Evidence-Based Guidelines for the Management of Neutropenia Following Outpatient Hematopoietic Stem Cell Transplantation

Fran West, DNSc, APRN-BC, FNP, AOCN®, and Sandra A. Mitchell, CRNP, MScN, AOCN®

Economic reforms, expanded treatment options, and a focus on improved outcomes have created an impetus to shift care from the hospital to the outpatient setting. Hematopoietic stem cell transplantation (HSCT) in particular has moved to the outpatient setting because of treatment advances such as hematopoietic growth factors, newer drug delivery systems, and expanded homecare services (Dix & Geller, 2000; Meisenberg et al., 1997; Meisenberg, Gollard, Brehm, McMillan, & Miller, 1996; Schmidt-Pokorny, Franco, Frappier, & Vyhlidal, 2003). Evidence suggests that a decrease in complications associated with transplantation, especially those related to neutropenia, can offset the costs of using some of the newer and more expensive treatment options (Feders & Camp, 1999; Hartmann et al., 1997; Lee, Klar, Weeks, & Antin, 2000; Meisenberg et al., 1998). However, outpatient care delivery models place expanded responsibilities on patients and their families for the management of this treatment side effect. Proactive management of neutropenia is critical to decrease the depth and duration of neutropenia following HSCT, limit exposure to opportunistic and nosocomial pathogens, and ensure prompt intervention should febrile neutropenia or infection develop. Patient and family education, psychosocial support, and coordination of care are key nursing responsibilities.

Key Words: neutropenia, bone marrow transplant

Hematopoietic stem cell transplantation (HSCT) involves the transfer of stem cells to establish hematopoiesis in patients who have received myeloablative chemotherapy with or without whole body irradiation. Following high-dose therapy and HSCT, all patients experience a period of neutropenia. Outpatient care delivery models place expanded responsibilities on patients and their families for the management of this treatment side effect. Proactive management of neutropenia is critical to decrease the depth and duration of neutropenia following HSCT, limit exposure to opportunistic and nosocomial pathogens, and ensure prompt intervention should febrile neutropenia or infection develop. Patient and family education, psychosocial support, and coordination of care are key nursing responsibilities.

Prevention of infection places additional responsibilities on patients for careful hygiene, oral care, and dietary changes and can affect patients’ lifestyle and disrupt usual routines (Crighton, 2004; Poe, Larson, McGuire, & Krumm, 1994; Shelton, 2003; Smith & Besser, 2000). Neutropenia affects patients’ symptom experience and quality of life (Shelton, 2003). The symptom experience of patients with neutropenia is not well described, but studies suggest that it is associated with fatigue, malaise, and diminished functioning in activities of daily living (Coleman, Coon, Mattox, & O’Sullivan, 2002; Crighton). In an effort to improve the symptom experience for HSCT recipients in a cost-effective manner, evidence-based clinical practice guidelines are essential for the management of neutropenia (Kapustay & Buchsel, 2000; Smith & Hilner, 2001).

Because of the complexity of care required for transplant recipients, a multidisciplinary team approach to education and care offers substantial benefits for patients.
A multidisciplinary team usually includes representatives from nursing, pharmacy, infectious disease, dietary, medicine, and social service departments (Kapustay & Buchsel, 2000).

Various studies have examined neutropenia in select patient populations receiving specific treatments (Crawford et al., 1991; Feld, DePauw, Berman, Heatman, & Ho, 2000); however, research exploring the nursing management of neutropenic HSCT recipients is needed (Larson & Nirenberg, 2004). A review of the literature indicates that research focusing on quality of life, dietary restrictions, sexual health, skin and oral hygiene practices, and the efficacy of protective clothing and environments is needed to establish evidence-based practice guidelines for the management of neutropenia in adult outpatient stem cell transplant recipients (Crighton, Kerr, 1999; Larson & Nirenberg; Ljungman, 2000). Only through the concerted research efforts of all disciplines involved in patient care will improved outcomes and cost-efficiency be realized (Bums, Tierney, Long, Lambert, & Carr, 1995; Coleman et al., 2002; Demetri, 1999).

Overview of Hematopoietic Stem Cell Transplantation

Since the 1980s, HSCT has evolved from an experimental treatment for patients with advanced acute leukemia to a therapeutically effective modality for selected malignant and nonmalignant diseases (Boyiadzis & Pavletic, 2004). Reductions in treatment-associated mortality and improved supportive care have helped to make this accomplishment possible (Baron, Storb, & Little, 2003; Johnson & Quiett, 2004). Astute nursing care is essential to preventing treatment-related complications and death (Mitchell, 2001).

HSCT refers to a transplant using hematopoietic stem cells and other blood cells at various stages of differentiation and maturation. HSCT involves replacing diseased, destroyed, or nonfunctioning hematopoietic cells with healthy progenitor cells, also called stem cells. Stem cells are primitive cells capable of self-renewal and are pluripotent, which means they are capable of maturation into red or white blood cells or platelets. Stem cells may be collected directly from the bone marrow spaces by a bone marrow harvest procedure or from the peripheral blood by apheresis. HSCT is an important advancement in restoring hematopoietic function in patients whose bone marrow has been destroyed by high-dose chemotherapy and radiation therapy given to treat their underlying malignancy.

In autologous (using the patient’s own stem cells) and allogeneic (using donated stem cells) transplants, peripheral blood stem cells have become the preferred source of cells for grafting. Collection of cells through apheresis is easier for patients and less costly and may result in a more rapid recovery of neutrophil and platelet counts (Wagner & Quinones, 1998). Research is under way to examine whether nonmyeloablative conditioning regimens prior to HSCT, where lower chemotherapy doses are given with immunosuppression, offer any advantages over myeloablative approaches. Nonmyeloablative transplants may provide a treatment option for patients who cannot tolerate the toxicities of the traditional approach (Wong et al., 2003). These patients still may encounter many of the same problems as myeloablative transplant recipients, particularly infection and graft-versus-host disease.

Significance of Neutropenia

Neutrophils are the body’s first line of defense against microbial invasion. They constitute approximately 40%–60% of the total white blood cell count that usually ranges from 4,000–10,000/mm³. Neutrophils are classified as bands (immature neutrophils) or segmented cells, which are mature neutrophils. Neutropenia exists when the total number of circulating neutrophils decreases and is measured by the absolute neutrophil count (ANC) (see Figure 1). Severe neutropenia is defined as an ANC less than 500/mm³ or an ANC from 500–1,000/mm³ that is predicted to decrease to 500 cells/mm³ or less within a 48-hour period (Alcoser & Burchett, 1999; Dykewicz, 2001b). The National Cancer Institute’s (2003) Common Terminology Criteria for Adverse Events Version 3.0 categorizes neutropenia as grade I–V based on the numbers of circulating neutrophils (see Figure 2). When the ANC is less than 500/mm³ (grade IV), the patient’s ability to fight infection is severely compromised, placing the individual at risk for the development of a life-threatening infection.

