

Nutrition in Crohn Disease

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Abstract and Introduction

Abstract

Nutrition plays an important role in the pathogenesis, treatment, and morbidity of Crohn disease. Approximately two thirds to three fourths of hospitalized patients with active disease and one fourth of outpatients with Crohn disease are malnourished. Malnutrition, which can be present even when Crohn disease is in remission, can affect growth, cellular and humoral immunity, bone density, and wound healing. Decreased nutrient intake, malabsorption, drug-nutrient interactions, anorexia, and protein-losing enteropathy can all contribute to the protein-calorie malnutrition and other specific nutrient deficiencies seen in Crohn disease. Therefore, by preventing and correcting nutrient deficiencies, nutritional therapy is an important component in the overall management of patients with Crohn disease.

Introduction

Crohn disease (CD) is a chronic transmural inflammatory disorder of the gastrointestinal tract of unknown cause. Since Drs. Crohn, Ginzburg, and Oppenheimer were initially credited with describing Crohn disease in 1932, weight loss has been recognized as a predominant feature of the disease.^[1] Many subsequent studies have demonstrated that nutrition and nutritional deficiencies are important factors in the pathogenesis, treatment and morbidity of CD. Malnutrition can be present even in patients whose disease is quiescent. In one representative study of outpatients with CD, 11 of 47 (23%) patients had abnormalities indicating protein-energy malnutrition.^[2] Significant deficiencies of vitamins, minerals, and

trace elements can also exist in patients with CD, whether they are inpatients or outpatients^[3-7**] ([Table 1](#)).

Causes of Malnutrition in Crohn Disease

Malnutrition, a broad term that refers to faulty or inadequate nutritional status, can be determined by insufficient dietary intake, poor appetite, muscle wasting, and weight loss.^[8] Malnutrition in CD is often multifactorial in origin and frequently insidious in its onset. Several factors may contribute to a patient's malnutrition, including anorexia; drug-nutrient interactions; malabsorption; and increased fluid, electrolyte, and blood loss from the gut. Anorexia is often the most prominent cause of malnutrition,^[9] which can result from increased levels of tumor necrosis factor (TNF)- α , interleukin-1, and other cytokines.^[10, 11] Patients also may have inadequate intake of nutrients secondary to fear of abdominal pain and diarrhea after eating. Deficiencies in zinc, copper, and nickel have been associated with altered taste sensation, leading to a cycle of decreased oral intake, and causing further malnutrition and mineral deficiencies.^[5, 12, 13] Even metronidazole, which is used in the treatment of CD, can produce a metallic taste and exacerbate a patient's anorexia.

Medications used regularly in the treatment of CD also can augment nutritional deficiencies. Corticosteroids suppress calcium absorption in the small intestine, increase calcium excretion by the kidneys, and alter protein metabolism. Sulfasalazine decreases folate absorption. Antibiotics alter gut flora and can affect vitamin K metabolism. Many medications (eg, sulfasalazine and 5-aminosalicylic acid) can be associated with nausea and vomiting, thus limiting nutritional intake.

Malabsorption can be another cause for malnutrition in patients with Crohn disease. Approximately one third of patients with CD have small intestine involvement. The absorptive surface area of the small intestine in CD may be limited by the degree of inflammation present. Small bowel resections also physically decrease the absorptive surface area. Ileal resections can result in vitamin B₁₂ deficiencies and bile salt malabsorption; the lack

of bile salts can lead to fat and fat-soluble vitamin deficiencies. Ileocecal valve resections can result in bacterial overgrowth causing malabsorption.^[14]

The intestinal inflammation seen in CD is often associated with exudative protein losses; the degree of protein loss correlates with the severity of disease activity.^[15] Inflammation also produces a catabolic response, which is probably a cytokine-mediated event, resulting in a negative nitrogen balance. To achieve a positive nitrogen balance, patients with CD require higher protein intake than the general population without a known gastrointestinal disorder.

