



Digest

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

Nutritional Intervention for IBS

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Background

Prior to medical school when I was a practicing dietician, I had the privilege of working with many patients who had irritable bowel syndrome (IBS). I found the subject of nutritional intervention related to IBS to be very rewarding and often challenging because there is no “perfect” diet for this syndrome. In light of the different etiologies potentially at work in each patient with IBS, nutrition therapy should be carefully and thoughtfully tailored to each person. This can be likened to times past when a cobbler hand-made each person’s shoes. Since each IBS patient can differ dramatically, careful documentation of exacerbating factors listed in the IBS diary maintained by patients may yield important clues to an effective approach to diet and nutrition.

One of the issues is that patients with IBS may have a lower threshold to stressors compared to people without IBS. An example of this is patients with carbohydrate intolerances as well as a diagnosis of IBS, who experience an even greater response to problematic carbohydrates such as lactose or fructose as compared to someone who does not have IBS. Another important issue is being alert to unnecessary food aversions. Individuals may experience abdominal discomfort and associate this with eating a certain food, so they decide to avoid eating that particular item, even for life. This may lead to excessive food restriction and the potential for a full-blown eating disorder. What must be kept in mind is that IBS is characterized by increased gut and central nervous system (CNS) reactivity to stressors, and that these stressors can include any dietary excesses as well as

sensitivities to particular foods that are unique to the individual rather than to the IBS condition.

This article reviews some of the literature in this area and then presents some treatment options to be considered in the nutritional management of IBS. It should be noted that the research and peer-reviewed published literature regarding IBS and diet is still very limited and, therefore, some of the resources cited in this article will date back several years.

Nutritional Factors Influencing Motility: Fiber, Fat and Caffeine

IBS is the most common of the functional GI disorder, affecting approximately 10-15% of the US population (1). IBS is a multifactorial illness with several different emerging pathophysiologies, including disorders of motility, visceral hypersensitivity, central processing dysfunctions, psychological factors, and post-infectious inflammation.

Fiber: A recent survey reported that close to 95% of general practitioners believe that fiber deficiency is the main cause of IBS. In fact, the most common dietary advice offered to patients with IBS is for them to increase their intake of fiber, primarily to address the constipation that may be associated with IBS. However, since IBS is also associated with visceral hypersensitivity, luminal distension -- as might be caused by the bacterial fermentation of insoluble fiber -- can also produce discomfort (2).

Dietary fiber is a non-starch polysaccharide derived from plant foods that are poorly digested by human enzymes. A fiber-enriched diet can relieve constipation, accelerate intestinal transit time, and may reduce intracolonic pressure. Furthermore, the intake of fiber is associated with a reduction in the intraluminal concentration of bile acids, which may reduce the contractile activity of the colon (3, 4).

There are two types of fiber -- soluble and insoluble. Soluble fiber is derived from fruits and grains, and is fermented in the colon to form short

chain fatty acids. Good sources of soluble fiber include oats, psyllium seed, pectin, and guar gum. Insoluble fibers consist of the outer husk of the grain and generally tend to decrease transit time. The national nutrition guidelines recommend an intake of 20-30 grams of fiber per day, yet the typical American consumes less than 10 grams of fiber per day. Fiber intake should be increased gradually in IBS patients with constipation, with an emphasis on including adequate water consumption (5).

The overall fiber picture can become a bit more confusing than a simple recommendation to increase fiber intake. Insoluble fiber may have a high content of cereal bran, which is the outer husk of the grain. A recent paper investigated the effects of adding or omitting bran and found conflicting results. It appears the primary care provider may see a greater benefit from patients adding fiber to their diet than the gastroenterologist, possibly because primary care physicians see mostly milder forms of IBS and gastroenterologists see patients with more severe IBS. Whorwell studied 100 patients in a primary care setting that were encouraged to increase cereal bran. The results in the primary care provider scenario produced a "mixed" picture -- 22% reported worsening of IBS symptoms while 27% who showed improvement. This may be the result of visceral hypersensitivity triggered by bran consumption. Whorwell recommends that patients identified with IBS and visceral hypersensitivity should be counseled to exclude cereal (insoluble) fibers for a brief period to see if symptoms improve, especially if this is within the care of a specialty clinic. Another study found that cereal fibers were associated with a 55% worsening of symptoms (6, 7). Thus, if the goal is to increase transit rate and increase the frequency of bowel movements (for IBS-C), one could add insoluble fiber to the diet; however, since IBS is also associated with visceral hypersensitivity, if discomfort/pain or bloating occurs, the patient may need to switch solely to soluble fiber.

Caffeine is a gastrointestinal stimulant. For IBS patients with diarrhea, a period of caffeine

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The Center's co-directors are Dr. Douglas Drossman, MD, Professor of Medicine and Psychiatry, and Dr. William Whitehead, PhD, Professor of Medicine and Gynecology. For more information about the Center, please visit our website at www.med.unc.edu/ibs.

exclusion may prove beneficial. The total intake of caffeine-containing beverages by many adults and children often reaches levels that can induce pharmacological effects. Evidence associating caffeine with GI symptoms suffered by patients with IBS is limited in the current literature, but one study revealed that caffeinated coffee stimulated colonic motor activity in a magnitude similar to that of an entire meal and had a 60% stronger effect than ingesting water (8).

Dietary fat is also a potent modulator of gut motor function. This macronutrient delays gastric emptying time and accelerates small bowel transit rates. Symptoms of bloating are commonly reported after consuming a high-fat meal. Serra et al. found that after an infusion of enteral fat, the volume of retained gas increased from 298 to 505 ml (9, 10). For patients who need to limit their fat intake, counting actual fat grams in the diet can be an excellent way to identify high-fat food sources. In general, IBS patients should aim for only 40-50 grams of fat per day. If weight loss becomes an issue with fat restriction, medium chain triglycerides (MCT) are an excellent source of calories. Unfortunately, MCT oils are expensive and, due to taste issues, are generally not well-received by patients.

Food Allergy, Hypersensitivity and Intolerance

Although up to 45% of the population reports adverse reactions to food, the actual prevalence of immune-mediated food allergy is unknown. Symptoms are more common in atopic individuals who often have allergies to non-food antigens as well, such as pollens, and in young children who tend to outgrow an allergy. The role of food allergy in IBS has not been studied well. Surveys indicate that 40-70% of food-allergic patients report GI symptoms including nausea, vomiting, abdominal pain, bloating, and diarrhea. Stefanini et al. conducted a 4-week multi-center study comparing the efficacy of the mast cell stabilizing agent sodium cromoglycate at 1500 mg per day with an elimination diet, and 67% of the patients reported improvement in their symptoms (11).

Attempts to “test” for food hypersensitivity in IBS have largely focused on the classic food allergy, which is based on the presence of IgE -- immunoglobulins of the “immediate type”. These

antibodies attach to certain cells in the body that release chemicals that cause anaphylaxis. Present speculation in the literature suggests that adverse reactions to food in patients with IBS might be due to forms of immunological mechanisms other than a dietary allergy, namely IgG antibodies. These tend to have a delayed response following exposure to a particular antigen and have been implicated in some cases of food hypersensitivity. IgG studies surfacing in the IBS literature are promising, but the issue of the validation of serum IgG testing is often raised. Atkinson et al. observed significant improvement in IBS symptoms in elimination diets using Elisa IgG antibody testing. Their results suggest that IgG antibodies may have a role in helping patients identify candidate foods for elimination (12). Collins et al. also found significant change in patients receiving the IgG exclusion diet. The foods that were most frequently associated with elevated IgG levels were yeast, milk, eggs, wheat, cashew nuts, peas, almonds, and barley. The mechanism by which the IgG antibodies have a detrimental effect is unclear, but most likely is associated with low-grade inflammation (12,13). For the most part, most patients with IBS do not have immune-mediated allergies to food and, more likely, have increased sensitivity to the direct effects of food on digestive function including increased food volume ingestion and the addition of fats, caffeine, carbohydrates, alcohol, etc.

Food Intolerance and Exclusion Diets

Niec recently summarized the literature on clinical trials using food elimination diets followed by rechallenge. Of the seven studies included in their review, positive response rates varied from 15 to 75 percent. A higher rate of response was correlated with diarrhea-predominant IBS. Milk, wheat and eggs were the most frequently implicated foods (14). Although the principle of food elimination or exclusion appears straightforward, it can be very demanding for the patient. If the patient appears hesitant or confused about food choices, physician referral to a registered dietitian may be helpful. With the exclusion of entire food groups, such as dairy products, the risk of developing a nutritional deficiency must be considered.