Research also indicates that the frequency and severity of infection are inversely proportional to the ANC and duration of neutropenia (Alcoser & Burchett, 1999; Dykewicz, 2001a). The diminished quantity of neutrophils and the inflammatory cytokines they produce also can limit the classic signs and symptoms that usually are seen with infections. The only symptom associated with a life-threatening infection may be fever, but other symptoms of neutropenic infection may include chills, myalgias, arthralgias, cognitive or mental status changes, anorexia, nausea and vomiting, dyspnea or cough, fatigue, pain or irritation at the site of infection, tachycardia, tachypnea, hypotension, hypoxemia, and oliguria (Cosby, Holzemer, Henry, & Portillo, 2000; Klastersky et al., 2000; Paesmans, 2000; Shelton, 1999).

Ineffective management of neutropenia can result in delayed treatment of febrile neutropenia, sepsis, septic shock, and poorer patient outcomes and can increase the overall costs associated with transplantation (Freifeld & Pizzo, 1996; Lee et al., 2000). Patients who are undergoing HSCT have a wide range of additional factors, such as immunosuppressive therapy, previous infections, malnutrition, and underlying hematologic malignancies (see Figure 3), that place them at an even greater risk for developing prolonged neutropenia, subsequently increasing their risk for developing other critical complications (Cairoli et al., 2004; Centers for Disease Control and Prevention [CDC], Infectious Disease Society of America, & American Society of Blood and Marrow Transplantation, 2000; Johnson & Quiett, 2004; Lipschitz, 1999; Lyman, 1998).

Proactive management of neutropenia is critical to decreasing the depth and duration of neutropenia following HSCT, limiting exposure to opportunistic and nosocomial...
• Disease site and stage (Hematologic malignancy is at a greater risk than solid tumors.)
• Stage of disease (increased risk of infection in patients with advanced stage or recurrent disease)
• Previous chemotherapy treatment
• Previous treatment with monoclonal antibodies, such as rituximab and alemtuzumab
• Previous hematopoietic stem cell transplant (autologous prior to allogeneic)
• Splenectomy
• Severe hypogammaglobulinemia
• Prolonged or profound neutropenia
• Breaks in the mucocutaneous barriers
• Graft-versus-host disease
• Immunosuppressive therapy
• Poor nutritional status with weight loss of more than 5% in one month
• Poor performance status
• The following comorbid medical conditions
  – Hypotension
  – Dehydration
  – Diabetes
  – Respiratory compromise
  – Acute abdominal pain
  – Previous febrile neutropenia
  – Ischemic heart disease
  – Recent surgery
  – Congestive heart disease
• Frequent vascular access and other invasive procedures including bone marrow aspirate and biopsy, as well as urinary catheterization
• Hospital treatment setting
• Anemia (< 8 g/dl)
• Older than age 60
• Antifungal therapy within six months for fungal infection
• Antiviral therapy within six months for active viral infection

**Figure 3. Factors That Increase the Incidence of Neutropenic Complications Following Hematopoietic Stem Cell Transplantation**


Patients, pathogens, and encouraging prompt intervention should febrile neutropenia or infection develop (Freifeld & Pizzo).

### Preventing Neutropenic Complications

The supportive management of neutropenic patients after HSCT includes measures to reduce the risk of infection, interventions to ensure that infection and febrile neutropenia are detected and treated promptly, and strategies to limit the duration of profound neutropenia. Neutropenic precautions may include using prophylactic antimicrobial therapy, restricting diet, decreasing community exposure, and improving oral and hygiene care.

Three major phases occur during the recovery of the immune system in all HSCT recipients. Patients are at risk for certain infections during the time prior to engraftment as well as during their delayed immune recovery period. Most HSCT recipients experience neutropenia for about two to four weeks, with the first evidence of neutrophils appearing 9–11 days after transplantation. Granulocyte counts of more than 500 cells/mm³ usually are found from days 18–26. Engraftment occurs when a patient’s granulocyte count reaches 500 cells/mm³ and remains more than 500 cells/mm³ for three consecutive days (Alcoser & Burchett, 1999; CDC et al., 2000).

Phase I of the recovery period, which begins the day of transplant and continues through day 30 following transplant, is referred to as the pre-engraftment period. Although prolonged neutropenia occurs in phase I, patients in phases II and III are still at risk for opportunistic infection. This is because although neutropenia has largely resolved, the immune system remains compromised. HSCT recipients treated in the outpatient setting have numerous risk factors, including neutropenia, which increase the possibility for development of opportunistic infection during this period. Infection is the primary cause of morbidity and mortality during phase I. Infections that can occur during the second and third phases are identified in Table 1 (CDC et al., 2000; Miller, 2001; however, during the time prior to engraftment, both autologous and allogeneic patients are at risk for developing the same infections. Autologous transplant recipients usually experience a more rapid recovery of the immune system function in phase III than allogeneic transplant recipients. Strategies to prevent opportunistic infections should be based on whether patients received an autologous or allogeneic transplant and the phase of recovery.

The risk for infection is proportional to the severity of graft-versus-host disease. Donor-recipient histoincompatibility and graft-versus-host disease, which are major determinants of immune reconstitution, increase HSCT recipients’ risk for developing infections (Alcoser & Burchett, 1999).

Eighty-five to ninety percent of all infections that develop in febrile neutropenic hosts are bacterial (Pizzo, 1989). Bacterial pathogens usually come from the endogenous flora colonizing the gastrointestinal tract, skin, and respiratory and genitourinary tracts. Breaks in the mucosa allow these organisms to enter the bloodstream. Gram-negative organisms cause the most deleterious infections and had been the major cause of infections in neutropenic patients until more recent years when granulocyte infections began to increase as a result of the increased use of implanted catheters and prophylactic antibiotics. The most common gram-negative organisms and gram-positive–causing infections in neutropenic patients are *Enterobacteriaceae* or *Pseudomonas aeruginosa* and the Staphylococcus, Streptococcus, Corynebacteria, and Clostridia species, respectively (Freifeld, 1993; Pizzo; Rubin & Ferraro, 1993).

The cells located in the gastrointestinal tract and oral cavity rapidly divide and, as a result, are affected easily by the dose-intensive regimens used in the transplantation procedure. This can cause breaks to occur in the gastrointestinal tract and oral cavity, allowing pathogens to colonize these areas, enter the bloodstream, and ultimately render patients vulnerable to developing life-threatening infections. How the advent of nonmyeloablative peripheral blood stem cell transplants will affect the incidence and prevalence of post-transplant infections is unclear because these regimen can cause less intregumentary breakdown (Junghans & Marr, 2002; Ruiz-Arguelles et al., 2001; Slavin et al., 2004). However, agents such as fludarabine often are included in the conditioning regimen and have the propensity to cause profound deficits in cell-mediated and humoral immunity (Tam et al., 2004).

