

# DIGEST



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SCHOOL OF MEDICINE

*Our mission is to advance the biopsychosocial understanding and care of patients with functional GI & motility disorders through research, training and education.*

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PATIENT SUBMITTED QUESTIONS ANSWERED BY UNC FACULTY AND FELLOWS

RESEARCH PARTICIPANTS NEEDED

LEGISLATIVE SUPPORT NEEDED TO HELP ADVANCE FUNCTIONAL GI RESEARCH BILL

## A LOW FODMAP DIET FOR IRRITABLE BOWEL SYNDROME



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*determinants of disease outcomes, and interactions of diet and gastrointestinal disease. Dr. Wolfe completed medical school and residence at UNC Chapel Hill.*

Irritable bowel syndrome (IBS) is defined by recurrent abdominal pain or discomfort at least three days per month with two of the following three features: 1) improves with defecation, 2) is associated with a change in stool frequency, or 3) is associated with a change in stool form.<sup>1</sup> IBS is subdivided by the dominant stool habit of each patient into diarrhea predominant, constipation predominant, and mixed type.

IBS is a common medical problem, affecting about one in ten adults in North America.<sup>[2]</sup> IBS patients

miss more work and require more physician visits than patients without the disease.<sup>[3]</sup> Unfortunately, the medications we use to treat IBS are not very effective. The mainstays of treatment are antidepressants. In a recent meta-analysis, antidepressants improved symptoms in 46% of IBS sufferers compared with 35% of patients on placebo.<sup>[4]</sup>

Patients with IBS often associate specific foods with their symptoms, and many restrict their diets.<sup>[5]</sup> The reactions that patients report, however, do not fit classic food allergies, and avoidance of trigger foods does not produce reliable symptom relief.<sup>[6]</sup> Because of the lack of a clear cause-and-effect relationship between foods and symptoms, using food avoidance to treat IBS has often been viewed with skepticism.

More recently, though, researchers have studied an elimination diet aimed at treating IBS. Called the low FODMAP diet, it aims to minimize levels of fermentable sugars (the FODMAP acronym stands for Fermentable Oligosaccharides, Disaccharides, Monosaccharides And Polyols). Patients minimize

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*DIGEST* is a quarterly publication of the UNC Center for Functional GI & Motility Disorders, a center of excellence within the Division of Gastroenterology and Hepatology, School of Medicine, University of North Carolina at Chapel Hill.

The Center's director is **William E. Whitehead, PhD**, Professor of Medicine and Gynecology.

Over the past decade, the UNC Center for Functional GI and Motility Disorders has enjoyed significant grant support from a number of private foundations and corporations. These grants have ranged from sponsorships of specific events (symposia or CME courses) to unrestricted grants in support of fellowships and the Center's education and training effort.

This activity is supported by an educational grant from Takeda Pharmaceuticals U.S.A., Inc. and Sucampo.

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# DIGEST

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FODMAP consumption and then slowly reintroduce foods to identify a tolerable level of FODMAP consumption. In this article, we will examine dietary sources of FODMAPs, mechanisms by which they may cause IBS symptoms, the evidence for low FODMAP diets in IBS, and ongoing areas of uncertainty in the science surrounding low FODMAP diets.

### FODMAP Mechanisms and Sources

The sugars targeted for elimination in the low FODMAP diet cause symptoms by two mechanisms. First, a subset of patients are unable to digest some of the sugars. These undigested sugars create an osmolar burden, pulling water into the gut, which can cause looser and more frequent bowel movements.[7] Second, many of these sugars can be fermented by gut bacteria resulting in gas production.[8] This gas may stretch the gut, resulting in bloating and abdominal pain.

The oligosaccharides avoided in the low FODMAP diet include fructans and galactans, both of which are largely indigestible in humans. Common food sources include artichokes, asparagus, beets, celery, wheat, garlic, onion, leguminous beans, Brussels sprouts, cabbage, and some soy products such as soy milk. Fructans and galactans may undergo fermentation in the colon, leading to gas production.

The disaccharide eliminated in the low FODMAP diet is lactose. Lactose malabsorption occurs in about 70% of the human race.[9] Dairy foods are the primary source of lactose. Non-absorbed lactose pulls water into the bowel which may result in loose stools or increased stool frequency.

The monosaccharide target for elimination in the low FODMAP diet is fructose. The primary sources of fructose in the diet are fruit and products containing high-fructose corn syrup. While fructose can be absorbed, doses of fructose consistent with average daily intake in the US are incompletely absorbed in about half of adults.[10] Much like lactose, unabsorbed fructose pulls water into the bowel.

