Dining With Inflammatory Bowel Disease: A Review of the Literature on Diet in the Pathogenesis and Management of IBD

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Inflammatory bowel diseases (IBDs) are chronic immune-related diseases hypothesized to be a sequela of an interplay of genetic predisposition and environmental exposures. The global incidence of IBD is increasing, and more patients are exploring diet as a means to explain and treat their IBD. In fact, many patients strongly believe diet plays a fundamental role in the onset and management of their IBD. However, a significant proportion of patients report limited nutritional education from their provider, and providers report limited nutritional resources to aid in discussions with patients. This imbalance between supply and demand likely reflects the previous paucity of available literature characterizing the influence of diet in IBD. To address this gap in knowledge, we review the available literature to characterize the role of diet in the pathogenesis, exacerbation, and treatment of IBD. We aim to provide patients and providers with resources to better understand and discuss the role of diet in IBD, with the overall goal of improving patient care and satisfaction.

Key Words: diet, inflammatory bowel disease, Crohn's disease, ulcerative colitis

INTRODUCTION

Inflammatory bowel diseases (IBDs), which include Crohn's disease (CD) and ulcerative colitis (UC), are chronic immune-related diseases that cause enteric inflammation and often result in debilitating gastrointestinal (GI) symptoms. In the United States, over 1 million patients are affected by IBD,[1] and studies have shown increasing incidence worldwide.[2] Although the pathogenesis of IBD remains elusive, investigators hypothesize IBD is a result of an interplay between genetic susceptibility and environmental exposures, resulting in inappropriate immune response to commensal bacteria and inflammation. The impact of environmental exposure on the pathogenesis of IBD is highlighted by epidemiological studies observing an increased incidence of IBD in developing countries after adopting a more Westernized lifestyle.[3–6] For example, between 1986 and 1988, the incidence of UC in Hong Kong was 0.3 per 100,000 but rose to 1.8 per 100,000 between 2004 and 2006.[7] There is also a higher incidence of IBD in immigrants who moved to developed countries compared with individuals of their native country.[8–10] Investigators and patients alike have sought to identify actionable environmental exposures that can ameliorate the burden of IBD.

Of the environmental exposures, patients often view diet as a vital component of their IBD management. In patients newly diagnosed with IBD, 1 study found 86% of patients identified knowledge about their diet as very important, but 69% of patients reported receiving little to no information about diet from their provider.[11] Similarly, another study reported 50% (n = 198) of patients never received any nutritional advice, even though 67% (n = 268) of patients wanted more nutritional advice.[12] In a survey of GI providers, only 46% (n = 91) reported adequate access to nutritional resources to initiate and guide discussions with patients.[13] This imbalance in supply and demand of information from both patient and providers can result in patients seeking advice from alternate sources such as the internet, which can result in highly restrictive diets, risking malnutrition. This consequence was highlighted in a review of patient-targeted dietary recommendations by Hou et al.[14] In their review, the authors performed an internet query of dietary recommendations and evaluated websites for recommendations to include or exclude certain diets. Their web search analysis found a majority of websites agreed on avoiding cruciferous vegetables, alcohol, carbonated beverages, and sugars. The majority of websites also agreed on including cooked vegetables, poultry, and lean protein. However, there was a discrepancy in recommendations for including/excluding "any vegetables," any fruit nuts, and whole grains. ("Any vegetable" indicated by the website's recommendation did not specify raw/cooked/cruciferous vegetables.) Ultimately, the authors concluded patient-targeted recommendations were highly restrictive and often conflicting. The imbalance of supply and demand of information and inconsistent recommendations found on other media outlets likely reflect the previous paucity of evidence characterizing the role of diet in the

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pathogenesis, exacerbation, and treatment of IBD and underlines the need for more research in this area.

To help patients and providers better address this gap in knowledge, we review the available data on the role of diet in the pathogenesis, exacerbation, and treatment of IBD. We aim to provide patients and providers with resources to better understand and discuss the role of diet in IBD, with the overall goal of improving patient care and satisfaction.

Role of Diet in Pathogenesis of IBD

Patients often wonder if their diet contributed to their development of IBD. In 2 studies surveying patients' dietary beliefs, 16%–48% of patients believed diet played a role in their developing IBD.[12, 15] Although there is no definitive evidence demonstrating a causal relationship between the two, there has been a growing body of literature suggesting diet contributes to the pathogenesis of IBD.

As discussed previously, several studies have observed an increased incidence of IBD in immigrants after moving to industrialized countries.[7–10] In addition to other environmental factors such as pollution associated with moving to an industrialized country, this may potentially be explained by the significant changes in the gut microbiome after immigrants adopt a Westernized diet.[16] Vangay et al found long-term US-resident Hmong first-generation immigrants harbored a gut microbiome that had an increased capacity for metabolizing sugars, whereas the native Hmong Thai-residents' gut microbiome were more enriched in pathways relating to the complex carbohydrate and plant fiber degradation. Thus, we will highlight the major components of the Western diet that could potentially contribute to the pathogenesis of IBD: high meat, high fat, low fiber, and emulsifiers.

Meat, particularly red meat, is a principal component of the Western diet that many suspect contributes to the development of IBD. Meat contains sulfur amino acid that, when fermented by bacteria in the gut, produces hydrogen sulfide. Studies have proposed that hydrogen sulfide contributes to the pathogenesis of UC by inhibiting butyrate oxidation in colonocytes and/or impairing the intestinal barrier function by reducing the disulfide bonds of the mucus layer, which increases intestinal permeability to enteric pathogens.[17, 18]

In a systematic review, Hou et al noted 5 studies have evaluated the association between meat and CD and 7 studies between meat and UC.[19] In CD, 2 studies observed an association between increased meat intake and risk of CD, but only 1 study reported a statistically significant association (odds ratio [OR] 2.48).[20, 21] In UC, 2 studies found a significant association with high meat intake (OR range 1.87–2.62).[20, 22] Additionally, there was an 87%–148% increased risk of developing IBD associated with high meat intake. Interestingly, in an observational prospective cohort study of 183 UC patients in remission, meat was significantly associated with increased risk of relapse (OR 5.19; 95% CI, 2.09–12.9).[23] Furthermore, dietary protein was positively associated with colitis severity in mice.[24]

Dietary fats have also been implicated in the pathogenesis of IBD, especially polyunsaturated fatty acids (PUFAs). In the Western diet, there is a high omega (n)-6 PUFA to n-3 PUFA ratio. Omega-6 PUFAs, which include linoleic acid and arachidonic acid, have been suggested to be pro-inflammatory, whereas n-3 PUFAs, particularly eicosapentaenoic acid and docosahexaenoic acid, which are major component of omega-3 fish oil, are suggested to be anti-inflammatory. Omega-3 PUFAs have been shown to have beneficial effects in other inflammatory conditions such as asthma and rheumatoid arthritis.[25]

In IBD, there have been a few prospective studies that have evaluated the impact of PUFA intake and the development of IBD. In a prospective study of 170,000 women enrolled in the Nurses' Health Study, higher n-3:n-6 PUFA ratio was associated with lower risk of UC (hazard ratio [HR] 0.69; 95% CI, 0.49–0.98; for highest vs lowest quintile; P_{trend} = 0.03).[25] Similarly, in 2 separate nested case-control studies in UC and CD patients, higher intake of docosahexaenoic acid was associated with lower risk of UC (OR 0.23; 95% CI, 0.06–0.97 for highest vs lowest quartile; P_{trend} = 0.03)[26] and CD (OR 0.07, 95% CI, 0.02–0.81 for highest vs quintile; P_{trend} = 0.04).[27] Higher linoleic acid intake was associated with increased risk of UC (OR 2.49; 95% CI, 1.23–5.07 for highest vs lowest quartile; P_{trend} = 0.02).[26] In mouse model studies, high-fat diets seemed to disrupt the gut barrier function and promote colonic inflammation.[28, 29] In 1 study, mice that were fed a "Western" diet comprised of high fat and high sugar had a decrease in mucus layer thickness and increase barrier permeability, which was associated with increased TNFα secretion. This later allowed for invasive *Escherichia coli* to more readily colonize the gut mucosa and induce inflammation.[28]

Recently, emulsifiers have gained increasing attention as pro-inflammatory food additives that may have a contributory role in the pathogenesis of IBD.[30] Emulsifiers are food additives commonly used to give food products a smooth texture, prevent separation, and extend shelf-life. Some common foods that contain emulsifiers include ice cream, non-dairy milk alternatives, salad dressing, and pasta, to name a few. While there are many different emulsifiers used in the food industry, carrageenan, carboxymethylcellulose (CMC), and polysorbate-80 (P80) have been strongly implicated in promoting intestinal inflammation. The majority of the research on emulsifiers and enteric inflammation has been in animal models, and the data have suggested that emulsifiers exert their inflammatory effects by altering the gut microbiome through decreasing diversity and promoting pro-inflammatory enteric bacteria.[31–33] Animal studies have also noted intestinal changes reminiscent of the effects of other foods implicated in IBD such as decreased colonic butyrate levels,[34] thinner inner mucus layer,[31] increased intestinal permeability,[31, 34, 35] and increased gut bacterial translocation.[31, 36] Several studies have also observed colonic ulcerations and intestinal histopathologic changes such as villous architectural distortion and lymphoid hyperplasia

with microgranulomas in animals exposed to emulsifiers.[37, 38] In fact, 1 study noted mice fed chow mixed with 2% carrageenan developed small bowel lesions during the first 2 to 6 weeks, followed by colonic lesions after 8 weeks,[39] which may have implications for the subphenotype of CD patients who experience extension of their disease during their disease course.

Although there is robust animal data supporting the deleterious effects of emulsifiers on the GI tract, there has been little in ways of studying their effects in humans. One small randomized control trial that included 12 UC patients evaluated carrageenan consumption and the risk of UC relapse and found carrageenan consumption was associated with a higher risk of relapse (3 of 5 patients in the carrageenan-exposed group vs 0 of 7 patients in the placebo group; $P = 0.046$).[40] Investigators also noted increases in interleukin (IL)-6 ($P = 0.02$) and fecal calprotectin levels ($P = 0.06$) in the carrageenan-exposed group. Although the study was not in humans, Chassaing et al exposed CMC and P80 to microbiota using the mucosal simulator of the human intestinal microbial ecosystem (M-SHIME), which is a model that allows a complex human microbiota to be maintained stably without a live host.[41] The investigators noted significant changes in the microbiome such as increased expression of bioactive flagellin, which has been hypothesized to promote inflammation via activation of toll-like receptor 5 (TLR5) and NOD-like receptor family CARD domain containing 4 (NLRC4).[31] Furthermore, after transplanting mice with emulsifier-treated M-SHIME or water-treated M-SHIME, investigators noted colonic shortening in mice that received the emulsifier-treated M-SHIME, suggesting presence of intestinal inflammation.[41] These findings provide evidence that emulsifiers can alter the human microbiome and promote its pro-inflammatory potential, which may contribute to the onset of IBD. Nonetheless, more human studies are needed to better understand the effect of emulsifiers on the human gut and its role in the pathogenesis of IBD.

Although the available data are limited, inorganic microparticles are also additives found in processed foods to prevent caking or preserve color that have been proposed as a contributing factor in the pathogenesis of IBD.[42] Microparticles are bacteria-sized, nonbiologic particles that are resistant to degradation, especially particulate oxides of titanium, aluminum, and silicon. Based on the available data, the role of microparticles in IBD is controversial. Mice models have found microparticles promote colitis and visceral hypersensitivity.[43, 44] However, a randomized-controlled trial of 83 patients with active CD did not show a low-microparticle diet improved clinical outcomes.[45] Though more studies are needed to further characterize their role in intestinal inflammation, microparticles further highlight the detrimental effects of food additives that potentially contribute to the development of IBD.

Whereas meat, dietary fats, and emulsifiers offer a glimpse into how diet can contribute to IBD, fiber has been proposed as protective of developing IBD. Fiber has always been regarded as having numerous health benefits but is severely lacking in the typical Western diet. In terms of inflammation, fiber is hypothesized to exert its anti-inflammatory effects via metabolization by intestinal bacteria to short chain fatty acids (SCFAs), and play a role in maintaining intestinal barrier function. In a systematic review of the literature, Hou et al generally found that both retrospective and prospective studies observed that high intake of dietary fiber was associated with decreased risk of UC and CD—but only 1 study found a statistically significant reduced risk in CD.[46] Similarly, in a large prospective study using the Nurses' Health study, Ananthakirshnan et al found higher intake of dietary fiber was associated with a lower risk of CD but not UC.[47]

Through interactions with gut microbiota, fiber appears to help maintain intestinal barrier function by preserving the inner mucus layer, which harbors antimicrobial peptides and immunoglobulins and acts as the first line of defense against mucosal pathogens.[48] Because fiber is a source of nutrition for gut microbiota, fiber depravation causes the gut microbiome population to shift toward mucin-degrading bacteria while fiber-degrading species decrease.[49] These findings are associated with thinning of the inner mucus layer and increased proximity of bacteria to the intestinal epithelium.[49, 50] In fact, the colonic mucus layer in fiber-deprived mice is 5 to 6 times thinner in fiber-deprived mice than mice fed a fiber-rich diet.[49] To further demonstrate the adverse effect of fiber depravation, Desai et al intentionally infected mice with an enteric pathogen and found the pathogen grew at faster and greater levels in fiber-deprived mice. Fiber-deprived mice also experienced severe weight loss after infection (>20% loss of body weight by day 10) and had greater surface area of inflammation on pathology.[49] Finally, Llewellyn et al found fiber intake was associated with reduced severity of DSS-induced colitis. Of the different fiber sources studied, psyllium was the most protective against DSS-induced colitis and was associated with increased concentrations of intestinal butyrate and T_{reg} cells.

Overall, it does not seem that one specific food causes IBD. Based on the available data, various components including meats, fats, fiber, and food additives (such as emulsifiers) interact with our microbiome to either strengthen or weaken our intestinal barrier function, allowing for varying degrees of enteric pathogens translocation (Fig. 1). This is potentially the role of diet in the pathogenesis of IBD.

Role of Diet in Exacerbation of IBD

Diet modification is common practice among IBD patients for various reasons, including relapse prevention. Studies have reported 57%–58% (total n = 407) of patients believe food has a role in triggering symptoms, and 68% (n = 273) of patients self-impose dietary restrictions

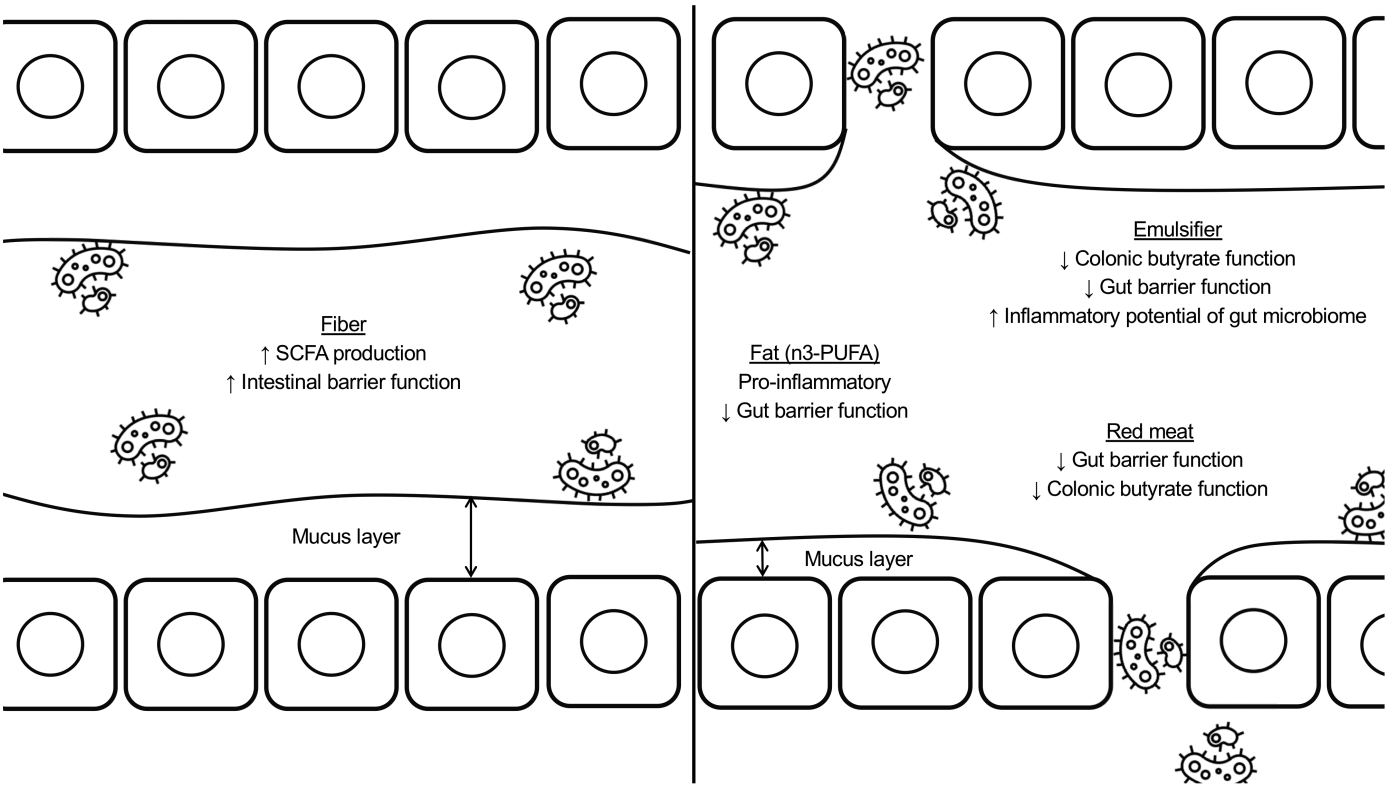

FIGURE 1. Proposed mechanism behind diet and the pathogenesis of IBD. Different dietary components interact with the gut microbiome to strengthen or weaken the gut barrier function that allows for varying degrees of enteric bacterial translocation, which may increase risk of developing IBD.

to prevent relapse.[12, 15] This results in a number of factors that can further dampen the quality of life in IBD patients, with 20% (n = 81) of patients refusing to dine out and 66% (n = 265) of patients depriving themselves of favorite foods to prevent relapse.[12]

Currently, there has not been data identifying specific "trigger" foods that exacerbate IBD. There is conflicting data on meat and relapse of IBD in 2 prospective studies.[23, 51] Patients often devise dietary restrictions based on anecdotal evidence, and there are common themes observed across several studies that surveyed dietary practices of IBD patients. In these studies, spicy foods, dairy products, fatty foods, and fibrous foods—particularly vegetables—were consistently identified as the most common "trigger" foods by patients.[12, 15, 52–54] Alcohol was also attributed to exacerbating symptoms but was not consistently surveyed across studies.[12, 52] Additionally, in their survey of 2329 IBD patients, Cohen et al found that patients with active disease were significantly more likely to avoid fruit, leafy and nonleafy vegetables, tomatoes, beans, and ice cream compared with IBD patients in remission.[52] Interestingly, IBD patients with active disease were more likely to consume soda than those without active disease. Finally, Cohen et al also found yogurt and rice were frequently reported to improve symptoms.

Despite certain foods exacerbating GI symptoms in IBD patients, studies have not demonstrated that these foods cause increased inflammation. Furthermore, as IBD patients frequently have GI symptoms despite quiescent disease, it can be difficult to discern if the exacerbation of symptoms from food is due to inflammation or dietary intolerance. This is demonstrated in a study of IBD patients in remission (total n = 110), where 7% had a low lactase level, but 72% met criteria for lactose sensitivity by breath test.[55] There was a higher rate of lactose sensitivity by breath test in CD (76%, n = 39) than UC (68%, n = 40) patients, and diarrhea was the most common symptom after lactose ingestion (UC 32%, CD 43%). Thus, although foods may not necessarily exacerbate inflammation in IBD, dietary avoidance nonetheless can improve symptoms and should be catered on an individual basis. Future studies will need to confirm the absence of inflammation in the setting of symptom exacerbation secondary to dietary exposures.

Popular Dietary Interventions in IBD

There are multiple diets that have been implicated in IBD treatment (Table 1) with varying degrees of quality of data to support their use. Table 2 summarizes the proposed mechanism and recommendations for each diet. We will highlight the 4 most studied diets in the literature

TABLE 1. Types of Studies Published on Various Dietary Interventions for IBD

Diet	Case Series	Retrospective	Prospective	RCT
Exclusive enteral nutrition	X	X	X	X
Specific carbohydrate diet	X	X	X	
Low FODMAP		X	X	X
Mediterranean		X	X	
Paleo			X	
CD Anti-inflammatory diet	X			
Semi-vegetarian			X	X

TABLE 2. Dietary Interventions that Have Been Proposed to Help Treat IBD

Diet	Proposed Mechanism	Typical Diet
Exclusive Enteral Nutrition (EEN)	• Possibly downregulates pro-inflammatory cytokines and alters the microbiome to decrease intestinal inflammation.	• Exclusive diet of formula (oral or via nasogastric tube) for 4–12 weeks. • The *CD-TREAT diet* aims to mimic EEN with real foods.[73] • The *CD exclusion diet* is a whole-food diet combined with partial enteral nutrition.[74]
Specific Carbohydrate Diet (SCD)	• Avoids foods that are thought to lead to intestinal injury caused by an overgrowth and imbalance toward pro-inflammatory gut microbes (i.e. poorly absorbed carbohydrates, specifically di- and poly-saccharide carbohydrates).	• Foods allowed include most fresh fruits and vegetables, meat, yogurt, nuts, seeds, hard cheeses, and certain legumes. • Avoid most grains such as wheat, barley, corn, rice, processed/canned foods, and milk.
Low FODMAP	• Avoids carbohydrates that are poorly absorbed, fermented by intestinal bacteria, and result in increased gas production and fluid load thus causing GI distress. • Likely improves functional symptoms more than inflammatory symptoms.	• Three-phase diet: 1. Elimination: avoid all high FODMAP food for 6–8 weeks. 2. Reintroduction: Gradually re-introduce back high FODMAP foods to tolerance to identify trigger foods. 3. Maintenance: Follow an individualized diet that avoids problematic high FODMAP foods.
Semi-Vegetarian	• Avoids meat and high-fat foods that may impair intestinal barrier function and promote inflammation.	• Low intake of animal proteins (fish once a week and meat once every 2 weeks).
Mediterranean	• Promotes diet high in omega-3's and low in omega-6's, which may reduce inflammation.	• High in vegetables, fruits, whole grains, healthy fat. • Moderate in fish poultry, beans and eggs. • Limited red meat intake.
Paleo	• Avoids foods and additives that may trigger intestinal inflammation, dysbiosis, and/or symptomatic food intolerance.	•Encourages fruits, vegetables, nuts/seeds, lean meats, fish, oils from nuts. • Avoids grains, legumes, dairy, sugar, salt, potatoes and highly processed foods. • Autoimmune protocol diet is an extension of this diet and includes gluten avoidance.[96]
CD Anti-inflammatory diet	• Aims to improve dysbiosis of the gut by modifying carbohydrates (reduced lactose and processed carbs), increased pre- and probiotics (soluble fiber, onions, fermented foods), increasing healthy fats. • Minimize irritants to promote healing. • Modifies textures of foods to improve absorption and minimize intact fiber.	• Allows lean meat, poultry, fish, omega-3 eggs, select carbohydrates, select fruits and veggies. • Encourages prebiotics in the form of soluble fiber (bananas, oats, flax). • Limits dairy intake.

and review their underlying pathophysiology, efficacy, and adherence rates.

Exclusive enteral nutrition

With exclusive enteral nutrition (EEN), patients obtain 100% of their nutrition through liquid formulations orally or via feeding tube for 4 to 12 weeks. It has gained increasing recognition, particularly in the pediatric IBD population, for inducing remission in CD. In fact, in the 2014 European Society of Pediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN) and European Crohn's and Colitis Organization (ECCO) guidelines, 96% of experts agreed that EEN is the recommended first-line induction therapy for children with active luminal CD.[56] The benefits of EEN in IBD were first described in the surgical literature when CD patients unexpectedly improved after being administered EEN to optimize their nutritional status, and a few patients even avoided surgery.[57] The mechanism of action behind EEN in IBD remains unclear, but many hypothesize that it downregulates pro-inflammatory cytokines and alters the microbiome to decrease intestinal inflammation.[58]

There are 3 major enteral nutrition formulations. Elemental formulations contain only amino acids and are administered via tube feeds. Semi-elemental formulations contain peptides of varying lengths. Finally, polymeric formulations contain intact protein and can be ingested orally. The polymeric formulations are as equally efficacious as the elemental and semi-elemental formulations.[59]

To date, there have been 9 meta-analyses evaluating the efficacy of EEN vs corticosteroids for inducing remission in CD (Table 3).[59–67] The overall consensus is mixed, but studies containing an exclusively pediatric population have shown EEN is equally efficacious as corticosteroids. In fact, 1 study found patients on EEN were 4.5 times more likely to achieve mucosal healing than corticosteroids (OR 4.50; 95% CI, 1.64–12.32).[66] In contrast, studies that include adults found EEN is inferior to corticosteroids. The reason behind the discrepancy between adults and children has not been established but may be a function of adherence and tolerability. On the other hand, data from 2 prospective observational studies have suggested that EEN may be effective for adults with penetrating CD. In 1 study of 41 CD patients with fistulas, strictures, and abscesses, 80.5% of patients achieved clinical remission, and 75% of patients with enterocutaneous fistulas achieved fistula closure.[68] Another study reported 331% increase in luminal cross-sectional area of inflammatory strictures on imaging after 12 weeks of EEN.[69] Exclusive enteral nutrition may also be effective in maintaining remission, especially in patients on biologics. In a meta-analysis comparing patients on infliximab (IFX) and EEN vs IFX monotherapy, 74.5% of patients on IFX and EEN therapy vs 49.2% of patients on IFX monotherapy remained in remission after 1 year (OR 2.93; 95% CI, 1.66–5.17; $P < 0.01$). Prior studies have suggested EEN may not be effective in UC or CD primarily involving the colon[70, 71]; however, Buchanan et al later observed disease location did not influence likelihood of clinical remission from EEN in children with CD.[72]

In an effort to maintain the benefits of EEN while improving its palatability, Svolos et al were able to design a diet with regular foods to mimic EEN (CD-TREAT diet) and demonstrated that it was easier to comply with than EEN, and in a small open-label trial in children with active CD (n = 5), 60% achieved clinical remission after 8 weeks, with a 55% decrease in fecal calprotectin compared with baseline.[73] Likewise, in a randomized controlled trial, Levine et al compared coupling CD exclusion diet (CDED), a whole food diet, with partial enteral nutrition (PEN) and EEN in pediatric patients with mild to moderate CD for tolerability and efficacy in inducing remission.[74] The results showed CDED+PEN was significantly better tolerated than EEN ($P = 0.002$; OR 13.92 for tolerance of CDED+PEN; 95% CI, 1.68–115.14) while being equally effective at inducing steroid-free remission at 6 weeks (75% [n = 30] on CDED+PEN vs 59% [n = 20] on EEN; $P = 0.38$). These studies not only offer promising dietary interventions but also help us better understand dietary factors that may contribute to the development and exacerbation of IBD.

In summary, EEN is a well-studied dietary intervention for treating CD, particularly in pediatrics. Further studies are needed to identify ways to improve EEN's efficacy in adults.

Specific carbohydrate diet

Specific carbohydrate diet (SCD) was first described in 1924 by Dr. Sidney Haas for the treatment of celiac disease in children. Initially, the diet was termed the "banana diet" because it required patients to eat numerous bananas daily along with milk, cottage cheese, meats, and vegetable while eliminating starches. In 1996, SCD gained interest for treating IBD from the book *Breaking the Vicious Cycle* by biochemist Elaine Gottschall, whose daughter was reportedly cured of UC after following the SCD diet for 2 years.

In SCD, the diet assumes that IBD and other intestinal disorders, such as IBS and celiac disease, are a consequence of intestinal injury caused by an overgrowth and imbalance toward pro-inflammatory gut microbes that is perpetuated by ingesting poorly absorbed carbohydrates, specifically disaccharide and polysaccharide carbohydrates. Thus, patients on SCD avoid most grains, such as wheat, barley, corn, rice, processed/canned foods, and milk. Patients eat monosaccharide carbohydrates, such as glucose, fructose, and galactose, which are easily absorbed to prevent further overgrowth and imbalance of pro-inflammatory gut microbes. Foods allowed include most fresh fruits and vegetables, meat, yogurt, nuts, and hard cheeses, just to name a few.

Studies evaluating the efficacy of SCD in IBD are sparse (Table 4), and the majority of the studies are conducted in the pediatric population and primarily include CD patients. Moreover, most of the data is limited by retrospective or case

TABLE 3. Summary of 9 Meta-analyses on Exclusive Enteral Nutrition (EEN) in IBD.

Study	No.studies	Total n	Population	Outcome: EEN vs Corticosteroid
Fernandez-Banares, 1995[60]	9	419	Adult	Inferior (0.35, (95% CI, 0.23–0.53)
Griffiths, 1995[61]	8	143	Adult	Inferior (OR 0.35, (95% CI, 0.23–0.53)
Messori, 1996[62]	7	N/A	Adult	Inferior (RTF 0.35, [(95%CI 0.23–0.53)
Heuschkel, 2000[63]	5	147	Pediatric	Noninferior (RR = 0.95, (95% CI, 0.67–1.34)
Zachos, 2001[64]	4	153	Adult & Pediatric	Inferior (OR 0.30, (95% CI, 0.17–0.52)
Zachos, 2007[59]	6	352	Adult & Pediatric	Inferior (OR 0.33, (95% CI, 0.23–0.56)
Dziechciarz, 2007[65]	4	144	Pediatric	Noninferior (RR = 0.97, (95% CI, 0.7–1.4)
Swaminath, 2017[66]	8	451	Pediatric	Noninferior (OR1.26, (95% CI, 0.77–2.05)
Narula, 2018[67]	8	223	Adult & Pediatric	Adult: Inferior (RR: 0.65, (95% CI, 0.52–0.82) Pediatric: Noninferior (RR 1.35, (95% CI, 0.92–1.97)

Abbreviations: RR, relative risk; RTF, risk of treatment failure

TABLE 4. Summary of available studies on Specific Carbohydrate Diet (SCD) and IBD

Study	Study Design	Total n	Cohort	Results
Obih 2016[66]	Retrospective observational	26	Pediatric IBD patients	• Mean PCDAI decreased from 32.8 ± 13.2 to 8.8 ± 8.5 after 6 months • Mean PUCAI decreased from 28.3 ± 10.3 to 18.3 ± 31.7 after 6 months.
Kakodkar 2015[67]	Survey study	50	Adult and pediatric IBD patients	• Mean time to symptomatic improvement: 29.2 days • 66% (n = 33) reported complete symptoms resolution • SCD was rated mean of 91.3% effective in controlling acute flare and mean of 92.1% effective at maintain remission
Suskind 2014[68]	Retrospective observational	7	Pediatric CD patients	• All patients' PCDAI decreased to 0 after 3 months on SCD. • Improvement to normalization of albumin, CRP, and Hct
Burgis 2016[69]	Retrospective observational	11	Pediatric CD patients	• Significant improvement of hct, albumin, and ESR on strict SCD (P = 0.006, 0.002, 0.002, respectively) • Lab values were stable on liberalized SCD • 90% (n = 10) gained weight percentile and 82% (n = 9) had stable or increased height percentiles on strict SCD
Suskind 2016[70]	Survey study	417	Adult and pediatric IBD patients	• 33% reported remission at 2 months on SCD and 42% reported remission at both 6 and 12 months • Of those who reported remission, 47% reported improvement in abnormal lab values. • Greater proportion of subjects requiring no IBD medication achieved remission on SCD (60.7 vs 35.6%; P < 0.001).
Cohen 2014[71]	Prospective observational	9	Pediatric CD patients	• Decrease in Harvey-Bradshaw Index (3.3 ± 2.0 to 0.6 ± 1.3; P = 0.007) and PCDAI (21.1 ± 5.9 to 7.8 ± 7.1, P = 0.011) at 12 weeks • Capsule endoscopy evaluation for mucosal healing showed decline in mean Lewis score (2153 ± 732 to 732 ± 433, P = 0.012) at 12 weeks.

Abbreviations: PCDAI, Pediatric Crohn's disease activity index; PUCAI, Pediatric ulcerative colitis activity index

series study designs. However, the available studies report promising results.[75–80] To the best of our knowledge, there has been 1 prospective study, and the investigators reported statistically significant clinical and mucosal improvement in the 9 pediatric CD patients that adhered to at least 12 weeks of SCD.[80] Similarly, a study that surveyed 417 patients reported significant improvement in GI symptoms including abdominal pain (80% before SCD and 7% after 12 months on SCD) and diarrhea (81% before SCD and 10% after 12 months on SCD). Additionally, 42% reported perceived clinical remission at both 6 and 12 months, and 47% of those patients observed improvement in laboratory values. In a 50-patient case series of both pediatric and adult IBD patients, 22 patients were able to maintain remission off medications while adhering to SCD, 16 of whom were able to wean off of steroids after starting SCD.[76] Currently, there is an ongoing study called the DINE-CD study that aims to compare the efficacy of the Mediterranean diet and SCD in reducing symptoms and inflammation in CD (NCT03058679). Additionally, the PRODUCE study is an ongoing prospective study aiming to compare the effectiveness of strict SCD with modified SCD in reducing symptoms and inflammation in pediatric IBD (NCT03301311).

In addition to its clinical benefits, SCD appears to have a high adherence rate. In their 50-patient case series, Kakodkar et al reported a mean adherence rate of 95% with the mean duration of following SCD for 35 months.[76] In a survey of 417 patients, Suskind et al reported 96% of patients were able to continue SCD, with only 7 patients citing difficulty to maintain as the reason for discontinuing the diet.[79] Additionally, the mean duration of following SCD was 32 months. Thus, despite limited data, IBD patients seem to respond to SCD with promising adherence rates. More prospective studies, particularly in adults, are needed to confirm the efficacy of SCD in IBD.

Low FODMAP

Conventionally, a low FODMAP diet, which stands for fermentable oligosaccharides, disaccharides, monosaccharides, and polyols, is prescribed to help treat patients with IBS and other functional GI disorders. Similar to SCD, FODMAP involves avoiding carbohydrates that are poorly absorbed, are fermented by intestinal bacteria, and result in increased gas production and fluid load, thus causing GI distress. The diet is divided into 3 phases: elimination, reintroduction, and maintenance—and it is notoriously difficult to follow given a laundry list of foods to avoid. Given its highly restrictive nature, particularly during the elimination phase, there are concerns for nutritional deficiencies with its long-term use. Studies have suggested the short-term exclusion of high FODMAP foods are associated with lower carbohydrate and calcium intake.[81] Data on nutritional intake with long-term exclusion of high FODMAP foods is sparse, but 1 study found no difference in those following an "adapted FODMAP diet" compared with those who returned to their previous diet.[82] However, it is important to note the investigators grouped subjects who continued to follow a strict FODMAP diet, followed a low FODMAP diet 50% of the time, and re-introduced high FODMAP foods to tolerance in the "adapted FODMAP diet" group. Thus, the nutritional profile of each subgroup is unclear. Nonetheless, it is important remember that the elimination phase is intended to be short-term because long-term strict avoidance of all high FODMAP foods may result in nutritional deficiencies.

Similar to SCD, data on using low FODMAP to treat IBD are lacking (Table 5). To the best of our knowledge, there have been 2 prospective trials evaluating efficacy of low FODMAP in IBD patients. A randomized controlled open-label study of 89 IBD patients with IBS-like symptoms reported a significant improvement in both GI symptoms and quality of life in patients who followed a low FODMAP diet for 6 weeks.[83] In fact, patients following low FODMAP were 5 times more likely to experience symptomatic improvement than patients following a normal diet (OR 5.30; 95% CI, 1.81–15.55; $P < 0.0$). In a randomized controlled cross-over trial, Halmos et al reported doubling in severity of GI symptoms after switching from a low FODMAP to a typical diet in CD patients in clinical remission, but there was no effect on fecal calprotectin.[84] There are also 2 other retrospective studies that demonstrate similar findings. In a retrospective analysis for 72 IBD patients, 70% of patients were adherent to the diet after 3 months and experienced improvement in symptoms of pain, bloating, and diarrhea.[85] Likewise, Prince et al stated that 78% of IBD patients (n = 69) reported improvement of symptoms after being referred to low FODMAP dietary education.[86] Additionally, there was significant improvement in stool consistency and frequency ($P < 0.002$). Based on the available literature, unlike SCD, a low FODMAP diet may not impact the inflammation in IBD but may offer relief for IBD patients with concurrent functional GI symptoms. This also underlines the fact that IBD patients often suffer from functional GI symptoms despite quiescent disease.[87]

Semivegetarian diet

Given the data suggesting high intake of meats and/or dietary fats may have a role in the pathogenesis of IBD, investigators have postulated that meat avoidance may have a beneficial role in the management of IBD. However, data supporting this practice are ambivalent and sparse. A small prospective study of 22 CD patients in Japan found following a semivegetarian diet, where only fish was allowed once a week and meat was allowed once every two weeks, was associated with remission in 94% (15 of 16) compared with 33% of patients (2 of 6) in the omnivorous diet group.[88] The investigators reported 73% (n = 16) of patients were able to maintain the study diet. Similarly, a small study using a IgG4-guided exclusion diet, where animal proteins were the most commonly eliminated foods, reported symptomatic improvement in 90% of patients (n = 26) who followed the dietary interventions.[89] Of note, of the 40 patients initially recruited, 5 subjects were

TABLE 5. Summary of Available Studies on Low FODMAP (LF) Diet and IBD

Study	Study Design	Total n	Cohort	Results
Pedersen 2017[74]	Randomized controlled open-label trial	89	Adult IBD patients with quiescent to mild/moderate disease and coexisting IBS symptoms	• Significantly larger proportion of responders (at least 50-point reduction in IBS symptom severity system) in LF group (81%) vs normal diet group (46%, OR:5.30 (95% CI, 1.81–15.55). •LF group had significantly greater increase than normal diet group in short IBD quality of life questionnaire score at week 6 (median 60, IQR51-65 vs median 50, IQR 39–60, $P < 0.01$).
Gearry 2009[75]	Survey study	52	Adult IBD patients who received instruction on low FODMAP diet	• ~50% of patients had improvement in ≥5 out of 10 overall symptoms on LF. •Significant improvement in abdominal symptoms, abdominal pain, bloating, wind, and diarrhea on LF ($P < 0.02$).
Prince 2016[76]	Retrospective observational	88	Adult IBD patients with functional GI symptoms independent of degree of inflammation	• Significant increase in proportion of patients reporting satisfactory relief of functional-like GI symptoms after LF (16% at baseline vs 78% at follow-up, $P < 0.001$). •Improvement in proportion of patients reporting normal stool frequency (once every 3 days to 3 times/day) (60% at baseline vs 81% at follow-up, $P < 0.001$) after LF.
Halmos 2016[77]	Randomized controlled cross-over trial	9	Adult CD patients in clinical remission	• GI symptom severity of GI symptoms was 50% lower on the LF compared with typical diet ($P < 0.001$). •Neither diets had effect on fecal calprotectin.

excluded due to dietary noncompliance. Although the 2 previous studies were limited by observational study designs and small sample sizes, a recent large randomized controlled trial involving 213 CD patients found reduced meat consumption (consuming ≤1 serving of red or processed meat per month) did not reduce the risk of CD flare compared with those with high meat consumption (consuming ≥2 servings of red or processed meat per week).[51] The average adherence rate was 57% throughout the study. Based on the available data, the benefit of reducing meat consumption in IBD is unclear. The discrepancies between the available data are potentially due to differences in study design (including intervention diet design) and regional dietary practices (Asian vs Western dietary practices despite eliminating meat). Lastly, the question of adherence is difficult to answer due to the different diets among the available studies, but the reported values are relatively similar to the reported rates of the other dietary interventions. Further multicenter—possibly multinational—studies are needed to better understand if reducing meat intake can treat IBD.

Finally, it is worth noting curcumin, which is a naturally occurring substance found in turmeric, might be a promising dietary agent for treating IBD via its action on NF-κB.[90–92] Current data have found 2 to 3 g daily in combination with 5-aminosalicylate is effective in inducing and maintaining remission in mild to moderate UC.[93, 94] Another study found curcumin resulted in clinical and endoscopic improvement in patients with active CD.[95] Though more prospective studies are needed to confirm its efficacy, curcumin may be a promising dietary supplement to conventional IBD therapies in select IBD patients.

CONCLUSION

Patients often view diet as a crucial component in the management of their IBD, but 50%–69% of patients report not receiving any information about it.[11, 12] With the anticipated increase in prevalence of IBD in the coming years, providers will more frequently be asked about diet in IBD. Thus, the aim of this review is to empower providers and patients with answers about diet in IBD based on the available literature. So, what can we answer?

1) Although the role of diet in the development of IBD remains unclear, the available literature suggests its impact on the gut microbiome and intestinal barrier function may make certain individuals more susceptible to IBD, but not one food causes IBD.
2) Data have not shown that foods can increase inflammation in IBD in humans, but they can exacerbate GI symptoms. This likely reflects a sensitized gut as a sequela of chronic inflammation. The most common foods patients avoid include spicy foods, dairy, fatty foods, and fibrous vegetables. However, one size does not fit all, and dietary avoidance must be individualized without sacrificing adequate nutrition.
3) There are a lot of diets for treating IBD, but data supporting their efficacy are sparse and primarily include pediatric patients. Exclusive enteral nutrition has the strongest data, but most of the studies support its use in pediatric patients. More studies are desperately needed to identify effective diets to treat IBD in adults.

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