Nutritional Assessment

When assessing a patient, it is important to conduct a detailed physical examination and elicit a thorough history. The subjective global assessment is a method of qualitatively assessing a patient's nutritional status. With this method, the patient is classified as generally well nourished, moderately malnourished, or severely malnourished, based on the patient's weight loss, dietary intake, gastrointestinal symptoms, CD activity, functional capacity, muscle mass, subcutaneous fat, edema, and ascites^[16] ([Table 2](#)). The subjective global assessment has been shown to be reproducible among observers, with better than 80% agreement when two independent observers assessed the same patient.^[16, 17]

As can be seen, both the history and physical examination are of paramount importance; however, laboratory studies also are integral components to the assessment of a patient's nutritional status when assimilating data regarding the cause of the patient's malnutrition. Anemia is common in CD and its cause is often multifactorial. It can be difficult to determine if the patient has an iron-deficient anemia or an anemia of chronic disease. In both, iron is low, but the ferritin concentration can be increased independently of iron status by infectious, inflammatory, malignant, and other disorders. The total iron-binding capacity (TIBC or transferrin concentration) can be useful in distinguishing between the two causes of anemia. In

uncomplicated iron deficiency, the TIBC increases and in the anemia of chronic disease the TIBC decreases. A combined microcytic and macrocytic anemia can be present, as is seen in some patients with CD who are deficient in vitamin B₁₂ or folate. Vitamin B₁₂-intrinsic factor complex is absorbed in the last half of the small intestine, but the greatest density of intrinsic factor receptors is in the distal ileum; hence, patients with ileal resections will require vitamin B₁₂ parenterally (intramuscularly or intranasally). Sulfasalazine competitively inhibits the jejunal folate conjugate enzyme, often producing folate malabsorption and requiring concurrent oral folate supplementation.^[6] Even patients not taking sulfasalazine should be considered for folate supplements as a result of frequent poor dietary intake of folate. Additionally, data exist to suggest that folate supplementation conveys protection against the development of colorectal cancer in patients with inflammatory bowel disease (IBD).^[18-20]

Osteoporosis and Vitamin D Deficiency

Osteoporosis represents a major public health problem, accounting for more than 1.5 million bone fractures in the United States each year.^[21] The estimated national direct expenditures (hospitals and nursing homes) for osteoporotic and associated fractures was estimated to be \$17 billion in 2001 (\$47 million each day).^[21] An average of 24% of patients with hip fracture 50 years of age and older die in the year following their fracture. The dual energy x-ray absorptiometry (DEXA) scan is commonly used in diagnosing osteoporosis. The *T*-score refers to the number of standard deviations (SD) above or below the mean for a young adult population (corresponding to peak bone mass); a World Health Organization (WHO) report formulated diagnostic ranges for osteoporosis based on *T*-scores. A *T*-score within one SD of the norm is considered to be within normal limits. A *T*-score that is 1.0 to 2.49 SD less than the norm is defined as osteopenia, and a value greater than 2.5 SD indicates the presence of osteoporosis. The *Z*-score refers to the number of SD above or below the mean for an age-matched population. Use of the *Z*-score can conceal normal age-related loss, thereby underestimating fracture risk.

Osteoporosis is a common extraintestinal complication of IBD. The prevalence of osteopenia is between 40% and 50% and the prevalence of osteoporosis is between 5% and 36% for patients with IBD.^[22-26] The underlying inflammatory process in CD may play a significant role in the induction of osteopenia in these patients.^[27] In CD, the principal cytokines released by the inflammatory cells of the intestine are TNF- α , interferon- γ , and interleukin-6. These cytokines, particularly TNF- α , stimulate osteoclast activity disproportionately, resulting in an imbalance in the regulation of bone metabolism. Additional risk factors for osteoporosis include corticosteroid use, decreased oral intake,^[28] small bowel resection,^[26] low body mass index,^[29] malabsorption, and vitamin D deficiency.^[30, 31] Of these, one of the most significant risk factors appears to be corticosteroid usage.^[24-26, 32] Patients with IBD on corticosteroids experience a 6.2% annual loss of total bone mass compared with only 0.9% annual loss of total bone mass in patients not using corticosteroids.^[33] It is estimated that one quarter to one half of patients on long-term glucocorticoids will experience bone fractures.^[34]

