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Behavioral and Complementary Approaches for the Treatment of Irritable Bowel Syndrome

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Irritable bowel syndrome (IBS) is one of the most common conditions seen in primary care settings. Despite this, there is no consensus as to the pathogenesis of this disorder or a consistently effective therapeutic regimen for many patients. This has encouraged the use of various alternative therapies from behavioral or complementary medicine. This review will address the evidence for alternative therapies, including the following: cognitive behavior therapy, hypnosis, elimination diets based on food antibody testing, nutrition supplements (such as fiber, probiotics, and prebiotics), and, finally, peppermint, L-glutamine, zinc, and cromolyn

sodium. The review also explores the evidence for and the therapeutic ramifications of the hypothesis that increased intestinal permeability underlies the symptoms of IBS in many patients, and how a therapeutic plan that addresses nutrition, elimination diets, and nutrition supplements may be useful in restoring the integrity of the gut immune barrier. (*Nutr Clin Pract.* 2008;23:284-292)

Keywords: inflammatory bowel diseases; cognitive therapy; hypnosis; imagery; complementary therapies; probiotics; dietary supplements; diet therapy; elimination diets; nutrition support

Irritable bowel syndrome (IBS) is a prevalent functional GI disorder that may affect as many as 20% of the adult population in North America. It is characterized by abdominal pain, altered bowel habits, and often bloating and abdominal distension. Although most patients are treated in primary care settings, referrals to specialists are frequent, and IBS accounts for 20%-50% of patients seen in gastroenterology offices. Furthermore, IBS is associated with significant impairment in quality of life, high absenteeism rates, and increased healthcare costs.¹

Conventional therapy of IBS has focused on systematic relief of symptoms such as pain, diarrhea, and constipation. Evidence of long-term benefit of pharmacologic agents has been sparse, and the development of new agents has raised issues concerning safety and therapeutic efficacy.^{2,3} In addition, managed care guidelines have limited the time that physicians can spend with patients. This is detrimental in view of the importance of the patient-physician relationship, which is considered a crucial determinant of treatment outcomes.⁴ Not surprisingly,

these considerations have led physicians and patients to consider alternative therapies.

There are 2 broad areas of therapies that are based on different but not mutually exclusive concepts concerning the pathogenesis of IBS. The first comprises so-called mind-body therapies, whereas the second comprises therapies that may alter existing changes in intestinal permeability, gut immunity, and intestinal inflammation, which are thought to produce IBS symptoms. This article reviews the literature about the best-studied psychological treatments such as cognitive behavior therapy (CBT) and gut-directed hypnotherapy (GDH), and then reviews relevant literature concerning complementary and alternative medications such as food intolerance, elimination diets, probiotics, prebiotics, peppermint, and nutrition therapies that may help sustain the integrity of the intestinal barrier, including fiber, L-glutamine, zinc, and cromolyn sodium.

Mind-Body Interventions

Mind-body interventions are predicated on the hypothesis that treatments designed to improve the ability of the mind to influence or control bodily functions may be effectively used to relieve IBS symptoms. The 2 most studied techniques are CBT and GDH.

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Cognitive Behavior Therapy

Most treatment trials involving psychological therapies in IBS have featured a specific treatment called CBT.⁵⁻⁷ This is a time-limited, structured, problem-focused, and prescriptive therapy⁵ based on the following 2 central underlying assumptions: (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 relieves symptoms. Components of CBT protocols typically include the following: (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 to increase a sense of mastery over IBS symptoms, or (5) cognitive restructuring to modify faulty appraisals of perceived threats that are thought to underlie physiologic and emotional reactivity.⁶

The improvements achieved with CBT are robust and are as good or better than those of recently developed drugs that act as serotonin receptors (such as alosetron hydrochloride and tegaserod).⁸ A recent meta-analysis⁹ of 17 studies regarding CBT for IBS that defined efficacy as >50% reduction of GI symptoms yielded an odds ratio of 12.0 (95% confidence interval [CI], 5.6-26.0) with a mean number needed to treat (NNT) vs control subjects of approximately 2. This may be compared with another recent meta-analysis¹⁰ of 6 large randomized, controlled trials of alosetron that showed a pooled odds ratio of 1.8 (95% CI, 1.6-2.1) with an NNT of 7, as well as a similar analysis¹¹ of 8 studies regarding tegaserod that showed a pooled odds ratio of 1.2 (95% CI, 1.1-1.3) with an NNT of 17. Similarly, antidepressant therapy for functional GI disorders in a meta-analysis¹² of 8 studies (primarily low-dose tricyclic agents) yielded a pooled odds ratio of 4.2 (95% CI, 2.3-7.0) with an estimated NNT of 4 (95% CI, 2.1-6.5) vs control subjects receiving placebo. However, it has been emphasized that comparisons of CBT with pharmacologic studies are inappropriate because a control condition comparable to a medication placebo control was not used in CBT investigations.⁶ In other functional pain disorders, such as migraine and chronic tension-type headaches, differences in overall efficacy between effective drug and psychological treatments have been negligible.¹³

