# Irritable Bowel Syndrome and Functional Dyspepsia: Different Ends of the Same Spectrum of Intestinal Barrier Dysfunction?

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# Irritable Bowel Syndrome and Functional Dyspepsia: Different Ends of the Same Spectrum of Intestinal Barrier Dysfunction?


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I read with interest the article from Nojkov et al. (1) describing the role of duodenal barrier dysfunction as an important underlying mechanism for the development of functional dyspepsia (FD).

More recently, the focus in FD has also increasingly shifted to the small intestine (more specifically the duodenum), in which the intestinal barrier dysfunction and the influx of inflammatory cells, in particular eosinophils and mast cells, have been indicated to being key players. The study by Nojkov et al. (1) elegantly demonstrates this using a combination of confocal laser endomicroscopy and *ex vivo* techniques and complements work performed previously by others (in particular the Tack and Talley groups) on the subject.

Small intestinal barrier function has also received considerable attention as a potential pathomechanisms in irritable bowel syndrome (IBS) (2), and this in fact predates similar hypotheses with regards to FD. More interestingly, other studies in patients with IBS using confocal laser endomicroscopy have demonstrated largely similar barrier defects in the distal duodenum (3), terminal ileum (4) and colon (5) to those observed in the Nojkov study in FD patients.

Considering the substantial symptomatic overlap between IBS and FD, one wonders whether these disorders are in fact part of the same underlying problem, i.e., intestinal barrier dysfunction. This overlap is further highlighted by the fact that in one of the landmark studies on FD and intestinal barrier dysfunction, 9 of 15 (60%) FD patients also had comorbid IBS (6).

The magnitude and the anatomical distribution (duodenum to colon) of this disturbance would then determine whether the symptoms are more skewed toward primarily upper or lower gastrointestinal phenomena. Importantly, abnormal sensations, in particular pain and discomfort, arising from the gastrointestinal tract are common denominators for both disorders, and the influence of the inflammatory infiltrate on afferent signaling function provides the rationale behind this hypothesis. In this sense, an overarching concept of barrier dysfunction is not necessarily at odds with the new Rome IV concept of interpreting these as disorders of the gut-brain interaction. On the contrary, it tributes to the need for identifying structural changes that allow us to move away from the negative connotations associated with a "functional" disorder.

What, however, remains a challenge is identifying the ways to improve or reinforce barrier function. Although the concept has been around for quite some time, we have yet to find effective ways to correct these defects. A phase III study currently ongoing in celiac disease, using larazotide acetate, a synthetic antagonist to zonulin, an endogenous protein that modulates intestinal tight junctions, might provide important leads to further research in other areas, such as FD or IBS. The solution need not necessarily be pharmacological because previous studies have pointed to specific food-derived substances driving barrier dysfunction (3). Either way, embracing the concept of leaky gut provides a unique opportunity to refining therapies for a large group of patients.

## CONFLICTS OF INTEREST

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