One recent retrospective study by Dear *et al.*^[7**] examined the effect of dietary treatment and corticosteroids on bone density in female patients with CD treated with and without long-term steroids. The prevalence of osteoporosis was 15% and of osteopenia was 45% in the cohort studied. Both hip and spine *T*-scores for all patients were significantly below peak bone mass. However, when compared with age-matched controls, the *Z*-score, the noncorticosteroid-treated patients did not differ significantly from controls; the mean *Z*-scores were -0.3 (95% CI: 0.15 to -0.75) and -0.04 (95% CI: 0.42 to -0.5) for the noncorticosteroid-treated groups. In contrast, the spine *Z*-score for the steroid treated group was -0.98 (95% CI: -0.6 to -1.36). Although the standard, both clinically and in research, is to use the *T*-score as it correlates best with the absolute fracture risk, the *Z*-score can be useful in comparing age- and gender-matched controls. This study demonstrates that all patients with CD are at risk for some level of osteopenia or osteoporosis, but that patients who are treated with steroids have a much higher risk of osteoporosis when compared with age-matched controls.

This study also shows that patients treated with dietary manipulations that often avoid dairy products and other sources of calcium are not necessarily at an increase risk of developing osteoporosis. However, more studies are needed to determine what the risk of developing osteoporosis is for men with CD.

In their study, Dear *et al.*^[7] also found a prevalence of vitamin D deficiency between of 8% and 14% in the cohort studied. Vitamin D is a hormone that is a positive regulator in calcium and phosphate homeostasis; it acts on calcium and phosphate levels by increasing their absorption in the small intestine, enhancing their mobilization from bone, and decreasing their excretion by the kidney. These processes maintain calcium and phosphate ion concentrations at levels that are appropriate and are needed for neuromuscular activity and bone mineralization. The intestinal absorption of calcium occurs mostly in the more proximal segments of the small bowel and is dependent on vitamin D-dependent Ca^{2+} -binding protein; calcium is also absorbed in the kidneys by both parathyroid hormone and vitamin D-stimulated mechanisms. Vitamin D is absorbed in the duodenum and jejunum; hence, when the small intestine has been resected in CD, both calcium and vitamin D absorption can be impaired, resulting in muscle weakness and skeletal demineralization.^[30] Vitamin D can also be synthesized in the skin from 7-dehydrocholesterol after exposure to ultraviolet B radiation. Interestingly, a recent case report looked at using ultraviolet B radiation to treat a woman with severe intestinal fat malabsorption caused by CD and multiple small bowel resections, leaving her with only 2 feet of small intestine.^[35*] She took daily vitamin D supplements and was dependent on total parenteral nutrition, but she continued to be vitamin D deficient and had bone pain and muscle weakness. After 6 months of ultraviolet B radiation treatment, which consisted of 10 minutes in a tanning bed time three times a week, her serum 25(OH) vitamin D level was in the normal range and she no longer complained of bone pain or muscular weakness. After only 4 weeks of treatment, her serum 25(OH) vitamin D level was increased by 357% from 7 to 32 ng/mL, her parathyroid hormone level decreased by 52%, and her calcium level increased from 7.8 to 8.5 mg/dL. Although only one case report, this offers a**

potential alternative for patients who are not responding to oral and intravenous vitamin D replacement.

