



# DIGEST

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

## FEATURE ARTICLE

# FUNCTIONAL HEARTBURN

*Ryan D. Madanick, MD*  
*Assistant Professor of Medicine*



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Heartburn is a very common symptom and is the most common presenting symptom of gastroesophageal reflux disease (GERD). Approximately 60% of Americans have experienced heartburn, and 20% have heartburn on a weekly basis. Although the most common cause of heartburn is GERD, other disorders including cardiac disease, esophageal motility disorders, and eosinophilic esophagitis can also present with heartburn. Currently most patients who consult a physician for heartburn are started on acid suppressing medication, commonly a proton pump inhibitor (PPI), as a therapeutic trial for uncomplicated heartburn. This therapeutic trial, often called the PPI test, has approximately 70-80% sensitivity and 40-70% specificity for diagnosing GERD.<sup>1</sup>

A significant proportion of patients do not respond to acid suppression as expected. In many patients, heartburn is incompletely controlled with standard doses of PPI and some patients have no response at all. The failure of a PPI to optimally control heartburn and other GERD-related symptoms is one of the most commonly encountered clinical scenarios in GI practice today.<sup>2</sup> Various labels have been applied to this group of patients, including "refractory GERD" or "PPI failures." However data indicate that many patients whose heartburn persists despite PPI do not actually have GERD.

### WHAT IS "FUNCTIONAL HEARTBURN"?

Functional heartburn (FH) has been defined by the Rome III Working Group by the following diagnostic criteria, which must be present for the previous 3 months, with symptom onset at least 6 months before the diagnosis<sup>3</sup>:

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

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1. Burning retrosternal discomfort or pain
2. Absence of evidence that gastroesophageal acid reflux is the cause of the symptom
3. Absence of histopathology-based esophageal motility disorders

The current definition has been revised from the previous Rome II definition.<sup>4</sup> According to the Rome II definition, all patients with heartburn, normal endoscopy and normal esophageal acid exposure were classified as FH. However, approximately 40% of these patients demonstrate a close relationship between symptoms and acid reflux events.<sup>5</sup> This group of patients is said to have an "acid-sensitive" esophagus. This change in the classification makes the definition of FH more stringent than previously discussed.

Uncertainty regarding the classification has led to difficulty in understanding the epidemiology of FH. Up to 70% of patients with heartburn do not have esophageal erosions on endoscopy. In the past, this large subset of patients was classified as having nonerosive reflux disease (NERD). The implication of such a classification is that *all* patients who present with heartburn but have a negative endoscopy have GERD, but that reflux has not produced gross esophageal mucosal damage. This dualistic view does not take into account that there may be other non-reflux etiologies or other functional components to heartburn. Failure to previously acknowledge this concept may account for the low rate of success with PPI therapy in studies of NERD.<sup>6</sup> The best estimate of the prevalence of FH can be gleaned from investigations of NERD. Thirty to fifty percent of patients with heartburn and negative endoscopy have normal pH studies.<sup>7</sup> Since 50-70% of patients with heartburn do not have erosions at endoscopy, the true prevalence of FH may range somewhere between 15 and 35%, depending on the definition of FH and the population sampled. One recent study indicates there is a gender difference in FH, with females accounting for 68% of FH patients.<sup>8</sup>

#### PATHOPHYSIOLOGY

At present, the underlying pathophysiology of FH remains incompletely understood. FH shares features of other functional gastrointestinal disorders, including psychological comorbidity and visceral hypersensitivity. Patients often complain that heartburn worsens under stress.<sup>9, 10</sup> A 1988 Gallup poll found that 64% of individuals with heartburn note an increase in symptoms under stress. Bradley et al found that stress tasks produced increased heartburn, especially in patients with a high gastrointestinal susceptibility score, with no change in objective acid reflux parameters.<sup>9</sup> The increase in heartburn under stress may represent a temporary esophageal hypersensitivity or alterations in cerebral cortical processing of peripheral signals.

In a recent study by Fass et al, 46 patients with GERD had their symptoms assessed during intraesophageal acid infusion at baseline, during auditory stress, and during an auditory control condition.<sup>11</sup> During auditory stress patients noted a reduction in lag time to symptom perception and an increase in sensory intensity ratings compared with baseline, but not during the auditory control condition. Stress, anxiety and anger all increased in GERD patients following the auditory stressor. The findings support the hypothesis that symptom perception is increased during periods of heightened levels of anxiety. In a study by Shapiro et al, endoscopy-negative heartburn patients underwent 24 hour pH monitoring and psychological testing.<sup>2</sup> Patients with a negative pH test were found to have increased somatization scores compared with those with an abnormal pH test.

Health-related anxiety may be another stressor that fuels functional heartburn. The rising epidemic of esophageal adenocarcinoma has led to widespread use of endoscopy to screen for Barrett's esophagus and perform surveillance. Although the risk of progressing to esophageal cancer from BE is quite low, patients markedly overestimate their risks, leading to marked anxiety.<sup>12</sup> Patients without BE on an index endoscopy rarely progress to BE, let alone adenocarcinoma. However many patients with heartburn are not aware of this, and continue to harbor concerns about developing esophageal cancer.

In certain patients, physiologic gastroesophageal reflux may sensitize the esophagus to develop symptoms of GERD in response to non-acid stimuli.<sup>13</sup> The underlying reason for this sensitization is unclear. This group of patients may be responding to minute changes in intraesophageal pH, an esophageal motor event, or some other intraesophageal stimulus. Bradley et al suggested that conditions of chronic stress or anxiety may play a significant role in this increased sensitivity.<sup>9</sup> Some patients may have heartburn symptoms in response to non-acid or weakly acid reflux, bile reflux, or gaseous reflux. According to the Rome III definition, these patients are considered to have FH, however it is debatable whether or not the heartburn is truly "functional" in this case, since an identifiable trigger (i.e., the reflux event) is closely associated with the symptom. Further studies are needed to establish if these patients behave similar to those with an acid-sensitive esophagus and respond to more aggressive anti-reflux measures, or if they behave more like patients with FH.

The role of abnormal cerebrocortical signaling in FH remains to be determined. There are only a few studies that have investigated the cortical processing of heartburn, and to date studies have not differentiated the symptoms in GERD patients from those in patients with FH. By using functional MRI scanning, acid stimulation has been found to increase sensitization of cingulate and insular cortices to distension of a barostat in the proximal esophagus.<sup>14</sup> It remains to be determined if patients with FH have similar cortical processing to those with GERD.

#### HOW IS FUNCTIONAL HEARTBURN DIFFERENTIATED FROM OTHER CONDITIONS?

The history and physical examination alone are not sufficient to diagnose FH. Neither severity nor frequency of heartburn symptoms adequately predicts endoscopic findings (erosive esophagitis or Barrett's esophagus). Based on Rome III criteria, a diagnosis of FH requires elimination of acidic gastroesophageal reflux (GER) as a cause of the symptoms. Current practice varies with respect to the method of eliminating acidic GER as the cause of heartburn depending on the setting. In primary care the most common practice is to employ a therapeutic trial of a PPI (the "PPI test"). This serves to both help patients' symptoms and make a presumptive diagnosis of GERD-related heartburn if there is a beneficial response. This technique is often used for younger patients who present with short-lived heartburn in the absence of "red flags" (e.g., dysphagia, weight loss, GI bleeding, anemia). Because of the recent release of an over-the-counter version of omeprazole, an increasing number of patients who present their primary care physicians have already tried PPI therapy to alleviate their symptoms. For the majority of young healthy patients who respond to PPI, little additional workup of their symptoms is required. By the time patients present to a gastroenterologist, most have been already started a PPI and are being referred for either endoscopy or because symptoms have not improved.

In an endoscopic setting, reflux as a cause of the symptoms can not actually be ruled out by a negative endoscopy, but can be "ruled in" with an examination that reveals erosions or other complications of  
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GERD (BE, stricture). Patients with functional heartburn should not have gross evidence of esophagitis on endoscopy. The utility of endoscopy in the setting of patients whose symptoms are refractory to PPI is evolving, and there is controversy about whether to perform endoscopy on or off PPI therapy. Proponents of performing endoscopy argue that the yield (for finding erosive esophagitis and thus diagnosing GERD) is higher when patients are not on therapy. Proponents of the opposing viewpoint argue that the sensitivity will increase at the expense of specificity for GERD as the cause of the persistent symptoms. This “positive” diagnosis of GERD can then lead to more aggressive treatment of reflux disease, including fundoplication, when in fact the refractory symptoms in patients with FH have little to do with GERD.

Nonetheless, endoscopy is a very important step in the evaluation of patients refractory to antireflux therapy and can identify select groups of patients who have other diagnoses. One small but important group of patients is the group with refractory severe (Los Angeles Class C or D) erosive esophagitis. This subset of patients often has a large hiatal hernia, significant esophageal motor dysfunction and free gastro-esophageal reflux despite maximal acid suppression. Even with excellent gastric acid control, the esophageal mucosa has little chance to heal because of the continued presence of gastric contents in the esophagus. The other group of patients in whom endoscopy shows a significant benefit is the group with eosinophilic esophagitis (EoE). This disorder is increasingly being recognized as a potential underlying diagnosis in patients with heartburn. When performing endoscopy in the setting of refractory symptoms, esophageal mucosal biopsies should be obtained to evaluate for EoE, preferably from both the distal and the proximal esophagus. Additional research is warranted to further delineate the significance of diagnosis and treatment of EoE in patients with refractory heartburn.

If endoscopy and mucosal biopsies in a patient with heartburn are negative, the differential diagnosis relies on esophageal reflux testing, with either pH- or pH-impedance testing. Esophageal manometry should also be considered to evaluate for conditions such as achalasia and diffuse esophageal spasm, which may present with heartburn or chest pain instead of dysphagia.

pH-testing can differentiate patients with normal and abnormal esophageal acid exposure. Patients with normal endoscopy and abnormal (elevated) esophageal acid exposure are said to have NERD. Those patients with heartburn and normal endoscopy whose esophageal acid exposure falls within the range of normal can be further differentiated by the presence or absence of the association of symptoms with acid reflux events. According to the updated Rome III criteria, the correlation of heartburn with acid reflux events by pH-testing is enough evidence to consider gastroesophageal reflux as the cause of heartburn.<sup>3</sup> As noted previously, this group of patients has been classified as having an “acid-sensitive” (or “acid-hypersensitive”) esophagus. It is only the group of patients with both normal esophageal acid exposure and negative symptom correlation that the diagnosis of functional heartburn can be made. A debate similar to the disagreement regarding diagnostic endoscopy exists for reflux testing as well (i.e., to test on or off therapy). The advent of pH-impedance testing has clarified the role of testing patients on therapy to some degree. With the addition of multiple impedance channels to the standard pH test, nonacidic or weakly acidic refluxate as well as gaseous refluxate can be detected in a patient with an otherwise normal pH test. A detailed discussion of impedance is beyond the scope of this paper.<sup>15</sup> pH-impedance has the potential role of detecting patients who have abnormal reflux of gastric contents irrespective of the pH, as well as identifying those patients who have a “reflux-sensitive” esophagus, not just an “acid-sensitive” esophagus. Even with a more sensitive test, approximately 50-70% of patients with refractory heartburn are still found to have normal reflux parameters and a negative symptom correlation.<sup>16, 17</sup> The clinical significance of abnormal findings on pH-impedance remains a subject of controversy and active research, although some experts will require a normal pH-impedance test with a negative symptom correlation before diagnosing FH.

## MANAGEMENT

At present there are sparse data to support any particular treatment option for patients with FH. Patients with FH have limited or suboptimal response to PPI therapy, so less traditional treatment options are generally prescribed. The principal goals of therapy for patients with functional heartburn are improving

symptom control and improving health-related quality of life. Similar to other functional GI disorders, it is also important to explore confounding psychosocial factors that may be contributing to the problem. For patients with esophageal hypersensitivity, peripheral pain modulating medications (e.g., gabapentin) may be effective, although there are no data examining their utility in patients with heartburn.<sup>18</sup> Centrally-acting medications, such as tricyclic antidepressants or selective serotonin reuptake inhibitors (SSRIs), have been used to improve symptoms and HRQOL in other functional disorders, including functional esophageal disorders, but there are limited data supporting their use in FH.

A small number of studies have demonstrated improvements in chest pain of presumed esophageal origin with select antidepressants, including imipramine, trazodone, and sertraline. In healthy male volunteers, imipramine has been found to increase the threshold for esophageal pain.<sup>19</sup> In patients with esophageal hypersensitivity, the SSRI citalopram has been shown to decrease the sensitivity to both acid perfusion and intraesophageal balloon distension.<sup>20</sup> However the activating effects of SSRIs may be less desirable in patients with FH, especially in those whose symptoms correlate with stress or anxiety. The tricyclic antidepressants and similar medications such as doxepin may improve symptom control to a larger degree.