Developing an evidence-based protocol for the management of neutropenia in HSCT recipients who are seen primarily in an outpatient setting requires that the transplant team implements a program that includes efforts to limit environmental exposure, provide comprehensive care, and offer systematic education to patients and caregivers. Patients, as well as staff, should be empowered with the knowledge that will assist them in understanding the complications associated with neutropenia and the measures that can be taken to limit the extent and duration of neutropenia and the risk of infection (Miller, 2001; National Comprehensive Cancer Network [NCCN], 2004; Smith & Besser, 2000).

### Practice Guidelines

The CDC et al. (2000) developed evidence-based guidelines for the managing neutropenia and preventing opportunistic infections in patients following HSCT. NCCN (2004) also published supportive care guidelines for the management of neutropenia and fever, encompassing the care of neutropenic stem cell transplant
TABLE 1. RISK FACTORS AND COMMON INFECTIONS BY IMMUNE RECOVERY TIME FOLLOWING HEMATOPOIETIC STEM CELL TRANSPLANTATION

<table>
<thead>
<tr>
<th>PHASE</th>
<th>RISK FACTORS</th>
<th>ASSOCIATED INFECTIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>I: pre-engraftment (0–30 days post transplant)</td>
<td>• Prolonged neutropenia</td>
<td>• Gram-negative bacteria</td>
</tr>
<tr>
<td></td>
<td>• Breaks in mucosal barriers (e.g., skin, mouth)</td>
<td>• Gram-positive bacteria</td>
</tr>
<tr>
<td></td>
<td>• Vascular access devices</td>
<td>• Clostridium difficile</td>
</tr>
<tr>
<td></td>
<td>• Community exposure</td>
<td>• Fungi (e.g., Candida species, Aspergillus species)</td>
</tr>
<tr>
<td></td>
<td>• Seropositive viral status</td>
<td>• Herpes simplex virus</td>
</tr>
<tr>
<td></td>
<td>• Graft-versus-host disease</td>
<td>• Cytomegalovirus</td>
</tr>
<tr>
<td></td>
<td>• Immunosuppressive therapy</td>
<td>• Herpes zoster (rare)</td>
</tr>
<tr>
<td>II: postengraftment (30–100 days post transplant)</td>
<td>• Impaired cellular immunity</td>
<td>• Aspergillus species</td>
</tr>
<tr>
<td></td>
<td>• Cytomegalovirus reactivation</td>
<td>• Cytomegalovirus</td>
</tr>
<tr>
<td></td>
<td>• Graft-versus-host disease</td>
<td>• Varicella zoster virus</td>
</tr>
<tr>
<td></td>
<td>• Immunosuppressive therapy</td>
<td>• Human herpes virus 6</td>
</tr>
<tr>
<td>III: late phase</td>
<td>• Cell-mediated immune deficits</td>
<td>• Respiratory syncytial virus</td>
</tr>
<tr>
<td></td>
<td>• Deficits in humoral immunity</td>
<td>• Herpes viruses</td>
</tr>
<tr>
<td></td>
<td>• Chronic graft-versus-host disease</td>
<td>• Pneumocystis carinii</td>
</tr>
<tr>
<td></td>
<td>• Immunosuppressive therapy</td>
<td>• Epstein-Barr virus (rare)</td>
</tr>
</tbody>
</table>

Note. Based on information from Miller, 2001.

recipients. The recommendations concerning antimicrobial prophylaxis, dietary restrictions, oral care, hand washing and hygiene practices, measures to limit community exposure, central venous catheter care, the use of colony-stimulating factors (CSFs), and the management of febrile neutropenia provided in these guidelines will be synthesized and discussed here.

Antimicrobial prophylaxis: NCCN (2004) developed evidence-based guidelines for the management of neutropenia and fever. The recommendations include prophylactic regimens for bacterial and fungal infections and herpes simplex virus reactivation in seropositive patients. The NCCN guidelines also offer recommendations for evaluating and managing infections in specific body sites. Helpful guidelines are provided for treating febrile neutropenia, including selection of empiric antimicrobial therapy for initial management of neutropenic fever, and evaluating and managing persistent and recurrent neutropenic fever.

Comprehensive evidence-based recommendations for preventing opportunistic infections in HSCT recipients have been collaboratively developed by the CDC et al. (2000) and summarized by Dykewicz (2001b). The CDC et al. guidelines concluded that evidence supporting the use of prophylactic antibiotics in afebrile, asymptomatic neutropenic patients is lacking. These guidelines indicate that if prophylactic antimicrobials are a component of the supportive care of patients with neutropenia, the team should review institutional susceptibility profiles routinely (Alcaide et al., 1995; Cometta, Calandra, Bille, & Glauser, 1994). The guidelines also recommend that if a provider does elect antibiotic prophylaxis during periods of neutropenia, it should be used for the shortest period possible and with the fewest patients possible.

Selection of an agent for prophylaxis should be guided by the knowledge of the spectrum of organisms that will be covered, vigilance for the emergence of antibiotic resistance, and a prospective monitoring of the impact of prophylaxis protocols on the spectrum of superinfection (Viscoli & Castagnola, 2002; Wingard & Anaissie, 2004). Efforts continue to develop more effective and less toxic agents to prevent fungal infections in HSCTs (Hamza, Ghanoum, & Lazarus, 2004; Leather & Wingard, 2002). Table 2 summarizes and compares the NCCN (2004) practice guidelines and the CDC et al. (2000) guidelines in terms of their recommendations for antimicrobial prophylaxis in neutropenic stem cell transplant recipients.

Dietary considerations: The CDC et al. (2000) guidelines recommend dietary restrictions for neutropenic HSCT recipients: All foods should be well cooked, and all raw foods, including seafood, mayonnaise, and raw eggs, should be avoided during the neutropenic period.

According to Smith and Besser (2000), a wide variety of institutional dietary practices for patients experiencing neutropenia exists. Smith and Besser reviewed dietary recommendations for patients with neutropenia at 156 institutions and found that 78% percent of the institutions initiated restrictive diets for patients. Ninety-two percent of the institutions surveyed initiated dietary restrictions only when neutropenia was documented, and 9% of the institutions commenced dietary restrictions when chemotherapy treatment was initiated. However, no studies are available to support dietary restrictions as a method of decreasing infection risk (Larson & Nirenberg, 2004; Poe et al., 1994; Wilson, 2002). In addition, an integrative review (Moody, Charlson, & Finlay, 2002) concluded that many of the studies attempting to address the question of the efficacy of low microbial diets are confounded by concurrent environmental manipulations such as protective isolation.

Oral care: Mucositis caused by dose-intensive chemotherapy is a frequent and costly complication of HSCT, often resulting in significant morbidity, discomfort, and diminished quality of life (Sonis et al., 2001).

In patients with neutropenia, mucositis represents a significant risk factor for systemic infection; in turn, the grade and duration of neutropenia have a direct effect on the severity of mucositis that patients experience (Kostler, Hejna, Wenzel, & Zielinski, 2001; Peterson & Cariello, 2004). Owing to their compromised immune system, patients who have received HSCT are at high risk to develop a bloodstream infection such as streptococcus viridans, originating from the oral cavity (Grabert et al., 2001).

