SPECIAL ISSUE
Gastrointestinal Health

AUDIO INTERVIEW WITH EAMONN QUIGLEY, MD
The Role of the Microbiome on Scientific Research and Human Health

LITERATURE REVIEW
Probiotics for the Treatment of Irritable Bowel Syndrome
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SPECIAL ISSUE GASTROINTESTINAL HEALTH

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MESSAGE FROM THE PUBLISHER

Please Enjoy Our Inaugural Special Issue

Welcome to the first special issue of the Natural Medicine Journal. Each year we will publish two special issues on topics with broad appeal. We begin with gastrointestinal (GI) health. Even if you don’t have specialty in this area, because of the increasing prevalence of GI disorders, this issue’s content covers topics you are likely to encounter.

The phrase “death begins in the colon” may be debatable, but certainly for millions of people worldwide, poor health can be traced back to the gastrointestinal tract. The National Digestive Diseases Information Clearinghouse reports that approximately 70 million Americans are afflicted with some type of digestive disease. Of those disorders, irritable bowel syndrome (IBS) has become one of the most common, affecting 1 in 5 women and 1 in 10 men. This special issue includes a peer-reviewed literature review on the topic of probiotics and IBS, beginning on page 14. In addition, leading gastrointestinal expert Eamonn Quigley, MD, discusses probiotics and IBS in the audio interview featured on page 6. Quigley also provides listeners with an update on the Human Microbiome Project.

In an audio interview on page 7, Mark Davis, ND, discusses the fascinating and controversial topic of fecal microbiota transplantation (FMT). Davis gives an overview of the science, procedure, and legal status of FMT. In the question and answer interview on page 22, researcher M. Mamadou, PhD, describes the use of enzymes in common digestive disorders.

As with every issue of the Natural Medicine Journal, this special issue also features our popular Abstracts & Commentary section. In this section your colleagues examine the latest published research and weigh in on the studies’ applications to clinical practice.

And finally, Teresa Silliman, ND, provides us with a review of the new textbook, Enteroinmunology: A guide to prevention and treatment of chronic disease, by Charles A. Lewis, MD, MPH. Silliman will tell you why she believes, “Every physician should have this insightful book at his or her side—especially those practitioners who follow the tenets of naturopathic medicine.”

If you are interested in contributing to the Natural Medicine Journal, please contact me at Karolyn@karolyngazella.com. Also, please remind your colleagues that they can visit our website — www.naturalmedicinejournal.com — and sign up to receive the journal and all special issues absolutely free.

We hope you find this special issue of the Natural Medicine Journal interesting and informative. On behalf of the staff, editorial board, and contributors, we appreciate your support.

In good health,

Karolyn A. Gazella
Publisher
The Role of the Microbiome in Scientific Research and Human Health
An Interview with Eamonn Quigley, MD

Highly respected gastrointestinal researcher and expert, Eamonn Quigley, MD, discusses the research significance of the Human Microbiome Project and what role it could play in terms of disease prevention and treatment. Quigley also explains his view of the role that probiotics, prebiotics, and synbiotics play in the treatment of gastrointestinal disorders and other health issues.

ABOUT THE EXPERT
Eamonn Quigley, MD, is the past president of the American College of Gastroenterology and the World Gastroenterology Organization. Presently he is the chair of the World Gastroenterology Organization Foundation and the division head of Gastroenterology and Hepatology at The Methodist Hospital System in Houston, Texas, where he is also developing a gastroenterology fellowship program. Quigley earned his medical doctorate from National University of Ireland, Cork, Ireland. He has been published in nearly 500 different peer-reviewed publications and has been the principal investigator or co-principal investigator of many research studies involving gastrointestinal issues.
In this audio interview, clinician Mark Davis, ND, explains what fecal microbiota transplantation (FMT) is, how to administer it safely in clinical practice, and what the present legal status is regarding administration of FMT in the clinical setting. He also describes how FMT differs from probiotic therapy and which conditions are most likely to benefit from FMT.

ABOUT THE EXPERT
Mark Davis, ND, is the medical director at the Good Life Medicine Center in Portland, Ore., where he focuses on gastrointestinal health. He received his medical doctorate with honors in research from Natural College of Natural Medicine. Davis is internationally known for his expertise in microbial medicine and is currently awaiting FDA approval for his clinical trial protocol to study fecal microbiota transplantation (FMT) for colonic inflammatory bowel disease. You can find out more about Davis at BrightMedicineClinic.com, FecalMicrobiotaTransplantation.com, and GoodLifePDX.com.

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Melatonin Treats H. Pylori and Gastric Ulcers

REFERENCE

DESIGN
An open clinical trial that added melatonin to a standard protocol for treating Helicobacter pylori infection. Clinical outcomes were compared with matched controls.

PARTICIPANTS
The study included 100 patients with duodenal ulcer (DU), 30 with chronic non-atrophic gastritis (CNAG), 30 with chronic atrophic gastritis (CAG), and 12 healthy subjects. All patients with DU and CNAG had morphologically confirmed H. pylori infection. The patients with DU were divided into 2 groups, each including age-matched subjects with endoscopically, morphologically, and immunohistochemically identical characteristics.

