The Neutropenic Diet Reviewed: Moving Toward a Safe Food Handling Approach

By Alison Freifeld, MD [2]

Review of the pathophysiology of foodborne illness and pertinent studies about the neutropenic diet lead to the conclusion that there is no clear benefit from the longstanding dietary restrictions that may be imposed during neutropenia. Instead, we propose adoption of standard safe food handling methods to allow for a more liberalized diet in the neutropenic patient.

Introduction

Chemotherapy-associated neutropenia is a well-known risk factor for increased vulnerability of cancer patients to infections. Serious neutropenia-related infections are seen particularly in those with prolonged neutropenic periods associated with treatment of hematologic malignancies or with stem cell transplantation. Bloodstream infections usually occur in about 15% to 25% of patients, most often when the absolute neutrophil count (ANC) is less than 500 neutrophils/μL.[1] Over the last 50 years, efforts to prevent serious bacterial infections in this population have largely included protective isolation measures, prophylactic antibiotics, and dietary restrictions. Despite a lack of supportive data, the neutropenic diet is still utilized in some centers. Re-evaluation of the available data relating to this diet—which is also referred to as the “sterile diet,” the “low-bacteria diet,” or the “low-microbial diet”—is provided here, with the goal of supplanting it with a more current guideline of safe food handling for all cancer patients.

Pathophysiology of Infection in Neutropenic Patients

Gram-positive bloodstream infections (with Staphylococcus species) predominate among neutropenic patients and are primarily derived from skin colonization.[1] In contrast, infections with gram-negative bacilli such as Escherichia coli, Pseudomonas aeruginosa, and Klebsiella pneumoniae, as well as Candida species (yeasts), are less frequent but more lethal; these organisms typically enter the bloodstream via translocation across the gastrointestinal tract. Starvation and protein malnutrition will promote bacterial translocation in animal models.[2] Disruption of the gut mucosal barrier, as a consequence of cytotoxic chemotherapy-induced mucositis, is also a significant contributing factor.[3] In the 1970s, nonabsorbable prophylactic antibiotics were evaluated for their ability to eradicate normal enteric flora and aerobic gram-negative bacteria, and thereby reduce the gut bacterial burden available for translocation. Limited success was achieved, but the drugs proved to be largely intolerable for patients.[4] During the same era, several studies revealed that enteric flora, including E coli, P aeruginosa, and K pneumoniae, could be cultivated from the surfaces of a variety of foods, usually fruits, cold meats, lettuce, and other fresh vegetables.[5-7] This raised concerns about the possible exogenous acquisition of pathogenic bacteria by the oral route, leading to the “neutropenic diet” concept of restricting specific foods. Typically, in a healthy person, consumed bacteria will pass through the gastrointestinal tract without adhering to the mucosal surface, will be destroyed by stomach acid, or will be competed out of existence by normal endogenous flora.[8] In the cancer patient, each of these mechanisms may be impaired: drugs to reduce stomach acidity may impair bacterial killing in the stomach, gastrointestinal mucositis promotes translocation of bacteria, and antibiotic suppression of endogenous flora prevents bacterial competition and allows overgrowth of potentially pathogenic bacteria. The essential question is whether or not food ingested by a neutropenic patient is a source of pathogenic bacteria that ultimately cause bloodstream or other serious infections. It is essential to understand the types of bacteria, both pathogenic and nonpathogenic, that are present in or on certain foods. Enterobacteriaceae (eg, Klebsiella species, E coli) are quite commonly carried on fresh fruits and vegetables, but since these organisms are essentially “normal flora” in the human colon, they are considered nonpathogens in healthy patients. A recent study from Finland found that Enterobacteriaeae...
bacteriaceae cultured from the surfaces of vegetables had significantly different antibiotic susceptibility profiles from Enterobacteriaceae cultured in stool samples from humans who consumed those vegetables.[9] The conclusion from this observation was that the antibiotic-resistant bacteria isolated from vegetables probably do not play a significant role in colonizing the human gut. In cancer patients, no studies exist that demonstrate a causal role for food-derived enteric bacteria (such as Enterobacteriaceae or Pseudomonas) in subsequent serious infections that occur during neutropenia.[10-12]

