UW Integrative Health

Department of Family Medicine and Community Health

Digestive Health: Integrative Approaches

Overview

An Integrative Health approach to gastrointestinal (GI) care focuses on the whole person, building on what matters most to each individual and drawing in mindful awareness and selfcare along with conventional and complementary approaches to health and well-being. Whether it is exploring healthy eating patterns, looking at the research related to the connection between the gut and other organ systems, or helping a person with a specific GI diagnosis, Integrative Health can prove beneficial.

Empowerment through self-care is key. The Circle of Health highlights eight areas of self-care: Surroundings; Personal Development; Nutrition; Recharge; Family Friends, & Co-Workers; Spirit & Soul; Mind and Emotions; and Physical Activity. Using an example of an Integrative Health patient, this overview and related tools offer an array of options to consider.

More details for specific conditions, including <u>GERD</u>, <u>irritable bowel syndrome (IBS)</u>, and <u>inflammatory bowel disease (IBD)</u>, are available in various digestive health clinical tools.

Meet the patient

Jake is a 36-year-old police officer who has always had a "sensitive gut." His symptoms "really got bad" after he required a broad-spectrum antibiotic for a pneumonia he was treated for two years ago. He also has a history of asthma, and the combination of poor sleep and a stressful mission took its toll. His asthma worsened, and he developed a secondary lobar pneumonia. He started on 5 days of the antibiotic, azithromycin. After his productive cough continued, he was then given 14 days of Augmentin. He reports that his bowels have never been the same since.

Jake has what many would label as having diarrhea-predominant IBS, with 5-6 watery stools a day, bloating, and diffuse gas pains. Any food seems to make his symptoms worse, particularly beer, which he enjoys drinking with his friends. His diet is rather poor. He eats processed, "white" foods with few vegetables and fruits. He has been using over-the-counter omeprazole with little change in his symptoms. The frequency of diarrhea seems to get worse as he starts to look for a job. He is worried about supporting his wife and young daughter.

Personal Health Inventory

On his Personal Health Inventory (PHI), Jake rates himself 4 out of 5 for his overall physical well-being and a 2 for overall mental and emotional well-being. When asked what matters most to him and why he wants to be healthy, Jake responds: "I want to be able to provide for and support my wife and daughter. I love playing with my daughter. I also enjoy deer hunting. It's not just about filling my tag. Sometimes, it is just sitting in my tree stand, connecting with nature, and having some time to slow down."

Digestive Health Overview University of Wisconsin Integrative Health www.fammed.wisc.edu/integrative

School of Medicine and Public Health UNIVERSITY OF WISCONSIN-MADISON

For the eight areas of self-care, Jake rates himself on where he is and where he would like to be. He decides to first focus on the areas of Nutrition and Mind and Emotions to better control his "broken bowels" and work on his stress levels.

For more information, see <u>Jake's PHI</u>.

Introduction

General Overview: key elements of healthy digestion

- Gastrointestinal Ecology
 - The Gastrointestinal (GI) environment is in a dynamic balance influenced by exposure to bacteria, nutrition, emotions, and medications.
- Intestinal Permeability
 - The integrity of the barrier between the gut and immune system can influence systemic illness and symptoms.
 - Key nutrients, positive emotions, and healthy bacteria can improve the integrity of this vital barrier.
- Adequate Acidity
 - Prolonged acid suppression can result in a decrease in protease activation that may reduce the digestibility of food proteins.
 - Acid is necessary to absorb key nutrients required for a healthy GI ecosystem.
- Establishing the Microbiome
 - Bacteria that populate the GI ecosystem are necessary for optimal GI and immune function.
 - Facilitating an optimal GI ecosystem can result in healthy bacterial growth.
 - Fiber promotes mucus and nutrients that the bacteria need to grow, allowing them to metabolize shortchain fatty acids that help maintain the health of the GI tract.

Gastrointestinal Ecology

Understanding how to facilitate health within the gastrointestinal (GI) system not only requires knowledge of medicine but also an understanding of ecology. The GI system is a dynamic living environment that relies on many interconnected influences to optimize function. In the field of afresh the term Intermediate Disturbance Hypothesis suggests that a small amount of stress to an ecosystem is healthy. It encourages nature to adapt and strengthen its defenses and promotes resiliency. However, too much stress can overpower these defense mechanisms and send the ecosystem into an imbalance of disrepair.

Jake's circumstances are an example of how the stressors he encountered overcame his GI ecosystem's ability to maintain this balance. Our goal is to help bring this dynamic ecosystem back to health.

To understand where to start, we need to review the communication mechanisms that create a healthy barrier between the lumen of the GI tract and the enteric immune system that allows nutrients to enter the circulatory system. The integrity of this system is vital. The enterocytes are covered by mucus and bacteria that are in constant communication with the gut associated

lymphoid tissue (GALT) that not only allows nutrients to pass into the blood stream, but can also influence systemic inflammation and disease.

Intestinal Permeability



Figure 1. Improving Intestinal Permeability.

Figure from University of Wisconsin Integrative Medicine depicting information from Farhadi.¹

Figure 1 shows how a disruption of this barrier can lead to an imbalance of the GI ecosystem. If the integrity of the GI lining is compromised, food proteins can cross and be recognized by the GALT as foreign, resulting in an inflammatory reaction that can lead to GI symptoms, worsening systemic disease, and production of pro-oxidants. This results in a snowball effect that promotes continued disruption of the ecosystem. This is called, "increased intestinal permeability" in the medical literature and "leaky gut" in the lay press.¹ An example of this process can be seen in Celiac Disease and Non-Celiac Gluten Sensitivity. To differentiate between the two, refer to the section below.

Both nutritional and emotional factors can influence whether one develops a "leaky gut." With the perception of stress, mast cells release histamine and serotonin that can encourage breakdown of the intestinal barrier. This is why it is so important to address both physical and emotional aspects of this ecosystem. Thus, in order to enhance the health of this barrier and reduce intestinal permeability, a whole-person approach is key.

Figure 2 compares the elements of an optimal GI environment and one that is unhealthy. It explores factors that positively and negatively affect GI health.

UW Integrative Health Department of Family Medicine and Community Health

School of Medicine and Public Health



Figure 2. Optimal Healing Environment for the GI Tract. Figure from University of Wisconsin Integrative Medicine depicting information from Farhadi.¹

Adequate Acidity

One of the key ingredients for an optimal GI ecosystem is an adequate gastric pH, which should fall in the 1-3 range. Many individuals may have chronic reflux with esophageal changes, placing them at risk of adenocarcinoma and making long-term acid suppression a requirement for them. Many others may inappropriately utilize these medicines to chronically suppress symptoms, which is not necessarily the best option. There are many potential risks to long-term acid suppression. To learn more, read the <u>"Coming off a Proton Pump Inhibitor</u>" Integrative Health handout.

Figure 3 shows how an acidic environment activates pepsinogen to create protease that helps break down proteins. If the pH is too high (greater than 4.5), the protease enzymes are not

activated.² This prevents the body from breaking down the protein into amino acids. If the protein cannot be digested appropriately, it may be recognized by the GI immune system as foreign, triggering an inflammatory response throughout one's body. Some would argue that this might explain the rise in the incidence of inflammatory conditions, such as eosinophilic esophagitis, ^{3, 4} and food protein intolerances. Within five days or less of taking a proton pump inhibitor (PPI) medication, pH will rise to greater than 4.0.⁵

This may also explain why there is a significant intolerance to the cow's milk protein, casein, in many people, and why they often feel better drinking raw milk. When milk is pasteurized, the heating process destroys bacteria and enzymes that help break down the casein protein. Because casein is not broken down, it may be seen by the immune system as a foreign protein and trigger inflammation.⁶



Figure 3. Difference in Protein Breakdown with Different Gastric pH Levels. Image care of David Rakel, MD.

The number of studies showing the potential harm of prolonged acid suppression is growing. Every prescriber of these medicines should be aware of the potential complications of persistent acid suppression.

Every prescriber of proton pump inhibitors (PPIs) should be aware of the potential complications of reducing acid and raising pH long-term.

Digestive Health Overview University of Wisconsin Integrative Health www.fammed.wisc.edu/integrative

School of Medicin <u>and Public He</u>alth

One of the important risks of chronic acid suppression is that it allows bacteria to grow where it should not. Acid suppresses much of the bacterial growth in the small intestine, and small intestinal bacterial overgrowth (SIBO) can result if acid is suppressed long-term.

Ideally, bacteria should populate the large, but not the small, intestine as this can have a significant impact on the health of the individual.

Potential Harms of Chronic Acid Suppression

The following information connects the known complications and mechanism of action associated with chronic acid suppression.⁷

Infection Risk

Community-acquired pneumonia

In a large cohort study, the use of acid suppressive drugs (both H2 blockers and PPIs) was associated with an increased risk of community-acquired pneumonia. This risk translated to one case of pneumonia per 226 patients treated with PPIs and 508 persons treated with H2 blockers. ⁸

Gastroenteritis and community-acquired pneumonia in children

In one study, two months use of ranitidine or omeprazole in children 4-36 months of age resulted in significant increases in gastroenteritis (47% vs. 20%) and community-acquired pneumonia (12% vs. 2%) versus controls. ⁹

C.difficile colitis

In a large population based case-control study, chronic use of histamine receptor antagonists and proton pump inhibitors increased the risk of community-acquired Clostridium difficile infection by 8% vs. 4% and 23% versus 8% respectively compared to controls.¹⁰

Small intestinal bacterial overgrowth (SIBO)

Infectious Risk: This study found that 26% of children treated with at least one month of a PPI had evidence of SIBO by hydrogen breath testing. ¹¹

Malabsorption Risk

Calcium malabsorption/hip fracture

Calcium is a relatively insoluble molecule and tends to bind to fiber. Thus, it needs HCl to dissolve and release it from its fiber carrier. ¹²⁻¹⁵

B12 malabsorption/neurological dysregulation

HCl is needed to release vitamin B12 from its carrier protein so that it can then combine with intrinsic factor to later be absorbed in the terminal ileum.^{16, 17}

Iron malabsorption/anemia

HCl releases non-heme iron from its fiber carrier and then dissolves it. ^{18, 19}

Magnesium malabsorption/cardiac arrhythmia

Long-term use of PPI is associated with greater risk. Magnesium levels can return to normal after one week of stopping PPI. Can cause cardiac arrhythmia, tremor, and seizures if low.²⁰

ool of

Public Health

Establishing the Microbiome

The volume of research on the types of bacteria that populate our bodies is growing quickly. Some types of bacteria are helpful, and others are potentially harmful. When the balance of good and bad bacteria tips toward the unhealthy side, it is called dysbiosis. Probiotics are beneficial bacteria and prebiotics are the food for these bacteria. Perhaps the most important and common prebiotic is fiber. Fiber not only feeds the bacteria, but it also stimulates the production of mucus, which the bacteria need to grow. Other prebiotic foods include those with strong smells, such as garlic, onions, and asparagus. In general, fruits (particularly bananas), whole grains, and vegetables are good prebiotics.

