

## FEATURE ARTICLE

# Putting Evidence Into Practice: Prevention of Infection

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The prevention of infection is an important outcome to measure in patients with cancer because infectious complications are a significant cause of morbidity and mortality. Nurses play a vital role in the prevention of infection in patients with cancer through nursing practice, research, and patient education. However, many common nursing interventions to prevent infection are based on tradition or expert opinion and have not been subjected to scientific examination. The 2005 Oncology Nursing Society Prevention of Infection Outcomes Intervention Project Team reviewed, critiqued, and summarized the research evidence for nursing interventions to prevent infections in patients with cancer. Pharmacologic and nonpharmacologic interventions were included because many advanced practice nurses prescribe medications. This article is an evidence-based review of nursing interventions to prevent infection in patients with cancer.

Nursing-sensitive patient outcomes are outcomes that are attained through or are significantly impacted by nursing interventions. The interventions must be within the scope of nursing practice and integral to the processes of nursing care.

*Editor's note.* This article is the first in a series on the Putting Evidence Into Practice project, in which best practices for patient care are presented.

Since the 1980s, initiatives have been directed at improving the quality of oncology care through clinical practice, research, education, and policy. The current climate of professional accountability has led healthcare professionals, organizations, insurers, and policymakers to identify outcomes that measure the quality of oncology care.

Outcomes can be generic, broad-based variables that pertain to all patients and healthcare providers, such as quality of care or patient satisfaction, or they can be specific to specialized populations, such as return to work after stem cell transplant or pain control in the palliative care setting (Given & Sherwood, 2005).

Nursing-sensitive patient outcomes (NSPOs) are outcomes that are attained through or are significantly impacted by nursing interventions. The interventions must be within the scope of nursing practice and integral to the processes of nursing care (Given & Sherwood). NSPOs validate the value and effectiveness of nursing practice and help nurses demonstrate their contribution to quality patient care.

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## Prevention of Infection

Infections in patients with cancer are a significant cause of morbidity and mortality, especially in those receiving chemotherapy. However, the overall mortality rate from bacterial infections has decreased from 21% to 7% since the mid-1970s. (Viscoli, 2002). Nurses play a vital role in the prevention of infection in patients with cancer through nursing practice, research, and patient education. The goal of the 2005 Oncology Nursing Society (ONS) Prevention of Infection Outcomes Intervention Team was to examine the relevant literature to determine the level of evidence for nursing interventions that contribute to the prevention of infection in patients with cancer (see Appendix).

## Methods

The team searched MEDLINE®, the National Library of Medicine's (2005) bibliographic database. Searches exploded the term *neoplasm plus infection, virus diseases, bacterial infection, or mycoses*. Research articles, systematic reviews, or meta-analyses were included if they were published from 1995–2005 and written in English. The National Guideline Clearinghouse was searched for the key words infection in cancer from 2001–2005 (Agency for Healthcare Research and Quality, 2005). Several organizations' Web sites also identified relevant guidelines (Centers for Disease Control and Prevention, 2006; Infectious Diseases Society of America, 2005; National Comprehensive Cancer Network [NCCN], 2005a, 2005b). Original articles cited before 1995 were reviewed as appropriate. Documents were excluded if they were devoted solely to pediatric or bone marrow transplant populations. A search of *mucositis* and *candidiasis* was conducted because of the strong link between mucositis and infection (Elting et al., 2003). A health services librarian was consulted to review the search terms and strategy.

## Synthesis and Evaluation

Reviewers used standardized worksheets to assist with literature synthesis. Specific criteria identified major and minor flaws with the study design (Hadorn, Baker, Hodges, & Hicks, 1996). The ONS levels of evidence framework was used to sort individual studies and reviews by strength of evidence (Ropka & Spencer-Cisek, 2001). After articles were sorted, each identified intervention was classified by a qualitative summation of the level of evidence. Three criteria were considered: evidence quality, magnitude of the outcome (effect size), and concurrence of the evidence. Six weight-of-evidence categories were devised and are described in Table 1. The evidence categories were adapted from other published schemas (Jones, 2002; U.S. Preventive Services Task Force, 2005). They differ because of the availability of evidence in the content areas as well as the unique aspect of evaluating biologic and behavioral interventions in the same project.

## Highlights of Reviewed Literature

### Pharmacologic

**Colony-stimulating factors:** In the 1990s, colony-stimulating factors (CSFs) were introduced to decrease the neuro-

penic complications of myelosuppressive chemotherapy (Dale, 2002) and to maintain chemotherapy dose intensity (Bohlius, Reiser, Schwarzer, & Engert, 2004). Since then, research has shown consistently that CSFs reduce the severity and duration of neutropenia (see Figure 1), febrile neutropenia, and infection in adults and children who receive chemotherapy for cancer, but they do not affect infection-related mortality or overall survival (Bohlius et al.; Lyman, Kuderer, Agboola, & Balducci, 2003; Lyman, Kuderer, & Djulbegovic, 2002; NCCN, 2005b; Sung, Nathan, Lange, Beyene, & Buchanan, 2004).