The mechanisms by which CBT works in IBS are not established. However, findings from a recent study⁵ suggest that CBT exerts a direct effect on GI symptoms that is independent of its effects on psychological distress. Results of this study also suggest that patients with increased chronicity and severity of symptoms were more likely to achieve the greatest improvement.

Gut-Directed Hypnotherapy

Gut-directed hypnotherapy is a form of hypnosis that has been frequently reported to have a beneficial effect on IBS symptoms. It uses hypnotic induction with progressive relaxation and other techniques, followed by imagery directed toward control of GI function. Therapy often includes education about self-hypnosis, which enables patients to manage their symptoms without reliance on care providers. Although study methods and the quality of reported studies vary, the preponderance of evidence suggests that hypnosis is effective in improving symptoms of IBS in most patients treated.

The first study¹⁴ to evaluate GDH in the management of IBS was published in 1984. Since then and without exception, outcome studies of hypnotherapy in IBS have been favorable, although many have lacked sufficient quality in terms of research design. Only 4 studies,¹⁴⁻¹⁷ including the original study in 1984, have used randomized and controlled treatment trials, but the reported success rates exceeded 75% in all studies. All 4 studies reported improvement in GI symptoms, and 3 of 4 reported improvement in affective symptoms as well. The benefits of hypnosis also may have long-lasting effects after therapy has been completed. In an uncontrolled prospective study¹⁸ of 204 patients with IBS, 81% of 143 initial responders to therapy had continued benefit 5 years later. In a small study,¹⁹ GDH was successful among 76% in the IBS group vs 59% in the control group, but this finding was not statistically significant.

In a controlled but nonrandomized trial of GDH vs standard care with a 12-month follow-up, GDH was more effective in reducing IBS symptoms, improving quality-of-life scores, and reducing healthcare use and disability.²⁰ Therefore, 5 controlled studies^{14-17,20} reported by 4 different centers seem to attest to the potential efficacy of hypnotherapy in IBS.

Nevertheless, the efficacy of GDH in IBS remains less than conclusive. Most of the studies were of modest to poor quality, and in some studies the placebo response rate is low (in a disorder in which placebo response rates vary from 25% to >50%). Patients included in the trials had refractory IBS, so it is not possible to generalize the results to all patients with IBS, many of whom are treated in the primary care setting. To our knowledge, no published studies have reported negative results; study samples have been small, suggesting the possibility of publication bias.¹⁵

Last, GDH is an intensive process, with most programs reporting 6-12 sessions, each lasting 30-60 minutes. Therefore, it seems that GDH would be most suitable for patients with severe and refractory IBS. Studies have sought to overcome this by offering home hypnotherapy using audiotapes²¹ or by directing therapy toward a primary care-based population.²² These results

seem to be promising, although the success rates do not approach those of therapist-directed GDH. This may be a promising less expensive approach, but further studies are needed.

Biologic and Nutrition-Based Therapies

Biologic and nutrition-based therapies use various strategies, including nutrition supplements, elimination diets, and probiotics, predicated on the hypothesis that they may correct altered gut immunity and intestinal permeability to reduce gut inflammation and IBS symptoms.

The Gut Immune Hypothesis of IBS

The gut immune interface is controlled by an active barrier of enterocytes that is constantly distinguishing nonharmful nutrients from potentially harmful antigens. This interface includes a dynamic communication between mucus, bacteria, and enterocytes.²³ If this interface becomes disrupted, chronic inflammation that further compromises its function can lead to increased intestinal permeability.²⁴ Common insults to barrier integrity include medications (antibiotics, corticosteroids, and nonsteroidal anti-inflammatory drugs), malnutrition,²⁵ infection,^{26,27} age, and stressors.^{28,29} Disruption of the barrier allows exposure of gut-associated lymphoid tissue to antigens that stimulate continued inflammation, increased intestinal permeability, and symptoms of IBS.^{30,31} Research to support this hypothesis is growing; if true, a multimodal therapeutic approach that recognizes the importance of physical and nutrition factors in the maintenance of IBS symptoms would be appropriate.