We are finding that the bacteria in our gut have many beneficial functions. Some of these include²¹ the following:

- Influencing the expression of glycoproteins on the surface of enterocytes, which foster communication with other immune cells
- Helping to promote (as does fiber) mucin production, enhancing the mucous layer that lines the GI mucosa
- Aiding in the defense of potentially pathogenic bacteria by the direct release of antimicrobial peptides
- Helping to regulate the release of inflammatory cytokines such as interleukin, tumor necrosis factor and interferon
- Sharing genetic material with the host to facilitate digestion of specific food groups²²

The research on using specific strains of probiotics is growing quickly, and the many benefits found highlight the importance of this synergistic human-microbiome relationship.

Summarized below are some of the more promising clinical studies of probiotics.

Conditions and Probiotics

The following information is a list of conditions that have the strongest evidence in support of using probiotics for prevention and treatment.

Prevention of Upper Respiratory Infection (URI) in children

- Bacteria strains: Lactobacillus acidophilus +/- Bifidobacterium animalis
- Benefits seen with Lactobacilli alone and combined with Bifidobacteria given twice daily for 6 months ²³

Prevention of colic, reflux, and constipation in infants

- Bacteria strains: Lactobacillus reuteri DSM 17938 during the first 3 months of life
- Mean duration of crying time was 38 minutes for probiotic group vs. 71 minutes in placebo group (P < .01)²⁴

Prevention of diarrhea in preschoolers

- Bacteria strains: Lactobacillus reuteri DSM 17938 1 x 108 CFU given daily for 3 months
- Not only reduces the incidence and duration of diarrhea but also reduced the incidence of URI ²⁵

Prevention of atopic dermatitis in infants

- Bacteria strains: Lactobacillus rhamnosus strain GG (Culturelle)
- Benefits seen when this was given to mothers prenatally and then to their offspring for 6 months. The benefit persisted at 4-year follow-up. ²⁶

Ability to store fat

- Bacteria strains: Bacteria from human twins (overweight and normal weight) were transplanted into sterile mice.
- Bacteria from overweight twin caused mice to gain more weight. Eating a high-fiber, lowfat diet negated the effect.²⁷

Irritable bowel syndrome

- Bacteria strains: Bifidobacterium infantis 35624
- The dose of 108 CFU worked best in this study of women. The available data supports Bifidobacteria to be more effective than Lactobacillus at reducing gas and bloating. ^{28, 29}

C. difficile colitis

- Bacteria strains: Donor stool infusion
- Significant benefits have resulted in this becoming the therapy of choice for drugresistant cases. ³⁰
- Single-strain probiotic (no clear species recommended); >50% reduction in colitis in hospitalized individuals when started within 2 days of antibiotics.³¹

Some of the best research regarding the benefit of probiotics has been conducted with infants and children. The environment and types of bacteria the newborn is exposed to is important. Once their microbiome is established, it may be difficult to alter.³² While a baby is *in utero*, it has a sterile intestine. At the time of delivery, the baby is exposed to bacteria as it travels through the birth canal (mainly *Lactobacilli*) and with breast-feeding and skin contact with the mother (mainly *Bifidobacteria*). The type of bacteria the baby is exposed to is different if he/she is born by cesarean section or bottle-fed.³³ Also, if a mother is group B *Streptococcus* (GBS) positive, she will receive peripartum antibiotics that change the vaginal bacterial growth. There are some early findings suggesting that birth via cesarean section is associated with a higher incidence of cow's milk allergy and atopy,³⁴⁻³⁶ although the data is conflicting.³⁷

While the mode of delivery and breast- versus bottle-feeding influences the unique microbiome early in life, the type of diet one eats has the biggest effect later in life. Eating a low-fat, high-fiber diet rich in vegetables and fruit is associated with more diversity of the human microbiome.³⁸ Eating a high-fiber, plant-based diet has also been associated with a higher growth of *Bacteroidetes* and *Bifidobacteria*. These bacteria reduce the efficiency of energy absorption in the gut and are associated with less obesity.^{39, 40}

Gut bacteria use soluble fiber (the type that absorbs water) to produce short-chain fatty acids (SCFAs) through fermentation. One of these SCFAs, butyrate, is the main source of energy for colonocytes. Colonocytes need SCFAs to repair themselves and reduce inflammation. The SCFAs acetate, propionate, and n-butyrate, can be measured in stool tests (<u>comprehensive</u> <u>diagnostic stool analysis</u>) to assess the amount of bacterial fermentation. Adequate production

of SCFAs has been associated with reduced risk of inflammatory bowel disease and colon cancer.⁴¹ Some clinicians use butyric acid enemas to treat ulcerative colitis. Both overuse of antibiotics and poor nutrition (including a low-fiber diet) can reduce the levels of SCFAs in the colon, because both reduce the healthy fermentation that normally occurs due to the interactions of fiber, food, and the microbiome.

Fermentation from fiber and gut bacteria produces short-chain fatty acids that help repair the gut lining and reduce inflammation.

To see if this intestinal fermentation can influence conditions beyond the colon, Trompette and colleagues showed that when mice were fed a high- vs. low-fiber diet, the high-fiber group produced more SCFAs. These SCFAs were associated with less inflammation and airway hyper-reactivity in the lungs when compared to the low-fiber group. The high-fiber diet also resulted in the growth of bacteria in the *Clostridium* genus, and they produced more SCFAs. In summary, fiber in the diet not only reduced inflammation and mucus in the lungs, but also promoted the growth of bacteria that were more likely to produce these anti-inflammatory effects.^{42, 43} For more information on probiotics, go to the "Promoting a Healthy Microbiome with Food and Probiotics" handout on the UW Integrative Health Website.

Summary

As indicated by reviews cited above, research data supports the fact that the GI tract has many influences that modulate the balance between health and disease. This balance starts at the time of birth and is influenced throughout the life cycle by nutrition, medications, emotions, and many other components of the Circle of Health.

Let us turn our attention back to Jake's situation and see how we can use the Circle of Health and specific therapeutic strategies to help Jake achieve his health goals.

Self-Care

Physical Activity

Jake feels pretty good about his physical health. We may want to encourage him to maintain his fitness. Activity is one of the most important triggers of regular bowel evacuation.

Movement and aerobic activity are powerful tools that use the autonomic nervous system to improve GI function. Movement helps promote peristalsis while also reducing emotional stress, allowing the parasympathetic nervous system to have a greater influence than the sympathetic nervous system. Most GI function works optimally when parasympathetic tone predominates. The fight or flight process (sympathetic stimulation) reduces blood supply to the gut. This reduces pancreatic enzyme secretion, which inhibits adequate digestion. This is why eating on the run or eating while under stress can cause havoc on digestive function. Stress also increases cortisol, a steroid that causes the body to store energy as fat.

Mild intensity physical exercise has been found to increase gas clearance and reduce bloating.⁴⁴ Women who are more physically active tend to have fewer and less-severe IBS symptoms.⁴⁵ One small randomized controlled trial (RCT) showed that increasing physical activity had symptomatic benefits in those with constipation-predominant IBS.⁴⁶ Regular

School of Medicin and Public Health

exercise helps reduce symptoms of gastroesophageal reflux disease, but vigorous exercise may worsen symptoms.⁴⁷ Despite these demonstrated benefits of exercise on GI symptoms, research does not support alternative exercise recommendations for those with IBS versus the general population.

With Jake's frequent loose stools, we would recommend that he maintain his current exercise and movement program, without increasing activity at this time, as this may promote more peristalsis, increasing his stool frequency.

Nutrition

Jake does not have much fiber in his diet. He reports eating lots of "white foods," and he has noticed that beer seems to exacerbate his symptoms.

The first-line approach to Jake's diet should be to optimize his adherence to guidelines for general, healthy eating. Given that most Americans do not adhere to general dietary guidelines, these recommendations should serve as a starting point. Further, those with IBS may be particularly sensitive to excessive consumption of alcohol, spicy foods, caffeine, and dietary fat, and inadequate consumption of hydrating fluids.⁴⁸

In determining if a food group could be exacerbating symptoms, we often ask if there are any foods that a person craves or eats frequently. It is thought that increased intestinal permeability might allow the foods we crave the most to cross the gut barrier and stimulate enteric endorphins; this may actually cause one to crave the very foods that may be triggering symptoms. Jake likes "white foods" such as bread and pasta. He also feels that his diarrhea is worse when he drinks beer. Both white foods and beer are rich in gluten. It is possible that the long course of antibiotics he required disrupted the integrity of his intestinal barrier, making his gut immune system sensitive to gluten. In other words, he may have non-celiac gluten sensitivity, which is different than having celiac disease.

Since celiac disease (CD) has long-term health consequences (GI malignancy, osteoporosis, etc.), it is important to accurately diagnose this condition. Many people with non-celiac gluten sensitivity (NCGS) receive the diagnosis of CD inappropriately. CD requires strict gluten restriction, while people with NCGS often do fine if they keep gluten load to a minimum while taking measures to improve their GI health. They can titrate the amount of gluten they eat based on the severity of their symptoms.

Celiac Disease and Non-Celiac Gluten Sensitivity

Celiac disease (CD) presents differently than non-celiac gluten sensitivity (NCGS).^{49, 50} Three main questions help us distinguish CD from NCGS.

- **Question #1.** Are CD serology tests positive? Check tTG IgA (transglutaminase IgA) and DGP (deamidated gliadin peptide antibodies). If positive, CD is likely.
- Question #2. Are there signs and symptoms of malabsorption? These include weight loss, diarrhea, and abnormal nutrient testing indicating low vitamin D, iron, B12 and/or zinc. (Low vitamin D and iron were most predictive for CD). *Note: Take care with*

Digestive Health Overview University of Wisconsin Integrative Health www.fammed.wisc.edu/integrative

School of Medicin <u>and Public H</u>ealth

patients on chronic acid suppression medications, as they can have malabsorption as well.

• **Question #3.** Is there a family history of CD or a personal history of autoimmune disease? (CD is more likely associated with other autoimmune disease).

If all these queries are negative and the patient feels better on a gluten-free diet, he/she has NCGS, and endoscopy with biopsy is unnecessary.

If serology is negative, but questions #2 and/or #3 are positive, order HLA genetic testing. If negative, the patient has NCGS. If positive, order endoscopy with biopsy.

Remember, serology testing needs to be done while a person has been eating gluten. Otherwise, there are risks of falsely negative results. Although recommendations vary, many experts recommend that gluten is eaten for 8 weeks to stimulate antibodies prior to CD testing. If your patient cannot tolerate gluten, consider genetic HLA DQ2/DQ8 genetic testing. If this is negative, the person likely has NCGS. Table 1 for a comparison between CD and NCGS.

Celiac	Non-Celiac Gluten Sensitivity
More diarrhea	More constipation
Presents later in life	Presents earlier in life
Positive serology (tTG IgA, DGP)	Negative serology (tTG IgA, DGP)
Symptoms of malabsorption (weight loss, diarrhea) are more common	Symptoms of malabsorption (weight loss, diarrhea) are less common
Order genetic testing (HLA DQ2/DQ8) if serology is borderline with symptoms of malabsorption. If negative then likely NCGS.	Not needed if serology is negative
Family history	No family history
Other autoimmune disease	No other autoimmune disease
Consider endoscopy and biopsy	Endoscopy and biopsy rarely needed

Table 1. Celiac Disease Versus Non-Celiac Gluten Sensitivity

tTG IgA = transglutaminase IgA

DGP = deamidated gliadin peptide antibody

HLA = human leukocyte antigen (DQ2/DQ8 = chromosome locations)

Note: Genetic Testing (HLA DQ2/DQ8) is positive in 40% of cases. Negative test is most useful to rule out Celiac Disease.

