

## ***An Integrative Approach for Treating Irritable Bowel Syndrome***

Irritable Bowel Syndrome (IBS) is a multi-factorial disorder that can have emotional, physical and nutritional influences. In treating this common condition, all areas should be addressed.

### **Emotional influence: Mind-Body Therapy**

The enteric nervous system has so many nerve endings and neurotransmitters that it has been referred as the “second brain.” When the mind is under stress, the GI tract often sympathizes by having spasms, bloating and discomfort. This strong interaction also gives insight to common metaphors such as, “I have a gut feeling” or “I have butterflies in my stomach” or “Something is eating me up inside.”

The mind-body therapies that have the best evidence for IBS include Cognitive Behavioral Therapy (CBT) and Gut-directed Hypnotherapy (GDH).

- **Cognitive Behavioral Therapy (CBT)**  
CBT focuses on two general themes regarding IBS: 1) IBS symptoms are learned and reflect specific skill deficits in the domains of cognitive and behavioral functioning and 2) teaching patients to modify maladaptive behaviors and thinking patterns can correct these deficits, which in turn relieve symptoms. Components of CBT protocols typically include: 1) information about stress and its relationship to IBS, 2) self-monitoring of events before and after IBS flare-ups, 3) problem-solving strategies about stressors that aggravate symptoms, 4) muscle relaxation exercises to lower arousal and increase a sense of mastery over IBS symptoms and/or 5) cognitive restructuring to modify faulty appraisals of perceived threats that are thought to underlie physiologic and emotional reactivity.<sup>1</sup>

- A meta-analysis of 17 studies of CBT for IBS which defined efficacy as >50% reduction of GI symptoms yielded an odds ratio of 12.0 (95% CI = 5.6–26.0) with a mean number needed to treat (NNT) vs. controls of approximately 2.<sup>2</sup> When these results are compared to similar meta-analyses of commonly studied drugs for IBS, CBT shows superior efficacy. Compiled research for these drugs showed a NNT of 7 for alosetron<sup>3</sup> and 17 for tegaserod.<sup>4</sup>

- **Gut-directed Hypnotherapy (GDH)**  
GDH uses hypnotic induction, progressive relaxation, imagery and other techniques towards improved control of GI function. Therapy often includes education towards self-hypnosis, which empowers patients to manage their symptoms without reliance on medical providers.

Four randomized controlled trials have shown success in greater than 75% of patients.<sup>5-8</sup> In refractory cases of IBS that were referred to a GI clinic, an uncontrolled prospective study of 204 patients showed that 81% responded to therapy. Of these initial responders 71% had continued benefit 5 years later.<sup>9</sup> In a controlled but nonrandomized trial of GDH versus standard care with a 12 month follow-up, GDH was more effective in reducing IBS symptoms, improving Quality of Life (QOL) scores, and reducing health care utilization and disability.<sup>10</sup>

Gut-directed Hypnotherapy can require 8-12, 30-60 minute sessions and may be most beneficial for severe, refractory cases.



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### • **Other Approaches**

For those patients who may not have access or a need for this therapy, other therapeutic tools can be utilized, such as:

- Journaling ([See handout, Using Journaling to Aid Health](#)).
- Balloon technique self-hypnosis for abdominal pain ([See handout on Self-Hypnosis, Balloon Technique for Abdominal Pain](#)).
- Guided imagery tapes (<http://www.healthjourneys.com/shop.aspx>) Enter “irritable bowel syndrome” in the search box.
- Breathing exercises ([See handout, Breathing Exercise](#)).