Disruptions of the mucosal barrier of the intestine may allow entry for antigens of dietary or bacterial origin into the enteral circulation to stimulate an inflammatory response and symptoms of IBS.²⁸ This inflammatory response is different if IBS results from infectious gastroenteritis such as *Campylobacter*²⁷ or if it is stimulated by emotional stressors.²⁹ Postinfectious alterations of intestinal permeability increase the numbers of immunocytes and cytokines,^{27,32} whereas stressors seem to work, at least in part, through mast cell stimulation³¹ and corticotrophin-releasing factor.³³ Increased intestinal permeability is associated with inflammation of the proximal³⁴ and distal³⁵ bowel. This inflammation includes the release of cytokines such as interleukin-4 and interferon- γ from T lymphocytes.³⁶⁻³⁸ In 77 patients meeting Rome criteria for IBS, 90% had immune activation in acute- and insidious-onset IBS and in diarrhea- and constipation-predominant cases.³⁹ These data suggest that inflammation of the bowel wall results in a vicious cycle that maintains increased intestinal permeability, allowing passage of

luminal antigens into the mucosa to continue the inflammatory process.

Elimination diets and Immunoglobulin G (IgG) antibody testing. Specific antigens derived from food sources can trigger inflammation if there is a breach in the gut barrier.³⁴ It is well established that gluten is a trigger of GI symptoms when the intestine mounts an immune response in celiac disease.⁴⁰ However, many patients with IBS symptoms and without evidence of pathologic changes on intestinal biopsy results benefit from the removal of gluten from their diet. True food allergy is uncommon, whereas food intolerances are far more prevalent; this may be related to the status of the intestinal barrier.²⁸ There is also evidence that gluten is not alone in its ability to aggravate IBS symptoms. The most common foods associated with food intolerance include milk, wheat, eggs, nuts, shellfish, soybeans, beef, pork, lamb, and sugars such as lactose, fructose, and sorbitol.^{41,42}

Antigens in certain foods (eg, cow's milk protein) may trigger GI symptoms via an immune response, but others such as lactose, fructose, and sorbitol may have their greatest effect via malabsorption. For example, of 126 children with symptoms consistent with IBS, 24% were diagnosed as having lactose intolerance by breath testing. When these individuals were placed on a lactose-free diet, 87% had improvement of symptoms during 5 years, with a 75% reduction in physician visits.⁴³

Although up to 65% of patients with IBS report food to be a common trigger of their symptoms,⁴⁴ only about 3% are related to IgE-mediated reactions, suggesting that another inflammatory trigger such as IgG may have 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.⁴⁵⁻⁴⁷ Nevertheless, food-related IgG tests are commonly used by many practitioners to help focus on foods that, if eliminated, may help reduce IBS symptoms.

Atkinson and colleagues⁴⁸ 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 2 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 second (control) group consumed a diet in which foods that did not correlate with IgG results were removed. After 3 months, those who complied with the "true" food elimination diet had 26% greater improvement in IBS symptoms than the control group. When the eliminated foods were reintroduced, there was 24% increased worsening of symptoms compared with the sham controls. In a smaller uncontrolled study, Zar et al⁴⁹ obtained IgG titers to 16 food types in 25 patients with IBS. IBS symptoms and rectal compliance

were measured after the high-titer foods were eliminated for 6 months. There was significant improvement in pain, bloating, satisfaction with bowel movements, and quality of life after removing these foods. There also was improved rectal compliance in 12 patients in whom this was measured using an infinitely compliant balloon connected to an electronic barostat. In essence, the changes observed were reduced pressure increases in response to increasing inflation volumes, resulting in less discomfort associated with rectal filling. In another study⁴² of 108 patients with IBS and 43 control subjects, IgG, IgE, and skin prick testing for 16 foods was performed to evaluate common IBS triggers. Compared with control subjects, patients with IBS had significantly higher IgG titers to wheat ($P < .001$), beef ($P < .001$), pork ($P < .001$), and lamb ($P < .009$). IgE titers and skin prick testing did not correlate with IBS symptoms. A more recent review by Zuo et al⁴⁷ also showed significantly higher IgG titers in patients with IBS to crab ($P < .001$), egg ($P < .001$), shrimp ($P < .001$), soybean ($P = .02$), and wheat ($P = .004$), but these findings did not correlate with IBS symptoms.