Jake had negative tTG IgA, DGP and no evidence of malabsorption or a history of autoimmune disease. To see if he may have NCGS, you suggest that he consider doing an elimination diet (ED) with a particular focus on gluten. He refrains from eating gluten for 3 weeks to see if his symptoms improve. Using one's own body as a laboratory to test sensitivity to a food protein can be both diagnostic and therapeutic. It is still the gold-standard test for diagnosing food sensitivity. For more information, refer to the "Testing to Assess the Gastrointestinal Ecosystem" Integrative Health tool.

Elimination diets

As reviewed in Figure 1, if there is a food protein that is triggering an inflammatory response through a disrupted intestinal barrier, removing this food can help reduce the intestinal permeability. This is an important part of improving the GI ecosystem. It is important to realize that a food sensitivity is different than an IgE mediated food allergy. A known food allergy must strictly be avoided to prevent a serious allergic reaction. A food that the body has become sensitized (not allergic) to needs to be removed to help the intestinal permeability heal. But once the barrier function and the GI ecosystem improve, it is possible that the body may be able to tolerate this food again.

It is also important not to create a fear of food. The gut-mind, mind-gut connection is so powerful that sometimes when people have such a positive response in symptoms by removing one food group, they can inappropriately attach fear and avoidance to other foods that may not actually be causing an inflammatory response. For example, maybe someone has a fight with a loved one and then eats a tomato, and the result is abdominal cramps and watery diarrhea. The fear that the mind attaches to the food can trigger symptoms that can result in a slippery slope of multiple food intolerances that can result in malnutrition and overall a poor health outcome.

Please refer to the following resources on elimination diets:

- "Elimination Diets" tool
- Chapter on elimination diets, Integrative Medicine 4th Edition, by David Rakel (2017).⁵¹

The FODMaP diet

Jake's fondness for "white foods" suggests that he may also benefit from the FODMaP diet, which is often considered a second-line approach after adhering to general dietary guidance. White foods are rich in bleached white flour, which converts to simple sugars in our digestive system. The FODMaP Diet is an acronym for Fermentable Oligosaccharides, Disaccharides, Monosaccharides and Polyol sugars. These particular sugars are not easily absorbed and thus go through the process of fermentation when exposed to microbes in the gut.

To put this into a context that is easy to understand, think of brewing beer. The combination of a sugar (malt) and a microorganism (yeast) causes the production of gas (fermentation). The same thing can happen in the gut. If our diets consist of an excessive amount of sugar, particularly those types that are difficult to digest, the sugar mixes with bacteria and yeast in the gut and produces a gas that can cause bloating and pain. An excessive amount of these specific sugars in the diet can also encourage the growth of yeast and bacteria that sustains the

Digestive Health Overview University of Wisconsin Integrative Health www.fammed.wisc.edu/integrative

School of Medicin <u>and Public He</u>alth

gaseous process. Foods to avoid in the FODMaP diet have shown to trigger an osmotic fluid shift into the lumen of the intestine, which worsens symptoms in those with diarrhea-predominant IBS.⁵² This may explain the findings in one study where the FODMaP improved symptoms by 50% for both diarrhea and constipation-predominant IBS, but only reduced stool frequency for IBS that was diarrhea-predominant.⁵³ Now that we have a better understanding of the pathophysiology of how certain sugars can worsen GI symptoms, we can treat the symptoms by modifying the diet.



→ Osmotic fluid shift into lumen of intestine → Watery diarrhea

Figure 4. The FODMaP Sugars. Image created by the University of Wisconsin-Madison Integrative Health Program for this document.

These mechanisms also help to explain why some people's GI symptoms significantly improve after taking an antibiotic. The antibiotic reduces the amount of bacteria needed to ferment dietary sugars. However, as discussed above, we need these healthy bacteria for many reasons, and using antibiotics to treat irritable bowel syndrome (IBS) has benefit that may be short-lived. The nonabsorbable antibiotic, Rifaximin, reduced the bacterial growth in the GI tracts of IBS patients by 70%, with a small benefit (10%) over placebo.⁵⁴ A 10-day course costs

about \$600. Since Rifaxamin is only mildly effective relative to placebo, may worsen the GI ecosystem, and is expensive, nutrition is a better initial and long-term therapy.



For more information, go to the "The Low FODMaP Diet" Integrative Health tool.

Figure 5. Summary of GI benefits from FODMaP for 90 patients followed for 15.7 months by de Roest. Reprinted with permission from John Wiley and Sons Ltd. Copyright 2013. ⁵⁵

Modified FODMaP. The FODMaP diet can lead to a significantly lowered intake of fiber from fruits and vegetables, which could lead to micronutrient deficiencies and adversely affect the microbiome. Although it has not been extensively studied, some people may benefit from a "modified FODMaP diet," which allows for continued intake of some higher FODMaP foods. Consider starting by having patients significantly reduce their FODMaP sugar load by avoiding dairy, wheat, rye, high-fructose corn syrup, honey, and polyol sugars. If this does not work, one can consider doing the full FODMaP diet.

Fiber

Regular consumption of fiber is a foundational nutritional requirement for optimal gastrointestinal health. Soluble fiber is a source of nutrition for the gut microbiome and also maintains the healthy intestinal mucous layer needed for bacteria to survive and support healthy gut immunity.

Fiber is beneficial for the following reasons:

• Fiber slows the glycemic index of carbohydrates. This is why it is much better to eat an orange in fruit form and not just drink orange juice. The fiber in the whole orange slows the absorption of the sugar within the juice. Slowing the absorption of sugar results in fewer insulin spikes and decreased insulin resistance.

 It inhibits the absorption of cholesterol. Plants are not only rich in fiber but also in plant stanols and sterols—plant cholesterols that humans cannot make. When eaten in plant form, cholesterol absorption is inhibited. Eating a diet that is specifically high in fiber, plant sterols, soy, and nuts has been found to equal the cholesterol-lowering effects of 20 mg of the drug lovastatin.⁵⁶

- Soluble fiber absorbs water and stimulates satiety. One tbsp of soluble fiber (e.g., psyllium or ground flaxseed) placed in 8-10 oz of water and consumed before meals can help with weight loss by filling up the stomach. This not only reduces postprandial sugars and cholesterol absorption, but it also causes a person to eat less during the following meal. Soluble fiber is an ideal therapy for a diabetic who wants to lose weight while lowering cholesterol and blood sugar levels.
- Fiber stimulates peristalsis of the GI tract, reducing constipation and helping with regular evacuation.
- It binds to hormones such as estrogen and helps with their excretion. This may have a beneficial influence on hormone-sensitive cancers (e.g., breast and prostate cancers).⁵⁷
- It provides an excellent source of nutrition for the bacteria in the gut; in other words, it is a prebiotic.
- Fiber stimulates mucus production along the GI tract.

Increasing dietary fiber intake should be considered a recommendation for the health plan of most anyone suffering from GI dysfunction.

Strategies to improve fiber intake. The American Dietetic Association (ADA) recommends eating at least 21-38 grams of fiber each day (varies depending on age and sex). Most people will get this if they eat 6-8 servings of vegetables and fruit daily. The following foods are considered good sources of soluble fiber:

- Oat bran
- Guar gum
- Dried beans and peas
- Apples (with their skins)
- Seaweed-based foods
- Flaxseeds

An important note: "Whole grains" are often considered by consumers to be a fiber surrogate, though the fiber content of whole grains various widely by grain and type of processing.⁵⁸

A good rule of thumb to optimize one's fiber intake is to examine food labels and determine the "total carbohydrate to fiber ratio." A ratio of less than 10 is good, and a ratio of less than 5 is ideal. For example, if a serving of cereal has 20 gm of total carbohydrates and 4 gm of fiber, this ratio is 20/4=5—an excellent choice.

If it is difficult for someone to get enough fiber by eating multicolored whole foods, you can recommend a supplement, such as one of the following:

Digestive Health Overview University of Wisconsin Integrative Health www.fammed.wisc.edu/integrative

School of Medicin <u>and P</u>ublic Health

- **Guar gum.** Dose is 5-10 gm a day or 1/2 tsp in juice or water before each meal 3 times a day. Low-cost guar gum is available online through websites such as Amazon (\$2.50 for 8 oz).
- **Psyllium (Metamucil).** This is available in many forms, including powder, capsules, and wafers. Dose is 1/2 tsp in juice or water before meals or 1 tbsp daily.
- **Ground flaxseed.** Advise patients to buy the seed form of flax, which stores well. They can use a coffee grinder to prepare a week's worth. Store flaxseed in the refrigerator, because once it is ground and the oils are released, it spoils quickly. Dose is 1 tbsp on food twice daily. It works well to sprinkle flaxseed over salads and in smoothies. Flaxseed is a good source of both fiber and omega-3 fatty acids.
- Methylcellulose (Citrucel) (. The dose is 1 tbsp in 8 oz of water or juice 2-3 times daily.
- Oat bran/oatmeal. You might recommend eating a bowl of this with fruit each morning.

Recharge

Jake has a disordered sleep-wake cycle. He reports that he often has trouble falling asleep due to racing thoughts. This disruption in the circadian rhythm is associated with worsening GI symptoms. As with many components of the Circle of Health, the benefits often go both ways. Not only does improving sleep improve GI function, but improving GI health also improves sleep.⁵⁹ A poor sleep-wake cycle triggers inflammatory cytokines that can exacerbate inflammatory bowel disease (IBD) and disrupt GI immunity.⁶⁰

Poor sleep can also result in lower melatonin levels. Melatonin reduces acid reflux by increasing the tone of the lower-esophageal sphincter and reducing acid excretion.^{61, 62} It makes sense that melatonin would have these effects. When we lie horizontally to sleep, reflux is more likely to occur, because gravity is no longer directing acid out of the stomach. Melatonin counteracts this, and it also reduces the intestinal permeability caused by nonsteroidal anti-inflammatory drugs (NSAIDS) in animal models.⁶³ Some individuals who have gastroesophageal reflux disease (GERD) and are bothered by symptoms when they are supine may benefit from a low dose (0.5-3 mg) of melatonin at bedtime. For more information on improving the sleep-wake cycle, see the "<u>Recharge</u>" overview.

Spirit and Soul

Hearing a person's unique story and understanding more about what provides meaning and purpose in his or her life is a key part of an Integrative Health approach. This exploration helps us break out of the find-it, fix-it model and redirects our focus toward the fundamental question of why each individual wants their health in the first place. This is relevant for all health conditions, including those of the GI tract. Understanding Mission, Aspiration, Purpose (MAP) — "what matters most"—helps clinicians co-create an optimal treatment plan based on individualized goals and can enhance self-efficacy. Jake wants to be able to support his family—this gives his life meaning. If this fact is not held at the center of his Personal Health Plan, it is unlikely Jake will make the necessary changes to align with this goal.