Carbohydrate Malabsorption

Carbohydrate intolerance can be seen in many



patients with IBS. Fructose, lactose and sorbitol malabsorption are common among patients who have IBS, and dietary restriction of these sugars may improve symptoms (15,16). One study found that 42% of IBS patients developed symptoms from sorbitol-fructose mixtures compared to 3.5 % in the control group (18). This could be an important factor when patients are consuming large amounts of weight-loss products or have diarrhea-predominant IBS.

Lactose malabsorption occurs when lactose, the primary sugar in dairy products, is not completely digested and absorbed in the small bowel. Lactase, the enzyme required to hydrolyze lactose for intestinal absorption, is found primarily in the tips of the jejunum. When unabsorbed lactose reaches the colon, colonic bacteria uses this substrate for fermentation, producing gas and short chain fatty acids. The unabsorbed lactose also affects osmolality, causing water to be drawn into the bowel and accelerating the intestinal transit time. If lactose intolerance is suspected, it can be confirmed with a hydrogen breath test. Lactose intolerance appears to be dose dependant. This means that many patients can tolerate small amounts of dairy products throughout the day, such as ½ cup of milk, but not larger amounts.

Although it may seem obvious which foods contain lactose, some sources may be difficult to discern. Patients should look for hidden sources in baked goods, salad dressings, and powdered mixes. Labels with the following words contain lactose: nonfat dry milk, milk powder, dry milk solids, whey curds, and caseinate milk sugar. Contrary to popular belief, acidophilus milk does not have the lactose sugar digested and is, therefore, a poor substitute for regular milk. Soy milk and rice milk do not contain lactose and are, therefore, good dairy substitutes. However, these products are often low in calcium and vitamin D. Hard cheeses and cultured yogurt are usually acceptable alternatives. For patients who do not tolerate lactose but want to consume dairy products, supplemental lactase enzymes are available. Several studies have shown that patients with lactose intolerance have significantly less calcium intake than those who tolerate lactose. In one study, patients who were lactose intolerant had a calcium intake of approximately 300 mg per day (18), which is only 20-40% of the recommended calcium intake for adults. Patients

with lactose intolerance have also exhibited decreased bone mass density (19). In light of the potential for compromised calcium and vitamin D intake, it would be prudent to evaluate all patients with lactose intolerance for a calcium supplement if needed.

Fructose is a hexose sugar that is highly utilized in the western diet. In the past 20 years, there has been a 10-fold increase due to its use in highly processed food products. It is often used as high fructose corn syrup in soda, fruit juices, cookies, baked goods, jellies, and candy. Unlike glucose, which is completely absorbed, fructose absorption capacity is limited. Therefore, when ingested in small quantities, dietary fructose will probably not be an issue. However, when consumed in larger amounts, fructose may serve to osmotically draw fluid into the intestinal lumen. This may cause distension of the small intestine and produce symptoms such as abdominal pain, bloating and discomfort. Furthermore, after reaching the colon, unabsorbed fructose may be fermented by colonic bacteria, producing excessive gas (20).

Probiotics

Several studies now exist defining the potential role of probiotics in IBS. These papers have exhibited a great degree of variability, possibly due to the use of different probiotic strains, their ability to adhere and colonize in the GI tract, and the number of colony-forming units actually ingested by the individual. The probiotics most often studied are lactobacillus, bifidobacterium, and some non-pathogenic forms of e-coli. In a recent study, bifidobacterium 35624 significantly alleviated symptoms of abdominal pain and discomfort, bloating, and distension. There was also a normalization of IL-10/IL-12 ratios (this skewed cytokine ratio may be indicative of a proinflammatory Th-1 state). The bifidobacterium used in this study is currently unavailable in the US marketplace in the concentrations used in this study (21,22).

Food products that are high in probiotics include fermented milk, pourable yogurt, and yogurt with live active cultures. Currently, there is no federal agency in the US that routinely tests or “polices” the market to ensure standardization and quality of probiotic products. Independent tests have

revealed that up to 30% of probiotics on the market are “laced” with reasonably adequate live bacteria. One study used DNA extraction to test five probiotic products at a local health food store. The PCR analysis revealed that 2 of the 5 products did not contain the bifidobacterium claimed on the label (23). I called a well-known dairy in the Midwest several years ago. The technician responsible for mixing the probiotic in the yogurt explained that the bacteria are added to a very large vat of product. The yogurt is then packaged in individual cartons and there is no final definitive measurement to ensure that the amount of probiotic stated on the label is actually in each individual container.

Putting It All Together

Due to the complex underlying pathophysiologies in patients with IBS, nutritional intervention will vary with each patient. The following general IBS categories attempt to help “map” an approach for dietary manipulation in the patient with IBS. For individuals with diarrhea predominant IBS, consider limiting nutrients that exacerbate GI motility or intestinal secretion -- caffeine, fat and some carbohydrates (fructose, lactose and alcohol sugars). Probiotics can also be of benefit, especially if post-infectious IBS or bacterial overgrowth is suspected, or the patient has had numerous antibiotic therapies in the past. If constipation is the main issue, make sure the patient has had an adequate trial of increased insoluble fiber. This usually means that the patient needs to count fiber grams and seek to attain 20 grams of fiber per day. When visceral hypersensitivity is suspected, ask the patient to limit the amount of food eaten in one session and instead to eat three small meals per day with snacks. A low-fat diet and avoidance of insoluble fiber may also be helpful for these patients.

Targeting nutritional intervention in the patient with IBS can be challenging due to the many different etiologies of this syndrome and the fact that some patients have heightened responses to different foods. A food diary kept by IBS patients can be a particularly helpful way to ascertain which foods may be problematic. It is recommended that the clinician look for food “trends” in the journal, with the goal of steering the patient away from excessive food restriction behaviors.

Note from the author: I would like to thank Dr. Drossman and the UNC Gastroenterology & Hepatology Department for the incredible hospitality and generosity of spirit that I experienced while I visited this fall. The clinicians’ provision of patient care at the UNC Center for Functional GI & Motility Disorders is among the best I have seen. It was a privilege to work with Dr. Drossman and his staff - my ability to practice medicine and care for patients in the future will be greatly enhanced by the time I spent here.

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Patient Symposium 2006

Understanding IBS and Other Functional GI Disorders

Saturday, July 15, 2006
The William and Ida Friday Center, Chapel Hill, NC

The UNC Center for Functional GI & Motility Disorders is hosting a Patient Symposium on Saturday, July 15, 2006. The theme is Understanding IBS and Other Functional GI Disorders. The symposium will be held at the William and Ida Friday Center for Continuing Education, in Chapel Hill, North Carolina.

The registration fee is \$25.00 and includes all plenary sessions, breakout sessions, lunch, refreshment breaks, and printed materials. Registration begins at 8:00am. The program runs from 8:30am until 5:30pm.

There will be Q&A sessions following plenary sessions as well as breakout sessions at the end of the day, providing plenty of opportunity for questions and answers with the symposium faculty.

Plenary topics (tentative):

- » **What is a functional GI disorder**
- » **Types of IBS and risk factors**
- » **Diagnosis and tests for IBS**
- » **IBS medications – effective treatments and new options**
- » **Behavioral and alternative treatments – CBT & other relaxation therapies, hypnosis, biofeedback**
- » **How to talk with your doctor**
- » **New leads in the biology of IBS**
- » **IBS diet and nutrition**
- » **Pediatric functional GI disorders**
- » **Incontinence, constipation, bloating**
- » **Functional dyspepsia and other upper GI symptoms**

Registration Form – Patient Symposium 2006

_____	Name	
_____	Street Address	_____ Primary Phone
_____		_____ Secondary Phone
_____	City	_____ State / Province
_____	Email	_____ Postal / Zip Code

Registration fee is \$25.00. Payment is due with registration, either check or credit card. **Pre-registration deadline is July 1, 2006.**

To register, make your check payable to:
UNC Center for Functional GI & Motility Disorders

OR: Include the following credit card information

If you prefer to phone in your credit card information or have any questions, please call Kirsten Nyrop at (919) 966-0289.

