cancer patients are at greater risk for HAIs than adults treated in highly attended intensive care units.[8,9] Velasco et al reported on a comparison of device use and health-care-associated infections and found a strong correlation between the presence of a central venous catheter (CVC) and HAI development.[10] Moreover, they found that the median infection rate was much higher in the oncology intensive care unit than in the nononcology intensive care unit—50.0 infections per 100 patients or 91.7 infections per 1,000 patient days compared to 9.2 infections per 100 patients or 23.7 infections per 1,000 patient days—and concluded that this was the result of a combination of factors related to underlying illnesses, neutrophil count, and the use of invasive procedures and catheters.

**Surgical Intervention**

A total of 27 million surgical procedures are performed each year in the United States, leading to the development of at least 920,000 surgical wound infections.[11] Surgical site infection rates ranging from 1.5% to 13.0% have been reported.[12-15] Studying cancer patients only, Barber et al found an 8.03% rate of surgical site infections.[16]

Treating patients who have intraabdominal cancer requires aggressive surgical intervention for proper diagnosis, staging, and cure and carries a high incidence of surgical site infections.[17] Moreover, surgery for abdominal cancer is associated with a higher degree of morbidity and mortality than other standard procedures.

A study at The Hospital of Cancer in Rio de Janeiro evaluated 236 consecutive patients who underwent surgery for intra-abdominal cancer. The surgical site infection rate was 22.5%, with 77 (32.6%) developing one or more infectious complications.[18] The researchers also found that the effect of antimicrobial prophylaxis decreased with increasing duration of surgery (> 2 hours). Factors associated with a significant risk of surgical site infections included duration of surgery beyond the predetermined cut-off point (5 hours), presence of remote infection at the time of surgery, length of preoperative stay (beyond 22 days), and use of abdominal drains. For surgeries that exceeded 5 hours, the infection rate jumped to 30.6% for the 215 to 300 minute range, and to 56.4% for the > 300 minute range. The mortality rate was higher among patients with postoperative HAIs than among patients without postoperative infections (24.7% vs 5%). Surgical site infections were the most prevalent (49.2%).

**TABLE 1**

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<thead>
<tr>
<th>Variables</th>
<th>Significantly Associated With Surgical Site Infections in Oncology Patients</th>
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<tr>
<td>Duration of Surgery (h)</td>
<td>0.301 (P = .001)</td>
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<tr>
<td>Preoperative Stay (d)</td>
<td>0.238 (P = .003)</td>
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<tr>
<td>Use of Abdominal Drains</td>
<td>0.265 (P = .002)</td>
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Similar results were reported by the National Cancer Institute in Mexico.[19] These investigators followed 3,372 surgeries to identify risk factors associated with infections in cancer patients. They found that surgical drains, diabetes, and obesity were associated with an increased risk of surgical site infections. The authors pointed out that, in their hospital, 57.5% of all surgeries require a drain. Moreover, they noted, in mastectomies and groin or axilla dissections, surgical drains remain in place for long periods, with the patient often being discharged with a drain in place. Emptying and cleaning the drain—often done by the patient—can allow bacteria to enter. Table 1 lists the significant variables associated with the development of a postoperative infection. It has been shown that drains placed through an operative incision increase the risk of surgical site infections,[20] and closed suction drains decrease the risk.[21]

**Invasive Technologies**

Potent neoplastic chemotherapies and advances in supportive care have resulted in prolonged survival rates for patients with malignancies. These powerful therapies have produced more severe and prolonged immunosuppression and thus a higher susceptibility to HAIs. In many cases, these HAIs stem from CVCs or intraarterial catheters.[22-24] The main sources of contamination are the hands of health-care personnel, the patient's own microflora, the needle hub, contaminated fluid, and contamination on insertion with subsequent spread through the bloodstream.

- **Central Venous Catheters**—Infection rates in one pediatric hematology/oncology study showed CVCs to be the most frequent source of HAIs.[23] Of 143 patients observed using a standardized surveillance system based on the National Nosocomial Infection Surveillance System, 28 (19.6%) had 40 documented HAIs, and the overall HAI rate was 10.8 per 1,000 patient-days. Of the 40 nosocomial infections, 26 (65%) were CVC-associated bloodstream or local infections more than any other cause of infection. Hospitalized patients are at great risk of acquiring infections via CVC, because the catheter is manipulated more frequently while they are in the hospital. The authors also noted that there is a higher degree of reduced compliance with the catheter-care protocol in a busy or overcrowded hospital environment than in a home-management program. Studies such as this one provide a good basis for recording specific infection rates in the hope of identifying risk factors that can be targeted with better preventive infection control programs. Hickman catheters are a specific type of CVC that are most commonly used in supportive care measures in oncology patients. In many hospitals, their use is preferred because of their low cost ($90 as opposed to a $450 implantable port system), durable nature, and lower risk of infectious complications.[25,26] One study of Hickman catheter-related infection in 316 cancer patients found that 156 (40%) acquired an infection. The risk of acquiring such an infection increased as the time the catheter remained in place increased, with a median time to infection of 90 days. A catheter-related infection developed in 50% at 90 days and in 62% by 180 days.[27] Peripheral inserted central venous catheters are associated with fewer mechanical complications and a lower rate of infection than are other nontunneled CVCs. This may be due to the fact that the antecubital fossa is less colonized, less oily, and less moist than the chest and neck.[28-30]

