

Nutrition In Inflammatory Bowel Disease

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An understanding of the pathogenesis of inflammatory bowel disease (IBD) continues to be the major focus of IBD research.

Environmental factors contribute to the increased incidence of **Crohn's disease (CD)** and the changing incidences of IBD in groups of people who have migrated from areas with low disease incidence to areas of higher incidence. (See "Epidemiology of Inflammatory Bowel Disease and Overview of Pathogenesis," by Bruce E. Sands, MD, MS, and Stacey Grabert, PharmD, MS, in March 2009 *Medicine & Health/Rhode Island*).

It is now widely accepted that IBD represents a dysregulation of the immune response to intraluminal antigens. Evidence to date has failed to identify specific food antigens and has focused on bacterial antigens. Although no specific dietary antigen, toxin or diet product has been linked to IBD, both the lay and scientific communities are interested in this possibility. Studies of pre-illness diet have implicated some dietary components, most notably refined sugars¹ and a high fat diet.² The popular appeal of incriminating refined sugar and high fat as signs of "westernization" of diet reinforces the widespread appeal and frequent citation of these theories. The studies, however, have too many methodological problems³ to be considered useful. Concern about nutritional deficiencies in IBD⁴ as well as the role of nutrition in pediatric IBD⁵ has been the subject of physician interest for many years.

NUTRITIONAL DEFICIENCIES IN IBD

Recommendations for nutrient intake generally cited as "daily values" on most food labels are derived from the **Dietary Reference Intakes (DRI)** published by the Food and Nutrition Board of the Institute of Medicine of the National Academy of Sciences.⁶ These values are intended as guidelines for healthy individuals and need to be used with caution as reference values for individuals with IBD. The DRIs consist of **Estimated Average Requirements (EAR)**, which should meet the needs of half the healthy

individuals in the population based on scientific research; **Recommended Dietary Allowances (RDA)**, a level based on the EAR, adjusted to meet the requirements of 97-98% of the healthy population; **Adequate Intake (AI)**, based on observation and approximations because adequate data are not available, and designed to be at levels at which deficiency has not been observed; and **Tolerable Upper Limits (UL)**, the highest level of daily intake found to pose no risk in healthy people. The commonly cited level for energy (calories) is an EAR and is often referred to as **estimated energy requirement (EER)**; i.e., an average requirement for healthy individuals that will exceed the needs of half the population and be inadequate for the other half. The commonly cited level for protein, and most vitamins and minerals, is the RDA, a level that meets the needs of almost everyone (97-98%) and easily exceeds the needs of the average healthy person.

Physicians and patients often focus excessively on the intake of protein, vitamins and minerals at the expense of adequate attention to caloric intake. In children and in adults trying to heal damaged tissue, positive nitrogen balance is vital, but so are adequate dietary calories, to ensure that protein in the diet can be used to maximum efficiency. All components of nutrition are critical.

The actual impact of disease on nutritional status depends on the location, extent and side effects of the disease and its therapies.

There are five general mechanisms by which nutritional depletion may occur in patients with IBD: (1) reduced or unusual pattern of intake; (2) increased turnover of nutrients; (3) malabsorption; (4) pharmacological interactions with drugs; and (5) inability to utilize nutrients that are present. A great deal has been hypothesized and written about each of these mechanisms, but an understanding of the actual mechanisms may be less important than determining whether a deficiency is likely to occur or already exists, and correcting the problem.

ALTERED PATTERN OF INTAKE

Reduced or unusual pattern of intake is common. Abdominal pain and diarrhea are inevitably associated with diet; rarely has a patient not attempted to reduce symptoms by altering his or her own diet. In addition to fad diets, we commonly see patients on low fat (low caloric density), low refined sugar (often less appetizing), lactose-free (low calcium), and low residue – "free of irritants" (often associated with low intake). Some patients gain symptomatic relief from some of these diets, but any restrictive diet increases the risk of being nutritionally incomplete. Furthermore, restrictions become cumulative and may exacerbate weight loss, nutrient deficiency, fatigue and general unhappiness of the patient.

INCREASED NUTRIENT TURNOVER

Hypoalbuminemia is a well-recognized complication of IBD. Decreased serum levels of albumin may reflect decreased synthesis as a result of long-standing protein intake deficiency or excessive loss through the gut. When synthesis decreases, the normal breakdown of albumin adjusts to slow turnover. In addition, albumin in the extravascular space shifts into the vascular compartment. Decreased serum albumin viewed through the context of the body's attempt to compensate may reflect disease activity. To reflect disease activity, however, there must be adequate protein (and calorie) intake to maximize synthesis. Even in patients reporting mild to minimal symptoms, protein loss (as well as minerals, blood and electrolytes) has been consistently found in stools.