Plasma Antioxidants

Although the cause of Crohn disease is unknown, oxidative stress is postulated to be an important factor in its pathogenesis.^[36, 37] In CD are seen low concentrations of endogenous antioxidant defenses, increased free radical production by neutrophils and monocytes,^[38] and decreased circulating antioxidants, all of which may be contributing to the increased oxidative stress seen.^[39**]

Lipid peroxidation is significantly higher in patients with CD than in healthy controls and the level of oxidative stress is independent of disease activity.^[40] The colon has relatively low stores of endogenous antioxidants; hence, circulating antioxidants (eg, carotenoids, vitamin A, vitamin E) may be important factors in the prevention of free radical-mediated tissue injury in CD.^[41] Low blood concentrations of vitamin A in patients with CD have been shown,^[42, 43] and a recent study by D'Odorico *et al.*^[39**] also demonstrated this; vitamin A levels in patients with CD were $1.67 \pm 0.1 \mu\text{mol/L}$ and in controls were $2.7 \pm 0.07 \mu\text{mol/L}$ ($P < 0.0001$). D'Odorico *et al.*^[39**] also measured carotenoid levels and found a statistically significant reduction in blood levels when compared with normal subjects ($P < 0.0001$). Beta-carotene, the carotenoid most reduced in concentration, was decreased by 50% when compared with controls ($P < 0.0001$). Despite these low blood levels of antioxidants, no overt clinical signs of vitamin deficiency were seen in any of the patients. The carotenoids also were decreased significantly more in active than in remission phase CD.

Decreased nutritional intake of vegetables and fruit was seen in patients with CD when compared with controls, which may contribute to the decreased antioxidant levels found in these patients. Other mechanisms also may contribute to reduced plasma antioxidant levels, including malabsorption, increased gastrointestinal losses, and increased vitamin requirements.

Further studies are needed to better elucidate the processes that result in the decreased plasma antioxidant levels in CD. Optimal vitamin status with adequate concentrations of antioxidants may improve the clinical course of CD, as patients with CD have higher concentrations of 8-OHdG (a measurement of DNA damage induced by oxygen-derived free radicals) regardless of disease activity or duration.^[39**] Although this seems plausible, it still needs to be demonstrated in a prospective randomized controlled fashion.

Long-Chain Triglycerides

An elemental diet (one that is very low in fat and contains primarily *L*-amino acids) is felt to be effective in inducing remission in patients with CD.^[44-48] Although originally believed that elemental diets were equivalent to standard corticosteroid therapy, further studies^[49, 50] and a recent meta-analysis^[51] have concluded that remission rates with corticosteroids are higher than with elemental diets. The decreased remission rates may be secondary to patients' noncompliance with ingestion of elemental diets, given their unpalatable nature.

Two meta-analyses have shown an inverse correlation between remission rates of a given enteral diet and the long-chain triglyceride (LCT) content in that diet.^[52, 53] A recent randomized controlled trial examined this question by giving patients with active CD two whole protein liquid enteral feeds which differed only in their LCT content.^[54**] The remission rates were 46% in the low LCT and 45% in the high LCT ($P = 0.99$). This study failed to show any difference in the remission rates between patients treated with high- or low-content long-chain triglycerides. Further studies need to be done to look at the source of fat in the diet or the emulsifiers and stabilizers used in the diets to determine if it is these, and not the LCT content, that influences remission. Regardless, the efficacy of elemental diets depends on the patient's ability to tolerate the feeds for prolonged periods of time.

Butyrate

Butyrate is a short-chain fatty acid produced by bacterial fermentation of dietary fiber and undigested starch in the colon. It is important in maintaining the health and integrity of colonic mucosa,^[55] as it provides greater than 70% of the energy supply of the colonocyte.^[56] Recently, it was demonstrated that butyrate inhibits the inflammatory response in CD by inhibiting the transcription factor nuclear factor kappa B (NF κ B) activation in immune cells.^[57] NF κ B is involved in inflammatory and immune responses and regulates TNF. By inhibiting NF κ B, TNF is downregulated and, theoretically, inflammation will be reduced. Already demonstrated in patients with steroid-resistant CD is marked improvement in those patients treated with monoclonal antibodies to TNF.^[58] Although further studies are needed to determine the best method of administering butyrate, it offers promise for an immune modulatory therapy for treating patients with CD. Of note, an oral precursor of butyrate has recently been used in ulcerative colitis and was successful in lowering corticosteroid dose. Further utility in CD might be of special interest.

