# ifigd DigestiveHealth Matters

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**Evaluating Health Information Online** *Tips on How to Find Reliable Health Information Online* 

Medical Research & Industry Treatment News Plus a Special Report from the 2015 ACG Meeting

Five Low FODMAP Diet Pitfalls And What You Can Do to Avoid Them

Melissa's Gastroparesis Story From Patient to Advocate

INTERNATIONAL FOUNDATION FOR FUNCTIONAL GASTROINTESTINAL DISORDERS

Information. Assistance. Support.

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"It is under the greatest adversity that there exists the greatest potential for doing good, both for oneself and others."

– Dalai Lama



Our Unique Mission: The International Foundation for Functional Gastrointestinal Disorders (IFFGD) is a nonprofit education and research organization dedicated to informing, assisting, and supporting people affected by gastrointestinal disorders. IFFGD has been working since 1991 with patients, families, physicians, practitioners, investigators, employers, regulators, and others to broaden understanding about gastrointestinal disorders and support research.

International Foundation for Functional Gastrointestinal Disorders



PO Box 170864 Milwaukee, WI 53217 Toll-free (U.S.): 888-964-2001 Business: 414-964-1799 Fax: 414-964-7176 E-mail: iffgd@iffgd.org

www.iffgd.org www.aboutconstipation.org www.aboutibs.org www.aboutincontinence.org www.aboutgastroparesis.org www.aboutgerd.org www.aboutgimotility.org www.aboutkidsgi.org www.giresearch.org www.dha.org

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# **DigestiveHealth** Matters



# **Evaluating Health Information Online**

Compiled by: Tegan Gaetano, Program Director, IFFGD, Milwaukee, WI

A s information becomes increasingly available online, more and more people are turning to the Internet for answers to their health questions. A report by the Pew Research Center revealed that adults in the United States use online resources, including search engines and social networks, as significant sources of information about symptoms, treatments, and support.

There are millions of websites containing health-related information. Some of the information on these websites is reliable. Some of it is not. Some of the information is current. And, some is not. Telling the good from the bad can be a challenge, but the following guide can help you be better informed about the health information you find online.

#### Who Wrote It? The Source

The first step in assessing the quality of health information found online is to consider the source. Any website that provides health information should make it easy to learn the identity of the individual, company, or organization responsible for the site and its contents.

Information on the source can usually be found in an "About Us" or "Contact Us" section of the site or on the website's homepage. This section should also contain a way to reach the source or sponsor, including an email address, phone number, and/or mailing address. Many health and medical websites post information collected from outside sources. The original source should be clearly indicated.

Check also to see if a review panel or editorial board fact checks information before it is made available online and is listed somewhere on the website. These individuals should be experts in the subject at hand and should make any financial interests in the content clear.

If you are unable to find any of this information on the website, ask yourself the following questions:

- 1. Why was the page created?
- 2. What does the person or organization that runs the website stand to gain from the information provided?
- 3. Are they trying to sell me something?

#### The Funding

Creating and running a website cost money. The funding source of the website should be readily apparent. In many cases, the web address of the site itself can give you a hint about the type of organization that sponsors the information:

- .gov identifies a government agency
- .edu identifies an educational institution
- .org identifies professional organizations, such as scientific or research societies and patient advocacy groups

• .*com* identifies commercial websites, such as businesses, pharmaceutical companies, and sometimes hospitals

If you can identify who maintains and pays for the site, this will help you evaluate the purpose of the information they publish.

#### Quackery on the Web

Health quackery is all too common on the Internet. When assessing health information online, be on alert for these warning signs and remember the old saying, "if it sounds too good to be true, it probably is."

- Does the page advertise "breakthrough" remedies that propose a cure to a variety of disorders or that rely on a "secret ingredient"?
- Does the page use sensational language, such as lots of exclamation points?
- Does the page use overly "scientific" sounding language?
- Does the page make claims that cannot be validated elsewhere?

Taking everything you read with a healthy dose of skepticism will help you avoid the many health-related half-truths, scams, and myths that exist on the Internet.

For more information about quackery on the web, you can visit *www.quackwatch.org*. Quackwatch is an online resource guide to avoiding health fraud.

#### **How Current is It?**

Findings from ongoing research can change the established recommendations for diagnoses, procedures, and treatments. So, it's important to have the latest information on hand in order to make smart health choices.

Websites hosting health information should post the date the content was last updated or reviewed. This date is often found at the bottom of the page. If the date isn't listed, check to see if the page has a copyright line. This will tell you when the information was originally written. If the site contains a lot of broken pages or links, this is a good indication that the site is not regularly maintained and may not have up-to-date information.

While it's a good idea to look for the most current health information available, older information isn't necessarily useless. Older articles are often provided to give readers an historical view of a disorder and its treatments.

#### **Privacy and the Internet**

Websites routinely collect information on how visitors use their sites to assess what pages are most popular and to better tailor content to meet visitor needs. However, many health-related websites may ask visitors to "Subscribe" or "Become a Member". This is often done in order to collect donations or to share relevant information as it becomes available. It is generally a good idea to register with a different username and password combination than what you use for your personal email and any online bank or credit card accounts you might have. In other cases, "aggregate" information, such as date of birth, zip code, or gender, may be sold to third party companies. To ensure that your information is kept private, take time to read the website's policy on information sharing. This is often found at the bottom of the site's homepage.

If you are asked for personal information, be sure to find out how the information will be used. Also, do not give out your Social Security number! This is important because, sadly, there is fraud on the Internet. Even when not used fraudulently, your information may be used or sold by the website (sometimes without your knowledge or consent) depending on the site's information sharing policy.

Be careful when making purchases online. Websites without security may not protect your credit card or bank account information. Look for confirmation that the website has a "secure server" before purchasing anything on the Internet. And, be suspicious if a site asks for your credit card or banking information if you are not making a purchase or donation.