Polyols are sugar alcohols including sorbitol and mannitol. Polyols are available in certain fruits and vegetables and are also found as sweeteners in sugar free products where they appear as sorbitol, mannitol,

maltitol, xylitol, and isomalt. These substances cause diarrhea at high doses, and in some countries, products containing polyol sweeteners must be labeled with a mandatory statement regarding their laxative properties.[11]

### Evidence for Low FODMAP diets in the Treatment of IBS

Five high quality randomized trials have examined low FODMAP diets for treating IBS. Four of the five have demonstrated benefits from a low FODMAP diet. Symptoms such as abdominal pain, bloating, gas, nausea, heartburn and fatigue improved in most patients. [8,12] Patients also had greater satisfaction with stool form,12 and bowel frequency was improved in patients with diarrhea predominant IBS.[13] A low FODMAP diet decreased total bacteria in the stool while increasing bacterial diversity.[14] The fifth study compared the low FODMAP diet to traditional IBS dietary advice encouraging regular meals with avoidance of large meals and reduced consumption of fat, fiber, caffeine, and gas producing foods such as beans, cabbage, and onions. In that study, both strategies improved IBS symptoms, but there was no difference between the two diets.[15] Taken together, these studies demonstrate that a low FODMAP diet produces consistent and rapid improvement in symptoms of IBS.

### Areas of Uncertainty

While the evidence from randomized trials demonstrates that a low FODMAP diet is effective in treating IBS, there are multiple areas which need further clarification. First, true placebo controlled dietary studies are difficult. Like patients with any disease, IBS patients may be more likely to report improvement if they believe they are undergoing active treatment, and it is hard to keep patients from recognizing changes in their diets. Second, compliance with low FODMAP diets was dramatically simplified in these trials by providing patients with the food to be consumed. It is unclear whether similar results can be obtained when patients attempt to maintain the diet independently. Third, all of these studies lasted only a few weeks to months. We do not know the long term effectiveness of a low FODMAP diet.

The health impact of consuming a low FODMAP diet over an extended period is also unknown. A low FODMAP diet restricts numerous healthy foods: fruits, vegetables, and whole grains. Dietitian consultation can assist in finding appropriate food substitutions to prevent nutritional deficits, but careless application of the low FODMAP diet could result in a high fat, low fiber diet which in turn can contribute to obesity and other health related illness.

Low FODMAP diets also reduce the intake of a variety of prebiotics, foods that help feed our healthy bacteria. For example, healthy colon bacteria utilize indigestible sugars such as inulin for fermentation, but inulin is restricted in a low FODMAP diet. The full impact of a low FODMAP diet on gut bacteria needs further study.

Another important issue is the role of low FODMAP diets in constipation predominant IBS. The reduction in intestinal water should be expected to produce firmer stools and decrease stool frequency. While this makes sense as a way to control diarrhea, it is unlikely to treat constipation. More research is needed to address this issue.

## Conclusion

Low FODMAP diets are effective at improving symptoms of IBS in multiple studies. Low FODMAP diets also appear to improve stool consistency in diarrhea predominant IBS. It is not clear whether low FODMAP diets are as effective in constipation predominant IBS. The cited trials, while well designed, do have important limitations including small numbers of subjects and the possibility of incomplete subject blinding. No research has assessed the effectiveness of a low FODMAP diet in maintaining long term symptom improvement. It is unclear if this complicated diet can be successfully implemented in a “real world” setting, particularly in areas which may lack ready access to dietician support. A decrease in intake of prebiotics and fiber may occur with the low FODMAP diet, and could cause detrimental health impacts in the long term. The benefits and risks of low FODMAP diets will have to be assessed on an individual basis, but the diets offer an alternative therapy to patients wary of pharmaceutical and psychiatric therapy or who have failed previous treatment attempts.

If you have IBS and are interested in trying a low FODMAP diet, please discuss it with your doctor. Numerous apps and online resources are available, including an excellent one from Monash University in Australia where much of the research cited here was performed. However, I recommend involving a dietitian in your care to ensure that your diet remains healthy and well balanced even while minimizing FODMAPs.

