NATUROPATHIC DOCTOR NEWS & REVIEW

VOLUME 15 ISSUE 1 JANUARY 2019 | GASTROINTESTINAL HEALTH / TOXICOLOGY / BARIATRIC

Tolle Totum

Prebiotics & Metabolic Regulation

Benefits Beyond the Gut

ERICK R. CERVANTES, MPH, ND
DALE PFOST, PHD

Human beings are host to a diverse ecosystem known as the microbiome. Characteristic of our microbiome, among many other things, is its now well-known diversity within the individual and from person to person, as well as its vast array of elaborate influences on our physiology. Our scientific knowledge of this symbiotic ecosystem has grown tremendously, and its clinical significance and implications cannot be ignored. This paper highlights how some microbiota within our intestinal tract, in particular the large intestine, influences

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Student Scholarship Honorable Mention

Psychiatric Disorders

Targeting the Microbiome

ALEXANDRA FRANCIS, ND, MS, CNS
MARIE WINTERS, ND, FABNO

All disease begins in the gut.
(Hippocrates)

When in doubt, treat the gut" is an excellent naturopathic rule of thumb that naturopathic doctors have relied on for decades. We have always understood that symptoms and chronic diseases often improve when we focus on treating the gut, but only recently has there been exploration into why this is so. We've been told that we have more microorganisms in our gut (meaning our whole digestive system, but primarily the small and large intestines) than we have cells comprising our bodies. "The human gut microbiota consists of a complex community exceeding 100 trillion microorganisms whose collective genome – the microbiome – encodes 100 times more genes than the human genome. It is now widely considered that the gut microbiota should be considered an 'exteriorized' organ placed within the body, which provides important physiological functions and is indispensable for human life."[1] These microorganisms are responsible for metabolizing dietary nutrients, xenobiotics, and drugs, as well as maintaining the integrity of the gut mucosal barrier, immunomodulation, and protection against pathogens.[2]

Our knowledge of the functions and roles the gut microbiome plays in our health and physiology has been expanding. The gut microbiome is a relatively new exploration in the field of medicine, and recent research has shed light on promising new clinical applications of focusing treatment efforts on the gut microbiome. Some of the conditions shown to benefit from optimizing the gut microbiome include several digestive disorders, such as irritable bowel syndrome (IBS) and inflammatory bowel disease (IBD), as well as systemic conditions such as diabetes mellitus, obesity, and cardiovascular disease.

Psychiatric Disorders

About half of US adults will experience a mood or mental disorder consistent with the diagnostic criteria in the DSM-IV at some point during their lives.[3] The onset of these disorders is usually during childhood or adolescence, which suggests that treatment methods should be directed at the younger population and emphasize prevention.[3] Use of conventional drug therapies for psychiatric disorders has been on the rise over the last few decades. Given the increasing rates of mood disorders and drug dependence trends, conventional drug therapy appears to have had relatively low efficacy in psychiatric patients, especially those with

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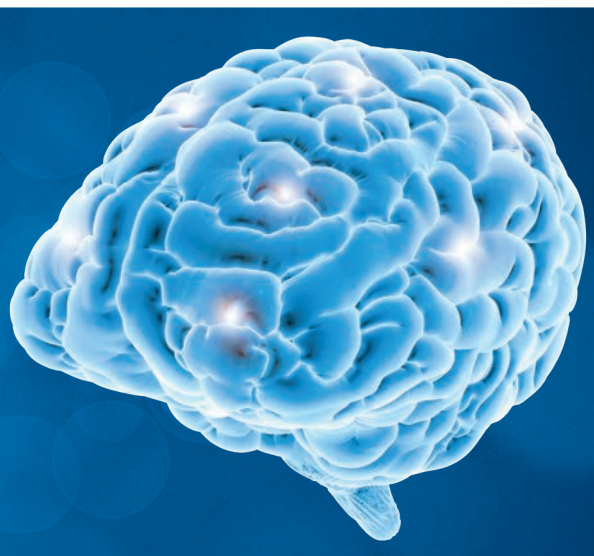

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our health through its fermentation of prebiotic dietary fiber and polyphenols and the resulting metabolite-driven feedback mechanisms. In addition, this paper discusses the clinical implications of prebiotic (dietary fiber and polyphenols) supplementation for various metabolic syndromes in terms of its influence on satiety and blood glucose regulation. To illustrate, we present findings from 2 clinical studies examining the health effects of a prebiotic blend referred to as a Gastrointestinal Microbiome Modulator, or GIMM. Both studies were conducted under the direction of Frank Greenway, MD, of the Pennington Biomedical Research Center in Baton Rouge, LA, one of the nation's leading centers for nutrition research.

In general, our Western lifestyle plays a detrimental role in our health and well-being. Characteristic of a Standard American Diet (SAD) and Western lifestyle is a decrease in physical exercise (sedentary lifestyle) as well as an increase in energy intake in the form of increased dietary sugars and processed foods.[1] Such diets have a high glycemic index, are high in calories, and contribute to both high blood sugar excursions and weight gain. Daily consumption of this type of diet has led to an increased incidence of complex symptoms collectively categorized as metabolic syndrome. The key characteristics of metabolic syndrome are obesity, loss of glycemic control, dyslipidemia, and hypertension.[1] The relationship of these conditions with gut health and our microbiota is explained here. It is also important to note that associated luminal dysbiosis due to poor dietary choices and other factors – such as food sensitivities/allergies, exposure to pesticides in our food supply, alcohol abuse, and antibiotics – plays a major role in gut permeability and impaired gut-barrier function.[2] The consequences are a variety of other associated clinical conditions: food sensitivities and allergies, allergic rhinitis, inflammatory bowel disease, celiac disease, autoimmune hepatitis, prediabetes, type 2 diabetes mellitus, multiple sclerosis, systemic lupus erythematosus, depression, and autism.

Prebiotics, SCFAs & Health

Our gastrointestinal (GI) health is greatly dependent not only on the foods we eat, but also on the health of our gut microbiota. The human microbiome is the entirety of the environment of microorganisms living in and on our bodies.[3] The majority of them symbiotically inhabit our GI tract.

Diets that are high in fruit and vegetables are richer in fiber than the SAD diet. On average, Western diets provide approximately 20-25 grams of dietary fiber per day, while high fruit and vegetable diets provide approximately 60 grams of dietary fiber.[1] Intestinal bacteria, specifically those residing in the cecum and large intestine, produce short-chain fatty acids (SCFAs) – key signaling metabolites from non-digestible nutrients, specifically fiber and polyphenols, that pass out of the small intestine unaffected.[1] The major types of fiber that pass through the gut are plant cell-wall polysaccharides, oligosaccharides, and resistant starches (eg, inulin and beta-glucan). The relationship between the health of our microbiota and high-fiber diets has been well established. Interestingly, the amount and type of fiber consumed has dramatic effects on the composition of the microbiota and consequently the type and amount of SCFAs produced.

The health of our GI tract and the health of our microbiota are thus directly correlated to our dietary intake of fiber. More specifically, daily intake of dietary prebiotics (polyphenols and non-digestible complex carbohydrates, aka fiber) directly affects the diversity of our microbiota, our metabolism, and therefore our health. Prebiotics cannot be digested by humans but are fermentable and serve as nutrients for the microbiota in the large intestine. The SCFAs (the products of fermentation) are used by the cecal and colonic epithelium cells for energy production, and they lower luminal pH, which inhibits the growth of pathogenic bacteria.

SCFAs also have far-reaching actions beyond the intestine. For example, SCFAs

Our Western lifestyle plays a detrimental role in our health and well-being. Characteristic of a Standard American Diet (SAD) and Western lifestyle is a sedentary lifestyle and an increase in energy intake in the form of increased dietary sugars and processed foods.

act as signaling molecules to G-protein receptors involved in satiety and glucose regulation, and they regulate the balance between fatty acid synthesis, fatty acid oxidation, and lipolysis. Specifically, fatty acid oxidation is activated by SCFAs in the liver and muscle tissue, while *de novo* synthesis and lipolysis are inhibited. This results in a reduction of free fatty acids in the plasma and a decrease in body weight.[1]

SCFAs inhibit fat storage in adipose tissue by suppressing insulin signaling in adipocytes, while promoting lipid and glucose metabolism in other tissues.[1] Moreover, SCFAs trigger the release of gut hormones, peptide YY (PYY) and glucagon-like peptide-1 (GLP1). PYY is known as a satiety hormone, helping to promote the feeling of satisfaction and early cessation of eating. GLP1 triggers the release of insulin and decreases the secretion of glucagon by the pancreas for glucose regulation; it also slows gastric emptying.[4-7]

Study #1

Prebiotic Effects on GI Microbes & SCFAs

In a placebo-controlled, double-blind randomized trial, 30 adults with a body mass index (BMI) ≥30 or a diagnosis of prediabetes were administered either a prebiotic formulation or placebo for 4 weeks. Stool and blood samples were collected at baseline and at 4 weeks, and markers for intestinal microbiome health and metabolic parameters were measured.

For the GI portion of the study, a GIMM, a strategic blend of 3 prebiotic nutrients, was studied for its ability to promote a healthy-functioning gut microbiome.[8] Fecal assessments included aerobic and anaerobic bacteria and yeast/fungi (as determined by DNA analysis); SCFAs; markers for digestion, absorption, and inflammation; and secretory IgA (sIgA) to assess immune function. This prebiotic blend was specifically designed to produce a greater yield of SFCAs in the large intestine by diverting biosynthetic pathways towards the SCFAs and shifting away from biosynthesis of methane and hydrogen sulfide, gases that have been associated with obesity,[9,10] type 2 diabetes,[11] irritable bowel syndrome and colitis.[12,13] The blend included inulin, beta-glucan, and polyphenols, totaling 8.8 grams of fiber in powdered form. A blend of xanthan gum and cellulose was used for the placebo. Participants were instructed to mix the powder into 6 oz water and take it twice daily on an empty stomach. No changes were made to their daily meal routine.

Inulin is a fermentable prebiotic that expands the microbiota populations, leading to an increased production of SCFAs (Figure 1).[14] With the growth achieved by inulin, the second ingredient – polyphenols extracted from blueberries – serves as a microbial substrate that is acetogenic, ie, uses hydrogen to produce acetate, a key SCFA (Figure 2).[15,16] This can result in a competitive advantage for the acetogens and helps shift the microbiome activity from microbiota that would otherwise produce methane and hydrogen sulfide. The third ingredient, beta-glucan, protects the GI tract by triggering the release of sIgA and acting as a decoy substrate for microbiota to consume instead of digesting the mucosal lining.[15,17-21]

Summary of Prebiotic Blend

- Inulin from agave promotes growth of microbial populations that produce SCFAs
- Polyphenol antioxidants from blueberries provide a substrate for the growth and activity of certain microbiota that produce acetate, a key SCFA
- Beta-glucan from oats protects the intestine's mucosal lining and supports the immune system

Prebiotic Effects on Glucose Regulation & Appetite

This same study[8] also assessed the effectiveness of GIMM on metabolic parameters, lipids, and satiety, at baseline and at 4 weeks. Evidence supports the significant role of the gut microbiota in the biochemistry of satiety – the feeling of reduced hunger and desire for smaller portions at mealtime.[22] A validated Visual Analog Scale (VAS) was utilized to assess satiety. Blood measurements included serum glucose and insulin (in a 3-hour oral glucose tolerance test [GTT]), hemoglobin A1c, hs-C-reactive protein (hsCRP), PYY, ghrelin, lipids, and other blood chemistry.

Compared to placebo, results for the prebiotic group showed reduced mealtime blood glucose measurements, as measured during the oral GTT (Figure 3); increased satiety, as measured by the VAS (Figure 4); and increased levels of sIgA, a fecal biomarker for immune preparedness (Figure 5).

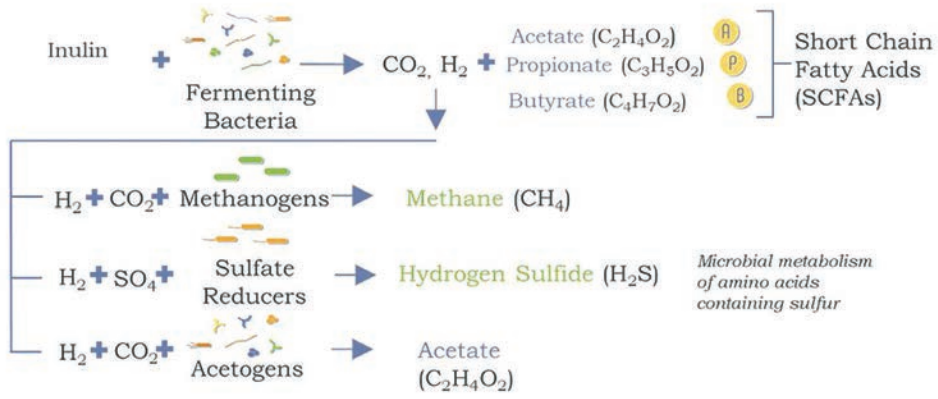
Study #2

Effect of Prebiotics on Metformin Tolerability

Not all drugs developed to be taken orally are completely absorbed into the blood and thus remain in the GI tract where there is potential for interactions with the microbiota. Individuals with high blood sugar are commonly offered metformin, an effective glucose-lowering therapeutic that is generally well tolerated; however, the drug can occasionally lead to diarrhea, constipation, heartburn, or nausea. For some people, this is enough to make it a challenge for them to achieve the recommended dosing. This second study showed that the same prebiotic blend (GIMM) provides nutritional support to counterbalance the occasional gastrointestinal effects that can accompany metformin.

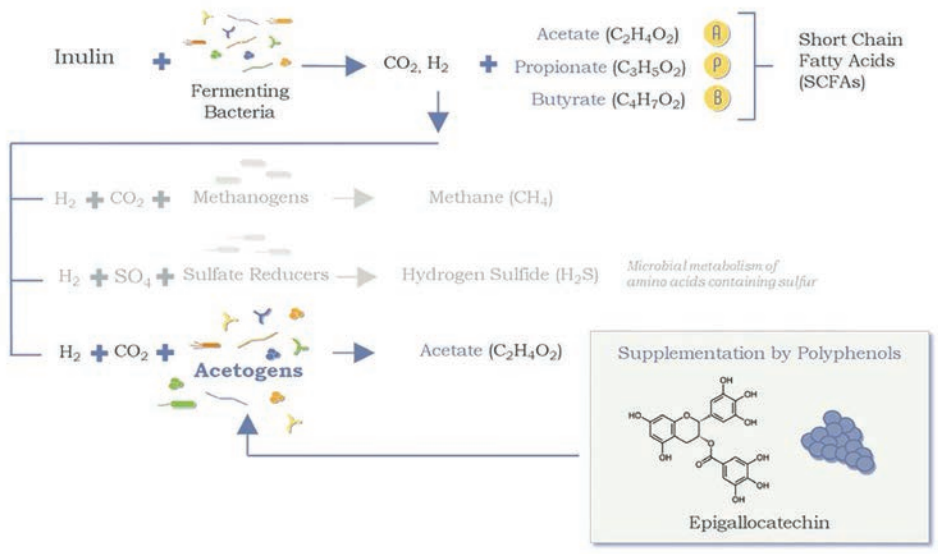
This placebo-controlled, double-blind, randomized, crossover study assessed type 2 diabetics with documented metformin intolerance.[23] Each of the 2 treatment periods lasted 2 weeks, with a 2-week washout period between them. All subjects continued to take daily metformin. In

Figure 1. **Production of SCFAs from Prebiotics**



Cross-feeding of microbiota: Use of hydrogen from an initial fermentation produces undesirable gases and more SCFAs through a competitive process

Figure 2. **Polyphenols Shift the Competitive Balance of H_2 Utilization**



Polyphenols serve as a key substrate for acetogens to produce acetate (thus reducing biosynthesis of undesirable gases)

Dietary prebiotics (fiber and polyphenols) have a major role in the diversification of microbiota and those microbes' subsequent role in host metabolism and overall health. The more diverse the diet, the more diverse the microbiota, and the more adaptable it can be to disruptions.

addition, subjects ingested either placebo (cellulose) or the GIMM. No changes were made to their daily meal routines. Frequency and consistency of bowel movements and metformin tolerability were assessed via questionnaires, and fasting blood glucose was monitored via morning finger-stick tests.

Results showed improved tolerance of metformin (Figure 6) in the prebiotic group, as compared to the placebo group, as well as improved bowel movement regularity and consistency (loose-to-firm stools), all without compromising the drug's usual therapeutic effect on regulating glucose levels.

In summary, the 2 clinical studies discussed here demonstrate that this prebiotic blend was effective at reducing the desire to eat and in reducing the amount of food anticipated or considered sufficient at the next meal, improving regularity from occasional GI disturbances, lowering mealtime blood sugar levels, protecting and preparing the GI immune system, and improving metformin tolerability.

Relevance of Prebiotics to SCFA Production

Dietary choices determine substrates for gut bacterial species, providing a competitive advantage to some microbes over others. As explained, dietary prebiotics (fiber and polyphenols) have a major role in the diversification of microbiota and those microbes' subsequent role in host metabolism and overall health. The more diverse the diet, the more diverse the microbiota, and the more adaptable it can be to disruptions.

During the past 30 years, the prevalence of metabolic disorders has sharply increased[24-26] while gut microbiome diversity has decreased.[27,28] Additions or losses of species with similar roles tend to only have small effects on overall microbiome function. However, domination by a few species or a reduction in species diversity can significantly impact physiological functions, specifically those related to host metabolism and host defenses (ie, gut barrier function and immunity).

As evidenced by both human and animal studies, diet can cause a shift in microbial populations in as little as 3 days.[29,30] Although temporary dietary changes will only briefly reduce diversity, some losses of microbiota may not be reversible after a prolonged absence of nutrients. This was suggested in a study in which mice inoculated with human microbiota and fed a low-fiber diet experienced an irreversible loss of microbial diversity over several generations despite a reintroduction of dietary fiber.[31] In addition, human use of antibiotics, the use of antibiotics in meat production, and the use of pesticides in crop agricultural practices can narrow the microbiome.[32-34] Pesticides can also subdue the plant's own defense system, as the plant has no need to produce phytoalexins (a plant polyphenol with antimicrobial actions); the end result may be that key micronutrients that normally nourish the gut microbiome are no longer available when these plants are consumed.[35]

Such factors can jeopardize the microbial production of the SCFAs and thus affect host health. As the body of evidence grows supporting the role of SCFAs as key mediators of host metabolism, it becomes increasingly clear

STAFF

Volume 15 Issue 1 | January 2019

Publisher
Razi Ann Berry
publisher@ndnr.com

Founders
Razi Ann Berry
David A. Tallman, DC, ND
publisher@ndnr.com

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Creative Direction
Jaclyn Threadgill
jaclyn@ndnr.com
www.jthreadgill.com

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ISSN 2169-1614
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Naturopathic Doctor News & Review

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Annual subscriptions (12 issues) are available to other healthcare providers and NDs outside of North America: US $99; Canada & Mexico $129USD; Europe and Overseas $179USD.

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that SCFAs represent a key molecular link between diet, microbiota, and health.

Studies designed to improve microbial diversity using prebiotics have demonstrated some success, suggesting that high levels of non-digestible carbohydrates may be needed in Western diets to produce relevant changes in SCFA production, along with nutritional counseling and behavior modification surrounding dietary choices.

Fortunately, the increase in prevalence of type 2 diabetes, obesity, inactivity, and the ubiquitous SAD diet has led to an increasing focus on disease prevention. Prebiotics have been proven in numerous studies to alter the gut microbiome in favorable ways, and continuing research is now illustrating the power of prebiotics to impact health beyond the gut as well, especially metabolic disorders. SCFAs' ability to affect appetite and glucose regulation suggests that they may play an important role in protecting the body against the deteriorating metabolic control and inflammation associated with Western lifestyles.

Nourishing the gut microbiota through diet and simple and cost-effective interventions such as prebiotics, including dietary fiber and polyphenols, offers significant promise in the prevention of metabolic syndrome and in slowing the progression of prediabetes to diabetes. As we all know, far more important than treating the symptom is to treat the cause.*

References available online at ndnr.com

* The statements in this paper have not been evaluated by the FDA. No product is implied or made reference to in this paper and all study materials or related supplements are not intended to diagnose, treat, cure, or prevent any disease.