MALABSORPTION OF FAT

Malabsorption is incorrectly incriminated as a frequent cause of malnutrition in IBD. Fat is the most concentrated form of energy (9 kcal/gm versus 4 kcal/gm for carbohydrate and protein). Digestion of fat is generally unaffected by CD or UC. In small bowel disease fat absorption may be altered as a result of loss of surface area due to extensive involvement by inflammatory disease or resection. Bile salt pool

depletion may also result from these causes or from bacterial overgrowth with deconjugation of bile salts. This is especially a problem in areas with poor motility, i.e., stasis loops or stricturous disease.

Nonetheless, studies have consistently confirmed that despite frequent steatorrhea, significant impairment of fat absorption occurs only with extensive disease and most prominently after extensive bowel resection. Filipsson et al⁷ report mild steatorrhea in 24% of patients with ileal disease. Ileal and ileocecal valve resection resulted in fat malabsorption in 48%. The extent of the malabsorption was highly correlated with the extent of ileal resection. In general, patients with resections reported to be less than 30 cm had minimal to mild steatorrhea. In the face of decreased intake or with increased demands for healing the "minimal" loss over time could become clinically relevant.

SPECIFIC NUTRIENTS

Water Soluble Vitamins:

Oxalate, the metabolic breakdown product of Vitamin C (ascorbate), has been linked to renal stones. This relationship between high ascorbate (vitamin C) intake and oxalate stones has been increasingly questioned. In general it is probably prudent to avoid excessive and unnecessary intake of Vitamin C (above 2 grams) especially if there is coexisting fat malabsorption. Except for isolated case reports, water soluble vitamin deficiency is rare in IBD. The exceptions are Vitamin B₁₂ and Folate. Both have been associated with anemia in deficient patients. Anemia has been noted in IBD from the earliest descriptions of the disease. The actual pathophysiology is multifactorial and has not always been clear.

Vitamin B12:

Vitamin B12 is absorbed in the terminal ileum. The body stores the vitamin so that depletion occurs only after a few years of decreased absorption or severe dietary restriction. Bacterial overgrowth may also contribute to depletion and should be monitored in patients with ileal disease and especially ileal resection. Depletion is directly proportional to the length of ileal resection, occurring in 71% of patients with 60-90 cm resection.⁸

Folic acid:

Folic acid deficiency is common in IBD. The etiology may not be straightforward. Dyer⁸ found that among 64% of patients with subnormal folate levels, the depletion was severe in 30%. There was a progressive fall in the RBC folate level as the disease became more active, and there was a positive correlation between serum and RBC folate. There was no correlation with disease location or prior resection. While some studies suggest that folate malabsorption may be significant, direct studies of folate absorption in small bowel CD have failed to show malabsorption.⁹ Impaired folate absorption has been found in patients with CD and UC who have been taking 5-ASA compounds. These compounds seem to have a direct effect on folate absorption. Decreased intake of fruits and vegetables, the use of 5-ASA compounds, and a general increase in folate requirement in intestinal mucosal cells undergoing rapid turnover all contribute to risk for folate deficiency. Subacute combined degeneration of the spinal cord after ileal resection and folate supplementation in a Crohn's patient⁴ serve as a reminder of the risks of supplementing folic acid while ignoring vitamin B12 requirements.

...any restrictive diet increases the risk of being nutritionally incomplete.

MINERALS

Iron:

Iron deficiency is common in IBD. Dietary intakes are frequently low in CD, and probably also in UC. Blood loss exacerbates the effects of reduced intake. The anemia of CD may be similar to the anemia of chronic illness as manifested by increased levels of inflammatory cytokines, especially IL-6.¹⁰ IL-6 had been associated with poor utilization of ingested iron and is probably an important determinant of iron deficiency in the IBD population.¹⁰ Therefore, in addition to dietary iron supplementation, optimal disease control is very important for preventing iron deficiency.