The 2005 NCCN practice guidelines recommended the primary use of CSFs in patients who are treated in a curative or adjuvant setting with regimens that carry a 20% or greater risk of neutropenic events, including neutropenic fever (NCCN, 2005b). Individual risk factors must be considered in all cases but are important particularly when determining the use of CSFs for regimens with less than 20% risk of neutropenic events. The factors include age, prior extensive chemotherapy, comorbid conditions, performance status, bone marrow involvement, and pretreatment blood counts. Treatment goals, such as prolonging survival or symptom management, also should be considered. The importance of age as a significant risk factor for neutropenia is underscored by a 2003 systematic review that reports the benefits of prophylactic CSFs in older adult patients, especially with regard to maintaining dose intensity (Lyman et al., 2003).

In 2002, Lyman et al. published a meta-analysis of eight randomized trials that evaluated the efficacy of CSFs in 1,144 adults with solid tumors or lymphoma and demonstrated a 27% risk reduction of febrile neutropenia. The reduction of risk was demonstrated for several subgroups of patients with varying degrees of risk for neutropenic events. The rate of documented infection was reduced, although no difference existed in the rate of infection-related mortality. The major adverse effect of CSF use, bone pain, was nearly three times more likely to be reported with CSF prophylaxis.

The results are echoed in two meta-analyses that studied more homogenous clinical populations. A 2004 Cochrane review of patients with lymphoma included 12 randomized studies with a total of 1,823 patients (Bohlius et al., 2004). Neutropenia was reduced by 33%, febrile neutropenia was reduced by 41%, and the rate of infection was reduced by 26%. Sung et al. (2004) reviewed 16 studies of CSFs in children receiving myelosuppressive chemotherapy and reported a 20% reduction in the rate of febrile neutropenia and a 22% reduction in the rate of documented infection in those receiving CSFs. Neither meta-analysis demonstrated a reduction in infection-related mortality with the use of CSF prophylaxis for patients undergoing chemotherapy.

### Antibiotic Prophylaxis

Antibiotic prophylaxis is defined as antibiotics prescribed for patients undergoing chemotherapy to decrease the risk of infection during chemotherapy-induced neutropenia. Historically, clinical practice guidelines, such as those published by NCCN (2005a) and the Infectious Diseases Society of America (Hughes et al., 2002), have not recommended antibiotic prophylaxis for neutropenic patients with cancer. Antibiotic prophylaxis with

**Table 1. Putting Evidence Into Practice Weight-of-Evidence Classification Schema**

WEIGHT-OF-EVIDENCE CATEGORY	DESCRIPTION	EXAMPLES
Recommended for practice	Effectiveness is demonstrated by strong evidence from rigorously designed studies, meta-analyses, or systematic reviews. Expected benefit exceeds expected harms.	At least two multisite, well-conducted, randomized, controlled trials (RCTs) with at least 100 subjects Panel of expert recommendation derived from explicit literature search strategy; includes thorough analysis, quality rating, and synthesis of evidence
Likely to be effective	Evidence is less well established for those listed under recommended for practice.	One well-conducted RCT with less than 100 patients or at one or more study sites Guidelines developed by consensus or expert opinion without synthesis or quality rating
Benefits balanced with harms	Clinicians and patients should weigh the beneficial and harmful effects according to individual circumstances and priorities.	RCTs, meta-analyses, or systematic reviews with documented adverse effects in certain populations
Effectiveness not established	Data currently are insufficient or are of inadequate quality.	Well-conducted case control study or poorly controlled RCT Conflicting evidence or statistically insignificant results
Effectiveness unlikely	Lack of effectiveness is less well established than those listed under not recommended for practice.	Single RCT with at least 100 subjects that showed no benefit No benefit and unacceptable toxicities observed in observational or experimental studies
Not recommended for practice	Ineffectiveness or harm clearly is demonstrated, or cost or burden exceeds potential benefit.	No benefit or excess costs or burdened from at least two multisite, well-conducted RCTs with at least 100 subjects Discouraged by expert recommendation derived from explicit literature search strategy; includes thorough analysis, quality rating, and synthesis of evidence

*Note.* Based on information from Mitchell & Friese, n.d.

