

ONCOLOGY NURSING SOCIETY WHITE PAPER

Neutropenia: State of the Knowledge Part II

Anita Nirenberg, RN, MS, AOCNP, Annette Parry Bush, RN, BSN, MBA, OCN®,
Arlene Davis, RN, MSN, AOCN®, Christopher R. Friese, RN, PhD, AOCN®,
Theresa Wicklin Gillespie, PhD, BA, BSN, MA, RN, and Robert David Rice, RN, NP-C, OCN®

Purpose/Objectives: To summarize the current available evidence for oncology nurses so that they may predict and prevent complications of chemotherapy-induced neutropenia (CIN), provide optimal education to patients, and become familiar with the state of the knowledge of neutropenia by understanding the evidence and guidelines for patients with cancer who may experience CIN.

Data Sources: Review of primary literature, meta-analyses, available systematic reviews, clinical practice guidelines, and discussions at the State of the Knowledge on Neutropenia Symposium.

Data Synthesis: The evidence for nursing interventions to prevent CIN complications is underdeveloped. Strong empirical support to prevent infection in patients with CIN (e.g., restrictions in diet, isolation procedures, providing accurate patient education) is lacking. Several areas of preventive measures by patients, hand washing, and skin care have a stronger evidence base and should have high priority on patient education plans.

Conclusions: Strong evidence is available for several nursing interventions to prevent infection in patients with CIN. Many existing practices lack empirical support and should be identified and reviewed in the clinical setting for appropriate patient management.

Implications for Nursing: Oncology nurses can use the findings from the symposium to revise their care standards for patients anticipated to experience CIN. Research and practice performance improvement projects may be undertaken by oncology nurses to improve the delivery of evidence-based nursing care to this vulnerable patient population.

In Part I of this two-part white paper, the project team of the State of the Knowledge on Neutropenia Symposium summarized the available evidence regarding chemotherapy-induced neutropenia (CIN), neutrophil physiology, chemotherapy dose intensity, approaches to risk assessment, national practice guidelines, and outcomes of neutropenia. The authors identified what currently is known and, importantly, what is not known about the most common dose-limiting toxicity of cancer chemotherapy. CIN affects all aspects of patients' lives, the healthcare system, and society. Downstream effects have been identified that are related to anti-infective use, either prophylactically or from treating actual infections resulting from the development of resistant organisms. This article presents the results of the team's literature review and discussion at the symposium pertaining to nursing interventions to prevent infection, patient education

Key Points . . .

- ▶ Prevention of infection for people with chemotherapy-induced neutropenia (CIN) includes recommendations that patients practice good hand hygiene with soap and water or alcohol-based hand rubs, that healthcare providers wear gowns when patients have respiratory secretions, and that visits from individuals with respiratory symptoms be avoided.
- ▶ A number of widely practiced interventions for the prevention of infection in patients with cancer and CIN, such as low-bacterial diets and inpatient isolation procedures, lack strong empirical evidence.
- ▶ The quality of life of patients who experience CIN and their families is negatively affected by this complication.
- ▶ Patient management and education for those at risk for developing CIN currently are not standardized.

Anita Nirenberg, RN, MS, AOCNP, is an assistant professor of clinical nursing and director of the oncology masters program in the School of Nursing at Columbia University in New York, NY; Annette Parry Bush, RN, BSN, MBA, OCN®, is a nurse planner and project manager in the education team at the Oncology Nursing Society in Pittsburgh, PA; Arlene Davis, RN, MSN, AOCN®, is an oncology clinical nurse specialist at Malcom Randall VA Medical Center in Gainesville, FL; Christopher R. Friese, RN, PhD, AOCN®, is a postdoctoral fellow in the School of Public Health at Harvard University and in the Center for Outcomes and Policy Research at the Dana-Farber Cancer Center, both in Boston, MA; Theresa Wicklin Gillespie, PhD, BA, BSN, MA, RN, is an assistant professor in the Department of Surgery and Winship Cancer Institute at Emory University and the director of health services research and development at the Atlanta VA Medical Center, both in Atlanta, GA; and Robert David Rice, RN, NP-C, OCN®, is a research nurse practitioner at Memorial Sloan-Kettering Cancer Center in New York, NY. (Submitted June 2006. Accepted for publication June 30, 2006.)

Digital Object Identifier: 10.1188/06.ONF.1202-1208

considerations, health policy, and gaps in clinical research. Conclusions and discussion from the entire project will be summarized with recommendations for practice, education, and research.

Prevention of Infection

Prevention of infection among patients with cancer was identified as a nursing-sensitive patient outcome (NSPO) measure by the Oncology Nursing Society (ONS) Outcomes Project Team (Given & Sherwood, 2005). As part of that effort, project teams were convened to conduct critical reviews of the literature to identify the level of evidence for nursing interventions for NSPOs. Specifically, the Prevention of Infection Team reviewed publications at varying levels of evidence to describe, summarize, and rank the quality of evidence available to recommend adoption by practicing oncology nurses and advanced practice nurses when managing patients with cancer (Zitella et al., in press). Following a standard ranking criteria based on the quantity and quality of available evidence, the team of staff nurses, clinical nurse specialists, nurse practitioners, and a doctorally prepared nurse scientist sorted the available interventions into several categories: recommended for practice, likely to be effective, benefits balanced with harms, effectiveness not yet established, and not recommended for practice (Mitchell, Friese, & Beck, 2006). Readers are referred to the full document, available at www.ons.org/outcomes for details, but salient results are reported here.

