■ Article

A Pilot Study Comparing the Neutropenic Diet to a Non-Neutropenic Diet in the Allogeneic Hematopoietic Stem Cell Transplantation Population

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Background: Historically, dietary restrictions imposed on patients undergoing hematopoietic stem cell transplantation (HSCT) were severe and limited to prevent exposure to foodborne organisms. With improvements in supportive care and anti-infective agents, the necessity of the neutropenic diet for this population has been in question.

Objectives: This study aimed to determine whether the incidence of infection differs and to analyze the nutritional status in patients undergoing myeloablative allogeneic HSCT with a neutropenic diet as compared to those with a diet without restrictions.

Methods: This study was a randomized, controlled prospective pilot study beginning within the first 24 hours of the start of the conditioning regimen. Patients were randomized to receive a neutropenic diet or a diet without restrictions. All patients received care in a high-efficiency particulate air-filtered room on the inpatient adult blood and marrow transplantation unit (ABMTU). All patients received antibacterial and antifungal prophylaxis. Patients were followed until the end of neutropenia (defined as absolute neutrophil count of greater than 500 for three days) or until discharge from the inpatient ABMTU.

Findings: In 46 evaluable patients, no significant difference was found between infection rates or nutritional status. The neutropenic diet did not offer a protective effect against infection in patients undergoing myeloablative allogeneic HSCT. No differences were found in nutritional status between the two groups.

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Each year, thousands of individuals undergo allogeneic stem cell transplantation for hematologic disorders (Tomblyn et al., 2009). For many individuals, receiving stem cells from another person is the only chance for cure or longer-term survival; however, the procedure is risky and has a potentially high mortality rate depending on the type of transplantation, donor source, and patient risk factors. The major complication of allogeneic stem cell transplantation is infection.

Patients undergoing myeloablative allogeneic hematopoietic stem cell transplantation (HSCT) develop a period of pancytopenia, during which occurs an increased risk of infection. In addition, conditioning regimens contain alkylating chemotherapy agents and total body irradiation that increase the development of stomatitis and mucositis. Mucositis enables microorganisms native to the endogenous intestinal flora to translocate from the intestine to the lymphoid tissue and blood (Boeckh, 2012). When mucositis and pancytopenia occur simultaneously, the risk of infection is even higher. Bloodstream infections by gram-negative bacilli and yeasts are an important cause of serious infections that cause considerable morbidity (van Tiel et al., 2007).

The physiologic basis of the neutropenic diet provides a theoretical basis for this topic. The primary function of the immune system is to recognize and destroy antigens in the body. This nonspecific immune response is promoted by polymorphonuclear

phagocytes, mononuclear phagocytes, and natural killer cells. Neutrophils are the most abundant polymorphonuclear phagocyte of the white blood cells and are the first line of defense against infection. When the neutrophil count falls to less than 1,000 cells per mcl, the risk of infection increases (Turvey & Broide, 2010).

The organisms found on food that most commonly cause infection are aerobic gram-negative rods, such as *Escherichia coli (E. coli), Pseudomonas aeruginosa,* and *Klebsiella pneumoniae*. These gram-negative organisms can cause lethal infections, which are often a result of bacteria translocation in the gut because of damage from cytotoxic therapy, allowing bacteria to move into the surrounding lymph nodes and visceral organs (Restau & Clark, 2008).

In an attempt to reduce bacterial infections, several measures have been used, including reverse isolation, prophylaxis with antibiotic and antifungal medications to selectively decrease the amount of aerobic gram-negative bacilli and yeast for the gut flora, and the use of the neutropenic diet. Historically, the Centers for Disease Control and Prevention (CDC) has recommend that a recipient of stem cell transplantation should have a restricted diet to decrease the risk of exposure to foodborne infections from bacteria, yeast, molds, viruses, and parasites (Tomblyn et al., 2009). This recommendation may not be practical because some patients may remain on immunosuppressive therapy long after they are discharged from the transplantation center.