- **Intra-arterial Catheters**—Although intra-arterial catheters have been used for over 3 decades for infusion of chemotherapy, little has been published on associated infection complications. In 1979, Maki et al found a 1.6% risk of *Staphylococcus aureus* bacteremia with the use of intra-arterial devices.[31] However, this risk index was calculated during an outbreak. More recently, Raad et al reported a very low risk of bacteremia associated with intra-arterial devices and attributed their finding to a relatively short period in which the catheters were inserted (median: 1 day; range: 1-6 days, compared to a mean of 21 days in the previous studies).[24] Therefore, it appears that a short placement period and excellent sterile barrier precautions are associated with a low risk of infectious complications.

- **Prevention**—During the past decade, new technologies to prevent intravascular catheter-related bloodstream infections have been pursued.[32] Among the technologic advances shown to reduce the risk of bloodstream infections are (1) an iodinated alcohol solution in the catheter hub (which produced a fourfold reduction in incidence of infection),[33] (2) short-term placement of a chlorhexidine/silver sulfadiazine-impregnated catheter (catheters in place ≤ 10 days reduced infection from 52% to 3%),[34] (3) minocycline/rifampin-impregnated catheters (catheters in place for an average of 6 to 7 days had a lower incidence of infections than chlorhexidine-silver sulfadiazine-impregnated catheters,[35-37] as with other antibiotics, however, resistance may develop as their use becomes more widespread), and (4) chlorhexidine-impregnated sponge dressing (which produced a threefold reduction in infections).[38]
Finally, nontechnologic strategies for reducing the incidence of infection should include barrier precautions during insertion, specialized nursing teams, and prospective infection control surveillance.

Environment

Oncology patients—especially those with neutropenia—vary in their susceptibility to HAIs, depending on the severity and duration of immunosuppression. They are generally at risk for bacterial, fungal, parasitic, and viral infections from both endogenous and exogenous sources.[39] In addition, recent updates have shown that malignancy is a significant risk factor for vancomycin-resistant bloodstream infection. One study reported that mucositis was independently associated with vancomycin-resistant bloodstream infection and that the risk of this infection increased with increasingly severe mucositis.[40]

Although the incidence of vancomycin-resistant infections in oncology patients is related to a depressed immune system, other opportunistic organisms are seen more often in immunosuppressed patients and are referred to as environmental risk factors. For example, *Aspergillus* (a fungal organism) and *Legionella* (a bacterial organism) are associated with high mortality rates among oncology patients but are strongly associated with the environment. *Aspergillus* is commonly found in the soil, water, and decaying vegetation. The most important HAI caused by *Aspergillus* is pneumonia, and the primary risk factor is severe and prolonged granulocytopenia with bone marrow transplants. Mortality from Aspergillus has been reported to range from 13% to 80% in leukemia patients.[41] The presence of *Aspergillus* spores in the hospital environment has been linked to periods of construction or renovation during which the number of spores increases. Other sources of infection in the hospital have been traced to such reservoirs as contaminated fireproofing material, damp wood, and bird droppings in air ducts.[41] *Legionella* also manifests as pneumonia in the immunosuppressed cancer patient. It is commonly found in aquatic environments and may enter hospital water systems in low or indeterminable numbers.[41] Patients with a hematologic malignancy are at greater risk for *Legionella* infection than patients with a nonhematologic malignancy. The mortality rate is 40% among patients who acquire the bacteria nosocomially.[41]

Reported HAI Clusters and Outbreaks

Because cancer patients are classified as being at high risk for HAIs, it is important to identify risk factors for possible outbreaks in hospitalized cancer patients. Bacteremia is a frequent complication in this population. The greatest risk of infection occurs when the absolute neutrophil count drops below 500/mm². Cancer patients who are undergoing chemotherapy frequently have neutrophil counts below 100/mm² during prolonged periods of neutropenia.