STUDY MEDICATION AND DOSAGE
Group 1 patients underwent a conventional 7-day course of treatment for H. pylori that included omeprazole (20 mg BID), clarithromycin (500 mg BID), and amoxicillin (1,000 mg BID). Group 2 received the same treatment with the addition of melatonin (3 mg before bedtime). Patients in group 1 continued omeprazole and those in group 2 omeprazole plus melatonin for a total of 2 months. Healthy subjects and patients with CAG served as controls.

OUTCOME MEASURES
All patients underwent fibrogastroduodenoscopy (FGDS) on weeks 2 and 4. Immunohistochemical studies were conducted for endothelin-1 and melatonin-positive cells. Apoptotic activity of mucosal epitheliocytes from gastric antrum was measured before and 6 weeks after the start of therapy.

KEY FINDINGS
The addition of melatonin to the standard treatment protocol for H. pylori increases efficacy of H. pylori elimination and accelerates DU healing. A 2-month therapy of omeprazole + melatonin is more effective at normalizing markers of healing than treatment with omeprazole alone.

PRACTICE IMPLICATIONS
Melatonin should now be considered in the treatment of H. pylori, gastric and duodenal ulcers, and gastrointestinal reflux disease.

Many patients are aware that melatonin may improve insomnia, but few are aware of its beneficial impact on the gastrointestinal tract. We think of melatonin only as the hormone produced in the brain by the pineal gland, yet far more melatonin is actually made by enteroendocrine cells that line the digestive tract.

Bowel habits follow clear circadian rhythms, and it is melatonin that regulates this timing. Dietary L-tryptophan increases blood levels of melatonin, even in animals that have had their pineal glands removed. L-tryptophan is converted to serotonin that in turn is converted into melatonin. The nighttime surge in melatonin comes from the pineal gland, but the gastrointestinal tract maintains baseline levels. Melatonin levels in the gut are 10 to 100 times higher than in the blood.

This is not the first study to report melatonin has benefit in treating H. pylori. In 2 studies published in 2011, Celinski et al reported that either melatonin or L-tryptophan helps heal gastric and duodenal ulcers resulting from H. pylori infections in humans. They gave all patients omeprazole 20 mg twice a day and then added either melatonin (5 mg BID) or tryptophan (250 mg BID). Both melatonin and tryptophan sped healing compared to omeprazole alone.

A number of reports suggest melatonin may be useful in treating gastro-esophageal reflux disease (GERD). This was first brought to our attention by de Souza Pereira who in a May 2006 letter to the editor of the Journal of Pineal Research described a 64-year-old woman whose GERD responded well to a formula containing melatonin (6 mg). Later the same year de Souza Pereira reported the results of a clinical trial in which 176 patients received this melatonin-containing product and 175 received omeprazole (20 mg). All the patients receiving melatonin supplements “reported a complete regression of symptoms after 40 days of treatment.” Only 65.7% of those receiving omeprazole reported similar improvement.

Madalinski in 2011 suggested that melatonin might protect against development of “erosive esophagitis, … esophageal stricture, Barrett’s esophagus and extra-esophageal damage (including the lungs, throat, sinuses, middle ear, and teeth),” all of which are “major risk factors for esophageal carcinoma.”

Jacob Schor, ND, FABNO
The benefits of melatonin aren’t limited to the esophagus and stomach but extend to the pancreas and liver. Melatonin “prevents various forms of gastritis and pancreatitis through the activation of specific MT2-receptors and scavenges reactive oxygen species (ROS). Melatonin counteracts the increase in the ROS-induced lipid peroxidation and preserves, at least in part, the activity of key anti-oxidizing enzymes such as superoxide dismutase.”

In a 2011 study of 75 patients with acute pancreatitis, high levels of endogenous melatonin played a protective role and were associated with a milder course of disease.

Melatonin may also protect against gallstone formation. It reduces biliary levels of cholesterol by inhibiting cholesterol absorption across the intestinal epithelium and by increasing conversion of cholesterol to bile acids. In a study of 45 patients with steatohepatitis, melatonin produced a “statistically significant reduction in GGTP, triglycerides and proinflammatory cytokine levels.”

The bottom line is simple: In melatonin we have a potent tool to help protect and heal the gastrointestinal tract. This study just adds further evidence to support its use.
Fiber, Bacteria, and Colorectal Cancer

Heather Paulson, ND, FABNO

PRACTICE IMPLICATIONS
This study supports what has been reported in several cell culture and epidemiological studies: The right gut bacteria, fiber, and SCFAs may reduce colon cancer cell growth.