TABLE 1

Pathogens Associated With Food

Food becomes a real danger to immunosuppressed individuals when it serves as a vehicle for pathogenic bacteria that typically cause illness in humans. Common foodborne pathogens include Campylobacter jejuni, Salmonella, E coli, and Clostridium perfringens (Table 1). Apart from E coli, these infections are rarely identified in neutropenic patients, but when they do occur they cause high degrees of morbidity and mortality.[1] The primary etiology of foodborne illness is the unsafe handling of foods.[13] In this regard, we stress that safe food-handling methods—rather than specific avoidance of raw fruit and vegetables—are of greatest importance for preventing infections in all patients, including those who are neutropenic. In contrast, the neutropenic diet (as it is understood in most centers) is not known to be definitively protective against foodborne pathogens. To understand how support for the neutropenic diet evolved, we will review the historical and published study information about how the neutropenic diet evolved as a part of cancer care.

Environmental Measures to Prevent Infection: Historical View

In the 1960s, most cancer treatments were administered in an inpatient setting, and patients remained hospitalized for prolonged periods. During this period, the low microbial or neutropenic diet emerged as part of a “total protective environment” approach to managing leukemia patients with prolonged neutropenia. This approach involved myriad environmental cleansing, sterilization, and isolation measures that were implemented when patients became neutropenic, in an effort to reduce exposure to both endogenous and exogenous bacteria.[14] The neutropenic diet, in which fresh fruits and vegetables were generally forbidden, was an integral part of the total protective environment. In addition, antimicrobial or protective procedures included the use of isolated laminar flow rooms; shaving of the genital area; thorough cleaning of toenails and fingernails; bathing in isopropyl alcohol or hexachlorophene; sterilization of clothes and linens; sterilization of food with ethylene oxide; cleansing of the gastrointestinal tract with castor oil and soapsuds enemas; sterilization of the gastrointestinal tract with antibiotics; and sterilization of all items taken into the isolation unit, including newspapers and procedure instruments.[14] Because
they are labor-intensive, expensive, and of no proven benefit, most components of the total protective environment are no longer employed.[15] In fact, a number of cancer treatments (eg, autologous stem cell transplants and consolidation therapies for acute leukemia) occur in the outpatient setting, and patients go through periods of neutropenia primarily as outpatients, with few restrictions on diet and activity.[11,16,17] Although total-protective-environment techniques have been mostly abandoned in the 21st century care of cancer patients, a notable exception has been the continued use of the neutropenic diet. This diet—in various forms—has remained a part of patient care based on the theoretical assumption that avoidance of foods that may carry gram-negative-rod bacteria may reduce bloodstream infections. In fact, this has never been proven.

Defining the Neutropenic Diet

No standard definition of the neutropenic diet exists. Indeed, it is unclear what fundamental features constitute a neutropenic diet: What foods should be restricted? How should foods be prepared to render them sterile or at least microbially reduced? When should limitations be instituted and discontinued? Surveys investigating institutional dietary prescriptions for neutropenic patients have revealed a wide range of definitions and practices.[17-19] Great variability exists in terms of specific foods restricted, timing of initiating restrictions, and food preparation methods such as washing and cooking techniques. Commonly prohibited are raw fresh fruits and vegetables, but some centers also avoid fresh-squeezed juices, dried fruits, yogurt and aged cheeses, raw herbs and spices, raw honey, deli meats, nuts, undercooked meats, undercooked seafood, and undercooked eggs for patients.[19] Food preparation methods to ensure low microbial content, including sterilization and autoclaving, are occasionally employed. These can affect the appearance, taste, and texture of food, thereby decreasing patients’ desire to eat and maintain their nutritional status at a time when it is critically important to maintain caloric intake.

Timing of diet initiation varies among institutions. Some hospitals use the absolute neutrophil count to determine when the diet is initiated, while others may initiate the diet upon hospital admission.[18,19]

