



The Neutropenic Diet: Fact or Fiction?

An update on evidence-based diet recommendations for immunocompromised oncology patients

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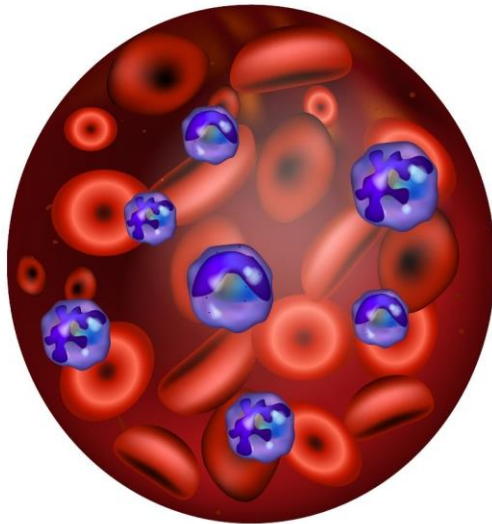
Objectives

- 1** Review the history of the neutropenic diet and cancer therapy
- 2** Evaluate the current literature regarding the efficacy of the neutropenic diet as it pertains to appropriate medical nutrition therapy for the oncology population
- 3** Describe the immunosuppressed diet

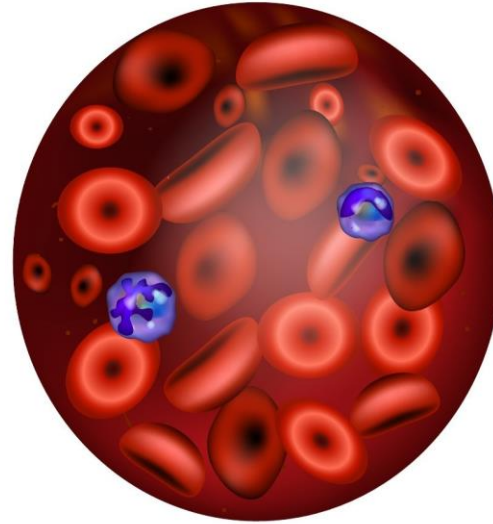
History of the neutropenic diet

What is neutropenia?

Neutropenia



Normal blood cells



Neutropenia

- Neutropenia: a condition in which there is a lower-than-normal number of neutrophils (a type of white blood cell) in the blood
- Absolute neutrophil count (ANC):
 $\leq 500 \text{ mm}^3 = \text{neutropenia}$ (Brown, 2019)
- Oncologic treatments, such as chemotherapy, radiation therapy, or hematopoietic cell transplantation (HCT), may lower blood neutrophil counts and induce neutropenia, thus increasing infection risk

Diet and neutropenia



- Specialized diets for neutropenic cancer patients established >50 years ago
- Rationale: minimize gastrointestinal exposure to pathogenic organisms (found in fresh produce, undercooked meats, and eggs, etc.) to decrease infection risk and reduce morbidity and mortality
- First published study regarding specialized diet:
 - AML patients maintained in isolation units fed “sterile” foods in attempt to decrease infection risk
 - Lower incidence of infections associated with oncologic therapies than would have been anticipated
 - Decreased caloric intake and subsequent weight loss noted (*Bodey, 1968*)

History of the neutropenic diet



- Over the next decade, growing interest in the use of specialized diets for oncology patients
- Modified diets frequently instituted for oncology patients and included:
 - sterile diet (e.g., all foods were made sterile through canning, baking, autoclaving, or irradiation)
 - low bacteria or low microbial diet (well cooked foods, only)
 - modified house diet (a regular diet omitting fresh fruits and vegetables)
- Neutropenic diet emerged based on guidelines created from microbial evaluation of common foods (<500 CFU/g) (*Pizzo, 1982*)

History of the neutropenic diet



- In recent years, the efficacy of the neutropenic diet has become controversial
- Question of interest: **Does evidence exist to support the effectiveness of the neutropenic diet in reducing infection rates in the neutropenic oncology population?**
- Multiple published randomized controlled trials have evaluated the association between the neutropenic diet and infection risk in oncology patients

Evidence-based studies related to the neutropenic diet

Review of neutropenic diets

General oncology population

- Out-patient pilot study showed no difference in rates of febrile admissions or positive blood cultures between compliant vs non-compliant patients (*DeMille, 2006*)
- Neutropenic diet did not prevent major infection in 153 AML patients maintained in a protected environment room (*Gardner, 2008*)
- Lack of effectiveness of neutropenic diet in 339 children with AML with respect to incidence of fever of unknown origin, bacteremia, pneumonia, and gastroenteritis (*Tramsen, 2016*)
- Pediatric oncology patients randomized to neutropenic diet vs standard FDA food safety guidelines had no difference in infection rates (*Moody, 2018*)