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## UNDERSTANDING IBS: NOT A SINGULAR CULPRIT

Factors involved in the development and perception of symptoms commonly associated with irritable bowel syndrome (IBS) can be attributed to, but are not limited to, maladaptive coping strategies, diversity and type of bacterial colonies and their associated symptoms, as well as an individual's diet.[3,6] Patients with IBS on average experience higher levels of stress related emotions (anxiety or depression) and visceral pain than the general population.[1,2,4] Visceral pain is associated with irregular distension or stimulation in the stomach and intestines.[1] Differences have also been noted between patients with IBS and the general population in regards to how their brains respond to pain.[2,4,5] This article will cover a general overview of symptoms associated with IBS and potential causes.

The brain is one of the most powerful and possibly the least understood organs in our body. It maintains the most basic of our bodily functions while allowing us to compute, analyze, and export solutions for complicated tasks. As wonderful as our brain is, it is also susceptible to the smallest of influences that can change how it and our GI tract interact. A recent study found women with IBS had greater brain activation, when exposed to an unexpected threat (uncued electrical stimulation to the abdomen), in their right amygdala, right ventral anterior INS, PCC, and precuneus.[2] Male and female IBS participants also had greater brain responses, compared to health controls, in the right amygdala, right ventral anterior INS, right MFG, right inferior occipital cortex, left thalamus, PCC and precuneus. This responses are important to note in that controls had a negative activation and positive activation in IBS participations. Activation was measured by the blood-oxygen level in a patient's brain during cued an uncued stimuli.

The increased activation of the amygdala is important factor in IBS as this part of the brain is the crossroads where emotional behavior and emotional memories, sensory information, learned behavior, and interpretation of fear and anxiety come together. [4] The amygdala is also one of several structures within the brain involved in the control of intestinal motor function.[5] This is where maladaptive learning techniques are thought to play a role in the perception

and expectation of unpleasant, unwanted, or painful stimuli, such as bowel distention, pain during defecation, or anxiety from all other symptoms.

There has been new revelations associating the link between microbiota colonies, hormones and cytokines, and how mood disorders [and our overall mental health and quality of life] are associated with functional GI disorders.[3] Changes in hormone and cytokine levels circulating in our body as well as the quantity and type of bacteria colonies in our GI tract have the potential to alter the symptoms experienced in IBS. From our first breath to our last, bacteria in our GI tract are influencing our intestinal health. Studies have suggested that microbiota colonies begin to develop in pregnancy and that the placenta and amniotic fluid may not actually be a sterile environment.[6] There are also noted differences in bacterial colonies in babies delivered vaginally versus caesarian section.[6,7] The difference in microbiota between delivery methods is notable in that caesarian delivered infants had significantly lower total microbiota diversity, specifically with the bacteria phylum of Bacteroidetes.[7]

Understanding a person's past as well as their emotional and psychological health is just as important as their physical wellbeing. Women with IBS had increased scores for depression and anxiety compared to female healthy controls, but there was no difference between IBS and controls in men and no significant difference between men and women who had IBS.[2]

In a recently published article, researchers found when comparing participants who have IBS versus those who did not have a functional gastrointestinal disorder (FGID) were more likely to have reported experiencing a form of physical, sexual, and emotional abuse as well as higher depression, anxiety, and somatic symptoms. [3] Additional findings from the same study reveal that participants with IBS with a history of abuse report poor health related quality of life (HRQOL) and that the impact of their symptoms were additive, meaning that with increased abuse, the patient's gastrointestinal symptoms would increase and their HRQOL would decrease. The researchers reported that the GI

symptoms were also impacted by the patient's mood. Anxiety, depression, and other mood dysfunctions have been linked to a disturbance in the guts microbiota.

It is important to acknowledge that there are multiple theories and proven facts about the development of symptoms associated with irritable bowel syndrome. The interaction between the brain and the gut is a pivotal axis that we must not separate them into different causal routes, but look at their mutual interaction when attempting to manage symptom development and disease etiology.

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## WHERE CAN I FIND INFORMATION ON PARTICIPATING IN A CLINICAL TRIAL?

UNC Chapel Hill has a website specifically designed to match eligible research participants to openly recruiting research studies. This includes individuals who are healthy and looking to participate as a control and those with specific diseases or symptoms.

Join the Quest (<https://jointhequest.org>) helps research participants search through the open clinical trials within the University of North Carolina at Chapel Hill. The research studies vary and include surveys, drug clinical trials, device clinical trials, procedure clinical trials, medical outcome studies, and research which needs healthy volunteers, which may also be referred to as a "control."

Another resource available to patients who do not live near Chapel Hill is [www.clinicaltrials.gov](http://www.clinicaltrials.gov). This is operated under the National Institutes of Health (NIH) and has information about clinical research studies available in the United States and globally.

