

Medical Nutrition Therapy for Resident with *C. difficile*-Associated Disease and Antibiotic Associated Diarrhea

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INTRODUCTION

Clostridium difficile (*C. diff*) is a spore-forming bacterium that releases toxins in the intestine causing mucosal inflammation, intestinal damage, and diarrhea. It is one of the most common nosocomial infections, with incidence and severity on the rise, reaching epidemic levels in the US. This is possibly due to the increased use of broad-spectrum antibiotics and the emergence of a *C. diff* strain that has increased virulence. Long-term care (LTC) residents are at especially high risk because of extended length of stay, advanced age, frequent hospitalizations, and the widespread use of antibiotics (1). From 50% to 75% of residents in LTC are exposed to 1 or more courses of antibiotics over a 12-month period (2-6). Up to 33% of LTC residents treated with an antibiotic acquire *C. diff*, with a 44% rate of recurrence within 1-2 months (7, 8). Furthermore, up to 65% of residents who have suffered 2 or more episodes will have another recurrence (8). In the last decade, there has been an increase of antibiotic-associated diarrhea (AAD) of 500%. *C. diff* accounts for 15% to 25% of all episodes of AAD (9). Even when an outbreak is not occurring, the prevalence of *C. diff* colonization in LTC ranges up to 20%, compared with less than 3% in healthy adults (10-12).

Studies have conservatively estimated the national cost of *C. difficile*-Associated Disease (CDAD) treatment to be between \$1 billion and \$3.2 billion (13, 14).

ROLE OF MICROBIOTA & DEVELOPMENT OF CDAD

The gut of a healthy adult contains an estimated 100 trillion bacteria of various species, known as the gut microbiota. Incidentally, this is 10 times as many cells as are contained in the entire body itself. These organisms are extremely active and interact continuously with each other and with the cells lining the gut, as well as with the immune, endocrine and central nervous systems. Together, their level of metabolic activity matches that of the liver (15). This 2-3 pound mass of microbiota could really be considered as a separate organ itself due to the multitude of indispensable functions it performs. Contained in this mix of 400-odd bacterial species are both beneficial and harmful microorganisms. The amount of these beneficial microorganisms, such as bifidobacteria and lactobacilli in the colon naturally decrease as we age putting older adults at increased risk for infection. The microbiota acts as a front line defense, protecting the body against numerous invaders and pathogens. However, the optimal microbiota composition hangs delicately in the balance and can be upset by a number of factors including stress, illness, recovery from surgery, poor diet, environment, medications, age, and antibiotics which kill the beneficial bacteria in the intestine. When this protective barrier is disturbed the host becomes susceptible to proliferation of *C. diff*. *C. diff* colonies produce toxins that damage the gut wall, causing problems ranging from mild diarrhea to severe pseudomembranous colitis, toxic megacolon, and bowel perforation. Symptoms include loose, watery, and foul-smelling stools, cramping, and abdominal pain, loss of appetite, and, in most cases, fever. Severe diarrhea is confirmed when there are more than 10 stools a day. Residents can develop signs and symptoms within the first week of antibiotic therapy and up to 10 weeks after its discontinuation (16, 17). Symptoms may be prolonged and debilitating and can lead to dehydration, electrolyte imbalance,

protein-energy malnutrition (PEM) and significant weight loss. CDAD can be a serious condition with a mortality rate as high as 25% in elderly patients who are frail.

PROTEIN-ENERGY MALNUTRITION (PEM)

PEM is a condition arising from sustained inadequacy in the quantity of protein and/or energy needed to meet the metabolic demands of the body. This can occur as a result of insufficient dietary intake or from an acute illness like CDAD, which can impair uptake and utilization of nutrients, increase protein and energy requirements, and increase nutrient losses. Acute illness causes systemic inflammation, leading to hypermetabolism and hypercatabolism, which significantly increase nutrient needs. In order to prevent PEM in residents with CDAD it is critical to ensure adequate protein and calories are consumed. A loss of 10% of usual body weight equals 15-20% loss of total body protein. A loss beyond 20% of total body protein leads to widespread impairments in physiologic systems (immunologic, pulmonary, cardiac, skeletal muscle function). Residents with sustained PEM have higher rates of morbidity and mortality, extended periods of rehabilitation or hospitalization, and a higher cost of medical care.

For residents with CDAD who have decreased appetite, high calorie supplements such as 2cal/ml, given 60 minutes after or before meals, may help them obtain the calories required to meet metabolic needs. Additionally, since breakfast is usually the meal where the most food is consumed, providing breakfast foods that have been enhanced with calories such as high calorie cereals may be a useful strategy. The use of fortified foods and beverages like soups, mashed potatoes, desserts, and juices should also be utilized to combat unintended weight loss. To further prevent PEM, concentrated, hydrolyzed liquid protein supplements can be given at med pass to help ensure adequate protein is consumed. Since older adults have decreased stomach acid, which is needed to break down protein, and residents with CDAD may have compromised intestinal absorption, the use of hydrolyzed (broken down) protein is most appropriate as it is readily absorbed and utilized. There are many liquid hydrolyzed protein supplements available that contain between 10-17 grams of complete protein per one ounce serving.