Calcium and Vitamin D:

Calcium and vitamin D must always be considered together. Calcium and Vitamin D deficiency are common in patients with CD.¹¹ The major circulating form of Vitamin D is 25-hydroxy vitamin D (25 OH-D, calcidiol). It is synthesized in the liver from vitamin D-2 (ergocalciferol), the commonly available form in the diet, and vitamin D-3 (cholecalciferol) which results from the action of sunlight on skin. The requirement for dietary vitamin D depends on exposure to sunlight. The actual requirement for vitamin D in the absence of sunlight is unknown. The final, metabolically active form of vitamin D is 1,25 dihydroxy-vitamin D (calcitriol) is responsible for stimulating intestinal absorption of calcium and phosphorous, renal tubular reabsorption of filtered calcium and the mobilization of calcium and phosphorous from bone. Osteoporosis in IBD may result from inadequate dietary calcium and/or vitamin D intake and may be exacerbated by inactivity and the use of corticosteroids. The widespread use of sunblock during the summer may also decrease the synthesis of Vitamin D3.

Magnesium:

Magnesium deficiency can be associated with any form of chronic diarrhea. If malnutrition coexists, the risk is greater. Some patients with IBD may have received magnesium deficient intravenous fluid for the treatment of dehydration. Intestinal capacity for upregulating magnesium absorption is probably very limited and the use of corticosteroids promotes further loss. Magnesium is primarily an intracellular ion and serum levels may not reflect total body load. Symptomatic and asymptomatic hypomagnesemia have been described⁴ in CD and IC.

Zinc:

In the pediatric literature, zinc deficiency has been associated with growth failure. The techniques used to assess zinc adequacy are highly controversial. Low zinc levels in the serum probably are a reflection of general hypoproteinemia.

MISCELLANEOUS:

Polyunsaturated fatty acids (PUFAs):

The omega-3 (w-3) polyunsaturated fatty acids have immunomodulatory activities. Those from fish oil,

eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) have been found to decrease levels of some of the pro-inflammatory cytokines. While there is a reasonable theoretical basis for expecting an anti-inflammatory effect from the dietary addition of PUFAs, existing data have failed to establish them as effective therapies.

Antioxidants:

Antioxidants inhibit lipid peroxidation. There is considerable evidence to support biological effects of these agents. Disappointing results from the use of dietary antioxidants in other diseases (some bioflavonoids have been shown to increase lung cancer in former smokers^{12,13}) warrant a careful approach to these agents. There is in general a greatly oversimplified view of these agents' possible benefits.

Fiber:

All fiber is not the same. Additionally, each individual's bacterial flora may metabolize the fiber to different end-products. The basis for a therapeutic effect of fiber is the belief that the end product of fiber digestion consists of short-chain fatty acids that promote colonocyte health. Apart from the limitation of fiber in patients with stenotic lesions (where it can trigger obstruction, hence the rationale for "low residue diet"), the effects of fiber in IBD patients are unproven. Therefore, as long as fiber does not increase patient symptoms, it should represent the same portion of the diet as it would for any healthy individual. Additionally, some patients with IBD also have symptoms from irritable bowel syndrome. For those patients the fiber may offer significant relief.

Pre and Probiotics:

Pre-biotics contain carbohydrate substrates that promote the growth of a particular microbial flora. Probiotics actually contain the bacterial flora. Because increasing evidence links the dysregulation of the immune system in IBD to altered response to intraluminal bacterial antigens, the use of flora altering agents is extremely appealing. The role for these agents is yet to be determined.

SPECIAL NUTRITIONAL REGIMENS:

Enteral Nutrition:

The potential for special defined formula diets to be used as primary therapy has been studied with varied and controversial results.^{14,15} In general the use of special diets is reserved for nutritional rehabilitation (and occasionally nutritional maintenance) in an overall pharmacologically centered treatment plan. In general, these "formulas-in-a-can" are administered via a naso-gastric tube that can be placed nightly by the patient for supplementation during sleep. As adjunctive therapy in the well-motivated patient (children, for example, can easily accept this therapy), it removes anxiety about nutritional intake during the day.

PARENTERAL NUTRITION:

Like enteral nutrition total parenteral nutrition has been proposed as both primary treatment and adjunctive nutritional support. No large prospective studies establish TPN as a primary therapy. It is used in specific situations¹⁵ almost always with other treatments. TPN is frequently employed as pre-surgical therapy to treat malnutrition and improve surgical outcome.

Both enteral and parenteral therapies are primary therapies for malnutrition. When malnutrition accompanies IBD, the choice of nutritional therapy is governed by clinical circumstances. The first goal is to provide therapy via the normal oral route. If this is not possible, then use of the enteral pathway via either a naso-gastric, naso-jejunal, or gastrostomy device is necessary. Only when it is not possible to use the alimentary canal is TPN the treatment of choice. The focus of nutrition in IBD patient care must be to prevent malnutrition whenever possible.

