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The Need to Reassess Dietary Fiber Requirements in Healthy and Critically Ill Patients

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SUMMARY

In conclusion, this article has provided evidence that current dietary fiber intake levels may be insufficient to maintain colonic mucosal health and defense, and reduce inflammation and cancer risk in otherwise healthy people. Secondly, current commercial tube feeds generally overlook the metabolic needs of the colon, and when combined with antibiotics may predispose patients to dysbiosis, bacterial overgrowth with pathogens such as *C difficile*, and acute colitis, thus perpetuating critical illness. These results raise concern about the wide-scale use of prophylactic antibiotics in the ICU and the use of elemental, fiber-depleted tube feeds. Nutrition support is not complete without the addition of sufficient fiber to meet colonic nutritional needs.

Keywords

Dietary fiber; Clinical studies; Fiber supplementation; Colon cancer; *Clostridium difficile*

NORMAL HUMAN DIETARY FIBER REQUIREMENTS

The definition of dietary requirements is extremely difficult.¹ Traditionally requirements have been based on the quantity of food needed to maintain a normal body weight, or in the case of micronutrients to maintain normal blood levels. This presupposes that the definition of normal levels is known. People can be slim and fit or fat and fit. Blood levels of vitamins have to drop precipitously before tissue deficiency occurs and a pathologic phenotype is displayed.

The explanation for this problem is that nutrients are stored in good times that allow people to survive feasts and famines. Thus, overweight has been associated with improved outcome from the ICU.² On the other hand, slimness is associated with prolonged lifespan.³

With dietary fiber, the definition of normal requirements becomes even more complex and difficult. Populations can survive on low fiber intakes for years, and patients with a colectomy do not need any fiber, as its chief role is to provide food for the colonic microbiota. However, the industrial and agricultural revolutions led to a massive increase in

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food production that supported the population explosion. Unfortunately, it also led to the progressive reduction in consumption of whole foods, which in turn led to dramatic reductions in food fiber content through food processing to promote storage and transportation. The development of fast foods through advanced food technology has culminated in the increased consumption of simple sugars, together with increased intake of processed meat and saturated fat, which characterize the western diet. This diet is responsible for the emergence of a group of chronic ailments, termed westernized diseases, which present the greatest challenge to health care in the United States today. Obesity, colon cancer, and cardiovascular diseases are perhaps the best examples. The lack of dietary fiber due to low intakes of coarse grains, fruits and vegetables is common to all, as their content of complex carbohydrate reduces satiety and glycemic responses to feeding, thereby reducing the risk of obesity. Obesity is associated with an increase in the incidence of at least 9 cancers, as documented by a recent review by the American Institute of Cancer Research, illustrated on Fig. 1.

The lack of fiber is particularly pertinent to the remarkably high incidence rates of colon cancer in westernized societies. For example, rates are uniformly high in all segments of the US population with levels of approximately 65 cases per 100,000 population in African Americans, 55 cases per 100,000 population in Caucasian Americans,^{4,5} and as high as 100 cases or more per 100,000 population in Alaska Native People.⁶ In stark contrast, colon cancer is rarely seen in rural African communities consuming their traditional high-fiber (~50 g/d), low-meat, and low-fat diets, at less than 5 cases per 100,000 population.

The explanation for this is the effect fiber has on the colonic microbiota. People have evolved over hundreds of million years on a high-fiber diet. Although people have characteristically been omnivores and hunter-gatherers, meat and fat intakes have been low and occasional, while foraging has been continual. Recent advances in dental micro-wear and stable isotope technology have provided evidence that grain consumption has always been part of the human diet.⁷ Thus, human digestive tracts evolved in tandem with dietary exposure, but the few hundred years since the agricultural revolution have been insufficient to enable people to do without fiber. Basically, the small intestine is extremely efficient in digestion, absorbing 95% of what we eat. These absorbed nutrients maintain general body composition and health. However, some starches and proteins contain carbohydrate structures that are resistant to human enzymatic digestion and enter the colon. The anatomy of the colon evolved to produce a reservoir to hold up the digestive stream to allow infrequent defecation, just as the stomach evolved to become a reservoir to enable people to eat periodic meals, rather than having to nibble all day like a rat. The colonic reservoir increased the ability of the gastrointestinal (GI) tract to reabsorb all the fluid and electrolytes secreted by the upper GI tract to enhance the digestive efficiency of human enzymes. Perhaps more importantly, it created a home for environmental microbes that have the missing enzymes needed to complete the digestion of dietary residues, such as complex carbohydrates and dietary fibers. A perfect symbiotic, or mutualistic, relationship was set up where the fiber provided food for the microbes, while the microbes only partially broke the carbohydrate skeletons down to short chain fatty acids, notably acetate, butyrate, and propionate. These metabolites were released into the lumen and became the preferred nutritional sources for the colonic epithelium. The colonocytes differ from all other body

cells in their preferred utilization of butyrate for energy production. Thus, naturally occurring foods provided sufficient fiber residues to maintain the health of the microbiota and the colon.