Fibers that initiate SCFA production from greatest to least are citrus pectin, soy fiber, sugar beet fiber, pea fiber, apple pectin, and oat fiber.1 Some of the possible protective effects of butyrate include its ability to nourish colonocytes, induce apoptosis, and increase glutathione transferases.2,3

Research has also supported the use of probiotics for reducing colon cancer cell growth in vitro and in vivo. Studies have supported the use of Lactobacillus species to decrease colorectal cell invasion.4 In patients with familial adenomatous polyposis, a 4-week intervention with the probiotic VSL#3, containing both Bifidobacteria and Lactobacillus strains, showed a reduction in cell proliferation and an increase in glutathione S-transferase (GST) enzyme, providing a protective benefit against colon cancer.5

Regarding fiber intake, human data supports the use of vegetable fiber in particular for reducing the risk of developing colon polyps. Another fiber that has been studied in animal models is inulin, which induced apoptosis in already transformed cells when used in the diet.

Although more research is needed, practitioners might suggest citrus pectin, probiotics containing Lactobacillus and Bifidobacteria, and butyrate to reduce colon cancer risk. I encourage my patients to eat a diet rich in vegetable fiber to increase the Bifidobacterium already present in their gut and thus SCFA production. These lifestyle and supplement interventions may provide the right fiber, gut bacteria, and SCFAs to reduce colon cancer cell growth and promote healthy colonocytes.

REFERENCES

REFERENCE
REFERENCE

DESIGN
Population study

PARTICIPANTS
Study included 140 children (37 with autism, 27 non-autistic siblings of those autistic children, and 76 healthy controls). The autistic children were diagnosed based on the Autism Diagnostic Observation Schedule (ADOS) and the Autism Diagnostic Interview, Revised (ADI-R). Serum specimens were collected from all groups and tested for reactivity to gliadin as well as celiac-specific markers.

KEY FINDINGS
Immunoglobulin G (IgG) reactivity to gliadin was higher in autistics compared to unaffected siblings and healthy controls. The presence of gliadin reactivity was also associated with a history of gastrointestinal symptoms. However, celiac-specific markers were not increased in autistics compared to controls. This study helps to clarify an immunological basis for symptomology in autistic children who appear to be intolerant to the gluten-containing grains.

PRACTICE IMPLICATIONS
A gluten-free, casein-free (GFCF) diet has been popular for many years among both families of children with autism and alternative-minded practitioners who treat these patients. Most of the evidence that has circulated in the past has been anecdotal in nature, but a small body of research does exist in this area. In 2008, Barcia reported a 3-fold higher prevalence of celiac disease in people with autism, which speaks to the importance of screening all autism patients regardless of gastrointestinal symptoms. This reactivity may have several etiologies. It is well known that there are immune aberrations in children with autism. It is not entirely clear whether these abnormalities are purely genetic in nature or if they are induced by diet and lifestyle factors. Cuchacovich and colleagues demonstrated in patients who had a myocardial infarction that streptokinase can promote autoantibodies to dipeptidyl-peptidase IV, the primary enzyme used to digest gluten and casein. Streptokinase is released in large amounts when antibiotics are used for streptococcal infections; many people with autism have extensive histories of antibiotic treatment for multiple infections, which may explain their gliadin intolerance. The science that explains gliadin intolerance only accounts for part of this complicated picture. Specific neurological impairment may result from an immunological response to gliadin. IgG to gliadin has been shown to cross-react with cerebellar peptides and Purkinje cells. The cerebellum, other than aiding in balance, is also involved with cognitive abilities like attention and language, as well as regulating fear and pleasure responses. These additional cerebellar functions are quite often impaired in autistic children. Purkinje cells are GABAergic, which may explain why a larger percentage of people with autism will have some seizure activity in their lifetime than will the neurotypical population: 1–2% of children in the general population will develop epilepsy, compared to 5–38% of children with autism spectrum disorder.

The benefits of a GFCF diet may also be explained by a decrease in systemic inflammation during dietary elimination. Milk and wheat ingestion has been shown to increase proinflammatory cytokines TNF-α, IFN-δ. Interestingly, autistic patients show higher serum TNF-α when compared to controls, and those patients exhibit more gastrointestinal symptoms. There is also a direct relationship between a GFCF diet and a decrease in colonic TNF-α compared to controls, adding validity to the diet’s use in the autistic population.

It is important to mention the research that many conventional physicians refer to as evidence that the GFCF diet does not work. Elder and colleagues performed a double-blind, placebo-controlled study on the GFCF diet in children with autism and reported no statistically significant findings. However, several parents in the study did report improvement in their children’s symptoms. It is also worth noting that the participants in the study only stayed on the diet for 6 weeks, which may be too short of a duration to see significant improvement. The results of another study that was presented at the 9th
Annual International Meeting for Autism Research also suggest that the GFCF diet is not effective.4 This research made headlines and was discussed extensively in the media as the definitive answer as to whether this treatment can be helpful. The design of this study was flawed in several ways. The study only included 14 participants, and they were put on a GFCF diet for only 4 weeks, which in my experience is not enough time. Furthermore, when challenging potentially offending dairy and wheat products in the diet, participants were not on a strict GFCF diet, which would obviously skew the results. Most importantly, patients who had gastrointestinal symptoms were eliminated from the study, which seems counterintuitive. Those patients are the ones who might benefit most from this diet, so eliminating those patients would also certainly affect the results.