Currently, a low bacterial diet is suggested for recipients of allogeneic HSCT until all immunosuppressive drugs are discontinued (Tomblyn et al., 2009). Little is known about how organisms from food colonize and infect immunosuppressed individuals or whether interventions, particularly the neutropenic diet, can help to reduce infection (Boeckh, 2012).

Evidence that supports the necessity of a neutropenic diet is lacking, and clinical practices around the world vary. In the United States, a descriptive study by Smith and Besser (2000) found that the implementation of a neutropenic diet in patients with neutropenia undergoing chemotherapy (excluding patients receiving stem cell transplantation) was inconsistent. Of the 120 institutions surveyed, 78% placed patients with neutropenia on a restricted diet. The diet restrictions varied widely between institutions. Although this study did not address infection rates, it did demonstrate that clinical practice is varied, further supporting the need for more research in this area. In a survey of Canadian pediatric bone marrow transplantation programs, five of seven hospitals that responded provided a low-bacteria diet to reduce the potential exposure to pathogens (French, Levy-Milne, & Zibrick, 2001). Practices ranged from preparing food in a separate kitchen using aseptic techniques to a modified hospital diet excluding fresh fruits and vegetables. In addition, no consensus was found on when to initiate or discontinue the dietary guidelines. A telephone survey of 21 institutions conducted by St. Jude Children's Research Hospital was used to describe the practice of using a neutropenic diet in immunocompromised patients (Todd, Schmidt, Christain, & Williams, 1999). That survey revealed that a neutropenic diet was provided to recipients of bone marrow transplantation at 19 of 21 hospitals. In a retrospective analysis conducted in Europe, Mank and van der Lelie (2003) surveyed adult transplantation centers in 13 Dutch hospitals and 141 European hospitals, yielding 101 responses. A questionnaire reviewed hospital standards and examined patient infection rates. Infection rates were quantified before and after a new standard was implemented. The previous standard was to provide a "germ-poor" diet on admission. Results were compared with the new standard, which had no diet restrictions. No differences were found between patients in median number of days with fever, use of amphotericin B, the number of documented infections, or mortality rates (Mank & van der Lelie, 2003).

With the possibility that the neutropenic diet is not beneficial in reducing infection rates, a second concern arises for clinicians—that the use of neutropenic diets may contribute to malnutrition in patients undergoing transplantation. Energy requirements of patients undergoing stem cell transplantation are believed to reach 130%–150% of predicted basal energy expenditure (Sheean, 2005). Impaired nutritional status prior to transplantation has been shown to be a negative prognostic indicator of outcome. Well-nourished patients have experienced earlier engraftment (Trifilio et al., 2012). Malnutrition ranges from 20%–80% in patients with cancer and has been associated with reduced response to treatment, survival, and quality of life (Kubrak & Jensen, 2007). Considering that patients undergoing HSCT struggle to consume adequate caloric intake orally because of treatment side effects, including mucositis, nausea, vomiting, and diarrhea, the use of a neutropenic diet may pose unnecessary restrictions and compound the diminished oral intake (Rock et al., 2012).

In the transplantation community, debate exists regarding the most appropriate diet for patients undergoing HSCT. Recommendations regarding the use of low-bacterial diets have been based on theoretical concepts of reducing the risk of contracting

TABLE 1. Sample Characteristics (N = 46)

		Control (n = 21)		Experimental (n = 25)	
Characteristic	Range	$\bar{X}$	SD	$\bar{X}$	SD
Age (years)	23–62	45	9.4	45	9.2
Characteristic		**n**		**n**	
Gender					
Male		13		9	
Female		8		16	
Diagnosis					
Acute myeloid leukemia		11		11	
Acute lymphoblastic leukemia		3		5	
Non-Hodgkin lymphoma		1		1	
Other[a]		6		8	
Preparatory regimen					
Total body irradiation/chemotherapy		13		16	
Chemotherapy alone		8		9	
Donor source					
Matched related donor		6		9	
Matched unrelated donor		9		10	
Matched unrelated donor (bone marrow)		–		1	
Dual umbilical cord blood		6		5	