### **Physical Influence: Exercise/Movement**

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Regular physical activity and movement have been found to be an important aspect of the management of conditions that are associated with a strong somatic influence. One of the key foundations in treatment is to empower patients to be active participants in creating lifestyle habits that will lead to improved quality of life. This is more effective than therapies where an individual is a passive recipient of care.<sup>11</sup>

Results from a small RCT indicate that exercise may be an effective intervention for symptom management in patients with IBS, especially for those whose condition is constipation predominant.<sup>12</sup> Women with IBS who are more physically active have fewer and less severe daily symptoms.<sup>13</sup> Mild physical exercise has also been found to increase gas clearance and reduce symptoms in those with abdominal bloating.<sup>14</sup>

- Encourage starting slowly and gradually increasing as able.
- Encourage group exercise programs to enhance a sense of community and social support.

- Use a perceived exertion scale to encourage exercise goals. On a scale of 1-20, with 20 being exercising to the point of exhaustion, direct the patient to shoot for a level of 14. At this stage, one should be able to talk but not sing. Encourage exercise for 25-40 minutes 3-4 times a week and work up to a “14” each time.

### **Nutritional Influences**

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It has long been known that eating certain foods can make the symptoms of IBS worse. Some of the latest thinking about IBS helps explain why food that caused no problems in the past may now be causing distress for a patient.

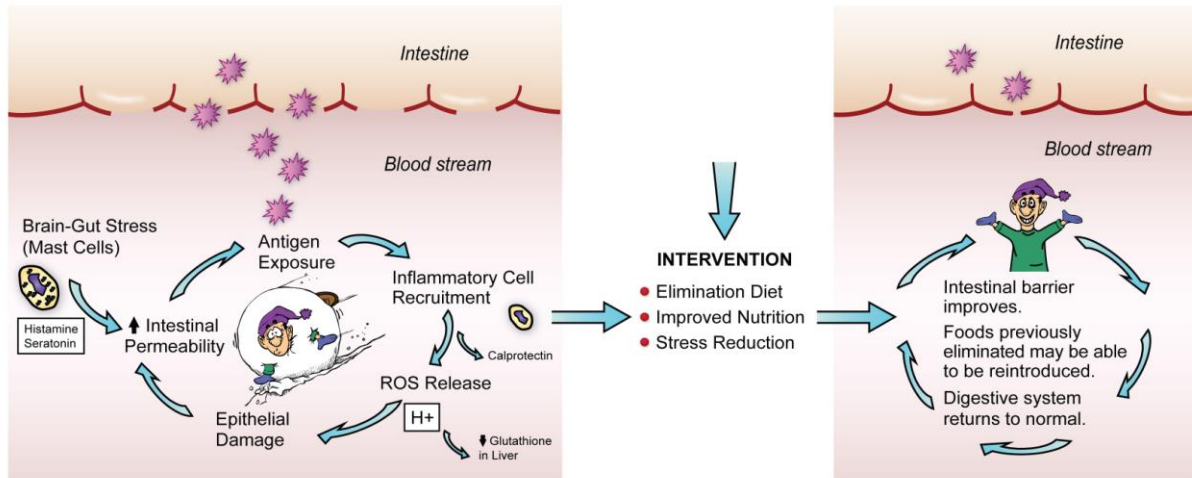
### **IBS that Results from an Insult to the GI Environment**

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Occasionally, IBS symptoms will arise after a significant stressor, illness, infection or medical treatment. This insult can disrupt the dynamic ecosystem of the GI environment which can change communication patterns that occur between mucus, bacteria and enterocytes.<sup>15</sup> If this interface becomes disrupted, chronic inflammation that further compromises its function can lead to increased intestinal permeability.<sup>16</sup> Common insults to barrier integrity include medications (antibiotics, steroids, NSAIDs), malnutrition,<sup>17</sup> infection<sup>18,19</sup>, age and psychosocial stressors.<sup>20,21</sup> Disruption of the barrier allows exposure of the gut associated lymphoid tissue (GALT) to antigens that stimulate continued inflammation, increased intestinal permeability and symptoms of IBS.<sup>22,23</sup> Research to support this hypothesis is growing, and if true, a multi-modal therapeutic approach aimed towards restoring a healthy gut-immune barrier would be warranted.