As for positive findings in the research, a small study (N=7) at Bastyr University did not show changes in the Gastrointestinal Symptoms Rating Scale (GSRS) or Childhood Autism Rating Scale (CARS), but parents of all children on the GFCF diet did report improvement of gastrointestinal symptoms and behaviors.5 At Pennsylvania State University, a parent-questionnaire study of 387 children with autism that have implemented the diet showed improvements in autistic behaviors, physiological symptoms, and other social behaviors.6

When considering treatments for children with autism, it is of utmost importance to consider all research on a particular therapy. However, not all safe and effective treatments have large bodies of data supporting their benefits. In such cases those who practice a biomedical approach to autism care may need to depend on information passed anecdotally. Therefore, a reasonable approach would be to weigh the benefits versus the risk of adverse effects of a therapy and proceed prudently.

REFERENCES
7 Vojdani A, Pangborn JB, Vojdani E, Cooper EL. Infections, toxic chemicals and dietary peptides binding to lymphocyte receptors and tissue enzymes are major instigators of autoimmunity in autism. Int J Immunopathol Pharmacol. 2003;16(3):189-199.
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Literature Review: Probiotics for the Treatment of Irritable Bowel Syndrome
By Lise Alschuler, ND, FABNO, and Karolyn A. Gazella

ABSTRACT
Interest in the use of probiotics to treat irritable bowel syndrome (IBS) has increased considerably over the past several years. The literature now provides us with a distinct picture as to how these beneficial bacteria impact health and relieve IBS symptoms. In many cases, probiotics can be a first-line treatment choice and provide a viable alternative to existing treatments that lack efficacy and may cause side effects. While more data is needed regarding strain, dosage, and sub-type application, it is clear that multistrain probiotics can play a significant clinical role in the treatment of IBS.

INTRODUCTION
Irritable bowel syndrome (IBS) is not a disease, but rather a functional gastrointestinal disorder. It has characteristic symptoms, the presence of which elucidate accurate diagnosis. IBS is a diagnosis of exclusion, and it is important to rule out other organic pathologies before making the final diagnosis and proceeding to treatment. Prevalence statistics vary dramatically, but most studies have shown that approximately 10% to 15% of the US population is affected by this disorder.\(^1\) Many experts believe prevalence may be higher, affecting up to 40% of adults in the United States.\(^2\) This prevalence range may be the result of the fact that less than 30% of people affected see their doctor for appropriate diagnosis and treatment.\(^3\) IBS can be difficult to diagnose because it is not associated with structural or tissue abnormalities. As such, physicians must rely solely on symptom presentation to make the diagnosis.

The Rome criteria were developed to classify functional gastrointestinal disorders based on clinical symptoms. The most recent revision is Rome III, in which IBS is diagnosed based on the following criteria:\(^4\)

- symptom onset at least 6 months prior to diagnosis
- recurrent abdominal pain or discomfort (ie, an uncomfortable sensation, not pain) for at least 3 days per month during the prior 3 months
- in addition to recurrent abdominal pain or discomfort, at least 2 of the following must also be present:
  1. symptom improvement with defecation
  2. onset associated with change in frequency of stool
  3. onset associated with a change in the form or appearance of stool

The Rome criteria specify that in order for a person to be eligible for pathophysiological research in clinical trials, he should report pain and/or discomfort frequency of at least 2 days per week during the screening evaluation.

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), National Institutes of Health, has identified 4 subtypes of IBS that help drive treatment decisions. The following categorizations are based on percentage of all bowel movements over a representative time period:\(^5\)

1. IBS with constipation
   - hard or lumpy stools at least 25%
   - loose or watery stools less than 25%
2. IBS with diarrhea
   - loose or watery stools at least 25%
   - hard or lumpy stools less than 25%
3. Mixed IBS
   - hard or lumpy stools at least 25%
   - loose or watery stools at least 25%
4. Unsubtyped IBS
   - hard or lumpy stools less than 25%
   - loose or watery stools less than 25%

The NIDDK National Digestive Disease Information Clearinghouse also states that secondary symptoms can include abdominal bloating, passing mucus, or feeling that the bowel movement was unproductive or incomplete.

Previously, IBS was thought to be a psychosomatic disorder; however, research has advanced our understanding of IBS to
include an organic etiology linked to altered gut microbiota and low-grade inflammation.⁶

Presently, conventional treatment for IBS symptoms includes the use of nutritional counseling, fiber or laxatives such as lubiprostone (Amitiza), prescription antispasmodics, or prescription antidepressants. The high treatment failure rate of current conventional management, combined with a challenging side effect profile associated with the drug therapy has prompted new explorations into the etiology and treatments of IBS. Foremost among these new approaches is the understanding of underlying dysbiosis as a prime cause of IBS, with the attendant rationale for the use of probiotics as a leading treatment.⁷–⁹