One additional option used at the esophageal clinic at UNC for treating patients with FH and other upper GI symptoms is a “GI cocktail.” Various concoctions are used in emergency rooms when patients present with a variety of upper GI complaints, although there are no specific data supporting their use in FH. The GI cocktail consists of lidocaine 2%, simethicone, Donnatal elixir, and a liquid antacid, mixed in equal parts, and administered in 5 mL doses as needed for esophageal symptoms. Anecdotal experience indicates that this compound can be highly effective in patients with intermittent or breakthrough symptoms that do not respond to acid suppression and seems to be most useful for patients with a notable component of visceral hypersensitivity, although patients occasionally complain of numbness in their throats. While there certainly may be a powerful placebo effect to this medication, the “on-demand” nature of a GI cocktail can improve patient’s symptoms and quality of life by increasing their internal health-related locus of control.

A final important aspect of management is the avoidance of fundoplication in patients with FH. Although the role of fundoplication has not been studied in functional heartburn, the prevailing belief is that patients with functional heartburn will not benefit from fundoplication.<sup>5</sup> The perceived “failure to do something” may need to be discussed at length with patients before they understand the rationale.

## CONCLUSION

Patients whose heartburn does not respond to acid suppression represent an important and challenging group of patients. In the era of potent acid suppression, the surgical dictum that failure to respond to medical therapy is an indication for anti-reflux surgery no longer holds true. It is clear that most of these patients do not have truly refractory GERD that needs more aggressive antireflux therapy but have a functional disorder that should be managed in a fashion similar to other functional gastrointestinal disorders. Additional research is sorely needed to further define the pathophysiology, evaluation and optimal management of functional heartburn.

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## FACULTY PROFILE

*Ryan D. Madanick, MD*  
*Assistant Professor of Medicine*

You never know where life will take you. The story of Dr. Ryan Madanick's medical career started fresh out of high school when he was accepted to medical school. He was a student in the Honors Program in Medicine at the University of Miami. This is a six-year program that includes both undergraduate studies and medical school. He completed the program in seven years, adding time to study in France.

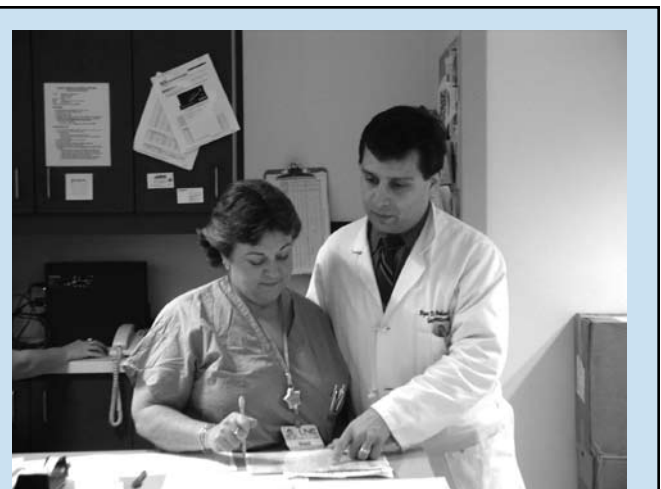
Once Madanick graduated from medical school, he returned to the Northeast where he grew up. He completed his internship and residency at Thomas Jefferson University in Philadelphia. Then he moved back to the University of Miami for a 3-year fellowship, followed by a faculty position.

Madanick chose to specialize in gastroenterology because he identified with an attending who was a gastroenterologist. "I also understood the disease processes of the GI tract really well, and this specialty allows me to work with my hands without becoming a surgeon," said Madanick.

Madanick joined the faculty at the University of North Carolina at Chapel Hill in 2007 to pursue his interests in research, teaching, and clinical work. "The ability to work with both the Center for Functional GI and Motility Disorders and the Center for Esophageal Diseases and Swallowing really appealed to me," said Madanick. "I am fortunate to be able to mix my interests in both esophageal diseases and functional disorders of the GI tract."

"I am also excited to work with such amazingly brilliant people, both in clinical gastroenterology and research," said Madanick. "This position gives me an opportunity to teach, too. I love seeing when students understand a concept, or come back to tell me they remember when I taught them something. I enjoy seeing the students grow."

Madanick's future plans include developing further classification and treatment paradigms for refractory and functional esophageal problems. He also hopes to concentrate on a specific group of patients repeatedly referred to GI specialists. These patients have extra-esophageal problems, often identified by throat clearing and coughing. After consulting with an Ear, Nose and Throat specialist, they are frequently referred to a gastroenterologist, who discovers the issue is not a GI problem, either. "There is no well-defined syndrome name, and no physician group has taken ownership of this condition. It is likely a functional issue, and I would like to conduct research to understand this better."



Dr. Madanick prepares for a procedure with Kris Barman





## ASK THE EXPERT

*Joseph Zimmerman, MD*

Associate Professor of Internal Medicine and Gastroenterology  
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Dear Editors,  
I have heard about the use of hypnotherapy for use in treating IBS. Can you tell me more about this type of treatment?

Answer: Hypnotherapy and the treatment of Functional Gastrointestinal Disorders

### BACKGROUND AND RATIONALE

Functional disorders of the digestive system are prevalent and may involve any level of the gastrointestinal (GI) tract. Functional heartburn, dyspepsia and noncardiac chest pain are the common functional disorders of the upper digestive system, while the irritable bowel syndrome (IBS) is the characteristic functional disorder of the lower GI tract. Functional gastrointestinal disorders (FGD) typically afflict young adults or even children, and tend to pursue a chronic course. These disorders, which frequently overlap, result from interplay of biological, emotional, behavioral and dietary factors. GI symptoms and some of the extraintestinal manifestations of FGD may reflect a reduced threshold for visceral pain. Several lines of evidence suggest a role of psychological factors in FGD: A frequent coexistence of psychiatric comorbidity, such as anxiety or depression; Exacerbation of symptoms during periods of emotional stress and an increased prevalence of these disorders in people who have been subjected to prolonged, extreme stress, such as holocaust survivors. Thus, FGD may be regarded as complex disorders, where physiological and emotional components intertwine. In view of their multifactorial nature, a holistic approach relating to the physical symptoms and their emotional content should be ideal for patients who have a severe or refractory course. Hypnotherapy is a modality that can relate to all these aspects of FGD.

### DEFINITION, METHODS, INDICATIONS AND CONTRAINDICATIONS

Numerous definitions have been proposed to describe the hypnotic state. For the purpose of this discussion, hypnosis may be defined as a state of altered awareness characterized by increased receptivity to suggestions. In this context, a suggestion is defined as an idea, or a set of ideas, conveyed to the hypnotized subject by an external agent (i.e., the therapist). Additional features stemming directly from this heightened

suggestibility are a capacity for modification of perceptions (such as visceral sensitivity or somatic pain sensation) and a potential for control of a variety of physiological functions that are not under voluntary control (such as gastric secretion). By analogy to surgical therapy, in hypnotherapy, the hypnotic trance may be regarded as the operating theatre, the ambiance, background, anesthesia etc., while the suggestions administered to the patient in this state may be regarded as the surgical scalpel, the instrument that produces the specific therapeutic effects. These suggestions, rather than the hypnotic trance per se, are the active ingredients of therapy. Indeed, a therapeutic effect may sometimes be achieved by administering suggestions to a patient in a state of normal awareness. Hence, some patients who lack any hypnotic capability may still benefit from appropriate suggestions. The term "hypnosis and suggestion", rather than hypnotherapy, may therefore be more suitable to describe this therapeutic modality.

Hypnotherapy may be administered using a generic instrument, a script of suggestions for general relaxation and "digestive well being". One such instrument, entitled "gut focused hypnotherapy" is in use in some centers. (1) Ease of administration is a major advantage of this approach. It is particularly useful for research purposes and for group therapy. The disadvantages of this method are in its "rigidity". No two patients are alike, and some suggestions may not work for certain patients. These disadvantages may be overcome using a treatment approach that is individually tailored to the specific patient. For instance, some patients exhibit a resistance to the mere induction of a hypnotic trance. Such resistance may be circumvented using specific induction methods. Moreover, the emotional content of symptoms, which may be important in many of the "refractory" patients, may be efficiently dealt with using "custom-made" suggestions. For example, guilt feelings, an important factor in some patients, may be effectively dealt with using specific suggestions, and this individual approach

may result in a therapeutic response without any specific reference to the digestive system, the focus of symptoms (and guilt feelings in such cases). Whatever method is used, a crucial prerequisite is that the patient practices self hypnosis (taught on the first therapeutic session) on a daily basis for the entire period of treatment, which may vary according to the specific case, but usually spans about 2 months or more.

Hypnotherapy is not necessary for most FGD patients. Mild to moderate cases usually benefit from reassurance, symptomatic treatment or dietetic counseling. Hypnotherapy should be reserved for the more severe or refractory cases. The main contraindications for this treatment are depression or a history of psychosis. Hypnotherapy should be administered only by trained, qualified professionals.

#### A BRIEF SUMMARY OF PUBLISHED RESEARCH

Since 1984, when the first controlled study of hypnosis in severe, refractory IBS was published (2), the efficacy of hypnotherapy has been demonstrated in several types of FGD. Well-designed, randomized controlled trials have shown it to be effective in IBS (2-6), in functional dyspepsia (7) and in noncardiac chest pain (8-9). In controlled studies, the rate of symptom improvement was about 70-80%, compared with about 20-30% in the control groups. The therapeutic effects of hypnotic interventions in these disorders were long-lasting (3,5,7,9), persisting as long as 6 years after cessation of therapy (5) and were manifest on multiple dimensions: improved quality of life (4,6-8), a decrease in symptoms (1-5,7-9) and a reduction in the use of medications and in consultation rates (4,7). Moreover, in IBS patients, hypnotherapy has been shown to be cost-effective (4).

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*The UNC Center for Functional GI and Motility Disorders is pleased to welcome Dr. Joe Zimmerman as he begins a 12-15 month sabbatical beginning in September 2008. Dr. Zimmerman is a graduate of the Hebrew-University-Hadassah Medical School in Jerusalem, where he completed his residency in Internal Medicine and a fellowship in Gastroenterology. During his stay in UNC, Dr. Zimmerman plans to validate some of the scales he has developed for measurement of symptoms in the English language, to study the course and results of detoxification protocol in treating narcotic bowel syndrome, and to interact with the various members on the GI faculty on mutual fields of interests. In addition he will serve as adjunct faculty in the functional GI and Motility clinic and the Division of Gastroenterology and Hepatology.*

The UNC Center for Functional GI and Motility Disorders has conducted research studies on the effects of hypnotherapy on IBS symptoms. Dr. Olafur Palsson has directed this important research.

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## INSTITUTE OF MEDICINE RELEASES ITS REPORT ON HEALTH CONSEQUENCES OF WAR TRAUMA

*Douglas A. Drossman, MD*

*Co-Director of the Center for Functional GI & Motility Disorders*

In 1998, the Institute of Medicine (IOM) began a series of congressionally-mandated studies to examine the scientific and medical literature on the potential health effects of chemical and biological agents related to the 1991 Gulf War. So far only limited evidence for a relationship of mental and physical illness had been found with regard to combustion products and chemicals. Now after 2 years of review and deliberation, the awaited report on the psychosocial effects of war trauma was released in book form. This report comprehensively reviews, evaluates, and summarizes the peer-reviewed scientific and medical literature regarding the association between stress and long-term adverse health effects in Gulf War veterans, as related to the physiologic, psychologic, and psychosocial effects of stress. The study found that there are substantial consequences of war trauma on physical and mental health including post-traumatic stress disorder and increased symptom reporting in many organ systems.

Dr. Doug Drossman, Co-Director for the UNC Center for Functional GI & Motility Disorders, was a member of the IOM Committee on Gulf War and Health: Physiologic, Psychologic, and Psychosocial Effects of Deployment-Related Stress who conducted this study and was responsible for compiling the data related to gastrointestinal and dermatological disorders.

With regard to the functional GI disorders, the committee reported several important conclusions in their report:

- “There are substantial physiological studies to support the association of acute and chronic stress with lowered pain sensation thresholds and visceral hypersensitivity, increased motility, altered brain circuitry involving pain regulation, and altered HPA axis reactivity”.
- “... it is possible that combat stress leads to central amplification of visceral and somatic

symptoms via a variety of CNS-peripheral mechanisms (e.g., HPA axis, pain modulatory circuits and autonomic function).

- “There are some limitations in this body of evidence, mostly related to methods of effect assessment. One is the self-reporting of GI symptoms in most cases not meeting criteria to diagnose a functional GI disorder. None of these studies used contemporary [Rome] criteria for assessment of FGIDs though in some cases the diagnoses can be inferred”.
- “Nevertheless, taken together the overall pattern of symptoms found across many primary and secondary studies confirms an association of deployment related stress and functional GI symptoms of abdominal pain, diarrhea, nausea and vomiting among others. Furthermore, the findings are suggestive for the development of deployment related IBS, functional dyspepsia and some other functional GI syndromes”.
- “Thus, while the association of deployment related stress with GI symptoms is accepted, the association with functional GI disorders is supported but not complete”. Accordingly the committee was cautious in its conclusion: **“There is limited but suggestive evidence of an association between deployment to a war zone and gastrointestinal symptoms consistent with functional gastrointestinal disorders, such as irritable bowel syndrome and functional dyspepsia”.**

These data were updated at DDW 2008 in San Diego, CA when 3 oral presentations showed clear associations of war trauma or abuse and the development of IBS.