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Farhadi A, Banan A, Fields J, Keshavarzian A. Intestinal barrier: An interface between health and disease. *J Gastroenterol Hepatol*. 2003; 18(5):479-497.

### Testing for Increased Intestinal Permeability

The status of the intestinal barrier can be assessed using a lactulose/mannitol absorption test, which measures absorption of both large (lactulose) and small (mannitol) sugars. Increased absorption of both, found in urine testing suggests increased intestinal permeability.

This test is not often covered by insurance and may not be necessary if the history suggests an insult that would be consistent with this hypothesis. Progressing to a therapeutic trial (see below) would be a reasonable option.

Information on Mannitol/Lactulose testing is at <http://www.gdx.net/home/assessments/ip/>. It costs approximately \$90.

Lactulose/Mannitol testing has been found to be a predictor of small intestinal disease particularly in the evaluation of celiac disease and chronic diarrhea.<sup>24, 25</sup>

### Therapy to Restore a Healthy GI Barrier

The "4R" approach to restoring a healthy gut-immune barrier was pioneered by our Naturopathic colleagues. Steps include:

1) removing mucosal irritants, 2) replacing agents for digestive support, 3) reinoculating with friendly bacteria and the foods they need to grow, and 4) repairing the mucosal lining. [See our handout, Therapy for Increased Intestinal Permeability](#), for a detailed outline of the approach. Highlights are offered here:

- **Elimination Diet**

Once the gut barrier is compromised, food proteins that were well tolerated in the past may penetrate across the GI barrier to the immune system, stimulating an inflammatory response and symptoms of IBS. This has been well documented in celiac disease<sup>26</sup> but can occur with other food proteins as well.<sup>27, 28</sup> The most common food triggers to remove are listed in the table below.

It is important to first remove foods that may be promoting this inflammatory response realizing that once the gut-immune barrier is restored, these foods can be slowly re-introduced, generally after about 3 months. It is important to note that this is not a true food allergy but an intolerance. The key is to significantly reduce the total "load" of the food protein.



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[See our handout on Elimination Diet.](#)

Foods To Consider Eliminating for a Two Week Therapeutic Trial in IBS <sup>27-29</sup>
Dairy (lactose)
Wheat (gluten)
High fructose corn syrup
Sorbitol (chewing gum)
Eggs
Nuts
Shellfish
Soybeans
Beef
Pork
Lamb

### o **IgG Food Antibody Testing**

Although up to 65% of patients with IBS report food to be a common trigger of their symptoms,<sup>30</sup> only about 3% are related to IgE mediated reactions, suggesting that another inflammatory trigger such as IgG may be playing a role. There is controversy about the clinical significance and specificity of IgG measured antibodies to commonly eaten foods as a potential cause of IBS symptoms.<sup>31-33</sup>

Atkinson and colleagues used an enzyme-linked immunosorbent assay to evaluate IgG food sensitivity in 150 outpatients with IBS. Once specific foods were identified, patients were randomized into two groups. The first group of patients received a food elimination diet in which those foods that correlated with elevated IgG titers were removed, whereas the control group consumed a diet in which foods that did not correlate with IgG results were removed. After three months, those who complied with the “true” food elimination diet had a 26% greater improvement in IBS symptoms than did the sham control group. When the eliminated foods were re-introduced there was a 24% greater worsening of symptoms than the sham controls.<sup>34</sup>

IgG food antibody testing requires further research and appropriate standardization. An elimination diet remains the gold standard of care.