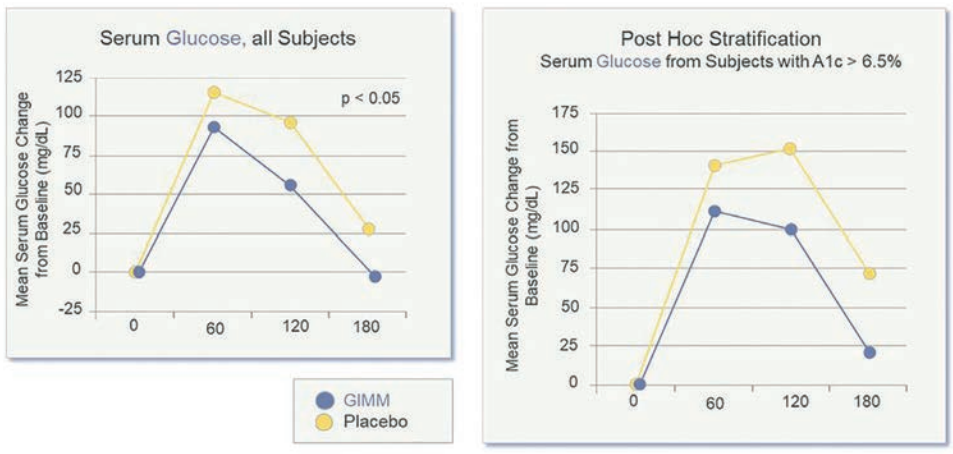
Financial Disclosures: Dale Pfost is the founding CEO of MicroBiome Therapeutics, the company that provided the prebiotic blend used in the 2 studies discussed in this article. Dr Erick Cervantes is an ambassador for MicroBiome Therapeutics, and recommends a proprietary version of the GIMM to appropriate patients.

Acknowledgments: The authors wish to acknowledge the primary contribution to the research and development of the GIMM described here by Mark Heiman, PhD, who is the CSO emeritus of MicroBiome Therapeutics. Dr Heiman and Dr Frank Greenway are both scientific advisors to MicroBiome Therapeutics.

Erick R. Cervantes, MPH, ND, is a 2011 graduate of NCNM in Portland, OR. Dr Cervantes is currently Program Chair and Assistant Professor of the Complementary and Alternative Health undergraduate program at Ashford University in San Diego, CA. He has taught within and led the program and has been practicing naturopathic medicine since 2011. Dr Cervantes joined the integrative health center, Body Craft, in October 2017. He uses an array of successful treatment interventions that include: Western herbs, homeopathy, massage, behavioral modification, nutrition, German bio-therapeutic drainage therapies, homeopathy, tissue cell salts, herbal stem-cell therapies, and micro-current therapy.

Dale Pfost, PhD, has 25 years of experience as a serial entrepreneur and executive in life sciences. He has been the founding CEO of 5 biotechnology companies – achieving 3 IPOs, 3 trade-sales and 3 companies with market capitalizations of over $2 billion. These include: Oxford GlycoSciences (IPO 1988); Orchid Biosciences (IPO 2000); Acuity Pharmaceuticals (now OPKO Health, 2007); and NuMe Health (founded 2010, now MicroBiome Therapeutics). Dale is also the US-based General Partner of the London venture capital firm, Advent Life Sciences. Dale holds a BS degree from the University of CA and a PhD in physics from Brown University.

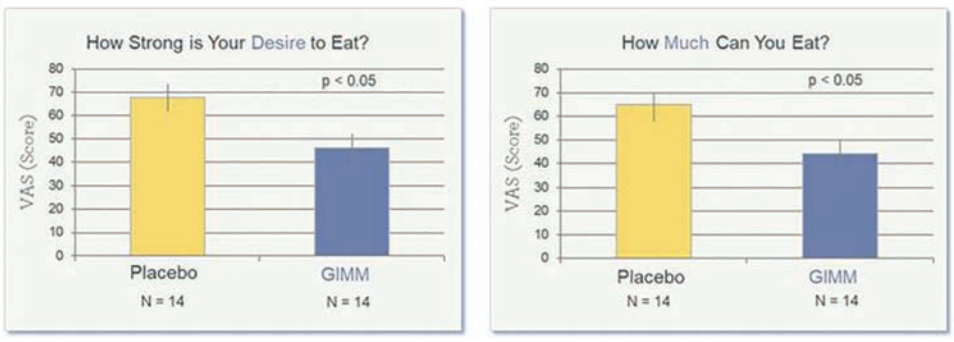
Figure 3. Serum Glucose After 4 Weeks of Prebiotics



Note: Blood glucose excursion was significantly improved after 4 weeks. There was a significant postprandial effect and greater effect in diabetic subjects (those with A1c >6.5%). Fasting blood glucose normalized to 0.

(GIMM = Gastrointestinal Microbiome Modulator)

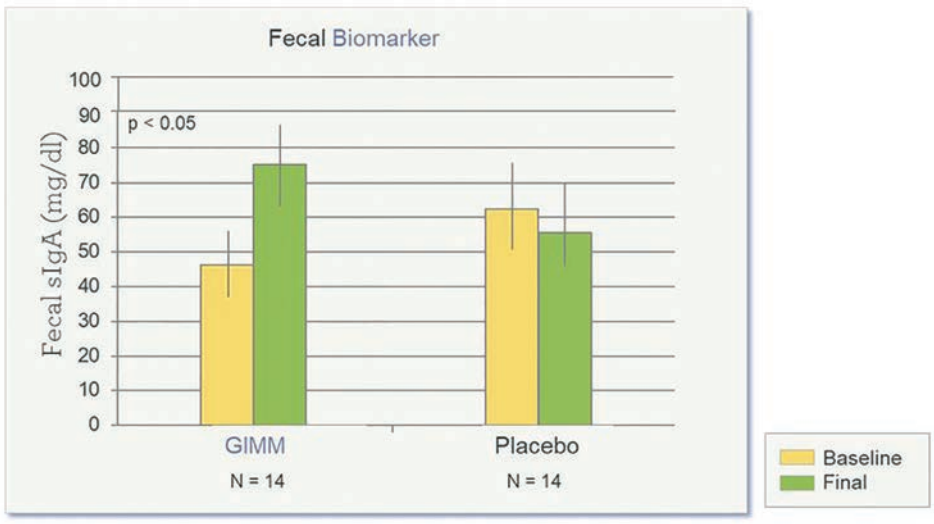
Figure 4. Increased Satiety After 4 Weeks of Prebiotics



A Validated Visual Analog Scale (VAS) was used to measure appetite. Data shown are from the final visit (Week 4).

(GIMM = Gastrointestinal Microbiome Modulator)

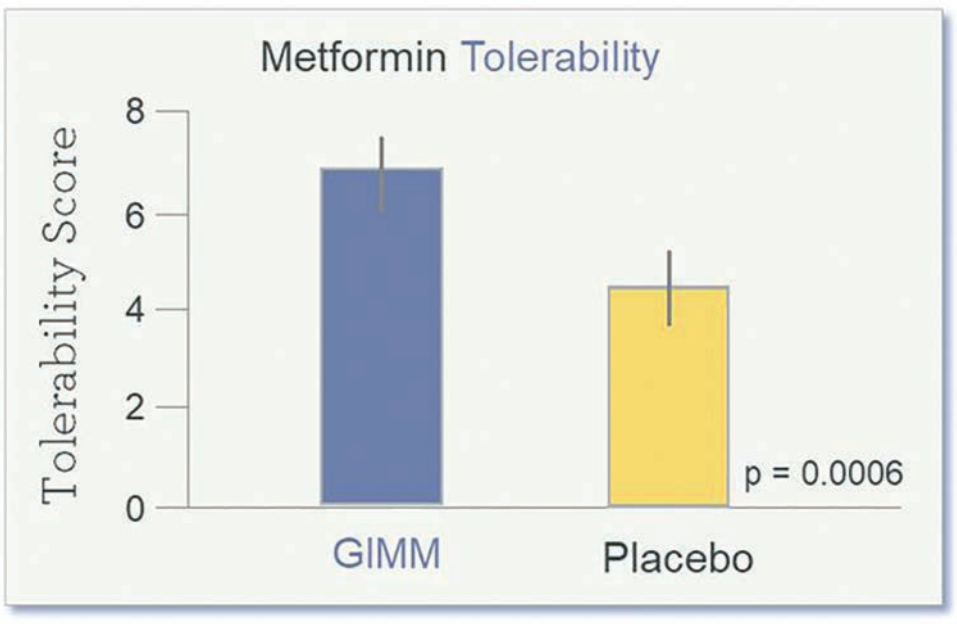
Figure 5. SIgA After 4 Weeks of Prebiotics



The intestinal antibody sIgA normally defends against food allergens and pathogens. Study showed significantly increased sIgA at the final visit (Week 4).

(GIMM = Gastrointestinal Microbiome Modulator)

Figure 6. Metformin Tolerability After 4 Weeks of Prebiotics



Tolerability Score is a symptom composite of bloating, urgency to evacuate, stool consistency, and flatulence.

(GIMM = Gastrointestinal Microbiome Modulator)

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depression.[4,5] Possibly in response to this, there has been increasing research into the composition of the gut microbiome in individuals with mood disorders. Many people with psychiatric illnesses have been found to have an altered gut microbiome composition and compromised integrity of the gut lining, and these patterns are theorized to affect the functioning of the nervous system.[6]

Ever since the 1950s, the only therapy widely used to treat mood disorders are pharmaceutical agents that target the monoamine neurotransmitters in the central nervous system (CNS) – serotonin, norepinephrine, and dopamine.[7] Recent research has established a strong connection between physiological health and mental health, including the extensive therapeutic potential of manipulating the gut microbiome in individuals with mood disorders.

The way that the gut communicates with the brain is likely the underlying factor in this relationship. Extensive research has been conducted on mice that has included manipulating their gut microbiota and observing their consequent behavioral changes (eg, increased or decreased depression and anxiety).[8] Findings from this research strongly support the theory that these behavioral/mood changes result from aberrant neurochemical transmission from the gut microbiome.[8] When mice are treated with oral neomycin (antibiotic), bacitracin (antibiotic), and primaricin (antifungal), their anxiety is reduced.[9] It has also been demonstrated that germ-free mice (mice devoid of gut microorganisms) have higher concentrations of the serotonin precursor, tryptophan, compared to control mice.[8] This could be due to the elimination of pathogenic or inflammation-inducing bacterial and/or fungal species in the gut. When in excess, some of these pathogenic enteric microbes can trigger inflammatory processes in the CNS. Acutely depressed patients have been shown to have higher gut levels of Bacteroidetes, Actinobacteria, and Proteobacteria, as well as lower levels of Firmicutes, compared to patients with milder depression.[7] Children with autism spectrum disorder (ASD) have been shown to have less gut microbial diversity and lower levels of *Prevotella*, *Coprococcus*, and Veillonellaceae compared to controls.[9] Spore-forming anaerobic bacteria and microaerophilic bacteria have also been found in gastric and duodenal samples from children with ASD, whereas control children showed no presence of these microbes.[9]

> Many people with psychiatric illnesses have been found to have an altered gut microbiome composition and compromised integrity of the gut lining, and these patterns are theorized to affect the functioning of the nervous system.

Probiotics & Prebiotics

The main immunomodulatory actions of probiotics and prebiotics include modulating the immune responses from the gut mucosa, enhancing the integrity of the epithelial barrier in the gut, and priming adaptive responses via antigen-presenting cells.[10]

Immunomodulation is primarily carried out through regulation of T-cell maturation, which is highly implicated in inflammation and autoimmune disease.[10] The 2 dominant genera of gut bacteria that are considered beneficial probiotics are Lactobacilli and Bifidobacteria.[11] Research has demonstrated that *Lactobacillus* and *Bifidobacterium* species modulate the production and secretion of various cytokines by acting on monocytes, macrophages, epithelial cells, peripheral blood mononuclear cells, and dendritic cells.[10] The eradication of "bad" species of gut bacteria and the addition of beneficial probiotic species may provide novel avenues for treatment of mood disorders. "Live bacteria that have a positive mental health benefit have been defined as psychobiotics."[7]

Disorders characterized by a deviation from normal gut bacteria include small intestinal bacterial overgrowth (SIBO), dysbiosis, IBS, and more. It should come as no surprise that there is a high prevalence of psychiatric illness among patients with IBS, including panic disorder, generalized anxiety disorder, social phobia, posttraumatic stress disorder, and major depression.[12] Probiotics can competitively inhibit disease- and inflammation-causing pathogenic bacteria by blocking attachment sites on epithelial cells. *Lactobacillus plantarum* and *Lactobacillus rhamnosus* upregulate the production of intestinal mucins, which greatly reduces the adherence of *Escherichia coli* O157:H7 and its damaging effects.[13] It has been demonstrated in humans that administering a combination of the probiotics *Lactobacillus helveticus* and *Bifidobacterium longum* has an anxiolytic effect and reduces serum cortisol.[14] *Lactobacillus reuteri* is another highly effective probiotic that modulates immune system functioning, reduces stress-induced increases in corticosterone, and reduces anxiety by altering the mRNA expression of $GABA_A$ and $GABA_B$ receptors in the CNS.[14] *Bifidobacterium infantis* has been found to have antidepressant effects, via suppression of stimulation-induced elevations in proinflammatory cytokines as well as increasing tryptophan levels.[14]

The Gut-Brain Connection

There have been rapidly coalescing clusters of evidence related to the gut-brain connection, with special focus on potential etiologies of anxiety, depression, behavior, and other mental or emotional disorders. "…[I]llnesses such as major depressive disorder are disproportionately prevalent in patients with gastrointestinal illnesses such as inflammatory bowel disease, which pathologically has been strongly linked to microbiome function."[15]

Intestinal hyperpermeability is a very important pathophysiologic mechanism implicated in dysbiosis and mood disorders. The hyperpermeability is characterized by weakened tight junctions between the enterocytes of mainly the small intestine. This creates "gaps" in the epithelial lining of the small intestine that allow for translocation of partially digested food products and bacterial toxins into the bloodstream, often triggering a low-grade immune response through the interaction of T-cells and compromised epithelium. It has been shown that intestinal hyperpermeability often coexists with altered gut microbiome composition and activity.[1]

Immune system hypersensitivity should also be explored as a possible contributing factor in the gut-brain connection. While the immune system is not usually occupied with reacting to non-harmful antigens, it can start to overreact to a normally harmless antigen; this is referred to as an immune hypersensitivity reaction. There are several types of hypersensitivity reactions, and they all promote inflammation that may affect mood and behavior. It has been found that germ-free mice have an increased stress response, higher cortisol levels, and lower levels of cortical and hippocampal brain-derived neurotropic factor (BDNF) compared to control mice; furthermore, these effects are no longer present when the mice are recolonized with Bifidobacteria species.[14] *Lactobacillus* strains have also been shown to trigger increased levels of 2 key anti-inflammatory/suppressive cytokines – transforming growth factor-beta (TGF-ß) and interleukin-10 (IL-10) via interaction with dendritic cells.[10] This produces a tolerogenic state such that immune cells do not hyper-react to non-harmful antigens (ie, they tolerate them), thereby keeping inflammation low.[10] TGF-ß has major regulatory activity, induces peripheral antigenic/immune tolerance, and suppresses cells of the innate immune system.[16] Because of its broad anti-inflammatory effects, TGF-ß has been considered a possible therapeutic for inflammatory diseases, autoimmune disease, cancer, and Alzheimer's disease; it might also be considered in the treatment of severe mood disorders.[16]

Nutritional Impacts on the Gut

The first time nutrition is thought to impact the gut microbiome is shortly after birth. Early life (the weeks and months following birth) serves as a critical window of opportunity for the development of the core microbiome from diet.[10] Human breast milk has profound beneficial effects on the gut microbiome and is considered the optimal source of nutrition for newborns. Breast milk contains several components that are essential for a maturing immune system, including colostrum,

immunoglobulins, lysozyme, lactoferrin, *Lactobacillus acidophilus* and *L gasseri*, *Bifidobacterium bifidium* and *B breve*, and human milk oligosaccharides (HMOs).[10]

Some of the general dietary changes that have occurred in the United States over the past 3 decades include higher caloric intake, higher proportion of calories derived from refined grains/carbohydrates, and increased intake of corn-derived sweeteners (ie, corn syrup).[17] These poor dietary patterns are likely a major culprit in the development of psychiatric disorders, mood disorders, and developmental disorders. A significant amount of evidence exists that shows how dietary interventions (especially gluten-free and casein-free diets) that help optimize the gut microbiome and reduce levels of inflammation also effectively improve behavioral and digestive symptoms in autistic children.[18] Foods shown to foster gut bacterial imbalances include sugar, eggs, soy, gluten, and dairy.[19] These foods trigger some of the most common food sensitivities in individuals with intestinal hyperpermeability ("leaky gut"). Food sensitivities can be the root cause of many common inflammatory manifestations, including mood disorders.

Short-chain fatty acids (SCFAs), such as butyrate, acetate, and propionate, have been shown to positively impact the gut microbiota and exert modulatory effects on the immune system.[17] Increased fiber intake can enhance SCFA status, since SCFAs are products of anaerobic microbial fermentation of non-digestible macronutrients (mostly plant polysaccharides and resistant starches).[17] SCFAs promote colonic water resabsorption and decrease fecal pH, which both beneficially affect bacterial growth in the colon.[9] Levels of SCFAs (butyrate, acetate, propionate), along with levels of different phylogenic microbial strains, can be measured via a comprehensive stool analysis.

Conclusions

Anxiety disorders, depressive disorders, and autism spectrum disorders have been rapidly increasing in prevalence over the past few decades, especially in the United States. Causes of this increase are still largely unknown, but etiologic factors are beginning to be considered at a deeper level. This fact highlights the need for more effective intervention strategies, which can be accomplished through research studies and clinical trials. Most studies of the gut microbiome to date have been conducted on mice, which only minimally translate to human health.

Today, there is a clear need for alternative treatment strategies for several common psychiatric conditions including anxiety and depressive disorders. Pharmaceutical therapy has demonstrated limited efficacy in the general population of psychiatric patients. Many patients with psychiatric illness are prescribed indicated medications and become reliant on them for a significant portion of their lives, despite their often-minimal efficacy and the fact that they are often intended to be used only for a short period of time. As an alternative to pharmaceutical therapy, treatment designed to reduce CNS inflammation and optimize the gut microbiome may be a novel and highly effective form of therapy. Many of the psychiatric and developmental disorders that are increasingly affecting young children are postulated to result from nutrition and diet during infancy and childhood – factors that significantly affect the composition of the gut microbiome.

Strong but complex connections exist between the gut microbiome, the immune system, CNS activity, mood, and behavior. Research is just beginning to reveal how these systems interact with each other. Although clinical applications are not yet well supported, it is likely that the growing interest in the gut microbiome will propel further investigation into more specific medical treatments that optimize the microbiome. Probiotics are already a useful clinical tool in the treatment of a wide variety of health problems, including psychiatric disorders. Diet therapy, functional foods, nutritional supplements, antimicrobial agents, and probiotic therapy are all avenues of treatment that have been shown to be highly effective in healing the gut, including balancing enteric bacteria, improving the integrity of the epithelial lining, and modulating the activity of gastrointestinal immunity. We now know that all of these factors are central to the functioning of the CNS and the pathophysiology of psychiatric disorders.

Nutritional therapy is one of the most powerful tools for altering the gut microbiome. It has been shown that even short-term dietary changes significantly affect (positively or negatively) the populations of microorganisms in the GI tract. In general, a high fiber, plant-based diet, in conjunction with fermented foods containing probiotics, is highly recommended for increasing the concentrations of beneficial gut microbes. The current average American diet is pro-inflammatory by promoting overgrowth of pathogenic microorganisms, both bacterial and fungal. Enhancing patients' dietary patterns can serve to balance their gut microbiome, decrease inflammation, optimize nutrient absorption and utilization, and modulate their immune system. All of these effects should significantly decrease their symptoms of anxiety and depression, and help to stabilize their mood.