Notably, Douglas Morgan MD at UNC and a member of our Center directed the 3rd study which showed a clear association between traumatic war experiences in the Sandinista rebellion in Nicaragua and the development of IBS. For example, females

who witnessed an execution, or in whom a family member killed or personally suffered physical or psychological abuse or other trauma were at 2.2 to 4.5 greater risk of developing IBS.

Dr. Drossman was invited to give a concluding presentation on “War Trauma and IBS” and he summarized the 3 studies as well as the Institute of Medicine report. He noted that all 3 of these recent studies used Rome criteria to confirm the diagnosis of IBS. Had these studies been available prior to the IOM report, the committee’s conclusions regarding the association of war trauma with IBS and other FGIDs would have been reported as “conclusive” rather than “suggestive”.

You can obtain a copy of the results of the report from the Institute of Medicine Website at [www.iom.edu](http://www.iom.edu).

**Positive Association Between Traumatic War Experiences in the Sandinista Revolution and Subsequent IBS: A Population Based Study in Nicaragua\***  
 Wurzelmann D, Pena R, Cortes L, Caldera T, Heidt P, Morgan D

- Household interviews of 1012 Residents with 19.3% (35%M, 9.3%F) having war experiences
- Prevalence of IBS 15.2% (Rome II, 17%F, 12%M)

Odds for IBS with:	Females OR (95% CI)	Males OR (95% CI)	>43 years OR (95% CI)
Witness execution	4.5 (1.6 -12.6)	2.4 (1.1 - 5.4)	
Family member killed or injured	2.2 (1.0 - 4.5)	2.1 (1.0 - 4.5)	2.1 (1.0 - 4.3)
Physical or psychological abuse	2.7 (1.0 - 7.6)	2.7 (1.2 - 5.7)	2.7 (1.2 - 6.0)
Multiple traumas	2.2 (1.1 - 4.6)	2.3 (1.0 - 5.3)	

\* Sponsored by Rome Foundation. Similar results for domestic violence also reported at DDW 2008. 2112

DDW 2008

Sunday, May 18, 2008  
 4:00 PM – 5:30 PM  
 AGA Research Forum  
 Chairs: **Douglas A Drossman**, G. Richard Locke  
 Sponsored by: Neurogastroenterology and Motility  
 Participants will be able to :  
 Learn about the role of war trauma on IBS prevalence.

#181 - Striking Prevalence of Irritable Bowel Syndrome in Former Prisoners of War: Analysis of Risk Factors  
 Michele C. Pulling, Mack Orsborn, Barbara J. Olson, Stephen Hunt, David J. Kearney

#182 - Bowel Disorders in Gulf War Veterans  
 Ashok K. Tuteja, Keith G. Tolman, Nicholas J. Talley, Matthew Samore, Gregory J. Stodard, Stacy Batt, G. Nicholas Verne

Sp272a – Overview Lecture: War trauma and IBS  
**Douglas A. Drossman**

Tuesday, May 20, 2008  
 4:00 PM – 5:30 PM  
 AGA Institute Distinguished Abstract Plenary  
 Chairs: William D. Chey, **Nicholas J. Shaheen**  
 Sponsored by: Clinical Practice  
**CLINICAL PRACTICE**

#799 – Positive Association Between Traumatic War Experienced in the Sandinista Revolution and Subsequent IBS: A Population-Based Study in Nicaragua  
 Daniel Wurzelmann, Rodolfo Pena, Loreto Cortes, Elette Valladares, Paris Heidt, **Douglas R. Morgan**

**Striking Prevalence of Irritable Bowel Syndrome in Former Prisoners of War: Analysis of Risk Factors**  
 Pulling MC, Orsborn M, Olson BJ, Hunt S, Kearney DJ

- Survey of 359 former POWs at VA setting
- Prevalence of IBS 69% (Rome II)

	OR for IBS (95%CI)	P
Psychological trauma	1.4 (0.68 - 2.94)	0.35 (NS)
Physical trauma*	.23 (0.06 - 0.91)	0.04
GI Diseases**	2.1 (1.1 - 3.9)	0.03
Psychiatric symptoms during captivity	3.0 (1.5 - 6.0)	0.002

\* e.g., Beating, torture forced marches \*\*Dysentery or worms

DDW 2008 2119

**Prevalence of Bowel Disorders in Persian Gulf Veterans**  
 Tuteja AK, Tolman KG, Talley NJ, Samore M, Stodard GJ, Batt S, Verne GN

- Persian Gulf War Vets in Gulf War Registry – VA Database
- Gastroenteritis during deployment a risk factor for IBS – OR 3.6 (95% CI 1.9-6.9)
- IBS (Rome III) associated with decreased HRQL

	Prevalence of Bowel Disorders Related to Deployment (%)		
	Before	During	Post
Diarrhea	6.8	39.3*	34.1
Constipation	17.0	49.5**	54.2
IBS (similar effects seen with subtypes)	0.3	15.9*	40.2***
Bloating	4.0	35.3**	44.2***

\* p<0.02 relative to before deployment  
 \*\* p<0.01 relative to before deployment  
 \*\*\* p<0.01 relative to during deployment.

DDW 2008 2111

## UNC CENTER AWARDED A SECOND BI-NATIONAL FOUNDATION GRANT WITH SOROKA MEDICAL CENTER, ISREAL

*Ami D. Sperber, MD, MSPH  
Soroka Medical Center  
Ben-Gurion University of the Negev*



A new US-Israel Binational Science Foundation (BSF) grant has been awarded to co-PI's Ami Sperber from Israel and Doug Drossman from UNC. The subject of the study will be sleep disturbances among women with IBS. As in our previous BSF award on the GI effects of elective gynecological surgery, which was completed last year, this study is also designed so that subject recruitment and testing will be carried out entirely in Israel and all data handling and analyses will be done by the biometry unit at UNC. The BSF awarded us \$138,000 for the 3-year study.

The previous study produced two papers. The first documenting the development of abdominal pain following elective gynecological surgery was published in *Gastroenterology* in 2008. The second, which shows that constipation is not an outcome of elective hysterectomy as previously thought, has been accepted for publication in *Neurogastroenterology and Motility* and will be published later this year.

The present study will involve patient reports and physiological measures of sleep impairment in IBS patients compared to healthy controls. While there is clear evidence of sleep impairment reported by IBS patients, physiological testing has yielded contradictory results and the issue remains very controversial. The present study will be conducted in the sleep lab in Beer-Sheva (a second Israeli co-PI is Dr. Ariel Tarasiuk, a prominent sleep physiologist) as well as through the use of modern, sophisticated ambulatory technologies to measure sleep disturbances in the patient's natural surroundings. Two additional aspects of the study will involve assessing the effect of sleep deprivation on IBS symptom severity and measurements of nocturnal urinary melatonin levels during the test periods.

Subject recruitment will begin in the fall/winter of 2008.

*Ami Sperber, MD will be visiting the UNC Center for Functional GI and Motility Disorders September 15-16, 2008. During his visit, Dr. Sperber will give the GI clinical conference presentation on "Can functional GI disorders be induced by stress?" as well as present to the Biometry Team at the Center. It is our great pleasure to welcome Dr. Sperber to Chapel Hill.*

I was born in the Bronx, NYC and moved to Israel at the age of 23. My association with UNC began in 1990 when I arrived for a two year stay to do a Masters of Science degree in Public Health (MSPH) in the Department of Health Behavior and Health Education of the School of Public Health. I had just finished my training in Gastroenterology in Israel and was developing an interest in functional disorders, so it was only natural to look up Doug Drossman. His secretary scheduled me for a short introductory meeting with Doug, which turned out to be the beginning of a wonderful personal relationship with Doug, Debbie and their family as well as a very satisfying and fruitful professional one. Doug has become friend, mentor and co-investigator for me and has helped me at every turn of my career. We have completed one Binational Science Foundation grant (US-Israel) and are now embarking on a second study funded by the BSF. I have worked particularly closely on those studies with Carolyn Blank-Morris, Shrikant Bangdiwala, and Yuming Hu (JB). Over the years I have also gotten to know many other members of the UNC Center, first and foremost Bill Whitehead. I knew Udi Ringel in Israel, as a friend and colleague, before he went to UNC, and have become colleagues and friends of many of the members of the biometry unit, a few of whom (Kant, JB, Steve Weinland) I have had the honor and pleasure of hosting on visits to and tours of Israel. I look forward to continuing this wonderful association and am happy to extend an invitation to one and all to come and visit Israel.

Ami Sperber, MD

# DDW 2008

*Center faculty and investigators were well-represented in presentations and posters at Digestive Diseases Week 2008, San Diego, CA, May 2008.*

DDW is the premier research and clinical forum for scientists and clinicians within digestive diseases which includes gastroenterology, liver disease and gastrointestinal surgery. The American Gastroenterology Association (AGA) is the group responsible for the gastroenterologists. The AGA has designated 12 research sections that include functional GI and motility (Neurogastroenterology), Esophageal Diseases, Clinical practice, Inflammatory Bowel Disease, and others. The program is developed annually by the section chairs and co-chairs with

the help of section councilors who are elected by the membership. We are fortunate that the UNC Center co-directors have been involved in this process. Dr. Drossman was the Neurogastroenterology co-chair and chair between 2001 and 2006 and Dr. Whitehead is the Neurogastroenterology Councilor for 2006 through 2011. Thus our Center is playing an important role that is spanning this decade in developing the programs that focus on research and education in the FGIDs.

## CLINICAL SYMPOSIA SESSIONS

*Clinical Symposia are 90 minute educational programs that highlight new or emerging areas of interest to practicing gastroenterologists or clinical investigators (there are also Basic Science Symposia for basic scientists who usually do not see patients). The speakers are selected by the AGA Section chairs who seek out the experts in the designated areas. Listed below are the symposia where the invited speaker is from our Center.*

Sunday, May 18, 2008

Symposia Title: **EMERGING ROLE OF GENETICS IN FUNCTIONAL GASTROINTESTINAL DISORDERS**

Chairs: Yuri A Saito, **William E. Whitehead**

*Sponsored by: Neurogastroenterology and Motility; Esophageal, Gastric & Duodenal Disorders*

Presented by **William E. Whitehead**

Title: Genetic Markers Associated with the Diagnosis of IBS and Subtypes of IBS

Tuesday, May 20, 2008

Symposia Title: **AN EVIDENCE BASED APPROACH TO CONTROVERSIES IN IBS MANAGEMENT**

Chairs: Richard J. Saad, **Kevin W. Olden**

*Sponsored by: Clinical Practice; Neurogastroenterology and Motility; Immunology, Microbiology & Inflammatory Bowel Disease; Esophageal, Gastric & Duodenal Disorders; Nutrition & Obesity; Intestinal Disorders*

Presented by: **Yehuda Ringel**, Kevin W. Olden

Title: Diet, Active Food and Complementary Medicines: Physiological Benefits or Placebo Effect?

Tuesday, May 20, 2008

Symposia Title: **FECAL INCONTINENCE – NEW PERSPECTIVES ON EARLY DETECTION, CURRENT AND FUTURE THERAPIES**

Chairs: **William E. Whitehead**, Tracy L. Hull

*Sponsored by: AGA Institute, SSAT*

Presented by: **Steve Heymen**

Title: Medical Management and Biofeedback

Wednesday, May 21, 2008

Symposia Title: **THE CHANGING FACE OF GERD**

Chairs: Donald O. Castell, Joel H. Rubenstein

*Sponsored by: Clinical Practice; Esophageal, Gastric & Duodenal Disorders; Neurogastroenterology and Motility*

Presented by: **Nicholas J. Shaheen**

Title: Diagnostic and Therapeutic Approach to NERD

Wednesday, May 21, 2008

Symposia Title: **NARCOTIC BOWEL SYNDROME**

Chairs: **Douglas A Drossman**, David M. Grunkemeier

*Sponsored by: Neurogastroenterology and Motility; Clinical Practice; Hormones, Transmitters, Growth Factors, & Their Receptors*

Presented by: **Douglas A. Drossman**

Title: Treatment Strategies

### THE ROME FOUNDATION/AGA INSTITUTE LECTURE

*The Rome Foundation sponsors a lectureship with the American Gastroenterological Association (AGA) held annually at Digestive Diseases Week (DDW). This year, Douglas A. Drossman, Co-Director of the Center and President of the Rome Foundation, was the Moderator for the session.*

Lecture Title: **LESSONS FROM OUR PATIENTS**

Guest Speaker: Gina Kolata

Moderators: **Douglas A. Drossman**, Lin Chang

### POSTGRADUATE COURSE SESSIONS

*On the Saturday and Sunday prior to DDW, the AGA offers Postgraduate Courses for attendees. These educational presentations are designed to update practicing gastroenterologists and trainees on the most up to date diagnostic and treatment methods. The UNC Center for Functional GI and Motility Disorders was proud to have Dr Nicholas J. Shaheen invited to present at two of these sessions.*

Course Title: **SSAT POSTGRADUATE COURSE: UNRESOLVED PROBLEMS AND EVOLVING SOLUTIONS IN SURGICAL GASTROENTEROLOGY**

Chairs: Myrddin Rees, Jean-Nicolas Vauthey, Thomas J. Howard, Fabrizio Mitchelassi, David M. Mahvi, Nathaniel J. Soper

Instructor: *Nicholas J. Shaheen*

Topic: Benign Esophageal Strictures: Non-Operative Options

Course Title: **SESSION IV GASTROINTESTINAL CANCERS: WHAT'S NEW?**

Chair: David A. Lieberman

Instructor: *Nicholas J. Shaheen*

Topic: The Rising Incidence of Esophageal Cancer: Genes or Fat?