Published Studies of the Neutropenic Diet

Studies evaluating the neutropenic diet have examined three main aspects of the diet: how and whether cancer treatment centers use neutropenic diets, factors influencing patient compliance, and the incidence of infection. Several of the more recent pertinent studies are reviewed here. In 2000, Smith and Besser[19] mailed surveys assessing use of the neutropenic diet to 400 institutional members of the Association of Community Cancer Centers. The survey queried institutions about use of a specialized low-microbe diet among nontransplant hospitalized cancer patients, the degree of neutropenia that triggered the initiation of such a diet, and a list of foods that were typically restricted. Of 400 centers queried, 156 surveys were returned. A total of 120 respondents indicated that patients with neutropenia were, in fact, placed on restricted diets, while the remaining 36 centers did not institute such diets. The investigators reported that 34 hospitals initiated neutropenic diets when the ANC was less than 1000/μL, and another 36 started when the ANC was less than 500/μL. Ten hospitals initiated the diet at the start of cancer treatment. Most hospitals that started the diet for inpatients also instructed patients to restrict their diets at home, while a minority allowed patients to resume a regular diet at home. The most commonly restricted foods were fresh fruits, fresh fruit juice, and fresh vegetables. About two-thirds of the hospitals restricted raw eggs and rare-to-medium-cooked meats, and nearly half restricted dried fruits, potato salad, and beer. These survey results show clearly the high inconsistency of dietary practices for neutropenic patients. In 2001, French et al[18] mailed a survey regarding use of the neutropenic diet to ten pediatric hospitals performing bone marrow transplantation. Seven of the ten hospitals replied to the survey. The survey included questions about whether or not a neutropenic diet was used and when restrictions were started and stopped. Five of the seven hospitals responding to the survey reported using neutropenic diet restrictions. Dietary restrictions ranged from preparing foods in separate kitchens using aseptic techniques, to focusing on safe food handling principles and avoiding foods associated with foodborne illness, to a modified in-house diet that only excluded fresh fruits and vegetables. The timing of initiation and discontinuance of the diet varied. Some hospitals initiated the diet upon hospital admission, whereas others did not begin restriction until transplant day or when the ANC was less than 500/μL. Criteria for discontinuing the neutropenic diet included specific neutrophil counts, a specific period of time following transplantation, or upon hospital discharge. Two of the five hospitals responding to the survey reported use of a step-down or transitional diet to
The Neutropenic Diet Reviewed: Moving Toward a Safe Food Handling Approach
Published on Physicians Practice (http://www.physicianspractice.com)

gradually reintroduce restricted foods prior to resumption of a regular diet. During this time, patients were allowed to eat raw fresh fruits that had been washed and peeled. In 2006, DeMille et al[17] conducted a pilot study to determine the effect of the neutropenic diet in the outpatient setting, excluding stem cell transplant and acute leukemia patients. Twenty-three patients between the ages of 33 and 67 years completed the 12-week study. Patients were educated about the neutropenic diet. Telephone interviews were conducted at weeks 6 and 12 to assess adherence to the diet. The study aimed to assess three outcomes: rates of compliance, febrile neutropenia, and bloodstream infections. Compliance with the diet was noted in 70% (16/23) of patients. Interestingly, four of the seven noncompliant patients perceived themselves as noncompliant. The investigators attributed the patients' noncompliance to difficulty following the requirements of the diet because of side effects of the chemotherapy. The second aim was to determine whether the rate of febrile admissions would differ between compliant and noncompliant patients. There were five admissions for febrile neutropenia. Four of the 16 compliant patients (25%) were admitted, and 1 of the 7 noncompliant patients (14%) was admitted. The third aim of the study was to determine whether a difference existed in the rate of blood cultures positive for gram-negative rods between compliant and noncompliant patients. Three of the four compliant patients who were admitted for febrile neutropenia (75%) had blood cultures positive for gram-negative rods. The one noncompliant patient admitted for febrile neutropenia also had blood cultures positive for gram-negative rods. Also in 2006, Moody et al[11] randomized 19 pediatric patients and their parents either to receive education about a neutropenic diet or to follow a plan of modified food safety guidelines approved by the US Food and Drug Administration (FDA). Patients included those being treated with myelosuppressive chemotherapy for malignant brain tumor, acute lymphoblastic leukemia (ALL), or sarcoma. The mean number of days of neutropenia (ANC < 500/μL) was 5.9 days for the neutropenic diet arm (n = 10) and 9.2 days for the food safety arm (n = 9), which was a nonsignificant difference (P = .29). Four patients in each arm (approximately 40%) developed a fever during neutropenia. In the neutropenic diet arm, there was one episode of *P. aeruginosa* bloodstream infection, but none in the food safety diet arm. The rate of adherence to the neutropenic diet was 94.1%, and the rate of adherence to the food safety guidelines was 99.9%. Patients on the neutropenic diet reported more difficulty adhering to the list of food restrictions.