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Please mail the completed registration form (with your check or credit card information) to:
Kirsten Nyrop, Center Coordinator, UNC Center for Functional GI & Motility Disorders, CB 7080 Bioinformatics, Chapel Hill, NC 27599-7080



Mary Ann Bella

Defining IBS

By Mary Ann Bella

Several years ago, a business associate told me she had been diagnosed with Irritable Bowel Syndrome. She was in good health, yet had frequent bouts of severe abdominal pain and diarrhea. Her doctor prescribed a low dose

antidepressant and told her to avoid dairy products and other fatty foods.

I had never heard of IBS and was puzzled. As a producer of medical videos, I was accustomed to hearing about laboratory indicators that defined an illness, yet she did not seem to have any. And, I wondered how could an antidepressant help diarrhea?

After extensive research and interviews, I now know that people with IBS suffer from what author Carol Sveilich calls “invisible chronic illness and pain.” People with IBS live with a brain-gut dysfunction that causes symptoms, yet does not show up on laboratory tests.

“Motility studies can help characterize these symptoms, but they are not sufficient for the diagnosis,” says Dr. Douglas Drossman, a leading IBS researcher and co-director of the UNC Center for Functional GI & Motility Disorders. “What makes the diagnosis of IBS is the very characteristic symptom pattern that these patients have, and it is the same pattern anywhere in the world.”

IBS is characterized by abdominal pain that must be associated with some change in bowel habit, which could be diarrhea or constipation or some mixture or combination of the two. It is a life-long illness that is not curable and there is no single medicine to treat all of the symptoms. IBS can be difficult to manage, particularly in severe and alternating constipation-diarrhea patients.

“Antidepressants are prescribed primarily for their analgesic effect to block pain signals from the bowel and also, when needed, to alleviate depression,” Dr. Drossman says. Depression may result from years of unpredictable IBS attacks and levels of pain that some compare to labor during childbirth and others describe as a sharp, jabbing ice pick to the loins.

“You have these plans, but that day you’re supposed to leave and you get these stomach cramps and you don’t go to the bathroom and you don’t know if you’re going to have problems on the road,” says a woman who has had severe alternating IBS for 16 years. “It’s a horrible feeling.”

“It’s like my body owns me,” says a man who has lived with severe diarrhea-predominant IBS for more than a decade. “And, if you were to talk about master and slave, I would be

the slave and my body would be the master.”

IBS causes visceral hypersensitivity, which is a low threshold for abdominal pain. Stretch in the bowel from even a small meal can trigger severe pain in people with IBS, which is sometimes relieved by a bowel movement.

Researchers do not know what causes IBS, but they do understand the physiology. When non-IBS people develop cramping, diarrhea or constipation from food, stress or other events of daily life, the brain receives that information and sends down serotonin or endorphins to block the pain. “But, in the more severe IBS, those signals are not working properly,” Dr. Drossman says. “So, in fact, the pain signals that come from the bowel are amplified and turned up. There’s actually a switch mechanism. And, in irritable bowel, that switch is not working properly.”

IBS affects about 10 percent of the people in the United States. That is 25 million people. IBS is second only to the common cold as the reason for work absenteeism and it is the most common GI disorder seen by primary care doctors and gastroenterologists. The combined annual cost for medical care and work absenteeism is estimated at \$20 billion.

“People think you can just go on with life without worrying about it,” says a woman who has had moderate diarrhea-predominant IBS for eight years. “And, I think often it’s difficult for people to do that, especially if you have diarrhea or incontinence. Anyone who’s ever had a virus where they were having diarrhea consistently for even a day or two can understand that.”

In a society that uses food to celebrate important occasions, people with IBS are especially challenged to avoid symptoms during the holidays. One man hates the holiday emphasis on food. “You gotta eat nuts for Christmas, you gotta have chocolate, you gotta have candy canes, you gotta have a bunch of fruit,” he says. “And turkey! Don’t get me started on Thanksgiving. All the rich disgusting food that tastes so good but is so bad for me.”

I have great respect for the people who talked candidly about their IBS symptoms during our interviews. Personal bowel habits are not comfortably discussed in public, but they wanted to educate others about IBS. “Everything else in my life is normal, but I have these symptoms,” says a woman who has coped with constipation-predominant IBS for 20 years. “I’m very grateful to know there are people who are willing to continue studying the illness and help people live normal lives.”

Mary Ann Bella is a writer and executive producer for Bella International Productions, Inc. in Chapel Hill. She recently completed “Doctor I have these symptoms,” a video on IBS produced for the UNC Center for Functional GI & Motility Disorders.

Please visit the Center website for various videos about IBS.: www.med.unc.edu/ibs



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ACG 2005

The UNC Center for Functional GI & Motility Disorders was well-represented by faculty and investigators at the 2006 meeting of the Annual Scientific Meeting of the American College of Gastroenterology (ACG), Honolulu, Hawaii.

Oral Presentation

Randomized Controlled Trial Shows Biofeedback to be Superior to Alternative Treatments for Patients with Pelvic Floor Dyssnergia-type Constipation

- » Steve Heymen, MS, Yolanda Scarlett, MD, Kenneth Jones, PhD, Yehuda Ringel, MD, Douglas Drossman, MD, and William E. Whitehead, PhD
- » UNC Center for Functional GI and Motility Disorders, University of North Carolina at Chapel Hill

Purpose: To conduct a randomized controlled trial comparing EMG biofeedback to two alternative treatments for patients with pelvic floor dyssnergia-type constipation (PFD).

Methods: 117 subjects participated in a 4-week run-in, in which 18 patients (15%) reported adequate relief. 15 patients (13%) withdrew from run-in. The remaining 84 patients (71 females) used in the intent-to-treat (ITT) analysis were randomly assigned to one of three treatment groups: 1) EMG biofeedback, n=30; 2) 5mg diazepam, n=30; 3) placebo pill, n=24. All patients were trained to do pelvic floor muscle exercises (PFME) during 6 biweekly 1-hour sessions. Diazepam/placebo pills were taken one hour prior to dinner. Instructions were given to all patients for proper defecation attempts following dinner. Diary data (cathartic use, straining effort, incomplete bowel movement sensations, Bristol stool scores, and compliance with PMFE homework) was reviewed in each session. The primary dependent measure was a report of adequate relief (yes or no) three months post-treatment. Hypothesis 1: A greater proportion of subjects receiving Biofeedback would report adequate relief compared to the diazepam and placebo groups. Hypothesis 2: One or more variables will be predictive of successful treatment. Hypothesis 3: Improvements in quality of life (QOL) will be associated with treatment success.

Results: *Hypothesis 1:* Biofeedback for PFD was superior to a placebo pill group. 70% of biofeedback vs. 38% of placebo patients were successful ($\chi^2 = 5.7, p=.017$). Biofeedback was also superior to the diazepam pill group. 70% vs. 23% were successful ($\chi^2 = 13.1, p<.001$).

Hypothesis 2: In an assessment of physiological, psychological, demographic, and symptom severity variables, no significant predictors of treatment outcome were found.

Hypothesis 3: Improved QOL predicted a successful treatment outcome (logistic regression, $p=.003$) and was significantly correlated with an increased number of unassisted bowel movements ($p = .001$). Prior to treatment, the groups did not differ on demographic variables [gender, race, age (mean 50, range 17-80 years)], physiological variables (rest or push anal canal values, first sensation threshold, or colonic transit time), psychological variables (depression, anxiety, or sexual abuse history), symptom duration (mean 15.6 years), or number of physician visits in the previous 6 months (mean 5.3 visits). In addition, there were no significant differences between groups in the expectation of benefit measured at the beginning of the second training session [biofeedback = 53, placebo=49, diazepam=51 (maximum possible score=63, $p=.27$ ANOVA)].

Conclusion: This investigation provides definitive support for the efficacy of biofeedback for PFD.

Poster Abstracts

An Algorithm Using CART Analysis to Identify IBS-C and IBS-A from IBS-D

- » DA Drossman¹, CB Morris¹, Y Hu¹, J Leserman¹, C Dalton¹, BB Toner², N Diamant², SI Bangdiwala¹
- » ¹UNC Center for Functional GI and Motility, Univ. of NC, USA; ²Centre for Addiction and Mental Health, Univ. of Toronto, Canada

Background: In Drossman, Gastro, 2005, we defined by prospective 1-yr evaluation, Rome II compatible IBS alternators (IBS-A) who alternate between IBS-C and IBS-D. IBS-A had similar bowel habit to IBS constipation-mixed (IBS-CM: alternates between IBS-C and IBS-M, but not IBS-D), while IBS diarrhea-mixed (IBS-DM: alternates between IBS-D and IBS-M, but not IBS-C) appears as a separate group. This suggests that treatments for constipation could apply to IBS-CM and IBS-A, but not IBS-DM, and treatments for diarrhea be restricted to IBS-DM. The aim of this study was to develop an

Poster Abstracts, cont.

algorithm to identify IBS-A, IBS-CM and IBS-DM patients for clinical trials, either as 3 distinct groups or with IBS-CM and IBS-A combined.

