



Digest

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

CENTER RECEIVES NIH GRANT: TO STUDY GENETIC RISK FACTORS FOR IBS

William E. Whitehead, PhD
Center Co-Director



The Center was recently awarded a 5-year, \$3.3 million grant from the National Institutes of Health (NIH) to study genetic risk factors in irritable bowel syndrome. This represents a competitive renewal of the “Psychophysiology of Irritable Bowel Syndrome” grant (R01 DK031369) which Dr. Whitehead has held for more than 20 years. Each of the 5-year cycles of this grant has built on previous grants from the NIH.

In the most recent 5-year cycle, we tested the hypothesis that IBS is not a single disorder but represents a collection of health problems with different causes that produce similar symptoms. By systematically collecting information on more than 50 physiological and psychological variables from 300 IBS patients and 60 healthy individuals, we were able to identify 4 different phenotypes or clusters of IBS patients: one group was defined by pain hypersensitivity, a second group had high levels of psychological distress but few physiological abnormalities, and the third and fourth groups were defined by predominant bowel habits of constipation and diarrhea. The symptoms and physiological findings that distinguish these IBS patient subgroups from each other were stable over years of follow-up. These results strongly support the notion that IBS has different causes for different clusters (subgroups) of patients, and that simple tests may in the future be able to show which IBS cause is at work in each patient.

In the previous grant we collected DNA from our subjects but did not have enough funding to test genetic risk factors except for the serotonin reuptake transporter gene. The new grant will enable us to carry out a systematic genetic analysis of the previous samples and to collect DNA and physiological and clinical data from a new sample of 300 IBS patients and 300 healthy controls. The goals of the new 5-year grant project are (1) to identify particular genetic patterns (i.e., certain polymorphisms) that are associated with each of the clusters of IBS

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

The Center's 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.

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

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patients found in our previous study and show that these are also found in the new sample; (2) to develop, for each of the clusters of IBS patients, a causal model to explain how IBS is generated, that includes gene-environment interactions as well as interactions between genes; and (3) to refine and validate these causal models through advanced statistical techniques such as structural equation modeling. The importance of this research is that it may eventually improve the treatment of IBS. If there are different underlying causes for symptoms in subgroups of patients, it is likely that they will respond to different treatments. Our hope is that this research will eventually enable us to individualize treatment by using simple tests to match patients to the treatments that are most likely to benefit them.

This study of genetic risk factors is technically complex and involves three teams of research staff: The phenotyping group which tests and identifies the patient subgroups includes investigators with expertise in GI physiology (Dr. William Whitehead, Dr. Motoyori Kanazawa, Dr. Lisa Gangarosa, and Dr. Doug Drossman) and psychology (Dr. Miranda van Tilburg and Dr. Olafur Palsson), as well as research nurses (Lenore Keck and Jane Tucker) who do the actual testing. The genetics team includes Tope Keku, Luda Diatchenko, and William Maixner. Data management is overseen by Oli Palsson with assistance from Gae Caudill, and study administration is the responsibility of Bill Whitehead and Marsha Turner. This area of research interest, supported by 20 years of grant support from NIH, has led to a number of publications, including the following:

1. Dorn SD, Palsson OS, Thiwan SIM, Kanazawa M, Clark WC, Van Tilburg MAL, Drossman DA, Scarlett Y, Levy RL, Ringel Y, Crowell MD, Olden KW, Whitehead WE. Increased colonic pain sensitivity in irritable bowel syndrome is the result of an increased tendency to report pain rather than increased neurosensory sensitivity. *Gut* 2007;56:1202-1209. PMID 17483191.
2. Whitehead WE, Palsson OS, Levy RL, Feld A, Turner M, Von Korff M. Comorbidity in irritable bowel syndrome. *Am J Gastroenterol* 2007;102:2767-76. PMID 17900326.
3. Grover M, Kanazawa M, Palsson OS, Drossman DA, Whitehead WE. Small intestinal bacterial overgrowth in irritable bowel syndrome: Association with colon motility, bowel symptoms, and psychological distress. *Neurogastroenterology Motil* 2008;20:998-1008. PMID 18482250.
4. Kanazawa M, Palsson OS, Thiwan SIM, Turner MJ, Van Tilburg MAL, Gangarosa LM, Chitkara DK, Fukudo S, Drossman DA, Whitehead WE. Contributions of pain sensitivity and colonic motility to IBS symptom severity and predominant bowel habits. *Am J Gastroenterol* 2008;103:2550-61. PMID 18684175/