TREATMENT FOR DIARRHEA

C. diff is the most common infectious cause of acute diarrheal illness in LTC (18,19). According to the nutrition care process, treatment for diarrhea should achieve the following: restore normal fluid, electrolyte, and acid-base balance; thicken consistency of the stool; stimulate the gastrointestinal tract by slow introduction of solid food without exacerbation of symptoms; and repopulate the gastrointestinal tract with normal flora.

Restore normal fluid, electrolyte, and acid-base balance

If the resident has mild diarrhea, clear juices and soups with small frequent feedings are recommended for rehydration. If the resident has moderate to severe diarrhea, the use of oral rehydration solutions such as Resol, Ricelyte, CeraLyte and Rehydralyte, which contain sodium, potassium and glucose, are recommended. Water losses should be replaced at a rate of 35 to 40 ml/kg. Beverage preferences should be obtained and provided to the resident possibly at the rate of 1-2 ounces every 1-2 hours. Liquids should be given at room temperature and advanced as tolerated. Beverages that are recommended and that should be avoided when the resident has diarrhea include:

Recommended	Avoid	Limit
Decaffeinated coffee, caffeine-free teas, soft drinks without caffeine, & rehydration beverages. High-sodium soups along with fruit, vegetable, or tomato juice can be used to help replace lost electrolytes.	Beverages sweetened with sorbitol and those containing caffeine, including regular coffee, regular tea, & colas	Beverages containing high fructose corn syrup should be limited to 12 oz per day

Thicken consistency of the stool

Banana flakes, apple powder, or other pectin sources can be added to foods. Historically, the use of the BRAT (bananas, rice, applesauce, and toast) eating pattern has been used to guide the initial food choices for acute diarrhea but does not provide a variety of nutrients. Also, antimotility agents such as loperamide should be avoided when the resident has *C. diff* associated diarrhea. This recommendation is based on anecdotal data indicating that diphenoxylate and atropine may predispose patients with CDAD to toxic megacolon.

Stimulate the gastrointestinal tract by slow introduction of solid food without exacerbation of symptoms

Low-residue, low-fat, lactose-free nutrition therapy should guide initial food selections. If there is no evidence of lactose intolerance, these foods should be added back to the meal plan. Small, frequent feedings with fluids between meals will help control diarrhea. Foods that are recommended and that should be avoided when the resident has diarrhea include:

Recommended	Avoid	Limit
Low-fat dairy products, yogurt with pre- & probiotics, tender, well-cooked meat, poultry, eggs, white bread, crackers, pasta, cereals, well-cooked vegetables without seeds or skin, strained vegetable juice, melons, & ripe bananas.	Whole milk products, fried meats, luncheon meats, fatty meats, whole wheat or whole grain products, raw vegetables except lettuce, all raw fruits except bananas & melons, dried fruit, fruit with pulp, canned fruit in heavy syrup, sugar alcohols such as sorbitol, & honey. High-fiber & gas-producing foods such as nuts, beans, corn, broccoli, cauliflower, or cabbage.	Fats should be limited to less than 8 teaspoons per day.

For severe diarrhea, a clear liquid diet is appropriate for 1 to 3 days and includes:

Juice, gelatin, ice water, popsicles, ice chips, sweetened tea or coffee, meat or vegetable broths, & hydrolyzed collagen based liquid protein supplements.

Repopulate gastrointestinal tract with normal flora

Probiotics

Probiotic and prebiotic supplementation can be used to repopulate gut flora, assisting with treatment and recovery of CDAD. Probiotics are live microorganisms which, when administered in adequate amounts, confer a health benefit to the host. Probiotics are available in foods and dietary supplements in the form of capsules, tablets, powders, gum, and straws. On their own, foods do not provide sufficient quantities of the probiotics needed to restore gut microbiota of older adults on antibiotic therapy. Probiotics in supplement form are required in order to provide the levels necessary to restore a favorable microbial balance after the devastating effects of antibiotics. Probiotics must be able to survive the aerobic condition of the product in which they are contained, as well as exposure to the acidic condition of the stomach, bile acid, and pancreatic secretions in the small intestine. It is therefore important to ensure the probiotics used are protected either by microencapsulation, a bio-film, or found naturally in a spore form. For example, the probiotic *bacillus coagulans* (*lactobacillus sporogenes*) is naturally encapsulated in a spore shell that does not dissolve until it reaches the intestine, where it multiplies rapidly, increasing the beneficial bacteria in the colon and producing lactic acid to lower the pH.