fluoroquinolones decreases the risk of gram-negative infections (Cruciani et al., 1996; Engels, Lau, & Barza, 1998; Gafter-Gvili, Fraser, Paul, & Leibovici, 2005; van de Wetering et al., 2005), gram-positive infections (Gafter-Gvili et al.), all infections (Bucaneve et al., 2005; Engels et al.; Gafter-Gvili et al.), and fever (Bucaneve et al.; Cullen et al., 2005; Engels et al.; Gafter-Gvili et al.). Despite strong evidence that the risk of infection is reduced with the use of prophylactic antibiotics, no evidence prior to 2005 has suggested that prophylactic antibiotics improve survival. In addition, researchers had serious concern that prophylactic antibiotics would promote antibiotic resistance. Therefore, guidelines from NCCN advise against antibiotic prophylaxis unless profound neutropenia (absolute neutrophil count less than 100) is expected to exceed seven days, such as in high-dose chemotherapy and stem cell transplant regimens (NCCN, 2005a). Likewise, the Infectious Diseases Society of America has not recommended routine antibiotic prophylaxis for neutropenic patients with cancer based on the absence of survival benefit and potential for antibiotic resistance (Hughes et al.).

However, in 2005, two meta-analyses showed a significant decrease not only in the incidence of fever, bacteremia, and infection but also in overall mortality (Gafter-Gvili et al., 2005) and infection-related mortality (Gafter-Gvili et al.; van de Wetering et al., 2005) with fluoroquinolone prophylaxis for neutropenic patients with cancer. A nonsignificant trend toward quinolone-resistant infections existed in one meta-analysis (Gafter-Gvili et al.) and one randomized, controlled

trial (Bucaneve et al., 2005) but no increase in fungemia or fungemia-related infection (Cullen et al., 2005; Gafter-Gvili et al.). Most of the patients evaluated in the studies had hematologic malignancies or were undergoing stem cell transplantation, which limits the generalizability of the results to patients with solid tumors who are generally less immunocompromised and, therefore, at lower risk for infection. One recently published randomized, controlled trial specifically evaluated levofloxacin prophylaxis (500 mg by mouth for seven days) after chemotherapy in 1,565 patients with solid tumors who did not receive CSF prophylaxis (Cullen et al.). The study demonstrated decreased rates of fever and probable infection but was not powered adequately to assess infection-related or overall mortality. In addition, the incidence of fever was 10.8% in the levofloxacin group and 15.2% in the control group, underscoring the low incidence of neutropenic fevers in patients with solid tumors undergoing chemotherapy. Controversy remains regarding the use of antibacterial prophylaxis for patients with solid tumors because of concerns about antibiotic resistance (Bucaneve et al.; Cullen et al.; Gafter-Gvili et al.; Hughes et al., 2002; NCCN, 2005a; van de Wetering et al.). Additionally, the benefit of antibiotic prophylaxis if patients are receiving CSFs requires further study (Lalami et al., 2004). Therefore, fluoroquinolones (e.g., ciprofloxacin 500–750 mg by mouth twice daily for seven days, levofloxacin 500 mg by mouth once daily for seven days) are recommended only for antibacterial prophylaxis in high-risk afebrile neutropenic patients with cancer after chemotherapy.

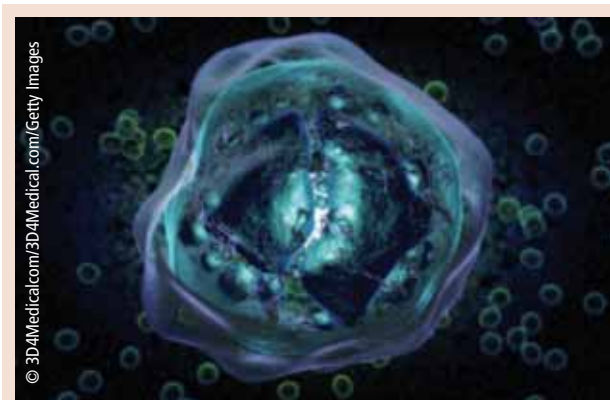


Figure 1. A Neutrophil

## Antifungal Prophylaxis

Fungal infections in neutropenic patients are associated with high rates of mortality and often are difficult to diagnose (Kanda et al., 2000). However, routine antifungal prophylaxis is not recommended for all neutropenic patients with cancer. Prophylaxis is recommended only for high-risk patients (e.g., those with acute leukemia) and patients undergoing stem cell transplantation (Bow et al., 2002; Cornely, Ullmann, & Karthaus, 2003; Glasmacher et al., 2003; Gotzsche & Johansen, 2004; Johansen & Gotzsche, 2004a; Kanda et al.; NCCN, 2005a). Antifungal prophylaxis reduces fungal colonization and risk of invasive fungal infection in patients with severe neutropenia such as those with acute leukemia or those undergoing hematopoietic stem cell transplantation (Gotsche & Johansen; Kanda et al.). Appropriate agents include fluconazole (Cornely et al.; Kanda et al.), itraconazole suspension, IV itraconazole (Cornely et al.; Glasmacher et al.), or amphotericin B (Gotsche & Johansen). Capsule formulations of itraconazole have inferior efficacy (Glasmacher et al.). Lipid formulations of amphotericin B are equivalent to nonliposomal formulations in reducing mortality, but lipid formulations may be better tolerated (Johansen & Gotzsche, 2004b).