References available online at ndnr.com

Alexandra Francis, ND, MS, CNS, was a 4th-year naturopathic medical student at the University of Bridgeport College of Naturopathic Medicine when she wrote this article; she graduated in May 2018. She is also pursuing a master's degree in Human Nutrition at the University of Bridgeport Nutrition Institute. Alexandra has given several lectures on subjects including naturopathic medicine, nutrition, therapeutic diets, lifestyle, and wellness. Alexandra plans to start consulting on nutrition, diet, and lifestyle, to complement her clients' medical treatment in Long Island, NY.

Marie Winters, ND, FABNO, received her ND degree from Bastyr University in 2006. Dr Winters is the former director of the Naturopathic Medicine Department at Cancer Treatment Centers of America in Philadelphia. She is also a Fellow of the American Board of Naturopathic Oncology, sits on the Board of Medical Examiners for the American Board of Naturopathic Oncology, and is currently President of the PA Association of Naturopathic Physicians. She is an adjunct professor at Bridgeport University's College of Naturopathic Medicine and maintains a private practice in Philadelphia. Dr Winters has spoken at several medical conferences across the country.

US Cannabis Regulation

What It Means for Naturopathic Doctors

SHAON HINES, ND

Much confusion exists regarding *Cannabis*, marijuana, and hemp. A better understanding of the terminology will help you to understand the legality.

The terms "Cannabis" and "medical marijuana" are often used interchangeably. *Cannabis*, however, is both marijuana and hemp. For example, marijuana and hemp belong to the Cannabaceae family, genus *Cannabis* L, and to the species *Cannabis sativa*.[1] The difference between marijuana and hemp is that marijuana has a higher tetrahydrocannabinol (THC) content (which is known for its euphoric or psychoactive properties), whereas hemp has a very low THC content and is non-psychoactive. The varying amounts of THC are accomplished by growing different varieties of the *Cannabis* plant to be either low-THC hemp or high-THC marijuana. The 2014 Agricultural Act, also known as the 2014 Farm Bill, originally separated marijuana from hemp by the amount of THC within the plant. To be considered hemp, the amount of THC in the plant must be less than 0.3%.[2] Prior to December 2018, the Controlled Substances Act (CSA) did not separate marijuana and hemp. The CSA defines marijuana as all parts of the *Cannabis* plant except for the mature stalks and sterilized seeds.[3]

> *(16) The term "marihuana" means all parts of the plant Cannabis sativa L., whether growing or not; the seeds thereof; the resin extracted from any part of such plant; and every compound, manufacture, salt, derivative, mixture, or preparation of such plant, its seeds or resin. Such term does not include the mature stalks of such plant, fiber produced from such stalks, oil or cake made from the seeds of such plant, any other compound, manufacture, salt, derivative, mixture, or preparation of such mature stalks (except the resin extracted therefrom), fiber, oil, or cake, or the sterilized seed of such plant which is incapable of germination.*[3]

Fortunately, due to the 2018 Farm Bill that was passed in Congress in December 2018, the definition of marijuana and hemp have been officially separated, making hemp no longer a "controlled substance."

Can NDs Prescribe Medical Marijuana?

Marijuana (*Cannabis*) is classified as a Schedule I Controlled Substance.[4] Such substances are not allowed to be prescribed by any type of physician in the United States. According to the Drug Enforcement Administration (DEA)'s Practitioner's Manual,[5]

> *All drugs listed in Schedule I have no currently accepted medical use in treatment in the United States and therefore may not be prescribed, administered, or dispensed for medical use. In contrast, drugs listed in Schedules II through V all have some accepted medical use and therefore may be prescribed, administered, or dispensed for medical use.*[5]

In states where medical marijuana is legal, physicians are allowed to recommend, certify, or authorize, but not prescribe.

- In the United States, medical marijuana is currently legal in 33 states and the District of Columbia (see Figure 1)[6]
- Naturopathic doctors are currently licensed or registered in 20 states, the District of Columbia, and the United States territories of Puerto Rico and the US Virgin Islands[7]
- Of the 20 states and the District of Columbia, naturopathic doctors have prescribing rights in 11 of those states and the District of Columbia.[8] Please note that a few states are awaiting regulation, so this could change.
- Of the 11 states with prescribing rights and the District of Columbia, only 2 states – Arizona and Washington – allow for naturopathic doctors to recommend, certify, or authorize for medical marijuana[9,10]

If you have prescribing rights and wish to recommend, certify, or authorize for medical marijuana, it is recommended that you contact your state medical board for the most current status to see if naturopathic doctors are eligible in your particular state.

Pharmaceutical Cannabis

Synthetic THC cannabinoid formulas that are available for prescription include Cesamet, Marinol, and Syndros. Epidiolex is a cannabidiol (CBD) product available

for prescription. Cesamet and Syndros are Schedule II; Marinol is Schedule III; and Epidiolex is Schedule V. Sativex (THC & CBD) is another formula but is not currently approved for use in the United States.[11]

Naturopathic doctors are able to prescribe these substances, depending on their individual state's formulary and whether they are able to prescribe controlled substances.

The End of Hemp Prohibition

The Agriculture Improvement Act of 2018, also known as the Farm Bill, was passed in December 2018. This was a monumental victory in the United States. Hemp cultivation and processing has been restricted since the Marijuana Tax Act of 1937. Prior to that, the hemp industry in the United States was encouraged between the 1600s and the late 1800s. It wasn't until the 1930s that the industry started to get demonized by powerful American industrialists that wanted it prohibited. Back then, hemp was used to make sails, rope, and clothing.[12] Bringing hemp back as an agriculture commodity will present many opportunities for farmers, manufactures, and retailers. We will see more hemp nutraceuticals, personal care products, textiles, biofuels, paper, and much more. Hemp also has the ability to detoxify soil and can be used to produce non-toxic building materials; thus, its uses are truly endless.

In December 2018, the Senate passed the 2018 Farm Bill by a vote of 87 Yea vs 13 Nay. The bill was then moved to the House, where it was passed by 369 Yea vs 47 Nay. Upon passage by both the Senate and the House, the bill was sent to the President of the United States and signed into law. History was made, ending the federal prohibition on hemp and establishing it as an agricultural commodity.

Before the passage of this bill, hemp was still considered a controlled substance and was federally illegal. Previously, hemp and marijuana both fell under the Controlled Substances Act because they are both *Cannabis* and the CSA's definition of marijuana included all parts of the *Cannabis* plant except for mature stalks and sterilized seeds.[3] Hemp was only able to be legally distributed within the United States if it represented the mature stalks and/or sterilized seeds and products made thereof or if it was imported from a different country, just as long as the products didn't fall within the CSA's definition of marijuana.

The definition of hemp per the 2018 Farm Bill is stated as: the plant *Cannabis sativa* L and any part of that plant, including the seeds thereof and all derivatives, extracts, cannabinoids, isomers, acids, salts, and salts of isomers, whether growing or not, with a delta-9 tetrahydrocannabinol concentration of not more than 0.3% on a dry weight basis.[13]

What Did the 2018 Farm Bill Change?[14]

- The definition of hemp was separated from that of marijuana
- Hemp is no longer a part of the Controlled Substances Act
- Hemp is now considered an agricultural commodity
- Interstate commerce of hemp can no longer be interfered by the DEA. This allows for e-commerce, banks, and credit card processors to conduct business freely.
- Hemp farmers, processors, and retailers will now be able to get insurance
- Hemp farmers will be able to participate in USDA programs for certification and competitive grants
- Growth and sale of hemp and hemp products can have separate restrictions mandated by individual states and tribes. They cannot, however, interfere with interstate transport and commerce.
- The US Food and Drug Administration (FDA) will continue to regulate ingestible and topical hemp products

The most important aspect regarding hemp in the 2018 Farm Bill was separating it from the definition of marijuana. This alone created many changes, removed

Figure 1. **Marijuana Legality in the United States[6]**

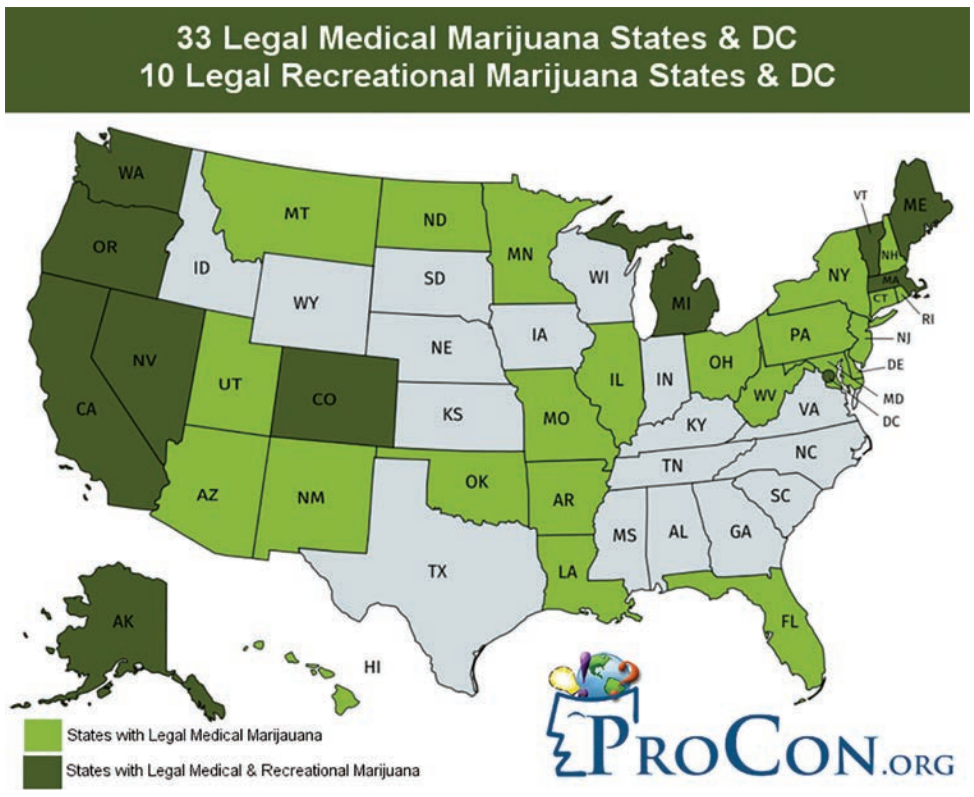


Image courtesy of ProCon.org.
(Source: ProCon.org; https://tinyurl.com/ya6y9xyc)

Now that hemp has been separated from the definition of marijuana, hemp is no longer under strict regulation.

restrictions, and opened many doors for hemp agriculture in the United States. The development and sales of hemp nutraceuticals will soon be bigger and better than what it seems to be today.

Hemp was Previously Federally Illegal

Many people have been under the impression that the 2014 Farm Bill made hemp legal in the United States. Unfortunately, this was not the case. In the Statement of Principles on Industrial Hemp, the 2014 Farm Bill did not remove industrial hemp from the CSA; as a result, it was still federally illegal prior to the current 2018 Farm Bill.[15]

> *Section 7606 did not remove industrial hemp from the controlled substances list.*

The Farm Bill of 2014 simply defined industrial hemp as containing less than 0.3% THC and also authorized institutions of higher education and state departments of agriculture to grow and cultivate hemp for research under state laws.[16]

The FDA was sending warning letters to many companies, and many consumers and retailers got in legal trouble; we just didn't hear about it. The law enforcement was minimal and mostly concentrated in states that didn't have laws regarding CBD. Some of the states that were receiving enforcement action for CBD were California, Wisconsin, Indiana, North Carolina, Texas, Wyoming, Arizona, Alabama, Montana, Ohio, Iowa, North Dakota, South Dakota, and Missouri.[17] These states had varying reasons for enforcement. Here are a few examples: CBD could not be contained in food products (California); CBD from other states could not be sold in dispensaries (Arizona); CBD with any amount of THC was not allowed (Texas); the purchase of CBD oil in another state led to felony charges (Wyoming); and retailers selling CBD were sent "cease and desist" letters (Alabama).[17] The lack of widespread enforcement by the FDA throughout the United States was most likely due to the lack of resources in the FDA as well as the fact that CBD and hemp extracts are very safe and don't pose a public health threat.[18] (See the FDA's statement on this in Table 1.)

Another reason the FDA was sending warning letters out and will continue to send those letters out is there is a widespread problem with false claims in regards to product descriptions and also what ingredients are actually in the bottles. This is a problem that will continue until more regulations are made. It's important to stay informed on what products you are using and where they came from.

CBD Legality Explained

The legality of CBD has drawn much confusion in the United States. The confusion lies in the terminology of *Cannabis*, hemp, and marijuana; differences between federal and state regulations; whether CBD is derived from hemp vs marijuana; and the percentage of THC in the plant.

CBD can be derived from hemp or marijuana. CBD derived from marijuana is still a controlled substance but can be sold in dispensaries in states where medical marijuana is legal. CBD derived from hemp was previously federally illegal, just like CBD derived from marijuana; however, the passing of the Farm Bill has changed that. Prior to the 2018 Farm Bill, hemp still fell within the Controlled Substances Act's definition of marijuana. Therefore, hemp was still considered a Schedule 1 Controlled Substance. Now that hemp has been separated from the definition of marijuana, that problem has been solved and hemp is no longer under strict regulation.

Another problem with CBD legality exists, though. This problem arises with the Food, Drug and Cosmetic (FD&C) Act. According to the FD&C Act, "an active ingredient in a drug product that has been approved under 21 U.S.C. § 355 (section 505 of the FD&C Act), or has been authorized for investigation as a new drug for which substantial clinical investigations have been instituted and for which the existence of such investigations has been made public, then products containing that substance are outside the definition of a dietary supplement."[19] Since THC and CBD are both active ingredients in FDA-approved drugs (ie, Cesamet, Marinol, Syndros, Epidiolex), they cannot be sold as dietary supplements. (Please read the full excerpt from the FDA's website in Table 2.)[19]

What About Hemp Extracts and Hemp Oil?

Many companies have started to use the term "Hemp Extract" instead of "CBD." Since hemp was previously not exempt from the CSA and CBD cannot be sold as a dietary supplement per the FD&C, many companies started to sell "Hemp Extracts" instead. The problem with this approach is that prior to the passing of the 2018 Farm Bill, the only legal way to form the product was to extract it from the mature stalks and sterilized seeds of hemp plants. The mature stalks and sterilized seeds only contain trace amounts of cannabinoids.[20] The excerpt regarding this from the DEA's website is below. Please note that at the time of this statement, hemp was still included in the definition of marijuana; thus, any mention of "marijuana" also means hemp:

> *According to the scientific literature, cannabinoids are not found in the parts of the cannabis plant that are excluded from the CSA definition of marijuana, except for trace amounts (typically, only parts per million) that may be found where small quantities of resin adhere to the surface of seeds and mature stalk. Thus, based on the scientific literature, it is not practical to produce extracts that contain more than trace amounts of cannabinoids using only the parts of the cannabis plant that are excluded from the CSA definition of marijuana, such as oil from the seeds. The industrial processes used to clean cannabis seeds and produce seed oil would likely further diminish any trace amounts of cannabinoids that end up in the finished product. However, as indicated above, if a product, such as oil from cannabis seeds, consisted solely of parts of the cannabis plant excluded from the CSA definition of marijuana, such product would not be included in the new drug code (7350) or in the drug code for marijuana (7360), even if it contained trace amounts of cannabinoids.*[20-22]

Many of the hemp extracts on the shelf that claim to be derived from stalks and seeds are hemp oil products with other beneficial ingredients, but not the sought-after cannabinoids. The companies will definitely change production now to include the whole hemp plant; however, if you are buying a product manufactured prior to the passage of the 2018 Farm Bill, I would be wary of its true ingredients if what you are looking for is cannabinoids.

Choose Products Wisely

The FDA is going to strengthen regulation for hemp products, but it will take some time to get things totally under control. Right now, it is the Wild West out there; millions of people have jumped at the chance to get involved with the CBD and Hemp Extract market, which has resulted in thousands of less-than-optimal products. Make sure your products are sourced from the whole hemp plant; have been properly tested for exact ingredients (ie, cannabinoids and terpenes), potencies, and contaminants; and ensure they are organic and were extracted using safe methods.

Cannabis Law: Helpful Resources

1. **National Conference on State Legislatures- State Medical Marijuana Laws:** http://www.ncsl.org/research/health/state-medical-marijuana-laws.aspx#4
2. **FDA and Marijuana: Questions and Answers:** https://www.fda.gov/NewsEvents/PublicHealthFocus/ucm421168.htm#dietary_supplements
3. **NORML:** https://norml.org
4. **ProCon.org**
   a. **Legal Marijuana States and D.C.:** https://medicalmarijuana.procon.org/view.resource.php?resourceID=000881
   b. **States with Laws Specifically for Cannabidiol (CBD):** https://medicalmarijuana.procon.org/view.resource.php?resourceID=006473
5. **US Hemp Roundtable:** https://hempsupporter.com
6. **Hoban Law Group:** https://hoban.law/frontpage
7. **Kight on Cannabis:** https://cannabusiness.law

References available online at ndnr.com

Table 1. FDA & Marijuana: Questions & Answers[18]

15. Will FDA take enforcement action regarding THC and CBD products that are marketed as dietary supplements? What about foods to which THC and CBD has been added?

A. When a product is in violation of the FD&C Act, FDA considers many factors in deciding whether or not to initiate an enforcement action. Those factors include, among other things, agency resources and the threat to the public health. FDA also may consult with its federal and state partners in making decisions about whether to initiate a federal enforcement action.

Table 2. FDA & Marijuana: Questions & Answers[19]

12. Can products that contain THC or cannabidiol (CBD) be sold as dietary supplements?

A. No. Based on available evidence, FDA has concluded that THC and CBD products are excluded from the dietary supplement definition under sections 201(ff)(3)(B)(i) and (ii) of the FD&C Act, respectively. Under those provisions, if a substance (such as THC or CBD) is an active ingredient in a drug product that has been approved under 21 U.S.C. § 355 (section 505 of the FD&C Act), or has been authorized for investigation as a new drug for which substantial clinical investigations have been instituted and for which the existence of such investigations has been made public, then products containing that substance are outside the definition of a dietary supplement. FDA considers a substance to be "authorized for investigation as a new drug" if it is the subject of an Investigational New Drug application (IND) that has gone into effect. Under FDA's regulations (21 CFR 312.2), unless a clinical investigation meets the limited criteria in that regulation, an IND is required for all clinical investigations of products that are subject to section 505 of the FD&C Act.

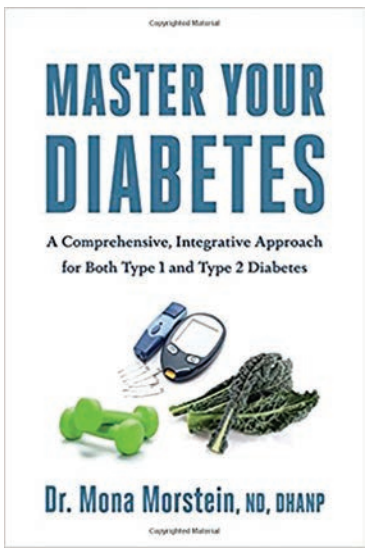
There is an exception to sections 201(ff)(3)(B)(i) and (ii) if the substance was "marketed as" a dietary supplement or as a conventional food before the drug was approved or before the new drug investigations were authorized, as applicable. However, based on available evidence, FDA has concluded that this is not the case for THC or CBD. For more information on this provision, including an explanation of the phrase "marketed as," see Draft Guidance for Industry: Dietary Supplements: New Dietary Ingredient Notifications and Related Issues.

FDA is not aware of any evidence that would call into question its current conclusions that THC and CBD products are excluded from the dietary supplement definition under sections 201(ff)(3)(B)(i) and (ii) of the FD&C Act. Interested parties may present the agency with any evidence that they think has bearing on this issue. Our continuing review of information that has been submitted thus far has not called our conclusions into question.