#### **A Final Word**

When looking for health information online, your greatest tool is your own common sense and good judgement. The Internet is home to websites on nearly every health topic, and you can find just as much misinformation, half-truths, and sensationalism as reliable information. Take some time to do your research before acting on any health information you find on the web. Lastly, don't count on any one source for your information. If possible, check several sites to confirm any information you find. A 2013 survey conducted by the Pew **Research Center's Internet and American** Life Project found that 35% of adults in the United States have used online information to diagnose a condition that they or someone they know might have. Of those individuals, 35% did not visit a clinician to obtain a professional opinion. While the Internet has made accessing health information easier than ever, it is not meant to take the place of a doctor's opinion. Make sure that you discuss your health concerns, along with any information you have gathered online, with a trusted clinician or other healthcare professional.

#### **Quick Checklist**

The following checklist can be used to help you make sure that the health information you find online is reliable.

- 1. Can you easily identify who sponsors and/or runs the website?
- 2. Does the site list contact information for the source or sponsor?
- 3. Can you find the date the information was written on or reviewed?
- 4. Is your privacy protected?
- 5. Does the website make claims that seem too good to be true?



# **Medical News from the 2015 ACG Meeting**

The following are some brief reports on research studies that were presented as abstracts at the 2015 American College of Gastroenterology (ACG) annual meeting, a conference for medical professionals.

The data and conclusions from these reports indicate new findings of possible treatments but *should be considered preliminary* until published in a peer-reviewed journal.

#### IBS

• A study of the intestinal bacteria (microbiota) of 83 patients with irritable bowel syndrome (IBS) and 24 healthy controls found that specific IBS symptoms (abdominal pain, discomfort, bloating, and changes in bowel habit) were associated with concentrations of different types of bacteria in the gut.

#### IBS-D

- Results of 2 double-blind, randomized, placebo-controlled Phase 3 studies involving a total of 2,428 patients with diarrhea predominant IBS (IBS-D) demonstrated that eluxadoline improved symptoms of abdominal discomfort and bloating, and reduced frequency of bowel movements and episodes of urgency and incontinence during the full 6 months of treatment.
- Repeat treatments (up to 2 repeat 2-week courses) of the antimicrobial drug rifaximin were not found to be associated with increased risk of infection among 2,579 patients who received repeat courses of the drug for treatment-resistant IBS-D.
- A national survey of 39,306 mostly female patients with IBS-D revealed that the disorder is associated with substantial direct healthcare costs compared with controls even after controlling for co-existing conditions. Those with IBS-D spent an average of \$2,696 more than their non-IBS counterparts annually.

#### **Chronic Constipation**

- A randomized, double-blind study of 62 patients with chronic constipation secondary to type 2 diabetes found lubiprostone to be safe and effective in increasing frequency of spontaneous bowel movements and decreasing colonic transit time compared with placebo.
- Among 115 patients with chronic constipation surveyed, a large number were found to engage in restrictive eating as a way to self-manage symptoms. Abdominal symptoms (i.e. bloating) more often predicted restrictive eating habits than bowel symptoms (i.e., straining, incomplete bowel movement).
- A survey of 105 mostly Caucasian patients with opioid induced constipation (OIC) revealed that 30% were not aware of the risks of OIC before starting opioids, 44% were unsatisfied with conventional treatments (i.e., stool softeners and osmotic and stimulant laxatives), 53% were unaware that prescription medications are available for the management of OIC, and 58% felt educational materials would help.

#### Gastroparesis

- The safety of domperidone was assessed in 21 mostly female patients with nausea and vomiting due to gastroparesis over a period of 6 months. The drug was not found to be associated with any cardiac or other adverse events.
- Gastric electrical stimulation (GES) was found to improve varying levels of abdominal pain in 53 patients with severe gastroparesis over a period of 3 years. The prevalence of abdominal pain was not found to differ between patients with diabetic and idiopathic gastroparesis in this population.
- A study of 8 patients with idiopathic gastroparesis (IGP) found that transcutaneous electroacupuncture (TEA), a method of stimulating acupuncture points (acupoints) without needles by using electrodes placed on the skin at acupoints, in synchronization with breathing is more effective than sham therapy in reducing nausea and improving gastric rhythms. This approach as potential as future therapy for treating symptoms of IGP. (A grant from IFFGD supported this study.) ■

## **Medical News Update**

#### FDA Announces Patient Advisory Committee on Medical Devices

The U.S. Food and Drug Administration (FDA) has announced the formation of their first-ever Patient Engagement Advisory Committee (PEAC) on medical devices. This panel of patients will provide input to the FDA on issues relating to medical devices, the regulation of devices, and their use by patients. This effort continues the FDA's increasing interest in obtaining the perspective of the patient when making decisions about the development of new therapies intended to improve patients' lives.

Source: FDA. September 2015.

#### Prucalopride Effective for Men with Chronic Constipation

A randomized, double-blind, controlled Phase 3 clinical trial of 374 male patients with chronic constipation found the drug prucalopride to be more effective than placebo in increasing the number of spontaneous bowel movements and improving quality of life over a study period of 12 weeks. Prucalopride has previously been demonstrated to alleviate symptoms of chronic constipation in women.

The treatment was well tolerated and had an acceptable safety profile. While currently licensed in Europe for the treatment of chronic constipation resistant to standard laxative therapy in women, prucalopride is not yet approved for use in the U.S. by the U.S. Food and Drug Administration (FDA).

Source: Yiannakou Y, et al. *Am J Gastroenterol*. May 2015.

#### Intestinal Tissue Differences in Individuals with IBS

A study analyzing tissue biopsy samples of the mucosal lining of the colon in 101 individuals with irritable bowel syndrome (IBS) and 20 healthy controls discovered cellular differences among individuals with IBS, which may help to provide future insight into the underlying mechanisms of the disease.

Source: Dothel G, et al. *Gastroenterology*. May 2015.

#### Reflux Symptoms Not Always GERD

A study of 106 individuals with typical reflux symptoms persisting despite treatment with proton pump inhibitors (PPIs), which limit acid secretion in the stomach, aimed to determine the underlying cause of reflux symptoms not responding to PPI therapy. The study found that approximately one-third of the patients suffered from disorders other than gastroesophageal reflux disease (GERD), predominantly functional heartburn, concluding that this explains, at least partly, why many patients will not benefit from acid inhibitory treatment.