### MEET THE PROFESSOR LUNCHEONS

*Meet the Professor Luncheons are smaller educational sessions (about 35 in attendance) that involve informal discussion of topic areas. They are usually facilitated by an expert in the area of interest. The luncheon facilitators are chosen by the section chairs. We were pleased to have two faculty members selected to lead sessions at DDW 2008.*

Barrett's Esophagus (M53)

*Nicholas J. Shaheen, Ganapathy A. Prasad*

Medical and Surgical Therapy for Fecal Incontinence (M57)

*William E. Whitehead*

## RESEARCH FORA

Research Fora are formal research presentations by six investigators in one 90 minute session (15 minute presentations). Since there are 12 sections in AGA, each AGA section is allotted only 5 or 6 research fora to develop for the meeting. These are oral sessions where the speaker presents his or her new research findings to the audience. The studies are submitted by investigators around the world in abstract form (about 250 word paragraph summarizing the research.) A panel of peers work in committee to vote on the quality of the work. While thousands of research abstracts are submitted each year, less than 10% are accepted for Research Fora presentations. Below are the presentations by the Center faculty who were selected based on the quality of the research.

Sunday, May 18, 2008

Forum Title: **FUNCTIONAL GI DISORDERS: EPIDEMIOLOGY AND SYMPTOMS**

Chairs: **Douglas A Drossman**, G. Richard Locke

Sponsored by: *Neurogastroenterology and Motility*

Presented by: **Douglas A. Drossman**

Title: Overview Lecture: War trauma and IBS

Tuesday, May 20, 2008

Forum Title: **FECAL INCONTINENCE, PELVIC FLOOR DISORDERS AND OTHER ANORECTAL DISORDERS**

Chairs: Jose Maria Remes Troche, Hiroshi Mashimo

Sponsored by: *Neurogastroenterology and Motility*

Presented by: **Steven Heymen, Yolanda V. Scarlett, William E. Whitehead**

Title: Twelve-Month Follow-Up of Randomized Controlled Trial (RCT) Comparing Biofeedback to Alternative Treatments for patients with Pelvic Floor Dyssynergia-Type Constipation (PFD)

Tuesday, May 20, 2008

Forum Title: **INTESTINAL MICROBIAL RESPONSE**

Chairs: Ralph A. Giannella, V.K. Viswanathan

Sponsored by: *Intestinal Disorders*

Presented by: *Matthew Benschhoff, Eliette Valladares, Rodolfo Pena, Loreto Cortes, Paris Heidt, Mercedes Caceres, Douglas R. Morgan*

Title: Post-Infectious IBS in the "Non-Sterile" Developing Nation Environment and the Role of Parasite Burden, a Population-Based Study in Central America

Wednesday, May 21, 2008

Forum Title: **IBD, INFLAMMATION AND INFECTION IN GASTROINTESTINAL CANCERS**

Chairs: Jan-Michael A. Klapproth, Ezra B. Burstein

Sponsored by: *Gastrointestinal Oncology*

Presented by: *Xiang Jun Shen, Lauren Burcal, Caroline N. Mpande, Natascha Jenkins, Thomas Randall, John F. Rawls, Robert Sandler, Temitope O Keku*

Title: Characterization of Mucosa-Associated Bacteria Species in Colorectal Biopsies from normal Mucosa of patients with and Without Adenomas

**PLENARY SESSION**

*The Plenary Session is another type of Research Forum; however, in this case the section chair and co-chair select the top six abstracts and place them in one forum. These are the very best of the abstracts selected by each of the 12 sections.*

Monday, May 19, 2008

Session Title: **CLINICAL SCIENCE PLENARY**

Chair: Robert S. Sandler

Sponsored by: AGA Institute

Presented by: **Nicholas J. Shaheen**, Prateek Sharma, Bergein F. Overholt, Charles J. Lightdale, Herbert C. Wolfson, Richard E. Sampliner, Kenneth K. Wang, Mary P Bronner, John R. Goldblum, Blair A. Jobe, Glenn M. Eisen, David E. Fleischer, Virender K. Sharma, Brenda Hoffman, Richard I. Rothstien, Hiroshi Mashimo, Kenneth J. Chang, V. Raman Muthusamy, Steven A. Edmundowicz, Stuart J. Spechler, Ali Siddiqui, Anthony Infantolino, Gary W. Falk, Michael B. Kimmey, Amitabh Chak

Title: A Randomized, Multicenter, Sham-Controlled Trial of Radiofrequency Ablation (RFA) for Subjects with Barrett's Esophagus (BE) Containing Dysplasia: Interim Results of the AIM Dysplasia Trial

**DISTINGUISHED ABSTRACT PLENARY SESSIONS**

Tuesday, May 20, 2008

Session Title: **GROWTH DEVELOPMENT AND AGING**

Chairs: Mark Lowe, Eric Sibley

Sponsored by: Growth, Development and Aging

Presented by: Denesh K. Chitkara, Nicholas J. Talley, Nilay Shah, Amy Weaver, Slavica Katusic, **Miranda A. Van Tilburg**, William E. Whitehead, G. Richard Locke

Title: Direct Medical Costs Associated with Constipation from Childhood to Early Adulthood: A Birth Cohort Study

Tuesday, May 20, 2008

Session Title: **CLINICAL PRACTICE**

Chairs: William D. Chey, **Nicholas J. Shaheen**

Sponsored by: Clinical Practice

Presented by: Daniel Wurzelmann, Rodolfo Pena, Loreto Cortes, Eliette Valladares, Paris Heidt, **Douglas R. Morgan**

Title: Positive Association Between Traumatic War Experienced in the Sandinista Revolution and Subsequent IBS: A Population-Based Study in Nicaragua

**TOPIC FORA**

*Topic Fora are similar to Research Fora, though the topic is considered important enough that there are usually two or more co-sponsor sections that develop the program (e.g., Neurogastroenterology and Clinical Practice sections may sponsor a session on Treatment of IBS because it appeals to both sections). Below are the Topic Fora and the sponsoring sections where abstracts from Center scientists were selected:*

Sunday, May 18, 2008

Forum Title: **OUTCOMES RESEARCH IN IRRITABLE BOWEL SYNDROME**

Chair: Nicholas J. Talley, Anil Minocha

Sponsored By: Clinical Practice; Intestinal Disorders; Neurogastroenterology and Motility

Presented by: William D. Chey, **Douglas A. Drossman**, Charles Scott, Raymond M. Panas, Ryuji Ueno

Title: What Symptoms Drive Global Symptom Improvement with Lubiprostone in patients with Irritable Bowel Syndrome and Constipation: Data from Two Multicenter, Randomized, Placebo-Controlled Trials

Tuesday, May 20, 2008

Forum Title: **CLINICAL ENDOSCOPIC ULTRASOUND**

Chairs: Julia K. LeBlanc, Mohammad R. Anees

Presented by: V. Raman Muthusamy, Amit Rastogi, Steven A. Edmundowicz, **Nicholas J. Shaheen**, Prateek Sharma, Kenneth J. Chang

Title: The Utility of Endoscopic Untrasound (EUS) in Patients with Barrett's Esophagus (BE) and High Grade Dysplasia (HGD): Analysis of the AIM Dysplasia Trial Experience

## POSTER SESSIONS

*There are many very good research abstracts submitted each year to DDW (and specifically to the AGA sections of DDW), but not all can be selected for the oral sessions (Research, Topic and Plenary sessions). About 50% of all abstracts submitted are selected for Poster Sessions. The Poster Sessions are held each day and each session has about 1,000 posters mounted on 4'x8' boards and grouped according to topic areas. The UNC Center is very successful in having many posters selected each year as shown below.*

Parental Employment and Marital Status: Indicators of Coping Style in Childhood Recurrent Abdominal Pain

Nader N. Youssef, Shelby Langer, Dennis L. Christie, Lynn S. Walker, Joan Romano, Andrew D. Feld, Sheri A. Ballard, **William E. Whitehead**, Rona L. Levy

Lubiprostone Is Effective and Well Tolerated Through 48 Weeks of Treatment in Adults with Irritable Bowel Syndrome and Constipation

William D. Chey, **Douglas A. Drossman**, Charles Scott, Raymond M. Panas, Ryuji Ueno

Twelve Month Follow-Up for Patients with Fecal Incontinence Reporting Adequate Relief After a 4-Week Education and Medical Management Run-in Intervention

**Steve Heymen**, Yolanda V. Scarlett, **William E. Whitehead**

Twelve Month Follow-Up for Patients with Pelvic Floor Dyssynergia-Type Constipation (PFD) Reporting Adequate Relief After a 4-Week Education and Medical Management Run-in Intervention

**Steve Heymen**, Yolanda V. Scarlett, **William E. Whitehead**

Health Care Costs Associated with Fecal Incontinence

**Steve Heymen**, **Olafur S. Palsson**, Michael Von Korff, Rona L. Levy, **Marsha J. Turner**, **William E. Whitehead**

National Health and Nutrition Examination Survey (NHANES): Association of Usual Stool Consistency and Frequency with Fecal Incontinence

**William E. Whitehead**

National Health and Nutrition Examination Survey (NHANES) of Fecal Incontinence: Characteristics of Incontinent Stools

**William E. Whitehead**

Health Care Costs and Utilization in Patients with Chronic Constipation

Thao V. Nguyen, **Olafur S. Palsson**, Michael Von Korff, Andrew D. Feld, Rona L. Levy, **Marsha J. Turner**, **William E. Whitehead**

National Health and Nutrition Examination Survey (NHANES) of Fecal Incontinence: Prevalence By Sex, Age, Race, Marital Status, Education, and Income

**William E. Whitehead**

Bone Health Quality Improvement in a Tertiary GI/Hepatology Clinic

Millie Long, **Lisa M. Gangarosa**, Robert Sandler

Both Bowel Symptom Severity and Visceral Anxiety Are Major Determinants of the Quality of Life Impact of Constipation

**Olafur S. Palsson**, Bruce D. Naliboff, **Marsha J. Turner**, Rona L. Levy, Andrew D. Feld, Michael Von Korff, **William E. Whitehead**

The Relative Effects of Clinical and Psychosocial Factors On Health Care Utilization and Disability in Women with Functional Bowel Disorders

Denesh K. Chitkara, **Carolyn B. Morris**, **Yuming J. Hu**, Brenda B. Toner, Nicholas E. Diamant, **Jane Leserman**, **Christine B. Dalton**, **Shrikant I. Bangdiwala**, **William E. Whitehead**, **Douglas A. Drossman**

Gastrointestinal Symptoms That Differentiate Pediatric FD from IBS

Shelby Langer, Lynn S. Walker, Kari F. Baber, **William E. Whitehead**, Joan Romano, Dennis L. Christie, Nader N. Youssef, Sheri A. Ballard, Melissa Young, Melissa J. Coffey, Sharon Brenner, Lila Garner, Rona L. Levy

## POSTER SESSIONS, CONT.

National Health and Nutrition Examination Survey (NHANES) of Stool Frequency and Consistency in U.S. Adults

**William E. Whitehead**

The ROME III Questionnaire Functional Constipation Module As a Constipation Severity Scale

**Olafur S. Palsson, Marsha J. Turner, Rona L. Levy, Andrew D. Feld, Michael Von Korff, Douglas A. Drossman, William E. Whitehead**

Persistence of the ROME Diagnostic Symptoms for Irritable Bowel Syndrome

**Olafur S. Palsson, Miranda A. Van Tilburg, Motoyori Kanazawa, Denesh K. Chitkara, Lisa M. Gangarosa, Douglas A. Drossman, William E. Whitehead**

Health-Related Quality of Life in Adults with Irritable Bowel Syndrome with Constipation: Results of a Combined Analysis of Two Phase 3 Studies with Lubiprostone

**Douglas A. Drossman, William D. Chey, Charles Scott, Raymond M. Panas, Ryuji Ueno**

Rifaximin for the Treatment of Diarrhea-Associated Irritable Bowel Syndrome: Short Term Treatment Leading to Long Term Sustained Response

Anthony Lembo, Salam F. Zakko, Nelson L. Ferreira, **Yehuda Ringel**, Enoch Bortey, Kecia Courtney, Ed Corsi, William P. Forbes, Mark Pimentel

Probiotic Bacteria Lactobacillus Acidophilus Ncfm and Bifidobacterium Lactis Bi-07 Improve Symptoms of Bloating in Patients with Functional Bowel Disorders (FBD).

