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# Crohn's Disease Prevention and Treatment with a Plant-Based Diet



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## Abstract

Epidemiologic studies show that IBD is prevalent in wealthy nations where dietary westernization usually occurs. Dietary westernization is characterized by increased consumption of animal protein, animal fat, and sugar. An epidemiological study found that the risk of Crohn's disease reduced by 70% in females and 80% in males following a vegetarian diet. Treatment with medications, though efficacious to a degree, all have significant adverse reactions. Many of these medications will also be contraindicated in a significant number of patients.

Treatment is aimed at inducing remission. A semi-vegetarian diet has been shown to achieve a 100% remission rate at 1 year and 92% at 2 years. Plant-based diets are rich in phytochemicals that help reduce inflammation by modifying several inflammatory mechanisms. A study of treatment with infliximab and a plant-based diet showed a remission rate of 96%, substantial reduction in CRP and CDAI and improvements in mucosa healing. This study shows that combining infliximab with a plant-based diet results in a strong clinical response.

Plant-based diets promote a more favorable gut microbial profile that is anti-inflammatory. Naturally occurring substances in plant foods, having anti-inflammatory bowel actions include phytochemicals, antioxidants, dietary fibers, and lipids. Many of these natural products exert their beneficial action by altering cytokine production. The plant-based diet has no adverse reactions or contra-indications and is affordable, so physicians can initiate therapy with a plant-based diet immediately, and prescribe it as a prophylaxis for all patients at risk of Crohn's disease.

**Keywords:** Crohn's Disease; Plant-based diet; Vegetarian; Vegan; Biologics; Microbiota; Cytokines; Inflammatory bowel disease; Phytochemicals

## Introduction

Crohn's disease is difficult to treat and can be frustrating for both the patient and their physician. Safer and more efficacious treatments are needed for this disease.

The current standard treatment for Crohn's disease involves medication to manage symptoms and induce remission, and when necessary, bowel resection. Medications used in the treatment of Crohn's disease include the following:

- I. 5-Aminosalicylic acid derivative agents (eg. mesalamine rectal, mesalamine, balsalazide)
- II. Corticosteroids (eg. prednisone, methylprednisolone, budesonide)
- III. Immunosuppressive agents (eg. mercaptopurine, methotrexate, tacrolimus)
- IV. Monoclonal antibodies (eg. infliximab, adalimumab, certolizumab pegol, natalizumab, vedolizumab)
- V. Antibiotics (eg. metronidazole, ciprofloxacin)

VI. Antidiarrheal agents (eg. loperamide, diphenoxylate-atropine)

VII. Bile acid sequestrants (eg. cholestyramine, colestipol)

VIII. Anticholinergic agents (eg. dicyclomine, hyoscyamine, propantheline)

These medications, though efficacious to a degree, all have significant adverse reactions. Many of these medications will also be contraindicated in a significant number of patients.

Most patients with Crohn's disease require surgical intervention during their lifetime, as it plays an integral role in controlling the symptoms and treating the complications of Crohn's disease, but operative resection is not curative. Because of the high rate of disease recurrence after segmental bowel resection, the guiding principle of surgical management of Crohn's disease is preservation of intestinal length and function [1].

Mean annual costs for Crohn's disease are about \$8265. 31% of costs were attributable to hospitalization, 33% to outpatient care, and 35% to pharmaceutical claims. The annual dollar cost for Crohn's disease in the United States is \$3.6 billion [2]. It can reasonably be concluded that Crohn's is both difficult and expensive to treat.

Symptoms of Crohn's disease may subside with total parenteral nutrition or total enteral nutrition, but it is well known to flare up after the resumption of meals. Therefore, the food in patient's meals are thought to be an etiologic factor in gut inflammation [3]. While parenteral nutrition is possible, nutrition taken orally is to be preferred if it won't cause a flare up, or even better, if it can prevent flare ups and induce remission. This is what a vegetarian diet seems to accomplish.

### Prevention

The etiology of Crohn's disease is unknown. Genetic, microbial, immunologic, environmental, dietary, vascular, and psychosocial factors have been implicated, as have smoking and the use of oral contraceptives and nonsteroidal anti-inflammatory agents (NSAIDs).

Epidemiology shows that IBD is prevalent in wealthy nations [4-6] where dietary westernization inevitably occurs [7,8]. Dietary westernization is characterized by increased consumption of animal protein, animal fat, and sugar. Diets rich in animal protein and animal fat cause a decrease in beneficial bacteria in the intestine [9,10]. However, the risk of Crohn's disease was found to be reduced by 70% in female and 80% in male young people following a nearly vegetarian diet [11].

### Treatment

Treatment is aimed at inducing remission. An important and well-designed study published in 2010, using a semi-vegetarian diet, achieved a 100% remission rate at 1 year and 92% at 2 years [12]. A more advanced study published in 2017 examined whether a substantial improvement of the relapse-free rate in Crohn's Disease could be obtained by incorporating three recently developed concepts in medicine: biologics, a plant-based diet and window of opportunity. This was followed by maintenance of remission with a plant-based diet, rather than further use of biologics with or without immunosuppressants [13].

Patients were treated with infliximab and a plant-based diet. The primary end point was clinical remission at week 6. Secondary end points were normalization of C-reactive protein (CRP) concentration at week 6 and mucosal healing. Crohn Disease Activity Index (CDAI) score was also evaluated [13].