As with all research studies, participation is completely voluntary and you make the decision to participate. If at any time you have questions about a research

study, you can always contact the research coordinator, study investigator, or the institutional review board (IRB). You should never feel coerced or pressured to participate in a research study. You also have the right to remove yourself from the research at any time and for any reason. The research investigator also has the ability to withdraw you from a study if s/he believes that it is unsafe for you to continue to participate. After all, your health and safety is paramount.

Most studies that involve a drug, device, or procedure must report their findings to the FDA if they want their product to be approved for sale. To learn more about the FDA's role in clinical trials, visit

<http://www.fda.gov/ForPatients/ClinicalTrials/ucm20041753.htm>

The Center for Functional GI and Motility Disorders has research opportunities for pediatric and adult patients and will add more throughout the year. You can find more information about these studies online at <http://www.med.unc.edu/ibs/research/research-subjects-needed>

## UPDATE ON THE DEVELOPMENT OF ROME IV CRITERIA

This is a brief outline of the development of the Rome IV diagnostic criteria for the functional gastrointestinal disorders (FGIDs), and the first attempts to use these criteria for research purposes. This summary is based on an article in the May 2016 issue of *Gastroenterology* titled “Development and Validation of the Rome IV Diagnostic Questionnaire for Adults.” The full citation is at the end of this article. Readers may find additional details in this article.

Diagnosis of a functional gastrointestinal disorders (FGID) is based primarily on exclusionary tests and the defining symptoms presented in the Rome Criteria. Like most patients, many have had workups prior to their diagnosis that can include, and exceed, colonoscopy, hydrogen breath tests, stool sample pathology, anorectal manometry, and the list goes on and on. The Rome Foundation, which publishes updates to the Rome Criteria for the past nineteen years, was developed in collaboration with Drs. William Whitehead and Douglas Drossman, in addition to several other distinguished doctors specialized in the field of functional gastrointestinal disorders.

The newest version is the fourth edition of the Rome Criteria, which was released in May 2016. This edition has been a long time in the making. The last time the criteria was updated, Rome III, was in 2006. The Rome IV criteria narrows the symptom threshold at which a person can be clinically diagnosed as having a disorder, thus making a diagnosis more specific.

To find this new threshold, several study sites within the United States were recruited and enrolled over 1100 adults without a gastrointestinal disorder. The survey asked about GI symptom frequency and defined the criteria for a clinically abnormal diagnosis threshold as the 90th percentile.[1] After establishing a threshold, the Rome Foundation then conducted another survey to identify the clinical sensitivity, specificity, and population prevalence of FGIDs. Using a combination of questions from the Rome IV Diagnostic Questionnaire, Rome III Diagnostic Questionnaire, and other physical and psychology questions, 5931 participants from the U.S., U.K., and Canada completed this online survey. This is meant to distinguish people with FGIDs from the healthy population controls. Some of the most prevalent FGIDs were functional dyspepsia (9.3%),

functional constipation (8.9%), and IBS (5.7%). In conducting this research study, they also found that many symptoms from different functional disorders often overlap one another.

| Disorder                       | Sensitivity | Specificity |
|--------------------------------|-------------|-------------|
| Irritable Bowel Syndrome (IBS) | 62.7%       | 97.1%       |
| Functional Constipation (FC)   | 32.2%       | 93.6%       |
| Functional Dyspepsia           | 54.7%       | 93.3%       |

Specifically for IBS, there were three main changes in the diagnostic criteria. The changes to these criteria made achieving a diagnosis more rigorous.[1]

- (1) The threshold for abdominal pain frequency was increased from 2 – 3 day per month (Rome III) to at least once a week (Rome IV).
- (2) Reporting discomfort as a primary symptom, such as abdominal discomfort and pain, was removed as a symptom, but abdominal pain remained a qualifying symptom in Rome IV.
- (3) When referencing pain during defecation, the requirement for pain or discomfort to improve after defecation was modified so that abdominal pain only has to be associated with a bowel movement.

In addition to making the criteria for diagnosis more specific, the Rome IV criteria also separated further functional constipation from opioid-induced constipation (OIC) and IBS-C. This creates a standalone diagnosis for functional constipation.