PATHOPHYSIOLOGY

While the specific cause of IBS remains somewhat unclear and continues to be debated, several well-established hypotheses exist regarding the pathophysiology of the condition. IBS is essentially a disorder of gut motility,¹⁰ characterized by hypertonic segmental contractions (spastic constipation) alternating with hypomotile bowel or increased peristaltic contractions (diarrhea). Several factors contribute to this disordered bowel motility. Food intolerance, considered a major contributing factor, is estimated to affect up to 50% of all patients with IBS.¹¹ For example, studies have shown that inadequate carbohydrate digestion can provoke IBS symptoms.¹² Serotonin receptor hypersensitivity in the bowel wall resulting in abnormal peristaltic contractions has also been implicated in IBS.¹³ Serotonin dysregulation can be provoked by acute histamine-mediated inflammation or significant stress with resultant increased secretion of corticotropin releasing factor and IL-1, which in turn stimulate the intestinal release of 5-hydroxytryptophan and activation of serotonin receptors. Alterations in bowel flora and associated immune dysregulation are also recognized as key factors in IBS.¹⁴ This review will focus on the pathophysiology of dysbiosis and immune dysregulation in IBS, and how probiotics may be indicated in treating patients with IBS.

From an immunoregulation standpoint, studies demonstrate that commensal bacteria provide an environment that encourages the effective modulation of both innate and adaptive immunity.¹⁵ Immunoregulation is also intimately connected to the composition of the microbiota environment in the gut.¹⁶ Additionally, immune homeostasis is critical to the control of inflammatory processes that can exacerbate IBS. In 2007, Liebregts and colleagues demonstrated that IBS patients had significantly higher proinflammatory markers, specifically TNF-alpha, IL-1beta, IL-6, and LPS-induced IL-6 levels.¹⁷ Immunoregulatory dysfunction has been found in IBS patients both mucosally, as well as systemically via a decrease of T regulatory cells.¹⁸ T regulatory cells, also known as suppressor T cells, play a critical role in gut-associated lymphoid tissue (GALT) antigen sampling and tolerance.¹⁹ Decreased intestinal T regulatory cells increase immune-mediated inflammation in response to ingested food compounds and intestinal microflora. This, in turn, alters the migratory motor complex of the intestines and contributes to the altered motility characteristics of IBS.

In large measure, due to the immune-disrupting effects from altered intestinal microflora, dysbiosis is a main etiologic factor in the development and worsening of IBS.²⁰ Furthermore, the subsequent correction of this imbalance may be an effective treatment for this condition.²¹

When the state of equilibrium in the large intestines is disrupted to favor an overgrowth of harmful bacteria, low-grade inflammation and immune dysregulation can result.²² Correcting large intestinal dysbiosis will in turn reverse inflammatory responses and normalize immunoregulation in the gut. A review by Hemarajata and Versalovic reinforce data showing that probiotics positively influence the composition and function of internal microbial communities and can reverse large intestinal dysbiosis, thereby alleviating corresponding IBS symptoms.²³

Dysbiosis in the form of bacterial overgrowth in the small intestines is referred to as small intestinal bowel overgrowth (SIBO) syndrome and has been implicated in IBS. In 2000, Pimentel and colleagues found that of their 202 patients with IBS, 78% had SIBO.²⁴ In 2005, Nucera et al found that 65% of their 98 patients with IBS had SIBO.²⁵ SIBO can be diagnosed via
breath trace-gas analysis. Hydrogen/methane breath tests have been shown to have good sensitivity and specificity and are less invasive than intubation and culture of intestinal aspirates.\(^{26}\) Both the Pimentel and Nucera studies utilized the breath trace-gas analysis. Most GI experts agree that SIBO plays a role in either the development or exacerbation of IBS symptoms.

Because correcting dysbiosis and SIBO plays a significant role in alleviation of IBS symptoms, proper diagnosis is important. Signs of dysbiosis can be detected in both stool and urine. One example of dysbiosis stool analysis is the Comprehensive Digestive Stool Analysis 2.0, which tests various aspects of digestion, absorption, microbiology, and metabolic markers.\(^{27}\)

Normalizing the gut microbial environment and associated GALT immunity can improve symptoms and severity of IBS. Probiotics influence both mechanisms of action.

**SYSTEMATIC REVIEWS**

Mounting evidence demonstrates that probiotics can be a clinically valid tool in the treatment of IBS. Based on existing data, as well as probiotics’ safety profile, it is prudent to consider probiotics as a potential first-line treatment choice for many patients with IBS.

Within the past few years, several systematic reviews have been published on the topic of probiotics and the treatment of IBS. In 2009, Brenner and colleagues looked at 16 trials that met the following selection criteria:

- randomized clinical trial
- adults with IBS using Rome II criteria
- single or combination probiotic versus placebo
- improvement in IBS symptoms and/or decrease in frequency of adverse events reported

The analysis clearly reflected the lack of research rigor in this field up to that point. Eleven of the 16 trials evaluated had suboptimal study design and did not have adequate data about tolerability and adverse events. The review did show that in 2 of the well-designed studies, *Bifidobacterium infantis* 35624 demonstrated significant benefit in improving abdominal pain and discomfort, bloating and distention, and/or constipation when compared to placebo.\(^{28}\)