Source: Herregods TVK, et al. *Neurogastroenterol Motil.* September 2015.

#### Novel Delivery System of Peppermint Oil Effective Therapy for IBS Symptoms

A 4-week randomized controlled study of 72 patients with irritable bowel syndrome with diarrhea (IBS-D) or mixed diarrhea and constipation (IBS-M) concluded that a novel peppermint oil formulation (IBgard) designed for sustained release in the small intestine is a safe treatment and more effective than placebo in providing rapid relief of non-constipated IBS symptoms.

Source: Cash B, et al. *Dig Dis Sci*. August 2015.

#### Amitriptyline Found to Relieve Some Symptoms of Functional Dyspepsia

Results of a randomized, double-blind, controlled clinical trial of 292 individuals with functional dyspepsia (FD) found the antidepressant amitriptyline to benefit some patients with FD more effectively than placebo, particularly those with ulcer-like (painful) FD, but not those with delayed gastric emptying or early fullness with meals (dysmotility-like FD).

Further research is needed to determine the therapeutic role of tricyclic antidepressants, including amitriptyline, in the treatment of FD.

Source: Talley NJ, et al. *Gastroenterology*. August 2015.

#### Annual Costs of Care for Pediatric IBS and Functional Abdominal Pain

A study of children in the Netherlands concluded that pediatric irritable bowel syndrome (IBS) and abdominal pain related functional gastrointestinal disorders impose a large economic burden on patients' families and healthcare systems. Inpatient and outpatient healthcare use plus parental productivity loss accounted for over threefourths of total annual costs.

Source: Hoekman DR, et al. *J Pediatr*. August 2015.



#### Neuronal and Structural Changes Identified in Individuals with Functional Dyspepsia

Tissue biopsies taken from the first part of the small intestine (duodenum) in 18 individuals newly-diagnosed with functional dyspepsia (FD) and 20 healthy controls revealed abnormalities in the cell structure and signaling of patients with FD, which may provide insight into the diagnosis of this condition.

Source: Cirillo C, et al. *Am J Gastroenterol*. August 2015.

#### Survey Finds that Patients Lack Access to Digital Health Tools

A survey of more than 5,000 adult Americans revealed that most are unaware of or don't have access to technology that could be used to communicate with their physician and health care team for better quality healthcare. Among the key findings of the survey were that just 14% have round-the-clock access to medical advice, 15% use email to communicate with their provider, only 1 in 5 have access to online appointment scheduling, and less than half of individuals polled receive even the traditional telephone appointment reminder.

Source: Council of Accountable Physician Practices (CAPP) and the Bipartisan Policy Center (BPC). November 2015.

#### Hypnotherapy for Esophageal Disorders

A published article reviewed the use of esophageal-directed hypnotherapy for the treatment of dyspepsia, globus sensation (lump in the throat), heartburn, non-cardiac chest pain, and dysphagia (difficulty swallowing) in patients where other therapies have been inadequate. In constructing a treatment plan for patients who will likely benefit from the hypnotherapy, researchers at Northwestern University have utilized structured, scripted protocols for most of these conditions. The authors conclude that in addition to an initial medical workup, hypnotherapy to manage disorders of the esophagus appears to be a viable consideration for the treatment of appropriate candidates.

Source: Riehl ME, et al. *Am J Clin Hyp*n. June 2015.

# Prescription Drug Use on the Rise in the U.S.

A survey of prescription drug use in the United States between 1999 and 2012 among 37,959 adult individuals revealed an increase in overall use as well as an increase in the simultaneous use of 5 or more prescription drugs even after accounting for changes in the age distribution of the study population. Drug classes that saw the greatest increases in use included antihyperlipidemic agents, antidepressants, prescription proton-pump inhibitors (PPIs), and muscle relaxants.

Source: Kantor ED, et al. *JAMA*. November 2015.

#### Ramosetron Found to Reduce Symptoms of IBS-D in Women

Ramosetron was demonstrated to reduce symptoms of abdominal pain and discomfort and improve stool consistency and quality of life better than placebo in a randomized, double-blind study of 576 female patients with diarrhea predominant irritable bowel syndrome (IBS-D) in Japan over a period of 12 weeks. While ramosetron is approved for the treatment of IBS-D in men in Japan, this demonstrates its efficacy in treating IBS-D in women. Constipation was the most common adverse effect of the drug.

Source: Fukudo S, et al. *Gastroenterology*. November 2015.

#### IBS Associated with Erectile Dysfunction

Incidence of erectile dysfunction (both of physiologic and psychologic origin) was found to be considerably higher among the 15,533 male individuals with irritable bowel syndrome (IBS) surveyed from the Taiwan National Health Insurance Program compared with 62,124 healthy controls. Other factors associated with an increased risk of erectile dysfunction included increasing age, higher income, living in urban areas, and co-existing kidney disease, diabetes, hyperlipidemia, and the use of antihypertensive drugs, antidepressants, and benzodiazepines.

Source: Hsu CY, et al. *Int J Impt Res*. October 2015.

#### Assessment of Long-Term GES in Children with Gastroparesis

A long-term study of gastric electrical stimulation (GES) in 97 mostly female patients with gastroparesis concluded that the therapy is safe and effective for certain children and adolescents with treatmentresistant gastroparesis who experienced improvement with GES in their symptoms for at least a full year.

Source: Islam S, et al. *J Pediatr Surg*. October 2015. ■



## **IFFGD INDUSTRY COUNCIL**

hen IFFGD began in 1991 there was little communication between patients living with functional GI and motility disorders and the companies with the means to develop treatment products and services. Subsequently, IFFGD has worked hard to make the needs of our members known – not only to the clinicians who see patients, but also to the researchers and providers of diagnostic and treatment methods and tools.

In an effort to strengthen our voice, in 1998 we formed the IFFGD Industry Council. The Council provides a forum to help ensure that the voice of our membership is heard. We invite participation from companies with a demonstrated interest in these disorders. While we are grateful to our Industry Council members for their support, we do not endorse any specific product or company. IFFGD retains unrestricted control over the planning, content, objectives, methods, and execution of all initiatives and projects.