1. Palsson OS, Whitehead WE, van Tilburg MA, Chang L, Chey W, Crowell MD, Keefer L, Lembo AJ, Parkman HP, Rao SS, Sperber A, Spiegel B, Tack J, Vanner S, Walker LS, Whorwell P, Yang Y. Rome IV Development and Validation of the Rome IV Diagnostic Questionnaire for Adults. *Gastroenterology*. 2016 Feb 13. pii: S0016-5085(16)00180-3.



## RESEARCH SUBJECTS NEEDED

## TREATMENT STUDIES

### Accidental Bowel Leakage Self Help Website (FISH)

The UNC Center for Functional GI and Motility Disorders is looking for eligible subjects to participate in the FISH Study/

Researchers in the UNC Center for Functional GI & Motility Disorders are finishing development of a complete 6 week online self-help program designed to enable individuals to reduce or get rid of accidental bowel leakage (fecal incontinence) on their own.

If you have been experiencing accidental bowel leakage, then the researchers would like your help to evaluate their new program in a research study that you can participate in entirely through your own computer.

You may be able to take part in this research study if you;

- Have experienced accidental bowel leakage at least once a week in the past 6 months.
- Are able and willing to log into a website and complete the learning tasks and answer diary questions for a few minutes each night for a six week period.
- Live in North Carolina or Virginia.
- Speak and write fluent English.

No study visits will be required. You will be reimbursed up to \$200 for completing the 6 week online self-help program.

For more information or to enroll in the study, click here to go to the online consent form: <http://bit.ly/1PFBv18> (The link is case sensitive)

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### Irritable Bowel Syndrome with Constipation Research Study for Patients age 18-85 years old.

The UNC Center for Functional GI and Motility Disorders is now recruiting subjects aged 18-85 years old to participate in a reserach study of an investigational research medication for Irritable Bowel Syndrome with constipation.

The research study is approximately 18 weeks long and requires 6-7 visits to the UNC CTRC clinic.

You may be eligible to participate if you are:

- Between 18 and 85 years of age.
- Currently experiencing abdominal pain and constipation due to your Irritable Bowel Syndrome condition
- Able and willing to make daily reports on your symptoms thoroughout the study
- Able and willing to participate in the clinical research study for approximately 18 weeks.

Eligible participants will recieve investigational medication and study related care at no cost. Compensation for time and possible other reimbursement.

**Principal Investigator**  
**Dr. Spencer Dorn**

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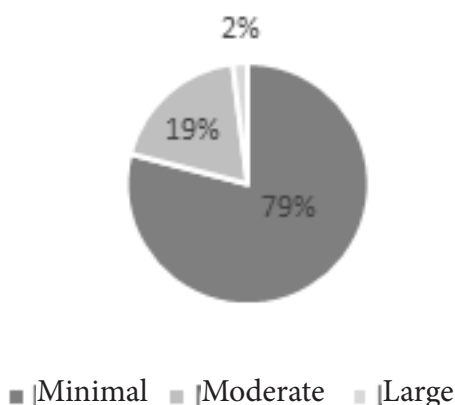
## PREVALENCE OF FECAL INCONTINENCE IN PATIENTS WITH IRRITABLE BOWEL SYNDROME

In the August edition of *Neurogastroenterology and Motility*, Drs. Olafur Palsson, William Whitehead, Steve Heymen, Magnus Simren, et. al., co-authored a paper, "Fecal Incontinence in irritable bowel syndrome" Prevalence and associated factors in Swedish and American patients." In the review of this article, information is presented comparing incontinence episodes in patient with irritable bowel syndrome (IBS) in two different countries, the United States and Sweden.

Fecal incontinence (FI), which is also known as accidental bowel leakage (ABL), was found to be common in patients diagnosed with IBS. This was found in both countries. When patients were asked if they experienced ABL more than one day a month, 19.7% of IBS patients in the US and 13.7% IBS patients in Sweden reported meeting this criteria. When the level of ABL incidence reporting was reduced to less than one day in the past three months, the numbers rose dramatically to 43.4% in the US and 29.8% in Sweden.

The amount of leakage was surprising as well. Categories of stool leakage were classified as (1) minimal, or only staining, (2) moderate, more than staining but not a full bowel movement, and (3) large or a full bowel movement. The chart below identifies the amount of stool lost in each country.