Shaon Hines, ND, is a licensed naturopathic doctor and a US Air Force veteran. Dr Hines is originally from Wisconsin, joined the Air Force right out of high school, and did tours of duty in Saudi Arabia and Qatar. She also served as Flight Sergeant for the MacDill AFB Honor Guard. Dr Hines earned her Doctor of Naturopathic Medicine degree from National University of Health Sciences in Lombard, IL. She is also a certified personal trainer, behavioral change specialist, master speed reader, and raw foods chef.

Medical Resources for NDs

A review of current publications for the naturopathic industry



BLAINE HARBOURNE, ND, LDN, CNS, CSCS

Master Your Diabetes: A Comprehensive, Integrative Approach for Both Type 1 and Type 2 Diabetes

Worldwide, there are 350 million people diagnosed with diabetes. In the United States, alone, there are an estimated 120 million prediabetic and diabetic patients (29 million diagnosed diabetics). The diabetes epidemic is growing and is no longer affecting just adults; diabetes is increasingly occurring in children and adolescence. Providing insight into the pathology and the physiology of diabetes is of paramount importance, not only for managing the disease but also for halting the epidemic.

After 25-plus years of practice in dealing with diabetes, Dr Mona Morstein provides us with a comprehensive resource that combats diabetes and helps patients understand their unique circumstances. With her "8 Essentials," Dr Morstein offers a thorough explanation for each aspect of diabetes as well as instructions in to manage it.

The 8 Essentials For Managing Diabetes

1. **Diet**: Diabetes at its core is a condition of dysfunctional carbohydrate metabolism. This book delivers an exceptional amount of nutritional information to patients, helping them to select what can work best for them.
2. **Exercise**: The prescription of exercise cannot be overlooked, as it is an important component of the diabetes management puzzle.
3. **Sleep**: This is a frequently overlooked and underrated part of the diabetes puzzle. Knowing that sleep plays a role in key biological processes should be enough to convince us to engage in proper sleep hygiene. Restorative sleep helps manage cravings, blood sugar, appetite, and a slew of other challenges associated with this disease.
4. **Stress Management**: Stress plays a pivotal role in lifestyle management, and not just for the diabetic patient. All of us are constantly faced with stressors in our lives. Learning how to deal with those stressors is crucial for keeping patients on their path toward optimal health.
5. **Healing the Gut and Microbiome**: This is the naturopathic doctor's backbone. Repairing the gut and balancing the microbiome helps optimize digestion and absorption of key nutrients. Dr Morstein provides enough detail to facilitate a full understanding of this area.
6. **Environmental Detoxification**: Our environment is toxic. Understanding how to avoid these toxins and remove them helps patients select specific avenues in their lives for reducing their toxic load.
7. **Supplementation**: Key supplements provide essential cofactors for multiple biological pathways in the body. Dr Morstein does a wonderful job of explaining exactly how they fit into the management of diabetes.
8. **Medications**: The book provides a comprehensive overview of all medications available to diabetic patients, including how to utilize each drug to its full potential.

Title:	*Master Your Diabetes: A Comprehensive, Integrative Approach for Both Type 1 and Type 2 Diabetes*
Author:	Mona Morstein, ND, DHANP
Publisher:	Chelsea Green Publishing
Available from:	All major book sellers
Pages:	560
Style:	Trade Paperback
Copyright:	2017
MSRP:	$21.73

Autoimmunity & GI Disorders

Sorting Out the Triggers

CHAD LARSON, NMD, DC, CCN, CSCS

Are you noticing the growing epidemic of autoimmunity? As the number of Americans suffering from autoimmunity has reached 25-50 million[1] and that figure continues to climb, we must consider new approaches for managing these patients. The evolution of laboratory science has provided new tools to help us investigate causes of immune dysregulation that can eventually manifest in autoimmune disease. It is generally accepted that autoimmunity is a result of an abnormal interplay between genetic predisposition and immune reactivity to non-self antigens (ie, environmental triggers). Since the gastrointestinal (GI) tract is such a key focus in naturopathic medicine, let's focus on that organ system in our discussion of how environmental triggers induce autoimmunity and how we can test for them.

Are you checking your GI patients for autoimmunity? I'm not just talking about the biggies like celiac disease, Crohn's, and ulcerative colitis (although make sure that you are ruling these out); I'm also talking about polyarteritis nodosa (PAN), autoimmune hepatitis, diabetes, eosinophilic esophagitis (EoE), and maybe even small intestinal bacterial overgrowth (SIBO) and irritable bowel syndrome (IBS). Having said that, it's less about naming the autoimmune condition and more about understanding the process. Discovering that a patient's condition is related to autoimmunity creates a valuable therapeutic branch point – one that helps open up other clinical opportunities.

When dysregulation of the immune system causes autoantibodies to be developed, the goal should be identification of the non-self antigen causing the dysregulation. If we can identify and remove the auto-antigen, the autoantibodies will decrease. I believe it's inappropriate to claim that autoimmunity can be cured; however, if we can identify and remove the environmental trigger that is causing the immune system to hyper-react, and bring about a decrease or normalization of the autoimmune markers, signs, and symptoms, this would be considered a successful clinical outcome. So, what kind of environmental triggers cause the immune system to dysregulate, potentially leading to autoimmunity?

It's Just Genetic, Right?

If you have been in clinical practice for any amount of time, you've undoubtedly noticed that autoimmunity can run in families. Typically, family members aren't necessarily suffering from the same condition. For example, your patient may have Hashimoto's thyroiditis, and her mom has rheumatoid arthritis, her sister has multiple sclerosis, and her son has celiac disease. There is clearly a genetic predisposition; however, the latest estimate suggests that only about one-third of an individual's risk of developing autoimmunity comes from genetics[2] – which leaves almost 70% of other stuff. So, what's the other stuff? There are 3 main trigger categories that we need to consider when evaluating for non-self antigens that are causing immune system dysregulation. These trigger categories include dietary proteins, chemicals, and pathogens. There is actually a very important fourth trigger that the science has added more recently, which we'll discuss toward the end of this discussion.

Models of Immune Dysregulation

Before we get to that, I'll mention as a quick reminder something about why the immune system dysregulates by misinterpreting a non-self antigen (such as a bacterial toxin or a dietary protein like gluten) as a self-antigen (such as your gut cells) and then attacking it. Since nearly the beginning of our understanding of autoimmunity, we've known that infections can trigger this process. There are 3 models that explain this.

Molecular Mimicry

The idea associated with the first model is that a part of the pathogenic antigen looks enough to the immune system like a piece of self-antigen that the immune system starts to attack the self-antigen with the same antibodies used to attack the pathogenic antigen. Once the self-antigen is on the radar of the immune system, the immune system keeps targeting it. Over time, this can lead to destruction of the tissue and organ system. This concept of immune dysregulation is called "molecular mimicry."

Bystander Effect

The second model suggests that the immune system's reaction to a non-self antigen (such as a pathogen) becomes so overzealous while working to destroy the pathogen that it inadvertently destroys some of the surrounding self-tissue as well. This is referred to as the "bystander effect."

Hygiene Hypothesis

The third model basically suggests that our overly antibiotic, antimicrobial, and anti-bacterial society eradicates the microbes that normally upregulate the Th2 immune response in childhood. This results in a more aggressive Th1 immune response, which is associated with predisposition to autoimmunity and chronic inflammation. This model is referred to as the "hygiene hypothesis."

With this information serving as a backdrop, we can better understand how environmental triggers cause the immune system to initiate an attack on self-tissue. Whether it's through molecular mimicry, the bystander effect, or the hygiene hypothesis, once an immune system reaction is blended with genetic predisposition, autoimmunity can result. Lab testing is the best way to take the guesswork out and identify which triggers are stimulating the immune system.

Autoimmune Triggers

Dietary Proteins[3-7]

The most common environmental trigger that constantly drags across the GI tract is dietary proteins. We know that certain foods, eg, wheat and dairy, are more immunogenic than others, especially when it comes to autoimmunity. The immunogenicity of different food constituents varies between individuals. Therefore, to decrease the chance of potential false-negative results, it's best to evaluate these foods comprehensively. For example, instead of just evaluating for wheat antibodies, it's recommended to look at multiple components of wheat, eg, alpha-gliadin, gamma-gliadin, omega-gliadin, glutenin, wheat germ agglutinin, and even non-gluten wheat proteins.

We also know that when a food is cooked or modified in some way, the immune-triggering antigens in that food can change. For example, an individual might be reactive to cooked salmon but not uncooked salmon. Not all laboratories test for both cooked and raw foods. How often do your patients consume uncooked grains, beans, and meat? Not often, so we should not only be testing for immune reactions to raw foods.

> When dysregulation of the immune system causes autoantibodies to be developed, the goal should be identification of the non-self antigen causing the dysregulation.

Chemicals[4,8-10]

Multiple chemicals have been implicated in GI dysfunction, including styrene, molds (eg, aflatoxin), formaldehyde, tetrachloroethylene, and heavy metals. Chemicals can covalently bind to human tissue. When this happens, the immune system will recognize it a problem and develop antibodies against the now-combined chemical and host tissue. This is an example of the "bystander effect" that can lead to autoimmunity. Many labs evaluate levels of chemicals in the body, which can be relevant in certain clinical situations; however, when it comes to autoimmunity, our main interest should be antibody reactions to chemicals or metals. The immune system's reaction to such chemicals with IgG, IgA, or IgM antibodies indicates loss of immune tolerance, and in susceptible individuals can result in autoimmunity. Make sure that you test through a laboratory that evaluates for immune reactions to chemicals/metals, not just their presence.

Pathogens[3,11-17]

Pathogens are ubiquitous in the GI tract, so should be considered in every case of GI dysfunction, especially GI autoimmunity. Viruses, bacteria, parasites, and molds can all trigger autoimmunity. Many labs evaluate for these pathogens, but the clinical challenge is determining where to start. Working with a lab that features the most common pathogens known to be related to autoimmunity is recommended; examples include *Klebsiella*, Epstein-Barr virus, and *Mycoplasma*, to name a few. Some labs also make it possible to evaluate these different pathogens in 1 panel from a single blood draw specimen, which can save your patients time, money, and the necessity of multiple needle sticks.

Intestinal Permeability (Leaky Gut)[18,19]

A more recently identified autoimmunity trigger is leaky gut. A breakdown of the tight junctions along the gut barrier causes increased intestinal permeability, which serves as a gateway through which a wide variety of immunogenic antigens can enter the circulation superhighway that otherwise would not, including undigested dietary proteins, pathogens, and other toxins. Multiple labs now test for these tight-junction gut-barrier proteins.

Conclusion

I'll leave it to Alessio Fasano, one of the top researchers in this area, to put it most succinctly:

> *Genetic predisposition, miscommunication between innate and adaptive immunity, exposure to environmental triggers, and loss of the intestinal barrier function secondary to dysfunction of intercellular tight junctions, seem to all be key ingredients involved in the pathogenesis of autoimmune diseases.*[18]

The pharmaceutical model of symptom suppression in autoimmune diseases is outdated and should be replaced by, or at least added to, an approach that aims to identify the environmental triggers for different individuals. This will allow physicians and patients to better manage these conditions, thereby minimizing the abnormal interplay between genetic predisposition and environmental triggers.

References available online at ndnr.com

Chad Larson, NMD, DC, CCN, CSCS, holds a Doctor of Naturopathic Medicine degree from Southwest College of Naturopathic Medicine, and a Doctor of Chiropractic degree from Southern California University of Health Sciences. Dr Larson is an advisor and consultant on the Clinical Consulting Team for Cyrex Laboratories. He is also a certified clinical nutritionist and a certified strength and conditioning specialist. Dr Larson particularly pursues advanced developments in the fields of endocrinology, orthopedics, sports medicine, and environmentally-induced chronic disease.

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FUT2 Secretor Status

Effects on Gut Health

GINGER NASH, ND

The significance of the fucosyltransferase-2 (FUT2) gene and "secretor status" has been written about by Dr Peter D'Adamo for over 20 years. Dr D'Adamo's research into ABO blood type led him to see a connection between the gene that codes for blood type and the FUT2 gene, which determines secretor status. Specifically, the FUT2 gene is responsible for the expression of our ABO blood-type antigens into all of our bodily fluids. Individuals who carry at least 1 functional allele are known as "*secretors*," whereas individuals who are homozygous for loss-of-function mutations are known as "*non-secretors*."[1]

Non-secretors do not secrete blood-type antigen into bodily fluids, ie, saliva, sweat, tears, vaginal secretions, semen, or digestive juices. Secretor status is completely independent of ABO status, so an individual can be a Type O secretor or non-secretor, Type A secretor or non-secretor, etc. It is estimated that about 18-20% of the general population are non-secretors, and this has an impact on various aspects of human physiology.[1] It is the impact of secretor status on gut health that will be the focus of the remainder of this article.

Secretor Status & the Gut

As naturopathic physicians focused on the health of the gut, most of us are well aware of the intensive research being conducted on the gut microbiome. We know that the composition of our gut microflora affects our ability to metabolize, digest and absorb nutrients, and to regulate immune function and defend against a multitude of pathogens. Indeed, it is our first "line of defense" against our environment, including the food we eat. The FUT2 secretor status gene is responsible for the synthesis of the type-1 H antigens, which act as precursors for the ABO blood-group antigens expressed on intestinal mucosa and deposited into digestive secretions (among individuals who are secretors).[1] Considering its significance, it is essential to understand a little bit about the relationship between ABO and FUT2 gene function with regards to intestinal health.

The ABO antigen is a carbohydrate food source for many bacteria and thus influences commensal bacterial levels.[2,3] The FUT2 gene plays such an important role in the composition of gut bacteria, that authors of a study from 2014 stated, "secretor status and *FUT2* polymorphism are associated with the composition of human intestinal microbiota, and appears thus to be one of the key drivers affecting the individual variation of human intestinal microbiota."[4] To understand why this is so, it is helpful to examine the role of ABO antigens in the gut mucosa.

> More work and attention may be required on the part of non-secretors to maintain or restore a healthy balance of commensals as well as adequate diversity in their GI tract.

Certain strains of bacteria have a greater affinity for the different carbohydrates, or blood-type antigens, found throughout the gut. Translation: your gut bacteria eat certain foods *based on your blood type*. Because secretors have blood-type antigen plentifully distributed throughout their digestive secretions in the intestine, the beneficial bacteria have a constant supply of food! Non-secretors, on the other hand, do not have such a plentiful food supply. As a result, more work and attention may be required on the part of non-secretors to maintain or restore a healthy balance of commensals as well as adequate diversity in their gastrointestinal tract.[5-8]

Because our ABO blood-group antigens are a source of food for various bacteria, the presence or absence of these antigens not only affect the population of various gut bacteria, they also provide a level of protection against the adherence of certain pathogenic bacteria. Several studies have shown that secretor status affects susceptibility to infection by Norwalk and respiratory viruses, *Vibrio cholera*, *Campylobacter jejuni*, rotavirus, and *Helicobacter pylori*.[8] In some cases, FUT2 non-secretor status confers an advantage.[8] Remember, ABO expression is heavily dependent on the inheritance of the Secretor/FUT2 gene.

The Role of Lectins

Another important factor in the relationship between diet, blood type, and secretor status is the role played by lectins. These are sugar-binding proteins that are found in abundance throughout the plant and legume world. Lectins are

highly specific to their sugar moieties. After all, the word "lectin" comes from the Latin word *legere*, meaning "I choose." Your ABO "blood type" is a sugar antigen – a carbohydrate structure found on the surface of many cells, not only in the blood. Blood-type antigen is found extensively throughout the lining of your gut and all your digestive secretions if you are a secretor.[9] When you consume incompatible lectins for your blood type, they can bind to your particular blood-type antigen and damage your intestinal lining; this in turn diminishes your ability to digest food and lays the foundation for inflammation in the gut.

Generalized "low-lectin diets" continue to be espoused by various health practitioners. D'Adamo's work, however, looks at the *specificity* of lectins for each person, based on his or her blood type. This is really the key to understanding any lectin-host relationship. In fact, some lectins are beneficial for certain individuals, in that their immune systems are more able to identify pathogens and, in some cases, defend against cell changes that might lead to cancer. This is because the lectins can cause aberrant cells to stick together, creating clumps of cells that are now more "visible" to the immune system. If an individual is a non-secretor, the potential for damage wreaked by adverse lectin relationships is much higher. This is because non-secretors lack that extra layer of protection afforded by ABO antigen in the digestive secretions whereby certain lectins can attach to "decoy" molecules instead of doing damage to the mucosal lining of the gut. In this way, blood groups can serve as false receptors, preventing binding to various target tissues. Consuming incompatible lectins for your genetic individuality promotes a proinflammatory state in the intestinal tract as a whole.

Secretor Status & Intestinal Disease

Secretor status effects on GI inflammation, in conjunction with its effects on host gut microbiome bacterial populations, likely contributes to the higher number of non-secretors among individuals with Crohn's disease.[10,11] All chronic inflammatory bowel diseases (IBDs) should be more extensively researched with an eye toward secretor status. Although the precise etiology of IBDs is not yet fully understood, abnormal host-microbial interactions have been implicated in the pathogenesis of IBD.[11-13] Mucosal and fecal bacterial analyses have revealed that patients with IBD have less diverse normal flora, and it has also been shown that non-secretors have less overall diversity in their microbiomes compared to secretors. This is one of the most important factors in overall gut health: a diverse bacterial population. Small intestinal bacterial overgrowth (SIBO) likely has connections to secretor status as well, if we consider the ability of certain bacteria to migrate into the small intestine more easily and propagate due to less mucosal layer protection. More research is needed in this area.

A review of the scientific literature will show definitive associations between non-secretor phenotype (or the FUT2 genotype AA) and celiac disease, peptic and duodenal ulcers, type 1 diabetes, primary sclerosing cholangitis, vaginal candidiasis, and urinary tract infections. Antibiotic treatment in non-secretors appears to promote easier overgrowth of known gut pathogens such as *Salmonella* and *Clostridium difficile*, making these enteric pathogens more difficult to treat in the non-secretor population.[14-18]

The activity of an important enzyme in the gut is also affected by FUT2 secretor status. It has been estimated that non-secretors have only 20% of the enzyme, intestinal alkaline phosphatase (IAP), that secretors possess.[9] IAP plays an essential role in intestinal homeostasis and health. This enzyme interacts with the resident microbiota and with our dietary intake of certain foods. One's secretor status will mightily influence the ability of this enzyme to protect us from both infectious agents and chronic inflammation.[19-23] Lastly, IAP also plays a role in the proper absorption and distribution of lipids such as cholesterol after the ingestion of a fatty meal, so there are implications far beyond the gut as well.

Treatment Considerations

FUT2 gene expression is fairly individual, especially based on the presence of various other genes, including ABO. Nonetheless, there are various therapeutic measures that are generally reliable for non-secretor individuals. Beta-glucans, a type of beneficial fiber, have been shown to help protect the intestinal wall in non-secretors, and several strains of "probiotics," most notably *Bifidobacterium*, will also enhance the expression of FUT2.[6] In addition, certain nutrients, eg, vitamin B12 or picolinic acid, may alter the activity of the FUT2 gene.[24,25] Dietary modifications can make a tremendous difference in overall gut health for non-secretors. It would be appropriate and important for any practitioner making dietary recommendations to his or her patients to identify their patients' secretor status and have a basic understanding of its impact on health. After all, true health, as we know, begins in the gut!

References available online at ndnr.com

Ginger Nash, ND, is an expert in the field of women's health and hormone balance, having lectured to both women and practitioners of natural medicine across the United States and Canada for 20 years. Dr Nash taught at the University of Bridgeport's College of Naturopathic Medicine clinic for 6 years and has also had a thriving practice in New Haven, CT, since 1999. She is a sought-after speaker and has recently launched a comprehensive online program for menopausal women.

Clostridia & Constipation

Using Organic Acid Testing in Diagnosis & Treatment

ANGELA KNAPP, ND

Although *Clostridium* species are typically present in the large intestine as a beneficial part of the gastrointestinal flora, the word clostridia generally elicits thoughts of intractable diarrhea and *Clostridium difficile*. However, despite the common association between clostridia and diarrhea, an imbalance of multiple *Clostridium* species can result in chronic constipation.