#### **IFFGD INDUSTRY COUNCIL**

Valeant Pharmaceuticals International, Inc.

Sucampo Pharmaceuticals, Inc. and Takeda Pharmaceuticals USA, Inc.

Shire

**QOL Medical, LLC.** 

Ironwood Pharmaceuticals, Inc.

Entera Health, Inc.

Allergan

#### Linaclotide for Treatment of IBS-C

Linaclotide, a guanylate cyclase type-C (GC-C) agonist, is a prescription drug used to relieve symptoms of abdominal pain, discomfort, bloating, and bowel symptoms in people who have irritable bowel syndrome with constipation (IBS-C) or chronic idiopathic constipation (CIC). It has been shown to be safe and effective in trials. It works by increasing the amount of fluid that flows into the bowel, allowing stool to pass more easily, and reducing abdominal pain.

Linaclotide (Linzess) has been available in the U.S. to treat IBS-C and CIC in adults aged 18 and older since 2012. It is currently available in several European countries with the EU brand name Constella.

Linaclotide should *not* be used in patients 17 years of age or younger or in patients with known or suspected mechanical gastrointestinal obstruction. The most common side effect reported during clinical studies was diarrhea.

Linaclotide is being co-produced in the U.S. by Ironwood Pharmaceuticals and Allergan. Ironwood has out-licensed linaclotide to Almirall, S.A. for development in Europe; to Astellas Pharma for development in Japan, Indonesia, Korea, the Philippines, Taiwan, and Thailand; and to AstraZeneca in China.

#### Positive Results Announced for Phase 3 Clinical Trial of Linaclotide in Japan

In December 2015, Astellas Pharma Inc. and Ironwood Pharmaceuticals announced that the Phase III clinical trial of linaclotide conducted in Japan in adults with IBS-C met its primary endpoints. Astellas expects to submit a new drug application to the Ministry of Health, Labor, and Welfare in Japan in 2016.

Linaclotide is currently approved in the U.S. for the treatment of adults with IBS-C and CIC. It is also approved for adults with IBS-C and CIC in more than 30 other countries.

#### Positive Results Announced for Phase 3 Clinical Trial of Linaclotide in China

In July 2015, Ironwood Pharmaceuticals and AstraZeneca Pharmaceuticals announced positive results of a Phase 3 clinical trial of linaclotide in China. Approval of the drug for marketing and distribution in China by the China Food and Drug Administration (CFDA) is pending. Linaclotide has met all primary and secondary endpoints, including multiple abdominal and constipation symptoms in all six of its Phase 3 and Phase 3b trials.

Linaclotide is currently approved in the U.S. for the treatment of adults with IBS-C or CIC and in a number of other countries for adults with IBS-C.



#### Seeking Participants with Chronic Idiopathic Constipation for Trial of Linaclotide

**Purpose of study:** This 12-week, Phase 3 study will assess the efficacy and safety of linaclotide in patients with chronic idiopathic constipation (CIC).

**Sponsor:** Ironwood Pharmaceuticals, Inc.

Collaborator: Forest Laboratories

**Participation:** Eligible male and female patients demonstrating CIC aged 18 and older

**Contacts:** Find a recruiting location online at *ClinicalTrials.gov*; Refer to this study by its *ClinicalTrials.gov* identifier: NCT02291679

#### Pediatric Patients with IBS-C Sought for Treatment Study

**Purpose of study:** The purpose of this multicenter, randomized, controlled Phase 2 study is to evaluate the safety and efficacy of linaclotide for the treatment of irritable bowel syndrome with constipation (IBS-C) in children ages 7–17 years. The study will last about 9 to 12 weeks, including up to a 4-week Screening Period and a 2 to 3-week Pretreatment Period.

**Sponsor:** Forest Laboratories

**Participation:** Male and female patients ages 7 to 17 years who meet inclusion criteria, including Rome III symptoms criteria for child/adolescent IBS and for modified Rome III criteria for child/ adolescent functional constipation.

**Contacts:** Cami Jamison, phone: 866-369-5227. Refer to this study by its *ClinicalTrials.gov* identifier: NCT02559817.

#### Pediatric Patients with Functional Constipation Sought for Treatment Study

**Purpose of study:** The purpose of this multicenter, randomized, controlled Phase 2 study is to evaluate the safety and efficacy of linaclotide for the treatment of functional constipation in children ages 6–17 years. The study will last about 9 to 12 weeks, including up to a 4-week Screening Period and a 2 to 3-week Pretreatment Period.

Sponsor: Forest Laboratories

**Participation:** Male and female patients age 6 to 17 years who meet inclusion criteria, including Rome III symptom criteria for child/adolescent functional constipation.

**Contact:** Cami Jamison, phone 866-369-5227. Refer to this study by its *ClinicalTrials.gov* identifier: NCT02259570.

#### Medical Food in the Management of Diarrhea

EnteraGam<sup>™</sup> is a prescription *medical food* product to help people manage ongoing problems with chronic loose and frequent stools (diarrhea). Medical foods are required to be used under physician supervision as part of ongoing medical care for a specific condition or disease.

EnteraGam is manufactured and distributed by Entera Health, Inc. It is indicated for the clinical dietary management of intestinal disease (enteropathy) in patients who, because of therapeutic or chronic medical needs, have limited or impaired capacity to ingest, digest, absorb, or metabolize ordinary foodstuffs or certain nutrients.

The main ingredient in EnteraGam is a specially formulated protein preparation

that consists of more than 50 percent of immunoglobulin (molecules involved with immune function). This ingredient, SBI (serum-derived bovine immunoglobulin/ protein isolate), is made up of beef serum proteins. The proteins in SBI remain in the intestine and are not absorbed whole. EnteraGam is contraindicated for patients with a hypersensitivity (allergy) to beef, or any components in EnteraGam.