[a] Other diseases included myeloma, myelodysplastic syndromes, chronic lymphocytic leukemia, acute erythroid leukemia, Hodgkin lymphoma, myelofibrosis, chronic myeloid leukemia, and follicular lymphoma.

infections from pathogens found in food sources rather than clinical trials. The evidence for the use of a neutropenic diet is weak (Tomblyn et al., 2009). To date, little to no randomized, controlled trials have been conducted that address the question of whether a neutropenic diet, in addition to prophylactic antibiotics, is necessary to prevent infection in patients receiving HSCT. Despite the CDC and U.S. Food and Drug Administration (FDA) stressing safe food practices rather than limiting actual food choices, variations of a neutropenic diet continue to be standard of care. The purpose of this study is to determine whether a difference exists in the incidence of infections and nutritional status in patients receiving myeloablative allogeneic HSCT with a neutropenic diet compared to those with a diet without restrictions.

Methods

Sample and Setting

The sample included patients admitted to the adult blood and marrow transplantation unit (ABMTU) at Duke University Hospital scheduled to receive a myeloablative allogeneic transplantation from any donor source. Potential participants were screened by the principal investigator (PI) and the research team from April 2009 to December 2011. Other eligibility criteria included being aged 20–70 years, no evidence of active infection, Karnofsky performance status score of greater than 80%, and ability to read and write in English. Ninety-six participants were screened and deemed to be eligible. Forty-nine elected not to participate in the study. Most refusals were because of the perception of additional risk of the regular diet during neutropenia. Patients also verbalized feeling overwhelmed about their upcoming treatment and other clinical trials. Forty-seven participants were enrolled in the trial for a 49% response rate. One participant experienced progressive disease during the conditioning regimen and was removed from the study, leaving 46 evaluable participants.

The mean age of participants was 45 years, and 48% of the participants underwent HSCT for a diagnosis of acute myeloid leukemia (AML) (see Table 1). All patients received care in a high-efficiency particulate air-filtered room. All of the patients had tunneled central venous catheters placed prior to beginning the conditioning regimen and were placed on standard antibiotic prophylaxis according to the ABMTU standard prophylaxis guidelines. Antibacterial coverage included ciprofloxacin 750 mg by mouth twice per day and metronidazole 500 mg by mouth three times per day, and antiviral therapy included acyclovir 400 mg by mouth twice per day. Antifungal therapy for patients with matched sibling and matched unrelated donors was fluconazole 400 mg by mouth daily, and patients with umbilical cord blood donors received voriconazole 200 mg by mouth twice per day. With the first neutropenic fever, all patients were started on IV antibiotic coverage of vancomycin 2 mg/kg daily and ceftazidime 2 grams every eight hours.

Procedures

The study was approved by the institutional review board at Duke University Health System. Individuals were asked to verbally recall key points about study participation, including risks and benefits. Participants were told that they could withdraw from the study at any time. Once informed consent was obtained by the study PI, the participants were assigned to their diet group using random numbering by the ABMTU pharmacist to avoid investigator bias. After assignment, patients were instructed on the particular diet arm. Patients received dietary instructions from their care nurse. Both groups received written instructions regarding the importance of good dietary intake. In addition, participants on the neutropenic diet received a written list of dietary restrictions.

Participants randomized to the neutropenic diet arm (n = 25) followed the standard hospital neutropenic guidelines of only cooked food and thick-skinned fruits. Those randomized to the unrestricted diet arm (n = 21) were allowed to eat any food product. All patients were instructed to follow safe food handling, storing, and preparation guidelines recommended by the FDA. Compliance was encouraged by signage on the patients' door and the use of food diaries. All patients remained on the randomized diet until the end of neutropenia (defined as absolute neutrophil count of greater than 500 for three days) or until discharge from the ABMTU. Standard care for individuals requiring total parenteral nutrition (TPN) is to encourage patients to continue with as much dietary intake as possible in addition to the supplementation. Institution of TPN is considered when the patient has lost greater than 5% of their body weight and is not expected to eat sufficiently for 3–5 days in severe malnutrition, 5–7 days in mild or moderate malnutrition, and 7–10 days in well-nourished patients.