Further research is needed to establish clinical relevance, specificity, and standardization of IgG food testing in relation to IBS. Until this is done, the current gold standard remains a 2-week elimination diet off the most common foods associated with this condition (Table 1). This can be therapeutic and diagnostic.^{48,50} The potential risk of this therapy is to create an unnecessary fear of food in an already hypersensitive individual. Therefore, the focus should not be to remove the food forever but to restore the GI ecologic balance to one in which the offending antigens are removed and intestinal permeability improves. If this hypothesis for IBS is true, the patient with IBS may be able to slowly reinstate these food groups after restoration of the gut immune barrier occurs. This requires not only that offending antigens be removed but also that appropriate gut flora be restored.

Alterations of the intestinal flora and probiotics. The bacteria within the mucus of the intestinal wall have a key role in the permeability of the tight junctions of enterocytes. The gut flora interact with toll-like receptors that are the gatekeepers in helping distinguish which antigens are helpful or harmful.⁵¹ This bacterial interaction with toll-like receptors affects susceptibility to food antigens and regulation of intestinal permeability.⁵² Bacteria have been shown to have a direct effect on intestinal permeability⁵³⁻⁵⁵ and on susceptibility to autoimmune diseases such as atopic dermatitis^{56,57} and pouchitis.⁵⁸ A growing body of evidence demonstrates a potential therapeutic benefit of probiotics in the treatment of IBS.⁵⁹⁻⁶²

A probiotic is a nonpathogenic microorganism that exerts a positive effect on host health or physiologic function. Among probiotics studied, *Lactobacillus* and

Table 1. Foods to Consider Eliminating for a 2-Week Therapeutic Trial in Irritable Bowel Syndrome^a

Dairy (lactose)
Wheat (gluten)
High-fructose corn syrup
Sorbitol (chewing gum)
Eggs
Nuts
Shellfish
Soybeans
Beef
Pork
Lamb

^aFrom Niec et al,⁴¹ Zar et al,⁴² and Gremse et al.⁴³

Bifidobacterium genera are the most commonly used. Several investigations have also been performed using a combination product called VSL#3 (VSL Pharmaceuticals, Fort Lauderdale, FL). Each VSL#3 sachet contains 450 billion viable lyophilized bacteria, including *Bifidobacterium* (*Bifidobacterium longum*, *Bifidobacterium infantis*, and *Bifidobacterium breve*), *Lactobacillus* (*Lactobacillus acidophilus*, *Lactobacillus casei*, *Lactobacillus delbrueckii* subspecies *bulgaricus*, and *Lactobacillus plantarum*), and *Streptococcus salivarius* subspecies *thermophilus*. The use of this agent is based on the finding that the stools of patients with IBS have a decrease in coliforms, lactobacilli, and, to a less extent, bifidobacteria.⁶³

Research on the use of probiotics and IBS is fraught with inconsistencies and is challenged by product variations. Few data support colony stability and viability. Many products include proprietary blends of bacteria that make specific clinical benefits difficult to quantify. Despite these challenges, there is increasing evidence of efficacy.

O'Mahony and colleagues⁶⁴ conducted a study in which 75 patients with IBS were randomized to receive 1×10^{10} colony-forming units (CFU) of *Lactobacillus 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 cytokines compared with placebo. In a study⁶⁵ using VSL#3, 48 patients with IBS were randomized to the probiotic or to placebo for 8 weeks; 48% in the treatment group and 33% in the placebo group had clinical benefit (not statistically significant), with the greatest benefit seen in the reduction of flatulence. A consistent finding of probiotics in the treatment of IBS is the reduction of bloating and flatulence.⁵⁹ In the largest study to date, Whorwell and colleagues⁶⁶ studied 362 female patients with IBS and randomized them to receive 3 different doses of *B infantis* (1×10^6 , 1×10^8 , or 1×10^{10} CFU) compared with placebo. After 4 weeks of treatment, the 1×10^8 dosage of CFU showed

significant benefit in reducing IBS symptoms, with 20% greater effect over placebo. There were qualitative improvements in bowel habits that were seen in diarrhea- and constipation-dominant cases. The results with the 1×10^{10} dosage of CFU were in contrast to the findings of O'Mahony et al.⁶⁴ A possible explanation is that the higher-concentration preparation in this study⁶⁶ congealed and may not have been adequately absorbed.⁶⁷

Nutrition Supplements and IBS

Dietary nutrients are important for maintaining integrity of the GI barrier and mucus. They also preserve a healthy and balanced intestinal ecosystem.