Dr. Whitehead's Research Team (from left to right): William Whitehead, Marsha Turner, Jane Tucker, Lenore Keck, Miranda van Tilburg, Olafur Palsson, and Steve Heymen





FACULTY PROFILE

Yolanda Scarlett, MD

Yolanda Scarlett, MD, is an Assistant Professor of Medicine, and Medical Director of the GI Motility Laboratory. Her duties include clinical evaluations, training gastroenterology and urogynecology fellows in diagnostic motility testing and researching anorectal motility disorders. She enjoys teaching medical students and likes to use an interactive approach incorporating “what if” scenarios. She describes herself as a clinician and a teacher.

Many doctors stay busy aside from the duties of their “day” jobs, and for Dr. Yolanda Scarlett this is no different. Every day is very busy for Dr. Scarlett; she wears many hats and some of them are not at UNC Hospitals.

With an attitude of **100% Care and 80% Effort**, she has a four-day work week at UNC that includes at least four jobs. As a practicing clinician, she sees patients for motility disorders such as constipation and fecal incontinence, and provides treatment. As Medical Director of the GI Motility Lab, she leads the motility lab for anal rectal monometry. As a Clinical Associate Professor of Medicine, she teaches medical students, instructs GI fellows, and meets with Visiting Fellows and Scholars. Some of her visiting scholars are American Motility Society Fellows – a program that places GI trainees from all of the United States in the care of Dr. Scarlett (and other faculty from the UNC Center for Functional GI & Motility Disorders) for a month in concentrated training and motility and endoscopic skills. Finally, being involved as a Researcher in two very different areas helps broaden her well-roundedness as a clinician and instructor: collaboration with Dr. William Whitehead and Dr. Steve Heyman in biofeedback, and various investigations in pharmacology. Her typical work week can be summarized in this manner:

Mondays: From 8am-noon, she sees patients in the clinic and provides treatment. After lunch, she turns to administrative activities, reading anal and rectal monometry studies, and interacting with vendors.

Tuesdays: Same as Mondays, but in addition teaches Visiting Fellows, reviewing anal/rectal tracings, conducting interviews, or other business.

Wednesdays: All day in Endoscopy.

Thursdays: Alternating Thursdays in either Endoscopy or Administrative Duties.

Fridays: Her day off, but she still takes time to conduct conference calls to Fellows and staff.

This “Jane of All Trades” resides in Hillsborough with her ophthalmologist husband and as a full-time mom of two active pre-teen boys. Each day, Dr. Scarlett puts on the chauffeur hat after the lab coat comes off: during her very impressive workweek, she has to juggle taking the boys to sports like basketball and track, along with keeping a visible role with the Parent Teacher Association at their schools. And, if that is not enough, she also has to make sure her wheelchair-bound father gets to his own doctor’s appointments.



Dr. Yolanda Scarlett with Dr. Yingxin Li, Clinical Fellow in the School of Pharmacy. Dr. Li came to UNC -CH from China where she is a dentist and has tried her hand at many fields, including the use of orthodontics 3D imagery to discover dental malfunction, pharmaceutical research, and mathematics.



ASK THE EXPERT

Reuben Wong, MD

Associate Consultant Gastroenterologist

"Doc, can I try this..."

Complementary and Alternative Medicine for IBS

The treatment of Irritable Bowel Syndrome (IBS) is very much a science in evolution, and to date, no single modality of treatment or "magic pill" has evolved. Indeed, many physicians find IBS one of the most frustrating conditions to manage, with most focusing their treatment on symptom control using a variety of pharmaceutical means, often with a poor outcome. From the patient's perspective, they are frustrated by the doctors' inability to find an organic problem, with multiple tests coming back as negative, and yet their symptoms are very real. Many of them either feel that the medicine they are on does not work, or they simply do not want to be on long-term medication. Therefore, it's no surprise that many patients turn to Complementary and Alternative Medicine (CAM) as a treatment for their symptoms or in their quest for a "cure" to their IBS.

IS THERE ANY EVIDENCE FOR CAM IN IBS?

CAM can be defined as any form of non-conventional treatment that is not based on the standard precepts of modern day Western medicine. CAM includes herbal remedies, homeopathy, acupuncture, physical manipulation techniques such as massage, or "holistic" healing such as yoga. The CAM options employed are very much shaped by the societal and cultural norms of the patient, and so it's not uncommon to see differences in CAM methods used for the same condition in patients coming from different backgrounds. It's been estimated that between 1997 and 2002 approximately 35% of the US population have reported using CAM, an obvious increase in popularity. An estimated \$34 billion a year is spent by US consumers on CAM therapies.