Pharmacologic interventions ranked as “recommended for practice” include antifungal prophylaxis for patients with severe, prolonged neutropenia; the use of trimethoprim-sulfamethoxazole for patients at risk for *Pneumocystis carinii*; antifungals absorbed by the gastrointestinal tract to prevent candidiasis; colony-stimulating factor for patients whose expected risk of febrile neutropenia (FN) is greater than 20%; and pneumococcal and influenza vaccines. Pharmacologic interventions not recommended for practice include routine antifungal prophylaxis in all patients receiving chemotherapy, nonabsorbable antifungals (e.g., nystatin) to prevent candidiasis, the use of chlorhexidine to prevent mucositis, and routine prophylaxis for gram-positive organisms or *Pneumocystis carinii*.

Environmental interventions at the highest level of recommendation include hand hygiene with soap and water or alcohol-based rubs, gown use by healthcare providers caring for patients with respiratory secretions, closed windows in healthcare facilities, and restrictions for visitors with respiratory symptoms. Effectiveness has not yet been established for several nursing interventions frequently delivered, such as the routine use of gowns, gloves, and masks when entering the room of a neutropenic patient and diet modifications (e.g., avoiding fruits and vegetables). In addition, laminar airflow units are not likely to be effective for preventing infection in patients with cancer.

The findings can help clinicians focus their attention on interventions with the maximum benefit to patients. For example, instead of strict enforcement of isolation procedures for inpatients, nurses can ensure that patients and families properly demonstrate good hand hygiene. Standardized protocols can clarify whether prophylaxis with antibiotics or antifungals are appropriate for the patient population. Provid-

ers also can track whether patients have been vaccinated for pneumonia and influenza, as appropriate.

The ONS Putting Evidence Into Practice (PEP) Team for Prevention of Infection recommended prophylaxis with fluoroquinolones to prevent infection in patients with cancer undergoing treatment with chemotherapy (Zitella et al., in press). However, the recommendation has several caveats. Although the majority of published trials and meta-analyses do report a significantly decreased risk of infection among patients receiving fluoroquinolone prophylaxis, data on antimicrobial resistance are lacking (Bucaneve et al., 2005; Cullen et al., 2005; Gafter-Gvili, Fraser, Paul, & Leibovici, 2005). Furthermore, many of the trials exclude or do not mention the use of colony-stimulating factor, which, in several instances, has been shown to reduce infectious complications. Some evidence in the neoadjuvant breast cancer population has suggested that optimal reduction in adverse events related to neutropenia might be achieved with the use of colony-stimulating factor and prophylactic fluoroquinolones (Martin et al., 2004; von Minckwitz et al., 2005). Finally, the Infectious Disease Society of America and the National Comprehensive Cancer Network (NCCN) have discouraged the use of fluoroquinolone prophylaxis for patients receiving chemotherapy (Hughes et al., 2002; NCCN, 2005).

Patient Education

Oncology nurses play a vital role in providing chemotherapy side-effect education to patients and their caregivers. Patient education includes teaching about the potential for and consequences of neutropenia, preventive measures to decrease the risk of infection, reportable signs and symptoms of infection, and what to do when signs and symptoms occur. However, wide variations exist in what patients are taught, and few evidence-based protocols are available to guide nursing practice and patient education in this area.

Although national patient guidelines and educational materials have been produced by the American Cancer Society and NCCN (2006), the American Society of Clinical Oncology (2006), and the Wellness Community (n.d.), not all are evidence based. A review of the guidelines revealed that all provide instruction on symptoms of infection (e.g., fever) as well as suggestions for preventing infection. They also include patient instructions to report the following signs and symptoms of infection: temperature of 100.5°F or higher, chills and sweating, sore throat, cough and shortness of breath, burning on urination, diarrhea, and redness or swelling at a site of injury.

Other signs and symptoms that are stated inconsistently are mouth sores, pain on swallowing, abdominal pain, rectal discomfort, and sinus tenderness; however, the most common sites of infection in patients with CIN are the oral cavity, lungs, gastrointestinal tract (including the perineal area), skin, and soft tissues (Pizzo, 1999). In addition, the reduced quantity of neutrophils may limit the classic signs and symptoms that usually are seen with infection, making fever the only sign of serious infection in neutropenic patients. Patients may have urinary tract infection without pyuria, skin infection without abscess formation, or pneumonia with normal chest auscultation and a normal chest x-ray at the onset of infection (Sickles, Greene, & Wiernik, 1975). About 60%–80% of febrile episodes in patients with neutropenia are the result of

infection, particularly when the absolute neutrophil count is less than 1,000/ml (Cruciani et al., 1996).

Although the available educational materials instruct patients to report a fever, they either omit instructions for patients to monitor their temperature or instruct patients to monitor their temperature one to four times per day or when they do not feel well. Tips for patients to reduce their risk of infection vary, but the most detailed list is in the American Cancer Society and NCCN (2006) patient guidelines. In a survey of more than 400 ONS members, Wivell and Fink (2003) determined that current practices in the care of neutropenic patients were varied. Instruction on a reportable elevated temperature ranged from less than 100°F to more than 101.5°F, with the majority of nurses instructing patients to report 100.5°F (almost 40%) or 101°F (approximately 25%). Instruction on other reportable signs and symptoms of infection as well as tips on preventing infection also showed variation among responders.