Prebiotics and synbiotics. Prebiotics are nondigestible nutrients that stimulate growth and activity of 1 or more microorganisms that act to promote health and well-being of the host.⁶⁸ These mainly consist of nondigestible oligosaccharides (inulin), which have traditionally been used in foods to add fiber without bulk. Foods rich in fructooligosaccharides include onion, asparagus, chicory, banana, and artichoke. Prebiotics help to stimulate the growth of bifidobacteria while inhibiting the growth of *Bacteroides*, clostridia, and coliforms. When prebiotics are packaged with probiotics in a supplement, they are called a synbiotic. There are limited data on the use of these products in IBS. A study⁶⁹ of the use of synbiotics in 21 patients with IBS showed no significant improvement in symptoms or bowel frequency.

Fiber. Fiber has been studied extensively in IBS, with mixed results. A Cochrane review⁷⁰ of bulking agents showed no clear benefit. Although there are limited data to support viscous fiber over insoluble fiber in IBS, viscous fibers such as psyllium or guar gum have many potential benefits. They enhance intestinal mucus, act as prebiotics supporting beneficial bacterial growth, relieve constipation, and lower cholesterol.⁷¹ In animal models, fiber prevents the disruption of the integrity of the intestinal barrier during the administration of parenteral nutrition⁷² or chemotherapy.⁷³

Since the Cochrane review⁷⁰ was published, some promising data regarding the use of guar gum and IBS have emerged. Guar gum is a soluble nongelling fiber that has the added benefit of acting as a prebiotic. It increases colonic contents of short-chain fatty acids, lactobacilli, and bifidobacteria.⁷⁴ When this fiber was given at 2 different dosages (5 g/d and 10 g/d) to 84 patients with IBS, both were found to reduce IBS symptoms and to improve overall quality of life. The benefits decreased after the 12 weeks of therapy were completed, suggesting the possible benefit of a maintenance dosage.⁷⁵ When guar gum was compared with bran fiber for IBS, there was benefit in symptoms seen with both, but patients preferred guar

gum over bran fiber.⁷⁶ The most important sources of fiber come from fruits, vegetables, and whole grains.

Other Treatments

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 neurotoxin and hepatotoxin.⁷⁷ Three systemic reviews have been performed on peppermint and IBS. The first article reviewed 5 double-blind placebo-controlled trials.⁷⁸ These studies showed promise in using peppermint to treat IBS symptoms, but there was insufficient evidence to claim benefit beyond reasonable doubt. A second review article included studies that enhanced heterogeneity and were longer in duration.² The findings supported a modest benefit of peppermint over placebo. The third article, which reviewed 16 clinical trials, showed a mean response rate of 58% for peppermint compared with 29% for placebo.⁷⁹ The authors compared this effect to that of pharmaceutical treatment for IBS (tegaserod, alosetron, and cilansetron) and concluded that the finding of similar efficacy with a much safer adverse effect profile suggests that "peppermint oil may be the drug of first choice for IBS patients."⁷⁹

Enteric-coated peppermint is recommended because it dissolves lower in the GI tract, reducing the risk of reflux symptoms due to the ability of peppermint to relax the lower esophageal sphincter. A common dosage is 0.2-0.4 mL 3 times daily of enteric-coated capsules, which are available over the counter. The pediatric dosage for those 8 years and older is 0.1-0.2 mL 3 times daily.⁸⁰

L-glutamine. Glutamine is a nonessential amino acid that is an energy source for rapidly dividing cells. Because enterocytes regenerate approximately every 3 days, glutamine has a key nutrition role in the integrity of the intestinal barrier. Glutamine also reduces inflammatory cytokine release within the bowel wall⁸¹ and increases heat shock protein, which protects enterocytes from injury. The benefits of glutamine on intestinal permeability occur only when inflammation is present, despite depletion of this amino acid in nutrition stores.⁸² Therefore, it seems to benefit intestinal permeability through its anti-inflammatory effects.