A meta-analysis in 2009 reviewed 14 randomized placebo-controlled trials in which the trials also varied in terms of length of treatment, dose, strains, and strengths of the probiotics. Their combined data, however, did show modest improvement in overall symptoms.\(^{29}\)

A 2010 review looked at 19 random clinical trials. In this review, Moayyedi P et al found that overall the trial quality was good and that “probiotics were statistically significantly better than placebo.”\(^{30}\)

The most extensive review done to date was completed and published in 2012 and looked at 42 trials. Clarke and colleagues found that 34 of the 42 trials reported beneficial effects in at least one of the symptom endpoints established.\(^{31}\) However, these researchers also pointed out deficits in trial design that included inconsistencies in strain and dosage. The researchers conclude: “Recent incremental advances suggest these areas are being addressed and that the future holds much promise for the use of lactic acid bacteria in the treatment of irritable bowel syndrome.”

Of note, there was minor overlap between the 2010 and 2012 systematic reviews with Clarke et al presenting the most comprehensive information available to date.

**RECENT RANDOMIZED CLINICAL TRIALS**

A 2010 randomized, double-blind, placebo-controlled trial using a multistrain probiotic for 6 months found improvement in dysbiosis (*P*=0.02) and overall GI microbiota.\(^{32}\) The intervention in this study included 4 different strains, including *Lactobacillus rhamnosus* GG, *Lactobacillus rhamnosus* LC705, *Propionibacterium freudenreichii* ssp. *Shermanii* JS, and *Bifidobacterium breve* Bb99. The researchers note that this same combination of strains had been shown previously to alleviate IBS symptoms; their study confirms the mechanism of action.

A study published in 2012 used “adequate relief (AR) of overall IBS symptoms” as its primary outcome measure for the 50 IBS patients they assessed weekly for a 10-week period. The treatment consisted of 7 species (*Lactobacillus acidophilus*, *Lactobacillus plantarum*, *Lactobacillus rhamnosus*, *Bifi-
**Conclusions**

Intervention Design

- The issue of the importance of bacterial viability is another understudied topic as even the implantation of dead bacteria is most effective for each of the IBS subtype categories.
- More worrisome is the repeated failure to confirm bacterial viability. That said, the rationale for probiotic use as it relates to mechanisms of action remains strong, with the body of clinical data taken as a whole consistent with expected results.

**DISCUSSION**

Over the past several years, the number of studies involving probiotics for the treatment of IBS has been growing. While many of the outcomes are encouraging, continuity in research design parameters has limited the significance of these findings. The biggest challenge is the lack of consistency regarding strain and dosage. More worrisome is the repeated failure to confirm bacterial viability. That said, the rationale for probiotic use as it relates to mechanisms of action remains strong, with the body of clinical data taken as a whole consistent with expected results.

Given the prevalence of IBS, its difficult management, and the lack of efficacy of existing treatments, probiotics offer a viable clinical strategy. Because probiotics have been proven to positively influence immunity and gut microbiota, they have the potential to offer long-term relief from a wide variety of symptoms associated with this condition. More data are needed to determine which strains and dosages are most effective for each of the IBS subtype categories. The issue of the importance of bacterial viability is another understudied topic as even the implantation of dead bacteria has been found to improve digestive function. In the face of the paucity of conclusive data, strict guidelines concerning the use of probiotics are premature. However, in consideration of the body of data on probiotics and IBS, clinicians are best served to use a high-quality, multistrain brand.

**SUMMARY OF STUDIES**

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**REFERENCES**

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A book’s table of contents is often a telling first glimpse of what to expect from the book—not just in terms of content, as the name would imply, but also in terms of style, tone, and personality. So when I opened *Enterobimmunology: A guide to prevention and treatment of chronic disease*, by Charles A. Lewis, MD, MPH, my interest was piqued immediately. With chapter titles like Meteorism, Trots and Foul Winds; Appetite, Satiation and Satiety; and Obesity, Syndrome X and the Company it Keeps, how could it not be?

Enterobimmunology is a field of medicine that focuses on how the enteric immune system’s response to bacteria, toxins (parasitic or food metabolites), and foreign proteins elicits inflammation and influences all other body systems. This book covers enterobimmunology as it relates to such diverse topics as acne, rage, biofilms, interstitial cystitis, diabetes, obesity, cancer, migraines, depression, sleep, osteoporosis, and autoimmunie disease. It also covers standard gastrointestinal (GI) conditions: small intestinal bacterial overgrowth (SIBO), dysbiosis, gluten disease, leaky gut, inflammatory bowel disease, and irritable bowel syndrome. The first 7 chapters cover the basics: GI function overview, proteins, fats, carbohydrates, sugar malabsorption (the aforementioned “Meteorism, Trots and Foul Winds”), and the colon and its inhabitants. I enjoyed the overview and learned quite a few more details that are applicable in my daily practice of naturopathic medicine. For example, the thorough table outlining the hormones that affect the GI tract will become a quick, easy reference in my practice. I also appreciate that each chapter is only a few pages but does not lack for depth of information. After the quick overview, the author delves into the nitty gritty of more complicated issues—hyperammonia, enterobimmune depression, leptin resistance, mast cell activation disorder, and leukotriene-associated hypersensitivity.