Open Questions Regarding Educating Patients on Signs and Symptoms of Infection

What should nurses teach patients? Should patients be taught to report a temperature of 100.5°F or greater as they are instructed to do in national patient guidelines (American Cancer Society & NCCN, 2006; American Society of Clinical Oncology, 2006; Wellness Community, n.d.)? Or do nurses teach their patients to report a fever as defined by NCCN (2005) and the Infectious Diseases Society of America (i.e., a single oral temperature reading higher than 100.9°F or an oral temperature higher than 100.4°F that lasts for more than an hour) (Hughes et al., 2002)? According to Bodey (2000), the definition of fever requiring antimicrobial therapy in neutropenic patients has been selected arbitrarily. Furthermore, how often should nurses tell patients to check their temperature? Do nurses take into consideration that neutropenic patients might have a life-threatening infection and remain afebrile or be hypothermic, especially if they are older, receiving oxygen, or taking anti-inflammatory drugs? Other signs and symptoms, such as unexplained hypotension, tachycardia, tachypnea, confusion, rigors, or oliguria, might mandate a comprehensive search for infection. So, what should the reportable list of signs and symptoms of infection include? Also, if patients have a fever or other signs or symptoms of infection, what should nurses tell them to do? Should nurses tell them to call, go to an emergency room, or, if available, go to a 24-hour clinic?

Prevention of Infection

In the absence of support for the efficacy of most nursing education regarding prevention of infection, unproved practices based on tradition, habit, and theoretical considerations continue to be used. Therefore, variations exist in what preventive measures neutropenic patients are taught. What measures are truly effective in preventing infections in neutropenic patients?

Neutropenic Diet

The efficacy of a neutropenic diet among patients receiving chemotherapy remains controversial. Carter (1994) recommended a low-microbial diet for neutropenic patients to reduce the potential for infection associated with bacterial translocation. Carter believed that infection will result from

ingested bacteria on food passing through the gastrointestinal tract to the mesenteric lymph nodes, other body organs, and the bloodstream. However, in a literature review, Wilson (2002) failed to identify studies that showed a direct relationship between a low-bacterial diet and prevention of infection in patients with CIN. In a recent pilot study with 23 evaluable patients, DeMille, Deming, Lupinacci, and Jacobs (2006) reported no significant differences in the rates of FN or positive blood cultures for gram-negative rods between patients compliant with a neutropenic diet and those who were not. Further complicating interpretation of the sparse available data is the fact that neutropenic diets are not standardized across settings. In a survey of 400 members of the Association of Community Cancer Centers regarding diet restrictions for neutropenic patients, Smith and Besser (2000) found that 78% placed patients on dietary restrictions, although the restrictions varied. Most commonly, fresh vegetables (98%), fresh fruits (93%), fresh juices (93%), and raw eggs (76%) were prohibited on neutropenic diets.

Hand Washing

Hand washing and personal hygiene appear to be important strategies for the prevention of infection when considering that a primary function of intact skin is protection against microorganisms, that normal human skin is colonized with bacteria (Boyce & Pittet, 2002), and that a large proportion of infections in patients with neutropenia is associated with patients' endogenous flora or normal environmental inhabitants. Backed by strong evidence, current interventions recommended for patients and caregivers in preventing infection in patients with cancer by the PEP Team for Prevention of Infection are conscientious and frequent hand washing with soap and water when hands are visibly soiled or with soap and water or alcohol-based hand rubs when not visibly soiled. In addition, the PEP Team recommended that hands need to be dried properly to avoid colonization with microorganisms (Zitella et al., in press). Although the reviewed patient education publications instruct patients and caregivers to wash their hands frequently or mention washing them before eating and after toileting, Wivell and Fink (2003) did not list hand washing as one of the most common instructions given to patients. Another concern regarding hand washing is whether to instruct patients on how long to wash their hands. If the length of time would be recommended for patients and caregivers, would it be the same as for healthcare workers? In the "Guideline for Hand Hygiene in Health-Care Settings," Boyce and Pittet strongly recommended that hands be rubbed together vigorously for at least 15 seconds after soap and water are applied, covering all surfaces of the hands and fingers. A summary of observational studies on hand washing by healthcare workers showed that the duration of hand washing ranges from 6.6–24 seconds, with the majority of studies revealing average times of 12.5 seconds or less (Boyce & Pittet). Furthermore, casual observation of individuals washing their hands in public facilities demonstrates that most individuals do not abide by a 15-second guideline. Because intact skin protects against infection, one last concern regarding patient education on hand washing is whether information on applying hand lotions or creams to minimize the occurrence of irritant contact dermatitis associated with hand washing should be included, as is strongly recommended for healthcare workers (Boyce & Pittet).

