INFLAMMATORY BOWEL DISEASE (CROHN'S DISEASE AND ULCERATIVE COLITIS)

Inflammatory bowel disease (IBD) encompasses both ulcerative colitis (UC) and Crohn's disease (CD). Both of these diagnoses likely have similar etiologies, but they each affect different locations and layers within the lower GI system. Unlike UC, CD can affect the upper GI tract as well.

The following focuses on the Whole Health approach to IBD. When possible, it will be specified whether a given study focused on UC, CD, or both disorders.

In the U.S. military population, prevalence of IBD is estimated to be 202 and 146 cases out of 100,000 individuals for UC and CD, respectively. Three main demographic variables in this population incur a higher risk: age, female sex, and Caucasian ethnicity.[1] The incidence of IBD has been increasing with increasing industrialization and marked dietary changes over recent decades.[2,3]

IBD is complex and multifactorial. Environmental factors (especially nutrition, smoking, and infections) and genetic factors interact, leading to a dysfunctional relationship between one's intestinal microbiome and immune system due to abnormal intestinal barrier function (reference Figure 1).

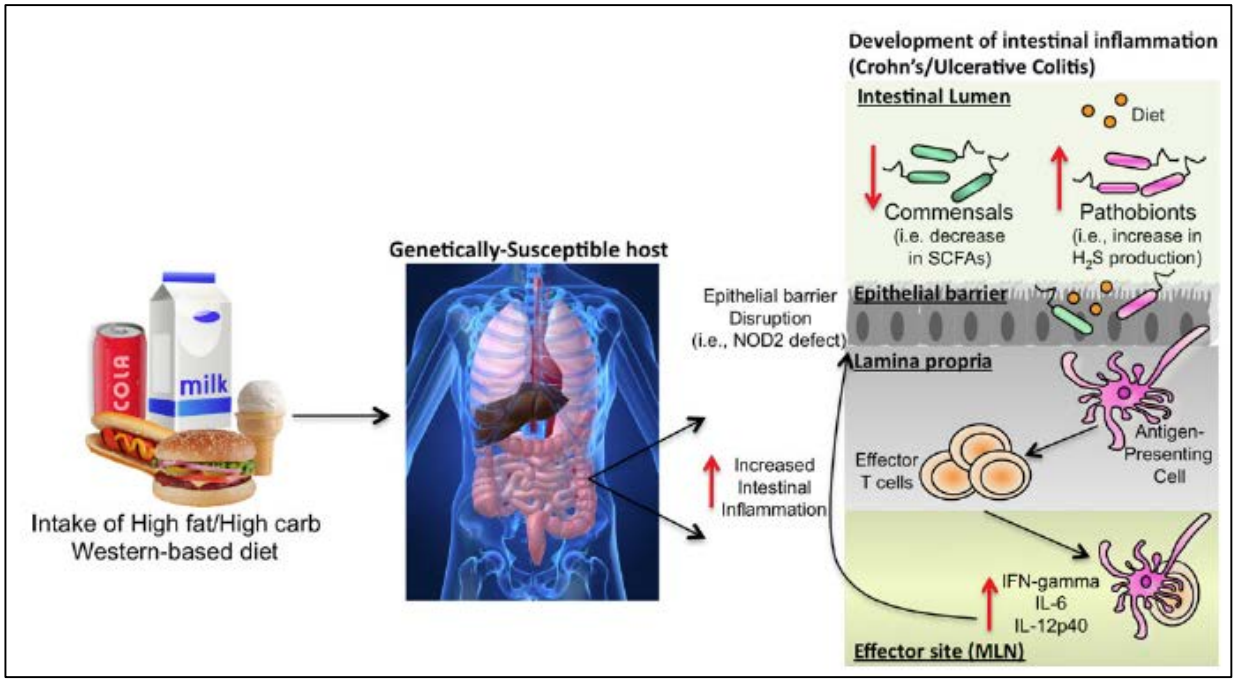

Figure 1. The Western diet and the development of IBD.[4]

An increased immune response to antigens (including foods) at the mucosal surface of the intestines leads to inflammation. With this inflammation, it becomes more possible for larger-sized molecules to cross from the gut into the bloodstream, which can precipitate

even more of an immune response and inflammation. Interrupting this process should form the basis for a Personal Health Plan (PHP) that specifically focuses on regulating the immune system by decreasing inflammation and by rebalancing and healing the gut microbiome. Every individual and his or her disease is unique; thus, a *personalized*, rather than a *one-size-fits-all*, approach may be most effective.

The following recommendations focus on the best available evidence. Although general healthy living recommendations are not included, it should be assumed that health-promoting behaviors are the default for any PHP.