When patients were asked if they felt their physician should ask about their spiritual health, 83% answered yes.⁶⁴ Among those who wanted to discuss spirituality, the most important reason for discussion was to enhance physician-patient understanding (87%).⁶⁴ Patients believed that information concerning their spiritual beliefs would favorably affect physicians' ability to

School of Medicin <u>and Public He</u>alth

encourage realistic hope (67%), give medical advice (66%), and positively change medical treatment (62%).⁶⁴

Mind and Emotions

Two studies illustrate the dynamic interaction of the gut ecosystem, mind, and body. A study of women, who were given a probiotic drink and then underwent functional MRI scanning of the brain, showed that the women given the probiotic drink had changes in the parts of the brain that process emotions and sensations. These areas of the brain were not stimulated in the control group who did not consume the probiotic.⁶⁵

A fascinating mouse study involved a probiotic, *Lactobacillus rhamnosus*, and its effects on mouse behavior. Researchers fed one group of mice a broth rich in the probiotic, while another group of mice received broth without it added. The mice given the probiotic broth not only had more explorative activity, but also had less anxiety and fewer signs of depression. Mice from each group were placed in water to elicit a fear of drowning. Mice that were given the probiotic not only were able to swim longer, but they had less anxiety and lower levels of the stress hormone, cortisol. Researchers repeated the same experiment with mice that had severed vagus nerves; the findings were not reproduced.⁶⁶

These studies suggest that the bacteria in our guts may influence emotional behavior and sensation. It would seem that the pathway in which this information is conveyed is through the vagus nerve. The vagus nerve is the super-highway of communication between the mind and the gut, and the gut and the mind. Information flows between the two in both directions. Just as bacteria may be able to influence our mood, our mood can also influence the gut.

Some consider the gut to be the body's "second brain." The intestinal tract actually contains more serotonin than the brain. It has been shown that when the mind perceives stress, the mast cells are activated along the enteric nervous system. They can exacerbate inflammation, worsening intestinal permeability (as noted in Figure 1). A study in rats demonstrates this nicely. One group of rat pups was separated from their mothers after birth. These highly stressed rat pups were found to have significant intestinal permeability as compared to the control group, which were not separated from their mothers. The highly stressed rat pups were fed supplements that included docosahexaenoic acid (DHA, an omega-3 fatty acid), arachidonic acid (ARA, fat found in breast milk), fructooligosaccharides (a prebiotic) and the probiotic lactobacillus. When the stressed rats were given these supplements, their intestinal permeability healed.⁶⁷

As is common in the culture of medicine, we often want to focus on the magic "fix" that comes from outside the living being, giving less attention to self-healing that comes from within. It might be tempting to focus on the supplements needed to help the gut barrier heal, forgetting that putting the rat pups back with the mothers facilitates healing from within without the need for the external "fix."

Ideally, when able, it is best to recruit the self-healing mechanisms of the body. It is also important to have tools to help move it along in the healing direction. One tool worth exploring involves metaphor, discussed under the Therapeutic Disclosure section that follows.

Therapeutic disclosure. We have two ears and one mouth, to be used in that proportion. Our empathic listening is likely one of our most-effective therapeutic tools.

Watch for nonverbal cues. During a visit with a patient, watching for nonverbal clues (such as welling up of the eyes), allows us to understand how gentle questioning may help someone discuss what truly matters to them.

Listen for metaphor "It's eating me up inside." "She is breaking my heart." Listening for metaphor in a patient's story can be a helpful. A memorable patient with proctalgia fugax (painful rectal spasms) once stated, "My boss is a pain in the ass." After this stressor was explored and brought into her conscious awareness, her pain resolved without the need for medications. Medications would only have treated the symptom, not its cause.

Metaphor can help us understand the relationship between the mind and the body. Lord Chesterfield said, "I find, by experience, that the mind and the body are more than married, for they are most intimately united; and when one suffers, the other sympathizes."

Getting something "off your chest" encourages disclosure of information that the body must work hard to keep suppressed. This work on the part of the body is thought to cause dysregulation of the autonomic nervous system (ANS) and the hypothalamic-pituitary axis (HPA), leading to elevated cortisol and immune suppression.⁶⁸ James Pennebaker, a leading researcher in this area, demonstrated this by monitoring the physiologic effects of disclosure in individuals connected to polygraphs. Once a person confessed to something he or she did wrong, the ANS returned to a more balanced state, with a reduction in heart rate, blood pressure, skin conductance, and respiratory rate.⁶⁹

Consider recommending journaling. Writing about emotional events is often referred to as journaling (summary of science for expressive writing therapy), and the process of expressing weighted emotions as disclosure. Many of the studies on journaling divide study participants into three groups. One group writes about an emotionally charged event, one writes about trivial topics (such as time management), and the third is the control group, who do not write at all. No study has found benefit to writing about time management. In contrast, writing about emotionally charged events has been found to do the following:

- Speed wound healing⁷⁰
- Improve lung function in asthmatics by 20%,⁷¹ and improve functional disability in adolescents with asthma⁷²
- Improve disease severity (inflammation) by 28% in people with rheumatoid arthritis⁷¹
- Improve memory function with less intrusive thoughts in college students⁷³
- Reduce number of visits to the infirmary in inmates of a psychiatric prison⁷⁴
- Improve marital satisfaction ⁷⁵
- Increase rates of smoking cessation in young adult smokers⁷⁶
- Reduce physical symptoms and number of cancer-related medical visits in women with breast cancer⁷⁷

No one has to read what is written. The therapeutic benefit comes from expressing the emotions in a way that enhances a sense of control and understanding. A patient can even consider

burning the writings and letting the wind carry the ashes away to add ceremony and closure to the process.

Researchers have started to analyze what it is about journaling that is most strongly associated with improved health. ⁷⁸ Key ingredients were threefold:

- 1. The writing tells a story with a beginning, middle, and end.
- 2. In creating the story, the writer develops insight into how the event influenced their life and uses words such as realize and understand. The writing demonstrates a sense of optimism with the use of more positive words.
- The writing changes to reflect less social isolation. As the story evolves, there is a change in the use of pronouns from first person singular (me, I) to second person pleural (we, us).

Key Healing Influences in Writing about Emotional Events

- Creation of insight
- Development of optimism
- Sense of community (feeling part of a larger whole)

Precautions. As with many therapies that have beneficial effects, there are precautions to remember with therapeutic disclosure. The body often keeps emotions repressed for a reason. If they are brought out when the individual is not yet ready to deal with them, the process can backfire. In working with Veterans, who have a high prevalence of PTSD, it is particularly important to keep this in mind.

Following are some points to keep in mind when exploring emotional stressors:

- Disclosure of past emotional events is most likely to occur within a trusting relationship. It is important to offer support for further processing if needed. Collaboration with a licensed counselor or therapist is beneficial.
- If the individual is not ready to discuss or write about emotional events, do not push.
- Be careful not to allow past events to create guilt. There is no evidence to support the often-misguided belief that past stressful events themselves cause disease. It is the individual's *reaction* to an event that plays a role, and guilt only exacerbates the problem.

Clinical Hypnosis

Clinical hypnosis is a method of deliberately using verbal cues to induce an altered state of awareness for a targeted therapeutic indication. These verbal cues can enhance relaxation, the ability to generate imagery, and focus. Evidence supports the use of either Gut-Directed Hypnotherapy (GDH) or audiotape hypnotherapy, and one trial found these to be equally effective for IBS with response rates of 50%-75%.⁷⁹ GDH is more resource-intensive than a self-directed audiotape, requiring 8-12 sessions that are ½-to 1-hour long. Several studies showed that clinical hypnosis seems to have consistent positive effects on IBS, with an estimated 25%-73% improvement in bowel symptoms, psychological distress, and quality of life that lasted over a year after treatment was completed.⁸⁰⁻⁸² In refractory cases referred to a GI clinic, an uncontrolled prospective study of 204 individuals found that 81% received benefit; 71% of these

continued to have benefits 5 years later.⁸³ Although larger randomized trials need to be done to verify the effectiveness of clinical hypnosis, its safety and potential benefit makes it a worthwhile therapeutic option. It also remains unclear how this intervention compares to other interventions.

For self-guided hypnosis audio resources, go the <u>Health Journeys</u> website. For a copy of a script you can use for yourself or with patients to ease abdominal pain, see the "<u>Balloon Self-Hypnosis Technique for IBS and Abdominal Pain: A Guide for Clinicians</u>" tool.

Cognitive behavioral therapy

Cognitive Behavioral Therapy (CBT) focuses on identifying behaviors and thought patterns, as well as negative emotions that hinder progress toward one's self-defined goals. This mind-body modality has the most robust evidence base for improvements in function. ^{84, 85} Some data suggests that online delivery may be as effective as live delivery, which may allow systems to greatly expand this often underutilized service. ⁸⁴

Dietary Supplements

A number of nutritional supplements are used to treat GI conditions. They can be categorized as those most useful for the upper GI tract and those most useful for the lower GI tract. This is not an exhaustive list, but it includes those that have the most evidence and historical use supporting benefit.

Note: Supplements are not regulated with the same degree of oversight as medications, and it is important that clinicians keep this in mind. Products vary greatly in terms of accuracy of labeling, presence of adulterants, and the legitimacy of claims made by the manufacturer.

The Upper GI Tract

Melatonin

If someone has reflux symptoms that get worse upon lying down, melatonin can be a useful tool. Melatonin may promote the secretion of gastric bicarbonate, protect the gut barrier from NSAIDS, and improve the activity of the lower esophageal sphincter by inhibiting nitric oxide.⁶¹⁻⁶³ Given that endogenous melatonin peaks in the evening, this may be one way that one's innate physiology help to minimize gravity-dependent reflux. Supplementing with melatonin may not only help with sleep initiation, but it may be as effective as a low dose PPI in treating GERD. Dose: 3-6 mg, 30-90 minutes before bedtime. ^{86, 87}

Licorice

A demulcent, or mucilaginous, botanical medicine can be used as mucoprotection of the esophageal mucosa, soothing irritated tissues to promote healing. For example, licorice (*Glycyrrhiza glabra*) is a well-known demulcent botanical used for GERD, gastritis, and duodenal and peptic ulcers. For long-term use, it should be prescribed as deglycyrrhizinated licorice (DGL) in order to avoid the side effects of one of its phytochemicals, glycyrrhizin, also called glycyrrhizic acid. The prolonged use of decoctions or infusions of dried, unprocessed licorice root can cause hypertension, hypokalemia, and edema, due to glycyrrhizin's mineralocorticoid effects. The common dosage is 2-4, 380 mg lozenges before meals.^{88, 89}

School of Medicin <u>and P</u>ublic Health

Slippery Elm

Slippery elm (*Ulmus fulva*) root bark powder is another useful demulcent for GERD. Mix 1-2 1-2 tbsp of the powder with a glass of water and take after meals and before bed. Advise patients to carefully titrate the proportions, as the preparation can be very thick and difficult for some people to tolerate; to increase its palatability they can add sugar or honey to sweeten it slightly. Most sources describe this botanical as very safe, though the hydrocolloid fibers may bind simultaneously administered medications and decrease their absorption.⁸⁸

Marshmallow

Marshmallow (*Althea officinalis*) is another mucilaginous herb for GERD symptomatic relief. Its demulcent properties also make it useful for pharyngitis, wound healing, cough, and bronchitis. The dose is 5-6 gm (about 2-3 tbsp) daily, in divided doses, as an infusion of the leaves or root. As with slippery elm, there may be a decrease in absorption of orally administered drugs taken simultaneously with marshmallow.⁸⁸

Chamomile

Chamomile (*Matricaria recituta*) is well-known for its mild sedative actions and for its antispasmodic effects on the GI tract. In GERD, it is used as a non-demulcent anti-inflammatory. Chamomile is most commonly used as a hot-water infusion (tea) of 1-3 gm (about 1 tbsp) of the flowers, steeped in a cup covered with a saucer, and taken 3-4 times daily.⁸⁸ Chamomile is generally well-tolerated, though individuals allergic to other plants in the daisy family (Asteraceae) may experience an exacerbation of their allergic symptoms with consumption of chamomile.⁹⁰

Combination botanical products

Iberogast® is a product that includes Clown's mustard, German chamomile, angelica root, caraway, milk thistle, lemon balm, celandine, licorice root, and peppermint leaf. A meta-analysis supported its use in the treatment of dyspepsia, showing a reduction in epigastric pain, cramping, nausea and vomiting compared to placebo.⁹¹ The usual dose is 1 ml, 3 times daily. Usually well tolerated, it may cause nausea, diarrhea, and skin rash in some people.