#### SBI may Improve IBS Symptoms

Researchers in a small study that followed 14 patients with various forms of irritable bowel syndrome (IBS: 2 IBS-C, 7 IBS-D, 2 IBS-Mixed, and 3 IBS-Undefined) concluded that SBI (EnteraGam<sup>™</sup>) as a medical food provides a safe option for patients with IBS with diarrhea (IBS-D), but may have application in other forms of IBS. Twelve of the fourteen patients indicated some level of overall improvement within 4 weeks after the addition of SBI to their standard therapy. The study results were published in March 2015 in the *World Journal of Gastroenterology*.

#### Review Looks at Effects of SBI on Managing Conditions like IBS-D

A review, which summarizes accumulated data from prior studies, concluded that specially formulated immunoglobulin sources like SBI have multiple effects which collectively serve to improve and maintain nutrient utilization, including water balance. This aids in the management of intestinal disorders (enteropathy) in patients with chronic loose and frequent stools in conditions like IBS-D.

The mode of action appears to be combined effects on inflammation, gut barrier function, and immune balance. The study review, by Petschow et al, was published in August 2014 in the journal, *Digestive Diseases and Sciences*. The authors are employed by Entera Health.

#### Study Evaluates Impact of SBI in People with IBS-D

Results from a randomized, double-blind, placebo-controlled pilot study suggest that nutritional therapy with SBI, the ingredient found in EnteraGam<sup>TM</sup> – used in addition to traditional medical care – can help manage various symptoms associated with IBS-D. The study, by Wilson et al., was published in 2013 in the journal, *Clinical Medicine Insights: Gastroenterology*.

A total of 45 persons completed the study per the protocol, with 31 in the SBI group and 14 in a placebo group. The symptom profile of each participant was determined during the first week, followed by a sixweek treatment period. The safety profile of SBI in the study was similar to that of placebo.

The study showed that nutritional therapy with either 10 g/day or 5 g/day of SBI in patients was well tolerated and resulted in statistically significant improvements in days with symptoms and a trend for improvement in symptom severity scores in participants with IBS-D. In particular, the 15 participants who received 10 g/ day of SBI showed significant reductions in abdominal pain, loose stools, bloating, flatulence, and urgency.

#### Participants Sought for Congenital Sucrase-Isomaltase Deficiency (CSID) Genetic Prevalence Study in Children with Chronic Diarrhea or Chronic Abdominal Pain

Congenital sucrase-isomaltase deficiency (CSID) is a rare genetic disorder that affects a person's ability to digest the sugars sucrose and maltose. Sucrose is found in fruits, and is also known as table sugar. Maltose is the sugar found in grains.

In this study, clinicians are looking at using two different tests to rule out CSID, which often causes chronic diarrhea and/ or abdominal pain for at least 4 weeks, may qualify to participate in this study.

If your child is eligible, there is the potential for up to three doctor's office visits that could include: having the inside of cheeks swabbed to look for common CSID genetic mutations, taking a breath test, providing a medical history review, and completing a few questionnaires.

**Purpose of Study:** Determine the prevalence of CSID genetic variants in subjects 18 years of age or younger with a primary symptom of chronic idiopathic diarrhea or chronic abdominal pain without constipation.

Sponsor: QOL Medical, LLC

**Collaborators:** 19 Medical Centers located throughout the U.S.

**Contact:** Healther Elser, Ph.D., 919-832-4949, *helser@qolmed.com*. Refer to this study by its *ClinicalTrials. gov* identifier: NCT01914003.

#### **Eluxadoline Available in U.S.**

In December 2015, Allergan announced the availability of eluxadoline (Viberzi<sup>TM</sup>) by prescription in the U.S. for the treatment of diarrhea predominant irritable bowel syndrome (IBS-D). Eluxadoline is a twice daily, oral medication indicated for use by adults suffering from IBS-D.

#### FDA Approves Eluxadoline (Viberzi) for Treatment of IBS-D in Men and Women

On May 27, 2015 the U.S. Food and Drug Administration (FDA) approved eluxadoline (Viberzi<sup>TM</sup>), a new drug treatment for IBS-D in adult men and women. Viberzi is taken orally twice daily with food. The drug activates receptors in the nervous system that can lessen bowel contractions. Viberzi is a novel drug compound to treat diarrhea and abdominal pain associated with IBS-D. The safety and effectiveness of the drug for treatment of IBS-D were established in two double-blind, placebocontrolled clinical trials in which 2,425 patients were randomly assigned to receive the eluxadoline or placebo. Results showed Viberzi was more effective in simultaneously reducing abdominal pain and improving stool consistency than placebo over 26 weeks of treatment.

In clinical trials the drug was generally well tolerated. The most common side effects in patients treated with Viberzi were constipation and nausea.

The most serious known risk associated with Viberzi is the risk of spasm in the sphincter of Oddi, the smooth muscle that surrounds the end portion of the common bile and pancreatic ducts, which can result in pancreatitis. Viberzi should *not* be used in patients with a history of bile duct obstruction, pancreatitis, severe liver impairment, or severe constipation, and in patients who drink more than three alcoholic beverages per day.

Viberzi has mixed opioid receptor activity. It is a mu receptor agonist, a delta receptor antagonist, and a kappa receptor agonist.

The FDA recommended that Viberzi be classified as a controlled substance, and subsequently it was classified as a Schedule IV controlled substance.

#### Teduglutide Granted Orphan Drug Status in Japan

In January 2015 the Japanese Ministry of Health, Labor, and Welfare (MHLW) granted teduglutide (Gattex in the U.S.; Revestive in the E.U.) orphan drug status for the treatment of adult patients with short bowel syndrome (SBS).

#### Data Supports Long-Term Use of Gattex for Treatment of Short Bowel Syndrome

In June 2014 the U.S. Food and Drug Administration (FDA) approved updated labeling for teduglutide (Gattex) for injection to include long-term data from adult patients with SBS. The revised labeling provides important information for healthcare professionals and patients about long-term use of teduglutide.