## Vaccinations

Currently, the rate of influenza vaccination among patients with cancer is low, presumably because of concerns regarding efficacy in that population (Ring, Marx, Steer, & Harper, 2002). Several studies have demonstrated that the immune response is equivalent in patients with cancer when compared to healthy controls, whereas others failed to confirm the findings (NCCN, 2005a; Ring et al.). Despite the conflicting evidence, the low incidence of adverse effects coupled with the potential benefit led the NCCN Fever and Neutropenia Clinical Practice Guidelines Panel to recommend that all patients with cancer and their household contacts receive annual influenza immunization (NCCN, 2005a). The timing of the vaccination in relation to chemotherapy treatments has not been established, but several small studies suggest that patients with cancer not receiving chemotherapy have a superior response to vaccination compared with patients receiving chemotherapy (Ring et al.).

Additionally, a small study suggested increased efficacy when the vaccination is administered between cycles rather than on the day of chemotherapy treatment (Ring et al.). Annual vaccination should be administered throughout the influenza season to patients at high risk for complications from influenza, including patients with malignancies and individuals who can transmit influenza to high-risk patients, such as healthcare workers and household contacts (Tablan, Anderson, Besser, Bridges, & Hajjeh, 2004).

Less research has evaluated the efficacy of pneumococcal vaccination in patients with cancer undergoing chemotherapy, but the Centers for Disease Control and Prevention recommended that the 23-valent pneumococcal polysaccharide vaccine be administered to all people aged 65 and older as well as patients aged 5–64 receiving immunosuppressive therapy or who have a malignancy (Tablan et al., 2004). The 7-valent pneumococcal polysaccharide protein-conjugate vaccine should be administered to all children younger than two years and to children aged 24–59 months with malignancies (Tablan et al.).

## Neutropenia

**Protective isolation:** A variety of practices exist regarding the use of isolation for immunocompromised patients; however, the effectiveness of protective isolation has not been established. A randomized study of adult neutropenic patients with cancer demonstrated no difference in infection for patients in protective isolation compared to those not in isolation; another study supported the findings, indicating no significant differences in median days with a fever, number of days before the first use of systemic antibiotics, or the use of antifungals (Mank & van der Lelie, 2003; Nauseef & Maki, 1981). Although the published studies had small sample sizes, no statistically significant differences existed in the incidence of febrile episodes, the number of infections, or the use of antibiotics for patients in protective isolation and those not isolated. Because no evidence suggests that protective isolation reduces the risk of infection, the practice is no longer recommended (Larson & Nirenberg, 2004; Schulster & Chinn, 2003; Shelton, 2003). However, healthcare providers should continue to recommend that neutropenic patients avoid or minimize exposure to potentially infectious people. Visitors should be screened for symptoms indicating potential respiratory infection and instructed not to visit patients if an infection is found (Larson & Nirenberg).

## Hand Washing, Gloves, and Gowns

Hand washing has been proven by multiple, well-designed studies to be one of the most effective ways to prevent the transmission of infection (Boyce & Pittet, 2002; Schulster & Chinn, 2003; Shelton, 2003; Smith & Kagan, 2005). The majority of the research has been conducted in noncancer settings but can be applied to all patients. Despite the strong evidence that hand washing decreases the risk of infection, clinicians are not always compliant in washing their hands before and after patient contact. The key to hand washing is friction during washing and thorough drying of the hands (see Figure 2). Either soap and warm water or an antiseptic hand sanitizer



**Figure 2. Hand Washing Can Prevent the Transmission of Infection**

may be used, although soap and water are preferable if hands are visibly soiled or contaminated with proteinaceous material (Boyce & Pittet). Thorough drying of the hands is important because hands may remain colonized with microorganisms after hand washing if hands are not dried properly (Boyce & Pittet). In clinical situations involving respiratory secretions or handling of objects that may have been contaminated with respiratory secretions, gloves and gowns should be worn (Schulster & Chinn).

## Diet

Although dietary restrictions for neutropenic patients with cancer have been common practice, research and evidence to support the effectiveness of the practice are surprisingly lacking. Despite the lack of evidence to demonstrate decreased risk of infection with dietary restrictions, nearly all institutions recommend dietary restrictions to their patients. The most common recommendation is to avoid uncooked meats, seafood, and eggs and unwashed fruits and vegetables (Larson & Nirenberg, 2004; Moody, Charlson, & Finlay, 2002; Smith & Besser, 2000; Somerville, 1986; Wilson, 2002). Many of the studies relating to diet are complicated by confounding institutional manipulations, such as protected environments and differences in restrictions, that may have an impact. Inconsistencies in the literature and practice illustrate the need for further research to define the role and effectiveness of the neutropenic diet in preventing infection.