IBS is a classic condition where patients often turn to alternative therapy options. A study done by

our team at UNC showed 38.4% of IBS patients used some form of CAM, with herbal supplements, massage therapy and yoga being the top three therapies utilized. However, very few doctors actually prescribe CAM, and so patients usually seek and obtain these alternative therapies without medical advice and often without their physician's knowledge.

Some of the main CAM therapies undertaken by patients with IBS, as found by the UNC study, include:

1. Herbal Remedies
2. Massage therapy
3. Yoga
4. Homeopathy
5. Aromatherapy
6. Acupuncture
7. Hypnosis

WHAT ARE SOME OF THE ISSUES WITH CAM?

In modern Western medicine, almost all of our prescription drugs have undergone a rigorous system of tests before approval by the FDA. Drugs are screened for efficacy (how well the treatment works) and potential adverse effects based on trials in animals and humans. With CAM, there is no such requirement for testing and regulation. As such, many of the success stories with CAM have been based on "word of mouth" or anecdotal evidence, and have not been verified or reproduced in clinical trials, so it has been difficult to quantify the efficacy of a given therapy. Similarly, the side-effects are often unknown, and when they do occur they often go unrecognized.

Many of the CAM remedies are "individualized" by the provider, and it is almost impossible to determine the active component within the medication, much less

determine their exact mode of action. A good example of this is the use of traditional Chinese herbs in the treatment of IBS. A number of rigorous trials have been undertaken by researchers which highlight a number of learning points. First, the active ingredients of herbs are often unknown, making it impossible to pinpoint which was the chemical component that worked. Second, standardization of dose and frequency has been difficult. To compound matters, many herbal and homeopathic cures are a combination of differing herbs and extracts, and the concoction is often “tailored” to the individual patient rather than being based on a standard set formula.

Third, treatment of functional gastrointestinal diseases such as IBS often have a large placebo effect. An analysis looking at major CAM treatment trials in IBS patients estimates the average placebo effect as 42%. As such, it’s difficult to tell if it’s the treatment that’s working or it’s a subjective improvement in symptoms based on the anticipation of a positive outcome.

SO WHAT SHOULD I DO?

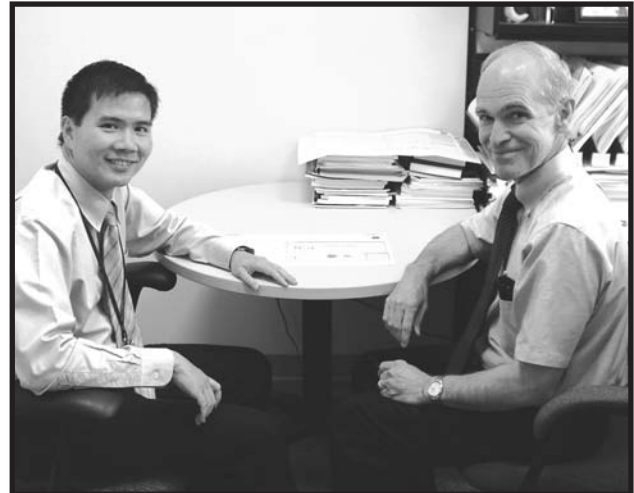
Does this mean that CAM has no role in the treatment of IBS? Certainly not. What we are advocating is a judicious and well-considered approach before embarking on any treatment, and this includes any CAM therapy.

First, make a well informed decision. This involves knowledge of IBS and the chronic nature of the disease. Take any cures that scream “100% instant & immediate cure” with a big pinch of salt! Also, perform a “due diligence” search of any treatment you are considering – with the advent of the internet and search engines, this has never been easier. Speak to people (not just one person!) who have tried the remedy you are contemplating, and get as broad a perspective as you can.

Second, understand the basis for the CAM, and ensure you are comfortable with it. Some alternative treatment options have strong religious or cultural roots that may clash with your own beliefs. You should never be coerced into a treatment with which you are personally uncomfortable.