In a study of gram-positive microorganisms as the cause of septicemia in cancer patients, gram-positive bacteria produced 1,073 monomicrobial bacteremias (49.5%), and gram-negative bacteria produced 733 such infections (33%).[42] The episodes of bacteremia or fungemia occurred during a period of neutropenia in 106 (58.6%) of 178 cases. This relative increase in bloodstream infections was not related to any specific source of contamination.

As approaches to the treatment of HAIs change, new invasive techniques tend to alter the mucosal skin barrier and allow the invasion of gram-negative microorganisms that colonize the skin. Drugs that were once highly active in the treatment of gram-positive infections now have little if any activity against gram-positive microorganisms. Also, antibiotic prophylaxis used to prevent bacteremias caused by gram-negative microorganisms allows increased colonization by gram-positive microorganisms.

An outbreak of water-borne gram-negative organisms among hematology/oncology outpatients enabled investigators to identify three risk factors—presence of a CVC, self-care, and longer duration of a recent hospital stay—to be associated with the development of bacteremia.[43] Although this study was retrospective, the authors noted that the likely sources of contamination were colonization of the patient's skin or needle hub during showering or the use of contaminated infusion solutions. *Bacillus*, an aerobic gram-positive bacteria, has also been associated with outbreaks. In one report, *Bacillus* species was isolated in 125 positive blood cultures taken from 39 cancer patients. The outbreak was traced to contaminated calcium gluconate solution and the presence of a CVC. Higher mortality rates were attributed to the patient's underlying diseases rather than bacteremias, but a
fourfold greater risk of death was observed in bacteremic patients.[44]

**Prevention and Future Developments**

Survival of immunocompromised patients, especially those with malignancies, depends mainly on the level of supportive care. Major advances in immunosuppressive therapy have extended the life span of cancer patients, but infections arising from host defense defects can jeopardize survival. Although surgical cancer patients should be no more susceptible to HAIs than other patients, those with altered immune systems and decreased neutrophil counts have a higher degree of morbidity and mortality due to postoperative infections.[17]

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<th>Risk Factors for Surgical Site Infections</th>
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With the purpose of developing a risk index for infections, Valesco et al in 1998 studied 1,205 patients who had surgery for malignant disease.[45] They identified six risk factors that predict the probability of acquiring a surgical site infection (Table 2). Patients with a score < 8 had a surgical site infection rate of 10.0%, whereas those with a score > 9 had a rate of 33.6%. This model would allow surgeons to modify their techniques and initiate selective intervention programs.

Appropriate antibiotic therapy in the cancer patient is another means of preventing infections. In 1998, Spanik et al looked at the outcome in 95 inappropriately treated patients.[46] In this group, 44% were given the wrong antibiotic, 18% received too short a course of appropriate antibiotics, and 14% were subjected to a delay in therapy for more than 48 hours after the onset of fever. The overall mortality for the inappropriately treated group was 45.3% vs 16.3% for the appropriately treated group. The authors suggested that educating physicians and developing clear guidelines for antibiotic use could decrease mortality in such patients.

Similar results were noted by Bodey et al in 1985.[47] They reviewed 410 episodes of health-care-associated *Pseudomonas* bacteremia occurring in cancer patients over a 10-year period. The overall cure rate was 62%. However, the cure rate for patients who received appropriate antibiotics was 67%, and for those who received inappropriate antibiotics, 14%.

Finally, hand hygiene—the single most important way to prevent the transmission of bacteria and HAIs—must be incorporated into all patient care practices. The use of alcohol-based hand rubs as the standard of practice for hand hygiene when hands are not visibly dirty should be followed by health-care workers treating the oncology patient.[48] Effective, ongoing, behavioral programs that involve patients, patient families, and health-care workers have been shown to increase hand hygiene compliance.[49,50]

**Conclusions**

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Oncology patients present a tremendous challenge to the health-care provider. Advanced technology and treatment options have improved long-term survival in these patients, but progress has been accompanied by many complications, including health-care-acquired infections. HAIs increase the length of hospitalization and cost of treatment, as well as mortality rates. In 1993, Shulkin et al performed an economic analysis of the care provided to cancer patients who were undergoing major abdominal surgical procedures. Compared with data from noninfected patients, infections added $12,542—a significant increase—to the cost of patient care.[51]

Although some of these infections cannot be prevented because of host factors, it is clear from the literature that certain steps can be taken to decrease the incidence of HAIs among oncology patients. Educating the health-care provider and the patient about hand hygiene, appropriate and timely use of antibiotics, careful insertion and monitoring of catheters, and preventive measures during construction can reduce the incidence of HAIs in oncology patients.

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References:


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