Antiseptic Bathing

Although the evidence associating hand hygiene with a reduced risk of infection is strong, the evidence associating antiseptic bathing with a reduced risk of infection in the neutropenic population is not clear (Larson, 2001). Primary infections of the skin and soft tissue are common in neutropenic patients and may disseminate via the bloodstream. Localized infections often arise at sites of minor trauma, venipuncture, or vascular catheters. Antiseptics have been shown to reduce microbial counts on the skin in the surgical population; however, no studies of antiseptic bathing specific to the neutropenic population were found (Larson & Nirenberg, 2004). Lay magazines and news reports have discussed the everyday use of antimicrobial soaps for the general population. Byrne, Napier, Phillips, and Cuschieri (1991) reported that suppression of normal flora, which has a role in protecting the body against potentially harmful pathogens, has led to colonization by the *Proteus* species; the authors suggested limiting antimicrobial soaps except in cleansing cuts and abrasions. However, recommendations made for one population cannot be applied to all populations or situations, and perhaps future investigation will examine whether antiseptic bathing is a prudent practice for neutropenic patients. Without evidence-based support, current national patient educational materials and guidelines instruct patients to bathe daily.

Oral Care

Patients experiencing neutropenia after cytotoxic chemotherapy almost always have breaches of physical defense barriers secondary to mucositis. Mucositis, which can involve the oropharynx and the gastrointestinal tract, may serve as an opportunity for local infection or direct invasion into the bloodstream. However, mucositis is not the focus of this article and will not be explored. Readers are invited to access the 2005 updated mucositis guidelines (Rubenstein et al., 2004).

Restrictions on Plants and Flowers

Instructing neutropenic patients to avoid gardening or working with soil and restricting plants and flowers in their rooms are fairly common practices. Dried and fresh flowers, plants, soil, and flower water harbor large numbers of resistant microorganisms (Kates, McGinley, Larson, & Leyden, 1991; Smith & Kagan, 2005). The ONS PEP Team for Prevention of Infection suggested several practices that are likely to be effective in preventing infection (Zitella et al., in press). Patients with cancer should avoid fresh or dried flowers and plants because of the risk of *Aspergillus* infection. The care of plants should be limited to individuals not directly caring for patients; however, if this practice is unavoidable, caretakers should wear gloves while handling plants and flowers and wash their hands after removing the gloves. These practices are not supported by well-designed experimental studies that prove that infection actually results from flowers and plants.

Restrictions on Visitors

Wivell and Fink (2003) found that 96% of oncology nurses reported instructing patients receiving chemotherapy to avoid contact with individuals with an infectious disease. National patient guidelines and materials provide similar instruction. Avoiding individuals with respiratory symptoms has been associated with a reduction in certain respiratory infections in patients undergoing bone marrow transplant (Garcia et al.,

1997; Raad, Abbas, & Whimbey, 1997), although no specific research is available among other neutropenic patients (Larson & Nirenberg, 2004). The ONS Team for Prevention of Infection has recommended avoiding contact with individuals with symptoms of respiratory infections (Zitella et al., in press). This recommendation leads to other questions. Should institutions permit afebrile staff with upper respiratory infections to don a mask and care for neutropenic patients? To avoid individuals with possible respiratory infections, should neutropenic patients be instructed to avoid crowds? Does that practice really reduce the infection rate or just increase feelings of social isolation and depression?

Restrictions Regarding Pets

Restricting animal encounters for neutropenic patients may be effective in preventing infection (Sehulster & Chinn, 2003; Zitella et al., in press). Therefore, neutropenic patients should avoid contact with animal feces, saliva, urine, or solid litter box material and direct or indirect contact with reptiles. Hand hygiene should be practiced after any animal contact, and scratches or bites that break the skin should be cleaned promptly. According to Duncan (2000), safety concerns exist regarding exotic species such as reptiles and birds, which have no available vaccinations to prevent them from contracting and transmitting similar zoonoses that are preventable in dogs and cats. However, no studies have determined the statistical risks associated with animals that are healthy, are vaccinated, and receive proper care.

Vast opportunity exists for research in the arena of patient education on fever, neutropenia, and infection. Few evidence-based protocols guide the practice of caring for and educating neutropenic patients. What remains unknown far exceeds the current knowledge base.

Discussion

The State of the Knowledge of Neutropenia Task Force focused its efforts on existing and nonexistent evidence regarding neutropenia, primarily CIN, in patients with cancer. The work of the group revealed many gaps in the evidence, but perhaps equally important is the question of oncology nurses' exact role in the management of neutropenia and CIN. The ONS Outcomes Resource Area (www.ons.org/outcomes/index.shtml) provides information for nurses who offer direct patient care as well as nurses searching for research evidence regarding outcomes. A similar resource is the Evidence-Based Practice Resource Area (www.ons.org/evidence), which focuses on the process and resources for evidence-based practice. Both of the sites refer to prevention of infection as the primary focus of oncology nurses' practice related to neutropenia rather than management of neutropenia. Given and Sherwood's (2005) white paper on NSPOs in oncology lists neutropenia as a symptom management issue; however, it identifies nursing's role as directed toward prevention of infection and FN.

Although the prevention of infection and FN certainly is a patient management issue of critical importance in oncology, the focus on infection, which is a wholly separate and complex clinical outcome, diminishes the significance of neutropenia in oncology nursing care. Neutropenia is a major cause of dose reductions and dose delays, with reduced dosing and lower relative dose intensity associated with inferior survival in patients treated for breast (Bonadonna, Valagussa, Moliterni, Zambetti,

& Brambilla, 1995; Budman et al., 1998; Lyman, Dale, & Crawford, 2003) and colon cancers (Neugut et al., 2006) as well as non-Hodgkin lymphoma (Kwak, Halpern, Olshen, & Horning, 1990). Dose reductions and delays also have resulted in heightened patient anxiety and decreased quality of life (QOL) (Calhoun, Chang, Welshman, & Cella, 2003). In the absence of fever or infection, neutropenia still leads to considerable morbidity and increased costs of care (e.g., use of prophylactic antibiotics, changes in treatment) (Crawford, Dale, & Lyman, 2004). Neutropenia, although frequently asymptomatic on its own, has been implicated in the exacerbation of other chemotherapy- or cancer-related toxicities that occur concomitantly. Studies have reported that the incidence, severity, and duration of other adverse events (e.g., anorexia, vomiting, dehydration, fatigue) were significantly higher when experienced during longer periods of neutropenia (Glaspy, Hackett, Flyer, Dunford, & Liang, 2001; Martin et al., 2004), and associated symptoms worsened when FN became more severe.