Variables

The following laboratory studies were performed at baseline and weekly following study enrollment: complete blood counts with differentials, prealbumin, transferrin, magnesium, calcium, and complete renal and liver panels. Food diaries were collected as a way to validate adherence to the assigned diet. In the case that a food diary was not completed, the clinic nurse verbally verified diet choices with the patient.

To assess nutritional status, the validated Patient-Generated Subjective Global Assessment (PG-SGA) tool was administered weekly to the patient by the PI or team member. The PG-SGA was adapted from the Subjective Global Assessment and developed for patients with cancer (Ottery, 2000). It includes questions regarding the presence of nutritional symptoms and short-term weight loss. The scored PG-SGA incorporates a

TABLE 2. Blood Culture Comparison Between Control and Experimental Groups (N = 46)

	Control[a] (n = 20)	Experimental (n = 25)
Blood Culture	n	n
Negative	14	18
Positive	6	7

[a] Missing data (n = 1)

Note. A positive blood culture indicates bacteria cultured from the bloodstream.

Control Group (Neutropenic Diet)

- *Escherichia coli*
- *Enterococcus faecium*
- *Pseudomonas aeruginosa*
- *Viridens streptococcus*

Experimental Group (Regular Diet)

- *Candida glabrata*
- *Escherichia coli*
- *Enterococcus faecium*
- *Gemella* species
- *Staphylococcus* coagulase-negative
- *Viridens streptococcus*

Note. Not all documented bloodstream infections are known to be foodborne pathogens.

FIGURE 1. Specific Blood Cultures and Their Distribution

numeric score and provides a global rating of well nourished, moderately or suspected of being malnourished, or severely malnourished. For the PG-SGA, 0–4 points are awarded depending on the impact of the symptom on nutritional status, food intake, weight, and activities (range = 0–32). A total score is then summed, which provides a guideline for the level of nutrition intervention required and facilitates quantitative outcome data collection (Ottery, 2000). A score of greater than 1 minimally requires patient and family education by a dietitian, nurse, or other clinician with pharmacologic intervention as indicated by the symptoms experienced by the patient. The scored PG-SGA is a continuous measure with a higher score indicating a greater risk for malnutrition. A score of 9 or greater indicates a critical need for nutrition intervention. The scored PG-SGA has been accepted by the Oncology Nutrition Dietetic Practice Group of the American Dietetic Association as the standard for nutrition assessment for patients with cancer (Isenring, Bauer, & Capra, 2007). Several studies have assessed the validity of the PG-SGA. Persson, Sjöden, and Glimelius (1999) correlated the PG-SGA scores with serum albumin, prealbumin, and percentage of weight loss and found that the PG-SGA scores were significantly associated with all three laboratory values. This validated tool was felt to be a strong method of objectively measuring nutritional status. Subjective global assessment has been found to have a high degree of inter-rater reliability (Detsky et al., 1987). It has also been found to have a predictive and convergent validity, correlating well with measures of morbidity and quality of life. Three studies provide data on the sensitivity and specificity of the PG-SGA as a screening tool, indicating how well it can determine which patients are truly malnourished and require referral for nutrition assessment (Biggs, 2012). In addition to laboratory and nutritional assessments, weekly weights, number of participants on TPN, and days of TPN were also recorded.

Infection rates were determined by the occurrence of positive blood cultures. Blood cultures were obtained at the time of febrile episode. The program at Duke University Health System has established a fever threshold of 100.5°F (38°C). The AMBTU standard operating procedure for fever workup includes blood cultures from the central venous catheter, peripheral blood if able, urinalysis, urine culture, and chest x-ray. The patient is assessed by a member of the healthcare team, and appropriate care is then provided.