Methods: Among 317 women entering an NIH treatment trial, Rome II compatible IBS-A, IBS-CM and IBS-DM subtypes were based on prospective assessment of stool habit. Subjects received clinical questionnaires at 3-mo. intervals for 1 yr. (N=190 evaluable). A Classification and Regression Tree (CART) analysis (SAS V.8) identified, using cross-sectional data from 2-weeks diary cards, which clinical items discriminated between IBS-A, IBS-CM and IBS-DM, that would otherwise require prospective assessment of bowel habit over at least 1 year.

Results: Several analyses were run to create a model that was parsimonious in the number of predictor items (N=2-4) and also robust in identifying the defined groups (misclassification range 12.6% to 34.2%). Efforts to classify subjects into 3 groups (IBS-A, IBS-CM, IBS-DM) were unsuccessful because IBS-A could not be separated from IBS-CM, thus confirming our initial findings. The best model contained only 2 items (average stool consistency using Bristol Stool Scale, and stool frequency) with a 14.7% misclassification rate. The final clinical decision rule was: 1) Is stool frequency <2/day? 2a) If Yes, is the stool consistency <5 [Yes=IBS-A+IBS-CM; No=IBS-DM]? 2b) If No, is the stool consistency <4 [Yes=IBS-A+IBS-CM; No=IBS-DM]?

Conclusion: Using CART analysis, we developed a simple algorithm using a 2-week assessment of average stool frequency + consistency that identifies with 85% accuracy subjects who will have IBS-A & IBS-CM vs. IBS-DM over the subsequent year. The algorithm may be of value in clinical trials and in planning treatments.

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Do Comorbid Dyspepsia and Reflux Symptoms Affect Morbidity, Utilization and Outcome in Irritable Bowel Syndrome (IBS)?

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Purpose: The impact of co-morbid gastroesophageal reflux disease (GERD) or functional dyspepsia (FD) on the health care costs and utilization, clinical response and symptom status of patients with IBS is largely unknown. The impact of these common IBS comorbidities was evaluated as a sub-study in a large survey assessing usual medical care for IBS (Aliment Pharmacol Ther 2004;20:1305-15).

Methods: Patients given a clinical diagnosis of IBS, abdominal pain, constipation, or diarrhea during a health maintenance organization (HMO) clinic visit completed mail questionnaires within two weeks of the visit. Responders were asked to complete follow-up questionnaires six months later. The study questionnaires included the ROME II questionnaire, the IBS-QOL, the IBS Severity Index, and ratings of satisfaction with medical care and satisfactory relief of bowel symptoms (yes/no) at 6-month follow-up. The total numbers of all health care visits and GI-related visits were obtained from the HMOs electronic records for one year after the index visit.

Results: 1,658 patients (ages 18-72, 73% female) completed baseline questionnaires, 73% also completed follow-up, and 87% of the patient records were manually reviewed. Data were analyzed from all of the 529 patients who met Rome II IBS criteria, had complete data, and had no organic cause for symptoms in their charts. Patients were divided into three comorbidity groups for analysis (see Figure at right): IBS-only (n=201); IBS+GERD (n=73) if they had current GERD diagnosis in their record; IBS+FD (n=255) if they reported upper GI pain often on the ROME II questionnaire and had no GERD diagnosis.

Conclusions: (1) Compared to IBS-only, both IBS+FD and IBS+GERD patients have more severe IBS symptoms. (2) IBS+FD patients have poorer health-related quality of life compared to those with IBS alone. (3) IBS+GERD are less likely to be satisfied with care or to have satisfactory relief after 6 months compared to patients with IBS alone. (4) Healthcare utilization is not significantly affected by the co-presence of upper GI symptoms in IBS.

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Why Do Irritable Bowel Syndrome Patients Take Multiple Drugs and What Are the Associated Costs?

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Aims: Most IBS patients use multiple medications and supplements. Previous studies have not assessed the reasons for this or the relationship to symptom severity or symptom relief. The aims of this study were to assess: whether polypharmacy is explained by symptom severity or poor treatment response; the incremental cost of polypharmacy; health care costs attributable to prescription and OTC drugs, herbs, and dietary supplements.

Methods: In 2001-2002, patients in a large health maintenance organization (HMO) diagnosed with IBS, constipation, diarrhea, or abdominal pain at a clinic visit were invited within two weeks of their visit to complete questionnaires. 1,665



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(59%) did so (mean age 53 years, 73% females). Completers were sent follow-up questionnaires 6 months later. Physician and hospital costs were calculated from automated medical records for this 6-month period, and out of pocket costs were estimated from patient questionnaires. IBS severity at enrollment was assessed by a validated questionnaire (APT 1997;11:395-402), and satisfactory relief and out-of-pocket expenses were assessed by questionnaire at the 6-month follow-up. Analysis was limited to 706 patients who met Rome II IBS criteria and had no known organic cause for their symptoms.

Results: (1) Relationship of polypharmacy to IBS severity and treatment outcome: The number of drugs taken was positively related to IBS symptom severity (regression analysis: $\beta = .201, p < .001$) and negatively related to attainment of satisfactory relief of symptoms ($\beta = -.140, p = .001$), together accounting for 7% of the variance.

(2) The incremental costs of polypharmacy: 64.1% of IBS patients used two or more OTCs, herbs or dietary supplements. Mean 6-month costs of drugs increased linearly, from \$128 if taking one medication to \$720 if taking 8+ medications, and number of drugs was positively correlated with total cost of care for IBS ($\rho = 0.476, p < .001$).

(3) Healthcare costs attributable to prescriptions, OTC medications, and supplements: The total 6-month health care costs including out of pocket expenses averaged \$3,816. Mean expenses for IBS were \$620, including \$308 for hospital and physician charges, \$104 for prescriptions, \$71 for OTCs, \$9 for herbal remedies, \$57 for dietary supplements, and \$69 for complementary/alternative treatments.

Conclusions: (1) The number of drugs taken by IBS patients is only in small part explained by IBS severity or unsatisfactory treatment response. **(2)** Number of drugs taken correlates with total health care costs for IBS. **(3)** Drugs and diet supplements account for 38.9% of health care costs for IBS, while OTCs, herbs and dietary supplements make up 56.8% of these costs.

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Patient Characteristics Determining Clinical Diagnosis of Constipation- predominant IBS (IBS-C) vs. Chronic Constipation (CC)

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Purpose: Our prior work (Gastroenterol 2004;126(4) Suppl 2:A-606) showed poor agreement between the Rome II criteria and clinical diagnosis of IBS-C and CC, suggesting that physicians probably take patient characteristics other than symptom criteria into account in assigning diagnoses. This study aimed to identify specific patient characteristics that might influence diagnostic decisions and differ between ROME II IBS-C patients diagnosed IBS vs. CC.

Methods: 1,658 patients (73% female, mean age 53 years) given clinical diagnoses of IBS, abdominal pain, functional constipation or diarrhea at a visit to health maintenance organization (HMO) doctors completed mailed questionnaires following their visit (59% response rate). Questionnaires included: Rome Diagnostic Questionnaire; IBS Severity Scale (IBSS); additional constipation severity questions; Brief Symptom Inventory-18 (BSI-18); Recent Physical Symptoms Inventory (RPSQ); demographic questions. Healthcare utilization for one year prior to the index visit was obtained from the HMO's electronic record.

Results: 255 patients met Rome II criteria for IBS-C, of which 109 were clinically diagnosed with IBS and 83 diagnosed with CC.

(a) Group comparisons on individual variables: Patients were compared on the following variables: Demographic characteristics -- Age (IBS < CC), Race (IBS = CC), Gender -- % Females (IBS > CC), Education -- years of school (IBS = CC). Symptoms -- Abdominal pain severity in the past 10 days (IBS > CC), Frequency of abdominal pain in the past 10 days (IBS = CC), Severity of abdominal distention (IBS = CC), Dissatisfaction with bowel habit (IBS = CC), Life interference from bowel problems (IBS = CC), Self-reported constant severe constipation in the past 6 months (IBS < CC; Figure 5), Amount of non-GI symptoms in the past month -- RPSQ scale (IBS > CC; Figure 6), Healthcare utilization in the past 6 months (IBS = CC), Psychological distress - BSI-18 scale (IBS = CC).