Importantly, neutropenia, when occurring separately from infection or FN, has been found to negatively affect QOL. QOL, in turn, has been shown to influence patients' willingness to continue treatment (Cella, Chang, Lai, & Webster, 2002) as well as affect treatment outcomes, including survival (Ganz, Lee, & Siau, 1991; Seidman et al., 1995). A prospective study of patients with cancer undergoing varied therapies demonstrated that more significant decreases in the absolute neutrophil count, without infection, correlated with decreased QOL during the absolute neutrophil count nadir in specific areas of QOL measurement (Fortner, Tauer, Okon, Houts, & Schwartzberg, 2005). Some effects of CIN on QOL were shown to continue even after the absolute neutrophil count had recovered (Okon et al., 2002).

Conversely, the control of other symptoms, as well as potential dose reductions or delays, through prevention and effective management of neutropenia has been reported by patients as having a positive impact on QOL during treatment by improving their physical and emotional well-being (Lyman & Kuderer, 2002). Some patients have expressed a preference to initiate myeloid growth factors at the time of the first cycle of chemotherapy to avoid negative outcomes associated with neutropenia (Erder, Fridman, & Weaver, 2001). Neutropenia management, however, may be associated with diminishing QOL because of the need for frequent injections and laboratory tests, often necessitating multiple clinic visits (Fortner et al., 2004).

Thus, neutropenia alone, in addition to the risk of infection and corresponding sequelae, represents a significant NSPO that requires attention by oncology nurses to identify and address continuing gaps in the evidence about optimal interventions to prevent and manage this symptom. The role of oncology nurses as it relates to prevention and management of neutropenia also needs further identification and clarification.

Application of the State of the Knowledge on Neutropenia: Role of Nurses in Clinical Practice, Research, and Education Settings

As outlined by Given and Sherwood (2005), oncology nurses might play multiple roles as related to NSPOs in different settings. Evidence with regard to the optimal methods for risk assessment of neutropenia, the best tools to use in

busy clinic practices, how to communicate risk and documented assessments to others on the healthcare team, and means of tracking outcomes related to assessments is lacking in the clinical practice setting. Although practice guidelines (American Society of Clinical Oncology, 2006; NCCN, 2005, 2006) exist, the best way to apply the guidelines to individual practice settings remains uncertain. Some clinical practices may work well using standing orders or algorithms derived directly from evidence-based guidelines, such as those of the American Society of Clinical Oncology. Other practices may need further assurance of the cost effectiveness of certain interventions used to prevent or manage neutropenia. Oncology nurses' role may range from becoming familiar with the evidence and practice guidelines to disseminating information to others in the practice and finding creative approaches to implement the evidence in direct patient care. Commonly held principles of neutropenia management (e.g., use of the neutropenic diet) should be examined carefully for supportive evidence. For example, a randomized pilot study of a neutropenic diet versus a diet following standard food safety guidelines was conducted in children receiving myelosuppressive chemotherapy. Infection rates were similar for patients enrolled in both arms, although more difficulty in adherence was reported for the neutropenic diet (Moody, Finlay, Mancuso, & Charlson, 2006). Nurses should serve as active participants as well as leaders in research to generate evidence when it is lacking.

In research settings, oncology nurses may evaluate the efficacy and effectiveness of specific interventions as described and investigate the outcomes associated with certain nursing interventions (Given & Sherwood, 2005). For example, questions as basic as defining the most effective patient hygiene methods to be followed during periods of neutropenia remain unanswered. The effect of nursing practice in neutropenia on patient-reported outcomes, such as health-related QOL or satisfaction with care, needs careful evaluation. Equally important is the need to identify useful, valid, and sensitive means to measure outcomes, as well as effective and practical tools to assess patient-related aspects of neutropenia (Lipscomb, Donaldson, & Hiatt, 2004). Given, Given, Jeon, and Sikorskii (2005) tested a cognitive-behavioral intervention to reduce symptoms and improve QOL in patients undergoing cancer chemotherapy in a randomized trial. Symptoms were more prevalent and severe among patients with neutropenia, but neutropenia also interfered with the effectiveness of the intervention. Of significance, the National Institutes of Health has funded few research studies focused on neutropenia (National Institutes of Health, 2005); most were basic science investigations or clinical trials. Only one funding program announcement (PA-05-004 Symptom Clusters in Cancer and Immune Disorders), sponsored by the National Institute of Nursing Research, was identified. The lack of a nationally funded pool of research studies with a shared focus on neutropenia may be interpreted as a lack of interest on the part of investigators applying for funding, a lack of funding earmarked specifically for neutropenia research, or a dearth of researchers with knowledge of the significance of the topic's relationship to quality oncology care or of the clear gaps in the neutropenia literature that could be addressed by carefully designed research studies.