The lower GI tract

Probiotics

The bacteria within the mucus of the intestinal wall play a key role in the permeability of the tight junctions of the enterocytes. The gut flora interact with toll-like receptors (TLRs) that are the gatekeepers in helping distinguish which antigens are helpful or harmful⁹², and composition of the gut flora directly influences intestinal permeability.⁹³ There is growing data showing a potential therapeutic benefit of probiotics in the treatment of IBS.⁹⁴⁻⁹⁸ The most positive single-species studies for IBS have shown the specific strain *Bifidobacterium infantis* (*B. infantis*) 35624 at a dose of 10⁸ colony-forming units (CFUs) to be the most effective.^{99, 100} However, multispecies probiotics seem to provide superior relief when used for at least 8 weeks and should contain Lactobacillus and at least one of either Streptomyces or Bifidobacterium species.⁹⁷

In one meta-analysis, the number of people who needed to be treated (NNT) with probiotics to have one person experience improvement was found to be as low as four. ¹⁰¹ Probiotics have significant favorable effects on abdominal pain, bloating, and bowel movement difficulty, especially in those with the diarrhea subtype.^{98, 102}

While using probiotics can be helpful, it remains unclear if they provide long-term benefits beyond several months. Some studies suggest that they do not, and other studies suggest that they may possibly worsen symptoms after 3-4 months.¹⁰³ Therefore, using probiotics during times of worsening symptoms, while incorporating other modalities, may be the best approach.

Peppermint

Peppermint is one of the most commonly used supplements for lower abdominal spasms that are common in IBS. Its main active ingredient is menthol, an antispasmodic. It works best to treat spasms that lead to abdominal pain as opposed to treating distention and flatulence. It has also been shown to improve diarrhea, constipation, urgency, and incomplete defecation.¹⁰⁴ One systemic review showed response rates in those using peppermint oil of 79% for abdominal pain, 83% for abdominal distention, and 73% for flatulence.¹⁰⁵ These findings are as good as those for pharmaceuticals—if not better—and peppermint oil has fewer side effects. In fact, the number needed to treat (NNT) is 2-3, making this possibly the single, most effective intervention for IBS.¹⁰⁶

L-glutamine

Glutamine is a nonessential amino acid utilized by rapidly growing cells. The enterocyte lining of the GI tract contains one of the most rapidly reproducing cells of the human body, and depletion of this protein can result in continued disruption of intestinal integrity. Research of L-glutamine has focused on severely ill individuals in the intensive care setting who develop increased intestinal permeability that leads to enteric derived septicemia. The breakdown of the intestinal barrier allows pathogenic bacteria into the blood stream resulting in sepsis.

This can be prevented by supplementing with L-glutamine, which maintains the integrity of the intestinal barrier and reduces the incidence of gut-derived infections.¹⁰⁷ Glutamine appears to have the most benefit when inflammation is present despite the depletion of nutritional stores.¹⁰⁸ It reduces inflammatory cytokine release within the bowel wall¹⁰⁹ and increases heat shock protein, which protects enterocytes from injury.

There is limited research on L-glutamine and IBS, but due to its safe side effect profile, a short course of therapy (5 gm BID for 2 weeks) may prove helpful in those patients suspected to have increased intestinal permeability. Since meat is the key nutritional source for glutamine, vegetarians may be at greater risk for deficiency.

Zinc

There is preliminary human data demonstrating that zinc has benefit in helping preserve intestinal integrity. In a randomized crossover trial, 10 patients were given 37.5 mg of prophylactic zinc to see if this would prevent the loss of intestinal integrity when given the medication indomethacin. There was no loss in intestinal integrity in those given zinc, but there was a three- to fourfold increase in intestinal permeability when zinc was not used. The group

School of Medicin <u>and P</u>ublic Health

treated with zinc also had a 75% reduction in gastric and small bowel injury and 50% less villous shortening.¹¹⁰ In vitro data is also supportive.¹¹¹

Since zinc deficiency is one of the most common mineral deficiencies in the Western diet,¹¹² a short trial of supplementation (20-35 mg daily for 14-30 days) may prove helpful. Zinc is necessary for appropriate immune function of the GALT and is deficient in those with IBS, although this may be secondary to zinc loss from diarrhea.¹¹³

Complementary Approaches

Chinese medicine AND acupuncture

Acupuncture is one of many therapies used within Chinese medicine (CM). It has a history of more than 2,000 years of use. Chinese medicine is a holistic system encompassing acupuncture, herbal medicine, nutrition, meditative practices (qi gong), and movement (tai chi). CM is based on the belief that health is maintained by balancing two opposing forces, yin and yang. Yin is the cold, slow or passive force and yang represents the hot, excited, or active force.¹¹⁴ Yin and yang balance is managed by qi, the body's vital energy source, believed to flow in channels throughout the body. Disease results from an imbalance of yin and yang with resultant blockages in the free flow of qi. The goal of CM modalities is to restore and maintain the balance of yin and yang. Acupuncture stimulates points on the body, usually with needles, altering the flow of qi attempting to achieve this balance. Even though acupuncture represents one piece of CM, it often is practiced as an independent therapy.

For more information, see the "Acupuncture" Integrative Health tool.

Acupuncture can help with pain and peristalsis of the GI tract in those with GERD or IBS.

Acupuncture may have clinical efficacy for GERD based on three possible mechanisms. Acupuncture may stimulate GI motility and decrease acid secretion via the vagus nerve and other parasympathetic pathways. Acupuncture also may increase esophageal sensory thresholds, which decrease in those with GERD. A recent meta-analysis of 12 small, heterogeneous trials showed that acupuncture improves quality of life and decreases recurrence of symptoms, and that the combination of acupuncture plus pharmaceuticals is more effective than either alone.¹¹⁵

Acupuncture may also be more effective than doubling the dose of a PPI in those with persistent symptoms on standard-dose PPIs.¹¹⁶ It can also be helpful for allowing patients to transition off a PPI. Stopping a PPI can lead to rebound hyperacidity. For more information, see the "<u>Coming off a Proton Pump Inhibitor</u>" Integrative Health tool. In the case of IBS, randomized controlled studies have not shown a clear benefit of acupuncture in reducing symptoms or severity or in improving quality of life. However, a few Chinese trials have shown that acupuncture may be more beneficial than antispasmodic medications. It may be that individuals who prefer acupuncture as a treatment modality, or have greater expectations of improvement with acupuncture, will benefit more from acupuncture than medications.^{117, 118} In many studies, quality of life improves in both treatment and sham acupuncture groups. Given that acupuncture

has a favorable benefit-to-risk ratio, it may be worth considering, though cost and accessibility must also be taken into account.¹¹⁹

Personal Health Plan

After going through the Personal Health Inventory (PHI), Jake was able to self-reflect on the areas that he feels are the most important to work on for his long-term health. He realized that he was not where he wanted to be with his personal development and emotional and nutritional health. The process of going through the PHI helped trigger insight, which aided in the facilitation of a personalized, proactive, patient-driven therapeutic process. It also helped him see that family support and his spiritual life are important for supporting his mission toward health.

Jake's main goal is to find a job to support his family. Assisting him with that will help reduce the stress that can exacerbate GI symptoms. He will be referred to a PACT social worker who can connect him with vocational resources, such as a counselor to help him identify his vocational interests and strengths, workshops on skill building and networking, resume-writing resources, a job-hunting support group, and/or sources of job-postings.

In taking Jake's nutritional history, it became evident that he enjoys a lot of "white food," such as breads and pasta. He also notices that his symptoms worsen when he drinks beer. All these foods are rich in gluten, which could be triggering sensitivity along his GI lining. After a trial of meeting basic healthy eating guidelines (with a focus on fiber), he can be encouraged to do an elimination diet, staying off gluten for two weeks to see if this reduces the frequency of his stools. For more information on how to use this tool, check out the "Elimination Diets Integrative Health tool.

If an elimination diet proves helpful, Jake would have two possible courses of action. Some clinicians might choose to challenge him again with gluten to see if his symptoms worsen again, while other clinicians might have him stay off the gluten for 3-4 months as he works on improving the health of his GI ecosystem. Ideally, once intestinal permeability improves, he could slowly start eating small amounts of foods containing gluten again. If he has no benefit from the elimination diet, trying the FODMaP diet could help reduce his symptoms.

To improve the GI environment, an Integrative Whole Health strategy would include the following recommendations.

Personal Development

Connect Jake to resources that may increase his likelihood of finding rewarding work and that will provide support throughout the job-seeking process. This will help reduce his stress and fear about not being able to provide for his family.

Nutrition

• Encourage Jake to meet with a nutritionist to improve his nutrition. He should be encouraged to include more vegetables, fruits and fiber. He should also be introduced to fermented foods (yogurt, sauerkraut, miso, tempeh, kefir) which can increase beneficial gut bacteria.

- Supplement with a soluble fiber, such as psyllium or guar gum: 1 tbsp in 6-8 oz of water daily. Using a soluble fiber with less water (6 oz instead of 12 oz) can reduce stool transit time, reducing the frequency of stools.
- Supplement with a probiotic of 10⁸ CFUs that contains both lactobacillus and bifidobacteria. Take both probiotics for 8 weeks.
- Make sure Jake is getting good sources of omega-3 fatty acids in his diet (fish, nuts, fruits), zinc (green leafy vegetables, peanuts, eggs), and glutamine (meat). If he doesn't get enough of these through his diet, consider supplementing with 1,000 mg of EPA and DHA essential fatty acids in the form of fish oil, L-glutamine (5 gm daily), and zinc (20-30 mg daily) for 4 weeks.

Mind and Emotions

Refer Jake to the team's psychologist, who will first explore the stressors of his experience as a police officer through CBT. Then, explore other therapies that can recruit the mind as a therapeutic ally. These may include journaling, Guided Imagery, and/or Gut-Directed Hypnotherapy.

Personal Health Plan

Name: Jake

Meaning, Aspiration, Purpose (MAP):

Provide for and support my wife and daughter.

My Goals:

In order to be able to support my family, I will work toward improving my overall health. In order to get my GI tract back into balance, I would like to start with the following items:

- Meet with a social worker who can direct me to vocational resources that may increase the likelihood of finding rewarding work and that will provide support throughout the jobseeking process.
- Do a 3-week elimination diet off gluten.
- Meet with a psychologist to develop tools to reduce stress.