Review of neutropenic diets

General oncology population

- Retrospective, case-control study of 2086 hematology/oncology patients showed no difference in infection-related end-points in patients randomized to a standard vs neutropenic diet (*Jakob, 2021*)
- Neutropenic diet was not effective in reducing febrile neutropenia and was associated with higher rate of neutropenic enterocolitis in children undergoing cancer treatment (*Gupta, 2022*)
- Randomized, controlled trial showed no benefit of a neutropenic diet compared with a regular diet for reducing infections and mortality in patients receiving induction chemotherapy for acute leukemia (*Radhakrishnan, 2022*)
- Systematic review and meta-analysis of 1114 patients (6 studies) showed that the application of a neutropenic diet did not reduce the risk of infection and mortality in oncology patients with neutropenia (*Ma, 2022*)

Review of neutropenic diets

Hematopoietic cell transplantation population

- Retrospective review of 726 transplant patients showed a higher infection rate in recipients who followed a neutropenic diet (*Trifilio, 2012*)
- Large, single-center retrospective review reported rare incidence of bacterial foodborne infections (0.3%) following transplantation in patients maintained on diet that allowed fresh fruits and vegetables (*Boyle, 2014*)
- Results of a randomized, controlled prospective pilot study of 46 allogeneic transplant patients showed no significant difference between infection rates or nutritional status (*Lassiter, 2015*)
- Patients maintained on a “modified” diet showed no differences in incidence of bloodstream infections, incidence of grade 3 to 4 graft-vs-host disease (GVHD), or 100-day overall survival (*Taggart, 2019*)
- Multi-center, randomized trial of adult patients undergoing transplantation or high-dose induction chemotherapy maintained on a low microbial protective diet vs a non-restrictive diet showed no differences in infection rates, feeding outcomes, or incidence of acute GVHD (*Stella, 2022*)

Other considerations

- Neutropenic diet restrictions may be associated with decreased nutrient intake (*Caceres, 2015*)
- Strict neutropenic diet contains less fiber and vitamin C (*Maia, 2017*)
- Patient dissatisfaction/compromised diet quality often reported with neutropenic diet (*Macris, 2020*)
- Maintaining a healthy and diverse gut microbiome (through intake of high fiber foods, including fresh fruits and vegetables) may lead to improvements in adverse outcomes in transplant patients (*Moody, 2019*)

Efficacy of the Neutropenic Diet

- Systematic reviews and meta-analysis confirm that there is NO evidence to support the use of the neutropenic diet or further food restrictions in neutropenic patients with cancer; safe food handling guidelines, as recommended by the FDA, are warranted (*Wolfe, 2018; Sonbol, 2019*)
- Guidelines from the European Society for Clinical Nutrition and Metabolism (ESPEN) and American Society of Clinical Oncology (ASCO): Neutropenic diets are not recommended to prevent infection in patients with cancer during active treatment (*Muscaritoli, 2021; Ligibel, 2022*)
- Restrictive diets continue to be prescribed by the oncology community (*Foster, 2014*)
- Survey of 198 member institutions of the Children's Oncology Group: 84% recommended a neutropenic diet for transplant patients (*Braun, 2014*)
- Most transplant centers (93%) utilize some type of neutropenic diet (*Peric, 2018*)
- Neutropenic diet continues to be recommended on the websites of 35% of United States cancer centers (*Brown, 2019*)

Food Safety Guidelines and Immunosuppressed Diet

Fred Hutchinson Cancer Center (FHCC)

Immunosuppressed diet

- Nutrition education regarding high-risk foods and safe food handling is necessary during immunosuppression, including food safety guidelines and immunosuppressed diet
- Food safety education: www.seattlecca.org/patients/patient-education/videos

Food safety guidelines and immunosuppressed diet

Allogeneic
transplant patients

Until off
immunosuppressive
medications

Autologous
transplant patients

For 3 months
post-transplant

Oncology/
Immunotherapy
patients

Anytime ANC*
< 1000 mm³

*ANC: absolute neutrophil count

Food safety guidelines for immunosuppressed patients



Source: <https://www.fda.gov/food/buy-store-serve-safe-food/safe-food-handling>

Dairy foods

Choose

- Pasteurized milk and milk products
- Pre-packaged hard and semi-soft cheeses
- Pasteurized yogurt and kefir
(live active cultures acceptable if made with pasteurized milk)