Amount of Stool Lost in US IBS Patients



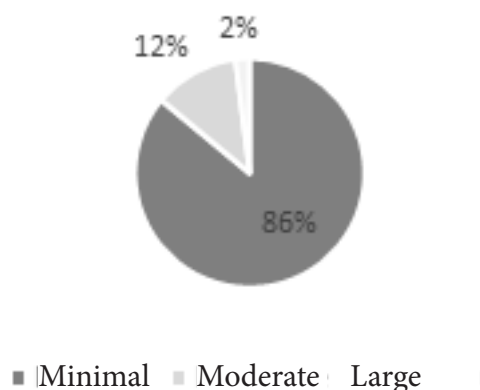
There was no statistical differences in IBS patients, both with and without ABL, in measurements capturing urge, pain thresholds, colorectal phasic motility response to stimuli, and smooth muscle tone and compliance.

The strongest risk factors for patients in the U.S. with IBS were urgency and age were independently associated with ABL, while in Sweden, urgency was the only independent risk factor. This article found associations between ABL and IBS that negatively impact a patient's quality of life, psychological symptoms, and work absenteeism.

The driving message of this article can be synthesized into one major point. IBS patients who report having loose, frequent stools and fecal urgency should be screened for ABL. This may be difficult as there are different social taboos for talking about incontinence between the countries sampled, but it is important for providers to ask and for patients to bring it up when talking about health history.

Simrén M, Palsson OS, Heymen S, Bajor A, Törnblom H, Whitehead WE. Fecal incontinence in irritable bowel syndrome: Prevalence and associated factors in Swedish and American patients. *Neurogastroenterol Motil.* 2016 Aug 31. Epub ahead of print.

Amount of Stool Lost in Swedish IBS Patients



## WHAT ARE THE FACTS ON LOW FODMAP RYE BREAD?

Low FODMAP's have been shown to be clinically effective to reduce symptoms associated with functional gastrointestinal disorders in diagnosis such as Irritable Bowel Syndrome.[1] We [The Center] have published a list in previous editions of our Digest newsletter and on Social Media about what foods are high and low FODMAP. Additional information on FODMAPs can be found on page 4 of the Digest.[3]

Recently, rye bread has been discussed as a food to help reduce symptoms, such as abdominal pain and abdominal distension, etc. A randomized clinical trial [2] investigated if low FODMAP rye bread was any better than regular rye bread at reducing symptoms. The study found that the low FODMAP rye bread did was more effective than regular rye bread in helping to reduce GI gas accumulation, which can influence perceived symptoms.

However, the study also noted that if individuals did not accommodate broader dietary changes, quality of life or symptom severity did not improve. So, the take away message? Low-FODMAP rye bread, in moderation along with other dietary changes, can

help with symptom reduction. Plus, it's a good way to increase fiber in your diet.

This is not an endorsement, but a reference of current literature. For more information on how you can modify your diet to help with symptom reduction, contact your health care provider or a registered dietician.

1. Halmos EP, Power VA, Shepherd SJ, Gibson PR, Muir JG. A diet low in FODMAPs reduces symptoms of irritable bowel syndrome. *Gastroenterology*. 2014 Jan;146(1):67-75. e5 PMID: 24076059
2. Laatikainen R, Koskenpato J, Hongisto SM, Loponen J, Poussa T, Hillilä M, Korpela R. Randomised clinical trial: low-FODMAP rye bread vs. regular rye bread to relieve the symptoms of irritable bowel syndrome. *Aliment Pharmacol Ther*. 2016 Jul 15. PMID: 27417338
3. Feast And Flatulence: How food choices may help your gi symptoms. Accessed 26July2016 <http://www.med.unc.edu/ibs/professional-training/digest/digest-folder/winter2014>

## INAUGURAL GASTROPARESIS AWARENESS MONTH

This year was the inaugural year for August being recognized as Gastroparesis Awareness Month. Many clinicians, patients, and patient advocates lobbied Congress and the House of Representatives and were successful at obtaining recognition.

For more information about Gastroparesis or which elected representative(s) were associated with recognizing August as Gastroparesis Month, you can visit IFFGD's website, <http://www.aboutgastroparesis.org/living-with-gastroparesis/gastroparesis-awareness-month.html> for more information.

## PATIENT SUBMITTED QUESTIONS ANSWERED BY UNC FACULTY AND FELLOWS



*Julia Hughes, MD*

*Dr. Hughes is a rising second year clinical fellow in the University of North Carolina Gastroenterology and Hepatology fellowship program. She graduated with a BA in Psychology from Boston College and*

*earned her MD from Tufts University. Subsequently, she completed Internal Medicine Residency and served as a Chief Resident at the University of North Carolina prior to starting fellowship training in Gastroenterology. Dr. Hughes's clinical interests include general and functional GI disorders, women's health, and medical education. She has also participated in research and published in the areas of IBD and Eosinophilic Esophagitis.*

**Question:** How does one know if they are experiencing abdominal pain along with FGIMD/FGID abdominal pain? Is there an effective diagnostic measure and/or treatment?

