

Things We Do For No Reason: Neutropenic Diet

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The “Things We Do for No Reason” series reviews practices which have become common parts of hospital care but which may provide little value to our patients. Practices reviewed in the TWDFR series do not represent “black and white” conclusions or clinical practice standards, but are meant as a starting place for research and active discussions among hospitalists and patients. We invite you to be part of that discussion.

For several decades, providers have routinely restricted the diets of neutropenic cancer patients by eliminating foods that might harbor pathogenic microbes to reduce infection rates. These diets, known as neutropenic or low-bacteria diets, are prescribed across the country with little uniformity in the extent or content of prescription. These diets are difficult to follow and force patients to omit fresh fruits and vegetables and limit dairy and meat products from their diet. These dietary omissions compromise nutritional intake in patients who are already at high risk of malnutrition. Randomized trials have shown that these restrictive diets are not superior in preventing infections than more liberalized diets. Evidence shows that adherence to the Safe Food-Handling guidelines issued by the Food and Drug Administration, a mandate for all hospital kitchens, provides adequate protection against food-borne infection, precluding the need for the neutropenic diet. Thus, routine use of the neutropenic diet should be abandoned.

CLINICAL SCENARIO

A 67-year-old man with acute myeloid leukemia who has recently completed a cycle of consolidation chemotherapy presents to the emergency room with fatigue and bruising. He is found to have pancytopenia due to chemotherapy. His absolute neutrophil count (ANC) is 380/mm³, and he has no symptoms or signs of infection. He is admitted for transfusion support and asks for a dinner tray. The provider reflexively prescribes a neutropenic diet.

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BACKGROUND

Although aggressive chemotherapy regimens have significantly improved survival rates in patients with cancer, these intensive regimens put patients at risk for a number of complications, including severe, prolonged neutropenia. Patients with neutropenia, particularly those with ANC < 500/mm³, are at a significantly increased risk for infection. Common sites of infection include the blood stream, skin, lungs, urinary tract, and, particularly, the gastrointestinal tract.¹ Oncologists and dietitians first designed neutropenic diets, or low-bacteria diets, to limit the introduction of pathogenic microbes to the gastrointestinal system. Neutropenic diets typically limit the intake of fresh fruits, fresh vegetables, raw or undercooked meats and fish, and soft cheese made from unpasteurized milk. Despite the widespread recommendation of the neutropenic diet, no standardized guidelines exist, and the utilization of the diet and its contents vary widely among and within institutions.²

The neutropenic diet is a national phenomenon. A survey of 156 United States members of the Association of Community Cancer Centers revealed that 120 (78%) of the members had placed patients with neutropenia on restricted diets.² The triggers for prescription (neutropenia, or starting chemotherapy), ANC threshold for prescription, and duration of prescription (throughout chemotherapy or just when neutropenic) were not uniform. A majority of centers restricted fresh fruits, fresh vegetables, and raw eggs, while some locations also restricted tap water, herbs and spices, and alcoholic beverages.² Similarly, a study of practices in 29 countries across 6 continents found that 88% of centers have some version of a neutropenic diet guideline with significant heterogeneity in their prescription and content. For example, dried fruits were unrestricted in 23% of centers but were forbidden in 43%.³

WHY YOU MIGHT THINK THE NEUTROPENIC DIET IS HELPFUL IN PREVENTING INFECTION

The rationale behind the neutropenic diet is to limit the bacterial load delivered to the gut. Studies have shown that organisms such as *Enterobacter*, *Pseudomonas*, and *Klebsiella* have been isolated from food, particularly fruits and vegetables.^{4,5} The ingestion of contaminated food products may serve as a source of pathogenic bacteria, which may cause potentially life-threatening infections. Mucositis, a common complication among cancer patients receiving therapy, predisposes patients to infection by disrupting the mucosal barrier, allowing bacteria to translocate from the gut to the bloodstream. Given that neutropenia and mucositis often occur simultaneously, these