Naturopathic doctors are trained to have a very good base of knowledge when it comes to the digestive system and how it affects health. We are thoroughly educated in nutrition and how the foods we eat or don’t eat can cause or perpetuate disease states. However, details and intricacies unique to each individual can be very difficult to tease out. As one example, I have a mother and daughter who react to everything. They react to certain foods, most supplements, some herbs, and most synthetic agents. For the mom, her issue is chronic sinus and bronchial issues. Her daughter gets skin reactions from acne to perioral dermatitis. After many years and trying every assessment and treatment I could think of, we’ve achieved a degree of success, but their symptoms still recur intermittently. I felt like I had run out of ways to help them before reading this textbook, which contains at least 8 chapters on immune hypersensitivity. In a brief aside, “Histamine in Pregnancy,” Lewis explains that the placenta creates an increased amount of diamine oxidase (DAO), which is the enzyme that catabolyzes/inactivates histamine. He writes, “High DAO levels may explain why some women feel so much better during pregnancy and also explain the reduction in the frequency of migraines and other histamine reactions during pregnancy. High DAO levels lower histamine reactions through much of the pregnancy and protect pregnant women from biogenic amines that otherwise have them not feel so well.”

With the mother and daughter I was treating, the daughter had just given birth, and she had not experienced any of her
usual hypersensitivities during her entire pregnancy. Perhaps the daughter benefited from the placental DAO, I thought. This idea solidified as I read the very detailed chapter on Mast Cell Activation Disorder. After reading and rereading this chapter, I have a few leads on where to go next to address my complicated hyperreactive patients.

This textbook is full of factoids and details that can be applied to daily practice. I found information on carbohydrates that was useful—especially if you utilize the fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAP) or SIBO diets in your practice. Each chapter is short and to the point and includes tables summarizing necessary details and references to other chapters to garner further clarification on difficult points. I also like that the author summarizes every chapter; at the end of the Leaky Gut chapter is a 20-point list on treating leaky gut, and only a few of the points are about a supplement. Lewis’s book is not a primer on what supplement to recommend but on what the possible causes or maintaining stressors are that perpetuate a state of disease. This is not another book on green pharmacy, but a book that follows the tenets of naturopathic medicine—treat the whole person, find the cause, and use food as your medicine.

In summary, I thoroughly enjoyed this textbook. I look forward to reading it more as I pick up some new tidbits that I can apply to my practice. I also enjoy Lewis’ writing style: He is clear and straightforward, and I can sense that he has plenty of experience behind what he is saying. I enjoy the sense of humor sprinkled throughout the book. This textbook does have its share of typographical errors and forgotten prepositions, but that seems a silly demerit when the content is so exceptional. Every physician should have this insightful book at his or her side—especially those practitioners who follow the tenets of naturopathic medicine.

ABOUT THE AUTHOR

Charles A. Lewis, MD, MPH, is an independent consultant to biomedical and technology companies. He also has more than 20 years in family practice medicine. He received his medical doctorate from Universidad de Tecnología de Santiago in the Dominican Republic and his master of public health from the University of Alabama at Birmingham.

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The Role of Digestive Enzymes in Gastrointestinal Health
A discussion with researcher M. Mamadou, PhD

Q. What role does poor digestion play in digestive discomfort and digestive disorders?

A. Digestion is a complex process that starts in the mouth and continues throughout the alimentary canal. First, the foods must be processed. This processing must be done progressively as the foods move from one section of the digestive system to the next. Any impairment in the process at any one segment can, over time, lead to complications ranging from discomfort to major disorders. Heartburn, colic, bloating, flatulence, and various bowel inflammations are all examples of conditions resulting from an impaired digestive system. Proper diet followed by an adequate and timely digestive process constitutes the first and last line of defense not only in maintaining gut health, but also in promoting overall general health.

Q. Conventional medicine often looks at digestive issues as an overproduction of acid. What is your view of this approach?

A. In many cases, the overproduction of acid is an attempt by the stomach (the organ responsible for producing the hydrochloric acid) to enhance the digestion of the proteins. This acid plays an important role in helping the digestion of proteins, and also in facilitating the absorption of minerals and some vitamins. However, as in most cases, the gut is no exception. The excess of anything could create problems. Thus, excess acid production must be avoided, and a good digestive function can do that.

When acid production is in excess, a healthy alternative approach is to improve the diet to make it more digestible, and to improve the digestive process so foods do not stay in the stomach too long and continue to stimulate acid production. Supplemental digestive enzymes that are proven effective in the conditions prevailing in the stomach and other segments of the alimentary canal can enhance the digestive process.

Q. What are the main enzymes used as supplemental digestive enzymes?

- *Proteases* help break down proteins, which are very difficult to digest. No single protease can digest all proteins efficiently. In digestive enzyme formulations, it is recommended to use a blend of proteases, also called proteolytic enzymes. Peptidases are also in this group. When proteins are not properly digested, they could create systemic health problems such as inflammation and behavior issues. They could also promote formation of foul-smelling gases when they are fermented by the microorganisms in the large intestine.