Mindful Awareness:

Mindful Awareness Sleep Induction Technique:

- Begin with abdominal breathing
 - Place one hand on chest and the other on abdomen. When taking a deep breath, the hand on the abdomen should rise higher than the one on the chest. This ensures that the diaphragm is expanding, pulling air into the bases of the lungs. Take a slow deep breath in through the nose for a count of 3-4 and exhale slowly through the mouth for a count of 6-7 (exhalation should be twice as long as inhalation.).This stimulates the vagus nerve, which increases the "relaxation response."
 - Clear the mind and focus on counting or breathing as the air gently enters and leaves the nose and mouth.

Digestive Health Overview University of Wisconsin Integrative Health www.fammed.wisc.edu/integrative

School of Medicin <u>and P</u>ublic Health



- o If the mind wanders, gently bring the attention back to the breathing.
- Repeat the cycle for an 8 breath cycles.
- After 8 breaths, change body position and repeat 8 breaths
 - After each 8 breath cycle, change body position in bed and repeat another 8 breaths.
 - It is rare to complete 4 cycles of breathing and position changes before falling asleep.

Areas of Self-Care:

- Nutrition
 - Start the 3-week elimination diet to remove gluten. Meet with a nutritionist to discuss other aspects of healthy eating, dietary goals, and its importance to my long-term health.
- Recharge
 - Work with a psychologist to learn tools to help quiet the clutter of thoughts and make it easier to fall asleep. The mindful awareness sleep-induction technique (described earlier in this plan) may be helpful.
- Personal Development
 - Do some additional training for my work.
- Spirit and Soul
 - I am lucky to have the support of my family and faith. It was my spiritual connection that got me through some tough times in my life. I'd like to keep growing this connection and as a foundation for my health.

Professional Care: Conventional and Complementary

- Prevention/Screening
 - o Up-to-date
- Treatment (e.g., conventional and complementary approaches, medications, and supplements)
 - Elimination/Low FODMaP diet
 - o Psychology
 - Peppermint oil, enteric-coated capsules 0.2 to 0.4 ml, 3 times daily as needed for abdominal cramping and spasm.
- Skill building and education
 - Vocational
 - Nutrition choices
 - Mind-body tools

Referrals/Consults

- Social work
- Psychology
- Nutrition

My Support Team

- Professional Care
 - Primary Care Clinician

Department of Family Medicine and Community Health

- o Social worker
- Psychologist
- o Nutritionist
- Personal
 - o Wife
 - o Daughter
 - Parents
 - o Chaplain

Next Steps

- Follow up in 3-4 weeks after making dietary changes.
- Start with social work and nutrition consults. Then see a psychologist as needed, depending on his response to these treatments.

Please Note:_This plan is for my personal use and does not comprise my complete medical or pharmacological data, nor does it replace the medical record.

Online Resources

- Promoting a Healthy Microbiome with Food and Probiotics
- Testing to Assess the Gastrointestinal Ecosystem
- Elimination Diets
- The Low FODMaP Diet
- Gastroesophageal Reflux Disease (GERD)
- Irritable Bowel Syndrome (IBS)
- Balloon Self-Hypnosis Technique for IBS and Abdominal Pain: A Guide for Clinicians
- Inflammatory Bowel Disease (Crohn's Disease and Ulcerative Colitis)
- Preventing Recurrent Diverticulitis
- Coming Off a Proton Pump Inhibitor

Author(s)

"Digestive Health" was adapted for the University of Wisconsin Integrative Health program from the original written by David Rakel, MD (2014) and updated by David Lessens, MD, MPH (2020). It was modified for the UW Integrative Health website in 2021.

This overview was made possible through a collaborative effort between the University of Wisconsin Integrative Health Program, VA Office of Patient Centered Care and Cultural Transformation, and Pacific Institute for Research and Evaluation.

References

- 1. Farhadi A, Banan A, Fields J, Keshavarzian A. Intestinal barrier: an interface between health and disease. *J Gastroenterol Hepatol*. May 2003;18(5):479-97.
- 2. Richter C, Tanaka T, Yada RY. Mechanism of activation of the gastric aspartic proteinases: pepsinogen, progastricsin and prochymosin. *Biochem J*. Nov 1 1998;335 (Pt 3):481-90.
- 3. Molina-Infante J, Zamorano J. Acid-suppressive therapy and eosinophilic esophagitis: friends or foes? *Am J Gastroenterol.* Mar 2010;105(3):699-700. doi:10.1038/ajg.2009.590
- 4. Orel R, Turk H. Re: Might the use of acid-suppressive medications predispose to the development of eosinophilic esophagitis? *Am J Gastroenterol*. Feb 2010;105(2):468; author reply 469. doi:10.1038/ajg.2009.603
- 5. Funaki Y, Tokudome K, Izawa S, et al. Comparison of the effect of a single dose of omeprazole or lansoprazole on intragastric pH in Japanese participants: a two-way crossover study. *J Chin Med Assoc*. Mar 2013;76(3):131-4. doi:10.1016/j.jcma.2012.11.006
- 6. Macdonald LE, Brett J, Kelton D, Majowicz SE, Snedeker K, Sargeant JM. A systematic review and meta-analysis of the effects of pasteurization on milk vitamins, and evidence for raw milk consumption and other health-related outcomes. *J Food Prot.* Nov 2011;74(11):1814-32. doi:10.4315/0362-028x.jfp-10-269
- 7. Wilhelm SM, Rjater RG, Kale-Pradhan PB. Perils and pitfalls of long-term effects of proton pump inhibitors. *Expert Rev Clin Pharmacol*. Jul 2013;6(4):443-51. doi:10.1126/science.124121410.1586/17512433.2013.811206
- 8. Laheij RJ, Sturkenboom MC, Hassing RJ, Dieleman J, Stricker BH, Jansen JB. Risk of communityacquired pneumonia and use of gastric acid-suppressive drugs. *JAMA*. Oct 27 2004;292(16):1955-60. doi:10.1001/jama.292.16.1955
- Canani RB, Cirillo P, Roggero P, et al. Therapy with gastric acidity inhibitors increases the risk of acute gastroenteritis and community-acquired pneumonia in children. *Pediatr Neonatol.* May 2006;117(5):e817-20. doi:10.1542/peds.2005-1655
- Dial S, Delaney JA, Barkun AN, Suissa S. Use of gastric acid-suppressive agents and the risk of community-acquired Clostridium difficile-associated disease. *JAMA*. Dec 21 2005;294(23):2989-95. doi:10.1001/jama.294.23.2989
- 11. Hegar B, Hutapea EI, Advani N, Vandenplas Y. A double-blind placebo-controlled randomized trial on probiotics in small bowel bacterial overgrowth in children treated with omeprazole. *J Pediatr (Rio J)*. Jul-Aug 2013;89(4):381-7. doi:10.1586/17512433.2013.81120610.1016/j.jped.2012.12.005
- 12. Corley DA, Kubo A, Zhao W, Quesenberry C. Proton pump inhibitors and histamine-2 receptor antagonists are associated with hip fractures among at-risk patients. *Gastroenterology*. Jul 2010;139(1):93-101. doi:10.1053/j.gastro.2010.03.055
- 13. Gray SL, LaCroix AZ, Larson J, et al. Proton pump inhibitor use, hip fracture, and change in bone mineral density in postmenopausal women: results from the Women's Health Initiative. *Arch Intern Med.* May 10 2010;170(9):765-71. doi:10.1001/archinternmed.2010.94
- 14. Kwok CS, Yeong JK, Loke YK. Meta-analysis: Risk of fractures with acid-suppressing medication. *Bone*. 2010;doi:10.1016/j.bone.2010.12.015
- 15. Insogna KL. The effect of proton pump-inhibiting drugs on mineral metabolism. *Am J Gastroenterol.* 2009;104:S2-S4.
- Valuck RJ, Ruscin JM. A case-control study on adverse effects: H2 blocker or proton pump inhibitor use and risk of vitamin B12 deficiency in older adults. *J Clin Epidemiol*. Apr 2004;57(4):422-8. doi:10.1016/j.jclinepi.2003.08.015
- 17. Lam JR, Schneider JL, Zhao W, Corley DA. Proton pump inhibitor and histamine 2 receptor antagonist use and vitamin B12 deficiency. *Nat Med.* Dec 11 2013;310(22):2435-42. doi:10.1038/nm.344410.1001/jama.2013.280490
- 18. Skikne BS, Lynch SR, Cook JD. Role of gastric acid in food iron absorption. *Gastroenterology*. Dec 1981;81(6):1068-71.

- 19. Sharma VR, Brannon MA, Carloss EA. Effect of omeprazole on oral iron replacement in patients with iron deficiency anemia. *South Med J.* Sep 2004;97(9):887-9.
- 20. Gau JT, Yang YX, Chen R, Kao TC. Uses of proton pump inhibitors and hypomagnesemia. *Pharmacoepidemiology and drug safety*. May 2012;21(5):553-9. doi:10.1002/pds.3224
- 21. Bermudez-Brito M, Plaza-Diaz J, Munoz-Quezada S, Gomez-Llorente C, Gil A. Probiotic mechanisms of action. *Ann Nutr Metab.* 2012;61(2):160-74. doi:10.1159/000342079
- 22. Hehemann JH, Correc G, Barbeyron T, Helbert W, Czjzek M, Michel G. Transfer of carbohydrateactive enzymes from marine bacteria to Japanese gut microbiota. *Nature*. Apr 8 2010;464(7290):908-12. doi:10.1038/nature08937
- 23. Leyer GJ, Li S, Mubasher ME, Reifer C, Ouwehand AC. Probiotic effects on cold and influenza-like symptom incidence and duration in children. *Pediatrics*. 2009;124(2):e172-e179.
- 24. Indrio F, Di Mauro A, Riezzo G, et al. Prophylactic use of a probiotic in the prevention of colic, regurgitation, and functional constipation: a randomized clinical trial. *JAMA Pediatr*. Mar 2014;168(3):228-33. doi:10.1001/jamapediatrics.2013.4367
- 25. Gutierrez-Castrellon P, Lopez-Velazquez G, Diaz-Garcia L, et al. Diarrhea in preschool children and Lactobacillus reuteri: a randomized controlled trial. *Pediatrics*. 2014;133(4):e904-e909.
- Kalliomaki M, Salminen S, Poussa T, Arvilommi H, Isolauri E. Probiotics and prevention of atopic disease: 4-year follow-up of a randomised placebo-controlled trial. *Lancet*. May 31 2003;361(9372):1869-71. doi:10.1016/s0140-6736(03)13490-3
- 27. Ridaura VK, Faith JJ, Rey FE, et al. Gut microbiota from twins discordant for obesity modulate metabolism in mice. *Science*. Sep 6 2013;341(6150):1241214. doi:10.1053/j.gastro.2013.09.04610.1126/science.1241214
- 28. Whorwell PJ, Altringer L, Morel J, et al. Efficacy of an encapsulated probiotic Bifidobacterium infantis 35624 in women with irritable bowel syndrome. *Am J Gastroenterol*. Jul 2006;101(7):1581-90. doi:10.1111/j.1572-0241.2006.00734.x
- 29. Wald A, Rakel D. Behavioral and complementary approaches for the treatment of irritable bowel syndrome. *Nutr Clin Pract.* Jun-Jul 2008;23(3):284-92. doi:10.1177/0884533608318677
- 30. van Nood E, Vrieze A, Nieuwdorp M, et al. Duodenal infusion of donor feces for recurrent Clostridium difficile. *N Engl J Med.* Jan 31 2013;368(5):407-15. doi:10.1056/NEJMoa1205037
- 31. Shen NT, Maw A, Tmanova LL, et al. Timely use of probiotics in hospitalized adults prevents clostridium difficile infection: a systematic review with meta-regression analysis. *Gastroenterology*. Jun 2017;152(8):1889-1900.e9. doi:10.1053/j.gastro.2017.02.003
- 32. Arumugam M, Raes J, Pelletier E, et al. Enterotypes of the human gut microbiome. *Nature*. May 12 2011;473(7346):174-80. doi:10.1038/nature09944
- 33. Huurre A, Kalliomaki M, Rautava S, Rinne M, Salminen S, Isolauri E. Mode of delivery effects on gut microbiota and humoral immunity. *Neonatology*. 2008;93(4):236-40. doi:10.1159/111102
- 34. Kero J, Gissler M, Gronlund MM, et al. Mode of delivery and asthma -- is there a connection? *Pediatr Res.* Jul 2002;52(1):6-11. doi:10.1203/00006450-200207000-00004
- 35. Pistiner M, Gold DR, Abdulkerim H, Hoffman E, Celedon JC. Birth by cesarean section, allergic rhinitis, and allergic sensitization among children with a parental history of atopy. *J Allergy Clin Immunol.* Aug 2008;122(2):274-9. doi:10.1016/j.jaci.2008.05.007
- 36. Eggesbo M, Botten G, Stigum H, Samuelsen SÖ, Brunekreef B, Magnus P. Cesarean delivery and cow milk allergy/intolerance. *Allergy*. Sep 2005;60(9):1172-3. doi:10.1111/j.1398-9995.2005.00857.x
- 37. Maitra A, Sherriff A, Strachan D, Henderson J, Team AS. Mode of delivery is not associated with asthma or atopy in childhood. *Clin Exp Allergy*. 2004;34(9):1349-1355. doi:10.1111/j.1365-2222.2004.02048.x [doi]; CEA2048 [pii]
- 38. Albenberg LG, Wu GD. Diet and the intestinal microbiome: associations, functions, and implications for health and disease. *Gastroenterology*. May 2014;146(6):1564-72. doi:10.1053/j.gastro.2014.01.058