Constipation: A Brief Review

Constipation is a digestive complaint that runs rampant in the United States and perhaps worldwide. It can cause enough discomfort to result in irritability. Constipation is defined as incomplete or infrequent stools, as well as difficulty passing stool. To diagnose constipation, at least 2 of the following symptoms must be present over a 3-month period. This is according to the Rome-III criteria[1]:

- Fewer than 3 bowel movements per week
- Straining
- Lumpy or hard stools
- Sensation of anorectal obstruction
- Sensation of incomplete defecation
- Manual maneuvering required to defecate

OR

- Loose stools are rarely present without the use of laxatives

Constipation is not only a symptom of an underlying problem; it also has the potential to create further dysfunction if not treated properly. Getting to the root cause of constipation requires identifying contributing factors.

The first step in uncovering the root of a patient's constipation is an in-depth history and physical exam. A proper physical exam includes listening for the sounds of digestion, percussing or drumming on the abdomen, and feeling for gas or impacted stool. While no sounds may indicate obstruction or slow motility, too much sound, aka borborygmus, suggests gas from offending foods, deficient digestive enzymes, lactose intolerance, or celiac disease. Additionally, assessing reflexes and motor strength is important in order to identify any potential nerve dysfunction.

The next steps in uncovering the root of constipation are lab tests and imaging. These are not always necessary to diagnose the cause of constipation, but can be helpful in some cases. For example, an organic acid test or microbial stool testing can point towards particular microbial disparities, such as clostridia overgrowth or yeast excess. Imaging may help diagnose bowel obstruction or gallbladder sludge that reduces digestive function. Food sensitivity testing can identify food triggers of constipation. Additionally, there are gastric emptying tests and tests for neuropathy, though these are rarely used to evaluate constipation.

When Clostridia Causes Problems

This particular article focuses on the use of organic acid testing to help identify clostridia as a causative factor in a patient's constipation. Clostridia's presence in the colon is generally not problematic. However, when the bacteria regurgitate into the small intestine, clostridia can wreak havoc on the digestive tract, resulting in systemic imbalances. Clostridia's access to nutrients in the ileum allows the microbes to produce short-chain triglycerides that promote water absorption, which dries up intestinal waste.[2] Clostridia are also capable of reducing fat absorption by deconjugating bile and consuming available lecithin.[2] Tryptophan – one of the most-scarce amino acids[3] and which is required for the production of 5-hydroxytryptophan (5-HTP), serotonin, and melatonin – may be metabolized by clostridia, reducing bioavailability.[2] Finally, clostridia's presence in the small intestine may result in impaired B12 metabolism, resulting in anemia.[2]

The short-chain fatty acid, butyric acid, is generally considered beneficial to the health of the gastrointestinal tract. In the case of clostridia overgrowth, however, butyric acid (along with propionic acid) may induce sodium and water absorption in the colon, furthering the solidity of the stool.[2,4,5]

Once constipation has worsened, backup of clostridia into the small intestine can allow for the sequestration of vitamin B12 prior to its absorption in the terminal ileum.[6] Resulting B12 deficiency may lead to anemia and eventual neurological damage by demyelination.[6]

Organic Acid Testing

Organic acids are byproducts of metabolism in the body that can be easily measured in a urine specimen. Levels of different organic acids can provide information about various functions and organ systems in the body, including the gastrointestinal tract.

Research since 1955 has shown that certain *Clostridium* species (and enterococci) are capable of bile salt deconjugation via the bacterial enzyme cholylglycine hydrolase.[7] Deconjugation of bile salts prevents the breakdown of fats, resulting in lipid malabsorption and fat-soluble nutrient depletion. Remaining fats in the intestine serve as a food source for pathogenic bacteria, producing malodorous gases from putrefactive fatty acids such as putrescine and cadaverine. On an organic acid test, elevated levels of suberic and adipic acids indicate a

reduction in the breakdown of fats. This, in combination with elevated levels of *Clostridium* metabolites, such as 4-hydroxyphenylacetic acid, HPHPA, 4-cresol, and 3-indolacetic acid, supports a link between reduced bile function and clostridial deconjugation of bile.[8-10]

Tryptophan metabolism is one of the more well-researched aspects of clostridia metabolism. Clostridia has been shown to cause tryptophan deficiency via 2 mechanisms. Firstly, *Clostridium* can consume the sugar necessary for tryptophan's absorption, which can then result in preferential absorption of other amino acids, such as tyrosine. Secondly, *Clostridium* can metabolize tryptophan. The resulting deficit in available tryptophan may cause niacin deficiency, due to tryptophan's role in niacin metabolism. Niacin as NAD plays an important role in oxidation-reduction reactions as well as non-redox reactions.[11]

On organic acid testing, urinary levels of tryptophan metabolites such as 5-hydroxyindolacetic acid (5-HIAA), quinolinic acid, kynurenic acid, and the ratio of quinolinic acid to 5-HIAA, can indicate a possible tryptophan deficiency and potential neurotoxicity (Figure 1). Along with markers for *Clostridium*, these tryptophan markers may suggest Clostridia involvement. Low serotonin levels, indicated by low 5-HIAA, can play a role in reduced peristalsis, further complicating constipation.

Treatment Options

Management of clostridia-mediated constipation can take any number of directions: diet, supplements, botanical medicine, or antibiotics. *Lactobacillus* species are known to be health-promoting gastrointestinal bacteria. Because lactobacilli balance and counter many of the actions of clostridia, a diet supporting lactobacilli and inhibiting clostridia can help prevent and reverse dysbiosis. *Lactobacillus* requires little iron and is unable to digest cellulose, many proteins, and lipids, whereas *Clostridium* can digest most foods other than lactulose and some proteins and lipids. Therefore, a diet low in protein and iron can help support lactobacilli species while at the same time reducing clostridia species. It has also been suggested that conservative use of lactulose can help alleviate constipation while also promoting growth of lactobacilli.

Just as a *Lactobacillus*-promoting diet can benefit the balance of the gut flora and inhibit *Clostridium* overgrowth, so can the use of probiotics comprised of *Lactobacillus* species, particularly *Lactobacillus rhamnosus*.[12] In combination or individually, research has also supported the clostridia-inhibitory effects of *Saccharomyces boulardii*.[13]

Clostridia has been shown to cause tryptophan deficiency via 2 mechanisms.

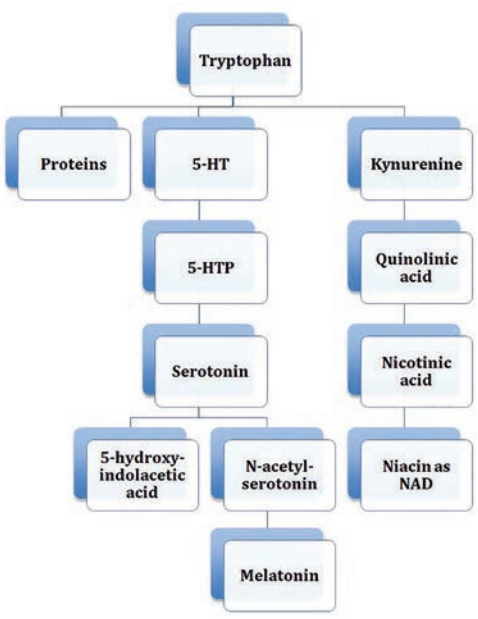
One of the most popular botanical approaches to dysbiosis that among clinicians is a proprietary blend of *Vaccinium myrtillus* (bilberry) extract (25% anthocyanosides), *Morinda citrifolia* (noni), *Silybum marianum* (milk thistle), *Echinacea* (*purpurea* & *angustifolia*), *Hydrastis canadensis* (goldenseal), shiitake, *Salix alba* (white willow bark), garlic, grapeseed extract (minimum 90% polyphenols), *Juglans nigra* (black walnut) hull and leaf, raspberry, *Fumaria officinalis* (fumitory), *Gentiana* (gentian), *Melaleuca alternifolia* (tea tree oil), *Ferula* spp (galbanum) oil, lavender oil (plant and flower), and *Origanum vulgare* (oregano) oil (plant and flower). Pulsing doses of this tincture may reduce clostridial burden similar to pulsing doses of antibiotics like vancomycin and metronidazole.[14]

Management of chronic constipation requires a complete work-up. Organic acid testing can help identify clostridia as a possible contributing factor in a patient's constipation. It can also help assess how clostridia may be affecting nutrient absorption, lipid breakdown, and neurotransmitter balance, as well as the severity of these imbalances.

References available online at ndnr.com

Angela Knapp, ND, believes in the symbiosis of humanity and the environment. It was during her work as a small farmer after college that Dr Knapp recognized her goal to heal the earth by helping its inhabitants heal themselves. In 2013, Dr Knapp received her doctorate from NCNM, with a specialty in Natural Childbirth. She currently practices at the Peirson Center for Children, in Portland, OR. Dr Knapp is Staff Physician at Kashi Clinical Laboratories. She enjoys spending time with her family, preparing meals with locally procured foods, and grounding herself by getting her feet wet in any nearby body of water.

Figure 1. **Tryptophan Metabolism**



SIBO as an Adaptation

A Proposed Role for Hydrogen Sulfide

GREG NIGH, ND, LAC

We can not solve our problems with the same level of thinking that created them.
(Albert Einstein)

It is an understatement to say that the microbiome is not what we thought it was. In the past decade we have seen an explosion of information regarding the multiple regulatory roles the gut bacteria play in the body. Almost every major organ in the body is now understood to function within an "axis" with the gut. These include a gut-brain axis,[1] gut-heart axis,[2] gut-kidney axis,[3] gut-lung axis,[4] diet-microbiota-immune axis,[5] gut-liver axis,[6] gut-joint axis,[7] and others. To designate an axis is to recognize the active role the microbiome plays in the beneficial modulation of these varied organs.

The case has been made that the microbiome constitutes an endocrine organ in itself due to its ability to produce a wide range of compounds that regulate distant cells, organs, and systems. These compounds include neurotransmitters and short-chain fatty acids, in addition to regulators of cortisol, ghrelin, leptin, secondary bile acids, and others.[8] Further, the microbiome can make changes in its composition that are adaptive for the host – changes that can take place within a single day of altering the macronutrient content of the diet. It will revert back to its original composition within 2 days of ending the trial diet.[9] There are numerous examples of the microbiota remodeling itself in order to utilize dietary constituents *for the benefit of the host*.[10,11]

The picture that has emerged is one of shocking complexity: these trillions of non-self organisms are sensing the changing nutritional environment[12] and constantly producing signaling molecules,[13] and fine-tuning and adjusting our entire physiology accordingly. It all works brilliantly until, it would seem, it doesn't.

An Alternative View

During my first year as a student at the National College of Naturopathic Medicine (NCNM), I made it a habit to regularly meet with Dr Jared Zeff over lunch. During those walk/talk sessions I would pepper him with as many questions as I could. Once I naively asked, "How do you treat a common cold?" His reply was quick and has stuck with me since: "A cold isn't the problem; it's the *cure*."

Regarding the microbiota, I would not suggest that there is no such thing as dysbiosis. However, when it comes to small intestinal bacterial overgrowth (SIBO), in particular, I do want to suggest that perhaps it is such a tenacious problem because we're thinking about it wrong. Maybe the problem with the durability of our therapies is that SIBO is not the problem. Rather, maybe SIBO is actually an adaptation, a symptom-laden solution to a *different* problem. Bear with me.

SIBO is as much a *clinically* diagnosed condition as it is diagnosed through testing. Patients with the standard SIBO symptoms but without a positive SIBO breath test are, in my experience, generally classified as hydrogen sulfide-type SIBO. I am not doing SIBO testing in my practice, but this is how patients commonly arrive at my office. I don't doubt that hydrogen sulfide is behind symptoms in those cases, and in fact I suspect it goes much further than that. Let's consider the prime suspects behind SIBO.

As much as 1 liter of hydrogen is produced by bacteria of the microbiome each day. It is important to keep in mind that molecular hydrogen plays a strong anti-inflammatory role in the body.[14] In fact, the antioxidant properties of lactulose have been attributed to its ability to promote bacterial production of molecular hydrogen,[15] and the cardioprotective effect of alpha-glucuronidase inhibitors has been attributed to their ability to increase hydrogen production in the microbiota.[16] Numerous articles have postulated beneficial effects from the molecular hydrogen produced by the microbiome.

Methane (CH_4) has been proposed as meeting all 6 requirements to be a "gasotransmitter."[17] While the physiological role(s) of CH_4 is unclear, it is well-established that microbial methane production acts as a sink for hydrogen produced "upstream" by the hydrogen-producing bacteria.[18]

Hydrogen sulfide (H_2S) has its own interesting history. Regarded for over a century as simply a noxious gas, it eventually joined carbon monoxide and nitric oxide as the third gasotransmitter in the human body. H_2S has a wide range of functions, including cognitive, neurological, gastrointestinal, cardiovascular, and others. Interestingly, its physiological effects are often opposite at low and high concentrations.[19]

When healthy cells are put under stress, the H_2S-generating enzyme cystathionine-gamma-lyase (CSE) translocates from the cytosol to the outer mitochondrial membrane, where it uses the high mitochondrial concentration of cysteine to generate H_2S. The H_2S then acts within the electron transport chain to improve efficiency of ATP production.[20] The point is that H_2S production is vital to the cellular adaptation to physiological stress.

H_2S is also generated by the microbiome through the action of the sulfur-fixing bacteria (SFB). As with CH_4 production, H_2S production is a means of trapping molecular hydrogen produced upstream. In fact, the SFB have a substantially stronger affinity for molecular hydrogen than do the methanogens, which means that H_2S is more likely to be produced than CH_4. In this way, the methanogens and the SFB maintain a functional balance with the hydrogen producers, while at the same time supplying the body with a crucial gasotransmitter.

H_2S as a Sulfate Substrate

Aside from its role in both health and diseases of the gastrointestinal tract,[21] there is another crucial role for H_2S in the body, a role that I believe is central to SIBO's adaptive function: H_2S is a substrate for sulfate (SO_4) production. Activated neutrophils can generate sulfate from H_2S,[22] while virtually all cells contain the enzymatic machinery to oxidize H_2S to thiosulfate in a 3-step process in which sulfite is an intermediate.[23] Sulfite can also likely be generated from H_2S via endothelial nitric oxide synthase (eNOS).[24] Sulfite, wherever it is generated, can be acted upon by the ubiquitous enzyme, sulfite oxidase, to generate SO_4. Given the body's constant need for SO_4 to build heparan sulfate,[25] carry out phase II detoxification, maintain proper blood viscosity,[26] and many other actions, any reduction in sulfate availability necessitates a "work-around," a compensatory shift. H_2S produced in the gut via SFB, symptomatic though it may be, will diffuse into the blood and a portion of it will ultimately be oxidized to sulfite and then sulfate via these mechanisms just described.

There are many reasons that sulfate might be in short supply, most of them, I believe, being environmental. Glyphosate, the active ingredient in many commercial herbicides, can chelate molybdenum and iron and can also impair heme synthesis – 3 consequences that would have profound impacts on the sulfate-generating heme enzyme, sulfite oxidase (SUOX).[27] Sunlight exposure is another important source of sulfate production within the skin. The dramatic increase in UV-blocking sunscreens would be expected to significantly reduce the average daily sulfate production in the population.[24]

Heavy metals, such as tungsten, copper, cadmium, and arsenic, have also been shown to insert themselves into the molybdenum cofactor within SUOX.[28]

Sulfur-containing products (eg, methionine, methylsulfonylmethane [MSM], lipoic acid, glutathione, N-acetylcysteine [NAC], and others) are used as detoxification therapies for a reason. Sulfur *binds*, and this includes the sulfur in the amino acid, cysteine, found within serum albumin, the sulfate in heparan sulfate, and elsewhere. It will bind metals[29] as well as various other pollutants.[30] An unfortunate result is that the heparan sulfate proteoglycans sustain damage when assaulted by byproducts of modern life such as reactive oxygen and nitrogen species, heavy metals, and aberrant copper and iron metabolism.[26,31]

Genetics comes into play in this as well, though my clinical experience suggests that outside of polymorphisms in the SUOX gene, the polymorphisms associated with cystathionine-beta-synthase (CBS) and CSE are usually playing a relatively minor role in sulfate production and processing.

It is within this context that hydrogen sulfide comes to the ironic rescue. Although linked to various symptoms, its ability to be oxidized to sulfate fills a biological vacuum that must be filled for sustained physiological functioning. In this

adaptation model, the many sulfur-fixing bacteria – which can convert sulfated steroids, sulfomucins, dietary cysteine, and other dietary sulfur into hydrogen sulfate – proliferate in order to supply this much-needed sulfate substrate. The sulfur fixers are not just in the genus of *Desulfovibrio*, but also include *Staph aureus*, *E coli*, *Campylobacter jejuni*, *Klebsiella* species, *Bilophila wadsworthia*, *Helicobacter pylori*, and over a dozen others.[32] Each of these can convert different sulfur substrates into H_2S, and H_2S can be transformed into SO_4.

I believe this is the reason that SIBO treatment that focuses on eradication of the bacteria causing the symptoms is doomed to fail, or at least has a high probability of failure. One study showed a 44% recurrence of SIBO 9 months after successful rifaximin treatment.[33] Patients who take the best herbal and prescribed antibiotic protocols, eat the right diets, and take all the indicated probiotics and nutrients have a tragically high probability of symptoms resurfacing. It doesn't make sense. However, this should be expected *if* the underlying issue is a sulfate deficiency, and *if* access to biologically useful sulfate has been limited.

I came to this adaptationist opinion rather incidentally. I was studying sulfur metabolism, seeing its connection to many maladies, and was working with sulfur issues as it related to hives, hot flashes, dermatitis, brain fog, inflammatory bowel disorders, and many other conditions. Then patients with a SIBO diagnosis started showing up to my office. I didn't know what the breath tests meant, but with the help of the nutrition therapist I work with, I put these patients through a protocol designed to "unlock" sulfur metabolism. Lo and behold, regardless of their SIBO test results, a large majority of these patients felt dramatically better, often for the first time after years of "standard" naturopathic SIBO diet and treatment. I don't claim any universal cure; however, I think that a significant number of SIBO patients are significantly lacking in sulfate, and therapies to restore sulfate will reduce the need for those sulfur-fixing bacteria, and thus reduce or eliminate symptoms.

Unlocking Sulfur Metabolism

Restoring metabolic sulfate production can be a tricky business in patients with an established dysbiosis, but a few therapies are almost universally helpful.

Epsom Salt Baths

RH Waring conducted a study[34] with 19 healthy subjects. He found that using 400 grams (about 4 cups) of Epsom salt and soaking for 20 minutes nightly for 7 nights in a row increased sulfate levels in the blood to a steady state. I have recommended this protocol for many patients and found that this alone can sometimes dramatically improve digestive symptoms in SIBO patients. A shower rinse after the bath is recommended.

Molybdenum

This trace mineral is crucial, though it is important to keep in mind that more is not always better. Molybdenum should be dosed in an organic form, and no more than 150 mcg twice daily with food should be taken. In my practice I have tried many supplemental forms, and only a few have worked.

Hydroxocobalamin

This particular form of vitamin B12 is able to bind H_2S and render it less biologically toxic.[35] Clinically, I'm using this both intramuscularly and as oral therapy.

Korean Red Ginseng

This form of ginseng has been shown to suppress the activity of the CBS and CSE enzymes, thus reducing production of H_2S internally.[36] This can obviously play an important dual role in those SIBO patients who struggle with fatigue or who manifest other low-adrenal symptoms.

Miscellaneous

In addition to these basic therapies, I utilize a wide range of homeopathics, other nutrients (as indicated per case), and with the assistance of the nutrition therapist in my office, recommend a specific low-sulfur diet that is customized to each patient. The common goal of all therapies is to reduce the need for SFB and reestablish healthy sulfate production. Most patients have had years or decades of inflammatory bowel issues that have to be repaired, so it takes time before dietary sulfur can be brought back in as a standard part of the diet. Gut rebuilding protocols have to be utilized incrementally, and only after sulfate-supporting nutrients have been brought into the program and biologically available sulfate has been supplied.