Thus, professional, patient, and family education settings demonstrate critical needs related to neutropenia. Although

the State of the Knowledge on Neutropenia and regional workshops are important initiatives to focus on neutropenia-related educational issues, these pursuits, in large part, serve to highlight what little high-level evidence currently exists on a topic so essential to cancer care. Nurses enrolled in undergraduate-, graduate-, and doctoral-level educational programs are ideal recipients of the findings of the state-of-the-knowledge conference and for understanding identified gaps in the evidence that would lend themselves well to research activities. Many educational and research initiatives will depend on multidisciplinary collaborative teams to address gaps in the evidence and design and implement educational programs focused on neutropenia prevention and management for physicians, nurse practitioners, physician assistants, staff nurses, pharmacists, and other healthcare providers. These individuals then would become key educators in creating effective approaches to educate patients and family members about the risk for neutropenia; assessment and management strategies, including self-care approaches; and associated outcomes (Donohue, 2006). Teaching patients about the known outcomes reported with low intensity or undertreatment with

cancer therapeutics can aid decision making about compliance with anticancer therapy and supportive care interventions (Gillespie, 2001). Setting treatment goals and communicating them to patients, families, and all members of the healthcare team should help to address the divergence between clinician- and patient-related goals of care.

Considerable gaps in established evidence exist in the areas of clinical practice, research, and education as related to the prevention and management of cancer- and chemotherapy-related neutropenia. Oncology nurses play critical roles in each of the areas and are charged with becoming familiar with the state of the knowledge of neutropenia and maintaining their understanding of the evidence and guidelines. In doing so, oncology nurses can be confident that sound rationale and clinical evidence are driving their decision-making processes to ensure quality cancer care and provide patients with the best opportunity for favorable long-term outcomes.

Author Contact: Anita Nirenberg, RN, MS, AOCNP, can be reached at an207@columbia.edu, with copy to editor at ONFEditor@ons.org.

References

- American Cancer Society & National Comprehensive Cancer Network. (2006). *Fever and neutropenia: Treatment guidelines for patients with cancer (version VII)*. Retrieved June 7, 2006, from http://www.nccn.org/patients/patient_gls/_english/pdf/NCCN%20FN%20Guidelines.pdf
- American Society of Clinical Oncology. (2006). *ASCO patient guide: White blood cell growth factors*. Retrieved May 21, 2006, from <http://www.plw.org/portal/site/PLWC/menuitem.169f5d85214941ccfd748f68ee37a01d/?vgnnextoid=e2215adc8851b010VgnVCM100000ed730ad1RCRD>
- Bodey, G.P. (2000). Fever in the neutropenic patient. In M.D. Abeloff, J.O. Armitage, A.S. Lichter, & J.E. Niederhuber (Eds.), *Clinical oncology* (2nd ed., pp. 690–706). New York: Churchill Livingstone.
- Bonadonna, G., Valagussa, P., Moliterni, A., Zambetti, M., & Brambilla, C. (1995). Adjuvant cyclophosphamide, methotrexate, and fluorouracil in node-positive breast cancer: The results of 20 years of follow-up. *New England Journal of Medicine*, *332*, 901–906.
- Boyce, J.M., & Pittet, D. (2002). Guideline for hand hygiene in health-care settings: Recommendations of the Healthcare Infection Control Practices Advisory Committee and the HICPAC/SHEA/APIC/IDSA Hand Hygiene Task Force. *Infection Control and Hospital Epidemiology*, *23*(Suppl. 12), S3–S40.