Conclusions

Malnutrition is common in patients with Crohn disease and may have serious potential consequences. The presence of malnutrition is associated with defects in cellular and humoral immunity, delayed growth, bone disease, and poor wound healing. A detailed history, thorough physical examination, and appropriate laboratory work are integral in diagnosing the cause of the patient's malnutrition so that therapy can be tailored accordingly. Nutritional support, with either elemental diets or parenteral nutrition, has been shown to be efficacious, but remains less effective than steroids in inducing remission in CD. Given the multitude of side effects associated with corticosteroids, alternative therapies are continually being studied, including short-chain fatty acids and elemental diets. Further studies are needed to better elucidate the relationship between nutrition and Crohn disease.

Tables

Table 1. Prevalence of decreased nutrient levels among patients with Crohn disease

Medscape®		www.medscape.com		
Nutrient	Prevalence (%)		Deficiency syndrome	
	Inpatients	Outpatients		
Albumin	25–80	0	Edema, ascites	
Calcium	13	ND	Osteomalacia, tetany, seizures, cardiac arrhythmia, prolonged QT interval	
Folate	56–62	10	Anemia	
Iron	25–50	37–53	Anemia	
Magnesium	14–33	ND	Anorexia, weakness, nausea, paresthesias, confusion	
Vitamin A	11–50	ND	Night blindness, corneal ulceration, increased infection risk, dry skin	
Vitamin B ₁₂	48	3–4	Anemia, paresthesias, optic neuropathy, glossitis	
Vitamin D	23–75	8–14	Rickets, osteomalacia, hypocalcemia, muscle weakness	
Zinc	40	1	Delayed wound healing, growth abnormalities, immune dysfunction	

ND, not determined.

Data extracted from [3–6,7**].

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Table 2. Subjective Global Assessment (SGA) of nutritional status

Medscape®		www.medscape.com		
Criteria	A (well nourished)	B (moderately malnourished)	C (severely malnourished)	
Weight loss in previous 6 mo	Loss <5%	Loss 5–10%	Loss >10%	
Dietary intake	>90% required	70–90% required	<70% required	
Gastrointestinal symptoms (nausea, vomiting, diarrhea)	None	Intermittent	Daily for >2 weeks	
Functional capacity	Full	Reduced	Bedridden	
Disease type	Inactive	Smoldering	Acute	
Subcutaneous fat	Normal	Decreased	Severely decreased	
Muscle mass	Normal	Decreased	Severely decreased	
Dependent edema	None	Slight	Marked	
Ascites	None	Slight	Marked	

Data extracted from [16].

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References

Papers of particular interest, published within the annual period of review, have been highlighted as:

* Of special interest

** Of outstanding interest

1. Crohn BB, Ginzburg L, Oppenheimer GD: Regional ileitis: A pathologic and clinical entity. *JAMA* 1932, 99:1323-1329.
2. Gee MI, Grace MG, Wensel RH, et al.: Protein-energy malnutrition in gastroenterology outpatients: increased risk in Crohn disease. *J Am Diet Assoc* 1985, 85:1466-1474.
3. Driscoll RH, Rosenberg IH: Total parenteral nutrition in inflammatory bowel disease. *Med Clin North Am* 1978, 62:185-201.
4. Imes S, Pinchbeck BR, Dinwoodie A, et al.: Iron, folate, vitamin B₁₂, zinc, and copper status in outpatients with Crohn disease: effect of diet counseling. *J Am Diet Assoc* 1987, 87:28-30.
5. McClain C, Souter C, Zieve L: Zinc deficiency: a complication of Crohn disease. *Gastroenterology* 1980, 78:272-279.