Conclusion

SIBO is a sign of the times. The modern world is built in a way that impairs sulfur metabolism, and SIBO is a reflection of that problem. If we treat SIBO as the problem, then patients are likely to struggle with recurrence; a body's gotta do what a body's gotta do, and producing sulfate is what a body's gotta do. Viewed in the light of sulfate-producing adaptation, I believe it is not only SIBO that becomes more understandable, but a wide range of modern maladies also become less mysterious.

References available online at ndnr.com

Greg Nigh, ND, LAc, is naturopathic physician and acupuncturist, graduating from NCNM (now NUNM) in 2001. Dr Nigh is co-owner of Immersion Health in Portland, OR, where he has a primary-care practice as well as a specialty in naturopathic oncology. He has done extensive research, writing, and speaking on the relationship between dysfunctional sulfur metabolism and the development of SIBO, inflammatory diseases, cancer, and other chronic conditions.

The Carroll Method

An Explanation

JARED C. PISTOIA
SUSSANNA CZERANKO, ND, BBE

The Carroll method is a technique performed to identify food intolerances. Traditionally oriented naturopathic doctors rely on the Carroll method in conjunction with other widely implemented dietary evaluation tests to identify foods that may be problematic for a patient. This method is especially important because there are very few available tests that can reliably identify food intolerances, also because clinical application of the results has anecdotally been a key step in preventing toxemia, ie, the buildup of toxic digestive byproducts, historically referred to as morbid matter by Henry Lindlahr.[1] When used in conjunction with the other available dietary evaluation tests, the result is a highly personalized diet that helps minimize the creation of morbid matter and ingestion of inflammatory or metabolically inefficient foods – a necessary first step in the naturopathic therapeutic order of cure.

The Carroll Method

Morbid Matter

The primary aim of the Carroll method is to reduce the production of morbid matter. Food that is incompletely broken down is destined to be digested by bacteria in the large intestine. Bacterial metabolism of meat, eggs, and dairy products increases the level of morbid matter (such as trimethylamine N-oxide) and the risk of developing its associated diseases.[2] Through simple urinalysis, a practitioner may detect levels of morbid matter in a patient's body,[3] thereby confirming that morbid matter is a veritable concern and not merely a concept. Toxemia is concerning because it increases the toxic load in the blood and taxes the organs of elimination. These disturbances can then manifest as inflammatory symptoms in the patient and disrupt normal bodily functions.

The ill effects of consuming intolerable foods is not unlike other forms of toxicity. For example, chronic lead exposure in children results in systemic symptoms in those children.[4] In this way, lead can also be thought of as morbid matter. The same principle applies to the internal environment of the body when it is exposed to intolerable foods.

Vibratory Properties of Food

In the early 1900s, naturopaths wrote about the vibratory properties of food and theorized that disturbances in harmonious vibration were a chief cause of disease.[5] The theoretical basis for such an idea is entirely plausible, considering that all material objects are composed of elementary particles that are neither stationary nor obey the known laws of physics[6]; light, sound, and all other detectable waves follow these same principles. Harmonious vibration refers to unimpeded cellular function and is therefore a governing concept of health. Of chief importance is understanding the precise cause of impeded cellular function. In clinical practice, a correlation between food intolerances, symptoms, and the disappearance of symptoms after removing the offending foods can be observed. In the same way that a lactose intolerance test implies a genetic lactase deficiency,[7] results of the Carroll method may imply enzyme deficiencies.

Methodology

The Carroll method uses an electrical device and glass rod to detect subtle electrical change at an acupuncture point (Stomach 25). The electrical device is used as a means of capturing and oscillating current sourced from the practitioner's electric field.[8,9] The field is honed by fastening a headband with a small conductive plate against the patient's forehead and then plugging the headband directly into the machine. Once the circuit is established, dials on the device are adjusted to manipulate the frequency of the established circuit to match that of the large intestine's frequency. Before the technique is performed, a sample of the patient's blood is drawn onto a small piece of filter paper; this sample is allowed to dry, and then placed between 2 metallic surfaces on the electrical device. This modifies the circuit and personalizes the results for the patient rather than the practitioner. Finally, a sample of dehydrated food – typically dairy, egg, potato, meat, or fruit – contained within a glass jar is placed individually on top of the metallic surface to detect any change in current.

The glass rod is the primary instrument used to detect changes in current. Before being used, it is briefly and vigorously rubbed with a wool cloth to temporarily transfer electrons from the wool onto the glass rod, much in the same way that one might rub a balloon on a shirt, essentially "charging it." The glass rod acts as a detector of current over the acupuncture point and will be met with a small level of resistance if the practitioner

gently and skillfully drags it upward past the acupuncture point. If the patient is intolerant to dairy and a sample of dairy is introduced to the current, current can no longer be detected and the glass rod will thus slide over the acupuncture point. If the person is not intolerant of dairy, the glass rod will be met with resistance, resulting in a slight sticking phenomenon. Such a reaction establishes dairy as a compatible food.

Although the mechanism of the Carroll method has no unanimous explanation in the medical community, it is theorized to be a bioenergetic phenomenon and is perhaps best explained by the late Dr Albert Abrams in his work, *The Electronic Reactions of Abrams*. In the "Conceptual Plausibility" section below, we offer a basis for understanding the technique based on known principles of physiology and electromagnetism.

Method Reliability

Typically, if more than 1 trained practitioner performs the Carroll method on a patient, the results will be the same. Although the execution of the method is subjective, its ability to reproduce the same result across multiple practitioners demonstrates objectivity. However, the method's objectivity can be undermined if the practitioner is incompetent in terms of skill or knowledge. There are several physical or energetic factors that can interfere with the practitioner's performance, such as body temperature, moisture at the site of testing, or a negative mental state, which also has been shown to induce both tissue-specific and generalized cellular changes over time.[10] The practitioner should regularly practice the fundamental tenets of health to achieve physical and mental competency.

Though empirical evidence is limited, studies support the Carroll method as a highly specific method for determining food intolerances. One double-blind study determined the Carroll method to have comparable specificity and positive predictive value as IgE/IgG/IgG4 testing for foods.[11] Further studies with larger sample populations are needed to help determine large-scale clinical efficacy, although the aforementioned study is consistent with anecdotal evidence from naturopathic doctors who utilize the Carroll method in conjunction with other traditional naturopathic modalities.

The specificity of the method is revealed clinically when the test results are applied to the patient. After the patient is directed to avoid their intolerable food(s), a series of treatments beginning with constitutional hydrotherapy are employed on a routine basis to facilitate the eliminative faculties of the body. According to the Therapeutic Order, the order of treatment to assist in toxin elimination begins with constitutional hydrotherapy and is followed by choice herbs and homeopathic remedies, etc, determined on a case-by-case basis. The protocol is considered successful if patients avoid their intolerable foods, resulting in restoration of tissue function and symptom dissipation. The use of diagnostic techniques such as iris examination or Chapman reflex points can also be performed to gauge the effectiveness of the healing protocol from an objective standpoint.

Conceptual Plausibility of the Carroll Method

The rationale behind the Carroll method is currently theoretical because the technology required to fully understand bioenergetics either does not yet exist or is ignored by the scientific community. Therefore, it's helpful to consider known principles of electromagnetism and physiology to facilitate an understanding of the potential mechanism of the Carroll method.

The technique can be understood conceptually by likening the body to that of a simple electric circuit. Imagine a circuit consisting of 2 wires, 1 bulb, and 1 battery. The battery is the source of electrical current – the electromotive force. The bulb is the resistor of current, and the wires transport the current. Under normal circumstances, current flows from the battery through the wire until it meets the light bulb, which resists the current as it converts electrons into heat and light. In the body, the bulb's conversion of energy is similar to mitochondrial conversion of electrons into heat and ATP. The large intestine and food sampled together can be likened to the bulb. Like bulbs of differing resistance, food likely also has a resistance value depending on the individual's ability to assimilate that food. More resistance results in decreased ability to assimilate the food, which translates into decreased current flow. Since the large intestine is ultimately digesting food as a means of accessing electrons to be packed into ATP molecules, the liberation of these electrons theoretically creates a detectable flow of current.

In this way, intolerable foods can be thought of as strong insulators. Thus, when tested, the glass rod will slide over the acupuncture point, unable to detect a flow of current. This simple explanation is plausible by considering Ohm's law, or I = V/R, where I is current flow, V is voltage, and R is resistance. Accordingly, more resistance decreases current output. A closer look at physiology helps one to understand the processes occurring at the cellular level.

Each cell in the body has a resting membrane potential. The cells are constantly exchanging ions, in different concentrations and rates of exchange. Different cells comprise different tissues with distinct functions, ultimately forming organs. The fact that different types of ions exist in the various tissues of the body allows for a reasonable assumption that each organ has a numerically dissimilar, summed electric field frequency. The value of organ frequencies has previously been produced by the late Bruce Tainio, whose original work is missing. Other work involving organ frequencies and diseases, discovered by the late Royal Raymond Rife, showed promise but was harshly criticized, rejected, and later tarnished by the AMA, and his Rife machine was confiscated by the Department of Public Health.[12] Rife was the highly acclaimed inventor of the first universal microscope, which at the time was considered a modern marvel and earned him the title of "scientific genius."[12]

Although these explanations offer an idea of the potential mechanism of the technique itself, 2 key questions yet remain: 1) What is the relationship between the blood sample, the device, and the practitioner? and 2) How does the technique provide information about an individual's digestive capabilities if that individual is not currently digesting that food or is not physically present for the test? Clearly, there is another force or factor at play that is not well understood and requires further study.

Present-Day Bioelectric Techniques

The Carroll Method is but one means of obtaining information coded in electromagnetics. Presently, the study and application of harmonious vibration falls under the category of bioenergetics. There are several modern-day techniques that seek to restore normal, harmonious cellular vibrations to the various organs of the body. Savely Yurkovsky, MD, utilizes a technique called "Field Control Therapy," proclaiming that it's a form of targeted homeopathy.[13] His method employs a machine that identifies disturbances in cellular frequency and then applies a homeopathic dose of electricity to draw out toxins from that organ.[14] Similarly, Pierre Nicolas created a form of energy medicine called Biosyntonie, capable of normalizing biorhythms and neuroendocrine functions.[15] Both methods of bioenergetic medicine are based on the concept that harmonious vibration is a function of unimpeded cellular function, and the varying forms of impedance include exposure to deleterious electric frequencies, ie, radiation, the internal effects of wrongful eating. Other techniques, such as music therapy, employ the use of sound waves to restore harmonious vibration.[16]

The concept of harmonious vibration, bioelectric fields, and bioenergetics all seems to point toward what could potentially be the cutting edge of medicine – a new wave of powerful healing methods. The ability of the Carroll method to identify a food intolerance, based presently on underdeveloped or unexplored principles of bioenergetics, is a phenomenon that cries out for attention in the scientific community. It is well worth exploring, considering the positive clinical outcomes of applying this technique. Dismissing such claims and devices as "pseudo-scientific," and eagerly dismantling the theories, does little to explain the clinical success, turns a blind eye to the essence of scientific inquiry, and potentially limits advancements in medicine, our understanding of health, and our evolution as a species.

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Jared C. Pistoia is a 2nd-year medical student at the National University of Natural Medicine (NUNM). He earned a bachelor's degree in Health Science from Stony Brook University and has a strong interest in vitalism and traditional naturopathic philosophy.

Sussanna Czeranko ND, BBE, a naturopathic physician licensed in Oregon, has been practicing since 1994. She incorporates nature-cure approaches such as balneotherapy, hydrotherapy, and breathing therapy into her practice. Dr Czeranko is a faculty member and works as the Rare Books Curator at NUNM. She has completed the 11th book in a 12-volume series, *The Hevert Collection*, based upon Benedict Lust's original journals. She is also the founder of the Breathing Academy, which trains NDs in the breathing therapy, Buteyko. She is a founding board member of the International Congress of Naturopathic Medicine. Dr Czeranko has established a traditional naturopathic clinic, *Manitou Waters*, in Manitou Beach, Saskatchewan, which is scheduled to open in August 2019.

Gallbladder Disease

Not Just a Problem for Women

ROBIN DIPASQUALE, ND, RH (AHG)

It is estimated that 15% of the US population – about 20 million people – have some degree of gallbladder disease (GBD). The prevalence of GBD increases with age and can often be asymptomatic, until it isn't anymore.

When a gallbladder attack comes on, there is often extreme and unrelenting pain, which can last for hours. People often go to the emergency room looking for relief. Analgesic medications such as acetaminophen or codeine may decrease pain. Anticholinergics, such as hyoscine butylbromide, may decrease the spasms. But nobody wants to experience this again… which is why cholecystectomy, ie, surgical removal of the gallbladder, has become the gold standard of treatment for GBD. Out of every 100 people diagnosed with biliary colic, 22 are referred for cholecystectomy.[1] People are increasingly choosing elective cholecystectomy as a preventative measure against the severe complications of acute cholecystitis, acute biliary pancreatitis, or acute cholangitis.[2] But is this really the best choice, to lose an organ when the condition might be managed more conservatively? Brazzelli reviewed 2 Norwegian studies including a total of 201 participants with symptomatic GBD.[3] During the 14 years of the study, 88% of the patients who had been randomized to surgery, and 45% of those who had been randomized to observation, underwent cholecystectomy. That meant that 12% of the surgery-randomized group, and 55% of the observation-randomized group, did not require surgery.[3] So perhaps there are other options, but patients have to be willing to make changes in their lifestyle and diets – not always an easy sell.

Contributing Factors to GBD

Everyone remembers the "5 Fs" mnemonic for cholelithiasis as a rule-out in upper abdominal pain: fair, fat, female, fertile, and forty. In a 2013 study, Bass et al confirmed most of these parameters, and included an additional parameter that begins with the letter F, that being family history.[4] Of 398 patients with upper abdominal pain, 198 cases were diagnosed with GBD by ultrasound. Of those, 150/198 were women, 144/198 were fair, and 135/198 were fertile, ie, of child-bearing age. Interestingly, although we often think of overweight and obesity as a contributing factor to GBD, only 56/198 had a BMI >30. And while the study found that 82/198 were over 40, those with a family history of at least 1 first-degree relative with GBD was 78/198 – close to the same number as the over-40 group.[4]

While Bass et al showed overweight and obesity to be a contributing factor for developing GBD in only 28% of participants, other studies have confirmed the correlation with weight. Radmar et al, for example, looked at the ability of abdominal/visceral fat to predict gallbladder disease.[5] Of 1494 participants, 51.4% were men over 50 years of age. Their research found a significantly increased risk of GBD among men with an elevated waist:hip ratio. For women, the BMI and waist:height ratio were found to be more significant in determining GBD risk.[5] In a prospective study of 29 847 men with no prior history of gallstone disease, 1117 new cases of symptomatic gallstone disease were documented over a 2-year period, linked to increased waist:hip ratio and waist circumference.[6] In other words, among these men, increased abdominal circumference was a more significant contributing factor to GBD symptoms than was BMI.

We know that a primary contributing factor to abdominal adiposity is metabolic syndrome, which can be a precursor to type 2 diabetes. A population-based study of 1250 men and 1656 women showed that the odds of developing GBD was 1.6 times greater when type 2 diabetes was present.[7] A retrospective cohort study, including 337 067 type 2 diabetics and the same number without diabetes, produced similar findings: the type 2 diabetes cohort had a 1.91-fold greater risk of biliary disease compared to the non-diabetic cohort.[8]

Although dietary fat intake may not contribute to increased GBD prevalence in women, it might in men. In a population-based study of Mexican Americans (who have a higher prevalence of GBD[9]), the women reporting the highest intake of total fat and linoleic acid showed reduced risk for GBD, whereas the opposite was observed in men.[10]

Hormones appear to be another gender difference in terms of GBD risk, as there seems to be a direct relationship between GBD and estrogen. The rates of GBD are 2-3 times higher in women compared to men, but primarily during the childbearing years.[11] Pregnancy is a major risk factor for gallstone formation. Higher estrogen levels increase biliary cholesterol secretion, causing cholesterol saturation of bile and reduced gallbladder motility.[11]

If this is the case, that estrogen is linked with the increased risk of GBD for women, then GBD risk should go down as women move into menopause and estrogen levels decline. Estrogen replacement therapy should restore that risk. It is also possible that as men age, and their estrogen levels increase through the aromatization of testosterone to estrogen, their own risk of GBD would increase.

Treatment Considerations

Diet can be the most significant contributor to GBD, and the most potent path to resolving it. A plant-based diet may be optimal for patients, including plenty of vegetables, some fruits, legumes, grains, nuts, and seeds. Lean meats can be included in small portions. High-quality oils, in small-to-moderate amounts, are an important source of fatty acids; examples include olive, avocado, flax, walnut, coconut, and sesame oils. Eating smaller meals overall can reduce the burden on the digestive system. The caffeine in coffee, tea, and chocolate can trigger contraction of the gallbladder, so have your patients be mindful when eating or drinking caffeinated products.

Bitter herbs are useful in GBD because of their ability to prime the entire digestive system, including the release of bile from both the liver and the gallbladder and the thinning of bile throughout the system. A comprehensive plant-based digestive enzyme taken with meals can be useful, as amylase, protease, and lipase will contribute to the breakdown of all 3 major macronutrients, including fats. Plant-based enzymes are more easily digested and absorbed compared to pancreatin, thus useful for a person with an already compromised digestive system.

There are 2 specific drinks that can be a supportive component of treatment for GBD. One of them is simply a cup of warm water with the juice of one-half lemon, to be sipped each morning. This drink will engage the liver, enhance bile flow, increase metabolic rate, and help maintain a balanced pH. This is actually a good idea for anyone, not just those with GBD. The second drink contains 8 oz water and 2 tsp apple cider vinegar (ACV), also to be sipped. Some people love this; some people hate it.

I had one patient add the ACV to a glass of apple juice every morning, hoping the malic acid in the apple juice would soften and dissolve his gallstones. I'm not sure about the effectiveness of this approach, since he wound up having his gallbladder removed a few months later. I did, however, have another patient who was in the middle of a gallbladder episode (milder than an attack) while traveling on a plane, and she appeared to resolve the spastic squeezing sensation by eating an apple.

For anyone with GBD, castor oil packs combined with 30 minutes of heat over the liver and gallbladder several days per week will help to decrease inflammation, soften any stones, and support the flow of bile. In my clinical experience, the essential oil of rose geranium is a valuable addition due to its antispasmodic action. If patients are not keen on the idea of the castor oil pack, or say they don't have time for it, I often have them massage the castor oil over the liver/gallbladder area, put on an old T-shirt, and climb into bed. The heat of their bodies will help with the absorption of the castor oil throughout the night.

Herbal Solutions

The Eclectic literature doesn't speak directly about GBD; however, discussions of the herbs that act on the liver make reference to it in several books. Following are a few pearls.

Chelidonium majus

Felter[11] holds *Chelidonium majus* (celandine) as a top choice of herbs for this condition. Felter's key notes include the following:

1. Biliary catarrh resulting from hepatic congestion
2. Jaundice due to swollen bile ducts as a result of subacute sluggish liver action
3. Light, pasty stools
4. Throbbing pain of the hypochondrium, with dull pains extending to beneath the right shoulder blade
5. This herb can prolong the intervals between attacks of gallstone colic

Ellingwood[13] wrote about *Chelidonium* being used for the treatment of biliary calculi, and comments that many physicians consider it superior to any other agent known for preventing gallstone formation.

Matt Wood, in *The Book of Herbal Wisdom*,[14] reports that *Chelidonium* is used almost the same way in both homeopathy and herbalism – as a liver remedy with an affinity for the bile. He also notes that *Chelidonium* is a very important herb for "gallbladder headaches," and includes it on the list next to *Sanguinaria*. Its bright yellow/orange sap exemplifies the doctrine of signatures.

Ellingwood[13] writes about herbs to prevent gallstones, listing *Chionanthus virginica, Iris versicolor, Leptandra virginica,* and *Podophyllum peltatum.* He doesn't mention *Fumaria officinalis,* but I'm adding it to this list.

Chionanthus virginica

Chionanthus virginica (fringe tree) is a cholagogue cathartic; however, its best effects are seen in acute congestion of the liver, with imperfect discharge of bile or catarrh of the common bile duct.[13] *Chionanthus* conquers catarrh, liquifies the bile, prevents the formation of calculi, and promotes the discharge of stones that have formed. It is not indicated for impacted gallstones.