In 2007, Van Tiel et al[12] randomized 20 adult patients receiving induction chemotherapy for acute leukemia to either a neutropenic (low-bacterial) diet or a normal hospital diet; all patients received antimicrobial prophylaxis and had neutropenic periods of about 2 to 3 weeks. Fecal samples were collected daily for evaluation of colonization with *Candida* species or gram-negative bacilli, quantitated as colony-forming units per gram of feces. No significant differences in the two groups were identified with regard to colonizing yeasts and gram-negative bacilli, number of days of fever, requirement for antimicrobial therapy, or rates of documented infections. One patient in each group had candidemia. Furthermore, calculated total medical costs were not different between the diet groups.

The largest study to date, published by Gardner et al[10] in 2008, randomized 153 patients undergoing induction for acute myelogenous leukemia (AML) to either a diet containing raw fresh fruits and vegetables (raw diet, n = 75) or one that excluded those items (cooked diet, n = 78) during their hospitalization for chemotherapy and neutropenia, until neutrophil recovery and hospital discharge. All patients received both antibacterial and antifungal prophylaxis. The primary endpoint was the incidence of major infection (pneumonia, bacteremia, or fungemia) in each group. Among those in the cooked-diet group, major infections occurred in 29%, compared with 35% in the raw-diet group (P = .60; 95% confidence interval [CI], 11% to 21%). There appeared to be a trend toward fewer fevers of unknown origin in the cooked-diet group vs in the raw-diet group (51% vs 36%; P = .07). Probability of death did not differ between the groups (P = .36). The authors concluded that survival was as expected in newly diagnosed AML. While the overall incidence of bacteremia was higher in the raw-diet group (23% vs 9%, P = .03), there was no difference in isolation of organisms normally resident in the gastrointestinal tract (*E coli, Enterococcus, Candida albicans, Enterobacter, Pseudomonas*, and *Klebsiella*) from blood cultures in raw-diet and cooked-diet populations (15% vs 6%; P = .12). The incidence of pneumonia tended to be higher in the cooked-diet group (15% vs 5%, P = .06).

Taken together, these studies indicate that the neutropenic diet is defined very variably and is not clearly of significant benefit to patients. Significant questions about the neutropenic diet remain unanswered, including which foods should be included; when such a diet should be initiated; which food preparation techniques best eradicate bacteria and improve patient compliance; and, most importantly, which populations (if any) will benefit from these manipulations. So far, the studies
reviewed give few answers and do not clearly point to any advantage for the neutropenic diet. In addition, the small sample sizes and numerous confounding variables (ie, prophylactic antimicrobials, growth factors, tumor types, degrees of mucositis and neutropenia, inpatient vs outpatient populations) limit a definitive interpretation.[10,12,20] It also has been suggested that awareness of the neutropenic diet by patients who have been assigned to a regular diet may result in study bias.[21] Thus, the aggregate data so far do not provide proof that a restrictive “low microbial” or neutropenic diet will protect neutropenic patients from invasive bacterial infections.

Moving From Unanswered Questions to What We Do Know

Although it is clear that fresh fruits and vegetables may carry enteric gram-negative rods on their surfaces, it is not clear what—if any—role they play in the pathophysiology of bloodstream infections in neutropenic patients. At this time, no cause-and-effect relationship has been or can be established to prove that the consumption of commonly restricted foods, particularly fresh fruits and vegetables, increases the likelihood of cancer patients developing bloodstream infections as a result of bacterial translocation. One could agree that the inclusion of raw fresh fruits and vegetables may actually be of benefit, as they are an excellent source of dietary fiber. Fiber may be considered a useful dietary component for cancer patients. Insoluble fibers are associated with improved intestinal transit and reduced incidence of constipation, and soluble fibers may help in managing diarrhea. Another benefit of dietary fiber is enhanced immune function. In fact, in a review of studies of bacterial translocation induced by total parenteral nutrition, Deitch[22] concluded that the addition of dietary fiber to low-residue oral diets improves the balance of intestinal flora and lessens bacterial translocation. One important exception to the liberalized consumption of raw vegetables is raw sprouts, including alfalfa, bean, clover, and others. This is the one food group that the FDA recommends avoiding, for both healthy and immunocompromised individuals. Unlike other fresh produce, seeds and beans need warm and humid conditions to sprout and grow. The warm, moist conditions in which sprouts are produced are also an ideal nourishing environment for the growth of bacteria, including Salmonella, Listeria, and E coli. A single bacterial pathogen on the outside of a seed can easily grow to an infectious dose after it has sprouted. The bacteria in and on growing sprouts cannot be washed off. Even though sprout growers attempt to use practices to decontaminate seeds before sprouting, no method has proven completely effective.[23]