6. Hoffbrand AV, Stewart JS, Booth CC, et al.: Folate deficiency in Crohn disease: Incidence, pathogenesis, and treatment. *BMJ* 1968, 2:71-75.
7. Dear KL, Compston JE, Hunter JO: Treatments for Crohn disease that minimize steroid doses are associated with a reduced risk of osteoporosis. *Clin Nutr* 2001, 20:541-546.
** This study investigated women with Crohn disease, treated with and without steroids, and demonstrates that steroids are an independent risk factor for osteoporosis. It also shows that dietary manipulation controls disease activity without increasing the risk for osteoporosis.
8. Chen CC, Schilling LS, Lyder CH: A concept analysis of malnutrition in the elderly. *J Adv Nurs* 2001, 36:131-142.
9. Schneeweiss B, Lochs H, Zauner C, et al.: Energy and substrate metabolism in patients with active Crohn disease. *J Nutr* 1999, 129:844-848.
10. Bodnar RJ, Pasternak GW, Mann PE, et al.: Mediation of anorexia by human recombinant tumor necrosis factor through a peripheral action in the rat. *Cancer Res* 1989, 49:6280.
11. Hellerstein MK, Meydani SN, Meydani M, et al.: Interleukin 1 induced anorexia in the rat: Influence of prostaglandins. *J Clin Invest* 1989, 84:228-235.
12. Tiomny E, Horwitz C, Graff E, et al.: Serum zinc and taste acuity in Tel-Aviv patients with inflammatory bowel disease. *Am J Gastroenterol* 1982, 77:101-104.
13. Solomons NW, Rosenberg IH, Sandstead HH, et al.: Zinc deficiency in Crohn disease. *Digestion* 1977, 16:87-95.
14. King CE, Toskes PP: Small intestinal bacterial overgrowth. *Gastroenterology* 1979, 76:1035-1055.
15. Crama-Bohbouth G, Pena AS, Biermond J: Are activity indexes helpful in assessing active intestinal inflammation in Crohn disease? *Gut* 1989, 30:1236-1241.
16. Detsky AS, McLaughlin JR, Baker JP, et al.: What is subjective global assessment of nutritional status? *J Parenteral Enteral Nutr* 1987, 11:8-13.
17. Baker JP, Detsky AS, Wesson DE, et al.: Nutritional assessment: a comparison of clinical judgment and objective measurements. *N Engl J Med* 1982, 306:969-972.
18. Lashner BA, Heidenreich PA, Su GL, et al.: Effect of folate supplementation on the incidence of dysplasia and cancer in chronic ulcerative colitis. A case-control study. *Gastroenterology* 1989, 97:255-259.
19. Lashner BA. Red blood cell folate is associated with the development of dysplasia and cancer in ulcerative colitis. *J Cancer Res Clin Oncol* 1993, 119:549-554.