TABLE. Summary of Notable Neutropenic Diet Studies

First Author	Population	Design	Number of Patients	Percentage of Patients Neutropenic	Average duration of Neutropenia	Duration of Study
DeMille et al. ¹⁴	Adults undergoing chemotherapy outpatient	Prospective Observational	28	Not reported	Not reported	12 weeks
Garder et al. ⁷	Adults with acute myelogenous leukemia or high risk myelodysplastic syndrome undergoing induction chemotherapy	Randomized controlled trial	153	Not reported	21 days in raw food arm, 20 days in cooked food arm	25 days
Lassiter et al. ¹⁸	Adults undergoing myeloablative hematopoietic stem-cell transplants	Randomized controlled trial	46	100%	Not reported	>4 weeks
Moody et al. (2006) ¹⁹	Children undergoing chemotherapy	Randomized controlled trial	19	89.5%	5.9 days in neutropenic diet arm, 9.2 days in food safety arm	Single chemotherapy cycle
Tramsen et al. ⁹	Children with acute myelogenous leukemia undergoing induction chemotherapy	Prospective Observational	339	Not reported	Not reported	Duration of intensive treatment of acute myelogenous leukemia
Moody et al. (2017) ⁸	Children undergoing myelosuppressive chemotherapy	Randomized controlled trial	150	74% in neutropenic diet arm, 71% in food safety arm	10.5 days in neutropenic diet arm, 9.6 days in food safety arm	24.5 days
Trifillio et al. ¹⁵	Adult hematopoietic stem-cell transplants	Retrospective	726	Not reported	Not reported	Duration of hospitalization
Van Tiel et al. ¹¹	Adults with acute leukemia undergoing induction chemotherapy	Randomized controlled trial	20	Not reported	Not reported	Not reported

patients are at an increased risk of infections.⁶ Cooking destroys bacteria if present, rendering cooked foods safe. Thus, the avoidance of fresh fruits and vegetables and other foods considered to have high bacterial loads should theoretically decrease the risk of infections in these patients.

WHY THE NEUTROPENIC DIET IS NOT HELPFUL IN PREVENTING INFECTION

Researchers have investigated the ability of the neutropenic diet to reduce infection in adult and pediatric neutropenic patients. A study involving 153 patients receiving chemotherapy for acute myeloid leukemia or myelodysplastic syndrome randomized 78 patients to a diet that restricted raw fruits and vegetables and 75 patients to a diet that included those foods.⁸ The groups had similar rates of major infection (29% in the cooked group versus 35% in the raw group, $P = .60$) with no difference in mortality.⁷ In a randomized, multi-institutional trial of 150 pediatric oncology patients, 77 patients received a neutropenic diet plus a diet based on the food safety guidelines approved by the Food and Drug Administration (FDA), while 73 children received a diet based on FDA-approved food safety guidelines.⁸ Infection rates between the groups were not significantly different (35% vs 33% respectively, $P = .78$).

Intensive conditioning regimens place hematopoietic stem-cell transplant (HSCT) recipients at an even greater risk of infectious complications than other patients and may increase gastrointestinal toxicity and prolong neutropenia. A study from a single academic US center included 726 HSCT recipients, 363 of whom received a neutropenic diet and 363 of whom received a general diet. Significantly fewer infections were observed in the general diet group than in the neutropenic

diet group. Notably, this study was a retrospective trial, and approximately 75% of participants were autologous HSCT recipients, who traditionally have low risks of infection. A survey and analysis of nonpharmacologic anti-infective measures in 339 children with leukemia enrolled in the multicenter Acute Myeloid Leukemia Berlin-Frankfurt-Munster 2004 trial also did not show that the neutropenic diet has protective effects on infection rates.⁹ A meta-analysis that compiled data from the studies mentioned above found the hazard ratio for any infection (major or minor) and fever was actually higher in the neutropenic diet arm (relative risk 1.18, 95% confidence interval: 1.05-1.34, $P = .007$) relative to that in the unrestricted arm.¹⁰

The inefficacy of the neutropenic diet may be attributed to the fact that many of the organisms found on fresh fruits and vegetables are part of the normal flora in the gastrointestinal tract. A Dutch prospective randomized pilot study of 20 adult patients with acute myeloid leukemia undergoing chemotherapy compared the gut flora in patients on a low-bacteria diet versus that in patients on a normal hospital diet. Gut colonization by potential pathogens or infection rates were not significantly different between the 2 groups.¹¹