(b) Logistic regression to assess predictive power: The five variables distinguishing the groups were used in a logistic regression analysis to assess their independent and collective contribution to prediction of diagnosis. All except age had additive power in predicting diagnostic assignment (binary logistic regression analysis). Collectively, severity of abdominal pain, a report of constant severe constipation in the past 6 months, the amount of non-GI symptoms, and gender explained 25% of the variance (Nagelkerke $R^2 = .25$) in assignment of IBS vs. CC diagnosis.

Conclusions: Severe abdominal pain and number of non-GI symptoms increase the likelihood of IBS diagnosis, whereas constant symptoms of constipation and female gender made a diagnosis of CC more likely.

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Which Medications And Food Supplements Are Associated With Bloating In Patients With Functional Bowel Disorders?

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Purpose: Abdominal distention accompanied by a subjective sensation of fullness or bloating adversely affects quality of life, and is often found to be the most distressing symptom of irritable bowel syndrome (IBS) (Am J Gastroenterol 1999;94:1320-6).

Aim: Identify which of 22 types of drugs and food supplements are associated with bloating.

Methods: In a large health maintenance organization (HMO), patients with clinical diagnoses of IBS, constipation, diarrhea, or abdominal pain at a clinic visit were invited within 2 weeks to complete questionnaires, and 1,665 (59%) did so (average age 53 years, 73% females). Patients who completed the questionnaires were requested to complete follow-up questionnaires 6 months later. Chart reviews were used to identify patients with organic disease explanations for functional bowel symptoms. This was an observational study of usual medical care, and treatments varied between patients. Patient questionnaires were used to identify which prescription and non-prescription medications and food supplements patients were taking. Patients rated the severity of abdominal distention over the last 10 days on a numeric rating scale (0-100). Nonparametric correlations were used to identify which of 22 drugs and food supplements were significantly ($p < .01$) correlated with distention, and these were entered into a linear regression analysis. Analyses were limited to 1,041 patients who had a functional bowel disorder, did not have malabsorption, inflammatory bowel disease, or gastrointestinal malignancy, and were not pregnant.

Results: (1) Nine types of drugs or supplements were significantly correlated with abdominal distention: fiber, bran, laxatives, glycerin suppositories, antispasmodics, antidepressants, gas-relief medications, and over the counter analgesics. Gas-relief medications, antispasmodics and pain-relievers were likely taken for the treatment of symptoms associated with distention and were consequently not entered into the regression model. (2) Regression analysis showed that three categories accounted for an adjusted R² of 4.2%: glycerine suppositories, bran and fiber.

Conclusions: This study shows that fiber and bran products and glycerine suppositories are associated with increased abdominal distention. Laxative use was not an independent predictor ($p = .08$), because it was correlated with use of bran, fiber and suppositories.

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ACG 2005 -- Palsson OS, Levy RL, Feld AD, Von Korff M, Turner MJ, Whitehead WE. Which medications and food supplements are associated with bloating in patients with functional bowel disorders? American Journal of Gastroenterology, 2005 in press.

Which Symptoms Predict Satisfaction With Treatment And Improved Quality Of Life In Irritable Bowel Syndrome (IBS)?

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Background: Satisfactory relief (yes or no) of IBS symptoms in general is commonly used to evaluate the effectiveness of investigational treatments, but limited data are available on how satisfactory relief relates to changes in specific symptoms.

Aims: Determine which of the 5 specific IBS symptoms on the IBS Severity Scale at baseline predict satisfactory relief and IBS-specific quality of life at 6 months follow-up. Determine whether changes in specific symptoms from baseline to follow-up are predictive of satisfactory relief or quality of life at 6 months.

Methods: 1,665 health maintenance organization patients with clinical diagnoses of IBS, constipation, diarrhea, or abdominal pain at a clinic visit completed mailed questionnaires within 2 weeks of their visit and 6 months later. Patients completed the IBS Severity Scale (Aliment Pharmacol Ther. 1997 11(2):395-402), which includes ratings of abdominal pain intensity and frequency, severity of abdominal distention, dissatisfaction with bowel habits, and impact of IBS symptoms on everyday activities, and the IBS-QOL (Am J Gastroenterol. 2000 Apr;95(4):999-1007), at enrollment and at 6-month follow-up. Satisfactory relief was assessed at follow-up only. Analyses were limited to 529 patients who met Rome II criteria for IBS, did not have a known organic cause for symptoms, and completed follow-up questionnaires.

Results: Subject Characteristics -- Gender: 418 women, 111 men; Age: mean 52.5 years; Ethnicity: 89.2% Caucasian, 3.5% Hispanic, 2.8% Asian, 2.8% African-American, 1.8% Other; Education: 47.2% college graduates. (1) Patients reporting satisfactory relief at six months reported less frequent abdominal pain, less severe abdominal distention, less dissatisfaction with bowel habit and less interference with life from their bowel symptoms, but not less abdominal pain severity, at baseline. (2) Baseline Predictors of Satisfactory Relief Identified by Regression Analysis: Variance explained = 14.2%. Significant independent predictors: i. Pain frequency (less baseline pain predicts greater satisfaction); ii. Dissatisfaction with bowel habits (less bowel habit dissatisfaction predicts greater satisfaction with treatment); iii. Interference with daily activities (less interference predicts greater satisfaction). (3) Patients who reported satisfactory



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relief at 6 months had higher IBS-QOL scores at baseline. (4) Patients who reported satisfactory relief at 6 months showed greater mean improvement across all 5 IBSS symptoms. (5) Logistic Regression Analysis: Changes in Individual Bowel Symptoms that predict Relief at 6 Months -- Baseline to 6 Months as Predictors of Satisfactory Relief at 6 Months. Variance explained = 24.8%; i. Significant independent predictors, ii. Reduction in pain severity; iii. Reduction in dissatisfaction with bowel habit. (6) Patients who reported satisfactory relief at 6 months showed greater mean improvement on the IBS-QOL. (7) Reductions in all five symptoms on the IBSS were significantly positively correlated with improvement in the IBS-QOL quality of life scores. (8) Regression Analysis: Improvement in Individual Bowel Symptoms that Predict IBS-QOL improvement at 6 months. Variance explained = 37.9%. Significant independent predictors: i. Reduction in abdominal bloating severity, ii. Reduction in life interference from symptoms, iii. Reduction in dissatisfaction with bowel habit.

Conclusions: (1) Baseline severity of bowel symptoms predicts satisfactory relief 6 months later: less severe IBS symptoms predict greater likelihood of satisfactory symptom relief. (2) Satisfactory relief of IBS symptoms also depends on improvements in both pain and altered bowel habits. (3) Improved quality of life is more closely tied to improvements in bloating and bowel habits than it is to pain.

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National Survey on Patient Education in Irritable Bowel Syndrome (IBS)

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Purpose: To identify patients' : 1) perceptions about IBS; 2) preferences on the type of information needed; 3) preferences about educational media; and 4) expectations from health care providers.

Methods: The study consisted of: 1) Questionnaire item generation using patient focus groups to develop the IBS-Patient Education Questionnaire (IBS-PEQ). 2) Cognitive item reduction of items considered important and relevant by IBS patients and 3) Data acquisition. The IBS-PEQ was administered to a national sample of IBS patients.

Analysis: Frequencies of the endorsement of items and their ranking (1-3) were obtained. A weight index = frequency of item endorsements, X mean rating per item was calculated to account for the importance of both endorsement and ranking. A higher index indicated greater importance (range 0-3).

Results: 200 outpatients completed the survey, mean age was 45.6 19.8 yrs., with an educational attainment of 14.8 2.8 yrs., and 89.5% were female. Illness duration was 8.9 4.7 years. The most prevalent misconceptions about IBS included (% of subjects agreeing with the statement and % unsure): 1) IBS will develop into colitis (18 %, 28%), 2) malnutrition (17%, 24%), and 3) cancer (14%, 29%). IBS patients were interested in learning about (% of subjects choosing an item, % ranking the item in the top 3 preferences, and weight index): 1) foods to avoid (60%, 16.5%, 1.0), 2) causes of IBS (55%, 16%, 1.05), 3) medications (58%, 15.5%, 0.95), 4) coping strategies (56%, 13%, 0.83), and 5) psychological factors related to IBS (55.5%, 15.5%, 0.81). Choice of presentation methods included: 1) M.D. (67.5%), 2) brochures (42%), and 3) newspapers and magazines (40.5%). 80 % of patients expected the M.D. to be available via phone or e-mail following a visit, and to provide information about sources of additional information and research studies. The most desired qualities of the physician were the ability to: 1) listen (80%), 2) provide hope (73%), and support (63%).