LONG-TERM NUTRITION-SUPPORT:

Some patients with CD cannot use their gastrointestinal tracts, often because of severe disease or multiple intestinal resections leading to short-gut syndrome. Options are generally limited to long-term total parenteral nutrition. In lieu of TPN and its complications (most notably hepatic failure secondary to TPN-induced cholestasis), some patients face small bowel or liver-small bowel transplantation. This is becoming a more frequent problem at major multi-visceral transplantation cen-

Nutritional Assessment of the Patient with Inflammatory Bowel Disease

<u>Subjective Assessment</u>	<u>Past course</u>	<u>Surgery (extent)</u> <u>Medications</u> <u>Special or fad diets</u> <u>Adherence to medications/diet</u>
	Current status	<u>Emotional state</u> <u>Psychological co-morbidities</u> <u>Medications</u> <u>Dietary habits</u>
	<u>Expected course</u>	
<u>Objective Assessment</u>		
<u>Anthropometrics</u>	<u>BMI</u> <u>Height</u> <u>Weight</u> <u>Weight loss</u> <u>Annualized growth velocity*</u> <u>Tanner Stage*</u> <u>Mid arm circ, triceps fatfold</u>	
<u>Laboratory</u>	<u>CBC</u> <u>Serum albumin, prealbumin</u> <u>RBC folate, vit B12</u> <u>Serum Fe, TIBC, ferritin</u> <u>Calcium/PO4/magnesium,</u> <u>alkaline phosphatase</u> <u>Cholesterol</u> <u>Bone age*</u> <u>25 hydroxy-vitamin D</u>	
<u>Possible</u>	<u>Prothrombin time</u> <u>Vitamin A, E</u> <u>Zinc</u>	

*Pediatric patients

Nutrient Mechanisms of Deficiencies and Potential Supplementation

Nutrient	Mechanisms		Potential Supplements (must be individualized) ** see text
	↓ intake	↑ loss with malabsorption	
Energy (calories)	↓ intake		
Iron	↓ intake	↑ loss (bleeding)	60 mg/day (assuming repletion of stores)
Calcium	↓ intake, ↓ activity	↑ bone turnover, ↑ loss, ↓ absorption ↓ Vit D intake	Steroid meds 1000mg/day+ Vitamin D
Vitamin D	↓ intake, ↓ sunlight	↑ sun blockers	Up to 2000 iu with Calcium
DHA	↓ diet		1 gm/day
Magnesium	↓ diet	↑ loss (diarrhea)	420 mg/day (elemental)
Folic Acid	↓ absorption	↑ loss, ↑ cell turnover	↓ interaction with 5-ASA
Vitamin B12	↓ intake	↓ absorption (distal ileal rx)	800 µgm (assuming adequate Vit B12 status) Requires parenteral (sub q inj or intra nasal route)
Prebiotics Probiotics Antioxidants Fiber	?	?	???

ters. It is hoped that with the newer therapeutic agents, the occurrence of short-gut syndrome will become even rarer.

APPROACH TO DIET

The best advice is to consume a diet from a variety of sources. The more restricted the diet, the greater the risk of nutritional inadequacy. Protein is important but for most patients it is probably over-emphasized. In order to maximize the efficiency of protein in the diet, the diet must contain adequate calories (otherwise the protein is broken down, the carbon skeletons of the amino acids being burned as fuel and the NH₃ component metabolized and excreted as urea.) The energy content must be adequate to maintain weight in adults and provide calories for growth in children. Attention to providing adequate calories simplifies the assessment and provision of all other nutrients. An approach that emphasizes any particular nutrient without adequate attention to energy runs the risk of not meeting either energy requirements or the requirements for the particular nutrient of concern.

Liquid diets are of unproven benefit. There is reason to believe that in those motivated patients who are compliant with liquid supplements, the actual intake over time of other foods is decreased so that there is no net benefit. More importantly, the lack of variety of food consumed poses a real risk of nutrient deficiency.

While particular foods may cause distress for some patients, dietary restriction without clear-cut symptomatic improvement is not beneficial. Restricted diets can be counter productive if they either lead to boring, unappetizing meals that decrease the overall quality of life of the patient, or lead to reduced intake.

When a patient reports symptomatic improvement on a restricted diet of any sort it is imperative to assure that the diet is nutritionally adequate. This requires the professional assistance of a registered dietitian.

Except in specific circumstances, such as high-residue diets leading to excessive colonic bleeding, or symptoms of intestinal obstruction (in the setting of intestinal stricture) a full “normal” diet for age and culture is appropriate.

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