- Bucaneve, G., Micozzi, A., Menichetti, F., Martino, P., Dionisi, M.S., Martinelli, G., et al. (2005). Levofloxacin to prevent bacterial infection in patients with cancer and neutropenia. *New England Journal of Medicine*, *353*, 977–987.
- Budman, D.R., Berry, D.A., Cirrincione, C.T., Henderson, I.C., Wood, W.C., Weiss, R.B., et al. (1998). Dose and dose intensity as determinants of outcome in the adjuvant treatment of breast cancer. The Cancer and Leukemia Group B. *Journal of the National Cancer Institute*, *90*, 1205–1211.
- Byrne, D.J., Napier, A., Phillips, G., & Cuschieri, A. (1991). Effects of whole body disinfection on skin flora in patients undergoing elective surgery. *Journal of Hospital Infection*, *17*, 217–222.
- Calhoun, E.A., Chang, C.H., Welshman, E.E., & Cella, D. (2003). The impact of chemotherapy delays on quality of life in patients with cancer [Abstract 2763]. *Blood*, *102*, 749a.
- Carter, L.W. (1994). Bacterial translocation: Nursing implications in the care of patients with neutropenia. *Oncology Nursing Forum*, *21*, 857–865.
- Cella, D., Chang, C.H., Lai, J.S., & Webster, K. (2002). Advances in quality of life measurements in oncology patients. *Seminars in Oncology*, *29*(3, Suppl. 8), 60–68.
- Crawford, J., Dale, D.C., & Lyman, G.H. (2004). Chemotherapy-induced neutropenia: Risks, consequences, and new directions for its management. *Cancer*, *100*, 228–237.
- Cruciani, M., Rampazzo, R., Malena, M., Lazzarini, L., Todeschini, G., Messori, A., et al. (1996). Prophylaxis with fluoroquinolones for bacterial infections in neutropenic patients: A meta-analysis. *Clinical Infectious Diseases*, *23*, 795–805.
- Cullen, M., Steven, N., Billingham, L., Gaunt, C., Hastings, M., Simmonds, P., et al. (2005). Antibacterial prophylaxis after chemotherapy for solid tumors and lymphomas. *New England Journal of Medicine*, *353*, 988–998.
- DeMille, D., Deming, P., Lupinacci, P., & Jacobs, L.A. (2006). The effect of the neutropenic diet in the outpatient setting: A pilot study. *Oncology Nursing Forum*, *33*, 337–343.
- Donohue, R. (2006). Development and implementation of a risk assessment tool for chemotherapy-induced neutropenia. *Oncology Nursing Forum*, *33*, 347–352.
- Duncan, S.L. (2000). APIC state-of-the-art report: The implications of service animals in health care settings. *American Journal of Infection Control*, *28*, 170–180.
- Erder, M.H., Fridman, M., & Weaver, C. (2001). Cancer patients' (CPS') perspectives about the impact of febrile neutropenia morbidity (FNM) on their well-being (WB) and preferences for filgrastim treatment versus dose reduction to prevent FN: An Internet survey [Abstract 2589]. *Proceedings of the American Society of Clinical Oncology*, *20*, 210b.
- Fortner, B.V., Tauer, K.W., Okon, T., Houts, A.C., & Schwartzberg, L.S. (2005). Experiencing neutropenia: Quality-of-life interviews with adult cancer patients. *BMC Nursing*, *4*, 4.
- Fortner, B.V., Tauer, K.W., Zhu, L., Okon, T.A., Moore, K., Templeton, D., et al. (2004). Medical visits for chemotherapy and chemotherapy-induced neutropenia: A survey of the impact on patient time and activities. *BMC Cancer*, *4*(1), 22.
- Gafter-Gvili, A., Fraser, A., Paul, M., & Leibovici, L. (2005). Meta-analysis: Antibiotic prophylaxis reduces mortality in neutropenic patients. *Annals of Internal Medicine*, *142*(12, Pt. 1), 979–995.
- Ganz, P.A., Lee, J.J., & Siau, J. (1991). Quality-of-life assessment. An independent prognostic variable for survival in lung cancer. *Cancer*, *67*, 3131–3135.
- Garcia, R., Raad, I., Abi-Said, D., Bodey, G., Champlin, R., Tarrand, J., et al. (1997). Nosocomial respiratory syncytial virus infections: Prevention and control in bone marrow transplant patients. *Infection Control and Hospital Epidemiology*, *18*, 412–416.
- Gillespie, T.W. (2001). Chemotherapy dose and dose intensity: Analyzing data to guide therapeutic decisions. *Oncology Nursing Forum*, *28*(2, Suppl.), 5–10.