Conclusion: Despite increasing education about IBS, many patients hold misperceptions about IBS developing into cancer, colitis, or causing malnutrition, and they most often seek information about dietary changes. They expect physicians to be the primary provider of information, to have good communication skills, and to provide hope and support.

Cilansetron Improves Health Related Quality of Life in Patients with Irritable Bowel Syndrome with Diarrhea Predominance (IBS-D)

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Introduction: Irritable bowel syndrome (IBS) is the most common chronic gastrointestinal disorder affecting 11.5% of adults in Europe and 10–15% of adults in North America. IBS has a marked negative impact on health-related quality of life (HRQOL). There is a growing consensus that HRQOL assessment should be a major component of clinical studies and treatment trials. Serotonin (5-HT) is well recognized and becoming better understood as a key factor in IBS. Cilansetron is a new 5-HT₃ receptor antagonist with demonstrated efficacy in men and women with irritable bowel syndrome with diarrhea predominance (IBS-D).

Objective: The objective of the sub-sample analysis was to evaluate the efficacy of cilansetron compared to placebo on HRQOL as measured by the IBS-QOL Survey in a Phase III 6-month multinational trial.

Methods: Study Design -- In a double-blind, placebo-controlled, 6-month multinational trial, male and female subjects meeting the Rome-defined IBS-D criteria were randomized to cilansetron 2 mg TID or placebo. Sample Population -- The

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intent-to-treat population consisted of 792 subjects (aged 18–84 from Australia, Belgium, Bulgaria, Canada, Denmark, France, Germany, India, Ireland, Israel, The Netherlands, New Zealand, Poland, Romania, Russia, South Africa, Spain and Ukraine). The IBS-QOL survey was completed only in countries for which there was a validated translation available. The subjects in the following countries did not complete the survey: Bulgaria, Israel, Poland, Romania, Russia and Ukraine. The IBS-QOL sub-sample size was a total of 338 subjects; 168 (91 females, 77 males) for cilansetron and 170 (90 females, 80 males) for placebo. Data Collection and Assessment of QoL -- The IBS-QOL survey, a validated 34-item condition-specific quality-of-life measure consisting of 8 subscales, was administered at baseline and at the end of treatment in order to assess possible changes in their quality of life. Subjects were asked to respond on a scale of 1–5 (1=not at all, 5=extremely or a great deal). QoL was assessed across eight subscale scores and an overall score was derived from the 34 individual item scores (Figure 1). Higher scores indicate better health-related quality of life (HRQOL).

Results: Cilansetron Treatment Associated with Improved IBS-QOL Scores in Male and Female IBS-D Subjects. Interference with activity, food avoidance, and dysphoria subscales showed the lowest scores at baseline (Figure 2). Subjects showed improvements in total scores, 17.7 for cilansetron and 9.6 for placebo, at end of treatment ($p < 0.005$). Cilansetron was statistically significant to placebo ($p < 0.005$) for all subscales except sexual ($p = 0.169$). The sexual subscale showed the highest scores at baseline and treatment reflects a trend in favor of cilansetron. (Table 2, Figure 3). **Conclusions:** Cilansetron treatment resulted in a significant improvement in HRQOL compared to placebo in men and women with IBS-D who were treated over a period of 6 months.

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Translation and Validation of a Japanese Version of the Irritable Bowel Syndrome-Quality of Life measure (IBS-QOL-J)

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Aims: To compare quality of life (QOL) for patients with irritable bowel syndrome (IBS) between the U.S. and Japan, it is indispensable to develop common instruments. The IBS-QOL (Dig Dis Sci 1998; 43: 400-11), which is widely used in Western countries, was translated into Japanese as there has been a lack of Japanese disease-specific QOL measures for IBS.

Methods: The original 34 items of the IBS-QOL were translated from English into Japanese through two independent forward translations, resolution, back translation, and resolution of differences. Forty nine patients who had GI symptoms but did not have any organic diseases (including 30 IBS patients diagnosed by Rome II criteria) were recruited from Tohoku University Hospital in Sendai, Japan and completed the IBS-QOL-J concomitant with the IBS severity index (IBSSI: Aliment Pharmacol Ther 1997; 11: 395-402) twice within 14 days.

Results: The IBS-QOL-J demonstrated high internal consistency (Cronbach's alpha; 0.96) and high reproducibility (intra-class correlation coefficient; 0.92, $p < 0.001$). Convergent analyses confirmed that the score of IBS-QOL-J was significantly correlated with overall severity of IBS symptoms on the IBSSI ($r = -0.36$, $p = 0.01$) and with the individual items on the IBSSI that assess interference with life in general ($r = -0.47$, $p < 0.01$) and dissatisfaction with bowel habits ($r = -0.32$, $p < 0.05$). Twelve patients who had consulted GI doctors more than 6 times in the past 6 months had significantly lower scores in the IBS-QOL-J than 37 patients who had consulted 6 times or less (59.6+/-18.9 vs 73.8+/-19.2, $p < 0.05$), whereas there was not a significant difference in the severity score of IBS symptoms between both groups (258+/-117 vs 207+/-92, $p > 0.10$). Age, sex, education or marital status did not affect the measure.

Conclusion: The IBS-QOL-J is a reliable instrument to assess the disease-specific QOL for IBS. Considering cross-cultural comparison, this measure is likely to be a valuable tool to investigate the QOL in Japanese patients with IBS.

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Christine Dalton

Ask the Expert

Christine Dalton, PA

Question What is a Functional GI disorder?

Functional gastrointestinal disorders (FGIDs) are common disorders that are characterized by persistent and recurring GI symptoms. These occur as a result of *abnormal functioning* of the GI tract. They are not caused by structural (tumors or masses) or biochemical abnormalities. As a result, many routine medical tests attempting to diagnose an FGID -- such as x-rays, CT scans, blood tests and endoscopic exams -- can have essentially normal/negative (non-disease) results.

More than 20 functional GI disorders have been identified. They can affect any part of the GI tract, including the esophagus, stomach, bile duct and/or intestines. The most common and best researched FGID is Irritable Bowel Syndrome (IBS) -- abdominal pain associated with altered bowel habits of diarrhea, constipation or alternating between both. Other common FGIDs include functional dyspepsia (pain or discomfort in the upper abdominal area, feeling of fullness, bloating or nausea), functional vomiting, functional abdominal pain, and functional constipation or diarrhea.

It is important to understand that these are *not* psychiatric disorders, although stress and psychological difficulties can make FGID worse. Approximately 25 million Americans have functional GI disorders. 50 -80% of people with FGID symptoms do not consult a physician, although they may take over-the-counter medications and report significantly more job absenteeism and disability than people without these symptoms. It has been reported that IBS is the second leading cause, after the common cold, for missing work or school.

There are three primary features of FGIDs - motility, sensation, and brain-gut dysfunction. *Motility* is the muscular activity of the GI tract, which is essentially a hollow, muscular tube. Normal motility (e.g., peristalsis) is an orderly sequence of muscular contractions from top to bottom. In FGIDs, the motility is abnormal. There can be muscular spasms that cause pain and the contractions can be very rapid, very slow or disorganized. *Sensation* is how the nerves of the GI tract respond to stimuli (e.g., digesting a meal). In functional GI disorders, the nerves are sometimes so sensitive that even normal contractions can bring on pain or discomfort. *Brain-gut dysfunction* is the disharmony in

the way that the brain and GI system communicate. With FGIDs, the regulatory conduit between brain and gut function may be impaired.

How are FGIDs diagnosed? Fortunately, attention to and understanding of FGIDs is increasing, as reflected in the growing base of research in this area over the last two decades. Because routine tests like x-rays, CT scans and others used for diagnosing organic disorders are generally negative for people with FGIDs, diagnosing these disorders cannot be based on test results. Expert clinicians and researchers from all over the world have met and studied the symptoms and other characteristics of FGIDs for many years and their collaboration has resulted in the development of the so-called 'Rome Criteria' -- symptom-based criteria for diagnosing FGIDs. As a result, the diagnosis of a functional GI disorder can be made when a patient's combination of symptoms and other factors meet the Rome criteria for a specific functional disorder. This is similar to other disorders, like migraine headaches, which also are not seen on x-rays, etc. but can be diagnosed based on the symptoms experienced by the patient.