Third, consider the risk-benefit ratio of the treatment

you are considering. FDA regulations require the side-effects and interactions of drugs to be declared, but there are no such requirements for CAM, and so you have to be aware there may be potential risks with ingested herbs and concoctions, such as Drug Induced Liver Injury. There may also be inherent potential risks associated with a particular treatment. For example, if you are undergoing acupuncture, ensure your therapist uses only new needles to avoid the transmission of Hepatitis B or C. Ask what the CAM entails and ensure that you have no existing health issues that may be unsuitable with the treatment you are undertaking, for example an intensive exclusion diet in a pregnant IBS patient.



Reuben Wong with William Whitehead

Sit down and work out the financial cost and time investment in the therapy to see if it is something you are prepared to undertake. Multiple regular sessions may be required, or there may be extensive costs involved with purchasing remedies or therapy sessions.

Finally, always keep your doctor informed about any CAM treatment you are undertaking. This may seem counter-intuitive, and there is always a fear by many patients that they will be berated for dabbling in “alternative stuff”. In reality, most physicians would respect a patient’s right to seek alternative treatment, and may even be able to share their own perspective on the CAM treatment. Ultimately, in your battle against IBS, your doctor should be your best advocate!



FUNCTIONAL GI DISORDERS: IRRITABLE BOWEL SYNDROME WITH CONSTIPATION AND CHRONIC CONSTIPATION

Christine Dalton, PA

Functional GI and Motility Disorders Physician Assistant

Synopsis of the November 26, 2008 feature Christine Dalton has on WebMD.

More can be found at <http://www.medscape.com/view program/17715>

Functional GI Disorders (FGIDs) are a result of abnormal functioning in the GI tract. They can occur anywhere in the GI tract: esophagus, stomach, bile duct, small and/or large intestine. Symptoms can include trouble swallowing, nausea, vomiting, stomach pain, constipation or diarrhea. More than 20 different FGIDs have been characterized. These disorders are characterized by:

1. Abnormal motility, or movement, of the muscles in the GI tract – they may be too fast or too slow or have a lot of spasms.
2. Increased sensitivity of the nerves in the GI tract – this can cause symptoms of pain, discomfort, nausea, etc.
3. There can also be dysfunction in the brain's ability to modify pain.

Functional GI Disorders occur in 10-20% of people in the general population. They can begin in childhood or result from infections, surgeries or other trauma to the organs of the GI tract.

CHARACTERISTICS OF IBS-C AND CC

IBS with constipation (IBS-C) and Chronic Constipation (CC) are commonly seen FGIDs in patients who come to the GI clinic.

- IBS-C symptoms include
 - Chronic intermittent abdominal pain in association with reduced stool frequency
 - Hard/lumpy stool consistency and
 - Difficult defecation (straining, infrequent stools, etc.)
- Chronic Constipation symptoms include
 - Hard/lumpy stool consistency and
 - Difficult defecation (straining, etc.)

The primary symptom that distinguishes between IBS-C and CC is abdominal pain. IBS-C pain is usually associated with a change in the form or frequency of the bowel movements, and the pain is often improved with the bowel movement.

POPULATION AND EFFECT OF IBS-C AND CC

In patients with IBS-C or CC, women are affected 2:1 compared to men. In general, health related quality of life is decreased in patients with these disorders. It is estimated that the cost of caring for these disorders is about \$30 billion per year: \$10 billion for doctor's fees, laboratory tests and medication cost and \$20 billion for indirect costs (loss of work or loss of productivity while at work).

THERAPEUTIC OPTIONS FOR TREATMENT

Lifestyle modifications: Increasing fluid intake, exercise, and dietary fiber

Traditional options: Osmotic stimulant

Emerging Therapy: Chloride channel activator, antibiotics (to treat bacterial overgrowth), and antidepressants (to treat pain in IBS-C)

Behavioral therapy: Hypnotherapy and biofeedback

POSSIBLE TESTS AND/OR PROCEDURES

- Colon transit studies
- Anorectal manometry
- Balloon Expulsion tests
- May also need – colonoscopy, blood tests, etc.

IMPROVING PATIENT-CLINICIAN COMMUNICATION

- Goal is to create patient-clinician partnership
- What is the effect of the disorder on the patient's life?
- What are the patient's concerns?
- Patient should have time to talk

RESEARCH SUBJECTS NEEDED

CAUSES OF SYMPTOMS STUDIES

Lenore Keck
(919) 966-8329

Genetic and environmental factors that cause or influence IBS. This 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 Clinical and Translational Research Center at UNC Hospital. No additional visits required.

Marsha Turner, MS
(919) 962-9787

Online Study - Characterization of IBS Symptom Episodes. The purpose of the 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 every day 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.