MOVING THE BODY

Increasing physical activity leads to improved quality of life, increased muscle mass, and decreased rates of osteoporosis in those with IBD.[5] This is important, given that those with IBD have a 40%-60% increased rate of osteoporotic fractures. This may be due to a combination of increased inflammation, steroid treatment, and micronutrient deficiencies.[6]

SURROUNDINGS

How important are our genes relative to our surroundings in determining our "genetic susceptibility" to IBD? There is a low concordance rate in identical twins for both CD (about 50%) and UC (about 10%), confirming that the environment is an important variable.[3]

Given that IBD is unevenly distributed around the world and in different socioeconomic strata in the United States, some hypothesize that the "hygiene hypothesis" may have an explanatory role. Humans living in industrialized countries of higher socioeconomic status are exposed to fewer microbes at an early age. This may cause them to have an immune system that is less able to tolerate microbial exposures later in life and which inappropriately activates, causing inflammation and possibly IBD.[2]

FOOD AND DRINK

Given that shifts toward more "Western" diets are likely the most significant variable increasing IBD rates worldwide, what one eats likely plays a major role in both developing and controlling IBD.

Our diets are directly associated with the characteristics of our intestinal bacterial community (our microbiome), which likely play a role in the development of IBD as well. The microbiome stays relatively stable throughout life, starting at the ages of 2 or 3, but it can be modified through significant dietary changes.[2] For more information, refer to Promoting a Healthy Microbiome with Food and Probiotics.

Although research supports a higher rate of food allergies and sensitivities in those with CD (approximately 61%), no recommended diet exists save eating liquid diets during disease flares.[7] Some studies support use of specific diets, such as the Specific Carbohydrate Diet or a Low Sulfur Diet, but control groups often were eating a more Westernized diet. It may be that these IBD diets are actually just "less Western" and therefore all have similar effects.

However, most with IBD change their diets after diagnosis. Several small studies have shown that *personalized* elimination diets can be helpful, and this dietary approach has the best clinical evidence for *both* symptom and histological improvements for CD.[2] For guidance, refer to "The Elimination Diet". Given that micronutrient deficiencies are common in those with IBD, one must ensure that elimination diets do not become overly restrictive.

The most common foods that seem to provoke symptoms include dairy (casein, lactose), gluten, wheat, yeast, corn, and certain fruits (citrus, grapes, melon) and vegetables.

Given the risk of nutritional deficiencies due to poor absorption or restrictive diets, consider ordering labs focused on determining one's nutritional health: red blood cell (RBC) magnesium, RBC zinc, serum albumin (or pre-albumin depending on context), serum iron, ferritin, transferrin, folate, B12, and 25-OH vitamin D. The most common deficiencies are folate, B12, and iron.[8]

Antioxidants have the ability to bind free radicals, which are often generated from inflammation in IBD. In-vitro evidence supports:[9]

- Vitamin E (and possibly A and C; all antioxidants)
- Selenium (anti-inflammatory)
- Iron (may need to be given IV given difficulties with absorption)
- Zinc (vital for GI healing)
- Calcium and vitamin D (bone strength)
- Folate and B12 (latter may need to be parenteral if the terminal ileum is involved)

With the advent of newer biologic medications, specific diet formulas have become less frequently used for those with active CD. Such diets have traditionally been used in pediatric populations for whom chronic steroid therapy is undesirable.[10] Enteral nutrition with elemental, semi-elemental, and defined formula diets are nearly as effective in inducing remission as corticosteroids, and they are much better than placebo with a nearly 60% response rate.[11]

The type of formula does not seem to matter because it is not the protein or nitrogen source but likely the fat content that leads to benefit. It is believed to work through both an anti-inflammatory interaction of lipids with the intestinal mucosa as well as by changing the colonic microflora.[12] In UC, this approach does not seem to be effective.[2] However, relapses after discontinuing these diets are common, and the diets are often unpalatable. Although few supporting data exist, it seems reasonable to suggest an anti-inflammatory

(or Mediterranean) diet given its better palatability and known positive effects on other aspects of health.

Finally, there are several plant-based compounds that have shown great promise as anti-inflammatory and antioxidants in basic science and animal studies. Clinical studies in those with IBD are lacking, and these should be highlighted in one's diet until more is known:[9]

- **Resveratrol.** This is naturally found in grapes, peanuts, and red wine.
- **Bromelain.** This is a mixture of enzymes derived from pineapples.
- **Pomegranate.** Likely quite safe, given it is a popular food.
- **Rutin.** This is a polyphenolic flavonoid found in citrus fruits, tea, and buckwheat seeds.

REST

Sleep modulates the immune response and therefore may affect the course of inflammatory diseases. Those with IBD often have disordered sleep, as exhibited by prolonged sleep latency, sleep fragmentation, higher sleep medication use, decreased daytime energy, and poor overall sleep quality. These observations are true even when IBD is not active.[13] Although there is likely a circular interplay between sleep dysfunction and inflammation, helping to restore healthy sleep patterns may improve quality of life and possibly disease severity.