The data, published in 2013, demonstrated that there was an increased response to treatment over time in all groups receiving teduglutide. The open-label extension study included 88 adult patients with SBS. Investigators reported that the long-term use of teduglutide in patients with SBS resulted in additional, clinically meaningful reductions in the volume and days per week of parenteral support requirements in this extension study. Thirteen patients in the study achieved complete independence from parenteral support with long-term teduglutide therapy. No new unexpected safety concerns were observed with long-term teduglutide treatment and the product's safety profile remains consistent with the product's label.

The drug works by regeneration of cells in the intestinal lining, slowing down transit through the gut and increasing blood flow, allowing for increased nutrient absorption.

In studies, the drug was associated with achieving and maintaining clinically meaningful reductions in parenteral nutrition (PN) and intravenous (IV) fluid volume in adult subjects with SBS.

Teduglutide was approved by the FDA as Gattex in 2012 for treatment of adult patients with SBS who are dependent on parenteral support. To help ensure that the benefits of the drug outweigh the risks for causing other serious conditions, the drug is approved with a Risk Evaluation and Mitigation Strategy, which patients need to discuss with their doctors. While the researchers found the safety profile to be acceptable, they advise that physicians closely monitor patients beginning the drug for side effects and possible need to adjust dosage.

SBS is a rare condition related to poor absorption of nutrients. It typically occurs in people who have a significant portion of their small intestine removed due to disease or injury.

#### Patients with SBS Sought for Long-term Study

**Purpose of Study:** This global clinical study is enrolling patients with short bowel syndrome (SBS) in order to provide additional long-term data on safety of teduglutide and on the natural history of SBS in patients in routine, real world settings. The information gathered is intended to assist health care providers in optimizing their clinical decision making in managing SBS patients.

Enrollment will include SBS patients treated and not treated with teduglutide.

Sponsor: Shire

**Study Population:** Male and female patients of any age with a diagnosis of SBS, including those who have never taken teduglutide, as well those who have or are using teduglutide.

#### Study Follow-up Duration: 10 years

**Contact:** Shire Clinical Operations; Phone: 908-450-5300; Email: *sbsregistry@quintiles.com*. Refer to this study by its *ClinicalTrials.gov* identifier: NCT01990040.identifier: NCT01990040

#### FDA Approves Rifaximin (Xifaxan) for Treatment of IBS-D in Adults

On May 27, 2015 the U.S. Food and Drug Administration (FDA) approved the antibiotic rifaximin (Xifaxan®) 550 mg for treating irritable bowel syndrome with diarrhea (IBS-D) in adult men and women.

The safety and effectiveness of Xifaxan for treatment of IBS-D were established in three double-blind, placebo-controlled trials. In the first two trials, 1,258 patients were randomly assigned to receive Xifaxan or placebo for 14 days, and then followed for a 10-week treatment-free period. More Xifaxan-treated patients reported improvements in abdominal pain and stool consistency than those on placebo.

A third trial evaluated repeat courses of Xifaxan, because patients with IBS-D can develop recurrent signs and symptoms after a single treatment course of Xifaxan. A total of 636 patients with recurrence were randomized to receive either Xifaxan or placebo for two additional 14-day courses separated by 10 weeks. More patients treated with Xifaxan than placebo were responders in abdominal pain and stool consistency in this phase of the study.

Xifaxan works by reducing or altering bacteria in the gut. It is only slightly absorbed in the gut and is generally tolerated well. The most common side effects in patients treated with Xifaxan for IBS-D include nausea and an increase in alanine aminotransferase (ALT), a liver enzyme measured in blood.

If diarrhea does not improve or worsens after treatment with Xifaxan, then evaluation for development of *C. difficile* enterocolitis should be performed. Caution should be used when using Xifaxan in patients with severe liver impairment or when combined with certain other drugs.

#### Guidance Issued in U.K. for Amitiza in Treating Chronic Idiopathic Constipation

The National Institute for Health and Care Excellence (NICE) has issued guidance on the use of lubiprostone (Amitiza) for treating chronic idiopathic constipation in the United Kingdom (UK). The guidelines stipulate that the drug should only be considered in adults who have tried at least 2 laxatives at the highest tolerated recommended doses for at least 6 months, but who have not seen an improvement in their symptoms. NICE clinical guidelines are recommendations on the appropriate treatment and care of people with specific diseases and conditions within the National Health Service (NHS) in the UK.

#### Lubiprostone Study Published Showing Efficacy in Opioid-Induced Constipation

A study published in 2014 in the medical journal *Pain Medicine* examined the efficacy and safety of lubiprostone (Amitiza) for relieving symptoms of opioid-induced constipation (OIC) in chronic non-cancer pain. The study found that patients treated with lubiprostone showed significant overall improvement for abdominal discomfort, straining, constipation severity and stool consistency when compared to placebo. The authors concluded that lubiprostone was effective and well tolerated in OIC patients with chronic non-cancer pain.

Lubiprostone is a prescription drug first approved by the U.S. Food and Drug

Administration (FDA) in 2006 to relieve abdominal pain, bloating, and straining and produce softer and more frequent bowel movements in men and women who have chronic idiopathic constipation (CIC). It is also FDA approved to treat irritable bowel syndrome with constipation (IBS-C) in women who are at least 18 years of age. Lubiprostone works by increasing the amount of fluid that flows into the bowel and allowing the stool to pass more easily.

The drug was FDA approved in 2013 for the treatment of OIC in patients with chronic, non-cancer pain. Opioids (such as morphine and codeine) are narcotics used to treat pain. The effectiveness of lubiprostone has not been established in those taking methadone. A number of gastrointestinal (GI) symptoms are potential side effects of using opioid-based medications. The most common symptom is constipation. Other symptoms may include decreased gastric emptying, abdominal cramping, spasm, bloating, and delayed-GI transit.

#### Two Studies of Lubiprostone in Pediatric Subjects with Functional Constipation

**Purpose of study 1:** This is a 12-week study to evaluate the efficacy, safety, and pharmacokinetics of oral lubiprostone as treatment for pediatric patients with functional constipation.