Miranda Van Tilburg
(919) 843-0688

Role of Mitochondria in IBS. The purpose of this research study is to learn about the role mitochondria can play in Irritable Bowel Syndrome. Mitochondria are the tiny parts inside the cells of our body that make the energy that we need. Mitochondrial disorders involve the ability of the body to produce sufficient energy. The study will involve 1 phone interview, completion of 1 questionnaire and providing a saliva sample for analysis. There are no visits to UNC required.

Katherine Baillie
(919) 843-7892

IBS Pocket PC Study with Immodium: Need Subjects with IBS-D and IBS-M. 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. It will study diarrhea-predominant and mixed IBS patients, and will also monitor how symptoms and bowel habits change in response to Immodium.

Ashley Messina
(919) 966-0147

Qualitative Analysis of Episodes of IBS. We are looking for patients with IBS to complete an online survey which allows them to answer open-ended questions regarding their personal symptom experience. By examining these reports, we hope to gain a better understanding of how patient symptoms change over the course of an episode and to identify any patterns in symptom experience.

RESEARCH SUBJECTS NEEDED

TREATMENT STUDIES

Katherine Baillie (919) 843-7892	<i>Need Men and Women with IBS and Chronic Functional Abdominal Pain.</i> The purpose of this research study is to try to improve functional bowel disorder symptoms with a combination of Seroquel and anti-depressant medication. Seroquel is an FDA-approved medication that is currently on the market and used in the GI clinic.
Jane Tucker, RN (919) 843-4906	<i>Treatment of Fecal Incontinence.</i> 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.
Albena Halpert, MD	<i>Writing and IBS.</i> Boston University School of Medicine is doing an online survey about writing and Irritable Bowel Syndrome. For more information, see www.bmc.org/ibs
Jane Tucker, RN (919) 843-4906	<i>Lubiprostone Effects on Visceral Pain Sensitivity.</i> Clinical trials of Lubiprostone have shown that this medication decreases clinical pain associated with IBS. This study is to determine how this medication works to decrease pain. It is predicted that it works by decreasing pain sensitivity.
Becky Coble (919) 966-8586	<i>Mindfulness for Women with IBS.</i> 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.
Kim Meyer (919) 966-8328	<i>Need men and women with IBS.</i> The purpose of this research study is to provide relief from abdominal pain and discomfort.
Kim Meyer (919) 966-8328	<i>Need men and women with constipation predominant IBS.</i> The purpose of this research study is to determine the efficacy of an investigational medication on constipation predominant IBS.
Kim Meyer (919) 966-8328	<i>Need women and men with diarrhea predominant IBS.</i> The purpose of this research study is to determine the efficacy of an investigational medication on constipation predominant IBS.
Jane Hankins (919) 260-2304	<i>Need men and women 18-70 years old with diarrhea-predominant IBS who are overweight.</i> The purpose of this study is to examine the impact of a low-carbohydrate diet (the Atkins diet) on Irritable Bowel Syndrome (IBS).



VISITING SCHOLAR

Francisco Marrero, MD
Gastroenterology Fellow Cleveland Clinic Foundation

I am a third-year gastroenterology fellow pursuing an academic career in gastrointestinal motility. I recently had the opportunity to spend one month at the UNC Center for Functional Gastrointestinal and Motility Disorders at the University of North Carolina in Chapel Hill. This opportunity was made possible by a training grant from the American Neurogastroenterology and Motility Society. I chose to spend time at UNC not only for their reputation for excellence in motility disorders and esophageal diseases but also in functional bowel disorders.

Patients with functional gastrointestinal disorders were among the most anxiety-provoking patients that I dealt with in my clinical practice prior to rotating at UNC. During my rotation at UNC, a significant portion of my time was spent working with Dr. Douglas Drossman. I learned a great deal about caring for patients with irritable bowel syndrome and functional abdominal pain in his clinic. The integrated approaches they used which incorporated the skills of physicians, psychologists, and physician assistants were impressive. Each patient underwent a comprehensive assessment. Great care was taken to establish a strong and meaningful physician-patient relationship. Each patient's expectations were explored and the team addressed these expectations with careful discussion and education. The team supported the patient with frequent in-office and over-the-telephone follow-up for symptom assessment, further treatment needs, and medication titration. After this rotation, I now feel much more comfortable caring for patients with functional gastrointestinal disorders and feel I am providing a better service to these patients in my own practice.