Recently, several agents, including keratinocyte growth factor (Finch & Rubin, 2004), glutamine (Savarese, Savy, Vahdat, Wischmeyer, & Corey, 2003), and interleukin 11 (Antin et al., 2002), have been examined and have shown promising results in reducing the severity and duration of oral mucositis (Gabriel, Shea, Olajida, Serody, & Comeau, 2003; Kwong, 2004; Peterson & Cariello, 2004; Scully, Epstein, & Sonis, 2003).
Rapport et al. (1999) observed that a diagnosis of leukemia, prolonged neutropenia, total body irradiation, and allogeneic transplantation all were associated with an increased duration and severity of oral mucositis. Pain and poor nutritional status can affect patients’ quality of life; therefore, preventive oral care should begin before transplant. A dental evaluation with the correction of any periodontal and dental disease prior to transplant or development of neutropenia should be done. The oral cavity should be assessed daily, and a consistent oral regimen should be used. Prophylactic and therapeutic measures for oral mucositis should include strategies that maintain a clean oral cavity while protecting fragile oral tissues and reducing pain and inflammation. A regimen for oral care is proposed in Figure 4.

Several oral-cleansing regimens are available for preventing and managing the perioral complications typically seen in patients following high-dose chemotherapy and HSCT, and several evidence-based reviews recently have been published (Eilers, 2004; Kostler et al., 2001; McGuire, Rubenstein, & Peterson, 2004), including a report of a consensus panel of experts (Rubenstein et al., 2004). Metabolic oral hygiene must be part of the protocol guidelines required for transplant recipients to prevent infection-related sequelae that often accompany mucositis in the setting of neutropenia (CDC et al., 2000). Table 3 identifies some of the more commonly used rinses for oral hygiene.

A wide variety of agents for oral care is available; however, many interventions have not yet undergone rigorous evaluation (McGuire et al., 2004). Consistent and meticulous examination of the oral cavity is an important facet of transplant nursing, and the use of prophylactic oral regimens and early recognition and treatment of mucositis are crucial in preventing complications associated with infections. Numerous mucositis assessments tools are available (Eilers & Epstein, 2004; Hyland, 1997; Sonis et al., 2000). Table 2 identifies some of the more commonly used rinses for oral hygiene.

### Table 2. Guidelines for Antimicrobial Prophylaxis in Neutropenic Transplant Recipients

<table>
<thead>
<tr>
<th>Infection Category</th>
<th>NCCN Fever and Neutropenia Guidelines: Indication and Treatment</th>
<th>CDC et al. Guidelines for Preventing Opportunistic Infection: Indication and Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacterial</td>
<td>Consider for expected grade IV neutropenia lasting more than seven days Quinolones</td>
<td>Not recommended except for severe hypogammaglobulinemia with allogeneic HSCT IVIG 500 mg/kg every week</td>
</tr>
<tr>
<td>Fungal</td>
<td>Allogeneic HSCT (marrow) Fluconazole 400 mg by mouth every day, itraconazole 400 mg by mouth every day, or low-dose amphotericin B formulation or voriconazole History of documented aspergillus infection undergoing intensive therapy; secondary prophylaxis with amphotericin B formulation or voriconazole</td>
<td>Allogeneic HSCT Autologous HSCT (limited to patients with underlying hematologic malignancy, recipients of fludarabine or cladribine, and patients expected to have prolonged neutropenia and mucosal damage from an intense conditioning regimen) Fluconazole 400 mg by mouth or IV every day</td>
</tr>
<tr>
<td>Viral: herpes simplex virus</td>
<td>Seropositive allogeneic stem cell transplant recipients Acyclovir or famciclovir</td>
<td>Seropositive only: allogeneic HSCT and autologous HSCT Start acyclovir at the beginning of conditioning therapy and continue until engraftment or mucositis resolves (i.e., about 30 days after HSCT for allogeneic recipients) Acyclovir 200 mg by mouth three times a day, acyclovir 25 mg/m² by IV every 12 hours, or valacyclovir 500 mg by mouth every day</td>
</tr>
<tr>
<td>Viral: varicella virus</td>
<td>Seropositive allogeneic HSCT recipients from time of transplant until all immunosuppression Acyclovir</td>
<td>Allogeneic and autologous HSCT with VZV exposure VZV immunoglobulin 625U intramuscularly</td>
</tr>
<tr>
<td>Pneumocystis carinii</td>
<td>Allogeneic BMT Autologous PBHSCT Trimethoprim or sulfamethoxazole (In patients with a history of sensitivity reactions, consider desensitization or atovaquone, dapsone, or aerosolized pentamidine.)</td>
<td>Allogeneic HSCT Autologous HSCT (with heme malignancy) Trimethoprim 80 mg with sulfamethoxazole 400 mg, one double-strength tablet by mouth three times a week or one single-strength tablet by mouth daily In patients with sulfia drug allergy: dapsone 100 mg by mouth every day, aerosolized pentamidine 300 mg every month, or pentamidine 4 mg/kg IV every two to four weeks Prophylaxis should begin one to two weeks prior to HSCT.</td>
</tr>
</tbody>
</table>

BMT—blood and marrow transplant; CDC—Centers for Disease Control and Prevention; HSCT—hematopoietic stem cell transplant; IVIG—IV immunoglobulin; NCCN—National Comprehensive Cancer Network; PBHSCT—peripheral blood hematopoietic stem cell transplant


---

**FIGURE 4. SUGGESTED ORAL CARE PROTOCOL**

- Have the patient suck on ice during the dose-intensive chemotherapy infusion.
- Gently brush the teeth at least twice daily with a soft, small toothbrush. Cleanse the toothbrush with hot water after each use and allow it to dry completely.
- Use foam toothettes when instructed by healthcare provider.
- Use fluoride-containing toothpaste.
- Remove and clean dentures each time oral care is performed; remove and store nightly in antimicrobial solution.
- Avoid wearing ill-fitting dentures, especially before, during, and immediately after treatment.
- Remove dentures during periods of mucositis.
- Rinse the mouth consistently with the recommended regimen best suited to the patient’s needs and preferences.
- Drink at least 3,000 cc of liquid daily unless otherwise contraindicated.
- Avoid tobacco, alcohol, and foods that are too hot or cold.

Note. Based on information from Beck, 1999; Eilers, 2004; Kostler et al., 2001; Miller, 2001; Rubenstein et al., 2004; Scully et al., 2004; Yeager et al., 2000.
al., 2001; Vogelsang, 2001); however, no clear evidence suggests that any one tool is better than another. Regularly performing and documenting an oral assessment allow nurses to identify patients at greatest risk for mucositis and helps to direct their further management.

**Colony-stimulating factors:** The primary goal for using CSFs is to prevent neutropenia; however, with HSCT, a period of neutropenia cannot be avoided. In this setting, CSFs are used to accelerate neutrophil recovery, thus limiting the severity and duration of neutropenia (Bolwell et al., 1998; Colby, McAfee, Finkelman, & Spitzer, 1998; Dale, 2002; Wingard & Bartfield, 2000). Three CSFs (i.e., filgrastim, sargramostim, pegfilgrastim) are used to limit chemotherapy-induced neutropenia; however, outside of clinical trials, only filgrastim and sargramostim currently are being utilized with HSCT (Amgen Inc., 2002) (see Table 4).