Glutamine has shown clinical benefit in critically ill patients who develop increased intestinal permeability that leads to enteric-derived septicemia. The breakdown of the intestinal barrier allows pathogenic bacteria into the bloodstream, resulting in sepsis. This can be prevented by supplementation with L-glutamine, which maintains the integrity of the intestinal barrier and reduces the incidence of gut-derived infections.⁸³ Intravenous glutamine was used in these investigations, but it is also well

Table 2. Summary of Complementary Therapies and Current Evidence Ratings for Irritable Bowel Syndrome

Therapy	Application	Evidence Rating (Strength of Recommendation Taxonomy Criteria) ^a
Cognitive behavior therapy	See text	A
Hypnosis	See text	B
Elimination diet	Remove foods in Table 1 for 2 wk	B
Probiotics	<i>Bifidobacterium infantis</i> (1×10 ⁸ colony-forming units daily) VSL#3	B
Prebiotics	Food sources include bananas, artichokes, onions, asparagus, and chicory	C
Fiber	Guar gum (5 g/d)	A
L-glutamine	5 g twice daily	C
Peppermint	0.2-0.4 mL enteric-coated capsules 3 times daily	B
Zinc	37.5 mg/d	C
Cromolyn sodium	400 mg 3-4 times daily	B

^aFrom Ebell et al.⁹² A indicates recommendation based on consistent and good-quality patient-oriented evidence; B, recommendation based on inconsistent or limited-quality patient-oriented evidence; and C, recommendation based on consensus, usual practice, opinion, disease-oriented evidence, and case series for studies of diagnosis, treatment, prevention, or screening.

absorbed orally. Although there are no studies (to our knowledge) to support the use of L-glutamine for IBS, its mechanism of action warrants research as a potential therapeutic agent.

Zinc. Of all the key nutrients, zinc deficiency is the most prevalent in North America.⁸⁴ Zinc is needed for appropriate immune function of gut-associated lymphoid tissue and is deficient in patients with IBS, although this may be secondary to zinc loss from diarrhea.⁸⁵ To our knowledge, there are no data regarding the use of zinc supplementation in IBS, but it has been found to reduce the duration of infectious diarrhea.⁸⁶ There also are preliminary human data that show benefit in helping repair intestinal integrity. In a randomized crossover trial, 10 patients were given 37.5 mg of prophylactic zinc to determine if this would prevent the loss of intestinal integrity when administered indomethacin.⁸⁷ There was no loss of intestinal integrity in those given zinc, compared with a 3-4-fold increase in intestinal permeability when zinc was not used. The zinc-treated group also had 75% reduction in gastric and small bowel injury and 50% less villous shortening.

Cromolyn sodium. Cromolyn sodium is a pharmaceutical agent that has shown promise in the treatment of IBS. The benefit may come in part from its anti-inflammatory effect through the stabilization of mast cells and the reduction of inflammatory cytokines. Cromolyn has been found to be most beneficial in diarrhea-predominant IBS.^{2,88} In a double-blind crossover trial, 8 weeks of cromolyn therapy resulted in significantly greater symptom reduction compared with placebo, and the effects lasted after the therapy was completed.⁸⁹

When cromolyn was compared with an elimination diet among 409 patients with IBS during 4 months, symptom

improvement was seen in 60% of those receiving the elimination diet and in 67% of those receiving cromolyn. Response rates were better in those who had positive skin test results to dietary antigens, supporting the anti-inflammatory effect of cromolyn in patients with IBS having food sensitivities.⁹⁰ In a group of 101 patients with diarrhea-predominant IBS who had previously shown a response to an elimination diet, 60% responded to cromolyn.⁹¹ Although neither of the studies was controlled or blinded, these findings support a potential benefit of using cromolyn with an elimination diet to help reduce inflammation that may occur with food sensitivities.

Future Research

A summary of current complementary and behavioral therapies for IBS is given in Table 2, which also summarizes the evidence to support their efficacy. Because IBS is a multifactorial disorder with many effects, further research should include prospective quality-of-life studies with lifestyle interventions that address intestinal integrity and the significant influences of emotion. Similar seminal studies have been performed by Ornish et al⁹³ and by Gould et al⁹⁴ that show improvement of atherosclerotic heart disease with aggressive lifestyle interventions.

The status of the intestinal barrier can be assessed using a mannitol and lactulose absorption test, which measures absorption of large and small sugars. Increased absorption of both sugars suggests increased intestinal permeability. Patients could then be randomized to a control group (usual care) or to a lifestyle modification group that includes therapies that are hypothesized to reverse increased intestinal permeability. These might include stress reduction classes (CBT and GDH), an elimination

diet, and key nutrients such as fiber, probiotics, L-glutamine, zinc, and cromolyn sodium.

Follow-up data would be collected to assess patient quality of life and to repeat mannitol and lactulose absorption test to determine if the therapy shows improvement in intestinal integrity and whether there is a correlation in overall quality of life. Such studies would address the potential importance of the role of intestinal permeability on IBS and incorporate measurements of what matters most in patient care and quality of life for patients.

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