- Given, B.A., Given, C.W., Jeon, S., & Sikorskii, A. (2005). Effect of neutropenia on the impact of a cognitive-behavioral intervention for symptom management. *Cancer*, *104*, 869–878.
- Given, B.A., & Sherwood, P.R. (2005). Nursing-sensitive patient outcomes—A white paper. *Oncology Nursing Forum*, *32*, 773–784.
- Glaspay, J., Hackett, J., Flyer, P., Dunford, D., & Liang, B. (2001). Febrile neutropenia is associated with an increase in the incidence, duration, and severity of chemotherapy toxicities [Abstract 1812]. *Blood*, *98*, 432a.
- Hughes, W.T., Armstrong, D., Bodey, G.P., Bow, E.J., Brown, A.E., Calandra, T., et al. (2002). 2002 guidelines for the use of antimicrobial agents in neutropenic patients with cancer. *Clinical Infectious Diseases*, *34*, 730–752.
- Kates, S.G., McGinley, K.J., Larson, E.L., & Leyden, J.J. (1991). Indigenous multiresistant bacteria from flowers in hospital and nonhospital environments. *American Journal of Infection Control*, *19*, 156–161.
- Kwak, L.W., Halpern, J., Olshen, R.A., & Horning, S.J. (1990). Prognostic significance of actual dose intensity in diffuse large-cell lymphoma: Results of a tree-structured survival analysis. *Journal of Clinical Oncology*, *8*, 963–977.
- Larson, E. (2001). Hygiene of the skin: When is clean too clean? *Emerging Infectious Diseases*, *7*, 225–230.
- Larson, E., & Nirenberg, A. (2004). Evidence-based nursing practice to prevent infection in hospitalized neutropenic patients with cancer. *Oncology Nursing Forum*, *31*, 717–723.
- Lipscomb, J., Donaldson, M.S., & Hiatt, R.A. (2004). Cancer outcomes research and the arenas of application. *Journal of the National Cancer Institute Monographs*, *33*, 1–7.
- Lyman, G.H., Dale, D.C., & Crawford, J. (2003). Incidence and predictors of low dose-intensity adjuvant breast cancer chemotherapy: A nationwide study of community practices. *Journal of Clinical Oncology*, *21*, 4524–4531.
- Lyman, G.H., & Kuderer, N.M. (2002). Filgrastim in patients with neutropenia: Potential effects on quality of life. *Drugs*, *62*(Suppl. 1), 65–78.
- Martin, M., Lluch, M.A., Segui, A., Anton, A., Ruiz, M., Ramos, A., et al. (2004). Prophylactic growth factor (GF) support with adjuvant docetaxel, doxorubicin, and cyclophosphamide (TAC) for node-negative breast cancer (BC): An interim safety analysis of the GEICAM 9805 Study [Abstract 620]. *Journal of Clinical Oncology*, *22*(14, Suppl.), 620.
- Mitchell, S., Friese, C.R., & Beck, S.L. (2006). Putting evidence into practice: Ranking criteria for nursing interventions. Retrieved June 1, 2006, from <http://www.ons.org/outcomes>
- Moody, K., Finlay, J., Mancuso, C., & Charlson, M. (2006). Feasibility and safety of a pilot randomized trial of infection rate: Neutropenic diet versus standard food safety guidelines. *Journal of Pediatric Hematology/Oncology*, *28*(3), 126–133.
- National Comprehensive Cancer Network. (2005). *Clinical practice guidelines in oncology: Fever and neutropenia*. Retrieved September 21, 2005, from http://www.nccn.org/professionals/physician_gls/PDF/fever.pdf
- National Comprehensive Cancer Network. (2006). *Clinical practice guidelines in oncology: Myeloid growth factors*. Retrieved June 20, 2006, from http://www.nccn.org/professionals/physician_gls/PDF/myeloid_growth.pdf
- National Institutes of Health. (2005). Computerized retrieval of information on scientific projects. Retrieved August 15, 2005, from <http://crisp.cit.nih.gov>
- Neugut, A.I., Matasar, M., Wang, X., McBride, R., Jacobson, J.S., Tsai, W.Y., et al. (2006). Duration of adjuvant chemotherapy for colon cancer and survival among the elderly. *Journal of Clinical Oncology*, *24*, 2368–2375.
- Okon, T.A., Fortner, B.V., Schwartzberg, L., Tauer, K.T., Durrence, H., Kovacs, A., et al. (2002). Quality of life (QOL) in patients with grade IV chemotherapy-induced neutropenia (CIN) [Abstract 2920]. *Proceedings of the American Society of Clinical Oncology*, *21*, 275b.
- Pizzo, P.A. (1999). Fever in immunocompromised patients. *New England Journal of Medicine*, *341*, 893–900.
- Raad, I., Abbas, J., & Whimbey, E. (1997). Infection control of nosocomial respiratory viral disease in the immunocompromised host. *American Journal of Medicine*, *102*(3A), 48–52.
- Rubenstein, E.B., Peterson, D.E., Schubert, M., Keefe, D., McGuire, D., Epstein, J., et al. (2004). Clinical practice guidelines for the prevention and treatment of cancer therapy-induced oral and gastrointestinal mucositis. *Cancer*, *100*(9, Suppl.), 2026–2046.
- Sehulster, L., & Chinn, R.Y. (2003). Guidelines for environmental infection control in health-care facilities: Recommendations of CDC and the Healthcare Infection Control Practices Advisory Committee (HICPAC). *Morbidity and Mortality Weekly Report: Recommendations and Reports*, *52*(RR-10), 1–42.
- Seidman, A.D., Portenoy, R., Yao, T.J., Lepore, J., Mont, E.K., Kortmansky, J., et al. (1995). Quality of life in phase II trials: A study of methodology and predictive value in patients with advanced breast cancer treated with paclitaxel plus granulocyte colony-stimulating factor. *Journal of the National Cancer Institute*, *87*, 1316–1322.
- Sickles, E.A., Greene, W.Y., & Wiernik, P.H. (1975). Clinical presentation of infection in granulocytopenic patients. *Archives of Internal Medicine*, *135*, 715–719.
- Smith, C.M., & Kagan, S.H. (2005). Prevention of systemic mycoses by reducing exposure to fungal pathogens in hospitalized and ambulatory neutropenic patients. *Oncology Nursing Forum*, *32*, 565–579.
- Smith, L.H., & Besser, S.G. (2000). Dietary restrictions for patients with neutropenia: A survey of institutional practices. *Oncology Nursing Forum*, *27*, 515–520.
- von Minckwitz, G., Blohmer, J.U., Lohr, A., Raab, G., Eidtmann, H., Gerber, B., et al. (2005). Primary prophylaxis with 3 weekly pegfilgrastim and ciprofloxacin effectively prevent (febrile) neutropenia and infection during neoadjuvant chemotherapy with docetaxel/doxorubicin/cyclophosphamide in breast cancer patients [Abstract]. *Journal of Clinical Oncology*, *23*(Suppl. 16), 8008.
- Wellness Community. (n.d.). *Managing symptoms and side effects: Managing the side effects of cancer treatment*. Retrieved May 13, 2006, from <http://www.thewellnesscommunity.org/programs/frankly/treatment/managing/managing.htm>
- Wilson, B.J. (2002). Dietary recommendations for neutropenic patients. *Seminars in Oncology Nursing*, *18*, 44–49.
- Wivell, B., & Fink, R. (2003, May). Neutropenic precautions: A journey to the development of evidence based standards. Poster presented at the Oncology Nursing Society 28th Annual Congress, Denver, CO.
- Zitella, L., Friese, C.R., Hauser, J., Gobel, B.H., Woolery-Antil, M., O'Leary, C., et al. (in press). Putting evidence into practice: Prevention of infection. *Clinical Journal of Oncology Nursing*.