What are the psychosocial aspects of FGIDs? Research on the psychosocial aspects of these disorders has yielded three general observations: *First*, psychological stress can exacerbate GI symptoms. *There is a bi-directional pathway between the brain and the GI tract*, often referred to as the 'brain gut axis'. External stressors and emotions or thoughts can affect GI sensation, motility and secretion. In other words, the brain affects the gut. But, just as significantly, activity in the gut can affect pain perception, mood and behavior in the brain. *Second*, *psychosocial disturbances can amplify illness experience* and adversely affect health status. Patients with FGIDs who were studied at medical centers have been found to have greater psychological difficulties than healthy subjects or other medical patients. However, patients at medical centers are generally sicker and their symptoms more severe as compared to patients seen in primary care clinics, so these results may overestimate the true difference. Also, persons with IBS who do not consult a physician for their symptoms are considered psychologically similar to people without IBS. This shows that IBS is not a psychiatric disorder. Instead, psychosocial factors modulate the illness experience and health outcomes, including physician visits. *Finally*, *having a functional*

GI disorder impairs the quality of one's life. Any chronic illness, including IBS, will affect a person's health-related quality of life (i.e., general well-being, ability to carry out everyday activities, concerns about the illness, and satisfaction with health care).

What are some of the treatments for FGIDs? The specific treatment depends on the particular symptoms a person is experiencing. Different medications will affect different symptoms, such as abnormal motility or hypersensitivity. *Anti-spasmodics*, such as Bentyl or Levsin, can be helpful in decreasing spasms in the GI tract. They are especially effective when taken prior to an event that might be expected to trigger spasms. For example, taken before a meal, they will blunt the exaggerated response often seen in FGIDs, which leads to cramping and pain. *Pro-motility* agents, such as Zelnorm, help accelerate the motility of the GI tract, which is especially useful for treating chronic constipation. Unfortunately, there are very few other motility-promoting medications on the market at this time. *Anti-diarrheals* or *laxatives* can be found over the counter at drug stores and many can be helpful for milder symptoms. *Prescription medications*, such as Lomotil for diarrhea or Miralax for constipation, can be used when symptoms are more severe.

Antidepressants are often prescribed, not for depression, but to decrease chronic GI pain. These medications can modify the messages between the brain and the gut in a way that 'turns down' the intensity of the pain. Some are also effective in decreasing pain by working on the GI tract directly, while others are effective in normalizing motility. Other miscellaneous medications that are helpful for FGIDs include Buspar, which can help relax the walls of the GI tract, and phenergan, which is used for nausea and vomiting. And, there are *psychological treatments*, such as relaxation therapy, hypnosis or cognitive behavioral therapy, that can help patients learn to better manage their symptoms and how they respond or react to their symptoms.

What is the future of FGIDs? As researchers in the US and around the world continue to study FGIDs, new and helpful information is becoming available. A better understanding of what might have caused IBS in certain people has resulted from the discovery of a connection between GI infections and subsequent chronic GI problems (post-infectious IBS). Investigations have also discovered a chronic, low-level inflammation in the GI tract in some people with IBS. There are also new diagnostic techniques and new medications being tested that appear promising. Basic research on the nature and causes of various functional GI disorders needs to continue along with clinical trials of new treatments.

Profile of On-Going Research Study

Clinical Efficacy of Probiotic Bacteria in Subjects with Irritable Bowel Syndrome (IBS), Functional Diarrhea, or Functional Bloating
Yehuda Ringel, MD

Probiotics are live bacteria which can be found in certain food like yogurt or cheese prepared with active cultures. Dr. Yehuda Ringel is collaborating with Danisco USA Inc to investigate the roll of probiotics on gastrointestinal (GI) symptoms. The purpose of this study is to see if probiotics bacteria, specifically Lactobacillus and Bifidobacterium, will improve GI symptoms in subjects with irritable bowel syndrome (IBS), functional diarrhea, or functional bloating.

The use of probiotics has been shown to be successful in several intestinal disorders, including chronic inflammatory bowel disease (IBD), childhood diarrhea (rotavirus infection), and traveler's diarrhea. This has led to increased interest in their use in patients with IBS. Data on the use of probiotics in IBS is still limited and the results are not consistent. However, a few reported studies show encouraging results and suggest symptomatic response and parallel improvement in quality of life.

Dr. Ringel hopes to recruit 50 subjects into this study here at UNC. Participants are assigned to take either the active supplement or a placebo, and the two groups will be compared to determine if taking the active supplement is superior to taking a placebo.

Individuals participating in this study will have four clinic visits where they complete questionnaires, have blood drawn, and complete a physical. They take a probiotic or placebo pill for 8 weeks, complete daily diary cards, and collect four bowel movements, one for each clinic visit. Study subjects will be compensated \$200 for completing the study.

For questions about this study, please contact the study coordinator, Sarah Causey at 919-843-1003 or toll free at 1-866-799-0092 or email at scausey@med.unc.edu.



Visitors this past quarter



Ronnie Fass

Ronnie Fass, MD
Associate Professor of
Medicine, University
of Arizona, Southern
Arizona VA Health Care
System, Tucson, AZ

Organized by Y. Ringel, MD, Dr. Fass visited October 20, 2005 and made a presentation on "Exploring Central and Peripheral Factors Responsible for Symptoms in GERD." He also participated in a discussion of Functional Bowel with the GI Fellows, led a luncheon presentation/discussion with Center investigators, and had one-on-one meetings with other faculty of the Division of Gastroenterology & Hepatology.



Susan Lucak

Susan Lucak, MD
Assistant Professor
of Clinical Medicine,
Division of Digestive
& Liver Disease at
Columbia-Presbyterian
Medical Center, New York
City; and Faculty, Dept.
of Medicine, College of
Physicians & Surgeons,
Columbia University.

Dr. Lucak visited the Center on November 7 through 11, 2005, to observe the approach to patient care of Dr. Drossman and other clinicians at the UNC Clinic on Functional GI Disorders. Her clinical interest is in functional bowel disorders, particularly the irritable bowel syndrome (IBS) and her research efforts have focused on evaluating the clinical safety and efficacy of treatments for patients with IBS.

Bette Bischoff

*Fourth Year Medical Student, University of Kansas
Medical Center*

Ms. Bischoff selected the UNC Center for Functional GI & Motility Disorders as the site for her month-long medical rotation on functional GI disorders (October 3-28, 2005). Please see her lead article in this edition of the Digest.



Freddy Squella Boerr

Freddy Squella Boerr, MD

Dr. Squella is a Gastroenterologist/Internal Medicine Service and ICU Resident at Hospital del Salvador in Santiago, Chile, as well as Adjunct Professor in Internal Medicine at the University of Chile. He is visiting the Center and the Division of Gastroenterology & Hepatology from November 1, 2005, through January 31, 2006. In addition to his interest in IBS and the activities of Drs. Drossman, Burnett and Ringel and PAs Chris Dalton and Danielle Maier in the UNC Functional GI Clinic, Dr. Squella is pursuing his interests in motility with Yolanda Scarlett, MD, Nick Shaheen, MD, Doug Morgan, MD, and Bill Whitehead, PhD. Dr. Squella is here with his wife and their daughter.



Frank Tu

Frank Tu, MD, MPH
Director of the Division
of Gynecologic
Endoscopic Surgery &
Female Chronic Pelvic
Pain, Dept. of Obstetrics
& Gynecology,
Evanston Hospital,
Evanston Northwestern
Healthcare, Evanston, IL.
Also Assistant professor
at Northwestern
University's Feinberg
School of Medicine

His meetings included Dr. Whitehead and his research team, Jane Leserman, PhD, Doug Drossman, MD and his clinical team to discuss clinical services, and Joanna Herath, Administrator of the UNC Division of Gastroenterology & Hepatology. Dr. Tu is a former Fellow at the UNC School of Medicine.