## Flowers and Plants

No research studies were found that evaluated the potential of infection from exposure to flowers and plants. However, the Centers for Disease Control and Prevention has recommended that no flowers and plants be allowed in the rooms of neutropenic patients. The guidelines permit flowers and plants in the rooms of immunocompetent patients but recommend that the water in the vase be changed every two days and discarded outside patients' rooms (Schulster & Chinn, 2003).

## Oral Mucositis

To date, no specific oral care products have been found to prevent oral mucositis in the general oncology population (Rubenstein et al., 2004). However, strong evidence indicates that oral care protocols significantly reduce the severity of mucositis from chemotherapy or radiotherapy (Rubenstein et al.). Oral care protocols generally include regular cleansing of the teeth and mucosal tissue as well as patient education. Although consistent and frequent oral care is currently the most effective intervention shown to prevent oral mucositis, no specific protocol is recommended. Research studies to date have not provided information on the frequency of activities such as brushing, flossing, and rinsing of the oral mucosa. More definitive studies are needed to help to guide nursing practice and education.

Of the numerous oral care products evaluated to prevent oral mucositis, none has proven to be more effective than oral saline rinses. However, several small studies suggest that amifostine, granulocyte-macrophage colony-stimulating factor, hydrolytic enzymes, or topical antibiotic pastille or paste may reduce oral mucositis in patients receiving cancer treatment (Clarkson, Worthington, & Eden, 2003). Additional studies with larger numbers of patients must be done to support their clinical application because the existing studies have small sample sizes or weak research designs. Other interventions studied include allopurinol mouth rinse, benzydamine, clarithromycin, and povidone, but the data are either insufficient or of inadequate quality to make a recommendation regarding their use. Interventions that are unlikely to be more effective than placebo based on adequate data include chamomile, folic acid, prednisolone, propantheline, prostaglandin, and Traumeel® (Heel Inc., Albuquerque, NM) (not approved by the U.S. Food and Drug Administration). Stronger evidence suggests that acyclovir, glutamine, and sulcrafate also are ineffective in preventing oral mucositis. Notably, well-designed studies demonstrate that the common practice of oral care with chlorhexidine mouth rinses is no more effective than a placebo and, in fact, may be harmful to patients (Clarkson et al.).

Strong evidence indicates that antifungal drugs that are absorbed from the gastrointestinal (GI) tract (e.g., fluconazole, ketoconazole, itraconazole) prevent oral candidiasis. Antifungal drugs that are partially absorbed from the GI tract (e.g., miconazole, clotrimazole) are also effective in preventing oral candidiasis. However, antifungal drugs that are not absorbed from the GI tract (e.g., amphotericin B, nystatin, chlorhexidine, nystatin plus chlorhexidine, thymostimulin, amphotericin B plus nystatin, polyenes, natamycin, norfloxacin plus amphotericin B) did not have significant benefit in preventing oral candidiasis and, therefore, are not recommended (Worthington & Clarkson, 2002; Worthington, Eden, & Clarkson, 2004).

Cryotherapy (ice chips) is another intervention to prevent oral mucositis associated with chemotherapy (Worthington & Clarkson, 2002). Cryotherapy significantly reduced the incidence of mucositis in patients receiving bolus 5-fluorouracil (5-FU) therapy (Cascinu, Fedeli, Fedeli, & Catalano, 1994; Clarkson et al., 2003; Mahood et al., 1991; Rubenstein et al., 2004). Patients were instructed to hold ice chips in their mouths starting five minutes prior to the bolus 5-FU and for 30 minutes after. The

effectiveness of the intervention is related to the short half-life of bolus 5-FU, so it cannot be generalized to other chemotherapy agents with longer half-lives. The results also should be viewed with caution because they are based on two trials with a total of only 177 subjects who were not blinded to the treatment (Cascinu et al.; Mahood et al.).

## Conclusion

Additional studies are needed to further define practice interventions that impact infection. Most of the interventions for managing hospitalized patients with neutropenia continue to be based on tradition and theoretical considerations; very few well-controlled research studies have been conducted. Many of the published studies are nonrandomized, single-institution studies with sample sizes too small to draw meaningful conclusions. Oncology nurses are in a key position to facilitate studies across institutions designed to improve the care of neutropenic patients.