Current recommendations from the American Society of Clinical Oncology (ASCO) support the use of CSFs for neutropenia; however, they advocate for additional research to assess the risks associated with CSFs used in combination with chemotherapy (ASCO, 1996; Ozer et al., 2000). ASCO guidelines recommend that CSFs be used to accelerate neutrophil recovery following peripheral blood stem cell transplantation because CSFs have been shown to shorten the duration of neutropenia following HSCT (Bolwell et al., 1998; Colby et al., 1998). Two additional studies (Hornedo et al., 2002; Lee et al., 1998) and an integrated review (Dempke, Von Poblozki, Grothey, & Schmoll, 2000) support the conclusion that the administration of CSFs after autologous HSCT will accelerate the recovery of neutrophils, reduce the rate of infection, and decrease length of stay and overall costs associated with HSCT. Controversy remains over whether CSFs should be administered shortly after stem cell infusion or after several days. In addition, once-weekly pegfilgrastim has been shown to have efficacy comparable to filgrastim and may contribute to improved patient quality of life (Anderlini & Champlin, 2002).

**Hand washing and personal hygiene:** The single most important factor for managing neutropenia is emphasis on strict hand hygiene for patients, caregivers, and healthcare personnel. Healthcare workers should decontaminate their hands prior to having any direct contact with patients, prior to applying sterile gloves, after contact with a patient’s intact skin, after contact with any inanimate object that is in the vicinity of a patient, and after using the restroom. Current guidelines indicate that conscientious and frequent hand washing by patients, family members, and healthcare workers is the most important precaution for neutropenia and preventing infection in transplant recipients (Larson, 1995; U.S. Department of Health and Human Services, 2002).

Numerous studies and reports (Larson & Killien, 1982; Mayer, Dubbert, Miller, Burkett, & Chapman, 1986; Scott, Barnes, Lister, & Arkell, 1991) have indicated that healthcare workers’ compliance with hand washing is related to several variables associated with product characteristics such as odor, consistency, color, and irritation properties, as well as convenience and availability of hand hygiene facilities. Additionally, observation studies have identified a correlation to poor hand hygiene adherence

<table>
<thead>
<tr>
<th>TABLE 3. COMMON ORAL CARE HYGIENE REGIMENS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ORAL CLEANSING AGENT OR PLAN</strong></td>
</tr>
<tr>
<td>---------------------------------------</td>
</tr>
<tr>
<td>Normal saline</td>
</tr>
<tr>
<td>Hydrogen peroxide</td>
</tr>
<tr>
<td>Peridex</td>
</tr>
<tr>
<td>Chlorhexidine</td>
</tr>
<tr>
<td>Sucralfate</td>
</tr>
<tr>
<td>Ice chips or ice pops</td>
</tr>
</tbody>
</table>

*Note. Based on information from Eilers, 2004; Kostler et al., 2001; McGuire et al., 2004; Rubenstein et al., 2004; Scully et al., 2004.*

<table>
<thead>
<tr>
<th>TABLE 4. COLONY-STIMULATING FACTORS USED TO ACCELERATE NEUTROPHIL RECOVERY TIME</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DRUG AND MANUFACTURER</strong></td>
</tr>
<tr>
<td>Neupogen® (filgrastim, Amgen Inc., Thousand Oaks, CA) G-CSF</td>
</tr>
<tr>
<td>Leukine® (sargramostim, Berlex, Montville, NJ) GM-CSF</td>
</tr>
</tbody>
</table>

*G-CSF—granulocyte-colony-stimulating factor; GM-CSF—granulocyte macrophage-colony-stimulating factor; sq—subcutaneous*

*Note. Based on information from Centers for Disease Control and Prevention et al., 2000; National Comprehensive Cancer Network, 2003.*
Transplant recipients should be taught to wash their hands before caring for a central venous catheter, before eating or preparing food, after using the restroom, after touching pets and animals, after going outdoors, and after touching any wound. Patients should be taught that touching their mucus membranes could lead to self-inoculation of an opportunistic infection; therefore, hand washing with antibacterial soap is essential prior to any mucus membrane contact by the hands. Additionally, personal physical hygiene practices, including daily baths or showers, should be maintained by patients experiencing neutropenia in an effort to decrease bacterial contamination (Alcoser & Burchett, 1999; U.S. Department of Health and Human Services, 2002). Skin care during neutropenic periods should include daily inspection of skin sites that are likely to be portals of infection, such as the perineum and vascular access sites. Protocols for perineal care should be developed to minimize loss of skin integrity (Haisfield-Wolfe & Rund, 2000).

The U.S. Department of Health and Human Services (2002) outlined specific guidelines for hand washing in healthcare settings, which should be incorporated into outpatient facilities. The preferred technique for visibly soiled hands is soap and water, whereas alcohol-based hand rubs are recommended in clinical situations that require routine decontamination. Transplant programs should have specific policies and procedures for hand washing and infection control that all hospital personnel should be expected to follow. Some questions still remain about which type of cleanser is best for certain environments and which method of cleansing is superior (U.S. Department of Health and Human Services). Additional research is indicated for hand hygiene preferences in the home and outpatient setting for this specific population.

Central venous catheter site care: Central venous catheters are used in most transplant recipients and carry a high risk of catheter-related infections. Infections associated with central venous catheters have a direct correlation with morbidity and mortality rates in the transplant population. Multidisciplinary teams caring for transplant recipients must identify standards of care for central venous catheters (Camp-Sorrell, 2004; Mermel et al., 2001). Transplant teams should have a well-organized program of staff education, continued quality improvement and monitoring of performance indicators and outcomes such as central venous catheter infection and complication rates, and staff and patient adherence to policy and procedure (O’Grady et al., 2002).

Central venous catheter care varies among institutions and often is based on institutional preferences and cost (Zitella, 2003). Evidence-based protocols help to ensure that central venous catheter care is based on current research findings and reduce practice variations that can increase the rate of local and systemic infection and decrease costs associated with the replacement of catheters (Penne, 2002). The Oncology Nursing Society (Camp-Sorrell, 2004) and the U.S. Department of Health and Human Services (O’Grady et al., 2002) offer comprehensive guidelines for central venous catheter care and represent a consensus of various professional organizations involved in infection control in the healthcare community. The guidelines should be reviewed and followed by all transplant teams to prevent the risk of central venous catheter-associated infections in this population.

The Guidelines for the Prevention of Intravascular Catheter Related Infections (O’Grady et al., 2002) recommend that a chlorhexidine gluconate agent be used in central venous catheter exit site care. Table 5 summarizes the Oncology Nursing Society’s access device guidelines (Camp-Sorrell, 2004) and the CDC (2002) guidelines. Figure 5 lists the indications for replacement of a central venous catheter device in neutropenic patients. Guide-wire replacement techniques should not be used in patients suspected of having catheter-related infection.

