EDITORIAL

The Role for Food Allergies in the Pathogenesis of Irritable Bowel Syndrome: Understanding Mechanisms of Intestinal Mucosal Responses against Food Antigens

See "Many patients with irritable bowel syndrome have atypical food allergies not associated with immunoglobulin E," by Fritscher-Ravens A, Pflaum T, Mosinger M, et al, on page 000.

Irritable bowel syndrome (IBS) is a common functional gastrointestinal disorder, which is a heterogeneous condition with multiple etiologies, including abnormal reactions related to foods.[1,2] Indeed, many patients with IBS commonly report adverse reactions against certain foods.[3,4] Moreover, many studies have investigated the role of food allergies in patients with IBS[5–8]; however, the underlying mechanisms related to certain foods have not been fully elucidated. In this issue of *Gastroenterology*, the study by Fritscher-Ravens et al[9] provides evidence of abnormal reactions to individual foods and associated pathophysiologic changes in patients with IBS.

Low-grade mucosal inflammation is now recognized as a pathophysiologic feature in IBS[10,11] and a variety of mechanisms may contribute to this, including diet. Certain foods may trigger an aberrant immune reaction and/or can increase intestinal permeability in patients with IBS.[6,12–14] Indeed, several studies have shown that in more than one-half of patients with IBS, their symptoms worsened after consuming specific foods such as wheat products, cow's milk, soy sauces, and eggs.[6,14] Moreover, several studies demonstrated that elimination diets for fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAPs) and other foods are effective for reducing IBS symptoms, in particular when patients suspect that their gastrointestinal symptoms are due to certain foods.[15–17] Because food allergies are generally caused by IgE-mediated type 1 hypersensitivity, several studies have tried to identify systemic responses to food antigens with skin prick tests or Ig E antibodies in patients with IBS.[18–20] The results of these studies were inconclusive, but questions remain as to whether abnormal responses to foods could be localized and limited to the intestinal mucosa.

Several studies used food allergen provocation tests, in which food allergens were injected into the cecal or rectal mucosa.[5,6,8,21] In these studies, about two-thirds of patients with IBS showed mucosal wheal and flare reactions along with increased mast cell and eosinophil activation, whereas healthy controls did not have these reactions. Furthermore, with a small number of cases, Fritscher-Ravens et al[8] examined the structural/functional changes of the intestinal mucosa, by using confocal laser endomicroscopy for real-time observation in patients with IBS and controls. They found that about two-thirds of patients with IBS showed abnormal mucosal changes including the formation of epithelial leaks/gaps and the widening of intervillous spaces after food challenge. About two-thirds of patients with IBS who had abnormal mucosal reactions to certain foods showed improvement of IBS symptoms after a 12-month exclusion diet. These findings indicated that hypersensitivity reactions against certain food allergens take place in the intestinal mucosa in a subset of patients with IBS. Consistent with these findings, Vazquez-Roque et al[7] also showed that a gluten-containing diet increased intestinal permeability in patients with IBS. Further, they found that patients with IBS on the gluten-containing diet had a decreased expression of *zonula occludens 1, claudin-1, and occludin* in rectosigmoid mucosa. Wheat, which has gluten in it, is one of the food antigens used in the study of Fritscher-Ravens et al[9] in the current issue of *Gastroenterology.*

Fritscher-Ravens et al[9] evaluated the underlying cellular and biochemical pathophysiology of atypical food allergies in a substantial number of patients with IBS who suspected their symptoms were related to food ingestion. Among patients who completed the study, 70% showed a positive reaction as demonstrated by confocal laser endomicroscopy, which was defined as a postchallenge increase of epithelial leaks with the secretion of fluorescein-labeled plasma into the lumen and the presence of fluorescent signal between enterocytes. Moreover, patients had improvement of IBS symptoms when they excluded those foods to which they reacted. More important, they showed that the confocal laser endomicroscopy positive patients with IBS had more intraepithelial lymphocytes, up-regulated *claudin-2* expression, decreased *occludin* protein, and higher eosinophilic cationic protein. These changes, therefore, reveal that a subset of patients with IBS had abnormal intestinal mucosal responses to food resulting in dysfunction of the barrier.

This study demonstrates the frequency of, a mechanism for, and the benefit of avoidance of reactive foods in patients with IBS. This work provides support for the identification of, and subsequent exclusion of specific foods as a treatment for IBS. This approach of identification and then exclusion differs from the empiric trials of diets that more broadly limit food categories such as FODMAPs or high fiber foods.[15,16,22] However, this field is still in its infancy, and further large studies are warranted to fully reveal the relationship of dietary factors, innate and adaptive immune responses, and mucosal interactions that occur in IBS. Understanding the structural changes in small intestinal mucosa provides the opportunity of targeting this effect as a therapeutic alternative to the often not so simple food avoidance.

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Conflicts of interest
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