POWER OF THE MIND

> *The gut is the body's emotional spinal cord.[14]*

People with IBD are at a greater risk of anxiety, depression, and impaired quality of life. They also have altered sensory perceptions, as suggested by increased sensitivity to hot and cold.[13] A review of mind-body approaches concluded the following:

- **Stress management techniques** can have a modest benefit on disease severity and quality of life.
- **Cognitive behavioral therapy (CBT)** improves mood but not IBD severity.
- **Hypnosis** has a positive impact on disease severity as well as mental health symptoms.[15]

These may be best utilized with people who have concomitant mental health disorders.

ROLE OF PREVENTION AND SCREENING

Diet. Western diets are high in total fat, animal fats, and omega-6 polyunsaturated fats as well as low in fiber and high in refined carbohydrates. High fiber and fruit intakes are

associated with a decreased UC risk.[2] Retrospective data suggest that a high intake of fiber and fruit (but not vegetables) is associated with a reduced risk of CD.[3] Conversely, a high intake of vegetables (but not fruit) is associated with a reduced risk of UC.[3]

Tobacco use. Smoking increases the incidence of CD and worsens its course. However, smoking is protective against UC, and patients with UC who smoke should not necessarily be encouraged to stop depending on an overall assessment of the risks and benefits.[5]

Breastfeeding. This protects against IBD, especially if continued for 6 months after birth.[11]

Avoiding antibiotics. There is a possible association between long-term antibiotic use (especially doxycycline) for acne and CD. This suggests that long-term and repeated exposure to antibiotics should be avoided unless absolutely indicated.[16]

Other risk factors for IBD include family history, age 15-35 and 55-65, female sex, urban dweller, high stress, Jewish ancestry, high socioeconomic status. Possible risks include NSAIDs, oral contraceptives, antibiotics, and bacterial intestinal infections.[7]

Screening for colon cancer. UC is associated with an increased risk of colon cancer, though this risk varies based on the site(s) of disease and duration of symptoms (and not its activity). Epidemiologic data has shown that proctitis alone confers no additional risk, but pancolitis that began in childhood confers a 162 times higher colon cancer risk compared to those who do not have UC.[17] It is best to be screened when the disease is in remission. The frequency of screening has not been rigorously studied and should be individualized. Many guidelines recommend screening initiation 10 years after diagnosis with follow up every 1 to 5 years. Patients with CD do not appear to have an increased risk of colon cancer, though this is still being investigated; however, they may have an increased risk of small bowel cancer, though no reliable screening methods exist for this. Also, women taking immunosuppressive therapy may be at higher risk of cervical cancer, so close adherence to current screening guidelines is recommended.

Note: Please refer to the *Passport to Whole Health*, Chapter 15 on Dietary Supplements for more information about how to determine whether or not a specific supplement is appropriate for a given individual. Supplements are not regulated with the same degree of oversight as medications, and it is important that clinicians keep this in mind. Products vary greatly in terms of accuracy of labeling, presence of adulterants, and the legitimacy of claims made by the manufacturer.

DIETARY SUPPLEMENTS AND BOTANICALS

Omega-3 fatty acids have not been shown to work in most studies and have had marginal benefit in others. While they have known anti-inflammatory properties *in vitro* and *in vivo*, they have not shown a clinical benefit in IBD. That said, they are often one of the most common supplements taken by those with IBD.[18-23]

Curcumin, a component of turmeric, showed promise in a few small studies for both CD and UC.[19] It has well-characterized anti-inflammatory and antioxidant effects. It is a COX-2 and lipoxygenase inhibitor. The dose is 1,000 mg twice per day with meals.[24] Curcumin has been used in trials along with pharmaceuticals, so the current best evidence supports using it as an adjuvant therapy.[25]

Aloe vera gel is the mucilaginous aqueous extract of the aloe leaf. It has been shown to be better than placebo in moderately active UC in a study of 30 patients over 4 weeks. It is the most popular botanical used by those with IBD. For UC, use 100 mL of a 50% solution twice daily. Be careful not to recommend aloe latex, as this acts as a laxative and can worsen diarrhea.[19]

Wheatgrass juice (*Triticum aestivum*) is better than placebo in inducing a clinical response for active distal UC in 23 patients over 4 weeks.[19] The amount used is 20 mL orally per day initially. This is increased by 20 mL per day to 100 mL total.