In addition to mucositis, the common gastrointestinal complications of chemotherapy include nausea, vomiting, diarrhea, food aversions, and changes in smells and taste, which limit oral intake.¹² Unnecessary dietary restrictions can place patients at further risk of inadequate intake and malnutrition.¹³ In the outpatient setting, compliance with the neutropenic diet is also problematic. In one study of 28 patients educated about the neutropenic diet, only 16 (57%) were compliant with the diet as revealed through telephone-based assessments at 6 and 12 weeks, and infection rates were not different be-

tween compliant versus noncompliant patients.¹⁴ Patients and family members reported that following the neutropenic diet requires considerably more effort than following a less restrictive diet.⁸ Maintaining nutrition in this patient population is already challenging, and the restriction of a wide variety of food items (fresh fruits, vegetables, dairy, certain meats, eggs) can cause malnutrition, low patient satisfaction, and poor quality of life.^{13,14}

WHEN MIGHT THE NEUTROPENIC DIET BE HELPFUL?

Evidence shows no benefit of the neutropenic diet in any particular clinical scenario or patient population. However, despite the dearth of evidence to support neutropenic diets, the overall data regarding neutropenic diets are sparse. Randomized control trials to date have been limited by their small size with possible confounding by the type of malignancy and cancer therapy; use of prophylactic antibiotics, growth factors, and air-filtered rooms; variation in contents and adherence to the prescribed diet; and inpatient versus outpatient status. The study that included HSCT recipients was a retrospective trial, and a majority of patients were autologous HSCT recipients.¹⁵ Although no study has specifically investigated the neutropenic diet in preventing infection in patients with noncancer-related neutropenia, no reason exists to suspect that it is helpful. The FDA advises safe food-handling practices for other immunocompromised patients, such as transplant recipients and patients with human immunodeficiency virus/acquired immunodeficiency syndrome, and the same principles can likely be applied to patients with noncancer-related neutropenia.

WHAT WE SHOULD DO INSTEAD

Although the neutropenic diet has not been proven beneficial, the prevention of food-borne infection in this population remains important. FDA-published guidelines, which promote safe food handling to prevent food contamination in patients with cancer, should be followed in inpatient and outpatient settings.¹⁶ These guidelines allow for fresh fruits and vegetables as long as they have been adequately washed. Cleaning (eg, cleaning the lids of canned foods before opening, hand washing), separating raw meats from other foods, cooking to the right temperature (eg, cooking eggs until the yolk and white are firm), and chilling/refrigerating food appropriately are strongly emphasized. These guidelines are also recommended by the American Dietetic Association. Despite additional flexibility, patients following the FDA diet guidelines do not have increased risk of infection.⁸ At our hospitals, the neutropenic diet can no longer be ordered. Neutropenic patients are free to consume all items on the general hospital menu, including eggs, meat, soft cheeses, nuts, and washed raw fruits and vegetables. The National Comprehensive Cancer Network guidelines for the prevention and treatment of cancer-related infections do not specifically address diet.¹⁷ We call upon them to note the lack of benefit and potential harm of the neutropenic diet in the guidelines. Such an action may persuade more institutions to abandon this practice.

RECOMMENDATIONS

- Neutropenic diets, or low-bacteria diets, should not be prescribed to neutropenic patients.
- Properly handled and adequately washed fresh fruits and vegetables can safely be consumed by patients with neutropenia.
- Patients and hospitals should follow FDA-published safe food-handling guidelines to prevent food contamination.

CONCLUSIONS

A general diet can be safely ordered for our patient in the presented clinical scenario. Available data from individual studies and pooled data provide no evidence that neutropenic diets prevent infectious complications in patients with neutropenia.

Hospital kitchens must adhere to the food-handling guidelines issued by the FDA, and following these guidelines should provide adequate protection against food-borne infection, even in patients who are immunocompromised. Instead of restricting food groups, the FDA guidelines focus on safe food-handling practices. Less dietary restrictions provide patient's additional opportunities for balanced nutrition and for food choices based on personal preferences or cultural practices.

Do you think this is a low-value practice? Is this truly a "Thing We Do for No Reason?" Share what you do in your practice and join in the conversation online by retweeting it on Twitter (#TWDFNR) and liking it on Facebook. We invite you to propose ideas for other "Things We Do for No Reason" topics by emailing TWDFNR@hospitalmedicine.org.

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