Transplant nurses should be aware of the possible complications that are associated with CVC care and should have the training needed to promptly identify and intervene with vascular access device complications. Each transplant program should develop systematic policies and procedures that outline CVC care and identify guidelines and instructional materials for delivering and documenting the education provided to patients and their families.

Neutropenic fever: Early detection and treatment of neutropenic fever in transplant recipients are critical to a successful outcome. The NCCN (2004) guidelines describe fever in neutropenic patients as any temperature that is higher than 38.0°C–38.5°C (100.4°F–101.3°F) when no apparent environmental cause exists. Transplant recipients with febrile neutropenia are considered at high risk for the development of sepsis, and because the progression of infection can be rapid and asymptomatic, IV antibiotic therapy must be initiated promptly (CDC, 2000; NCCN, 2004). The use of a third- or fourth-generation cephalosporin (e.g., cefepime, ceftazidime), a carbapenem (e.g., imipenem), or a combination of aminoglycoside plus an antipseudomonal offers broad-spectrum coverage for initial management of neutropenic fever (Bertz et al., 2003; Hughes et al., 2002; NCCN, 2004). The routine use of vancomycin has been discouraged by multiple expert consensus panels, owing to concern about the emergence of vancomycin-resistant enterococci.

Nurses have a responsibility to coordinate the delivery of care to ensure that all transplant recipients with neutropenic fever are evaluated immediately and the appropriate treatment is initiated within one hour of the first fever (Hughes et al., 2002; Koh & Pizzo, 2002; Shelton, 1999). Transplant programs should have a protocol defining fever and the diagnostic procedures, agents for treatment of neutropenic fever, and antipyretics to be used (Foundation for the Accreditation of Cellular Therapy [FACT], 2002; Reed & Franco, 1992).

Limiting community exposure: Every effort should be made to limit patients’ community exposure to bacterial, viral, and fungal infections. Patients who are neutropenic and are being seen in the outpatient clinic will need to wear a mask to and from the clinic and when out in public. Neutropenic patients should not go to shopping malls or other places in the community where crowds are present (CDC et al., 2000). Outpatient clinics should have a designated protective environment for immunocompromised patients and must be able to accommodate patients who require long infusion times. Outpatient and inpatient clinical environments must minimize the airborne microbial contamination, and patients should never be placed in semiprivate or group rooms (CDC et al.; FACT, 2002).

Although evidence is not conclusive about the relationship between patient exposure to plants and flowers and incidence of fungal infections, experts agree that HSCT recipients who are neutropenic should not have fresh or dried flowers or plants in their homes or hospital rooms. These recommendations are based on evidence that fungi and protozoa have been isolated from soil, fresh plants, and flowers and have been found on the surfaces of dried arrangements. Neutropenic HSCT recipients should be instructed to avoid locations being remodeled or construction areas (Dykewicz, 2001a, 2001b).
**Patient education**: Education is required for patients and their caregivers throughout the stem cell transplant process. Patient education is particularly essential for effective management of neutropenia in outpatient settings following HSCT (Franco et al., 1996). Lorig (2001) described patient education as a program that incorporates planning specific educational activities that are designed to improve a patient’s health status through improved behavior patterns. Patient education is not about acquiring information but rather is a process for patients and their informal caregivers to develop the knowledge, skills, and behaviors necessary for effective care. Nurses’ language and actions must stress the relationship between adherence to prescribed therapies and improved outcomes for patients (Hayes, 2001). Patients may delay or underreport side effects and complications related to neutropenia because of fear of hospital readmission or because they are uncertain about the significance and optimal management of neutropenic symptoms. Teaching patients about the importance of accurate and timely reporting of symptoms and appropriate self-management ensures an optimal outcome of outpatient neutropenia management.

Patient education should begin after a careful needs assessment has been completed and before neutropenia occurs. The transplant team should not assume that patients have preexisting knowledge regarding the protective measures that are required following dose-intensive therapy and HSCT. Patients should be taught to take their temperatures daily during periods of neutropenia. Personal hygiene practices should be assessed, and the need for consistent and meticulous hygiene should be reinforced. Teaching should include proper food-handling tips (Stevens, 2004). Other recommendations should include avoidance of all yard work or gardening, safest sexual practices, travel safety, and measures to reduce exposure to potential pathogens (CDC et al., 2000; Ezzone, 2000). Topics that should be incorporated into the patient education process are outlined in Figure 6. NCCN and the American Cancer Society have translated the NCCN practice guidelines used by professionals for fever and neutropenia into a patient-friendly resource outlining appropriate self-management of fever and neutropenia (NCCN, 2002).

**Follow-up care**: HSCT recipients should be seen daily in the outpatient clinic throughout their period of neutropenia and then monitored closely until immune recovery. Follow-up visits may vary based on individual status; however, a comprehensive physical examination, including evaluation of all blood work, should be performed daily until neutropenia has resolved. The physical examination should be comprehensive and include a thorough skin and oral cavity examination and assessment of nutritional status. Advanced practice nurses and physician assistants often perform daily assessments and manage patients following HSCT in the outpatient setting, and they should consistently follow the transplant program’s policies and procedures for follow-up care and assessments. Education provided to patients and caregivers must be reinforced, and an evaluation of adherence must be assessed at each follow-up visit. This comprehensive patient assessment and all changes in the plan of care and treatment should be documented clearly (FACT, 2000; Kapustay & Buchsel, 2000; Reed & Franco, 1992).

**Table 5. Recommendations for Catheter Care Following Hematopoietic Stem Cell Transplantation**

<table>
<thead>
<tr>
<th>Catheter Type</th>
<th>Dressing Type and Change</th>
<th>Site Cleanser</th>
<th>IV Tubing and Cap Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central venous</td>
<td>Sterile transparent: every five to seven days and as needed</td>
<td>2% chlorhexidine gluconate</td>
<td>Tubing: ≥ 72 hours; cap: every week and both as needed or per manufacturer’s recommendations</td>
</tr>
<tr>
<td></td>
<td>Sterile gauze: every other day and as needed</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Semipermeable: every five to seven days and as needed</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>24-hour post insertion for all dressing types</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Implanted port</td>
<td>Sterile transparent: every five to seven days with needle change and as needed</td>
<td>2% chlorhexidine gluconate</td>
<td>Tubing: ≥ 72 hours; cap: every week and both as needed or per manufacturer’s recommendations</td>
</tr>
<tr>
<td></td>
<td>Sterile gauze: every other day and as needed</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(dress only while accessed)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pheresis</td>
<td>Sterile transparent: every five to seven days with needle change and as needed</td>
<td>2% chlorhexidine gluconate</td>
<td>Tubing: ≥ 72 hours; cap: every week and both as needed or per manufacturer’s recommendations</td>
</tr>
<tr>
<td></td>
<td>Sterile gauze: every other day and as needed</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tunneled</td>
<td>Sterile transparent: every five to seven days and as needed</td>
<td>2% chlorhexidine gluconate</td>
<td>Tubing: ≥ 72 hours; cap: every week and both as needed or per manufacturer’s recommendations</td>
</tr>
<tr>
<td></td>
<td>Sterile gauze: every other day and as needed</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peripheral venous</td>
<td>Sterile transparent: as needed and with catheter change</td>
<td>2% chlorhexidine gluconate</td>
<td>With catheter change</td>
</tr>
<tr>
<td></td>
<td>Sterile gauze: as needed and with catheter change</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Note.** Based on information from Camp-Sorrell, 2004; Centers for Disease Control and Prevention, 2002.