Statistical Analysis

The laboratory measurements were compared between the control (neutropenic diet) and experimental (regular diet) arms using the two-sided Wilcoxon rank-sum test. The two-sided chi-square test of proportions was used to compare the percentage of patients with positive blood cultures in the two diet groups. Statistical analyses were performed by the Duke Cancer Biostatistics Department using SAS®, version 9.2.

Results

All demographic variables and other variables demonstrated no significant difference between the control group and experimental group at the two-sided 0.05 significance level, using the Student's t test for the continuous variable of age and the chi-square test for all other variables. Fifteen participants in the experimental arm required TPN for a median of 21 days. The control group had 13 participants requiring TPN for a median of 20 days, which was not significantly different ($p = 0.7$). Across all time points, no significant difference was found in any of the laboratory values with the exception of the total protein level. The median in the total protein level across all time points was 20% in the control arm and 16% in the experimental group, which reached significance ($p = 0.023$).

No differences were found between the groups in the percentage of positive blood cultures (see Table 2). Six of 20 participants in the control group and seven of 25 participants in the experimental group had positive blood cultures ($p = 0.99$).

This pilot study shows that, in this setting, no difference exists in the infection incidence between those patients undergoing HSCT receiving a neutropenic diet or those receiving a diet without limitations. *E. coli* is the only identified bacteria that can be potentially contracted from undercooked food (see Figure 1). *E. coli* is also a common enteric bacteria that may be transgressed into the bloodstream following high-dose chemotherapy or radiation therapy because of the disruption of the gut flora. Both arms of the study followed safe food handling and preparation, which includes cooking meat to the proper temperature. In this way, it is unlikely that the *E. coli* infections were caused by food. More likely, they were caused by transgression from the disrupted gastrointestinal system. By limiting the enrollment to those patients who were hospitalized and monitoring food that was brought in by family members, more control was established over the food choices.

With regard to the PG-SGA scores, patient scores in both arms showed an increase in the number of symptoms and degree of nutritional intervention needed during the period of mucositis and neutropenia. Profound neutropenia and mucositis are expected effects of myeloablative chemotherapy and radiation. Many patients develop gastrointestinal toxicity within 7–14 days following therapy, limiting their nutritional intake. Sixty percent of patients in both groups required TPN support during the period of neutropenia. Based on the PG-SGA scores, a more liberal diet does not appear to influence symptoms during this phase of treatment in this patient population. The subjective

portion of the PG-SGA scores showed little variability in either arm (see Figure 2).

Implications for Nursing Practice

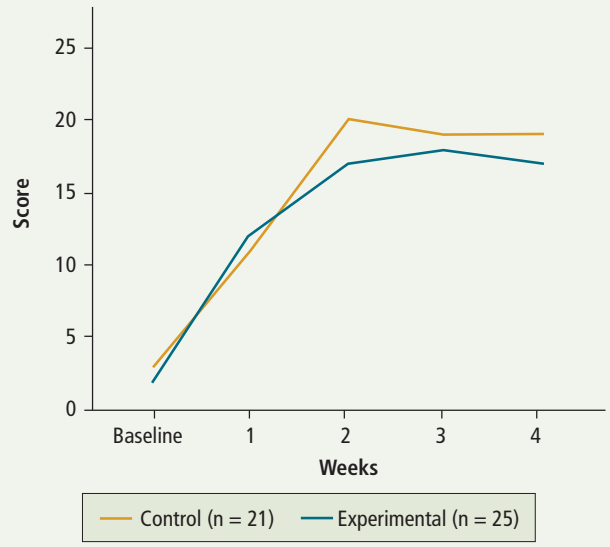
As discussed previously, dietary restrictions vary widely across oncology practices. The concept of a neutropenic diet carries no consistent definition or guideline. These inconsistent practices can cause confusion and stress for patients and caregivers when they receive care in different areas. Simplifying safe nutrition guidelines can reduce the anxiety patients and caregivers may experience during treatment and follow-up care.