All patients in this study who completed the protocol achieved remission at week 6. Remission rates by intention-to-treat and per protocol analysis were 96% and 100%, respectively. The rates of CRP normalization at week 6 were 92% among adults with a new diagnosis, 82% among children with a

new diagnosis and 67% among relapsing adults. The mean CDAI score was significantly decreased from 314 before treatment to 163 after the first week. The scores were further decreased chronologically: 115, 98, 82, 74, and 63 at weeks 2, 3, 4, 5, and 6, respectively. Mucosal healing was achieved in 46% patients. This study has shown that a plant-based diet can improve the efficacy of biologics such as infliximab.

Plant-based dietary patterns may promote a more favorable gut microbial profile. Such diets are high in dietary fiber and fermentable substrate (i.e. non digestible or undigested carbohydrates), which are sources of metabolic fuel for gut microbial fermentation and, in turn, result in end products that may be used by the host (i.e. short chain fatty acids such as butyrate). These end products may have direct or indirect effects on modulating the health of their host [14].

The naturally occurring substances in plant foods having anti-inflammatory bowel actions include phytochemicals, antioxidants, microorganisms, dietary fibers, and lipids. The literature indicates that many of these natural products exert their beneficial action by altering cytokine production. Specifically, phytochemicals such as polyphenols or flavonoids are the most abundant, naturally occurring anti-inflammatory substances. The effects of lipids are primarily related to the n-3 polyunsaturated fatty acids. The effects of phytochemicals are associated with modulating the levels of tumor necrosis factor  $\alpha$  (TNF- $\alpha$ ), interleukin (IL)-1, IL-6, inducible nitric oxide synthase, and myeloperoxidase. The anti-IBD effects of dietary fiber are mainly mediated via peroxisome proliferator-activated receptor- $\gamma$ , TNF- $\alpha$ , nitric oxide, and IL-2, whereas the effects of lactic acid bacteria are reported to influence interferon- $\gamma$ , IL-6, IL-12, TNF- $\alpha$ , and nuclear factor- $\kappa$  light-chain enhancer of activated B cells. These results suggest that the anti-IBD effects exhibited by natural products are mainly caused by their ability to modulate cytokine production [15].

Studies, conducted using in vivo and in vitro models, provide evidence that pure polyphenolic compounds and natural polyphenolic plant extracts can modulate intestinal inflammation [16]. Polyphenols may thus be considered able to prevent or delay the progression of Crohn's disease, especially because they reach higher concentrations in the gut than in other tissues [17].

While not perfect, of all the laboratory markers, C-Reactive Protein (CRP) is the most studied and has been shown to have the best overall performance. CRP is an objective marker of inflammation and correlates well with disease activity in Crohn's disease [18]. It is produced as an acute phase reactant predominantly in the liver, in response to stimulation by interleukin (IL)-6, TNF- $\alpha$  and IL-1 $\beta$ , which are produced at the site of inflammation [19].

Adipocytes in hypertrophied mesenteric adipose tissue produce and secrete significant amounts of adiponectin, which

may be involved in the regulation of intestinal inflammation associated with Crohn's disease. Furthermore, adiponectin concentrations in hypertrophied mesenteric adipose tissues of Crohn's disease patients correlated inversely with serum CRP levels ( $r=-0.51$ ,  $p=0.015$ ) [20] There is a good correlation between CRP and other measures of inflammation such as the Crohn's Disease Activity Index, radioactive labelled fecal granulocyte excretion and fecal calprotectin [21-23].

Plant-based diets have been shown to increase adiponectin in diabetics, and reduce CRP in both diabetics and patients with coronary artery disease, and may well be doing the same in Crohn's disease patients [24-26]. This improved profile of cytokines may be part of the therapeutic efficacy of plant-based diets in Crohn's disease.

### Discussion

To put the efficacy of a vegetarian diet into perspective one must compare it to standard treatments. Overall, despite the use of oral mesalazine treatment in the past, new evidence suggests that this approach is minimally effective as compared with a placebo, and less effective than budesonide or conventional corticosteroids. Induction of remission was noted in 52% of Crohn's disease patients.

Maintenance of remission was reported in 71% of Crohn's disease patients on azathioprine over a 6-month to 2-year period. Induction and maintenance of remission was noted in 70% of Crohn's disease patients on methotrexate over a 40-week period. Induction of remission was reported in 32%, 26%, and 20% of Crohn's Disease patients on infliximab, adalimumab or certolizumab, respectively. Approximately one-fifth of Crohn's disease patients treated with biologicals require intestinal resection after 2-5 years in referral-center studies [27]. The adverse reactions of the above medications are well-known, as are the risks and complications of surgery. The safety and efficacy of a plant-based diet to treat Crohn's disease would seem quite advantageous. It has no contraindications and no adverse reactions. Therefore, it may be safely combined with standard treatments.

Treatment with a plant-based diet also reduces the risk of common diseases that the Crohn's patient will face in common with all patients, such as coronary artery disease and type II diabetes mellitus. Given the substantial advantages more study is warranted. However, given its safety the physician can institute therapy with a plant-based diet immediately.

Finally, every physician should practice prevention. The decreased risk of Crohn's disease obtained with a plant-based diet is considerable. It is a safe prophylaxis, and should especially be prescribed for patients at risk because of family history or because of cigarette smoking.

### Conflict of Interest

The authors have no conflicts of interest to disclose.

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