Nursing professionals are dedicated to the provision of quality care to improve health outcomes for patients. Evidence-based practice helps nurses determine which interventions are effective to improve patient outcomes and allows nurses to abandon ineffective interventions that are based solely on custom or tradition. Additionally, embracing the initiative to identify, define, and measure NSPOs provides a means for nurses to articulate and objectively demonstrate their contribution to quality patient care. The oncology NSPOs outlined by members of ONS provide a framework for classifying nursing interventions. Through a collaborative effort among ONS, nurse scientists, advanced practice nurses, and staff nurses, the existing literature should continue to be reviewed to develop evidence-based summaries for these NSPOs. Because a tremendous amount of additional research is necessary to evaluate the effectiveness of nursing interventions, nurse scientists also can contribute to evidence-based practice by developing the research protocols to study NSPOs.

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## Appendix. Putting Evidence Into Practice Card on Infection Prevention

### What Interventions Are Effective in Preventing Infection in People With Cancer?

#### RECOMMENDED FOR PRACTICE

Interventions for which effectiveness has been demonstrated by strong evidence from rigorously designed studies, meta-analyses, or systematic reviews and for which the expectation of harms is small compared to the benefits

#### Hand hygiene using soap and water or an antiseptic hand rub for all patients with cancer and their caregivers<sup>1-7</sup>

- Wash hands with soap and water, especially if hands are visibly soiled or contaminated with proteinaceous material.
- Use either soap and water or alcohol-based hand rubs when hands are not visibly soiled or contaminated.
- Hands may remain colonized with microorganisms after handwashing if hands are not dried properly.

#### Colony-stimulating factors (CSFs) for all patients with cancer undergoing chemotherapy with > 20% risk of febrile neutropenia<sup>6,8-12</sup>

#### Influenza vaccine annually for all patients with cancer<sup>1,3,14</sup>

- The potential benefit significantly outweighs the low risk for adverse effects. The timing and efficacy of influenza vaccination have not been clearly established based on conflicting evidence in the literature.

#### 23-valent pneumococcal polysaccharide vaccine for all patients with cancer older than five years of age and 7-valent pneumococcal polysaccharide protein-conjugate vaccine for all patients with cancer younger than five years of age<sup>1</sup>

#### Trimethoprim-sulfamethoxazole (TMP-SMZ) to prevent *Pneumocystis carinii* pneumonia (PCP) for all patients at risk<sup>15</sup>

- Consider TMP-SMZ desensitization, atovaquone, dapsone, or aerosolized pentamidine when PCP (recently renamed as *Pneumocystis jir-oveci*) prophylaxis is required and patients are TMP-SMZ intolerant.<sup>14</sup>

#### Antifungal drugs absorbed or partially absorbed from the gastrointestinal (GI) tract to prevent oral candidiasis in patients with cancer undergoing chemotherapy<sup>16,17</sup>

- Antifungal drugs absorbed from the GI tract (fluconazole, ketoconazole, and itraconazole) or partially absorbed from the GI tract (miconazole and clotrimazole) prevented oral candidiasis.
- Antifungal drugs not absorbed from the GI tract (amphotericin B, nystatin, nystatin plus chlorhexidine, thymostimulin, amphotericin B plus nystatin, polyenes, natamycin, and norfloxacin plus amphotericin B) did not prevent oral candidiasis.

#### Antifungal prophylaxis for severely neutropenic afebrile patients (absolute neutrophil count [ANC] < 1,000 for more than one week)

- In general, antifungal prophylaxis is not recommended for all neutropenic patients with cancer; however, it is recommended for high-risk patients such as those with acute leukemia or those undergoing hematopoietic stem cell transplantation (HSCT).<sup>14,15,18-23</sup>
- Antifungal prophylaxis reduces fungal colonization and risk of invasive fungal infection in severely neutropenic patients (ANC < 1,000 for more than one week).<sup>14,18,19,21-23</sup>

- Effective agents include fluconazole,<sup>14,18-20,23,24</sup> itraconazole suspension 400 mg po,<sup>14,18,20,21</sup> itraconazole 200 mg IV daily,<sup>18,20,21,23</sup> or IV amphotericin B.<sup>14,18,20,22-24</sup> Lipid-based formulations of IV amphotericin B may increase efficacy because of increased patient tolerability.<sup>22</sup> Itraconazole capsules are not effective.<sup>21</sup>

#### Antibacterial prophylaxis with quinolones for high-risk afebrile neutropenic patients with cancer undergoing chemotherapy

- Quinolones (e.g., ciprofloxacin 500–750 mg bid x 7 days or levofloxacin 500 mg qd x 7 days) are recommended for the prevention of infection in high-risk afebrile neutropenic patients after chemotherapy.<sup>6,14,25-30</sup> Patients at high risk for infection include patients with hematologic malignancies, HSCT patients, or patients expected to have prolonged neutropenia. Most of the patients evaluated in clinical trials had hematologic malignancies or were undergoing HSCT, although one recent randomized controlled trial demonstrated a decreased rate of infection in patients with solid tumors undergoing chemotherapy. Nonetheless, controversy exists regarding its use in patients with solid tumors because of concerns about antibiotic resistance.<sup>14,15,25-30</sup> The benefit of antibiotic prophylaxis if patients are receiving CSFs requires further study.<sup>31</sup>