Ensuring proper nourishment for patients undergoing HSCT is challenging. A multidisciplinary approach using registered dietitians and the most current evidence is essential to minimize nutritional deficits for patients. Oncology nurses have the opportunity to educate patients about the importance of maintaining good nutrition to promote healing, provide energy, and maintain muscle mass. The FDA (2011) has published comprehensive guidelines for food safety for transplantation patients. These guidelines provide a starting point for discussion regarding food safety for practice. In addition, Tomblyn et al. (2009) provides diet recommendations to minimize infection risk that are consistent with the FDA recommendations without resorting to a neutropenic diet.

Discussion

The results of this pilot study suggest that altering diet choices for patients undergoing myeloablative allogeneic HSCT during neutropenia does not increase the risk for bloodstream infections or improve nutrition. To the authors' knowledge, this is the first published prospective, randomized study examining this issue in the myeloablative allogeneic transplantation population and should be replicated in larger samples from more institutions. As more data emerge from similar patient populations, recommendations focusing on safe food storage and preparation may become more important for infection control than limiting specific food choices. More research specific to the HSCT population research is needed. Although this pilot study had a small sample size from a single institution, the study group was among the most at-risk populations for infection. In other transplantation populations using other donor sources (autologous) or reduced doses of chemotherapy, the risk of mucositis may be decreased. If patients are not experiencing mucositis, more food choices may be appealing to increase caloric intake. Because immunocompromised patients generally have decreased oral intake, the priority should be to avoid restrictions that would further limit food choices. Many of the foods restricted on a neutropenic diet are cool and odorless (e.g., fresh fruit and vegetables being less odorous than canned). These foods tend to be appealing to patients undergoing transplantation and experiencing mucositis, nausea, or vomiting.

Another issue can be raised regarding participation in clinical trials. Only about half of those eligible for enrollment participated in the study. Many of those who declined to participate cited the potential for increased risk of infection despite the potential risk and benefits being thoroughly explained. Many had been maintained on a neutropenic diet during prior therapies in community oncology practices. Lack of consistent guidelines of when to stop and start the diet restrictions were anecdotal comments shared with the study staff. This observation highlights the inconsistencies in nutrition consultation and education for all patients with cancer as well as recipients of transplantation.



Note. Higher scores indicate greater risk for malnutrition.

FIGURE 2. Average Scores Using the Patient-Generated Subjective Global Assessment Tool (N = 46)

Implications for Practice

- Simplify safe nutrition guidelines to reduce anxiety for patients and caregivers.
- Use a multidisciplinary approach with registered dietitians as standard of care for patients undergoing hematopoietic stem cell transplantation.
- Provide consistent guidelines for all members of the healthcare team to encourage adherence to recommendations.

Conclusions

This study does not support the current standard of the neutropenic diet in the allogeneic transplantation population. A restrictive diet also may place an unnecessary burden on patients and caregivers in a less controlled outpatient environment. Focusing on safe food purchasing, food preparation, and good hand hygiene will likely offer better infection prevention for recipients of transplantation.

References

Biggs, K. (2012). Malnutrition screening programs in adult cancer patients: Clinical practice is hungry for evidence. *Current Oncology, 19,* E305–E307. doi:10.3747/co.19.1006

Boeckh, M. (2012). Neutropenic diet—Good practice or myth? *Biology of Blood and Marrow Transplantation, 18,* 1318–1319. doi:10.1016/j.bbmt.2012.07.006

Detsky, A.S., McLaughlin, J.R., Baker, J.P., Johnston, N., Whittaker, S., Mendelson, R.A., & Jeejeebhoy, K.N. (1987). What is subjective global assessment of nutritional status? *Journal of Parenteral and Enteral Nutrition, 11,* 8–13. doi:10.1177/014860718701100108

French, M., Levy-Milne, R., & Zibrik, D. (2001). A survey of the use of low microbial diets in pediatric bone marrow transplant programs. *Journal of the American Dietetic Association*, *101,* 1194–1198. doi:10.1016/S0002-8223(01)00292-9

Isenring, E.A., Bauer, J.D., & Capra, S. (2007). Nutrtiion support using the American Dietetic Association medical nutrition therapy protocol for radiation oncology patients improves dietary intake compared with standard practice. *Journal of the American Dietetic Association, 107,* 404–412.