The author recently reviewed the overwhelming human study and experimental evidence for the overarching importance of butyrate in maintaining colonic health, resistance to disease, and prevention of colon cancer, summarized on Fig. 2.

This figure helps explain the mechanisms whereby diet affects colonic inflammation and colonic carcinogenesis. First, food is digested by the small intestine, releasing simple sugars, fats, amino acids, fluids and electrolytes and micronutrients into the bloodstream, supporting vital organ function and life. The content of fat, meat, and fiber determines what residues then enter the colon to provide substrate for the microbiota. The microbiota forms a complex system whose structure and activity depend upon what it is fed. Thus, a high-fiber diet stimulates the growth and function of microbes that contribute to saccharolytic fermentation, notably starch degraders such as *Ruminococcus. bromii* and *Bifidobacterium adolescentis* that cross-feed to produce acetate, which is the major energy source for the final major butyrate producers *Eubacterium rectale*, *Roseburia* subspecies, and *Faecalibacterium prausnitzii*.⁸ Bifidobacteria are also induced by starch and soluble fiber to produce lactate, which is released into the lumen and fuels other butyrate-producers such as *E. hallii*. Increased lactate production reduces luminal pH, which further stimulates the growth of butyrate producers, and, importantly, suppresses overgrowth by pathogens. The figure outlines the remarkable pleiotropic beneficial effects of butyrate on maintaining mucosal health and defense, immunologic modulation via stimulation of regulatory T cells, the promotion of microbial metabolism and homeostasis, and the epigenetic modulation (ie, butyrate acts as a histone deacetylase inhibitor) of inflammation and epithelial proliferation, which suppresses long-term risk of carcinogenesis. Further reading on the evidence supporting each of these pathways is available elsewhere.⁴ Microbes also digest the remaining plant cell walls, releasing phytochemicals at a mucosal level, where their powerful antioxidant, anti-inflammatory, and antineoplastic properties fortify the effects of short chain fatty acids in promoting mucosal health, microbial balance, and cancer resistance. Finally, increased colonic metabolism enables microbes to synthesize a remarkably wide spectrum of water-soluble vitamins, such as folate, B12, biotin, and nicotinamide, which are available in high local concentrations.^{9,10} Recent studies have demonstrated that the view that such vitamins only become of benefit if coprophagia is practiced, as in rabbits, is incorrect, as specific transporters have been demonstrated in human colonic tissue.^{11,12} Thus, the efficacy of these vitamins in regulating DNA synthesis and repair will likely further reduce the risk of neoplastic change and progression.

On the other hand, an unbalanced diet, rich in meat and fat, generates several mechanisms that increase mucosal inflammation, proliferation, and risk of colitis and cancer. A high-fat diet stimulates the liver to synthesize more bile acids, which are primarily needed for the small intestinal digestion and absorption of long chain fatty acids. Although most bile acids are reabsorbed in the proximal small intestine, a proportion enters the colon, where they are conjugated by specific microbes to secondary bile acids, which are recognized human carcinogens.¹³ Furthermore, a recent study showed that high saturated fat consumption

stimulated the production of taurine, one of the bile acids that has a high sulfur content.¹⁴ On entering the colon, taurine stimulated a blossom of *Bilophila wadsworthiae*, which utilizes the sulfur to produce hydrogen sulfide, which caused acute colitis in experimental animals and has been shown to be genotoxic.¹⁵

High meat and protein diets are also not totally digested and stimulate colonic microbes to engage in proteolytic fermentation. Although this process also generates short chain fatty acids, it releases nitrogenous metabolites, such as nitrosamines, phenolics, and p-cresol, which are inflammatory and proneoplastic.¹⁶ Furthermore, over-cooked or burned meat produces heterocyclic amines, which are powerful carcinogens in their own right. Thus, the overall balance is shifted from colonic health to inflammation and neoplasia. It is critical to understand, however, that a high-fiber diet counteracts many of these inflammatory and neoplastic pathways,¹⁷ and so a moderate quantity of meat and fat is well tolerated in a fiber-rich balanced diet.

