

# Diet Affects Symptoms and Medication Response in Inflammatory Bowel Disease

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Crohn's disease (CD) and ulcerative colitis (UC) are chronic relapsing inflammatory bowel diseases (IBD) of which the etiologies are not fully understood. Genetic and environmental factors are likely central to both diseases. In societies that adapt a Westernized diet consisting of increased refined sugars, decreased complex carbohydrates, and increased fats, the incidence of IBD is rising. There is a possible role of diet in the etiopathogenesis of IBD coupled to increasing evidence in support of the significance of diet in the management of IBD.

The mechanism by which diet affects inflammatory bowel disease remains unclear. The intestinal microbiome has been associated with IBD, obesity [1], and diabetes [2, 3]. IBD patients have a loss in biodiversity in their intestinal flora coincident with an increase in the proportion of fungi [4]. There are three predominant variants of the gut microbial community, known as “enterotypes” dominated by *Bacteroides*, *Prevotella*, and *Ruminococcus* [5], which are strongly associated with long-term dietary habits and do not change with short-term changes in diets [6]. Long-term dietary interventions may modify an individual's enterotype, which could possibly alter the natural history of disease in IBD.

In the study by James Lewis and colleagues published in this issue of *Digestive Disease and Sciences*, the authors recruited 8,000 participants from 250 countries derived from a large-scale Internet-based cohort (e-cohort) of

patients living with IBD [7]. A semi-quantitative food frequency questionnaire (FFQ) revealed that yogurt and rice more frequently improved symptoms in all subjects whereas bananas improved symptoms in subjects with UC who have a pouch (UC-pouch). In contrast, non-leafy and leafy vegetables, high fiber foods, corn, spicy foods, fruit, nuts, fried foods, milk, red meat, soda, popcorn, dairy, alcohol, fatty foods, seeds, coffee, and beans were more frequently reported to worsen symptoms. Moreover, when compared to CD without an ostomy, CD patients with an ostomy reported a greater consumption and more liberalized dietary items including cheese, pizza, milk, sweetened beverages, and processed meats. As suggested by the authors, dairy was reported to worsen symptoms across most of the subjects, which could have reflected inherent lactose intolerance. Red meat was more commonly reported to worsen symptoms in all subjects except UC-pouch patients. This is the largest study to date on the relation of dietary intake to IBD and one of the first studies to link diet to IBD symptoms. Using the Likert scale, the authors assessed patients' symptoms, using logistic regression to associate IBD activity with specific food items. The large size of the patient cohort enabled the authors to include patients with ostomies and ileoanal J pouches.

This study demonstrates the recruiting power of a multinational internet cohort, a population which will no doubt serve as the basis for many future epidemiologic and clinical trials. The lack of detailed measurements of disease activity and mucosal healing pales in comparison to the amount of novel information gained from this huge database reliant on subject self-reporting. These findings will be very useful for physicians in counseling patients about modifying their diets during states of remission to prevent symptom relapse and during flares of disease to decrease symptoms.

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The therapeutic value of diet is greater for CD when compared to UC. Enteral nutrition (EN), administered orally or via tube feeds, reduces inflammatory markers [8] and mucosal cytokines [9], while improving gut permeability [10] and modifying gut flora [11]. In one non-randomized trial, the relapse rate at 1 year was 25 % in the EN group versus 65 % in the non-EN group, with reported significant improvement in average endoscopy scores, with decreased mucosal concentrations of IL-1b, -6, and TNF [9]. In a meta-analysis of seven studies, EN with elemental, semi-elemental or polymeric diets orally or via tube feeds had higher clinical remission rates compared to groups ingesting ordinary foods [12].

The benefit of EN in the maintenance of remission in CD was further supported by the retrospective study by Fumihito Hirai and colleagues published in this issue [13]. The goal of this study was to determine whether EN added to infliximab (IFX) therapy is effective for maintaining remission in adult CD patients compared with IFX alone. In the EN group, 31.1 % (14/45 patients) had recurrence compared to 57.8 % (33/57 patients), recurrence being defined as an increase in C-reactive protein (CRP) to  $\geq 1.5$  or a shortened interval of IFX administration of  $\leq 4$  weeks. Weaknesses of the study were several, including using the CRP and a shortened IFX administration interval to measure recurrence rather than clinical activity scores such as the CD Activity Index or the Harvey–Bradshaw Index. Further, EN is often not palatable, requiring administration via nasogastric or gastric tubes. Lastly, the non-EN group had some exposure to EN. If this group had no EN exposure, perhaps the difference between the two groups may have been greater.

In conclusion, the two studies published in this issue of *Digestive Diseases and Sciences* highlight the influence of nutrition in the management of IBD. The first article should inform physicians and nutritionists regarding the recommendation of specific diets based on disease and bowel anatomy. Although these specific diets may help improve symptoms during remission states and during flares of disease, further studies to evaluate whether there is an improvement in endoscopy scores or inflammatory markers are needed. The second study, which used objective data to assess recurrence of disease, should strengthen the notion that EN can be an important part of CD treatment, especially for those patients refusing or failing conventional therapy. Dietary therapy has already been adopted in other countries: in Japan, guidelines recommend nutritional therapy as a first-line therapy and as a maintenance therapy after inducing remission in CD [14]. Perhaps it is time for us in the Western world to learn from the Japanese and incorporate EN or at least more specific nutritional therapy into our algorithm for treating CD.

## Key Concepts

- Diet can influence symptoms in UC subjects, with some responses predicated on gut anatomy.
- In CD, EN combined with IFX therapy achieves greater remission rates when compared to IFX therapy alone.

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