**Collaborators:** Sucampo Pharmaceuticals, Inc. and Takeda Pharmaceuticals USA, Inc.

**Participation:** Eligible male and female patients aged 6–17 years.

**Contact:** Shadreck Mareya, Ph.D., phone: 301-961-3400, email: *pedgen@sucampo*. com; Refer to *ClinicalTrials.gov* identifier: NCT02042183.

**Purpose of study 2:** This is a 9-month study to evaluate the long-term safety, efficacy, and pharmacokinetics of oral lubiprostone as treatment for pediatric patients with functional constipation.

**Collaborators:** Sucampo Pharmaceuticals, Inc. and Takeda Pharmaceuticals USA, Inc.

**Participation:** Eligible male and female patients aged 6–17 years.

**Contact:** Shadreck Mareya, Ph.D., phone: 301-961-3400, email: *pedgen@sucampo.com*; Refer to *ClinicalTrials.gov* identifier: NCT02138136.

#### Seeking Participants with Diabetic Gastroparesis

**Purpose of Study:** To assess the safety of IW-9179 in individuals with diabetic gastroparesis and its effects on the principal symptoms of diabetic gastroparesis.

Sponsor: Ironwood Pharmaceuticals, Inc.

**Study Population:** Eligible male and female patients over the age of 18 and with a diagnosis of type 1 or type 2 diabetes mellitus and a diagnosis of diabetic gastroparesis.

**Contacts:** Find a recruiting location online at *ClinicalTrials.gov*; refer to *ClinicalTrials.gov* identifier: NCT02289846. ■





# Five Low FODMAP Diet Pitfalls (and What You Can Do to Avoid Them)

By: Patsy Catsos, M.S., R.D.N., L.D., Private Practice Dietician and Co-Author of IBS-Free Recipes for the Whole Family

People with functional gut symptoms have known for years that food choices can impact symptoms. Yet, common diet advice (such as to eliminate red meat and spicy foods and add highfiber foods and increase fluids) often fails to deliver relief. Cathy F., a 55-year old client of mine, had constipation predominant irritable bowel syndrome (IBS-C) for years. As a result, she suffered from hemorrhoids, anal fissures, and a rectocele, for which she'd had several surgeries. Her well-meaning doctors recommended a high-fiber diet. Cathy did her best for many years to follow this advice, and her regular diet included bran cereal for breakfast every day, apples for soluble fiber, fiber-fortified breads and bars, and large portions of nuts. She kept a food and symptom diary for years, yet was unable to spot individual food triggers.

FODMAP is the acronym for a group of osmotically active, rapidly fermentable, shortchain carbohydrates. It stands for Fermentable Oligo- Di- and Monosaccharides and Polyols. Examples of FODMAPs are lactose, fructose, sorbitol, mannitol, fructooligosaccharides, and galactooligosaccharides. The concept originated with scientists at Australia's Monash University.

I suggested Cathy try a short dietary experiment: a FODMAP elimination diet. This is a new evidence-based approach to helping people with IBS identify which foods are well-tolerated and which foods are not. *The FODMAP elimination diet is a process, not a list of acceptable foods.* She began by eliminating high FODMAP foods from her diet for a few weeks. Then she followed a detailed plan that we created together to reintroduce each type of FODMAP back into her diet one at a time, monitored her symptoms, and adjusted her diet accordingly.

FODMAPs are an irresistible topic for bloggers, social media, and mainstream print media, with some of the best hooks an editor could want: *What Your Doctor Never Told You, An Apple a Day* – *Not, Australian Researchers Discover New Diet Secret*, and so on. Unlike many other diets making headlines, the low-FODMAP diet does have a developing body of solid research to back it up. Studies have shown it can help up to 85% of well-selected patients with IBS achieve relief of their symptoms. But, it isn't right for everyone.

"The FODMAP elimination diet is a process, not a list of acceptable foods."

Have you been thinking about trying a low FODMAP diet, or have you already started? If you do decide to try it, be sure to avoid these common low FODMAP diet pitfalls:



#### Starting the Diet Without Medical Advice

Don't diagnose yourself with IBS. Start with your primary care provider (PCP) to discuss your symptoms, diagnosis, and treatment. If necessary, your PCP will refer you to a gastroenterologist. Once you have a confirmed diagnosis of IBS, seek out a registered dietician with FODMAP experience, if available. Most physicians don't have the time or skills to perform a thorough nutrition assessment. In my practice I find some people are not good candidates for an elimination diet, particularly those at risk for eating disorders, those with little control over their food (such as people living in community situations), and those whose diet history reveals that they are already following an instinctively-determined low FODMAP diet. If there are many foods you can't eat due to other medical conditions, inflexible food preferences, or your food philosophy, you will need extra help meeting your nutrient needs on a low FODMAP diet.

#### **Expecting Too Much**

It's important to have realistic expectations about what FODMAPs can do for you. Leaning more about how your body reacts to FODMAPs can empower you to manage your IBS more effectively. How important is that? Ask Cathy, who revealed at our second visit, "Until now, I never knew what it felt like to be normal." However, since FODMAPs themselves are *not* the root cause of IBS, eliminating them won't cure the condition. Though most people eventually return to a modified version of their preferred diet, there will probably be some foods you must learn not to overdo.

#### **Changing Everything at Once**

If you are changing your diet, medications, and supplements all at the same time, how will you know what worked? You will learn more from the FODMAP elimination and reintroduction process if you keep the rest of your regimen stable for a few weeks while you experiment. Work with your other health care providers to negotiate this, perhaps delaying proposed new prescription medications or supplements until after the first few weeks on the diet. If you are to be treated with antibiotics for small bacterial intestinal overgrowth (SIBO), it is often best done immediately before beginning a low FODMAP diet.

> Learning more about how your body reacts to FODMAPs can empower you to manage your IBS more effectively.

#### **Over-Limiting Your Diet**

Be sure to eat a wide variety of low FODMAP foods unless you have an important reason not to. For example, lactose is the only component of dairy products that must be avoided on a low FODMAP diet. Unless you are a vegan or are allergic to milk, you can continue to use low-lactose milk products such as aged cheeses and lactose-free yogurt on a low FODMAP diet. Likewise, oligosaccharides (certain fibers) are the component of soy or wheat that should be avoided on a low FODMAP diet. Processing methods that reduce oligosaccharides can make certain wheat or soy foods suitable for the diet. Authentically made sourdough bread and tofu, for example, are low FODMAP foods.