Based on the fiber composition of the traditional African diet of greater than 50 g/d, which is associated with remarkably low rates of colon cancer, and the results of experimental studies that show there is a threshold quantity of fiber that needs to be met before the anti-inflammatory and antineoplastic effects of butyrate become active,¹⁸ the author and colleagues believe the current US Department of Agriculture (USDA) recommendations that a normal diet should provide at least 22 g of fiber per day for women and 38 g/d for men, are insufficient. The author and colleagues believe that the ideal intake should be more like 50 g/d to prevent colitis and colon cancer. This proposal is further supported by the results of the Polyp Prevention Study, which recommended an increase on fiber to 35 g/d, and failed to achieve its primary endpoint, which was a reduction in adenomatous polyp recurrence.¹⁹ Critically, it was demonstrated that in the segment of the population who increased their consumption of fiber rich foods and dry beans most, there was a significant reduction in the development of premalignant advanced polyps.²⁰ It is noteworthy that the current USDA dietary recommendations were based on the amount of fiber shown to reduce risk of cardiovascular diseases, not colonic health.

CLINICAL STUDIES

Following the previously cited evidence, the author and colleagues are concerned that the current nutritional recommendations for tube feeding of hospitalized patients are also inadequate. Most tube feed formulae have sufficient nutrients for maintain small intestinal health, but are grossly deficient for the support of colonic nutrition. Critically ill patients are commonly fed for prolonged periods on elemental diets that are either devoid of fiber, or only contain 4 g/L. A further concern is that most patients are treated with a variety of broad-spectrum antibiotics, which all but wipe out the microbes that are essential for using what little fiber there is to maintain colonic mucosal nutrition and defense. Thus, the colon is starved, increasing the risk of overgrowth of pathobionts such as *Clostridium difficile* and acute colitis.

In evidence, a recent study by Alverdy's group in a group of long-stay intensive care unit (ICU) patients²¹ showed a dramatic contraction in the numbers of fecal microbial

communities to between one to 4 taxa, mostly *Enterococcus* and *Staphylococcus* and the family *Enterobacteriaceae*. Furthermore, there was a rise in antimicrobial resistance, and overgrowth with fungal communities was common, including *Candida albicans* and *C. glabrata*. Fig. 3 illustrates one such patient who had received 14 courses of antibiotics and was left with a skeleton fecal microbiome consisting of 1 *Enterococcus* and 1 *Enterobacteriaceae*.

FIBER SUPPLEMENTATION STUDIES

In an attempt to help the recovery of the colonic microbiota in a group of 13 critically ill ICU patients predominantly suffering from the consequences severe acute pancreatitis, the author and colleagues tested the utility of progressive soluble fiber supplementation of their enteral feeds for up to 36 days.²² Table 1 shows that all patients had been, or were receiving broad-spectrum intravenous antibiotics, and most were also treated with gastric acid suppression by proton pump inhibitors (PPIs). Previous studies had shown that PPIs were associated with disturbed gut function and small bowel bacterial overgrowth,²³ and had raised the concern that the combination of elemental diets, antibiotics, and PPIs were a prescription for *C. difficile* infection and colitis.²⁴ The tube feed given was semielemental and contained 4 g soluble fiber per liter. Following fecal microbial analysis for microbes and short chain fatty acids, progressive supplementation was commenced at 4 g 3 times daily, and increased progressively every 3 days, with tolerance, to a goal of 24 g/d. The supplementation was well tolerated from a GI point of view, with no significant increase in stool output or diarrhea. In fact, bowel function was unchanged in those without diarrhea, and in the 4 with diarrhea, it improved in 2 patients, remained the same in 1 patient, and worsened in the fourth patient, whose progress was hindered by recurrent sepsis and the need for continued antibiotics.

Fecal studies revealed that microbial counts before fiber supplementation were dramatically suppressed in the group as a whole (Fig. 4), with a 97% reduction in the predominant potential butyrate producers at the genus level, namely *Clostridia* cluster XIVa (which include *Eubacterium rectale*, *Roseburia intestinalis*) and cluster IV (including *Faecalibacterium prausnitzii*), and in starch degraders (*Ruminococcus bromii* and *R. obeum*). Similarly, fecal short chain fatty acid concentrations were several-fold lower. Following maximal fiber supplementation, there was partial, but not complete, restoration of microbial numbers and their metabolites, including butyrate (Fig. 5). The partial response could be explained by the continued use of antibiotics in some and to the well-recognized long-term disturbance of the microbiota following a course of antibiotics.²⁵

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KEY POINTS

- Human dietary fiber requirements are based on the quantity known to be associated with cardiovascular health. It is more appropriate that they should be based on the nutritional needs of the colonic microbiota, which maintain colonic health and homeostasis.
- Diets containing more than 50 g of fiber per day are associated with low colon cancer risk.
- Current nutritional support of hospitalized patients overlooks the nutritional needs of the colonic microbiota, leading to colonic starvation and increased risk of dysbiosis, *Clostridium difficile* overgrowth, and acute colitis.