Kubrak, C., & Jensen, L. (2007). Critical evaluation of nutrition screening tools recommended for oncology patients. *Cancer Nursing*, *30*(5), E1–E6. doi:10.1097/01.NCC.0000290818.45066.00

Mank, A., & van der Lelie, H. (2003). Is there still an indication for nursing patients with prolonged neutropenia in protective isolation? An evidence based nursing and medical study of 4 years' experience for nursing patients with neutropenia without isolation. *European Journal of Oncology Nursing, 7,* 17–23. doi:10.1054/ejon.2002.0216

Ottery, F.D. (2000). Patient-generated subjective global assessment. In P.D. McCallum & C.G. Polisena (Eds.), *The clinical guide to oncology nutrition* (pp. 11–23). Chicago, IL: American Dietetic Association.

Persson, C., Sjöden, P.O., & Glimelius, B. (1999). The Swedish version of the patient-generated subjective global assessment of nutritional status: Gastrointestinal vs urological cancers. *Clinical Nutrition, 18,* 71–77. doi:10.1016/S0261-5614(99)80054-5

Restau, J., & Clark, A.P. (2008). The neutropenic diet: Does the evidence support the intervention? *Clinical Nurse Specialist, 22,* 208–211. doi:10.1097/01.NUR.0000325363.31174.9e

Rock, C., Doyle, C., Denmark-Wahnefried, W., Meyerhardt, J., Courneya, K.S., Schwartz, A.L., . . . Gansler, T. (2012). Nutrition and physical activity guidelines for cancer survivors. *CA: A Cancer Journal for Clinicians, 62,* 243–274. doi:10.3322/caac.21142

Sheean, P.M. (2005). Nutrition support of blood or marrow transplant recipients: How much do we really know? *Practical Gastroenterology, 26,* 84–97.

Smith, L.H., & Besser, S.G. (2000). Dietary restrictions for patients with neutropenia: A survey of institutional practices. *Oncology Nursing Forum, 27,* 515–520.

Todd, J., Schmidt, J., Christain, J., & Williams, R. (1999). The low-bacterial diet for immunocompromised patients: Reasonable prudence or clinical superstition? *Cancer Practice*, *7,* 205–207. doi:10.1046/j.1523-5394.1999.74009.x

Tomblyn, M., Chiller, T., Einsele, H., Gress, R., Sepkowitz, K., Storek, J., . . . Boeckh, M.J. (2009). Guidelines for preventing infectious complications among hematopoietic cell transplantation recipients: A global perspective. *Biology of Blood and Marrow Transplantation*, *15,* 1143–1238. doi:10.1016/j.bbmt.2009.06.019

Trifilio, S., Helenowski, I., Giel, M., Gobel, B., Pi, J., Greenberg, D., & Mehta, J. (2012). Questioning the role of a neutropenic diet following hematopoietic stem cell transplantation. *Biology of Blood and Marrow Transplantation, 18,* 1385–1390. doi:10.1016/j.bbmt.2012.02.015

Turvey, S.E., & Broide, D.H. (2010). Innate Immunity. *Journal of Allergy and Clinical Immunology, 125*(Suppl. 2), S24–S32. doi:10.1016/j.jaci.2009.07.016

U.S. Food and Drug Administration. (2011). *Food safety for transplant recipients: A need-to-know guide for bone marrow and solid organ transplant recipients.* Retrieved from http://1.usa.gov/1xe6UFO

van Tiel, F., Harbers, M., Terporten, R., van Boxtel, R.T., Kessels, A.G., Voss, G.B., & Scouten, H.C. (2007). Normal hospital and low-bacterial diet in patients with cytopenia after intensive chemotherapy for hematological malignancy: A study of safety. *Annals of Oncology, 18,* 1080–1084. doi:10.1093/annonc/mdm082