**Yehuda Ringel, Olafur S. Palsson, Gregory Leyer, Sarah Causey, Sarah E. Yeskel, Steven M. Faber, Tamar Ringel-Kulka**

Predictors of Clinical Response from a Phase 2 Multi-Center Efficacy Trial Using Rifaximin, a Gut-Selective, Nonabsorbed Antibiotic for the Treatment of Diarrhea-Associated Irritable Bowel Syndrome

**Yehuda Ringel, Salam F. Zakko, Nelson L. Ferreira, Enoch Bortey, Tina Wu, Kecia Courtney, William P. Forbes, Anthony Lembo, Mark Pimente**

Diffuse Noxious Inhibitory Controls (Dnic) Are Compromised in Patients with Irritable Bowel Syndrome Compared to Healthy Controls

**Steve Heymen, William Maixner, William E. Whitehead, Rebecca R. Klatzkin, Beth Mechlin, Kathleen C. Light**

Small Intestinal Bacterial Overgrowth in Irritable Bowel Syndrome: Association with Colon Motility, Bowel Symptoms, and Psychological Distress

Madhusudan Grover, Motoyori Kanazawa, Denesh K. Chitkara, **Lisa M. Gangarosa, Olafur S. Palsson, Douglas A. Drossman, Marsha J. Turner, William E. Whitehead**

The Development of IBS, Abdominal Pain and Constipation Following Elective Hysterectomy

Ami D. Sperber, Carolyn B. Morris, Lev Greemberg, **Shrikant I. Bangdiwala**, David Goldstein, Eyal Sheiner, Yefim Rusabrov, **Yuming J. Hu**, Miriam Katz, **Douglas A. Drossman**

Characterization of the Fecal Microbiota in Patients with Diarrhea Predominant Irritable Bowel Syndrome.

Ian M. Carroll, Xiang Jun Shen, Temitope O. Keku, R. Balfour Sartor, **Yehuda Ringel**

Meal Induced Symptoms in Patients with Irritable Bowel Syndrome - Clinical and Physiological Characteristics.

**Yehuda Ringel, Amit Ringel, Olafur S. Palsson, Motoyori Kanazawa, William E. Whitehead**

Psychological Well-Being and Quality of Life (QOL) in Barrett's Esophagus (BE) Compared to Gastroesophageal Reflux Disease (GERD)

Quinn K. Lippmann, **Ryan D. Madanick**, Melissa Spacek, Paris Heidt, **Douglas R. Morgan**, Stephanie D. Bright, Catherine Zimmer, **Nicholas J. Shaheen**

Positive Association Between Intimate Partner Violence and Irritable Bowel Syndrome in Latina Women: A Population-Based Study in Nicaragua

Sylvia I. Becker-Dreps, Eliette Valladares, Rodolfo Pena, Loreto Cortes, Christopher Martin, **Douglas R. Morgan**

## KEY POSTERS FROM THE UNC CENTER

*This year, the Center co-directors decided to identify several poster presentations that may be of particular interest to the readership. They are listed in full abstract form over the next six pages:*

### Health-Related Quality of Life in Adults with Irritable Bowel Syndrome with Constipation: Results of a Combined Analysis of Two Phase 3 Studies with Lubiprostone

**Douglas A. Drossman**, William D. Chey, Charles Scott, Raymond M. Panas, Ryuji Ueno

Lubiprostone is a selective activator of type-2 chloride channels approved for the treatment of chronic idiopathic constipation. Combined analyses of the quality of life (QOL) data from two phase 3, double-blinded trials comparing lubiprostone and placebo in adults with irritable bowel syndrome and constipation (IBS-C) are presented here. Two randomized, doubleblinded, phase 3 clinical trials compared lubiprostone (8 mcg twice daily [BID]) to placebo BID over a 12-week treatment period. All subjects had IBS-C as confirmed by Rome II criteria and were at least 18 years of age. Subject-reported outcomes of IBS-C symptoms (abdominal pain/discomfort, abdominal bloating, constipation severity, straining, stool consistency, and overall symptom relief) were collected via electronic diaries prior to treatment and at Weeks 4 and 12. QOL was collected using the IBS-QOL questionnaire, which has 8 subscales: dysphoria, interference with activities, body image, health worry, food avoidance, social reaction, sexual, and relationships. A higher IBS-QOL score indicates improved QOL; a difference of 14 points is clinically meaningful. At Week 12, change from baseline overall IBS-QOL score was higher for the lubiprostone patients compared to the placebo patients ( $p=0.066$ ). There was statistically significant improvement for lubiprostone patients vs. placebo in health worry ( $p=0.025$ ) and body image ( $p=0.015$ ), and a trend for improvement with dysphoria ( $p=0.086$ ). Lubiprostone also provided improved symptom response at Week 12 compared to placebo (also in: Drossman DA et al. *Gastroenterology*. 2007;132:2586-7[abstr]). Lubiprostone produced clinically meaningful changes (>14 points) in the IBS-QOL domains of social reaction, food avoidance, health worry, body image, and dysphoria. Symptoms associated with IBS-C impact all aspects of QOL, with the most serious concerns being health worry and food avoidance. Lubiprostone produced clinically meaningful improvement in these important QOL domains.

### Post-Infectious IBS in the "Non-Sterile" Developing Nation Environment and the Role of Parasite Burden, a Population-Based Study in Central America

Matthew Benschoff, Eliette Valladares, Rodolfo Pena, Loreto Cortes, Paris Heidt, Mercedes Caceres, **Douglas R. Morgan**

**BACKGROUND** Post-Infectious IBS is well described in developed nations. The role of common intestinal infections in IBS in developing nations is unclear. The University of Nicaragua (UNAN) maintains a population epidemiology surveillance system for western Nicaragua, encompassing 24% (11,000 homes) of the region's population (200,000) - relatively unique in Latin America. Our aim was to investigate the role of parasite burden, both pathogenic and commensal, in IBS in the third world environment. **METHODS** We conducted a population-based, cross-sectional survey in western Nicaragua ( $n=1624$ ). The validated Spanish Rome II Modular Questionnaire (R2MQ) was used for the identification of IBS cases, with MD confirmation. Stool was examined for ova and parasites per protocol. Pathogens included *G. lamblia*, *Ent histolytica*, *A lumbricoides*, *H nana*, *T trichiura*. Commensals included *B hominis*, *Ent coli*, *Ent dispar*, *I butschlii*, *E nana*, and *C mesnili*. Household socioeconomic status was assessed with a validated poverty index [Renzi 1993], which was calculated with the United Nation's unsatisfied basic needs measurement, based on housing, sanitation, education, unemployment. **RESULTS** In this population-based survey of randomly selected subjects ( $n=1624$ ), the prevalence of IBS was 13.2% (15.9% F, 9.3% M). Of the IBS cases, 163 subjects had evaluable stool exams, with 194 age and gender matched controls. In this cohort ( $n=357$ ), 75% were female, 40% less than age 35, 40% with less than a 6th grade education, and 35% in moderate to severe poverty. The overall prevalence of intestinal parasite carriage was 16%, without differences based upon age, gender, or residence. There was no significant difference in parasite burden between IBS cases and controls, 16.6% versus 15.5% (OR=1.09, 95%CI 0.62-1.9). The carriage of pathogenic parasites was low among clinically diagnosed cases, 6.1% ( $n=10$ ). There was no significant difference in risk for IBS with pathogens vs commensals, OR = 1.52 (95%CI, 0.6-4.0). None of the individual parasites showed a correlation with IBS. Also, household socioeconomic status did not affect IBS risk: presence of a water system (OR=1.08, 95%CI 0.61-1.9), indoor sanitation (OR=1.5, 95%CI 0.7-3.2), and severe poverty (OR=0.68, 95%CI 0.3-1.7). **CONCLUSIONS** Intestinal parasite burden with either pathogenic parasites or commensals did not increase risk for IBS in the developing nation setting of Nicaragua. In this population-based study, the overall IBS prevalence was comparable to developed nations, suggesting that the infectious-IBS attributable risk may be limited in this setting. (Funding: Rome Foundation).

## National Health and Nutrition Examination Survey (NHANES): Association of Usual Stool Consistency and Frequency with Fecal Incontinence

**William E. Whitehead**

**Background:** Epidemiological studies of fecal incontinence (FI) show a consistent association with self-reported diarrhea and an inconsistent association with self-reported constipation. However, subjects differ in what they mean by diarrhea and constipation. **Aim:** Determine whether usual stool consistency and stool frequency are associated with FI in a national population based sample. **Methods:** Subjects in the NHANES survey for 2005-2006 were asked to rate their usual or most common stool type using the 7 descriptions from the Bristol Stool Scale (Gut 1994;35:1455). We pooled ratings 1 and 2 (hard and lumpy), ratings 3-5 (normal consistencies), and ratings 6 and 7 (mushy and watery). Subjects were also asked how often they usually have bowel movements, and responses were merged into 3 ranges: <3/week, 3-21/week, and >21/ week. FI was defined as any involuntary loss of mucus, liquid, or solid stool during the last 30 days. NHANES oversamples minorities and the elderly for increased precision; it provides weights for each subject's data to obtain estimates for the national population. Subjects were 2079 males and 2229 females aged 20 or older. Prevalences (in percent) for the national population are estimated and their 95% confidence intervals (CI) are given. **Results:** See table. For both females and males, having stools that are typically loose or watery or stools that are more frequent than 21/week was associated with a 3-4 fold increase in the rate of FI. Neither typically hard/lumpy stools nor infrequent stools were associated with significant increases in FI for males or females. **Conclusions:** Having typically loose/watery stools and/or stools more than 3 times per day is significantly associated with the presence of FI and may be a target for preventing or treating FI.

[Supported by grants from the National Institute of Child Health and Human Development and the NIH Office of Research on Women's Health (U01 HD41249, U10 HD41250, U10 HD41261, U10 HD41267, U10 HD54136, U10 HD54214, U10 HD54215, and U10 HD54241)]

Prevalence of FI as a function of stool consistency					
Female (p=0.0006)			Male (p=0.021)		
Hard	Normal	Watery	Hard	Normal	Watery
8.2%	7.7%	22.6%	15.3%	6.4%	28.9%
[3.5-13.0]	[5.8-9.6]	[17.7-27.5]	[3.7-26.9]	[5.2-7.6]	[12.2-45.7]

Prevalence of FI as a function of stool frequency					
Female (p=0.082)			Male (p=0.075)		
< 3/wk	3-21/wk	>21/wk	< 3/wk	3-21/wk	> 21/wk
11.2%	8.1%	35.4%	13.0%	7.1%	30.7%
[2.7 - 19.8]	[6.4 - 9.9]	[16.1 - 54.7]	[4.9-21.0]	[5.7-8.7]	[11.6-49.8]

Probiotic Bacteria *Lactobacillus Acidophilus Ncfm* and *Bifidobacterium Lactis Bi-07* Improve Symptoms of Bloating in Patients with Functional Bowel Disorders (FBD).

**Yehuda Ringel, Olafur S. Palsson, Gregory Leyer, Sarah Causey, Sarah Yeskel, Steven M. Faber, Tamar Ringel-Kulka**

FBD are the most common gastrointestinal disorders seen in primary care and GI clinics; however, the etiology still remains unknown. Evidence suggests that intestinal bacteria play a role in the pathophysiology and symptomatology of these disorders and that modulation of intestinal microflora by antibiotics or probiotics may be beneficial in the treatment of patients with these disorders. Aim: To investigate the effect of probiotic bacteria *Lactobacillus acidophilus* NCFM (L-NCFM) and *Bifidobacterium lactis* Bi-07 (B-LBi07) in patients with non-constipation IBS, functional diarrhea, or functional bloating. Methods: Patients with FBD who met the Rome II criteria of non-constipation-IBS, or functional diarrhea, or functional bloating were enrolled in a prospective double-blind, placebo-control clinical trial. Patients were randomized into a placebo arm and an active arm of oral probiotic bacteria containing equivalent amounts of L-NCFM and B-LBi07, 1x10<sup>11</sup> cfu total probiotic bacteria in each dose. The placebo and probiotic products were administered bid in a capsule form over 8- weeks. Patients were evaluated for the following endpoints: global relief of GI symptoms (GSA), specific functional GI symptoms, overall symptoms severity (IBS-Severity Index), satisfaction with treatment, overall well being, and Health Related Quality of Life (IBS-QOL). Results: A total of 57 (probiotic n=30; placebo n=27) patients were enrolled. Study population consisted of 72% females, 84% whites, and mean age of 37 years. Baseline demographics were similar among the two groups. Bloating and distention scores (measured on a 10 points scale) improved significantly in the probiotics group compared to the placebo group at 4 weeks (4.10 +3 vs. 6.17+3, p=0.009 respectively) and showed a strong trend of improvement at 8 weeks (4.26 +3 vs. 5.84+3, p=0.06 respectively). Secondary analyses using only the IBS subgroup (n=33) showed similar results with significant improvement in bloating and distention in the probiotics group (n=17) compared to the placebo (n=16) group (4.24 +3 vs. 6.73+3, p=0.03 respectively). Conclusions: Supplement of diet with L-NCFM and B-LBi07 BID (2x10<sup>11</sup> cfu total probiotic bacteria per day) significantly improved symptoms of bloating and distention in patients with FBD. This data support the role of intestinal bacteria in the pathophysiology of FBD and suggest an important role for these probiotic bacteria in the management of patients with these disorders. (Supported by grants K23 DK075621, RR00046, and Danisco USA Inc.)