Fig. 1. Obesity and risk of cancer. (From American Institute for Cancer Research. What You Need to Know About Obesity and Cancer. AICR Infographics 2017. Available at: <http://www.aicr.org/learn-more-about-cancer/infographics/infographic-obesity-and-cancer.html>; © American Institute for Cancer Research, <http://www.aicr.org>; with permission.)

Fig. 2.

Illustration of the influence of dietary composition on colonic microbial metabolism to enhance saccharolytic fermentation, colonic mucosal health, and cancer prevention, in the case of high fiber foods, or promote the production of inflammatory mediators or carcinogenesis in the case of fiber deficient, high-meat and high-fat diets. (From O'Keefe S. Diet, microbes and their metabolites, and colorectal cancer. *Nat Rev Gastro & Hep* 2016;13:691–706; with permission.)

Fig. 3.

Time course of 1 long-stay ICU patient who received multiple courses of antibiotics, illustrating the decimation of the fecal microbiota. (From Zaborin A, Smith D, Garfield K, et al. Membership and behavior of ultra-low-diversity pathogen communities present in the gut of humans during prolonged critical illness. *MBio* 2014;5:e01361–14; with permission.)

Fig. 4.

Illustration of the gross suppression of fecal microbial counts in ICU patients recovering from severe acute pancreatitis. (*From* O'Keefe SJ, Ou J, Delany JP, et al. Effect of fiber supplementation on the microbiota in critically ill patients. *World J Gastrointest Pathophysiol* 2011;2:138–45; with permission.)

Indices of Fermentation before and after Fiber Supplementation

Fig. 5.

Evidence of recovery of saccharolytic fermentation in ICU patients given progressive fiber supplementation of their tube feeds. (From O'Keefe SJ, Ou J, Delany JP, et al. Effect of fiber supplementation on the microbiota in critically ill patients. *World J Gastrointest Pathophysiol* 2011;2:138–45; with permission.)

Table 1

Results of testing the utility of progressive soluble fiber supplementation of patients enteral feeds for up to 36 days

Patient	Diagnosis	Age (y)	Sex	Body Mass Index (kg/m ²)	Duration of Fiber Suppl (d)	Maximum Fiber (g/d)	Medications, Gastrointestinal Symptoms Before Feeding, Outcome
Group 1: bolus injections: short term							
1	Trauma	59	M	34.7	3	15	Metronidazole, lanzoprazole, diarrhea, d/c to snf
2	SAP	65	M	38.0	8	29	Cefepime, lanzoprazole, diarrhea, discharge home
3	SAP	85	F	31.0	3	24	Omeprazole, diarrhea, discharge home
4	SAP	89	F	29.4	6	32	Fluconazole, lanzoprazole, transfer rehab
5	SAP	43	M	34.7	9	12	Fluconazole, vancomycin, pantoprazole, discharge home
6	SAP	34	M	44.8	3	18	Ertapenem, omeprazole, diarrhea, d/c to snf
7	SAP	81	F	35.5	3	15	Omeprazole, discharge home
8	SAP	62	M	27.0	7	22	Famotidine, metronidazole discharge home
9	SAP	56	M	28.7	6	24	Trimethoprim-sulfamethoxazole, voriconazole, pantoprazole, discharge home
Group 2: continuous infusions: long term							
10	SAP	88	F	30.3	19	35	Metronidazole, aztreonam, famotidine, diarrhea transfer to snf
11	SAP	65	F	27.6	36	36	Piperacillin-tazobactam, doripenem, metronidazole, pantoprazole, cefuroxime, diarrhea, distension, pain, d/c to snf
12	SAP	47	F	31.0	33	18	Piperacillin-tazobactam, pantoprazole, fluconazole, metronidazole, vancomycin, diarrhea, distention, d/c to snf
13	Chronic Sepsis C diff	79	F	34.9	23	24	Metronidazole, vancomycin, lanzoprazole, diarrhea, distension, pain. C difficile, d/c to snf

Abbreviations: d/c, discharge; SAP, severe acute pancreatitis; snf, skilled nursing facility.

From O'Keefe SJ, Ou J, Delany JP, et al. Effect of fiber supplementation on the microbiota in critically ill patients. World J Gastrointest Pathophysiol 2011;2:138-45; with permission.