- 39. Kalliomaki M, Collado MC, Salminen S, Isolauri E. Early differences in fecal microbiota composition in children may predict overweight. *Am J Clin Nutr.* Mar 2008;87(3):534-8.
- 40. Bäckhed F, Ding H, Wang T, et al. The gut microbiota as an environmental factor that regulates fat storage. *Proc Natl Acad Sci U S A*. 2004;101(44):15718-15723.
- 41. Hijova E, Chmelarova A. Short chain fatty acids and colonic health. *Bratisl Lek Listy*. 2007;108(8):354-8.
- 42. Trompette A, Gollwitzer ES, Yadava K, et al. Gut microbiota metabolism of dietary fiber influences allergic airway disease and hematopoiesis. Feb 2014;20(2):159-66. doi:10.1038/nm.3444
- 43. Huffnagle GB. Increase in dietary fiber dampens allergic responses in the lung. *Nat Med.* Feb 2014;20(2):120-1. doi:10.1038/nm.3472
- 44. Villoria A, Serra J, Azpiroz F, Malagelada JR. Physical activity and intestinal gas clearance in patients with bloating. *Am J Gastroenterol.* Nov 2006;101(11):2552-7. doi:10.1111/j.1572-0241.2006.00873.x
- 45. Lustyk MK, Jarrett ME, Bennett JC, Heitkemper MM. Does a physically active lifestyle improve symptoms in women with irritable bowel syndrome? *Gastroenterol Nurs*. May-Jun 2001;24(3):129-37.
- 46. Daley AJ, Grimmett C, Roberts L, et al. The effects of exercise upon symptoms and quality of life in patients diagnosed with irritable bowel syndrome: a randomised controlled trial. *Int J Sports Med.* Sep 2008;29(9):778-82. doi:10.1055/s-2008-1038600
- 47. Festi D, Scaioli E, Baldi F, et al. Body weight, lifestyle, dietary habits and gastroesophageal reflux disease. *World J Gastroenterol*. Apr 14 2009;15(14):1690-701.
- 48. McKenzie YA, Bowyer RK, Leach H, et al. British Dietetic Association systematic review and evidence-based practice guidelines for the dietary management of irritable bowel syndrome in adults (2016 update). *J Hum Nutr Diet*. Oct 2016;29(5):549-75. doi:10.1111/jhn.12385
- 49. Carroccio A, Mansueto P, Iacono G, et al. Non-celiac wheat sensitivity diagnosed by double-blind placebo-controlled challenge: exploring a new clinical entity. *Am J Gastroenterol*. Dec 2012;107(12):1898-906; quiz 1907. doi:10.1038/ajg.2012.236
- 50. Kabbani TA, Vanga RR, Leffler DA, et al. Celiac disease or non-celiac gluten sensitivity? An approach to clinical differential diagnosis. *Am J Gastroenterol.* May 2014;109(5):741-6; quiz 747. doi:10.1038/ajg.2014.41
- 51. Rindfleisch A. Forgiveness. In: Rakel D, ed. Integr Med. 4th ed. Elsevier; 2017:940-944.
- 52. Staudacher HM, Whelan K, Irving PM, Lomer MC. Comparison of symptom response following advice for a diet low in fermentable carbohydrates (FODMAPs) versus standard dietary advice in patients with irritable bowel syndrome. *J Hum Nutr Diet*. Oct 2011;24(5):487-95. doi:10.1111/j.1365-277X.2011.01162.x
- 53. Halmos EP, Power VA, Shepherd SJ, Gibson PR, Muir JG. A diet low in FODMAPs reduces symptoms of irritable bowel syndrome. *Gastroenterology*. Jan 2014;146(1):67-75.e5. doi:10.1001/jama.2013.280490 and 10.1053/j.gastro.2013.09.046
- 54. Pimentel M, Lembo A, Chey WD, et al. Rifaximin therapy for patients with irritable bowel syndrome without constipation. *N Engl J Med.* Jan 6 2011;364(1):22-32. doi:10.1056/NEJMoa1004409
- 55. de Roest RH, Dobbs BR, Chapman BA, et al. The low FODMAP diet improves gastrointestinal symptoms in patients with irritable bowel syndrome: a prospective study. *Int J Clin Pract.* Sep 2013;67(9):895-903. doi:10.1111/jjcp.12128
- 56. Jenkins DJ, Kendall CW, Marchie A, et al. Direct comparison of a dietary portfolio of cholesterollowering foods with a statin in hypercholesterolemic participants. *Am J Clin Nutr*. Feb 2005;81(2):380-7.
- 57. de Lorgeril M, Salen P, Martin JL, Monjaud I, Boucher P, Mamelle N. Mediterranean dietary pattern in a randomized trial: prolonged survival and possible reduced cancer rate. *Arch Intern Med.* Jun 8 1998;158(11):1181-7.

58.

Quagliani D, Felt-Gunderson P. Closing America's fiber intake gap: communication strategies from a food and fiber summit. *Am J Lifestyle Med*. Jan-Feb 2017;11(1):80-85.

- doi:10.1177/1559827615588079
 59. Kanaly T, Shaheen NJ, Vaughn BV. Gastrointestinal physiology and digestive disorders in sleep. *Curr Opin Pulm Med.* Nov 2009;15(6):571-7. doi:10.1097/MCP.0b013e3283318539
- 60. Ali T, Choe J, Awab A, Wagener TL, Orr WC. Sleep, immunity and inflammation in gastrointestinal disorders. *World J Gastroenterol*. Dec 28 2013;19(48):9231-9. doi:10.3748/wjg.v19.i48.9231
- 61. Lahiri S, Singh P, Singh S, Rasheed N, Palit G, Pant KK. Melatonin protects against experimental reflux esophagitis. *J Pineal Res*. Mar 2009;46(2):207-13. doi:10.1111/j.1600-079X.2008.00650.x
- 62. de Oliveira Torres JDF, de Souza Pereira R. Which is the best choice for gastroesophageal disorders: Melatonin or proton pump inhibitors? *World J Gastrointest Pharmacol Ther.* 2010;1(5):102.
- 63. Mei Q, Diao L, Xu JM, Liu XC, Jin J. A protective effect of melatonin on intestinal permeability is induced by diclofenac via regulation of mitochondrial function in mice. *Acta pharmacologica Sinica*. Apr 2011;32(4):495-502. doi:10.1038/aps.2010.225
- 64. McCord G, Gilchrist VJ, Grossman SD, et al. Discussing spirituality with patients: a rational and ethical approach. *Ann Fam Med.* Jul-Aug 2004;2(4):356-61.
- 65. Tillisch K, Labus J, Kilpatrick L, et al. Consumption of fermented milk product with probiotic modulates brain activity. *Gastroenterology*. Jun 2013;144(7):1394-401, 1401.e1-4. doi:10.1053/j.gastro.2013.02.043
- 66. Bravo JA, Forsythe P, Chew MV, et al. Ingestion of Lactobacillus strain regulates emotional behavior and central GABA receptor expression in a mouse via the vagus nerve. *Proc Natl Acad Sci* U S A. Sep 20 2011;108(38):16050-5. doi:10.1073/pnas.1102999108
- 67. Garcia-Rodenas CL, Bergonzelli GE, Nutten S, et al. Nutritional approach to restore impaired intestinal barrier function and growth after neonatal stress in rats. *J Pediatr Gastroenterol Nutr*. Jul 2006;43(1):16-24. doi:10.1097/01.mpg.0000226376.95623.9f
- 68. Kiecolt-Glaser JK, Glaser R, Cacioppo JT, Malarkey WB. Marital stress: immunologic, neuroendocrine, and autonomic correlates. *Ann N Y Acad Sci*. May 1 1998;840:656-63.
- 69. Pennebaker J. Opening Up: The Healing Power of Expressing Emotions. The Guilford Press; 1997.
- 70. Gouin JP, Kiecolt-Glaser JK, Malarkey WB, Glaser R. The influence of anger expression on wound healing. *Brain Behav Immun.* 2007;doi:10.1016/j.bbi.2007.10.013
- 71. Smyth JM, Stone AA, Hurewitz A, Kaell A. Effects of writing about stressful experiences on symptom reduction in patients with asthma or rheumatoid arthritis: a randomized trial. *JAMA*. Apr 14 1999;281(14):1304-9.
- 72. Warner LJ, Lumley MA, Casey RJ, et al. Health effects of written emotional disclosure in adolescents with asthma: a randomized, controlled trial. *J Pediatr Psychol*. Jul 2006;31(6):557-68. doi:10.1093/jpepsy/jsj048
- 73. Klein K, Boals A. Expressive writing can increase working memory capacity. *J Exp Psychol Gen*. Sep 2001;130(3):520-33.
- 74. Richards JM, Beal WE, Seagal JD, Pennebaker JW. Effects of disclosure of traumatic events on illness behavior among psychiatric prison inmates. *J Abnorm Psychol*. Feb 2000;109(1):156-60.
- 75. Baddeley JL, Pennebaker JW. A postdeployment expressive writing intervention for military couples: a randomized controlled trial. *Journal of Traumatic Stress*. Oct 2011;24(5):581-5. doi:10.1002/jts.20679
- 76. Ames SC, Patten CA, Werch CE, et al. Expressive writing as a smoking cessation treatment adjunct for young adult smokers. *Nicotine Tob Res.* Feb 2007;9(2):185-94. doi:10.1080/14622200601078525
- 77. Stanton AL, Danoff-Burg S, Sworowski LA, et al. Randomized, controlled trial of written emotional expression and benefit finding in breast cancer patients. *J Clin Oncol*. Oct 15 2002;20(20):4160-8.
- 78. Smyth JM, Pennebaker JW. Exploring the boundary conditions of expressive writing: In search of the right recipe. *Br J Health Psychol*. Feb 2008;13(Pt 1):1-7. doi:10.1348/135910707x260117