The addition of probiotics to the diet of residents undergoing antibiotic therapy replaces natural bacteria that would normally counteract *C. diff* by competing for resources in the colon. Probiotics

have been associated with diminished rates of *C. diff* and reduced costs associated with treatment of these infections (20). It is important to understand that not all probiotics work on all conditions and therefore appropriate selection should be based on those clinically proven for specific disease states. For AAD and *C. diff*, *Saccharomyces Boulardii* (*S. Boulardii*) has been shown to be the most effective probiotic against AAD and *C. diff*, with over 50 years of clinical research and use (21-29). Doses of *S. Boulardii* in these studies ranged from 500 mg (250 mg twice daily) to 1 g (two 250 mg capsules twice daily) administered each day either during antibiotic therapy, or continued for up to 2 weeks after completion of antibiotic regimens. *S. Boulardii* is a non-pathogenic yeast, unlike most probiotics, which are bacteria. It is acid and heat stable and antibiotic resistant unlike probiotic bacteria which can be destroyed by antibiotics. *S. Boulardii* grows well at body temperature, is not systemically absorbed into the circulation, reaches a high steady-state level of 10^7 to 10^8 CFUs within the colon in a matter of days, but is rapidly eliminated within 2–5 days of discontinuing use. *S. Boulardii* produces an enzyme that destroys the *C. diff* toxins and their receptor sites in the intestine helping to prevent recurrence. This unique probiotic organism also stimulates chloride absorption, reduces symptoms of CDAD, and permits normal bacterial gut microbiota to be reestablished (24).

Prebiotics

Unlike probiotics, which are live bacteria or yeast, prebiotics are non-digestible food ingredients that positively affect the host by selectively stimulating the growth and/or activity of one or a limited number of beneficial bacteria in the colon (30). In effect, prebiotics act as food for gut bacteria. A number of food ingredients have been shown to act as prebiotics. These include fructooligosaccharides (FOS), inulin, galacto-oligosaccharides (GOS), lactulose, polydextrose, and digestive resistant maltodextrin (30). They have been added to foods and beverages such as yogurt, kefir and other dairy drinks, functional waters, nutrition bars and supplements, soymilk, mineral supplements, and medical foods.

FOS are a very well-researched prebiotic, found naturally in certain foods such as bananas, onions, garlic, and Jerusalem artichokes. FOS resist degradation by digestive enzymes and pass intact through the stomach and small intestine. Once FOS reach the colon, anaerobic bacteria ferment them to obtain energy and carbon for their own growth. During this process, bacteria also generate short-chain fatty acids (SCFAs), which reduce pH in the gut creating a less favorable environment for harmful bacteria. As a result of the fermentation, there is an increase in the concentration of beneficial bacteria (bifidobacteria) in the large intestine, an increase in calcium absorption, an increase in fecal weight, and a shortening of gastrointestinal transit time, all of which help normalize bowel function (31). FOS are also used to help to manage diarrhea and constipation. The production of SCFA, like butyric acid, serves as the primary fuel for the cells of the large intestine and helps maintain their health and integrity, which can become damaged by *C.diff* toxins. FOS may help in the prevention and treatment of *C. diff* infections by aiding in the restoration of microbiota and the strengthening of intestinal barrier integrity. Additionally, polydextrose has been shown to increase both bifidobacteria and Lactobacilli, inhibit pathogen growth through the decrease of fecal pH, and increase butyrate production in a dose dependent manner with a dose as low as 4 grams per day (32). Bifidobacteria are beneficial because they stimulate the immune system, increase resistance to infection and diarrheal disease, reduce markers of chronic gut problems and enhance overall gut health (33).

Synbiotics (Probiotics + Prebiotics)

A prebiotic can be combined with a probiotic to make a synbiotic, which improves the survival rate and proliferation of the probiotic in the gastrointestinal tract and helps ensure that they reach the colon in numbers adequate enough to confer a health benefit. On their own, probiotics are vulnerable to pH and temperature variations as well as the negative impact of oxygen and bile secretions. The benefits of probiotics are dependent on their viability, growth, and metabolic activity, which can be maximized with the addition of prebiotics. Probiotics must also compete with resident bacteria in the

gastrointestinal tract. With the addition of a prebiotic food substrate, the probiotic cells are better equipped to survive and proliferate. This greater stability, which a synbiotic combination facilitates, also translates into longer shelf-life. For example, in a randomized, double blind, placebo controlled clinical study, a supplement containing *bacillus coagulans* (*lactobacillus sporogenes*) and FOS significantly reduced the number of days and duration of events in children with AAD (34). Providing foods and supplements that contain synbiotics to residents with *C. diff*, AAD, or those at risk, will help ensure optimal delivery to the gut, strengthening their front line defense and improving quality of life.

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