Iris versicolor

Ellington's key notes for *Iris versicolor* (blue flag) are as follows[13]:

1. When the stools are clay colored, the urine scanty, and the skin inactive and jaundiced

2. Gastralgia and gastrodynia with vomiting or regurgitation of food, especially after eating fats or rich pastry
3. Diarrhea, with a burning sensation after the passage of stool
4. Jaundice arising from duodenal catarrh and obstruction of the biliary ducts

Matt Wood writes this about *Iris*: "Causing a liquidification of the bile, so that it flows freely from the hepatic structures, producing yellow to orange diarrhea with itching of the anus, which showed up in the homeopathic proving."[14]

Leptandra virginica

Here are Ellington's key notes for *Leptandra virginica* (Culver's root)[13]:

1. Pressure in the right hypochondrium
2. Torpor of the liver
3. Jaundice

Podophyllum peltatum

Ellington lists these key notes for *Podophyllum peltatum* (May apple),[13] many of which you will recognize as signs and symptoms of GBD:

1. This remedy is demanded in inactive conditions of the gastrointestinal tract
2. Heavily coated tongue, thick and broad and pale, with a coat of dirty yellow color, especially at the base
3. Biliousness with inactive liver, sallow skin and conjunctiva, constipation, and highly colored urine
4. Enlargement of the liver with general indisposition, soreness over the liver, and pain through the right side and under the right scapula

For these symptoms, Ellington offers the following formula, warning the reader that it will not taste good[13]:

- *Podophyllum* tincture: ½ dram
- *Leptandra* tincture: ½ dram
- *Capsicum* tincture: 20 minims
- Syrup of licorice: ½ oz
- Port wine, to make 4 oz total

Directions: Take 1 tsp every 2-3 hours

For removal of gallstones, Ellington recommends ½ to 1 grain dose of *Podophyllum*, repeated once or twice, followed by ½ pint of olive oil.[13] He says the results may be painful, but the patient will have subsequent relief.

Fumaria officinalis

Fumaria officinalis (fumitory) is a plant in the Fumariaceae family, which used to be the Papaveraceae family; other useful members of the Fumariaceae family include *Corydalis* (turkey corn) and *Dicentra* (bleeding heart and Dutchman's breeches). All of these herbs work to diminish gallbladder pain.

Here are Felter and Lloyd's key notes for *Fumaria*,[15] which are not so specific about GBD:

1. Used in jaundice
2. Obstruction of the abdominal viscera
3. In cases of debility of the digestive organs

Other Considerations

Herbal formulas for GBD can also include these liver herbs: *Cynara scolymus* (globe artichoke), *Taraxacum officinalis* (dandelion root), *Mahonia* spp (Oregon grape), *Silybum marianum* (milk thistle), and *Arctium lappa* (burdock).

Gemmotherapy

I always like to bring up the gemmotherapy remedies whenever they might be indicated for a condition, as they work to bring drainage to specific organs and systems. In the case of GBD, the most indicated of all gemmo remedies is *Rosmarinus officinalis* (rosemary). *Rosmarinus* is specific for liver and gallbladder drainage, it regulates motility of the gallbladder, and it acts as a cholagogue and choloretic, helping to move bile and stimulate its production, respectively.

Here are some additional gemmo remedies that have been found useful:

- *Fraxinus excelsior* (ash): helps with drainage of liver and kidney; reduces cholesterol
- *Acer campestris* (hedge maple): regulates the saturation of bile with cholesterol, preventing the formation of sand and stones in the gallbladder
- *Prunus amygdalus* (sweet almond): reduces lithiasis in the bile ducts
- *Secale cereale* (rye): supports drainage and decreases inflammation in the liver
- *Corylus avellana* (hazel): helps regulate cholesterol metabolism in the liver
- *Juniperus communis* (juniper): supports liver and kidney drainage

Closing Comments

As gallbladder disease involves a great deal of spastic action, remember to include antispasmodic herbs in your formulas. Ellingwood writes about herbs for pain during the passing of stones, listing *Dioscorea villosa, Hydrastis canadensis, Lobelia inflata, Piscidia erythrina,* and *Podophyllum peltatum*; *Dioscorea* and *Lobelia* are specifically antispasmodic.[13]

One of our brilliant colleagues has formulated an antispasmodic combination that includes *Viburnum opulus*, *Actaea racemosa*, *Petasites*, *Valeriana, Matricaria*, *Mentha piperita*, *Viburnum prunifolium*, *Glycyrrhiza*, and *Atropa belladonna*.[16]

Lastly, keep in mind the emotions related to the liver and gallbladder (per TCM), including anger, irritability, frustration, resentment, jealousy, and envy. Whether you work with Family Constellation Therapy, EMDR, EFT, flower essences, hypnosis, or some other modality when working with your patients, remember to work holistically by also attending to the mental, emotional, and spiritual aspects of gallbladder disease – or any disease, for that matter. It's essential.

References available online at ndnr.com

Robin DiPasquale, ND, RH (AHG), has been practicing in the healing arts for over 30 years. Dr DiPasquale served as faculty at Bastyr University for 15 years where she chaired the Botanical Medicine department, was a clinical supervisor, and taught botanical medicine and homeopathy. After moving to Madison, WI, she opened a family practice, Red Lotus Healing Arts. She was also the first ND to work directly in patient care through the U of WI Integrative Medicine Clinic. Dr DiPasquale now lives and practices in Fort Collins, CO. She has been teaching on-site and on-line courses in Gemmotherapy for over 10 years. Her newest passion is Family Constellation Therapy.

Dyspepsia

SUSSANNA CZERANKO, ND, BBE

There are probably more persons in the world today suffering from indigestion than from any other known ailment. And so long as people eat too much, too fast, and improperly, they will have stomach troubles.

William James Cromie, 1902, p.506

Should you suffer from indigestion, fast awhile and take physical exercise. Eat only when hungry.

Benedict Lust, 1908, p.149

Never eat to satiety. Eat only when hungry, never because it is meal time, or because invited to eat.

John Harvey Kellogg, 1908, p.320

Digestive disorders are on the rise. Functional dyspepsia is widespread – 20% prevalence worldwide – and despite extensive research, "the underlying causes of dyspepsia in a majority of patients remain [elusive and] unknown." (Addula et al, 2018, p.831) Full-blown indigestion in the form of GERD (gastroesophageal reflux disease) is increasing globally. According to the World Health Organization, more than $10 billion was spent on antacids alone in 2017. (Marketwatch, 2018) More money is apparently spent on antacids than on politics in the United States. The significant economic burden due to healthcare costs and constraints on daily activities of patients remains a challenge for those afflicted with indigestion.

While proton-pump inhibitors (PPIs) are the first line of drugs used, the over-reliance on these drugs and their increased unsubstantiated long-term use have become a concern. Importantly, aside from side effects, taking medications has not resolved the inherent problem of indigestion.

A century ago, Edwin Ross noted, "Great industries the world over are kept busy producing 'cures' and the newspapers, magazines and other avenues of publicity are cluttered with their advertisements." (Ross, 1922, p.65) Indigestion is as old as history, and yet despite the well-oiled scientific machinery of the American medical industry, rather than seeing any improvements in dyspepsia, the numbers are escalating.

The early Naturopaths of that era were quick to recognize symptoms of dyspepsia, and treated their patients without drugs. Then, as now, allopathic medicine was often successful at eliminating the symptoms of indigestion while completely overlooking why these very symptoms arose in the first place. The early Naturopaths, on the other hand, studied closely the causes of indigestion; as a result, their treatment plans were multifaceted.

9 Rules to Prevent Indigestion

William James Cromie (Figure 1) was one such Naturopath very interested in indigestion. He was one of Benedict Lust's students, and he specialized in Physical Culture. Cromie published often in Lust's magazine, *The Naturopath and Herald of Health*. In a 1902 article (Cromie, 1902, p.506), he compiled a list of 9 causes of indigestion that included:

1. eating too fast
2. drinking too much fluid
3. mental effort
4. fatigue
5. eating too much
6. sedentary habits
7. tight clothing
8. alcohol
9. irregular eating habits

Eating quickly resulted not only in food being poorly masticated, but also in preventing enzyme production by the salivary glands; this, in turn, resulted in unwanted fermentation in the digestive tract.

Fletcherizing, by Horace Fletcher

The man whose namesake became associated with chewing was Horace Fletcher (Figure 2). He wrote the book, *The A B Z of Our Own Nutrition* (1903), which revolutionized the act of eating. Fletcher declared that "Americans eat too much and unwisely. The result … is a loss of energy and an invitation to disease." (Lust, 1905, p.53) Fletcher observed that when "food [is] properly chewed, there is marked absence of fermentations and putrefactions which are so often present in the alimentary canal, not only in the stomach, giving rise to flatulence, but also in the small intestine, particularly in the colon, resulting in the formation of poisonous substances which thin the blood and permeate the tissues, interfering with all the vital functions, giving rise to a variety of chronic diseases." (Lust, 1905, p.56) The multitude of chronic diseases listed by Fletcher continue to plague society.

Fletcher differentiated between cravings and hunger. He emphasized that one "be sure he or she is really hungry and not pampering a false appetite." (Lust, 1905 p.54) Fletcherism entailed chewing one's food until it is virtually liquefied, and then swallowing. This practice became common and was adopted by Naturopaths, persisting long after Fletcher's book retreated into the shadows. John Kellogg also instructed patients to chew their food well. He wrote, "Chew every morsel until reduced to liquid in the mouth … thorough chewing develops *appetite juices* [hydrochloric acid] in the stomach." (Kellogg, 1908, p.321)

J. Devereux summarizes the importance of mastication and saliva: "To those suffering from acidity and flatulence, denoting forms of indigestion or dyspepsia, it should be carefully noted that the natural antacid is the alkaline saliva." (Devereux, 1926, p.327) Thorough mastication creates the conditions for the correct balance of gastric juices, thus preventing indigestion.

After eating a meal, Cromie recommended giving the brain a rest so that blood is available for the stomach to digest. "There is not enough blood in the body to supply muscles, mind and stomach, or any of the two organs at the same time." (Cromie, 1902, p.507) Orison Marden adds,

Many intelligent people do not know that the reason for being so sleepy and dull after a hearty meal is because Nature has sent just as much blood as possible to the digestive organs, and the brain is left without stimulation. Nature makes it difficult for us to work right after a meal by withdrawing from the brain the blood, which supplies the thinking forces. (Marden, 1915, p.177)

Naturopaths would counsel patients to sit down to eat, focus on chewing their food thoroughly, and on being patient and aware of the digestive process.

Drinking too fast and consuming too much fluid during meals reduces the amount of saliva to mix with foods and drink, and also leads to fermentation. J. Neff described drinking during meals as "one of worst acts of gluttony." (Neff, 1911, p.181) He writes, "When you drink at meals, you wash the food down long before it is chewed finely enough, or before it has received half of the saliva needed to prepare the food for the gastric operation [of digestion]." (Neff, 1911, p.181) The presence of saliva in the mouth determines the secretion of gastric juices to be produced in the stomach. Harris Luntz writes, "Digestion, as we all know, begins in the mouth, that of mixing the food with saliva." (Luntz, 1921, p.94) Mastication increases the flow of saliva and enzymes, which "stimulates the flow of the acidic stomach juices." (Luntz, 1921, p.94) Cromie continues: "Too much liquid taken at meal time tends to dilute the gastric juice and thus weakens its power in the process of digestion." (Cromie, 1902, p.507) On the other hand, J. Neff counseled against any drinking of liquids during meals. He wrote, "Never, never drink a drop of any liquid at meals. … It only prevents digestion and causes ill health." (Neff, 1911, p.381)

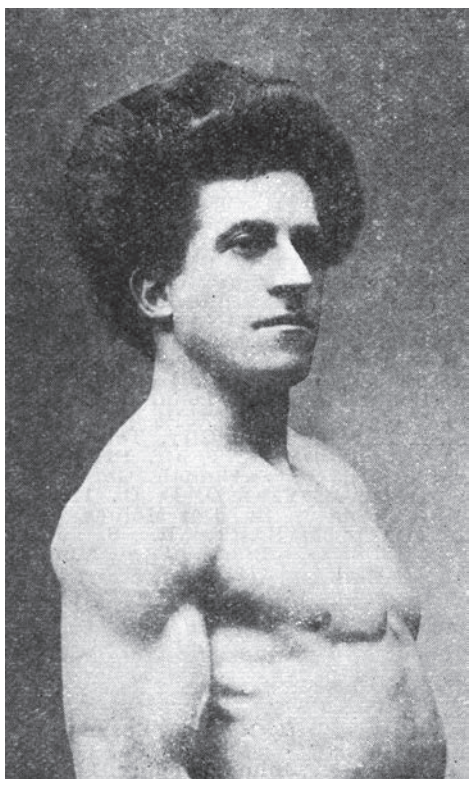
"Nervous dyspepsia" was common and seen as a diagnostic category of its own. People who were seen as nervous or suffering from "neurasthenia," or what we today call stress, would be prone to dyspepsia. "Mental exertion, haste of our busy life, mental disturbances of all kinds, such as anger, sorrow, the constant fear of the future and all sorts of excesses may bring about nervous diseases," leading to dyspepsia. (Lust, 1900, p.38)

When stressed or exhausted, eating should be postponed until a feeling of repose returns. When agitated, digestive processes are impaired, the early Naturopaths contended, and gastric secretions thus decrease. Emotions such as "worry, fear, anger, discontent, jealousy, malice," (Cromie, 1902, p.507) also contributed to dyspepsia. These same naturopathic pioneers also felt that digestion began in the brain. We only need to say "lemon juice" to feel the salivary glands activated, they would declare.

Figure 1. **William James Cromie**

Cromie was Physical Director of the YMCA, in Easton, PA

Figure 2. **Horace Fletcher (1849-1919)**



Eating when emotionally charged or stressed is a sure recipe for indigestion.

Evils of Overeating

Excessive consumption of food not only leads to weight problems; it is also reasonable to conclude that there is a limit to the amount of digestive fluids our bodies can produce so that food can be digested. The digestive fluids must permeate the contents of the stomach to complete the digestive process; otherwise, the "parts of the mass which are not digested will soon decompose, producing acidity and a pressure of gas." (Cromie, 1902, p.507) Lust suggested taking a break from eating: "People who are in the habit of gorging themselves every day should better fast one day in each week and thus give their overworked digestive organs a little rest so that many diseases, beginning with stomach troubles, can be prevented." (Lust, 1901, p.27) Eating too often also contributed to indigestion. In this regard, Lust remarked, "Many diseases are caused by eating a second meal before the first has been fully digested." (Lust, 1905, p.271)

Cromie made his living teaching people to exercise. He counseled that when people adopt a sedentary lifestyle, peristalsis also follows suit. "General exercise is effective in the cure of indigestion as it increases the circulation of the blood and this in turn stimulates the stomach, and … all [organs]. (Cromie, 1902, p.509) Luntz adds, "Most of us suffer from lack of exercise. We sit in chairs and work with our heads. Nature made our body for muscular work." (Luntz, 1921, p.95) Accordingly, Luntz included poor posture as a factor in poor digestion. He summarizes many of the previous causes of indigestion identified by Cromie:

> *Habit comes in as another important point in digestion. By habit, I mean, how we dress, how we walk, how we breathe, the amount of exercise we take, and generally our amount of willpower and poise. (Luntz, 1921, p.94)*

Alcohol was on Cromie's list of digestive culprits because alcohol caused inflammation and ulceration … and changed the gastric fluids. Alcohol was often lumped together with spices and condiments such as pepper, catsup, and mustard. (Cromie, 1902, p.508; Kellogg, 1908, p.320) John Harvey Kellogg, the famous Hydrotherapist of Battle Creek, counseled against condiments as well, including sugar, which he considered very irritating for the digestive tract, causing indigestion. (Kellogg, 1908, p.320)

Medications

The effects of medications upon the digestive tract were also recognized by the early Naturopaths. Benedict Lust writes, "In our increasingly degenerated conditions, the sins of the fathers are visited on the children more often than ever." (Lust, 1901, p.298) Vincent Priessnitz, in his lifetime, had successfully treated a multitude of patients who were ravaged by the golden standard of care used by doctors of his day. The medical doctor would have relied upon calomel, considered as the very best that medicine offered to sick people. Patients, invariably heavily dosed with mercury or calomel, sought out Priessnitz and others using hydrotherapy. Cold water cured these patients, not only of their mercury toxicity but also of their original diseases.

Lust writes, "Father Kneipp … could distinctly trace in children that their father had been treated for a length of time with mercury, and had still in his system the poisoned blood which had naturally been transmitted to the poor innocent offspring." (Lust, 1901, p.298) These early hydrotherapists recognized that offspring from parents treated with mercury inherited poor digestive organs.

Symptoms

Patients suffering from nervous dyspepsia had a variety of symptoms that included "bad taste in the mouth, gaping, belching of wind, and sometimes intense pain." (Lust, 1900, p.38) The presence of gas or bloating did not come immediately after a meal but "often appeared one-half or three-quarters of an hour later; … with others, they occur upon an empty stomach." (Lust, 1900, p.38)

Dietary Counsel

Lust commented that "the treatment of nervous dyspepsia should never be a mere dietetic one, but must be directed more at the improvement and strengthening of the whole organism and especially the nervous system of the patient." (Lust, 1900, p.38) He emphasized individualized dietary recommendations tailored to the conditions of each patient. (Lust, 1907, p.290) Those with nervous dyspepsia "should live on a light vegetarian diet, the use of butter and eggs is also permitted." (Lust, 1907, p.289)

Lust considered rice an easily digestible food, requiring only 1 hour to digest, unlike other foods that required hours. Shorter digestion times allowed the stomach to have a rest. (Lust, 1905, p.271)

The early Naturopaths knew about food combinations too. Morgan writes, "Some fruits have acids that hinder the digestion of starch." (Morgan, 1901, p.305) Another early Naturopath, Eugene Christian, was an important author of books and home courses on diet. He comments, "About 90% of all human disease originates in the stomach caused by errors in eating." (Christian, 1912, p.6) He believed that people should "know how to select [and combine] food that would remove causes of indigestion and constipation." (Christian, 1912, p.7)

Many of the Naturopaths spoke about the merits of a vegetarian diet for indigestion. Louisa Lust herself published a cookbook that became a valuable source book for those initiating into vegetarianism. She writes, "Such vegetarians should remember that the secret of physical health lies just as much in discarding sugared beverages and starchy, devitalized foods as in leaving out the meat." (Lust, 1921, p.323) Continuing, she adds,

> *Green and root vegetables are antiseptic. They neutralize poisons and toxins as well as stop gaseous fermentation and eradicate poisons from the walls of the bowels. Any treatment for indigestion must be directed toward cleansing the stomach and bowels of their poisonous accumulations. (Lust, 1921, p.323)*

In her view, adopting a healthy vegetarian diet was the ticket to heal indigestion.

Fiber

Naturopaths also emphasized the inclusion of fiber or cellulose in the diet to counter indigestion and its sequela, constipation, that often accompanied indigestion. Fiber was recognized as one of the constituents of foods that stimulated "proper peristaltic activity." (Ross, 1922, p.65) Foods that contained fiber included "apples, oranges, lettuce, celery, spinach, etc., [and] are in reality far superior to concentrated foods such as grains, cereals, beans, peas, lentils, eggs, cheese, meats or nuts." (Ross, 1922, p.65) Naturopaths taught their patients that fruits and vegetables contained more water than legumes and helped lubricate the digestive tract.