Welcome to the Center



Denesh Chitkara

Denesh K. Chitkara, MD
Assistant Professor of Pediatrics

In October 2005, Denesh Chitkara, MD joined the Center. Dr. Chitkara is a pediatric gastroenterologist who moved from Boston with his family to become an Assistant Professor in Pediatrics at UNC. He will conduct collaborative studies on functional gastrointestinal disorders (FGIDs) in children

with other researchers in our Center. His involvement in the Center will increase the focus on pediatric functional GI disorders.

Dr. Chitkara received his MD from The Ohio State University College of Medicine and completed his fellowship training in pediatric gastroenterology at The Floating Hospital for Children/Tufts School of Medicine and at Children's Hospital Boston/Harvard Medical School. He went on to complete a clinical and research fellowship in Clinical Enteric Neuroscience under the mentorship of Michael Camilleri, MD and Nicholas J. Talley, MD, PhD at Mayo Clinic Rochester.

Dr. Chitkara's previous research involved studying mechanisms responsible for symptoms in children with FGIDs. He initially studied GI motility in children with disorders in mitochondrial function, and prolonged esophageal manometry in normal children and those with gastro-esophageal reflux disease. At Mayo Clinic Rochester with mentorship from Dr. Camilleri, Dr. Chitkara utilized novel non-invasive techniques to study GI transit and gastric accommodation in common childhood FGIDs, such as functional dyspepsia, and constipation in children. He also studied the specificity of symptoms in functional upper GI disorders such as functional dyspepsia and aerophagia, a condition caused by repeated swallowing and retention of air with increased burping, abdominal pain and distension, in both children and adults.

In addition to his physiologic studies, Dr. Chitkara has initiated population-based research studies in order to evaluate patterns of symptom complaints and medical presentation in children with common FGIDs. In collaboration with the Department of Health Sciences Research at Mayo Clinic Rochester and Dr. Nicholas Talley, Dr. Chitkara has completed studies examining the medical presentation of gastro-esophageal reflux disease (GERD), functional abdominal pain, and constipation in children from birth to 5 years in a single community and followed them through adulthood.

Dr. Chitkara has received a seed grant funded through the Gastrointestinal Biopsychosocial Research Program at the Center (NIH grant R24 DK067674) under mentorship from Dr. William Whitehead (UNC) and Dr. Nicholas Talley (Mayo Clinic). With this grant, he will examine the incidence of functional abdominal pain from birth to adulthood, and identify risk factors for the presentation of functional abdominal pain

during the lifespan such as early symptoms, having a parent with IBS, and co-morbid conditions.

Dr. Chitkara's research focus at UNC will involve examining psychosocial and physiologic factors that contribute to the manifestation of symptoms in children with FGIDs. With mentorship from Dr. Whitehead, Dr. Chitkara will build on the information from his epidemiologic and physiologic studies to expand the understanding of psychosocial and physiologic mechanisms on the symptoms and treatments of pediatric functional dyspepsia and constipation.



Sarah Yeskel

Sarah Yeskel
Research Assistant to Dr. Ringel

Ms. Yeskel has recently joined the staff of the Division of Gastroenterology & Hepatology as Dr. Udi Ringel's research assistant. The research she will be working on includes functional dyspepsia, IBS, probiotic bacteria, and intestinal microflora. She is a recent graduate of Dickinson College

in Carlisle, PA, where she received her bachelor's degree in Biology. Ms. Yeskel has research experience in ecological and biomedical research; specifically oncology, small mammal ecology, and forest ecology. Last summer, she was a research assistant at the University of Michigan Biological Station in Pellston, MI, and two summers ago she was a research assistant in oncology at the UNC.



Patrena Patterson

Patrena Patterson
Assistant to Dr. Drossman

Patrena Patterson recently joined the Center as an Assistant to Dr. Drossman, working with Susan Schneck and Linda Miller. She is a Junior at Strayer University studying Human Resource Management, with less than 12 classes to go before she finishes with a Bachelors Degree. She already has an Associates Degree with a double major

with in HRM and Business Management, as well as a Medical Certificate and Paralegal Certificate. She plans to continue on with school in the Medical Coding Area, which she had begun earlier, and then aim for a Masters Degree in Human Resource Management.

Center News

On-line REGISTRY of Potential Research Study Participants – The Center recently received approval from the UNC Institutional Review Board (IRB) to launch an on-line REGISTRY to recruit volunteers for on-going and future research studies conducted by Center investigators. Please see further information in this edition of the Digest and sign up with our REGISTRY.

Bill Whitehead, PhD, Center Co-Director, gave an invited address titled “Biofeedback for Fecal Incontinence and Constipation” at the 6th annual Chinese Gastrointestinal Motility Society meeting in Wuhan, China, on November 12, 2005.

Doug Drossman, MD, Center Co-Director, is among the nominees for Vice President of the American Gastroenterological Association (AGA), as is Robert Sandler, MD, Chair of the UNC Division of Gastroenterology & Hepatology. Bill Whitehead, PhD, is a member of the AGA Nominating Committee.

Participate in a Research Study

The UNC Center for Functional GI & Motility Disorders always has a number of research studies underway for which volunteers are welcome and needed. The Center has launched a REGISTRY that volunteers can join to be contacted by Center research coordinators about on-going and future studies; more information is on our website at:

www.med.unc.edu/ibs

Interested persons are also welcome to contact us directly about participating in any of the following on-going studies. For more detailed information regarding the following studies, please visit our website at:

http://www.med.unc.edu/medicine/fgidc/research_subjects.htm

Research Studies Sponsored by the National Institutes of Health (NIH)

- » Determining Factors that Cause or Influence IBS – *need men and women with IBS and healthy controls* — Contact: Lenore Keck (919/966-8329)
- » Treatment Options for Patients with Fecal Incontinence – *need men and women with fecal incontinence* — Contact: Steve Heymen (919/966-2515)

Research Studies Involving Mechanisms and Outcomes

- » Validation of the Bloating & Diagnostic Severity Questionnaire – *need men and women with bloating and only one of the following conditions – IBS, constipation or congestive heart failure* — Contact: Jane Tucker (919/843-4906)

Research Studies Involving Drugs and Treatment

- » *Need men and women with IBS.* Contact: Kim Meyer (919/966-8328)
- » *Need women experiencing fullness while eating, abdominal pain or discomfort, bloating, nausea or vomiting.* Contact: Sarah Causey (919/843-1003)
- » *Need men and women with constipation-predominant IBS.* Contact: Kim Meyer (919/966-8328)
- » *Need healthy men and women and those with IBS for a study looking at gene markers in IBS.* Contact: Sarah Causey (919/843-1003)
- » *Need women and men with diarrhea-predominant IBS.* Contact: Kim Meyer (919/966-8328)
- » *Need men and women with functional diarrhea, functional bloating or IBS for a supplement treatment trial of probiotics.* Contact: Sarah Causey (919/843-1003)

SAVE THIS DATE

On-line Chat Room

Mark your calendar for the **Tuesday, February 14, 2006**, on-line chat room. Topic and speaker to be announced. Please check the home page of our website www.med.unc.edu/ibs in February 2006 for latest update on the chat room.

SAVE THIS DATE

Patient Symposium 2006

Please see the full-page announcement in this edition of the Digest and mark your calendar for the Patient Symposium scheduled for Saturday, July 15, 2006, at the Friday Center in Chapel Hill, NC. The registration fee for this all-day event is only \$25.00.

Contact Information

_____	Name	_____	_____
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I would like to make a donation to the Center. Enclosed is my donation in the amount of:

\$1,000 and above

\$500

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Please send me more information on the following:

- Functional GI and Motility Disorders
- Irritable Bowel Syndrome (IBS)
- Psychological Services
- Research Studies
- Constipation
- Fecal Incontinence
- Other _____

- Check here if your contribution is designated for the Alan Wayne Ducoff Memorial Fund
- Check here if you do NOT want to be publicly acknowledged for your contribution to the Center

Send your contribution to:
 UNC Center for
 Functional GI & Motility Disorders
 CB 7080, Bioinformatics Bldg
 Chapel Hill, NC 27599-7080

Phone: (919) 966-0289
Fax: (919) 966-8929
www.med.unc.edu/ibs

Make your check payable to:
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OR: Include the following credit card information

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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.

Memorial Research Fund

The Alan Wayne Ducoff Memorial Fund provides an opportunity for families and friends to remember and honor their loved ones by making a designated contribution to the Center's research program. To make a donation to the Alan Wayne Ducoff Memorial Fund, please check off the appropriate box on the donation form.

Opportunity to Support



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SEASONS Greetings

from

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