20. Lashner BA, Provencher KS, Seidner DL, et al.: The effect of folic acid supplementation on the risk for cancer or dysplasia in ulcerative colitis. *Gastroenterology* 1997, 112:29-32.
21. National Institutes of Health. Fast Facts on Osteoporosis. Available at: <http://osteoporosis.nih.gov/docs/47.821117075.html>. Accessed September 21, 2002.
22. Bernstein CN: Risk factors and prevalence of bone disease in IBD. In: Williams CN, Bursey RF, Gall DG, et al., eds: *Trends in IBD Therapy*. The Netherlands: Kluwer Academic Publishers; 1999:147-162.
23. Bjarnason I, Macpherson A, Mackintosh C, et al.: Reduced bone density in patients with inflammatory bowel disease. *Gut* 1997, 40:228-233.
24. Silvennoinen JA, Karttunen TJ, Niemela SE, et al.: A controlled study of bone mineral density in patients with inflammatory bowel disease. *Gut* 1995, 37:71-76.
25. Bernstein CN, Seeger LL, Sayre JW, et al.: Decreased bone density in inflammatory bowel disease is related to corticosteroid use and not disease diagnosis. *J Bone Miner Res* 1995, 10:250-256.
26. Compston JE, Judd D, Crawley EO, et al.: Osteoporosis in patients with inflammatory bowel disease. *Gut* 1987, 28:410-415.
27. Staun M, Tjellesen M, Thale M, et al.: Bone mineral content in patients with Crohn disease. A longitudinal study in patients with bowel resections. *Scand J Gastroenterol* 1997, 32:226-232.
28. Rigeaud D, Angel LA, Cerf M, et al.: Mechanisms of decreased food intake during weight loss in adult Crohn disease patients without obvious malabsorption. *Am J Clin Nutr* 1994, 60:775-781.
29. Felson DT, Zhang Y, Hannan MT, et al.: Effects of weight and body mass index on bone mineral density in men and women: The Framingham Study. *J Bone Miner Res* 1993, (Suppl): 567-573.
30. Driscoll RH, Meredith SC, Sitrin M, et al.: Vitamin D deficiency and bone disease in patients with Crohn disease. *Gastroenterology* 1982, 83:1252-1258.
31. Scarla SH, Minne HW, Lempert UG, et al.: Bone mineral density and calcium regulating hormones in patients with inflammatory bowel diseases (Crohn disease and colitis ulcerosa). *Exp Clin Endocrinol* 1994, 11102:44-49.
32. Motley RJ, Clements D, Evans WD, et al.: A four-year longitudinal study of bone loss in patients with inflammatory bowel disease. *Bone Miner* 1993, 23:95-104.
33. Roux C, Abitbol V, Chaussade S, et al.: Bone loss in patients with inflammatory bowel disease: a prospective study. *Osteoporos Int* 1995, 5:104-156.
34. Lukert BP, Raisz LG. Glucocorticoid-induced osteoporosis: pathogenesis and management. *Ann Intern Med* 1990, 112:352-364.

35. Koutkia P, Lu Z, Chen TC, et al.: Treatment of vitamin D deficiency due to Crohn disease with tanning bed ultraviolet B radiation. *Gastroenterology* 2001, 121:1485-1488.
* This is an interesting case report of a woman with severe Crohn disease and subsequent vitamin D deficiency who is treated with ultraviolet B radiation. Her vitamin D levels improved with time and her symptoms resolved.
36. Nielson OH, Ahnfelt-Ronne I: Involvement of oxygen-derived free radicals in the pathogenesis of chronic inflammatory bowel disease. *Klin Wochenschr* 1991, 69:995-1000.
37. McKenzie SJ, Baker MS, Buffinton GD, et al.: Evidence of oxidant-induced injury to epithelial cells during inflammatory bowel disease. *J Clin Invest* 1996, 98:136-141.
38. Kitahora T, Suzuki K, Asakura H: Active oxygen species generated by monocytes and polymorphonuclear cells in Crohn disease. *Dig Dis Sci* 1988, 33:951-955.
39. D'Odorico A, Bortolan A, Cardin R, et al.: Reduced plasma antioxidant concentrations and increased oxidative DNA damage in inflammatory bowel disease. *Scand J Gastroenterol* 2001, 36:1289-1294.
** This study, which was conducted to determine vitamin A, E, and carotenoid concentrations in patients with inflammatory bowel disease (IBD), found a depletion in these antioxidants. It also demonstrated that patients with IBD have an increase in free radical peripheral leukocyte DNA damage.
40. Wendland BE, Aghdassi E, Tam C, et al.: Lipid peroxidation and plasma antioxidant micronutrients in Crohn disease. *Am J Clin Nutr* 2001, 74:259-264.
41. DiMascio P, Murphy ME, Sies H: Antioxidant defense systems: the role of carotenoids, tocopherols, and thiols. *Am J Clin Nutr* 1991, 53 (Suppl): 194S-200S.
42. Imes S, Pinchbeck B, Dinwoodie A, et al.: Vitamin A status in 137 patients with Crohn disease. *Digestion* 1987, 37:166-170.
43. Kuroki F, Lida M, Tominaga M, et al.: Multiple vitamin status in Crohn disease. Correlation with disease activity. *Dig Dis Sci* 1993, 38:1614-1618.
44. O'Morain C, Segal AW, Levi AJ: Elemental diet as primary treatment of acute Crohn disease: a controlled trial. *BMJ* 1984, 288:1859-1862.
45. Saverymuttu S, Hodgson HJF, Chadwick VS: Controlled trial comparing prednisolone with an elemental diet plus non absorbable antibiotics in active Crohn disease. *Gut* 1985, 26:994-998.
46. Giaffer MH, North G, Holdsworth CD: Controlled trial of polymeric versus elemental diet in treatment of active Crohn disease. *Lancet* 1990, 335:816-819.