#### Herpes viral prophylaxis (acyclovir or valacyclovir) for selected seropositive patients with cancer<sup>14</sup>

- During cytotoxic therapy–induced neutropenia in patients with cancer who have had prior reactivations requiring treatment
- Patients receiving T-cell–depleting agents (i.e., fludarabine)
- During allogeneic marrow transplant until day 30 post-transplant
- During induction or reinduction therapy for acute leukemia through the neutropenic period

#### Protective gowns if soiling with respiratory secretions is anticipated<sup>1</sup>

#### Do not allow visitors with symptoms of respiratory infections.<sup>1</sup>

#### Environmental interventions<sup>4</sup>

- Keep windows closed.
- Patients with airborne respiratory viruses (e.g., varicella, tuberculosis) should be placed in rooms equipped with an anteroom to maintain proper air balance. High-efficiency particulate air (HEPA) filters should be used for air recirculation. Portable HEPA filters should be used when anterooms are not available.
- Negative-pressure rooms should be used for patients with documented or suspected airborne infections or viral hemorrhagic fever.

#### LIKELY TO BE EFFECTIVE

Interventions for which the evidence is less well established than for those listed under “Recommended for Practice”

#### Oxygen and respiratory care<sup>1</sup>

- Oxygen humidifiers: Change the humidifier tubing, nasal prongs, and/or mask when it malfunctions or becomes visibly contaminated.



- Small-volume medication nebulizers: (1) Disinfect, rinse with sterile water, and dry between uses on the same patient; (2) use only sterile fluid for nebulization, and dispense fluid aseptically; (3) single-dose dispensing is preferred.
- Mist tent: (1) Replace mist tents and their nebulizers, reservoirs, and tubing with those that have undergone sterilization or high-level disinfection between uses on different patients; (2) mist tent nebulizers and tubing that are used on the same patient should undergo daily low-level disinfection or pasteurization followed by air drying.

#### HEPA filters and HEPA filter masks for patients with prolonged neutropenia<sup>4,6,14</sup>

- It is reasonable to use HEPA filters in nontransplant patients with prolonged neutropenia. Immunocompromised patients placed in protective environments should have mask protection when traveling outside of their protected area.

#### Flower and plant guidelines

- Patients with cancer should avoid fresh or dried flowers and plants because of the risk of *Aspergillus* infection.<sup>4,6,32</sup>
- Limit plant care to staff not directly caring for patients.<sup>4</sup>
- If plant care by patient care staff is unavoidable, staff should wear gloves while handling plants/flowers and perform hand hygiene after glove removal.<sup>4</sup>
- Change vase water every two days; discharge water outside the patient's room.<sup>4</sup>
- Clean and disinfect vases after use.<sup>4</sup>

#### Ice handling<sup>4</sup>

- Automated ice-dispensing systems are preferred to ice bins, but adherence to cleaning procedures and schedules is essential.
- Do not handle ice by hand, and wash hands prior to obtaining ice.

#### Animal encounters<sup>4</sup>

- Advise patients to avoid contact with animal feces, saliva, urine, or solid litter box material.
- Promptly clean and treat scratches, bites, or other wounds that break the skin.
- Advise patients to avoid direct or indirect contact with reptiles.
- Practice hand hygiene after any animal contact.

#### Preconstruction planning<sup>4</sup>

- Planning should include risk assessment, documentation and monitoring of the construction barrier, and education to the clinical staff about appropriate precautionary measures.
- High-risk patients should wear high-efficiency masks when not in a functioning protective environment room during construction/renovation activities.

#### Uniform/protective garment washing by employer when contaminated<sup>4</sup>

#### Mattress maintenance to maintain integrity of mattress<sup>4</sup>

- Replace mattresses that have lost integrity. Do not puncture mattresses with needles.

### EFFECTIVENESS NOT ESTABLISHED

Interventions for which insufficient data or data of inadequate quality currently exist

**Immune globulin for respiratory syncytial virus<sup>1</sup>**

#### Enhanced infection control policy to prevent the transmission of vancomycin-resistant enterococci (VRE)<sup>33-35</sup>

- Nonrandomized, single-institution studies suggest that enhanced infection control measures may decrease the transmission of VRE. Interventions evaluated include contact isolation, limiting the use of empiric vancomycin, spatial separation of patients based on VRE status, infection control surveillance, and staff and patient education. Multiple interventions were implemented simultaneously, so the effect of each intervention is unknown.