Safe Food Handling Guidelines Should Replace the “Neutropenic Diet”

Safe food handling can be defined as “protecting food from contamination.”[24] Currently, safe food handling is advocated by the US Department of Agriculture (USDA), the FDA, and the US Centers for Disease Control and Prevention (CDC) as the main method of preventing food-related illness in immunocompromised patients. Two USDA publications, the “Dietary Guidelines for Americans 2010” and “Food Safety for People with Cancer,”[25,26] do not make reference to a neutropenic diet at all. Instead, the emphasis is strongly on safe food handling and preparation. The “Dietary Guidelines for Americans 2010” advocate the need for following four core food safety principles: cleaning, separating, cooking, and chilling. Furthermore, in its “Nutrition Care Manual,”[27] the American Dietetic Association recommends that patients with neutropenia follow the USDA’s food safety guidelines. Hospital food and nutrition services are required by their state’s health department to follow FDA food safety guidelines, ensuring the safety of foods provided to the most immunosuppressed individuals.[28]TABLE 2
Safe Food Handling Guidelines Used by The Nebraska Medical Center

Foodborne illnesses are defined by the World Health Organization (WHO) as diseases that are either infectious or toxic in nature, caused by agents that enter the body through the ingestion of food.[29] Signs and symptoms of foodborne illnesses can include fever, muscle aches, nausea, vomiting, abdominal cramping, and diarrhea. The onset of symptoms can vary greatly, occurring in just a few hours to several days after ingestion. Since these symptoms mimic some of the side effects seen in cancer treatments, identification of foodborne illness may be delayed. In the neutropenic patient, any delay in identifying and treating infection could be life-threatening. The goal, therefore, is to prevent the occurrence of foodborne illness by employing methods of food selection and preparation that will reduce the chances of transmission, as described in Table 2.

At The Nebraska Medical Center (TNMC), our review of the existing data has led us to abandon the old and restrictive neutropenic diet in favor of safe food handling techniques for immunosuppressed patients. There is a striking lack of evidence to support the view that a neutropenic diet will prevent infection in neutropenic patients. On the other hand, the anticipated benefits of a more palatable diet and the improved oral intake and better quality of life afforded by a liberalized diet are welcomed by caregivers and patients. At TNMC, our recently revised policy is to educate patients, caregivers, and staff about implementation of safe food handling as recommended by the USDA. In the inpatient setting, the importance of food safety is stressed not only in the hospital food services kitchens, but also on nursing units. Undercooked eggs, undercooked meats, unpasteurized dairy products, unpasteurized juices, and raw sprouts are not provided to any patient. Meal trays are not allowed to sit at the patient bedside for more than 1 hour. In the outpatient setting, patients and caregivers are educated about safe food handling, preparation, and storage at home as well as food safety guidelines for foods eaten outside the home. Table 1 lists the safe food handling guidelines adopted at our institution for outpatients.

In the setting of a diagnosis of cancer, with patients facing many fears, stressors, and an uncertain future, liberalization of neutropenic diet restrictions may make patients feel more empowered to gain control over a very essential aspect of their lives. Allowing patients to follow a more generous dietary pattern (with an emphasis on safe food handling) is likely to increase interest in food and therefore improve intake of calories and protein, resulting in less unintentional weight loss.

In summary, the available evidence does not implicate food as a direct cause of bacteremia in neutropenic patients. We suggest that until a cause-and-effect relationship can be proven, the neutropenic diet should not be imposed on cancer patients. Safe food handling guidelines are geared toward preventing acquisition of foodborne pathogens in the broader population. We recommend that these guidelines supplant the neutropenic diet restrictions previously imposed on cancer patients.

Financial Disclosure: The authors have no significant financial interest or other relationship with the manufacturers of any products or providers of any service mentioned in this article.
References:


Source URL: http://www.physicianspractice.com/neutropenic-diet-reviewed-moving-toward-safe-food-handling-approach

Links: