

ADVANCES IN IBD

Current Developments in the Treatment of Inflammatory Bowel Disease

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The Role of Diet in Inflammatory Bowel Disease



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G&H What is the current understanding of the pathogenesis of inflammatory bowel disease? Does diet play a role?

JL Inflammatory bowel disease (IBD) is caused by a combination of one's genetic makeup and environmental exposures. Presumably, both of these factors contribute to an overly robust immune response to the organisms living in an individual's intestines.

In terms of the potential role of diet as a contributor to the cause of IBD, current evidence does point in that direction. Observational studies have shown associations between dietary patterns and the risk of being newly diagnosed with Crohn's disease and ulcerative colitis. These studies have typically demonstrated that greater consumption of meat and animal products is associated with the onset of Crohn's disease and ulcerative colitis, whereas greater consumption of fruits and vegetables is typically associated with a lower incidence of these diseases.

G&H What mechanisms could explain why diet has a role in causing IBD?

JL Many hypotheses have been put forth as to how diet could contribute to the etiology of IBD. Some of these hypotheses feature a direct relationship between diet and IBD. For example, it has been suggested that diet can directly alter the composition of the microbiome to cause IBD. Another hypothesis has suggested that dietary antigens trigger an immune response. Finally, diet influences the production of metabolites by the organisms living in the gut (ie, the organisms produce small molecules that may initiate or perpetuate IBD).

It should also be pointed out that diet has the potential to impact the mucous layer, which protects the epithelium from the contents of the gut. This is important because not only does the gut include microorganisms that live there, it also includes the small molecules that are derived from food products or that are directly produced by the organisms that inhabit that area.

Other hypotheses have suggested that diet has an indirect effect on IBD, such as changing bile acid profiles or causing direct or indirect effects on immune function. Many basic science investigations have been undertaken to explore these different hypotheses.

G&H Does diet have a role in terms of treating IBD?

JL A number of different diets have been used as treatment for people who have active IBD. Most of this work, at least the most promising, has been in Crohn's disease, rather than in ulcerative colitis.

The strongest evidence for the role of diet as a therapeutic modality for Crohn's disease comes from studies of exclusive enteral nutrition, meaning the provision of nutrients with a defined formula, or a formula-based diet. The studies that have shown the greatest promise typically have used these formula-based diets to provide 90% or more of caloric intake. The makeup of the formula does not seem to be as important. For example, some of the formulas have completely hydrolyzed protein, vs partially hydrolyzed protein, or even intact proteins, and the efficacies of these formulas appear to be comparable. Similarly, studies have directly compared formulas that have a high fat concentration or a low fat concentration, and the efficacies of these formulas appear to be comparable.

There is currently much interest in identifying more palatable and easier-to-use diets for the long-term management of IBD because these formula-based diets are generally impractical for long-term use.

G&H Are there any other disadvantages or limitations to formula-based diets?

JL There are a number of substantial limitations to these diets. The most obvious is that people like to eat. In the Western world, eating is a very social event, and it is disadvantageous to patients if they are not able to participate.

Another disadvantage is cost; for example, a month's supply of a formula-based diet is generally more expensive than standard food bought at a grocery store. In certain situations, an insurance company will pay for formula-based diets, but that is not uniformly the case.

A third major disadvantage is that most of these diets do not taste very good. In fact, these diets are often administered by a nasogastric tube while people sleep at night. For all of these reasons, it is difficult to envision using these diets for long-term maintenance therapy for most IBD patients.

G&H Why do formula-based diets help patients with IBD?

JL Understanding how formula-based diets work in Crohn's disease is an important area of ongoing research. A number of potential hypotheses have been put forth. One hypothesis is that these diets are better able to provide specific nutrients that may be needed for healing the mucosa. An alternative hypothesis suggests the opposite—that formula-based diets are an extreme example of an exclusion diet and that their effectiveness may be related to what the patient is not eating, as opposed to what he or she is eating.

There are also a number of intermediary hypotheses suggesting that formula-based diets improve IBD because they alter the gut microbiome and/or change the metabolome that is present in the gut lumen.

G&H Have any controlled clinical trials been conducted on formula-based diets in IBD patients?

JL Unlike clinical trials of drugs, it is not possible to conduct a placebo-controlled trial of a diet because all people need to eat something. It is possible to conduct blinded trials of 2 different formula-based diets, but not a blinded trial of a formula-based diet vs a regular diet, with or without another treatment.

However, a number of trials have compared formula-based diets to corticosteroid therapy. One of the most compelling observations comes from a randomized, controlled trial of formula-based diet vs corticosteroids. While patients demonstrated clinical improvement with both

treatments, evidence of healing of the epithelium was only seen in those treated with the formula-based diet.

G&H What research has been conducted on the effects of other diets on IBD?

JL Both observational studies and small clinical trials have been conducted on other dietary interventions for patients with Crohn's disease and ulcerative colitis. Over a decade ago, a study was published that looked at patients with ulcerative colitis who had recently gone into remission and asked them about their normal dietary patterns. These patients were then followed to see whether their normal dietary patterns were associated with the risk of having a relapse of their disease. In this study, patients who consumed more eggs, meat (particularly red and processed meat), and alcohol were more likely to experience a relapse of their disease than patients who consumed low levels of those items. This was one of the earlier modern-day studies that suggested that altering a patient's regular diet in less extreme ways might improve the patient's outcomes for IBD.

Other studies have largely been small and observational in nature, although there was a large, randomized trial from nearly 30 years ago of a diet that included refined sugars vs one that included carbohydrates only in their natural form (ie, no sugar or white flour). This study found a difference in the rate of people undergoing surgery for Crohn's disease over a period of 2 years. However, a number of other outcomes that were examined were not significantly different between the treatment groups. Continued investigation of this issue is warranted.

More recently, there has been some interest in semi-vegetarian diets for Crohn's disease, based on a small study that suggested that patients who followed a semi-vegetarian diet may be more likely to remain in remission than those who were eating a more meat-heavy diet. Perhaps one of the most interesting studies that was recently put forth was by Ari Levine and colleagues. In this study, patients followed a fairly extreme exclusion diet (which required the avoidance of gluten, dairy products, gluten-free baked goods and breads, animal fats, processed meats, any products containing emulsifiers, canned foods, and so on) and also received up to 50% of their calories from a formula-based diet. This was a very compelling preliminary study because over 70% of the participants experienced resolution of their symptoms, normalization of their C-reactive protein levels, and, in the small group that underwent repeated colonoscopies, healing of the mucosa. These types of studies point to the idea that exclusion diets could be useful in the treatment of Crohn's disease.

G&H Based on all of the information currently available, should any patients with IBD make adjustments to their regular diet?

JL The simplest answer for almost any patient with IBD is that he or she should be eating a healthy diet, if he or she is not already doing so. In the absence of other evidence, I would define a healthy diet as a Mediterranean-style diet because of its many health benefits. This type of diet also offers the possibility of a therapeutic benefit for patients with IBD, in part because it is characterized by lower consumption of red and processed meats and increased consumption of fruits and vegetables.

In addition, I recommend that patients eat fresh foods, meaning that they should go to the grocery store, buy ingredients, and prepare their own food, as opposed to buying food that is prepackaged and processed. There are not much data to support this recommendation for IBD other than some animal models that suggest that emulsifiers may be harmful to the intestines and could contribute to inflammation. Most of the studies discussed above rely on people eating fresh foods, as opposed to processed foods.

In terms of altering diets, we know that many patients already do so, avoiding foods that they believe worsen their symptoms and, to a lesser extent, eating foods that they believe help their symptoms. As long as people are getting adequate nutrition, I think that it makes sense for them to avoid foods that exacerbate their symptoms. For patients with strictures in their bowel, such exclusions might include high roughage foods. However, even patients who do not have strictures in their intestines have identified certain foods that they think worsen their symptoms and, therefore, often avoid these foods.

In terms of restriction diets, there are many that are popular for patients with Crohn's disease, such as the diet put forth by Levine, or a similar diet referred to as the Specific Carbohydrate Diet. The decision to follow one of these diets should be made after a discussion between the patient and the physician. If the physician and the patient agree to use diet as a primary therapy, I think that it is important that the diet is held to the same standard as other therapy; in other words, the physician should look for evidence not just that the patient is feeling better, but that the dietary intervention is actually reducing inflammation in the patient's bowel.

G&H Is the ultimate hope that dietary modification by itself might be able to induce or retain IBD remission in the future?

JL We should not view dietary intervention as an all-or-nothing phenomenon. When looking at medical therapy, there are some patients who are adequately managed with one medication, while others require multiple medications. In the future, there will likely be a subpopulation of patients with Crohn's disease or ulcerative colitis whose inflammation can be controlled with a therapeutic diet. For other

patients, dietary manipulation may be an ancillary therapy that can allow them to use less immunosuppression and still remain in remission. Finally, as with all medical therapies, there will almost certainly be a subset of the population in which dietary therapy is completely ineffective.

G&H What are the next steps in research?

JL There are 3 lines of research that are actively being pursued. One involves clinical trials of dietary interventions for patients with IBD that are aimed at either inducing or maintaining remission. The second line of research is trying to understand the mechanisms by which defined formula diets and/or extreme restriction diets are able to improve the symptoms and inflammation that characterize IBD. The third line is related to the second—continuing to examine the fundamental impact of diet on immune function as well as the composition and function of the gut microbiome and other related biochemical processes.

As mentioned above, we already know that patients are routinely altering their dietary practices because they are often convinced that what they eat impacts the course of their disease. It is beholden to us as physicians and scientists to listen to patients and apply scientific principles to figure out if there is a diet that would offer a therapeutic benefit, such that we could advance the science to the same level as that for drug therapy.

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Suggested Reading

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