#### Protective isolation<sup>5,6,36,37</sup>

#### Diet modifications for neutropenic patients

- No recent studies have linked dietary restrictions with a lower risk of infection for neutropenic patients with cancer; however, basic principles, such as avoiding uncooked meats, seafood, eggs, and unwashed fruits and vegetables, may be prudent.<sup>6,7,32,36,38-40</sup> Multivitamin supplementation for patients with cancer anticipating neutropenia requires further study.<sup>41</sup>

### EFFECTIVENESS UNLIKELY

Interventions for which lack of effectiveness is less well established than for those listed under "Not Recommended for Practice"

**Laminar air flow<sup>4,14</sup>**

### NOT RECOMMENDED FOR PRACTICE

Interventions for which clear evidence has demonstrated ineffectiveness or harmfulness or for which the cost or burden necessary for the intervention exceeds the anticipated benefit

#### Antifungal prophylaxis for neutropenic patients with cancer with solid tumors<sup>14,15,18-23</sup>

- Antifungal prophylaxis is not recommended for all neutropenic patients with cancer. It is only recommended for high-risk patients such as those with acute leukemia and those undergoing HSCT.

#### Itraconazole capsules are not effective for any cancer population<sup>21</sup>

#### Nonabsorbable topical antifungal drugs to prevent oral candidiasis<sup>16,17</sup>

- Antifungal drugs not absorbed from the GI tract (amphotericin B, nystatin, nystatin plus chlorhexidine, thymostimulin, amphotericin B plus nystatin, polyenes, natamycin, and norfloxacin plus amphotericin B) did not have significant benefit in preventing oral candidiasis.

#### TMP-SMZ for antibacterial prophylaxis in afebrile neutropenic patients with cancer<sup>15,26-28,42</sup>

#### Gram-positive prophylaxis and fluoroquinolone in combination for antibacterial prophylaxis in afebrile neutropenic patients with cancer<sup>42</sup>

**FluMist® (intranasal attenuated influenza vaccine)<sup>14</sup>**

## What Interventions Are Effective in Preventing Oral Mucositis in People With Cancer?

Mucositis was included in this review because it is associated with a significantly increased risk of infection when present in people with cancer.<sup>43</sup>

### RECOMMENDED FOR PRACTICE

Interventions for which effectiveness has been demonstrated by strong evidence from rigorously designed studies, meta-analyses, or systematic reviews and for which the expectation of harms is small compared to the benefits

#### Oral care protocols

- Oral care protocols, including regular cleansing of the teeth and mucosal tissue, as well as patient education, significantly reduce the severity of mucositis from chemotherapy or radiotherapy.<sup>44</sup>

#### Cryotherapy for patients receiving bolus 5-fluorouracil (5-FU)<sup>17,44-47</sup>

- Patients should be instructed to hold ice chips in their mouth starting 5 minutes prior to the bolus 5-FU and for 30 minutes after. The effectiveness of this intervention is related to the short half-life of bolus 5-FU and is NOT proven for other chemotherapy agents.

### LIKELY TO BE EFFECTIVE

Interventions for which the evidence is less well established than for those listed under "Recommended for Practice"

#### Amifostine for patients with head and neck cancer treated with radiotherapy<sup>46</sup>

#### Granulocyte macrophage–colony-stimulating factor for patients with solid tumors<sup>46</sup>

#### Hydrolytic enzymes for patients with head and neck cancer<sup>46</sup>

#### Topical antibiotic pastille or paste for patients with solid tumors<sup>46</sup>

### EFFECTIVENESS NOT ESTABLISHED

Interventions for which insufficient data or data of inadequate quality currently exist

#### Allopurinol<sup>17,46</sup>

#### Benzydamine<sup>46</sup>

#### Clarithromycin<sup>46</sup>

#### Povidone<sup>46</sup>

### EFFECTIVENESS UNLIKELY

Interventions for which lack of effectiveness is less well established than for those listed under "Not Recommended for Practice"

#### Chamomile<sup>17,46</sup>

#### Folinic acid<sup>46</sup>

#### Pentoxifylline<sup>46</sup>

#### Prednisolone<sup>46</sup>

#### Propantheline<sup>46</sup>

#### Prostaglandin<sup>17,46</sup>

#### Traumeel<sup>46</sup>

### NOT RECOMMENDED FOR PRACTICE

Interventions for which clear evidence has demonstrated ineffectiveness or harmfulness or for which the cost or burden necessary for the intervention exceeds the anticipated benefit

#### Acyclovir<sup>46</sup>

#### Chlorhexidine<sup>17,44,46</sup>

#### Glutamine<sup>46</sup>

#### Sucralfate<sup>46</sup>

Recommendations are intended for the prevention of infection for the general hematology and oncology patient population. Recommendations for the prevention of infection for transplant (HSCT) recipients are excluded. Recommendations for the treatment of febrile neutropenia or established infections are excluded.

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Definitions of the interventions and full citations: [www.ons.org/outcomes](http://www.ons.org/outcomes)  
Literature search completed through June 2005.

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