If compliance with an elimination diet is difficult and you choose to consider ordering IgG food antibodies despite their limitations, a resource for this test is <http://www.usbiotek.com/>

### • **Restoring Healthy Gut Flora**

The bacteria within the mucus of the intestinal wall play a key role in the permeability of the tight junctions of the enterocytes. The gut flora interact with Toll-Like Receptors (TLRs) that are the gatekeepers in helping distinguish which antigens are helpful or harmful<sup>35</sup>, and composition of the gut flora directly influences intestinal permeability.<sup>36</sup> There is growing data showing a potential therapeutic benefit of probiotics in the treatment of IBS.<sup>37-40</sup>

In the largest study to date, Whorwell and colleagues studied 362 female IBS patients and randomized them to receive three different doses of *B. infantis*,  $1 \times 10^6$ ,  $1 \times 10^8$  or  $1 \times 10^{10}$  compared to placebo. After 4 weeks of treatment, the  $1 \times 10^8$  dosage showed a significant benefit in reducing IBS symptoms with a 20% greater effect over placebo. There were qualitative improvements in bowel habits that were seen in both diarrhea and constipation dominant cases.<sup>41</sup> In another study conducted by O'Mahoney and colleagues, 75 patients with IBS were randomized to receive  $1 \times 10^{10}$  of *L. salivarius* or *B. infantis* or placebo for 8 weeks. The *Bifidobacterium* group had the greatest reduction in IBS symptoms (20-25%), which also correlated with a reduction in inflammatory cytokine compared to placebo.<sup>42</sup>



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A common finding in the research regarding probiotics and IBS is that *Bifidobacterium* appears to consistently reduce flatulence and bloating<sup>37</sup> and also has a beneficial influence on the inflammation of the bowel wall.<sup>42</sup>

[See our handout on Probiotics.](#)

- **Fiber**

In animal models, fiber prevents the disruption of the integrity of the intestinal barrier during the administration of total parenteral nutrition (TPN)<sup>43</sup> or chemotherapy.<sup>44</sup> In human research the benefits of fiber on IBS have been mixed, a 2005 Cochrane review reveals.<sup>45</sup> Since this review was published, there have been some promising results with the use of guar gum for IBS. Guar gum (like psyllium and ground flax seed) is a viscous fiber that helps maintain a healthy mucous layer in the intestine while also helping lower cholesterol, improve constipation and acting as a prebiotic (nutrient for the growth of healthy bacteria).<sup>46,47</sup>

When guar gum was given at two different doses (5 gm/day and 10 gm/day) to 84 IBS patients, both were found to reduce IBS symptoms and improve overall quality of life. The benefits decreased after 12 weeks of therapy was completed, suggesting the possible benefit of a maintenance dose.<sup>48</sup> When guar gum was compared to bran fiber for IBS, both were found to be beneficial, but patients preferred the guar gum over the bran.<sup>49</sup>

- **L-Glutamine**

Glutamine is a non-essential amino acid that is utilized by rapidly growing cells. The enterocyte lining of the GI tract is one of the most rapidly reproducing cells of the human body, and depletion of this protein can result in continued disruption of intestinal integrity. Research of L-glutamine has mainly been done on severely ill individuals in the intensive care setting who develop increased intestinal permeability that leads to enteric derived septicemia. The breakdown of the

intestinal barrier allows pathogenic bacteria into the blood stream resulting in sepsis. This can be prevented by supplementing with L-glutamine which maintains the integrity of the intestinal barrier and reduces the incidence of gut derived infections.<sup>50</sup> Glutamine appears to have the most benefit when inflammation is present despite the depletion of nutritional stores.<sup>51</sup> It reduces inflammatory cytokine release within the bowel wall<sup>52</sup> and increases *heat shock protein* which protects enterocytes from injury.

There is no research on L-Glutamine and IBS, but due to its safe side effect profile, a short course of therapy (5 gms BID for two weeks) may prove helpful in those patients who are suspected of having increased intestinal permeability.

- **Zinc**

There is preliminary human data to show benefit in helping repair intestinal integrity with zinc. In a randomized cross-over trial, 10 patients were given 37.5 mg of prophylactic zinc to see if this would prevent the loss of intestinal integrity when given the medication Indomethacin. There was no loss in intestinal integrity in those given zinc compared to a 3-4 fold increase in intestinal permeability when zinc was not used. The zinc treated group also had a 75% reduction in gastric and small bowel injury and 50% less villous shortening.<sup>53</sup>

Since zinc is one of the most common mineral deficiencies in the western diet,<sup>54</sup> a short trial of supplementation (20-35 mg daily for 14-30 days) may prove helpful. Zinc is needed for appropriate immune function of the GALT and is deficient in those with IBS, although this may be secondary to zinc loss from diarrhea.<sup>55</sup> There is no current clinical data regarding the use of Zinc supplementation in IBS.