Cook

- Sliced cheeses from deli

Avoid

- Cheeses containing molds, such as blue cheese
- Cheeses containing uncooked vegetables that are not pasteurized after addition



Meat and meat substitutes

Choose

- Cooked commercially packaged or deli sliced pre-cooked meats (*cold cuts, hot dogs*)
- Cooked or pasteurized tofu
- Pasteurized eggs or cook until yolk is firm

Cook

- Pre-cooked meats (*packaged or deli sliced*)
to steaming hot or 165° F

Avoid

- Raw fish (*sushi, poke*)



Fruits and vegetables

Choose

- Whole fruits and vegetables
- Dried herbs and spices
- Shelf-stable salsa and fruit
- Pasteurized juices

Avoid

- Fresh, refrigerated salsa
- Raw sprouts (all kinds)
- Salads from deli
- Pre-cut fruits and vegetables
- Kimchi, non-pasteurized sauerkraut



Fruits and vegetables

Washing

- **All fresh fruits and vegetables should be thoroughly washed under clean, running water**
 - Includes produce that may be peeled, such as bananas, melons, oranges, and pre-washed, bagged produce (salad kits)
- **Scrub produce that has a firm or rough skin or rind, such as cantaloupe, potatoes, and avocados**
- **Rinse leaves of leafy vegetables thoroughly** (includes bagged lettuce)

Nuts and seeds

Choose

- Shelled roasted nuts, or nuts cooked into foods
- Commercially packaged peanut butter or other nut butters

Avoid

- Raw nuts or seeds (*including flax or chia seeds*)
- Nuts in the shell (*pistachios, “baseball” peanuts*)
- Ready-to-eat bulk foods (*acceptable if cooked before eating*)



Bread, grain, and cereal products

Choose

- All breads and baked goods
- Cooked grain products and cereals

Avoid

- Raw grains (*muesli cereal, some granola bars*)
- Bread, grain, and desserts open to the public (*bread cases*)
- Ready-to-eat bulk foods (*acceptable if cooked before eating*)



Fats

Choose

- Any vegetable oils
- Lard, margarine, and butter (*refrigerate*)
- Shelf-stable mayonnaise, salad dressings (*including blue cheese*)

Avoid

- Fresh, refrigerated commercially-prepared salad dressings, unless made with pasteurized eggs



Entrées and soups

Choose

- Choose entrées and soups
- Commercially prepared pasteurized miso products

Avoid

- Home-made or restaurant prepared miso products
- Self-serve soups at grocery stores and restaurants



Beverages

Choose

- Clean and maintain single-serve coffee machines
- Make tea and coffee with boiling water (212°F)
- Loose-leaf tea is acceptable if made with boiling water (212°F)
- Commercially bottled/canned cold-brew coffee

Avoid

- Kombucha (*fermented beverage*)
- Sun tea



Desserts

Choose

- Cream or custard filled pastries are acceptable if refrigerated or shelf-stable
- All homemade and commercially baked cookies, cakes, pies, and puddings

Avoid

- Desserts from self-service areas (doughnuts, in case, etc.)



Other

Choose

- All shelf-stable condiments and dry goods are acceptable
- Pasteurized honey

Avoid

- Raw honey or honey in comb



Water safety

Choose

- City or municipal well water (*tested daily for contaminants*)
- Bottled water (*treated by reverse osmosis, distillation, or filtered through absolute 1 micron or smaller filter*)
- Well water that has been boiled for 15-20 minutes, stored in the refrigerator, and used within 48 hours

Avoid

- Private or small community well water
- Portable water filter systems such as Brita® or Pur®
(**Acceptable** – *if used on safe water supply to improve water flavor*)



Dining out

Choose

- Cooked vegetables (*steamed, stir-fried, baked, sauteed, roasted, grilled, boiled, etc.*)
- Baked fruit (*pie, etc.*)

Avoid

- Raw fruits and vegetables
- Food that are open to the public (*buffets, salad bars*)
- Food sold by street food vendors (*food trucks, farmer's markets*)

Dining out

Safe choices

- Eat hot foods hot and cold foods cold
- Check color/juices of meat (no pink or red; meat should be well-cooked)
- Request new, unopened bottles or individual packets of condiments
- Pack up your own leftovers
- Make sure restrooms are clean
- Make sure tables and dinnerware are clean

Dining out

Fast foods

- Request foods be freshly prepared
- Avoid raw fruits and vegetables, such as lettuce/tomato on burger or in taco, side salads, coleslaw
- Avoid special sauces



Summary

Summary



- Evidence in support of the neutropenic diet has not been established
- Oncology patients should be educated on high-risk foods and safe food handling

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Thank you!

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