**Answer:** Visceral abdominal pain is a common feature of many functional GI disorders and refers to pain that is experienced as a result of stimulation of visceral nerves with activation of pain receptors in the abdomen. This type of pain is typically diffuse in nature, or difficult to localize to a particular area of the abdomen. In contrast, somatic abdominal pain refers to a more specific, localized pain in the abdomen, typically caused by an established organic etiology, such as an abscess, ulcer, or the later stages of acute appendicitis. Visceral hypersensitivity refers to the experience of heightened pain and discomfort in response to abdominal distension, tension, contraction, and pressure.

It often occurs in the absence of any identifiable organic cause. It also includes the complex interplay between the nerves supplying the abdomen and those of the central nervous system, including the brain. Thus, visceral hypersensitivity can be experienced as a result of an increased perception of pain or discomfort from various external or internal stimuli and can often be associated with abdominal distension, constipation, or diarrhea as in Irritable Bowel Syndrome (IBS). Additionally, visceral hypersensitivity may occur in response to eating.

While various diagnostic modalities, including the use of balloon distension of various portions of the GI tract, MRI, and PET scan following injection of

<sup>99m</sup>Tc pertechnetate isotope are being performed experimentally, there is no validated testing for the diagnosis of visceral hypersensitivity currently. Therefore, at present, diagnosis hinges on the clinical evaluation of each individual patient, with the treatment plan tailored to the specific symptoms the patient is experiencing. For example, patients with visceral hypersensitivity associated with cramping and diarrhea may benefit from an antispasmodic medication with anticholinergic effects that will also decrease diarrhea. Conversely, a patient with visceral hypersensitivity in the context of bloating and constipation may benefit from a bowel regimen to help produce regular stools.

Functional Abdominal Pain Syndrome (FAPS) is a specific type of functional GI disorder in which chronic abdominal pain occurs in the absence of any structural abnormalities and is associated with a loss in daily functioning. In contrast to above, however, it is not associated with changes in bowel habits, abnormal gut motility, eating, or increased visceral pain/visceral hypersensitivity. In this condition, the primary driver of pain is thought to be an overactive central nervous system, which leads to an increased pain response associated with various cognitive and psychosocial components. This is often managed through both cognitive-behavioral and pharmacologic therapies, which are individualized and can be discussed with your doctor.

**Question:** Functional dyspepsia and Gastroparesis are very similar with their symptoms and treatments for symptom management. What are the most important distinguishing factors for diagnosis and treatment?

**Answer:** Functional Dyspepsia is characterized by a sensation of fullness after eating either prematurely or beyond what would be typically expected, or symptoms of epigastric pain or burning. These symptoms must be present in the absence of any identifiable organic, systemic, or metabolic disease that could otherwise explain these symptoms, such as H. pylori, Peptic Ulcer Disease, NSAID use, or Gastroesophageal Reflux Disease. Interestingly, there is no identifiable cause of dyspeptic symptoms in approximately 75% of patients. Initial treatment for Functional Dyspepsia typically consists of a trial of a once daily proton pump inhibitor (PPI), such as omeprazole or esomeprazole, for four to eight weeks. If symptoms continue to persist, it is then reasonable to initiate a tricyclic antidepressant (TCA) such as amitriptyline or desipramine. If symptoms fail to improve with this next step, then prokinetics such as metoclopramide may be a reasonable option, however potential side effects such as tardive dyskinesia need to be

carefully considered prior to initiation. Further treatment options, including psychological therapy, may need to be considered if symptoms are refractory beyond this.

In contrast to Functional Dyspepsia, Gastroparesis is the presence of delayed gastric emptying with symptoms of nausea, vomiting, early satiety after eating, bloating, and/or upper abdominal pain in the absence of mechanical obstruction. Mechanical obstruction must first be excluded via upper endoscopy and imaging studies such as a CT or MRI. Once obstruction is effectively ruled out, diagnosis is then established typically via a gastric emptying study, which will confirm slow emptying of the stomach. There are many conditions that can be associated with delayed gastric emptying, or gastroparesis, including Diabetes, previous gastric or thoracic surgery, various medications, neurologic disease, or post-viral autoimmune disease. Additionally, a number of cases of gastroparesis are due to unknown etiology. The initial treatment for gastroparesis should emphasize lifestyle modification, including stopping or limiting exacerbating