**Figure 5. Indications for Replacement of a Central Venous Catheter**

Note. Based on information from O’Grady et al., 2002; Vento & Cainelli, 2003.
• Personal hygiene
  – Oral care four to six times a day and as needed
  – Bathe daily.
  – Skin care
• Meticulous hand hygiene
• Sexual activity
  – Do not have sexual intercourse during periods of severe neutropenia.
  – During nonsevere periods of neutropenia, use condoms and water-soluble lubricant during intercourse.
  – During nonsevere periods of neutropenia, practice effective postcoital hygiene.
• Stress the importance of avoiding high-risk sexual behaviors, including anal sex, genital contact, and oral-anal contact.
• Stress the importance of safe sex practices for patients with multiple partners.
• Dietary restrictions and food safety
• Pet safety
  – Avoid all pet and animal excrement.
  – Do not clean litter boxes, bird cages, or fish tanks.
  – Do not provide direct care for domestic or farm animals.
  – Wash hands thoroughly after any contact with pets.
• Water and beverage safety
  – Wash foods well.
  – Cook food thoroughly.
  – Do not eat raw seafood.
  – Do not share eating utensils.
• Travel safety
  – Do not plan to travel during periods of neutropenia.
• Preventing environmental exposures
  – Avoid crowds, and wear a mask when out of the house while neutropenic.
  – Avoid exposure to people with colds or other contagious diseases.
• Central line care
• Compliance with prophylactic medications and follow-up care
• Monitor temperature daily.
• When to call the physician or nurse
  – Temperature greater than 100.4°F
  – Any new signs or symptoms
  – Abdominal pain
• Miscellaneous
  – Do not use tampons.
  – Do not use enemas, rectal suppositories, or thermometers.

**Figure 6. Education Topics for Patients Following Hematopoietic Stem Cell Transplantation**

*Note.* Based on information from Centers for Disease Control and Prevention et al., 2000; Klustersky et al., 2000.

---

**Recommendations for Practice**

**Program Development**

Planning a transplant program should include identifying a model of care, articulating clinical practice guidelines that incorporate national standards for transplant programs, and writing policies and procedures that define staff education and development, patient education, and a quality assessment program (Burns et al., 1995; FACT, 2002).

The Cooperative Model of Care is an innovative service delivery model developed to support outpatient HSCT (Schmit-Pokorny et al., 2003). The model recognizes that as transplant programs shift care to the outpatient setting, patients and their families have increased self-care responsibilities during what was traditionally a high-acuity inpatient hospital stay. A focus on patient and family education, skill development, continuity of care, and collaboration in care delivery among patients, caregivers, and professional nursing staff is of paramount importance to the success of an outpatient transplant model.

Policies, procedures, and practice standards should outline how the transplant team will manage all aspects of caring for patients in the outpatient setting, as well as the complications associated with neutropenia, such as fever (Neumann & DeJesus, 1998). The policies and procedures should identify all methods that will be incorporated in staff development and patient education throughout the different phases of recovery for patients following HSCT. An outpatient program should have adequate coordination with an inpatient facility to ensure that all patient needs can be met if a change in a patient’s status requires admission (Reed & Franco, 1992).

Developing a new or restructuring an old transplant program that is patient-focused, cost-efficient, and meets the needs of the staff, should incorporate standards for the delivery of high quality with consideration for the experience of other transplant programs (Giles & Vaughan, 1999; Morabito et al., 2002) and an analysis of national outcomes data (DeMeyer, 2000; Russell et al., 2004). Another important consideration in program development is accreditation by a nationally recognized organization. Accreditation for transplant centers in the United States is voluntary; however, accreditation with FACT implies that the transplant program uses national standards for practice, is dedicated to the quality care, and voluntarily participates in ongoing quality evaluation (Clifford, 2000; FACT, 2002).

Preparation for accreditation should involve an evaluation of the current program if one exists. Accreditation evaluation models generally examine an organization to determine whether it is meeting acceptable standards and whether improvements are needed (Johnson & Olesinski, 1995). Accreditation by FACT involves two parts: (a) evaluation of the documentation supporting compliance with standards and (b) a successful on-site inspection (FACT, 2002). The standards also address requirements for operating procedures, including preventive measures such as clinical environment standards for neutropenic patients.

**Staff Development and Education**

Nurses working with transplant recipients require special training and must possess excellent judgment. A training program should include didactic and clinical education components to assist nurses in preparing for this demanding role (see Figure 7). Staff must receive specialty education in the care of HSCT recipients, and assessment of competency must be evaluated. Staff development is critical to achieving positive outcomes, and nurses have a pivotal role in preventing infections in neutropenic patients. Nursing educators should incorporate a flexible, yet comprehensive, orientation period that is customized to each nurse’s experiences and background. The transplant team should be made up of individuals from different disciplines, and nurses should be recruited from various backgrounds as well. Hiring nurses with backgrounds in areas other than oncology, such as critical care and emergency medicine, will ensure a versatile staff that will be able to care for the complex needs that can arise in HSCT recipients.

**Research**

Instruments to evaluate quality of life in patients with neutropenia have been developed and are undergoing validation (Callhoun, Chang, Welshman, & Cella, 2002; Ozer, 2003). In clinical practice and research, quality of life may be a useful outcomes measure to evaluate the impact of care delivery models and nursing interventions on neutropenia. Other important outcomes are costs, length of stay, and readmission rates. Research that examines the impact of family or the support system on quality of life and caregiver burden also is needed. Nursing research is needed to (a) develop outcome
measures to evaluate the impact of evidence-based practice protocols for the management of neutropenia following HSCT; (b) evaluate the impact of staff development and patient education on outcomes; (c) determine patient preferences for teaching strategies, personal hygiene, diet choices, and oral care regimens; (d) evaluate the effects of antibiotic and heparin flushes on the incidence of catheter-related infections (van de Watering & van Woensel, 2003); and (e) determine the effect of specific patient education tools, such as audio, visual, and written material, and classroom instruction, on clinical and financial outcomes of neutropenia following HSCT.

**Conclusion**

By carefully planning and developing a comprehensive program that initiates an evidence-based approach to managing neutropenia, community-based centers will be able to successfully achieve accreditation and improve the quality of care for HSCT recipients in the outpatient setting. Nurses must be aware of the significance of neutropenia in patients following HSCT, the risk factors associated with it, and the effect it can have on patient outcome. The use of prophylactic antimicrobial therapy, improved personal hygiene, exposure safety, care of central venous catheters, oral care, meticulous hand washing, dietary restrictions, and systematic patient and caregiver education have been shown to influence patient outcomes during prolonged periods of neutropenia. A well-organized system for staff and patient education, and a program for monitoring performance indicators and outcomes are important aspects of an evidence-based approach for managing neutropenia following HSCT.