## Lubiprostone Is Effective and Well Tolerated Through 48 Weeks of Treatment in Adults with Irritable Bowel Syndrome and Constipation

William D. Chey, **Douglas A. Drossman**, Charles Scott, Raymond M. Panas, Ryuji Ueno

Lubiprostone is a selective activator of type-2 chloride channels approved for the treatment of chronic idiopathic constipation. Two double-blinded, placebo-controlled phase 3 trials studying the effects of lubiprostone in patients with irritable bowel syndrome with constipation (IBS-C) were conducted, along with a follow-on study to assess the efficacy and safety of lubiprostone in a 36-week open-labeled extension (OLE) period. Subjects who exhibited >70% study drug compliance in their blinded trial were eligible for the OLE. A total of 476 subjects entered the OLE and received lubiprostone 8 mcg twice daily (BID); those who originally received placebo are designated as “placebo-lubiprostone,” and those originally randomized to lubiprostone are denoted as “lubiprostone-lubiprostone.” The primary endpoints were long-term safety and efficacy, defined as monthly responders (subjects with overall symptom relief ratings of at least “moderately relieved” for all 4 weeks within a month or “significantly relieved” for 2 or more weeks within a month). Response was based on a subject-reported 7-point scale ranging from “significantly worse” to “significantly relieved,” provided that the subject did not discontinue treatment during the month due to a lack of efficacy, and there was no reported rating during the month of “moderately worse” or “significantly worse.” Prior to entry into the OLE study population and at the conclusion of double-blinded treatment, the monthly responder rate was significantly higher with lubiprostone vs. placebo (15% vs.8%;  $p=0.001$ ). Overall, 58% of subjects completed the OLE (63% of placebo-lubiprostone subjects and 56% of lubiprostone-lubiprostone subjects). The monthly responder rate with the lubiprostone-lubiprostone subjects increased in the OLE to 37% by Week 36 (Table 1). All symptoms of abdominal discomfort/pain, abdominal bloating, spontaneous bowel movement frequency, stool consistency, straining, and constipation severity had statistically significant improvement over baseline at each month during the OLE. Lubiprostone-lubiprostone subjects had an average of 285 days of drug exposure. There were no treatment-related serious adverse events reported during the 36-week treatment period. Diarrhea (4.8%) and nausea (3.5%) were the most common treatment-related adverse events. These data indicate that treatment with lubiprostone confers long-term efficacy and safety in subjects with IBS-C. Table 1: Monthly Response Rates 1

Treatment Group	Monthly Response	
	Month 3	Month 12
Placebo-Lubiprostone	8%	31%
Lubiprostone-Lubiprostone	15%	37%

### Persistence of the ROME Diagnostic Symptoms for Irritable Bowel Syndrome

**Olafur S. Palsson, Miranda A. Van Tilburg, Motoyori Kanazawa, Denesh K. Chitkara, Lisa M. Gangarosa, Douglas A. Drossman, William E. Whitehead**

**Background:** Little is known about the long-term persistence of the individual symptoms that form the basis for IBS diagnosis in the Rome system. **Aims:** To evaluate the persistence of the central Rome IBS symptoms, as well as the associated impairment in patient well-being, across 1-3 years. **Methods:** 124 patients (84% female; mean age=36.2 years) with IBS (Rome II criteria + physician diagnosis) who provided baseline data in our laboratory were surveyed via mail at either one (n=58), 2 (n=44) or 3 (n=22) years follow-up (fu). Patients completed the Rome diagnostic questionnaire (Rome II at baseline, Rome III at fu), IBS Severity Scale (IBS-SS; APT 1997;11:395-402), IBS-QOL (Dig Dis Sci. 1998;43:400-11) and BSI-18 (NCS Pearson, Inc.) both at baseline and at follow-up, and reported any new diagnoses at fu. Rome III responses at fu were scored using Rome II criteria. **Results:** At fu, 4 patients (3%) reported new diagnoses other than IBS that could account for their bowel symptoms: 2 bacterial infections; 1 possible Crohn's disease; 1 colonic atonia). These subjects were omitted from data analysis. All except one patient still had bowel symptoms at follow-up. Persistence of individual Rome diagnostic and bowel activity sub-typing symptoms are presented in the table. IBS severity decreased (change from baseline in fu years 1, 2, and 3: 1.0%, -5.5%\*, -22.5%\*) and quality of life scores increased (5.2%\*, 6.8%\*, 16.5%\*) during fu, but in contrast, BSI-18 general psychological distress was elevated in fu years 1 and 2 (9.1%\*, 6.1%\*, 1.0%); significant paired t-tests ( $p < 0.05$ ) are indicated with an asterisk. Baseline versus fu Pearson correlations were high and consistent across fu years 1, 2, and 3 for psychological distress ( $r$ : 0.56, 0.61, 0.54) and IBS-QOL ( $r$ : 0.74, 0.64, 0.69). **Conclusions:** The symptoms that form the current Rome system for diagnosing and categorizing IBS are highly persistent over 1 to 3 years. Over that timeframe, IBS severity and associated QOL impairment decrease. Patients rarely receive alternative diagnosis to account for their symptoms. [Supported by grants RO1 DK31369, R24 DK67674, and MO1 RR00046] Table: % of patients reporting each Rome IBS symptom at baseline who also reported the same at follow-up. Each fu year shows data from a different group of patients. (BM=bowel movement).

Symptom:	1 year fu	2 year fu	3 year fu	Overall
Abdominal pain $\geq$ 2-3days/mo	94.5%	92.7%	72.2%	90.5%
Pain relief with BM	95.0%	100%	100%	97.6%
BM frequency change with pain onset	97.3%	96.0%	100%	97.3%
BM form change with pain onset	66.7%	45.8%	71.4%	60.0%
Hard stools $\geq$ 25% of BMs	66.7%	80.0%	75.0%	73.1%
Loose stools $\geq$ 25% of BMs	70.6%	70.5%	75.0%	71.1%

### Small Intestinal Bacterial Overgrowth in Irritable Bowel Syndrome: Association with Colon Motility, Bowel Symptoms, and Psychological Distress

Madhusudan Grover, Motoyori Kanazawa, Denesh K. Chitkara, **Lisa M. Gangarosa, Olafur S. Palsson, Douglas A. Drossman, Marsha J. Turner, William E. Whitehead**

**Background:** Small intestinal bacterial overgrowth (SIBO) has been implicated in the pathogenesis of irritable bowel syndrome (IBS), but the significance of SIBO in IBS is unclear. **Aims:** To determine the prevalence of SIBO and its association with colonic motility, bowel symptoms and psychological distress in IBS patients. **Methods:** 158 IBS patients, diagnosed by Rome II criteria and confirmed by physician diagnosis, and 34 healthy controls were tested for SIBO using a Quintron hydrogen and methane analyzer for 2 hours following ingestion of 50 g sucrose. Balloon distensions in the descending colon were performed using a G&J Electronic barostat to assess pain and urge thresholds by the ascending method of limits. Colonic phasic motility was determined with the motility index (MI, average area under the curve of phasic contractions). Subjects completed questionnaires on psychological distress (Brief Symptom Inventory-18, Recent Physical Symptom Questionnaire, and Catastrophizing Scale), IBS Symptom Severity scale (IBS-SS), IBS Quality of Life (IBS-QOL) and self reported bowel symptoms. **Results:** 52/158 (32.9%) of IBS had abnormal breath tests compared with 6/34 (17.9%) of controls ( $\chi^2=0.079$ ). Patients with SIBO (SIBO+) and Non-SIBO (SIBO-) did not differ in the prevalence of IBS-subtypes, IBS-SS, IBS-QOL or psychological distress. SIBO- showed a trend towards lower pain thresholds compared to SIBO+ (25.9 vs. 30.1,  $p=0.055$ ). Compared to controls, both SIBO+ and SIBO- had a greater post-distension increase in MI (625.6 and 642.9 vs. 313.3,  $p<0.05$ ) but the MI was not different between these two groups. Predominant methane producers (PMP) had higher urge thresholds (28.4 vs. 18.3,  $p<0.05$ ) and higher baseline MI (461 vs. 301.45,  $p<0.05$ ) than SIBO- IBS, and they were more likely to report hard or lumpy stools at least 25% of the time when compared to predominant hydrogen producers (PHP) (90% vs. 52%,  $p<0.05$ ) and SIBO- IBS (90% vs. 53%,  $p<0.05$ ). The IBS-SS scale did not significantly correlate with peak hydrogen in the PHP group ( $\rho=-0.06$ ) or peak methane production in the PMP group ( $\rho=-0.11$ ). **Conclusions:** SIBO is unlikely to contribute significantly to the pathogenesis or morbidity of IBS. Visceral hypersensitivity and SIBO appear to be independent mechanisms for the development of IBS symptoms. It is unlikely that psychological distress could mediate the association between SIBO and bowel symptoms. Methane production is associated with constipation bowel pattern. [Supported by RO1 DK31369, R24 DK067674, & MO1 RR00046]

## IFFGD ANNOUNCES GRANT AWARDS

In August, the International Foundation for Functional Gastrointestinal Disorders (IFFGD) awarded competitive grants in the amount of \$50,000 each to three investigators. The grants awarded were selected from among 25 applications by a committee of independent reviewers. IFFGD grants provide funding for clinical or translational research related to functional gastrointestinal and motility disorders, and neurogastroenterology. The mission of IFFGD is patient-oriented and their goal is to support high-quality research that will lead to improvements in the understanding of these disorders and the care of patients.

IFFGD thanks all of those who submitted a grant application for their dedication to serving the patient community, and is pleased to announce the following research projects selected to receive 2008 IFFGD Grants:

IBS SUSCEPTIBILITY GENOTYPES AND GASTROENTERITIS EXPOSURE IN THE DEVELOPING NATION SETTING

Primary Investigator: **Douglas R. Morgan, MD, Associate Professor of Medicine, University of North Carolina at Chapel Hill.**

ROLE OF EOSINOPHIL ACTIVATION ON MUCOSAL INFLAMMATION IN DIARRHEA-IBS PATIENTS

Primary Investigator: Javier Santos, MD, Senior Staff Physician, Hospital General Universitario Valle de Hebron.

MATERNALLY INHERITED MTDNA SEQUENCE VARIANTS, IRRITABLE BOWEL SYNDROME AND OTHER FUNCTIONAL DISORDERS

Primary Investigator: **Miranda A.L. Van Tilburg, PhD, Research Assistant Professor, University of North Carolina at Chapel Hill.**

Find more information online about IFFGD grants and awards at [www.giResearch.org](http://www.giResearch.org).

### CONGRATULATIONS TO:



DOUGLAS R. MORGAN, MD



MIRANDA A.L. VAN TILBURG, PHD



## CENTER VISITORS

Norman Clark, Medical Student  
*Medical School for International Health, Israel*

I'm currently a fourth year medical student, studying at the Medical School for International Health, a collaboration between Ben-Gurion University in Israel and Columbia University in New York. What attracted me to MSIH and what makes it unique was that it was the first program established with the specific goal of training medical students for careers in global health and cross-cultural medicine. Such a program has exposed me to a diverse range of patients, including Jews, Palestinians, Bedouins, Ethiopians, immigrants from Eastern Europe, migrant workers from Southeast Asia, and refugees from Sudan and the Ivory Coast. My interests include cross-cultural medicine, biopsychosocial medicine, cognitive medicine, and improving doctor-patient communication. Naturally, the field of functional gastroenterology incorporates expertise in each of these areas.

My initial attraction to gastroenterology and functional bowel disorders was fuelled by my mentor, Professor Ami Sperber of Ben-Gurion University in Israel. Prof. Sperber was the first to tell me of the work being done at UNC in functional GI and motility. And as he had been mentored by Dr. Drossman while studying at the UNC School of Public Health, my choice of where to gain more exposure to my chosen field was all but settled. At the recent Binational U.S. - Israel AGA Meeting on IBS and Functional GI Disorders in Tel Aviv, I essentially begged Drs. Drossman and Whitehead to let me come to Chapel Hill.