- *Lipase* helps digest fats. In the area of supplemental digestive enzymes, there are various lipases used, mostly based on their fungal sources. Improper digestion of fats could lead to diarrhea and deficiency of the fat-soluble vitamins A, D, E, and K.

- *Amylase* helps digest starch. Improperly digested starch could reach the large intestine and cause major gas formation.

- *Cellulase* helps break down the big molecules of cellulose found in plant foods. Cellulose is a fibrous molecule that also serves to cement many other health-promoting molecules in the plant-derived foods, so it is important to digest it. However, no human cell produces the enzyme cellulase necessary to break down cellulose. By incorporating the enzyme cellulase in digestive enzyme formulations, we can digest cellulose molecules totally or partially to help free the various molecules in the plant-derived foods, but also to enhance the toxin-binding ability of the cellulose.

ABOUT THE EXPERT

M. Mamadou, PhD, is the chief science officer of Phytomedic Labs. He earned his doctorate from the University of Cincinnati and has been actively involved in enzyme-based formulations for health and wellness. His present research activities focus on isolating new phytochemicals and enzymes for dietary supplements. He has taught and conducted research at several universities and has provided consulting and research services for many health and nutrition companies, including EnzymeScience, Inc, a key sponsor of the *Natural Medicine Journal*.
• **Lactase** breaks down lactose. Many people have lactose intolerance because lactase is lacking or not working properly. A supplemental enzyme product containing lactase helps prevent the symptoms associated with lactose intolerance.

• **Alpha galactosidase** helps people tolerate beans and prevent the excess gas they can cause.

**Q. How can supplemental digestive enzymes support overall digestive health?**

A. By enhancing the breakdown of food molecules, supplemental digestive enzymes reduce the digestive organs’ workload. Moreover, if foods are not digested in a timely manner, they tend to accumulate and promote potentially damaging local inflammations. If the walls of the intestines become damaged, intestinal permeability (ie, leaky gut syndrome) may occur. This condition can lead to the passage of relatively large food molecules into the general blood circulation.

The digestive system is very complex. It has a large surface area, and all the cells lining the alimentary canal are alive and continuously functional. While some of the molecules in the foods and beverages we consume are beneficial, others could be harmful. The cells of the intestinal lining have a replacement rate of 3–5 days. This high turnover rate implies a very active DNA metabolism, including DNA replication to ensure continuity of the genetic make-up within the cells. Such continuous duplication and renewal of cells, with constant exposure to all types of outside molecules, makes the cells vulnerable to injury, including DNA mutations. A good way to maintain digestive health is to introduce healthy foods and ensure their digestibility.

It is important to remember that what goes on in the gut does not stay in the gut. This is critically important, because the gastrointestinal tract

- has its “own” nervous system that could function independently of the central nervous system.
- produces more serotonin than the rest of the body.
- has an intricate immune system that is continuously in contact with the rest of the immune system. An estimated 75% of the immune system in the body transits through the gastrointestinal tract.

A healthy diet, free of harmful components, supplemented with effective digestive enzymes, helps ensure digestive structural and functional integrity, and thus its health.

**Q. Are there any contraindications healthcare providers should keep in mind when using digestive enzymes in clinical practice?**

A. For general digestive support, there are no known contraindications against taking supplemental digestive enzymes. In some cases dealing with health challenges such as improper blood flow, inflammatory processes, and other systemic conditions beyond the gastrointestinal tract, check that the patient does not have blood-clotting disorders, as enzymes tend to thin the blood. Additionally, if a patient is taking other blood-thinning medications, there could be some synergistic effect that must be avoided.

**Q. What should practitioners look for when choosing digestive enzymes to recommend to their patients?**

A. The main points I recommend in selecting supplemental enzyme products are that the products should be made from effective enzymes that can sustain the conditions in the digestive system, and that they should be produced by reputable companies with good manufacturing practices and sound quality control protocols.

Over the years, I have visited and worked with enzyme producers, dietary supplement manufacturers, and enzyme product distributors that are very strong in every aspect of safety and quality and using standards and norms as in the pharmaceutical industry. Additionally, innovative approaches continue to be developed for selecting organisms that produce effective enzymes for use in the digestive process, inflammation control, and even in cases of emergency dealing with stroke or heart attack.

These are some key points to consider when selecting an enzyme for gastrointestinal health:

- pH stability within the digestive system
- Effectiveness within the alimentary canal
- Lack of allergenicity or toxicity

Some of the key and reliable supplemental enzyme companies have scientific, safety, and quality control staff that can address specific questions a practitioner may have to help in using the products.

For Dr M. Mamadou’s round-up of specific conditions that respond to digestive enzymes, visit Natural Medicine Journal
Americans’ demand for “natural medicine” is greater than ever before. This presents unlimited opportunities and significant challenges. While others provide care in natural medicine, NDs bring a profound, comprehensive, and unique quality to the table. We owe it to our patients and community to stand up for our profession to make clear that we are the experts in natural medicine.

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