Digestive Health Overview University of Wisconsin Integrative Health www.fammed.wisc.edu/integrative

School of Medicine and Public Health UNIVERSITY OF WISCONSIN-MADISO

- Forbes A, MacAuley S, Chiotakakou-Faliakou E. Hypnotherapy and therapeutic audiotape: effective in previously unsuccessfully treated irritable bowel syndrome? *Int J Colorectal Dis.* Nov 2000;15(5-6):328-34.
- 80. Whitehead WE. Hypnosis for irritable bowel syndrome: the empirical evidence of therapeutic effects. *Int J Clin Exp Hypn*. Jan 2006;54(1):7-20. doi:10.1080/00207140500328708
- Wilson S, Maddison T, Roberts L, Greenfield S, Singh S. Systematic review: the effectiveness of hypnotherapy in the management of irritable bowel syndrome. *Aliment Pharmacol Ther*. 2006;24(5):769-780.
- 82. Peters SL, Muir JG, Gibson PR. Review article: gut-directed hypnotherapy in the management of irritable bowel syndrome and inflammatory bowel disease. *Aliment Pharmacol Ther.* Jun 2015;41(11):1104-15. doi:10.1111/apt.13202
- 83. Gonsalkorale WM, Miller V, Afzal A, Whorwell PJ. Long term benefits of hypnotherapy for irritable bowel syndrome. *Gut.* Nov 2003;52(11):1623-9.
- 84. Laird KT, Tanner-Smith EE, Russell AC, Hollon SD, Walker LS. Comparative efficacy of psychological therapies for improving mental health and daily functioning in irritable bowel syndrome: A systematic review and meta-analysis. *Clin Psychol Rev.* Feb 2017;51:142-152. doi:10.1016/j.cpr.2016.11.001
- 85. Ford AC, Moayyedi P, Chey WD, et al. American College of Gastroenterology monograph on management of irritable bowel syndrome. *Am J Gastroenterol.* Jun 2018;113(Suppl 2):1-18. doi:10.1038/s41395-018-0084-x
- 86. Dossett ML, Cohen EM, Cohen J. Integrative medicine for gastrointestinal disease. *Prim care*. Jun 2017;44(2):265-280. doi:10.1016/j.pop.2017.02.002
- 87. Korzenik J, Koch AK, Langhorst J. Complementary and integrative gastroenterology. *Med Clin North Am.* Sep 2017;101(5):943-954. doi:10.1016/j.mcna.2017.04.009
- 88. Shulz V, Hansel R, Tyler V. Rational Phytotherapy: A Physician's Guide to Herbal Medicine. 3rd ed. Springer; 1998.
- Liu H, Wang J, Zhou W, Wang Y, Yang L. Systems approaches and polypharmacology for drug discovery from herbal medicines: an example using licorice. *J Ethnopharmacol.* Apr 19 2013;146(3):773-93. doi:10.1016/j.jep.2013.02.004
- 90. Singh O, Khanam Z, Misra N, Srivastava MK. Chamomile (Matricaria chamomilla L.): An overview. *Pharmacogn Rev.* Jan 2011;5(9):82-95. doi:10.4103/0973-7847.79103
- 91. Melzer J, Rosch W, Reichling J, Brignoli R, Saller R. Meta-analysis: phytotherapy of functional dyspepsia with the herbal drug preparation STW 5 (Iberogast). *Aliment Pharmacol Ther*. Dec 2004;20(11-12):1279-87. doi:10.1111/j.1365-2036.2004.02275.x
- 92. Fasano A, Shea-Donohue T. Mechanisms of disease: the role of intestinal barrier function in the pathogenesis of gastrointestinal autoimmune diseases. *Nat Clin Pract Gastroenterol Hepatol.* Sep 2005;2(9):416-22. doi:10.1038/ncpgasthep0259
- 93. Bashir ME, Louie S, Shi HN, Nagler-Anderson C. Toll-like receptor 4 signaling by intestinal microbes influences susceptibility to food allergy. *J Immunol*. 2004;172(11):6978-6987.
- 94. Quigley EM. Bacteria: a new player in gastrointestinal motility disorders-infections, bacterial overgrowth, and probiotics. *Gastroenterol Clin North Am.* 2007;36(3):735-748. doi:10.1016/j.gtc.2007.07.012
- 95. Quigley EM. The use of probiotics in functional bowel disease. *Gastroenterol Clin North Am.* Sep 2005;34(3):533-45, x. doi:10.1016/j.gtc.2005.05.008
- 96. Kajander K, Krogius-Kurikka L, Rinttila T, Karjalainen H, Palva A, Korpela R. Effects of multispecies probiotic supplementation on intestinal microbiota in irritable bowel syndrome. *Aliment Pharmacol Ther.* Aug 1 2007;26(3):463-73. doi:10.1111/j.1365-2036.2007.03391.x
- 97. Dale HF, Rasmussen SH, Asiller Ö, Lied GA. Probiotics in irritable bowel syndrome: an up-to-date systematic review. *Nutrients*. Sep 2 2019;11(9)doi:10.3390/nu11092048

- Liang D, Longgui N, Guoqiang X. Efficacy of different probiotic protocols in irritable bowel syndrome: A network meta-analysis. *Medicine (Baltimore)*. Jul 2019;98(27):e16068. doi:10.1097/md.00000000016068
- 99. Brenner DM, Moeller MJ, Chey WD, Schoenfeld PS. The utility of probiotics in the treatment of irritable bowel syndrome: a systematic review. *Am J Gastroenterol*. Apr 2009;104(4):1033-49; quiz 1050. doi:10.1038/ajg.2009.25
- 100. Floch MH, Walker WA, Madsen K, et al. Recommendations for probiotic use-2011 update. *J Clin Gastroenterol*. Nov 2011;45 Suppl:S168-71. doi:10.1097/MCG.0b013e318230928b
- 101. Moayyedi P, Ford AC, Talley NJ, et al. The efficacy of probiotics in the treatment of irritable bowel syndrome: a systematic review. *Gut.* Mar 2010;59(3):325-32. doi:10.1136/gut.2008.167270
- Chey WD, Maneerattaporn M, Saad R. Pharmacologic and complementary and alternative medicine therapies for irritable bowel syndrome. *Gut Liver*. Sep 2011;5(3):253-66. doi:10.5009/gnl.2011.5.3.253
- 103. Didari T, Mozaffari S, Nikfar S, Abdollahi M. Effectiveness of probiotics in irritable bowel syndrome: Updated systematic review with meta-analysis. *World J Gastroenterol*. Mar 14 2015;21(10):3072-84. doi:10.3748/wjg.v21.i10.3072
- 104. Chang FY, Lu CL. Treatment of irritable bowel syndrome using complementary and alternative medicine. *J Chin Med Assoc*. Jun 2009;72(6):294-300. doi:10.1016/s1726-4901(09)70375-2
- 105. Mann NS, KS S. Peppermint oil in irritable bowel syndrome: systematic evaluation of 1634 cases with meta-analysis. *J Integr Med*. 2012;19(1):5-6.
- 106. Hawrelak JA, Wohlmuth H, Pattinson M, et al. Western herbal medicines in the treatment of irritable bowel syndrome: A systematic review and meta-analysis. *Complement Ther Med.* Jan 2020;48:102233. doi:10.1016/j.ctim.2019.102233
- 107. De-Souza DA, Greene LJ. Intestinal permeability and systemic infections in critically ill patients: effect of glutamine. *Critical care medicine*. May 2005;33(5):1125-35.
- 108. Hulsewe KW, van der Hulst RW, van Acker BA, von Meyenfeldt MF, Soeters PB. Inflammation rather than nutritional depletion determines glutamine concentrations and intestinal permeability. *Clin Nutr.* Oct 2004;23(5):1209-16. doi:10.1016/j.clnu.2004.04.001
- 109. Wischmeyer PE. Can glutamine turn off the motor that drives systemic inflammation? *Critical care medicine*. May 2005;33(5):1175-8.
- Mahmood A, Fitzgerald AJ, Marchbank T, et al. Zinc carnosine, a health food supplement that stabilises small bowel integrity and stimulates gut repair processes. *Gut.* 2006;doi:gut.2006.099929 [pii]; 10.1136/gut.2006.099929 [doi]
- 111. Shao Y, Wolf PG, Guo S, Guo Y, Gaskins HR, Zhang B. Zinc enhances intestinal epithelial barrier function through the PI3K/AKT/mTOR signaling pathway in Caco-2 cells. *J Nutr Biochem*. May 2017;43:18-26. doi:10.1016/j.jnutbio.2017.01.013
- 112. Cordain L, Eaton SB, Sebastian A, et al. Origins and evolution of the Western diet: health implications for the 21st century. *Am J Clin Nutr.* 2005;81(2):341-354. doi:81/2/341 [pii]
- 113. Cavallo G, De Magistris R, Miluccio V, Iannuzzi R. [Changes in the blood zinc in the irritable bowel syndrome: a preliminary study]. *Minerva Dietol Gastroenterol*. Apr-Jun 1990;36(2):77-81. Alterazioni della zinchemia nella sindrome dell'intestino irritabile: studio preliminare.
- 114. Ammendolia C, Furlan AD, Imamura M, Irvin E, van Tulder M. Evidence-informed management of chronic low back pain with needle acupuncture. *Spine J*. Jan-Feb 2008;8(1):160-72. doi:10.1016/j.spinee.2007.10.014
- 115. Zhu J, Guo Y, Liu S, et al. Acupuncture for the treatment of gastro-oesophageal reflux disease: a systematic review and meta-analysis. *Acupunct Med.* Oct 2017;35(5):316-323. doi:10.1136/acupmed-2016-011205
- 116. Dickman R, Schiff E, Holland A, et al. Clinical trial: acupuncture vs. doubling the proton pump inhibitor dose in refractory heartburn. *Aliment Pharmacol Ther*. Nov 15 2007;26(10):1333-44. doi:10.1111/j.1365-2036.2007.03520.x

- 117. Manheimer E, Cheng K, Wieland LS, et al. Acupuncture for treatment of irritable bowel syndrome. *Cochrane Database Syst Rev.* 2012;5
- 118. Sun JH, Wu XL, Xia C, et al. Clinical evaluation of Soothing Gan and invigorating Pi acupuncture treatment on diarrhea-predominant irritable bowel syndrome. *Chin J Integr Med*. Oct 2011;17(10):780-5. doi:10.1007/s11655-011-0875-z
- 119. Schneider A, Streitberger K, Joos S. Acupuncture treatment in gastrointestinal diseases: a systematic review. *World J Gastroenterol.* Jul 7 2007;13(25):3417-24.

Digestive Health Overview University of Wisconsin Integrative Health www.fammed.wisc.edu/integrative

School of Medicine and Public Health UNIVERSITY OF WISCONSIN-MADISON