With the help of Dr. Drossman, I hope to further develop and hone my clinical skills in functional GI, such as patient interviewing, understanding and conceptualizing illness schemas, as well as applying a biopsychosocial perspective to patient-focused care. Furthermore, I plan on becoming more

proficient in research and database management by assisting Dr. Whitehead's team with ongoing research into the psychological correlations of chronic constipation. Additionally, I'll be traveling to Kenya in the upcoming months as required by my medical school, in order to pursue a research project in international health. While there, I hope to implement what I have learned during my time here at the Center.

One thing that has thoroughly impressed me is how everyone with whom I've interacted at the Center has made themselves available to help me feel at home. The team atmosphere in the clinic is invigorating and inspiring, and a high level of support and mutual respect exists among everyone involved. The dedication exhibited here to furthering research and improving the lives of patients is palpable.

Each day since arriving in Blue Heaven, I've been more and more pleased with my decision to visit the UNC Center for Functional GI and Motility Disorders. I'm fortunate to have chosen to pursue a field which has attracted such intelligent and inspiring professionals. I've seen patients receive guidance, support, and hope when, before they came here, they had little left.

I'm honored to be treated as a colleague by such leaders in their field as the professionals at the Center, particularly at this early stage in my training. I hope to take with me their commitment to advancing the field of medicine through mentoring, patient care and investigational research. In short, I'm thrilled to be a part of the groundbreaking research and patient care that happens at the UNC Center for Functional GI & Motility Disorders, and I'd like to express my gratitude to all the people at the Center who have made me feel so welcomed.

## CENTER VISITORS

Reuban Wong, MD  
*National University Hospital, Singapore*



I obtained my basic medical degree (MBBS) in 1998 from the National University of Singapore, and obtained a postgraduate degree in Internal Medicine from the Royal College of Physicians (UK) in 2004. I was admitted in 2008 as a Fellow of the Academy of Medicine (Singapore) as a specialist in Gastroenterology.

I am currently practicing as an Associate Consultant in the Department of Gastroenterology and Hepatology at the National University Hospital, Singapore. I am also an appointed clinical tutor to the Department of Medicine, National University of Singapore. My practice encompasses general gastro-intestinal and liver disorders, with special interests in functional gastrointestinal diseases, especially Irritable Bowel Syndrome (IBS).

In addition to IBS, I also have research interests in esophagitis, colorectal adenomas and Primary Biliary Cirrhosis. As part of my research work, I have been awarded

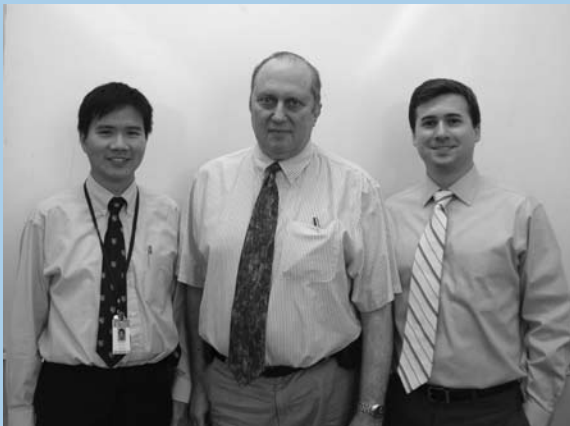
the “Young Investigator’s Award (2nd prize)” at the 15th Asia Pacific Association for the Study of the Liver Conference 2005, the “Young Investigator’s Award” at the 6th Asia Pacific Digestive Week Conference 2006, and “Poster-of-Distinction” Awards at the GI-Hep Annual Scientific Meeting 2006. In my undergraduate and pre-university years, I was the recipient of Community Service Awards from the Rotary Club, the Singapore Medical Association and AIA-International. I was also a Ministry of Education scholar.

I also serve as a medical officer with the Combat Support Hospital. I am married to Jane, a lawyer, and my greatest joy is spending time tumbling with my two beautiful daughters.

I am pleased to be here for a year on a grant from the Singapore Health Ministry, to sub-specialize in functional gastrointestinal diseases, and who better to learn from than the two architects of the Rome criteria!



Dr. Wong with Dr. William Whitehead, one of the Center Co-Directors, to discuss a research project



Reuben Wong, Douglas Drossman and Norman Clark



## RESEARCH DAY 2008

## BIOPSYCHOSOCIAL GASTROINTESTINAL RESEARCH AT UNC

October 3-4, 2008

Auditorium, Bioinformatics Bldg. (130 Mason Farm Rd.), UNC at Chapel Hill

In 2004, the UNC Center for Functional GI & Motility Disorders was awarded a grant (R24 DK067674) from the National Institutes of Health (NIH) to foster interdisciplinary research on interactions between the mind and body in health and disease, with a specific focus on the causes and treatment of functional gastrointestinal disorders. As part of this NIH grant, the Center will host the fourth of what has now become an annual Research Day on October 3-4, 2008, on the campus of the University of North Carolina at Chapel Hill. This year, the program for this symposium is focused on five areas of on-going research at our Center: (1) Pelvic Floor and Fecal Incontinence, (2) Pathophysiological Mechanisms of FGID Symptoms, (3) Treatments, Symptoms, Health Status and Health Care Impact, (4) Inflammation and Infection, and (5) Pediatric FGIDs. The format includes presentations on the state-of-the-art in each of these areas by visiting senior scientists, followed by overviews of on-going studies involving UNC faculty and investigators.

People interested in attending should contact Kirsten Nyrop at [knyrop@med.unc.edu](mailto:knyrop@med.unc.edu).

**TOPIC: PELVIC FLOOR & FECAL INCONTINENCE****State of the Art: Evaluation and therapy of fecal incontinence: Plugging the breach**

Satish Rao, MD, PhD, FRCP (LON), Professor of Medicine; Director, Neurogastroenterology & GI Motility, Carver College of Medicine, University of Iowa, Iowa City, Iowa

**NHANES: Epidemiology of fecal incontinence**

William Whitehead, PhD, Professor of Medicine, Division of Gastroenterology & Hepatology, UNC at Chapel Hill

**AGS Survey**

Madhusudan Grover, MD, PGY-3 Internal Medicine, School of Medicine, Michigan State University, East Lansing, Michigan

**Conservative treatment for fecal incontinence**

Steve Heymen, PhD, Assistant Professor of Medicine, Division of Gastroenterology & Hepatology, UNC at Chapel Hill

**Dysregulation in pain sensitivity, psychological state, and pro-inflammatory cytokines in patients with VVS and IBS**

Denniz Zolnoun, MD, MPH, Assistant Professor of Obstetrics & Gynecology, UNC at Chapel Hill

**TOPIC: PATHOPHYSIOLOGICAL MECHANISMS OF FGID SYMPTOMS****State of the Art Lecture**

Robin Spiller, MD, MSC, Professor of Gastroenterology, University Hospital, Queens Medical Centre, Nottingham, England

**Genetics of IBS**

William Whitehead, PhD, Professor of Medicine, Division of Gastroenterology & Hepatology, UNC at Chapel Hill

**The role of intestinal bacteria in the pathophysiology of functional bowel disorders**

Yehuda Ringel, MD, Assistant Professor of Medicine, Division of Gastroenterology & Hepatology, UNC at Chapel Hill

**Lubiprostone effects on abdominal pain**

William Whitehead, PhD, Professor of Medicine, Division of Gastroenterology & Hepatology, UNC at Chapel Hill

**Utility of pH-impedance testing in patients with refractory GERD Symptoms**

Ryan Madanick, MD, Assistant Professor of Medicine, Division of Gastroenterology & Hepatology, UNC at Chapel Hill

**Development of a more sensitive test of visceral pain**

Chloe Hill, BA, Third Year Medical Student, Cornell University, Ithaca, New York

**Endogenous ghrelin and gastric emptying in patients with postprandial distress syndrome**

Kimberly Brownley, PhD, Assistant Professor of Psychiatry, UNC at Chapel Hill

**TOPIC: TREATMENTS, SYMPTOMS, HEALTH STATUS & HEALTH CARE IMPACT****State of the Art Lecture**

Kevin Olden, MD, Jerome S. Levy Professor of Medicine, Division Director, Division of Gastroenterology & Hepatology, Little Rock, Arkansas

**Suicidal Ideation and Attempt in Adolescents with Chronic Abdominal Pain**

Miranda Van Tilburg, PhD, Assistant Professor of Medicine, Division of Gastroenterology & Hepatology, UNC at Chapel Hill

**CONQUEST: Impact of constipation on quality of life and healthcare costs**

Olafur Palsson, PsyD, Associate Professor of Medicine, Division of Gastroenterology & Hepatology, UNC at Chapel Hill

**Ecological Momentary Assessment (EMA): what is an episode?**

Stephan Weinland, PhD, Instructor of Medicine, Division of Gastroenterology & Hepatology, UNC at Chapel Hill

**Psychosocial influences on Celiac disease**

Spencer Dorn, MD, MPH, Clinical Fellow of Gastroenterology & Hepatology, UNC at Chapel Hill

**UNC-IFFGD national survey of health status, severity and risk factors in patients with IBS**

Douglas Drossman, MD, Professor of Medicine & Psychiatry, Division of Gastroenterology & Hepatology, UNC at Chapel Hill

**Partner burden in Irritable Bowel Syndrome**

Reuben Wong, MD, Associate Consultant, Gastroenterology & Hepatology, National University Hospital, Singapore

**Mindfulness treatment for IBS**

Susan Gaylord, PhD, Assistant Professor of Physical Medicine & Rehabilitation, UNC at Chapel Hill

**Seroquel and the treatment of IBS**

Stephan Weinland, PhD, Instructor of Medicine, Division of Gastroenterology & Hepatology, UNC at Chapel Hill

**Natural history of IBS symptoms, episodes of illness**

Olafur Palsson, PsyD, Associate Professor of Medicine, Division of Gastroenterology & Hepatology, UNC at Chapel Hill

**TOPIC: INFLAMMATION & INFECTION****State of the Art Lecture**

Jack Wood, PhD, Professor of Medicine, Department of Physiology, College of Medicine and Public Health, The Ohio State University, Columbus OH

**Enteric neuropathy**

William Whitehead, PhD, Professor of Medicine, Division of Gastroenterology & Hepatology, UNC at Chapel Hill

**Stress, enteric corticotropin-releasing factor (CRF), and colon dysfunction**

Sumei Liu, MD, Ohio State University, Columbus OH

**IBD-IBS and post-infectious IBS: A conceptual model**

Madhusudan Grover, MD, PGY-3 Internal Medicine, School of Medicine, Michigan State University, East Lansing MI

**Gene-environment interactions in IBS: A prospective study of post-infectious IBS**

Reuben Wong, MD, Associate Consultant, Gastroenterology and Hepatology, National University Hospital, Singapore

**The role of serine-proteases in gastrointestinal function and IBS**

Ian Carroll, PhD, Microbiologist, Division of Gastroenterology & Hepatology, UNC at Chapel Hill

**TOPIC: PEDIATRIC FGIDS****State of the Art: An Overview of where we have been and thoughts for next directions for research on pediatric FGIDs**

Rona Levy, PhD, Professor, School of Social Work, University of Washington, Seattle

**Long-term follow-up on guided imagery for pediatric FGIDs**

Miranda Van Tilburg, PhD, Assistant Professor of Medicine, Division of Gastroenterology & Hepatology, UNC at Chapel Hill

**Constipation in children**

Denesh Chitkara, MD, Merck Pharmaceuticals, New Jersey

**Feasibility and efficacy of a school nurse guided imagery program for childhood recurrent abdominal pain: a pilot study**

Nader Youssef, MD, MBA, Goryeb Children's Hospital/Atlantic Health, New Jersey



## RESEARCH SUBJECTS NEEDED

*The UNC Center for Functional GI & Motility Disorders regularly conducts research on a variety of topics. At present, various research teams within the organization are involved in projects for which we are looking for research volunteers. All studies have been evaluated by the university institutional review board.*

### CAUSES OF SYMPTOMS STUDIES

Lenore Keck  
(919) 966-8329

This NIH study involves measuring the relationship between genes, the environment, and various psychological and health factors in men and women with IBS. Individuals who participate will spend one overnight visit in the General Clinic Research Center at UNC. No additional visits required. [Participants completing the study will receive \$250-\$300]

Katherine Baille  
(919) 843-7892

IBS Pocket PC Study: Need Subjects with IBS. The purpose of this research study is to learn about how bowel symptoms vary throughout the day and in response to specific stresses people encounter. [Participants completing the study will receive \$200]

Marsha Turner  
(919) 962-9787

Online Study-Characterization of IBS Symptom Episodes. The purpose of this study is to learn about the natural history of IBS, that is, how it changes from day to day with respect to bowel symptoms, pain and bloating. The study will involve keeping track of your IBS symptoms everyday for 90 days by logging into a secure website. You will have a unique study ID and password to ensure your responses are anonymous and confidential. There are no visits to UNC required. [Participants completing this study will receive up to \$180]

### TREATMENT STUDIES

Katherine Baille  
(919) 843-7892

Need Men and Women with IBS and Chronic Functional Abdominal Pain The purpose of this research study is to try to improve functional bowel disorder symptoms with a combination of Seroquel and antidepressant medication. Seroquel is an FDA-approved medication that is currently on the market and used in the GI clinic. [Participants completing the study will receive \$350]

Jane Tucker, RN  
(919) 843-4906

Treatment of Fecal Incontinence The purpose of this study is to determine if a medical and behavioral treatment program for fecal incontinence needs any changes to make it more effective and easier to use. This treatment has already been used successfully in a previous NIH study. [Participants will receive any medications needed.]