#### **Inadequate Fiber Intake**

Fiber intake can take a hit on a low FODMAP diet. That's not ideal, since fiber is an important food source for the good bacteria in our gut. In addition to producing gas, those gut bacteria perform other services important to human health. The solution is to deliberately increase your intake of fiber from low FODMAP foods: eat a wide variety of low FODMAP fruits and vegetables, low FODMAP grain and legumes, and small servings of low FODMAP nuts and seeds. Low FODMAP fibers are fermented more slowly and are less likely to disrupt fluid balance in the gut. See the chart accompanying this article for specific suggestions.

The last time I saw Cathy her symptoms were well controlled on a moderately low FODMAP diet. During the reintroduction process she discovered that lactose and oligosaccharides were significant symptom triggers for her, so she consumes low-lactose milk products only; sticks to small portions of foods like wheat, beans, and nuts; and gets more fiber from foods like quinoa and chia seeds. With choices like these, Cathy is avoiding common low FODMAP pitfalls and eating the most varied and nutrient-rich diet she can tolerate.

Adapted from IBS-Free Recipes for the Whole Family by Patsy Catsos, Lisa Rothstein, and Karen Warman and used by permission.

Food/Beverage	Portion	Fiber Grams (g)
Brown rice	1 cup prepared	3.5g
Corn pasta	1 cup prepared	6.7g
Low-FODMAP fruits (especially wild blueberries, kiwi, oranges, starfruit, papayas)	½ cup	2 – 8g
Low-FODMAP vegetables (especially butternut squash, cabbage, carrots, collard green, green beans, kale, okra, spinach, summer squash tomatoes, turnips, radishes)	½ cup	2 – 4.8g
Low-FODMAP nuts (almonds, peanuts, walnuts, pecans, brazil nuts, pine nuts)	2 tablespoons	1 – 1.6g
Low-FODMAP seeds (pumpkin, sesame, sunflower)	2 tablespoons	1 – 2.1g
Oatmeal	<sup>1</sup> ∕₂ cup prepared	2g
Quinoa	1 cup prepared	5.2g
White potato (with skin)	1 medium	3.6g
Sweet potato (with skin)	½ cup	4.1g
Gluten-free bread (without added fiber)	2 slices	1g



# **Melissa's Gastroparesis Story: From Patient to Advocate**



n February 12, 2014 out of the clear blue, I found myself vomiting, in excruciating pain, and on the verge of collapse. Within the course of a week, I was hospitalized, put through a battery of unpleasant tests, diagnosed with gastroparesis, given only a brief explanation of this illness, and sent home. I had no idea how severe my condition was and honestly believed that if I could simply endure the first few weeks of a special diet (liquids only, followed by soft foods), I would be able to return to my "normal" life. I was stunned when I was unable to progress through the given dietary steps, and after a time, I realized that this would likely never occur. The illness I thought would be shortlived was instead chronic and incurable. In a desperate search for help, I turned to the Internet. And that is when I found the online gastroparesis community and began advocating for the people who, like me, have been left with little information and few solutions – people who struggle with this cruel disease every day of their lives.

I had never heard of gastroparesis and had limited involvement with the healthcare system prior to my diagnosis. So, as I became more and more involved in the groups, the lack of awareness and help for the gastroparesis community I discovered was shocking to me, to say the least. In addition to our daily struggle with physical symptoms, many in my community face a medical system that lacks knowledge and understanding of our condition. There are few reliable, effective medications/treatments available and little guidance regarding how to cope with this illness. There is sparse research and lack of funding for such research. There are also deep personal and emotional struggles within my community. Many have no one to fight for them and no one to comfort and support them. They have family members who do not understand, friends who have deserted them, and financial hardships.

My involvement with the support groups left a meaningful impression on me and a strong desire to persuade and empower others to fight for our community. As a result, about a year ago a few other group members and I formed a separate online advocacy group (https://www.facebook.com/groups/ Gastroparesis. Fighting for Change) where we could unite to promote awareness; better education of our community, friends, the medical world, and the general public; changes in legislation and policies; and other such efforts advantageous to our cause. Since our formation, we have grown to over 1,000 members and have become heavily engaged in letter-writing campaigns to elected officials, policymakers, healthcare providers, the media, and others to support efforts that might increase awareness and benefit our community in a tangible way.

We have made a huge push to persuade our elected officials to support bills such as The Functional Gastrointestinal and Motility Disorders Research Enhancement Act of 2015 (H.R. 2311), and we have begun petition drives to convince our policymakers to consider including gastroparesis as a disability and to establish a National Gastroparesis Awareness Month. We have also submitted several state-level proclamations for awareness weeks and currently have 13 of these approved and in effect. (We plan to continue this effort and hope to have proclamations in every state as well as in several cities). In addition, we have increased our online presence on Facebook, Twitter, and various medical/chronic illness sites and have even created our own website (*https://www.curegp.com*). We have held several online "Go Green for GP" events, produced a few videos, and participated in significant healthcare transformation efforts such as the Lown Institute's Right Care Action Week. We have made enormous strides and are pleased with our progress to date, but we hope to accomplish far more in the upcoming year.

We applaud IFFGD and the DHA for their efforts to bring attention to our illness and to the needs of our community. We seek to support and further such labors and hope to make 2016 a banner year for the gastroparesis community. We seek awareness, better treatments, and, ultimately, a cure. ■

#### For information about gastroparesis, visit IFFGD's website at www.aboutgastroparesis.org.



# INTERNATIONAL FOUNDATION FOR FUNCTIONAL GASTROINTESTINAL DISORDERS

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International Foundation for Functional Gastrointestinal Disorders IFFGD PO Box 170864 Milwaukee, WI 53217 Toll-free (U.S.): 888-964-2001 Business: 414-964-1799 Fax: 414-964-7176

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