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### **Other Biologic Agents for IBS**

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- **Peppermint**

Peppermint is rich in menthol, a smooth muscle relaxant that is proposed to reduce the amount of cramping and pain with IBS. Most quality products have at least 44% menthol and less than 1% pulegone (a neuro- and hepatotoxin).<sup>56</sup>

A review<sup>57</sup> of 16 clinical trials showed an average response rate of 58% for peppermint compared to 29% with placebo. The authors compared this effect to that of pharmaceutical treatment for IBS (tegaserod, alosetron, cilansetron) and concluded that similar efficacy with a much safer side effect profile suggests that, “peppermint oil may be the drug of first choice for IBS patients.”

Enteric-coated peppermint is recommended since it dissolves lower in the GI tract, reducing the risk of reflux symptoms because of peppermint’s ability to relax the lower esophageal sphincter. A common dose is 0.2-0.4 ml three times daily of enteric-coated capsules. The pediatric dose for those 8 and older is 0.1-0.2 ml three times daily.<sup>58</sup>

- **Cromolyn Sodium**

Cromolyn appears to have the most benefit on the inflammatory component of IBS through its stabilization of mast cells and reduction in inflammatory cytokines. It appears to be most helpful in diarrhea dominant cases.<sup>59, 60</sup>

When cromolyn was compared to elimination diet for 409 patients with IBS over 4 months, symptom improvement was seen in 60% in those on the elimination diet and 67% in those on cromolyn. Response rates were better in those who had positive skin tests to dietary antigens supporting cromolyn’s anti-inflammatory effect in those IBS patients with food sensitivities.<sup>61</sup> In a group of 101 diarrhea predominant IBS patients who had previously shown a response to an elimination diet, 60% responded to cromolyn.<sup>62</sup>

In those patients who respond to an elimination diet, short term use of cromolyn sodium may help calm the inflammatory reaction that can occur when a food triggers enteric cytokine production.

### **Relationship Centered Care**

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Due to the complex nature of IBS, it is best treated by a continuous relationship with a practitioner who knows the patient well. This relationship will give insight into how to best organize the many therapeutic options towards an efficient health plan that will result in a greater quality of life with fewer symptoms.

### **Additional Information**

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For additional information on treating IBS with complementary and alternative medicine (CAM) therapies, see the [May 2011 edition of the NCCAM Clinical Digest](#) by the National Institutes of Health, National Center for Complementary and Alternative Medicine. This issue summarizes research on some of the most popular CAM therapies people try to treat symptoms of IBS.



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## Therapeutic Review for IBS

Therapy	Application	Evidence Rating (SORT Criteria) <sup>63</sup>
Cognitive Behavioral Therapy	Referral to health psychology Consider journaling	A
Hypnosis	Self-hypnosis techniques	B
Relaxation Training	Breathing exercises, progressive muscle relaxation, guided imagery	C
Exercise/Movement	Regular aerobic activity	C
Elimination Diet	Remove foods listed in table above for two weeks	B
Probiotics	<i>B.infanti</i> 1 x 10 <sup>8</sup> CFU daily (Brands: Floragen #3)	B
Fiber	Guar Gum 5 gms daily Ground Flax Seed, 1 Tbsp on food or in juice, smoothie BID Psyllium, 1 Tbsp in 8-10 oz of water or juice BID	A
L-Glutamine	5 gms BID	C
Zinc	37.5 mg daily	C
Peppermint	0.2-0.4 ml enteric coated capsules TID	B
Cromolyn Sodium	400 mg TID to QID	B

An accompanying handout for patients is also available.

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