Albena Halpert, MD  
(978) 557-8867

Writing and IBS Boston University School of Medicine is doing an online survey about writing and Irritable Bowel Syndrome. For more information, see [www.bmc.org/ibs](http://www.bmc.org/ibs) [Participants completing the study will receive \$25]

## TREATMENT STUDIES, CONT.

Jane Tucker, RN  
(919) 843-4906

Lubiprostone Effects on Visceral Pain Sensitivity. Clinical trials of Lubiprostone have shown that this medication decreases clinical pain associated with IBS. This study is designed to determine how this medication works to decrease pain. It is predicted that it works by decreasing pain sensitivity. [Subjects will be paid up to \$500 for completing this study. If interested, subjects may also choose to participate in another add-on study with additional compensation.]

Becky Coble  
(919) 966-8586

Mindfulness for Women with IBS. This study compares the effects of two group treatments for IBS. The first group, a support group, will center on sharing information about successful strategies for coping with and reducing symptoms of IBS. The second, the mindfulness group, combines gentle yoga with a meditation technique. Both programs have shown promise for helping people with long-standing illnesses. Participation will include attending group meetings two hours per week for 8 weeks, with a longer session on a Saturday after the 6th group meeting. Study participants will also be asked to complete questionnaires. A total of 20 subjects with IBS will be invited to participate in this study. [Participants completing the study will receive UNC parking vouchers and \$60]

Kim Meyer  
(919) 966-8328

Need women with IBS. The purpose of this research study is to provide relief from abdominal pain and discomfort. [\$250 - \$275 depending on the study]

Kim Meyer  
(919) 966-8328

Need women with constipation predominant IBS. The purpose of this research study is to determine the efficacy of an investigational medication on constipation predominant IBS. [\$50 per visit to UNC, up to \$250 total]

Kim Meyer  
(919) 966-8328

Need women with diarrhea predominant IBS. The purpose of this research study is to determine the efficacy of an investigational medication on diarrhea predominant IBS. [\$125 to \$250 depending on the study]

Kim Meyer  
(919) 966-8328

Need women with chronic constipation. The purpose of this research study is to determine the efficacy of an investigational medication on chronic constipation. [\$50 per visit to UNC, up to \$250 total]

Jane Hankins  
(919) 966-0147

Need men and women 18-70 years old with diarrhea-predominant IBS who are overweight. The purpose of this study is to examine the impact of a low-carbohydrate diet (the Atkins diet) on Irritable Bowel Syndrome (IBS). [\$150 for completing the study and all free meals for 6 weeks]



## CLINIC CORNER

*One of the four goals of the Center is to provide state-of-the-art evaluation and treatment for a full range of functional gastrointestinal and motility disorders (FGIDs). Patients come from throughout North Carolina, the United States, and other countries to benefit from the Center's unique biopsychosocial approach to understanding and treating FGIDs.*

## FUNCTIONAL GI AND MOTILITY DISORDERS CLINIC

Established and directed by Dr. Douglas Drossman, the Functional GI and Motility Disorders Clinic at UNC Hospitals is the premier site, both nationally and internationally, for referral of patients with functional GI and motility disorders (FGID). The clinic's unique multi-disciplinary, patient-centered approach integrates medical, physiological and psychological factors in the evaluation, understanding and treatment of patients with these disorders. The clinic also serves as a leading tertiary referral

site for patients who have difficult-to-diagnose illnesses or challenging disease/disorder management issues. The clinic's services and educational activities have expanded over the last few years with the addition of two faculty. Dr. Yehuda Ringel has a referral service for patients with functional upper GI symptoms (e.g., dyspepsia, non-cardiac chest pain, chronic nausea, vomiting) and/or complicated motility disorders,

in addition to IBS and other functional bowel disorders. Dr. Ryan Madanick has also joined the staff and focuses his work on Functional Esophageal Disorders. In addition, Dr. Joe Zimmerman from Hadassah Hospital in Jerusalem will be spending a 1 year sabbatical in the clinic. Other FGID Clinic staff include Christine B. Dalton, PA-C; Lynn Eckert, PA; Danielle Maier, PA-C, MA PAS; Charles K. Burnett, PhD, DrPH; and Stephan Weinland, PhD. On Wednesday afternoons, the clinic is also staffed with a Fellow (gastroenterologist in training), who is supervised by Dr. Drossman or Dr. Ringel. The Center's clinical personnel are also routinely involved with consulting on patients at UNC Hospitals with severe functional GI or motility disorders

and with physicians who call for advice regarding their patients. The clinic often has visiting gastroenterologists and trainees from other states and countries who are interested in learning more about the clinical approach, diagnosis and treatment of FGID patients. They also learn how to improve their interviewing and patient skills.

## CLINICAL CASE CONFERENCE

An important part of improving patient care is the Clinical Case Conference (see photo), held every Thursday morning in the FGID Clinic. Clinicians



**Clinical Staff:** Lynn Eckert, PA; Rueben Wong, MD; Norman Clark, Medical Student; Chris Dalton, PA; Douglas Drossman, MD; Spencer Dorn, MD; Ryan Madanick, MD

have the opportunity to present difficult cases and exchange ideas regarding patient evaluation and treatment. Participants in the Clinical Case Conference address the physical, social and psychological factors that are relevant to a specific case, utilizing the group's overall expertise to maximize the impact on patient care. This weekly forum also provides a learning opportunity for resident fellows, investigators, and others interested in

the clinical aspects of caring for patients with functional GI and motility disorders.

## GI MOTILITY PROGRAM

The GI Motility Program at UNC Hospitals was established by Dr. Whitehead. Diagnostic evaluations are now managed by Dr. Yolanda Scarlett (Medical Director), Dr. Yehuda Ringel, and Danielle Maier, PA, for lower GI motility disorders, and Dr. Nicholas Shaheen, Dr. Doug Morgan and Dr. Ryan Madanick for swallowing disorders and ambulatory pH testing. Sheila Crawford, RN, is the head nurse for the UNC Hospitals GI Motility Lab, and Jennifer Williams, RN, also performs diagnostic testing in the Laboratory.

## Clinical Case Conference



Patients with GI motility disorders may be seen initially in the Functional GI and Motility Disorders Clinic, or they may be referred directly to the medical staff of the GI Motility Lab if referring physicians anticipate that diagnostic motility testing or biofeedback training will be needed. Diagnostic motility tests may be scheduled directly by outside physicians, but a medical consultation from one of the clinicians affiliated with the GI Motility Lab is recommended.

### PELVIC FLOOR BIOFEEDBACK CLINIC

A state of the art pelvic floor biofeedback clinic is directed by Steve Heymen, PhD. Appropriate referrals for this clinic are patients with fecal incontinence or dyssynergic defecation (a form of constipation in which the patient has difficulty emptying the rectum). Angel Moore, NA, assists Dr. Heymen in this clinic.

The Pelvic Floor Disorders Case Conference is held monthly and is central to the training, patient care and research objectives of the GI Motility Service. The format for the conference is a discussion of cases that have been seen by the gastroenterology and urogynecology services, focusing on cases that present complex decision making about patient care or important teaching points. There is also discussion of whether certain patients are appropriate for referral to one of the ongoing research studies at the Center. The conference also provides an opportunity for updates on new publications, research conferences, and new research initiatives.

### PSYCHOLOGICAL SERVICES

Charles K. Burnett, PhD, DrPH, Clinical Associate Professor of Medicine, and Stephan Weinland, PhD, Instructor of Medicine, provide psychological services to the Functional GI & Motility Disorders Clinic. Patients are referred to the two psychologists through the Center and by outside physicians. When the medical evaluation of a patient visiting the FGID Clinic suggests that psychological evaluation and/or treatment that could include pain management or psychological treatments would be beneficial, Drs. Burnett or Weinland or a psy-

chology intern working with them is brought into the patient's overall care as part of our multi-disciplinary team approach. Drs. Burnett and Weinland specialize in the treatment of patients with chronic gastrointestinal illnesses, using one or more of the following techniques or therapies, in collaboration with the patient's other health care providers:

**Stress Management:** Stress management therapy seeks to help a person understand the role of stress in his/her life and how it relates to the person's FGID symptoms. It also seeks to provide the patient with a variety of ways for dealing with stressful events in ways that minimize their impact on the person's FGID symptoms and quality of life.

**Cognitive Behavioral Therapy (CBT):** CBT focuses on the interrelationship between a patient's thoughts (cognitions), actions (behaviors) and feelings (affect), and the role they play in their FGID symptoms. A common example is to beat the "vicious cycle" that occurs when chronic severe symptoms lead to psychological distress which, in turn, worsens the symptoms. By understanding and focusing on the psychological components of the "brain-gut axis", changes can be made in how a patient thinks, acts and feels about his/her GI difficulties, and thereby help reduce the frequency and intensity of FGID symptoms.

**Relaxation Therapy:** Relaxation therapies to reduce a person's current state of physical and psychological activation include progressive muscle relaxation (PMR), autogenic training, breath regulation, and meditation. With these techniques, a person can learn how to "turn down the volume" on their GI symptoms by becoming more calm and relaxed about them.

**Hypnosis:** Hypnosis or hypnotherapy is a set of techniques designed to help a person focus their attention and concentration in more positive directions. This can be accomplished with the help of a therapist or by oneself (self-hypnosis). It creates a very deep state of relaxation and imagining through which the patient is open to ideas or concepts that may help him/her manage certain problems, such as FGID symptoms.



**Psychological Services:** Stephan Weinland, PhD and Charles Burnett, PhD



## CENTER NEWS



Congratulations to Spencer and Emily Dorn, MD on the birth of Mischa Ivy Dorn, born on 7/23/08, weighing 8 pounds.

**Moneika Owens** has left the Center to obtain an MS in Medical Science from Hampton University. This 2 year post-baccalaureate program is designed to increase the number of minority and disadvantaged students into medical school. Moneika began working at the center as a work study student and continued on to play an important role conducting pharmaceutical studies with Kim Meyer and as an also coordinating manuscripts and bibliographic retrieval in Dr. Drossman's group.



Congratulations to **Yehuda Ringel, MD** for his promotion to Associate Professor of Medicine at the University of North Carolina School of Medicine.



Congratulations to Ryan and Naomi Madanick, MD on the birth of Micah Shoshan Madanick, born 7/28/08, weighing 7 lb 4 oz.



Drs. Whitehead and Drossman facilitating a Center Staff Meeting

## WELCOME TO THE CENTER

**Katie Baillie** is a social research assistant working on Investigator Initiated studies for Dr. Drossman and research studies for Dr. Weinland. She graduated from UNC Chapel Hill in 2006 with a double major in Journalism and Psychology, and is interested in pursuing a PhD in clinic psychology. Katie is involved with many aspects of the research process, from recruitment and subject screening to clinic visits and data collection and is also a grant and contract administrator.



**Ashley Messina** graduated from UNC-CH in May 2008 with a bachelor's in Biology. She is a clinical research assistant for Drs. Drossman and Weinland.

"My job here keeps me busy, as I am responsible for recruitment and the day-to-day running of the investigator initiated studies. In the future I plan to attend a Physician Assistant program and hope to specialize in women's health or surgery. In my spare time I enjoy listening to music, arts and crafts, hanging out with my cat Mr. Magoo, and traveling."

**Sarah Hubeny** is a research project coordinator working for Dr. Ringel on studies related to intestinal bacteria and inflammation in IBS. She recently graduated from UNC School of Public Health with a Master of Public Health in Nutrition, and is particularly interested in probiotic and nutrition-related research regarding GI health, permeability, and allergy. Previously, she worked for U.S. Surgical / Tyco Healthcare in medical device regulation, and obtained a Master of Health Administration from Quinnipiac University.



**Hollie Edwards** is a clinical research assistant for Dr. Drossman and Dr. Weinland, and is currently working on three investigator-initiated studies. She is involved with recruitment, clinical visits, and data collection as well as administrative activities. Hollie recently graduated from UNC Chapel Hill with a BS in Biology and a minor in Chemistry. She plans to attend medical school in the future.



**Ceciel Rooker** has joined the Center for Functional GI and Motility Disorders as the Director of Public Relations, Development and Clinical Services. Ceciel is also currently working for the Rome Foundation as a consultant for Marketing and Public Relations. She will be assisting Dr. Drossman with Sponsorship recruitment as well as development and marketing of our Center's research and clinical programs



## OPPORTUNITY TO SUPPORT

### CONTACT INFORMATION

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Street Address	
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	Postal/Zip Code
Email	

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

\$1,000  
 \$500  
 \$100  
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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](http://www.med.unc.edu/ibs)

Make checks payable to:  
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OR: Include your 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.