**Author Contact:** Fran West, DNSc, APRN-BC, FNP, AOCN®, can be reached at fwest@utcancer.com, with copy to editor at CJONeditor@jsobel.com.

**References**


Dix, S.P., & Geller, R.B. (2000). High-dose...
chemotherapy with autologous stem cell rescue in the outpatient setting. *Oncology*, 6, 185–186.


Rapid Recap

Evidence-Based Guidelines for the Management of Neutropenia Following Outpatient Hematopoietic Stem Cell Transplantation

- Centers that participate in hematopoietic stem cell transplantation (HSCT) in the outpatient setting should develop and implement protocols that are grounded in evidence-based practice.
- To ensure quality of care for all transplant recipients, centers participating in HSCT should prepare for and participate in accreditation from the Foundation for the Accreditation of Cellular Therapy.
- Further research that focuses on dietary restrictions, sexuality, and oral care regimens are needed; identification of patient preferences should be included in this research.
- Research that evaluates the effectiveness of staff development and patient education on outcomes following HSCT also is needed.
**DIDACTIC ELEMENT**

Basic fundamentals of oncology
- Hematology and oncology nursing
- Chemotherapy administration
- Cytotoxic safety precautions
- Biotherapy administration
- Oncologic emergencies
- Pain management
- Blood component administration
- Nausea, vomiting, and anorexia
- Constipation
- Anemia
- Neutropenia
- Thrombocytopenia
- Psychosocial issues
- Central venous catheter care
- Patient education and discharge planning

Intermediate hematopoietic stem cell transplantation
- Use of growth factors
- Use of immunoglobulins
- Use of immunosuppressive drugs
- Management of neutropenia
- Recognition and management of neutropenic fever
- Management of bacterial, fungal, and viral infections
- Nursing implications of clinical research for transplantation
- Patient education

Basic critical care
- Basic care for critically ill patients
- Physical assessment of critically ill patients
- Pulmonary and cardiac complications of critically ill patients
- Ventilator support and management
- Basic and intermediate electrocardiogram interpretation
- Recognition of arrhythmias and treatment
- Impaired renal function and required support
- Hemodynamic support

Basic hematopoietic stem cell transplantation
- Basic immunology
- Diseases treated by transplantation
- History of transplantation
- Side effects and management of side effects of high-dose chemotherapy
- Management of patients receiving radiation therapy
- Nursing care of transplant recipients in inpatient and outpatient settings
- Acute complications
- Patient education
- Discharge information
- Introduction to clinical research

**PRACTICUM ELEMENT**

12 months of experience
- Orient to unit routines and standards.
- Complete a competency evaluation of physical assessment of patients with cancer.
- Care for various patients with hematologic or oncologic diseases with preceptor.
- Complete chemotherapy administration training and a competency evaluation.
- Complete chemotherapy safe-handling training and a competency evaluation.
- Complete biotherapy administration training and a competency evaluation.
- Care for patients with disseminated intravascular coagulation, sepsis, spinal cord compression, syndrome of inappropriate secretion of antidiuretic hormone, and other emergencies.
- Participate in the management of patients receiving patient-controlled analgesia and other pain delivery systems for conscious sedation.
- Participate in the administration of blood, platelets, fresh frozen plasma, and other blood products with a preceptor, and then complete a competency evaluation.
- Participate in the care of patients receiving antiemetics, appetite stimulants, and laxatives.
- Observe and participate in collecting daily laboratory tests and evaluating complete blood counts and other laboratory results.
- Participate in rounds with a social worker and dietitian.
- Observe and participate in central venous catheter site care, and complete a competency evaluation.
- Participate in discharge planning meetings.

9–12 months of experience
- Orient to unit routines and standards.
- Orient to unit policies and procedures.
- Review treatment protocols and, with preceptor, use different protocols.
- Participate in the care of transplant recipients with a preceptor.
- Orient with the outpatient transplant coordinator and assist with pretransplant workup.
- Observe catheter placement and removal.
- Participate in the mobilization process while working with a preceptor.
- Observe apheresis and a bone marrow harvest.
- Observe and participate in a stem cell infusion with a preceptor.
- Participate in discharge planning meetings.

12 months of experience
- Orient to the critical care unit.
- Work with a nurse caring for critically ill transplant recipients.
- Participate in a skills laboratory for electrocardiogram, ventilator support, hemodynamic monitoring, and dialysis.
- Participate in daily rounds.
- Participate in patient treatment planning.
- Participate in research activities.

18–24 months of experience
- Care for transplant recipients in acute and outpatient settings.
- Rotate through the critical care unit working with a preceptor.
- Continue to participate in a skills laboratory for ventilator support, hemodynamic monitoring, and dialysis.
- Participate in research activities.
- Participate in daily rounds.
- Attend weekly multidisciplinary team meetings.

(Continued on next page)

**FIGURE 7. COURSE OUTLINE FOR TRAINING AND EDUCATION OF HEMATOPOIETIC STEM CELL TRANSPLANTATION NURSES**

*Note.* Based on information from Clifford, 2000; Foundation for the Accreditation of Cellular Therapy, 2002; Reed & Franco, 1992.
DIDACTIC ELEMENT

ADVANCED HEMATOPOIETIC STEM CELL TRANSPLANTATION
- Hemorrhagic emergencies in transplantation, disseminated intravascular coagulation, and diffuse alveolar hemorrhage
- Veno-occlusive disease
- Acute graft-versus-host disease
- Chronic graft-versus-host disease
- Prophylaxis and acute treatment for cytomegalovirus
- Long-term complications
- Current trends and research in hematopoietic stem cell transplantation

Advanced critical care
- Recognition and treatment of sepsis
- Recognition and treatment of multisystem organ failure
- Recognition and treatment of advanced arrhythmias
- Use of various drug therapies in hemodynamically unstable transplant recipients

PRACTICUM ELEMENT

24–36 MONTHS OF EXPERIENCE
- Work with a new orientee caring for a transplant recipient.
- Collaborate with advanced practice nurses and physicians in case study analysis.
- Assist in the development and implementation of nursing research studies.
- Care for transplant recipients in all settings.

24–36 months of experience
- Obtain advanced cardiac life support certification.
- Mentor a new orientee caring for a critically ill transplant recipient.
- Collaborate with advanced practice nurses and physicians in case study analysis.
- Assist in the development and implementation of nursing research studies.

FIGURE 7. COURSE OUTLINE FOR TRAINING AND EDUCATION OF HEMATOPOIETIC STEM CELL TRANSPLANTATION NURSES (CONTINUED)

Note: Based on information from Clifford, 2000; Foundation for the Accreditation of Cellular Therapy, 2002; Reed & Franco, 1992.