47. Gonzalez-Huix F, de Leon R, Fernandez-Banares F, et al.: Polymeric enteral diets as primary treatment of active Crohn disease: a prospective steroid controlled trial. *Gut* 1993, 34:778-782.
48. Okada M, Yao T, Yamamoto T, et al.: Controlled trial comparing an elemental diet with prednisolone in the treatment of active Crohn disease. *Hepatology* 1990, 37:72-80.
49. Malchow H, Steinhardt HJ, Lorenz-Meyer H, et al.: Feasibility and effectiveness of a defined-formula diet regimen in treating active Crohn disease. European Cooperative Crohn Disease Study III. *Scand J Gastroenterol* 1990, 25:235-244.
50. Lochs H, Steinhardt HJ, Klaus-Wentz B, et al.: Comparison of enteral nutrition and drug treatment in active Crohn disease. *Gastroenterology* 1991, 101:881-888.
51. Griffiths AM, Ohlsson A, Sherman PM, et al.: Meta-analysis of enteral nutrition as a primary treatment of active Crohn disease. *Gastroenterology* 1995, 108:1056-1067.
52. Middleton SJ, Rucker TJ, Kirby GA, et al.: Long-chain triglycerides reduce the efficacy of enteral feeds with active Crohn disease. *Clin Nutr* 1995, 14:229-236.
53. Evans RC, Rhodes JM: Understanding the mechanism of dietary therapy in Crohn disease—a meta-analysis of polymeric enteral feeding studies and pilot study of maintenance with low fibre/low fat diet. *Gut* 1996, 38:A637.
54. Leiper K, Woolner J, Mullan MMC, et al.: A randomized controlled trial of high versus low long chain triglyceride whole protein feed in active Crohn disease. *Gut* 2001, 49:790-794.
** This study gave patients with active Crohn disease enteral feeds either high or low in long-chain triglycerides and examined their effects on inducing remission. Contrary to previous meta-analyses, no difference was seen in induction of remission between the two groups.
55. Scheppach W. Effects of short chain fatty acids on gut morphology and function. *Gut* 1994, 35 (Suppl 1): S35-38.
56. Roediger WEW. The colonic epithelium in ulcerative colitis: an energy-deficiency disease. *Lancet* 1980, 2:712-715.
57. Segain JP, Raingeard de la Bletiere D, Bourreille A, et al.: Butyrate inhibits inflammatory responses through NF κ B inhibition: implications for Crohn disease. *Gut* 2000, 47:397-403.

58. Targan SR, Hanauer SB, van Deventer SJ, et al.: A short-term study of chimeric monoclonal antibody cA2 to tumor necrosis factor alpha

for Crohn disease. Crohn Disease cA2 Study Group. N Engl J Med 1997, 337:1029-1035.

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