Water Applications

Cold-water applications had the primary purpose of strengthening the whole body. Special considerations for weak patients included beginning with a washing or affusion, using a small amount of vinegar mixed with water. One part vinegar to 2 parts water was the preferred ratio for vinegar used in bathing. (Lust, 1907, p.290) Patients who suffered from anemia, or chlorosis, especially needed to be warm before and after any cold-water treatment, and these patients were advised to rest in bed until their bodies warmed up. (Lust, 1900, p.39)

Wet wraps were also used as one of the hydrotherapies to begin with. Again, vinegar would be added to the water, which was used to wet the sheets. Lust provides clear instructions on how the wet packs were applied:

> *The wet linen, wrung out well, must cover the whole abdomen. This linen, which must reach around the whole body, must be covered with a woolen cloth to produce the heat necessary to create that beneficial effect which will cure. The packings will stop that painful pressure in the abdomen, remove the gas and help the stool. (Lust, 1900, p.39)*

Once patients were accustomed to these preliminary cold-water treatments, other applications such as gushes, sitz baths, and half-baths were given. A combination of these would be applied 3 or 4 times a week. (Lust, 1900, p.39)

Closing Comments

The Naturopaths understood dyspepsia or indigestion and were successful in not only treating the symptoms but also in teaching their patients preventative measures. In the next issue, we will explore some of the roots of naturopathic thoughts on the theories of nutrition based upon Louis Kuhne (1835-1901).

Excessive consumption of food not only leads to weight problems; it is also reasonable to conclude that there is a limit to the amount of digestive fluids our bodies can produce so that food can be digested.

Sussanna Czeranko ND, BBE, a naturopathic physician licensed in Oregon, has been practicing since 1994. She incorporates nature-cure approaches such as balneotherapy, hydrotherapy, and breathing therapy into her practice. Dr Czeranko is a faculty member and works as the Rare Books Curator at NUNM. She has completed the 11th book in a 12-volume series, *The Hevert Collection*, based upon Benedict Lust's original journals. She is also the founder of the Breathing Academy, which trains NDs in the breathing therapy, Buteyko. She is a founding board member of the International Congress of Naturopathic Medicine. Dr Czeranko has established a traditional naturopathic clinic, *Manitou Waters*, in Manitou Beach, Saskatchewan, which is scheduled to open in August 2019.

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Naturopathic Medical Education

What a Russian Soldier Taught Me About Its Value Proposition

DAVID J. SCHLEICH, PHD

Naturopathic educators toil with the right language and content to describe the value proposition for the medicine for students. In an era of confusing messages flying hither and thither among naturopathic doctors, holistic medical doctors, functional medicine doctors, holistic nurse professionals, and – in recent years – integrative medicine doctors, a calming, guiding framework for action is in order.

I'd like to invite you back to the wild east of former Soviet Russia in 1983, where I found such counsel about value propositions in professional medical education even before I knew I would need to know about such things, and which insight has helped me navigate through today's brave new world of ROI (return on investment) in post-secondary and higher education.

Siberian Mentors

It all began after a midsummer fortnight up at the top end of Lake Baikal in Siberia 35 years ago. There I was in a remote eastern USSR village surrounded by the magnificent hinterland of Siberian taiga (forest), smitten by rhododendrons and wildflowers profuse and cascading down to the shores of that unique, deep, deep lake. And in that village, I was charmed by the robust, resilient people who made their living there. There too were the peculiar and wonderful cries of cuckoo birds, distinct among the meadow pipits, dunnocks, and reed warblers sharing the terrain. In the late afternoon, the bubbly, chuckling calls of the cuckoos didn't fool the locals, like Irene. She lived in one of the larch-built cabins – of mostly a chill jade color – that peppered the slopes descending to the lake.

Irene had rented me a room near the church. She warned me that the cuckoo is clever (in mimicking sparrowhawks), and proffered wisdom about those birds. They are, after all, she said, nest parasites. Know who's doing what and why, she was telling me.

Her pretty little village had an impossible name (see below) that not only Irene, but also an old Russian soldier I met a few days later, challenged me to pronounce properly. Irene had been a fisher's wife in the village for decades. The solider turned out to be a retired history professor at the Irkutsk State Technical University of Siberia. When I met him he was retired from both the military and the university, but now had a volunteer security job at the Irkutsk railhead. I learned that village name with difficulty.

As I passed through Irkutsk, en route slowly back home to North America via Leningrad and Helsinki, I was delayed by a very late train. I was standing at the Mikrorayon Batareynaya station with my backpack, waiting for the decrepit transcontinental Trans-Siberian train, which I could see wending its way westward along the Angara River. It finally arrived 3 hours late on its way to Krasnoyarsk and other points west, such as Krosnoyarsk, Omst, Perm, and eventually Moscow itself. On the platform on that very hot August afternoon, I happened to take up a spot on the crowded platform near a severe, tall, old soldier who suddenly began scolding a group of a dozen cadet pioneers to "priderzhivat'sya vyazaniya" ("stick to the knitting"). Angling for tips among the disembarking travelers, one of the young women in the group played her guitar and sang, surrounded by several of the train workers, performing for the Eastern European and Japanese "intourists" who had descended from the heat of the train during what soon developed into a prolonged delay. It was when one male tourist handed her some money that the soldier barked his admonition. The uniformed boys and girls quickly scurried away to and boarded a white and orange Liaz 5256 bus (that model was all over the Soviet Far East, sometimes in the most unlikely of places). I watched the whole thing uncomfortably. The old soldier sensed my minor chagrin about his officious behavior. He commented in elegant Russian, "They should not be bothering Intourist guests." "But they enjoyed it," I countered, in poor Russian.

It was when one male tourist handed her some money that the soldier barked his admonition.

A Russian Hit Song

The young girl had been singing a popular Latvian hit song, "Million Alyh Roz," or "million red roses," immortalized everywhere that year in the Soviet Union by Alla Pugacheva. I later bought an old Russian equivalent of a 45 record, which I have to this day. In any case, he stared down right into my face, probably surprised

by my awkward Russian, and ready to coach me in pre-perestroika politics.

"Where do you come from, that you are waiting here for a train to go to Moscow?"

"I am from North America. I was in a little town up north."

"Which town?"

I tried my best at the name. He laughed. He then said the name correctly. I imitated his pronunciation, repeated it twice, and later successfully did it again after we had a few hours together. I can say it right even today, but still have to break it down into syllables to make it through: Baykalo-Lenskiy Gosudarstvennyy Priorodnyy Zapovednik.

What he also said, in addition to straightening me out on the village name – and what is most relevant here – has stuck with me for a quarter-century. He said, more or less, pointing at my backpack with its big maple leaf, "My friend, you are a guest in our fatherland Soviet Union. We are in perilous times, and the future lies with our children. They cannot waste time with foolish songs about a million scarlet roses and a lovesick painter. They must stick to the knitting."

"But," I protested, presumptuously, when I should have known better, "should they not be permitted to be young?"

"They are *not* young. Russians cannot be young for more than a moment in this world," he said slowly.

We were still standing on the platform, his assigned post. Many travelers were waiting to hear about the train's likely departure time. Eventually, an announcement from the monstrous loudspeaker over the station next to a huge clock with 3 hands (the third hand always pointing to Moscow time), declared that the train would leave the following day at 2 PM.

We were both standing in the shade of a massive billboard blasting red and green letters to all and sundry about a sprawling monument behind it that honored Russians killed in what the sign proclaimed as "The Great Patriotic War." Every quarter-hour in the time we had been standing there, a phalanx of young students in dark-blue uniforms oddly goosestepped up to the monument to salute its eternal flame.

In those hours we talked about many things: the compromises of the vanguard of the proletariat, my assertions about the impossibility of central planning, awful consumer reports on the Lada, and good ones on Soviet tractors.

The soldier's name was Krispin. He had served many years in the Red Army in the Soviet Far East and had been among the 4 waves of very young Russian soldiers who occupied South Sakhalin and the Kuril Islands in 1945. Early into our conversation, I discovered that he spoke excellent French, which allowed me to abandon my terrible Russian and he, his labored English, and we were away to the races. The lessons came quickly.

"What we value in Soviet Russia is what lasts," he said. "These young pioneers you like can have their songs, but they must stick to what matters," he insisted. Later he repeated these same aphorisms in a pub where we retreated once we knew the train was not going anywhere. I drank tepid Kalinkin pivo and he swilled back long funnels of alcoholic fermented milk, which I did not favor as an afternoon repast. He chomped toothlessly on black bread and natural butter. I kept drinking pivo.

"What matters for them?" I asked him.

"What matters is only what we decide to teach them and only what they decide to learn," he said. The implied transaction was clever. "And if what they learn are pretty songs only," he went on, "that is not enough. They must know where it all came, even the sad painter soldier's lament from the song, and why he and they are where they are this day."

I have remembered that conversation from so long ago, not just because of the exotic, faraway city where it took place, but because Krispin's words stuck and made sense in many contexts. He and I became pen pals (the best one could do back then). We kept up our conversations discretely about many topics over the next 20 years. His country collapsed in 1989 and he went silent for some months. Krispin last wrote me in 1996, the year I first became president of CCNM in Toronto. He understood what naturopathy was and sent me a parcel of information about Russian botanicals and the medical system in Siberia. More than once I have thought about his counsel. I have thought about what value propositions we have for new naturopathic doctors. How have they arrived at where they are?

I think Krispin would have said that our model for naturopathic medical education must assume what matters for health for all people. "So, the doctors of your country do not agree among themselves and they fight about who is the boss of the patient? Is a doctor not a doctor? Why do you have different doctors? What fuss and rattle is that?" he asked me in bold letters in the French language in one of his letters, reacting to a comment I made about naturopathic doctors not being the same as medical doctors in North America. Krispin passed in 1997 at age 92.

Value Proposition in Naturopathic Medical Education

I'm embellishing what Krispin said here, but a Krispin-approved model, had I been able to run it by him, likely would involve 3 simultaneous variables: customer (student or patient) buy-in to the value proposition, a value chain in the delivery of education and licensing, and a realistic revenue formula. He would never have used that language. We are asking a great deal of our ND programs, just as the pre-Gorbachev leaders in the USSR were asking a great deal of the newest generation of "pioneers" in the crazy end-game of the Cold War. Those young Siberians had

never experienced a German invasion or a Stalinist pogrom, and were expected to understand and honor the traditions that preceded them.

Our value propositions might be these:

- A credential that is accredited and valued by a growing community
- A credential that is convenient and fairly priced
- A credential that emphasizes the experience of getting it, and not the course installments or final degree credential
- A credential that the experience of getting motivates lifelong learning and the commitment to solve crucial health problems on the planet
- A credential that leads to work and income every time because it is grounded in the integration of content with real-world experience
- A license that works where the licensee wants to work with what s/he has learned for a long, long time
- A credential recognized and honored by individuals and by third-party payers
- A growing profession on all fronts (numbers of states and provinces, cohorts in training, and clinical and residential venues in which to work)

In a world of integrative medicine, holistic medicine, and functional medicine – variegated forms with a similar core content – the values we attribute to our educational efforts must address what our deans and faculty are dealing with:

- the need for a strong, consensual definition of naturopathic medicine;
- a hotly competitive landscape where detractors have an edge;
- faculty workload and employment model issues;
- credentialing challenges;
- financial models that address student debt; and
- persistent cash flow vulnerabilities

Our students are not only experiencing the confusion of terminology and philosophy in the marketplace, but are also bringing their digital skills and habits into the equation at the same time as many of them continue to demonstrate great respect for the traditions and elders of the profession in a pre-digital age. The "revitalization" efforts at NUNM, SCNM, and Bastyr, and the recent growth of the NMI (Naturopathic Medicine Institute), indicate the persisting interest from what some would depict as a less complex era. Krispin would disagree. He would have said that all eras have their complexities. We know that smartphones, tablet computers, and lightweight laptops in our lecture halls are replete with conflicting messages and data about the location of naturopathic medicine in the healthcare terrain. All eras have their tools, but underlying everything are resilient values.

The ROI our students expect includes learning what Oblinger characterizes as "experiential, socially constructed, and interdisciplinary" (2012, p.14). Furthermore, she contends, "[In the post-course era], our classrooms may no longer be the place where the most significant learning takes place." (2012, p.14) She emphasizes – in a way that reminds me of Irene and Krispin – participation and social connection, however achieved, whether via blogs, wikis, visualizations, digital information, simulations, or MOOCs. Those are not necessarily massive disrupters if they too can convey the traditional into the contemporary and both can propel forward the profession in the volatile terrain of health care and the militant politics of health, not to mention tight timing and cash flow realities.

Sticking to the Knitting

During some breakfasts and evening meals with Irene and her family, and during that delightful afternoon and evening of conversation and feasting with Krispin, along with our many letters over a number of years, I learned how concerned they both were about keeping the values and priorities of the past robust in the face of new challenges and priorities. Krispin, for example, worried that even though his country had emerged after the war as one of the world's 2 great military powers, there was a solemnity and seriousness about the work at hand that was not embraced with the same conviction by the young people around him. I think of our contemporary naturopathic students who don't understand their mission as particularly solemn and serious, tinged as it is with the practicalities of licensing and making a living.

Krispin once wrote to me about the infamous Zhdanovshchina Campaign (think McCarthyism, Soviet style) and how the answer to going forward was not by adopting an adversarial posture, but by focus and hard work that is grounded in shared values. He went on to talk about the days after the war when young people and old people alike squatted on their hams eating discarded vegetable rinds and scraping hopefully on the discarded bones of other people's soups. "We were crafty back then," he said. "We had eyes like the fox." The naturopathic profession is not in starvation mode, but it is in scarcity mode in many jurisdictions.

As we continue to refine our naturopathic programming, adjusting to the complex interprofessional interplay before us means contending with a confused identity, along with a checkered, messy marketplace. We need elders like Krispin and Irene who can remind us about what to value most in our educational product and processes. Our graduates can emerge confident that way, and anchored to a long history of value-added contributions to civil society. Throughout it all, though, Krispin (and Irene too, probably) would insist that we have to stick to the knitting.

David J. Schleich, PhD, is president and CEO of the National University of Natural Medicine (NUNM), former president of Truestar Health, and former CEO and president of CCNM, where he served from 1996 to 2003. Previous posts have included appointments as vice president academic of Niagara College, and administrative and teaching positions at St. Lawrence College, Swinburne University (Australia) and the University of Alberta. His academic credentials have been earned from the University of Western Ontario (BA), the University of Alberta (MA), Queen's University (BEd), and the University of Toronto (PhD).

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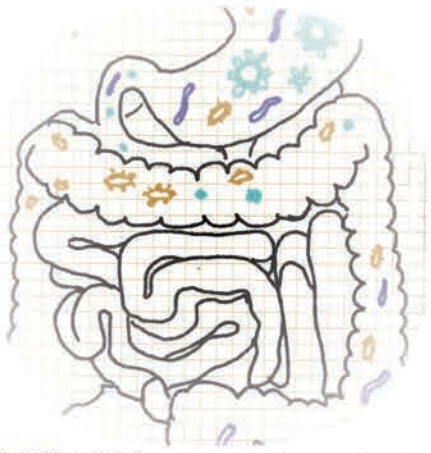
Preventing SIBO Relapse

Utilizing Prokinetic Agents & More In Post-Eradication SIBO Recovery

Dr. Tomah Phillips, ND



While SIBO treatment involves eradication of the bacterial overgrowth and is often followed by a specific diet low in fermentable foods, there is a high rate of recurrence. In order to prevent relapse it is essential to address the root cause.

Impaired MMC – The Main Cause of SIBO Relapse

SIBO often develops following a bout of gastroenteritis (an estimated 7-31% of GI infections will develop SIBO). Many of these bacteria (e.g. C. jejuni, E. coli, Clostridium spp.) can secrete neurotoxins (i.e. CdtB) that impair nerve conduction and through an autoimmune-type process can inactivate the migrating motor complex (MMC). Impaired MMC function is the main underlying cause in development of SIBO, and this issue must be addressed to prevent relapse.

How Does The MMC Work?

The migrating motor complex (MMC) is a cyclic, recurring motility pattern that moves through the stomach and small intestine during fasting states and is interrupted by feeding. Also known as the "housekeeping wave," it sweeps out any undigested food, bacteria and debris from the small intestine. The MMC can be subdivided into four phases, of which phase III is the most active, with a burst of contractions originating from the antrum or duodenum and migrating distally. Phase III activity can be induced by both 'prokinetic' pharmaceuticals and natural agents.

Pharmaceutical Options & Their Potential Side Effects

Low Dose Naltrexone (LDN)

LDN has a good safety profile and can be used to stimulate the MMC; however, it is not without potential side effects. In one survey from a gastroenterologist's clinic involving 121 patients, 48% had one or more neurological complaints, and 26% had one or more gastrointestinal side effects. LDN was terminated owing to side effects in 27.0%. The same report found that in 85 patients with IBS/SIBO treated with LDN, only 17.6% were markedly improved.

Low Dose Erythromycin & Prucalopride

Low dose erythromycin and Tegaserod have been studied for SIBO relapse prevention following antibiotic use, and both significantly increased the number of days before relapse compared to placebo. Prucalopride is also a 5-HT(4) agonist, but with a better safety profile than Tegaserod due to its being highly selective. However, prucalopride can be cost-prohibitive for some patients, and potential side effects include headache and GI symptoms such as abdominal pain, nausea, and diarrhea, especially in diarrhea-dominant SIBO.

Natural prokinetic agents and adjunctive remedies can be a safe and effective alternative to provide a comprehensive approach to preventing SIBO relapse.

Natural Prokinetic Agents

Ginger is well-known for its prokinetic action as it is commonly used to treat nausea, vomiting, and constipation.

It has been shown to modulate serotonin signaling by binding 5-HT(3) (antagonist) and 5-HT(4) (agonist) receptors in the enteric nervous system on top of its cholinergic action on M3 receptors, supporting gastric emptying, intestinal transit, healthy visceral sensation and upper GI comfort.

Ginger has also been shown to significantly increase interdigestive antral motility during phase III of the migrating motor complex in healthy adults, making it a safe and effective natural prokinetic agent.

5-HTP is able to stimulate the MMC through activation of 5-HT(4) receptors. Moreover, 5-HTP is readily absorbed by enterochromaffin cells in the small intestine, in which it is decarboxylated to serotonin to further support gut motility.
However, 5-HTP may cause nausea in some people, partly due to its binding to 5-HT(3) receptors in the stomach (ie. stimulates regurgitation).

Taking ginger with 5-HTP can help alleviate this side effect because ginger, with its antagonistic and agonistic actions on the 5-HTP(3) and 5-HTP(4) respectively, can exert anti-emetic effect while providing additive prokinetic effects.

Natural Adjunctive Agents to Help Prevent SIBO Relapse

Carminatives to Balance PNS & SNS

Digestive function is inhibited by stimulation of the sympathetic nervous system (SNS), which is why chronic stress is often involved in various GI disorders, including IBS and dyspepsia. While SIBO has been identified as one of the major causes of IBS, IBS has long been recognized as a "psychosomatic" disorder where its physical symptoms are closely associated with mental and emotional wellness.

Herbs, such as Cinnamon, Chamomile and Peppermint, are well known for their carminative & anti-spasmodic (ie. modulatory) actions on the enteric smooth muscles. They also exert a significant calming action on the SNS and indirectly up-regulate vagus nerve stimulation to help relieve anxiety and insomnia, and promote digestion and gut motility.

Digestive Tonics to Increase Stomach Acid, Digestive Enzymes, and Bile

Our digestive juices (ie. stomach acid, enzymes, and bile) work together to inhibit the growth of bacteria in the upper GI tract by directly killing them or limiting the availability of nutrients. Utilizing digestive tonics, such as betaine HCl, bitter herbs (eg. gentian, cinnamon), and broad-spectrum digestive enzymes plays an integral part, especially in those with pancreatic insufficiency, in preventing SIBO relapse.

B-Vitamins - Support Neurotransmitter Synthesis & Nerve Regeneration

In addition to stimulating the MMC, supporting nerve conduction and regeneration may be of additional benefit in preventing SIBO relapse.

Incorporating active B-vitamins, such as pyridoxal-5-phosphate (vitamin B6), 5-MTHF, and methyl-B12, can support the synthesis of serotonin and dopamine – two major neurotransmitters in our gut, as well as nerve cell development and integrity.

Tolle Causum

SIBO can be a complex condition that necessitates a multi-faceted treatment approach. While eradication of the bacterial overgrowth is key to improving symptoms, addressing the root cause is fundamental to preventing relapse. **A dysfunctional MMC is most often at the core of SIBO, and natural prokinetic agents are a safe and effective means of improving treatment success and preventing relapse of SIBO.**

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