medications if possible, improving glycemic control in Diabetics, and dietary modification with smaller, more frequent, meals that are low in fat and high in soluble fiber. If these measures are unsuccessful, prokinetic agents such as metoclopramide should be considered. Cycled erythromycin can also be used cautiously, with careful monitoring for gastrointestinal toxicity, ototoxicity (toxicity to the ears/hearing), and QT prolongation, which may produce dangerous cardiac arrhythmias. Antiemetic therapies such as ondansetron and prochlorperazine and antihistamines such as diphenhydramine may have some utility in managing symptoms as well. In refractory cases, tricyclic antidepressants (TCAs), gastric electrical stimulators, and various endoscopic therapies such as percutaneous gastrostomy tube placement for decompression of the stomach or placement of a jejunal feeding tube to bypass the stomach can be employed. Surgery is rarely indicated, and it is typically limited to completion or subtotal gastrectomy in patients whose symptoms are thought to be related to the effects of a previous partial gastrectomy.

## LEGISLATIVE SUPPORT NEEDED TO HELP ADVANCE FUNCTIONAL GI HEALTH RESEARCH BILL

Did you know there is legislation pending in the U.S. House of Representatives that could help aid research efforts into the treatment of functional gastrointestinal disorders? H.R. 2311 "Functional Gastrointestinal and Motility Disorders Research Enhancement Act of 2015" was introduced into the 2015-2016 114th Congress.

This legislation is budget neutral, which means it does not ask for additional money in the budget.

- Expanding basic and clinical research into FGIMDs by implementing the research recommendations of the National Commission on Digestive Diseases,

- Providing support for the establishment of centers of excellence on FGIMDs,

- Supporting innovative approaches to educating health care providers and patients regarding strategies that improve patient-provider relationships and care,

- Directing the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) to provide the necessary funding for the continued expansion and advancement of the FGIMDs research portfolio, and

- Directing NIDDK and the Eunice Kennedy Shriver National Institute of Child Health and Human Development to expand research into FGIMDs that impact children.

So far, 11 representatives have cosponsored this important piece of legislation that has the potential to help many patients, including military veterans who developed a

chronic multisymptom illness (which includes IBS) or other functional gastrointestinal disorder due to deployments and stress. (<http://www.dha.org/advocate-change/veterans-issues>)

|                                 |                      |
|---------------------------------|----------------------|
| Rep Sensenbrenner, F. James Jr. | [R-WI-5]             |
| Rep. Carson, Andre              | [D-IN-7] 06/11/2015  |
| Rep. Lofgren, Zoe               | [D-CA-19] 06/25/2015 |
| Rep. Moore, Gwen                | [D-WI-4] 09/08/2015  |
| Rep. Young, David               | [R-IA-3] 11/30/2015  |
| Rep. Loebsack, David            | [D-IA-2] 12/08/2015  |
| Rep. Rothfus, Keith J.          | [R-PA-12] 12/11/2015 |
| Rep. Joyce, David P.            | [R-OH-14] 06/22/2016 |
| Rep. Duffy, Sean P.             | [R-WI-7] 06/28/2016  |
| Rep. Engel, Eliot L.            | [D-NY-16] 07/05/2016 |
| Rep. Pocan, Mark                | [D-WI-2] 07/06/2016  |
| Rep. Kind, Ron                  | [D-WI-3] 07/06/2016  |

Senator Thom Tillis (R) from North Carolina has written Stefanie Twist, Center Coordinator for UNC's Center for Functional GI and Motility Disorders, directly and stated "If HR 2311 comes before the Senate floor, I will carefully consider everything you have stated in making a decision on what is best for North Carolina and the country."

We need your help as patients, advocates, and health care providers to make this legislation pass the House of Representatives and continue onto the Senate floor. If your representative isn't listed, contact them today and ask them to cosponsor this important legislation now!

More information about the bill can be found at <http://bit.ly/29ARHnk>



## OPPORTUNITY TO SUPPORT

To donate to the Center, simply print this form, fill in the blanks, and mail to the address

below with your donation. Please be sure to let us know if you are making your contribution to the Alan Wayne Ducoff Memorial Research Fund or directly to the Center, and let us know if you DO NOT wish to be publicly acknowledged.

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Contributions from individual donors and grants from foundations and corporations are essential to enhancing and expanding the Center's comprehensive and multi-disciplinary approach to clinical care, research, training and education in functional GI and motility disorders.

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