Boswellia serrata is a traditional Ayurvedic remedy and a component of incense. It is also known as Indian frankincense. It has been shown to be equal to sulfasalazine for moderately active UC and equal to mesalamine for CD in inducing a clinical response and/or remission. The dose used in the research was 300 mg three times daily for 6 weeks.[19]

Psyllium reduced symptoms and increased remission times in those with UC who took 20 grams with their mesalamine versus using mesalamine alone. Use caution, as taking this during flares can make symptoms worse.[26]

Probiotics—Given that specific bacterial species exhibit anti-inflammatory effects and can positively alter the intestinal ecosystem, studying the effects of probiotics on IBD makes logical sense. Although significant research is being done, each individual likely has a uniquely dysfunctional gut microbiome, so individualized therapies will likely prove the most useful.[27,28] Novel, culture-independent DNA sequencing is revolutionizing our ability to understand this, and the research is becoming more positive over time. Several probiotic species alone or in combination have been studied and show the most promise in relapse prevention and remission induction in mild to moderate UC.[6,29] A meta-analysis examining probiotics' effectiveness in CD revealed no overall benefit, but there is some suggestion that *Lactobacillus rhamnosus GG* or *Saccharomyces boulardii* may be beneficial.[30-32] The following can be considered:

- VSL#3 (active UC, inactive pouchitis).[33,34] One sachet twice per day. This contains eight strains of *Bifidobacterium*, *Lactobacillus,* and *Streptococcus* species. This product contains corn.
- *Lactobacillus rhamnosus* strain GG 10 to 20 billion colony-forming units (CFUs) per day.
- *Saccharomyces boulardii* 250 mg three times per day or 500 mg twice daily.

For more information, refer to "Promoting a Healthy Microbiome with Food and Probiotics."

Prebiotics. These are nonabsorbable carbohydrates that enhance the growth of beneficial intestinal bacteria (e.g., *Lactobacillus*). They provide a substrate for the generation of short-chain fatty acids (SCFAs), which possess anti-inflammatory properties; the most representative of these is butyrate.[4] Enteric-coated butyrate capsules (4 grams daily) in combination with mesalamine versus mesalamine alone improved symptoms in patients with mild to moderate UC.[26]

TABLE 1. FOOD SOURCES OF PREBIOTICS [35]

Food	Amount to Eat to Get 10 Grams (g) of Prebiotics
Raw Chicory Root	15.5 g (0.6 oz)
Raw Jerusalem Artichoke	31.7 g (1.1 oz)
Raw Dandelion Greens	40 g (1.4 oz)
Raw Garlic	57.2 g (2 oz)
Raw Onion	116.3 g (4.1 oz)
Cooked Onion	200 g (7.1 oz)
Raw Asparagus	200 g (7.1 oz)
Cooked Whole Wheat Flour	208.3 g (7.3 oz)
Raw Banana	1000 g (2.2 lbs.)

OTHER SYSTEMS

In two meta-analyses including 48 randomized controlled trials, acupuncture with moxibustion and moxibustion alone demonstrated better efficacy than oral sulfasalazine in treating IBD. However, results were quite variable, and the studies were of low methodological quality. These therapies show promise, but research is insufficient to support making a strong recommendation.[36,37]

Non-pharmaceutical treatment recommendations for CD versus UC are summarized in Table 2.

TABLE 2. SUMMARY OF NON-PHARMACEUTICAL TREATMENTS

Treatment	Crohn's disease	Ulcerative colitis
Defined formula diets	Effective but may be unnecessary; consider elimination diet	Not effective
Colon cancer screening	Unknown interval	10 years after diagnosis, then every 1-5 years
Probiotics	*Lactobacillus rhamnosus GG* *Saccharomyces boulardii*	VSL#3

Treatment	Crohn's disease	Ulcerative colitis
Prebiotics	Not applicable	Via food; consider butyrate capsules or enemas
Curcumin	1 gram twice daily with meals	1 gram twice daily with meals
Aloe vera gel	—	100 mL twice daily
Boswellia serrata	300 mg three times daily	300 mg three times daily
Psyllium husk	20 grams daily	—
Wheatgrass juice	—	20-100 mL orally/day

For everyone with IBD, the following should be strongly considered:

- Cease use of tobacco products
- Increase physical activity, especially weight-bearing activities.
- Start an individualized elimination diet. Refer to the "Elimination Diet" tool.
- Promote colorful anti-inflammatory foods.
- Consider a multivitamin to reduce pro-oxidant load.
- Address stress management by one or more therapies including hypnosis, CBT, or other mindfulness-based techniques.
- Address suboptimal sleep.
- Test for possible nutritional deficiencies: RBC magnesium, RBC zinc, serum albumin (or pre-albumin depending on context), serum iron, ferritin, transferrin, folate, B12, and 25-OH vitamin D.
- Caution in using NSAIDs and oral contraceptives (the latter are a risk factor for CD and may not be as effective in those with IBD).
- Consider acupuncture and/or moxibustion.

AUTHOR(S)

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