In addition to learning how to better manage patients with functional bowel disorders, I had the opportunity to explore many other aspects of motility. Another goal of my experience at UNC was to become more comfortable with anorectal manometry. I had the opportunity to read many anorectal manometry studies with Dr. Yolanda Scarlett. Her comprehensive approach helped me learn how to properly select patients for manometry, interpret the manometric findings, and integrate these findings with plans-of-care. Also, I gained a better understanding of when to order and how to interpret colonic transit studies, anal ultrasound, and defacography. Many patients with anorectal disorders were enrolled in biofeedback sessions in which I was able to participate. Dr. Steve Heyman is a renowned expert in biofeedback and provided excellent insight into the purpose, implementation, and goals of biofeedback. This experience has greatly improved my clinical skills with constipation and fecal incontinence patients and has given me a much broader array of diagnostic and treatment options in my own practice.

Other aspects of my training at UNC included esophageal manometry, impedance, and pH testing. There were also many opportunities to observe and/or discuss barostat testing, electrogastography, breath testing, and other techniques for assessing gastric, small bowel, biliary, and colonic motility. Additionally, I was able to participate in endoscopic sessions in which radiofrequency ablation and cryotherapy were used to ablate Barrett's esophagus. Not only did I observe many of these procedures, but I also had the opportunity to discuss these techniques in detail with the expert faculty who use these techniques for research and in clinical practice.

I feel my time at UNC was very well spent. My confidence in assessing, diagnosing, and managing patients with functional and motility-related issues is much greater for having done this rotation. This training has also greatly impacted my marketability as a fellow about to enter academic practice. Furthermore, I have gained many new colleagues at UNC that will be resources throughout my career. I cannot state more strongly how much I appreciate the great learning opportunity UNC provided and how wonderful it was to have been supported by an American Neurogastroenterology and Motility Society Clinical Training Program grant in this endeavor.



CENTER VISITOR

Chloé Hill
Doris Duke Clinical Research Fellow

Chloé Hill is at UNC for a year as a 2008-2009 Doris Duke Clinical Research Fellow. She is working under the mentorship of Dr. William Whitehead at the UNC Center for Functional GI and Motility Disorders. Ms. Hill attended Brown University, where she was a participant in the Program in Liberal Medical Education, and received her Bachelors of Science in Neuroscience with a focus in cognition. She is currently a student at Weill Cornell Medical College, and has completed her 3rd year of medical school. Ms. Hill's previous research experience includes basic science work on the differentiation of neurons in the brain, retrospective analysis of breast tumors, and clinical trials of Alzheimer's drugs. Her fellowship with Dr. Whitehead focuses on the etiology of IBS, specifically exploring the hypothesis of visceral hypersensitivity.

Through physiological testing of IBS patients and healthy controls, Ms. Hill's study aims to investigate the underlying mechanism of hypersensitivity to elucidate whether this phenomenon is psychological or neurological. The goal of this work is to advance the understanding of the disease, as well as to clarify a target for effective therapy. Ms. Hill was recently awarded a North Carolina Translation and Clinical Sciences Institute Pilot Grant to further her study of hypersensitivity in IBS patients. Ms. Hill has loved getting her feet wet in clinical research, and is thrilled to be gaining a solid foundation on which she hopes to build throughout the rest of her training and career. She has long been interested in alternative medicine, and hopes both to pursue an integrative clinical practice where she sees patients as a neurologist, and to continue her clinical research in the field of pain. She will return to New York this fall to complete her fourth year of medical school. In addition to research, Ms. Hill enjoys singing, running, and hip-hop dance.



Chloé Hill with William Whitehead, PhD



VISITING FELLOW

Jaya Agrawal, M.D., M.P.H.

I graduated from the 8-year Program in Liberal Medical Education at Brown University in 2003. During my time in this program, I obtained a B. A. in Religious Studies and a Master of Public Health from the Harvard School of Public Health in addition to my medical degree. I became very interested in health policy and spent a year in Washington DC, serving as the 52nd National President of the American Medical Student Association.

During that year, we began a medical student campaign to address conflict of interest, led coalitions advocating for national health insurance, and worked with John Conyers (D-MI) office to introduce legislation to federally regulate resident physician work-hours. This work lead ultimately to the ACGME adopting voluntary work-hour restrictions for trainees in all specialties.

I left this exciting life to begin my own residency in internal medicine at the Brigham and Women's Hospital and started a fellowship at the same institution in 2006. I had a research interest in the use, utility and overuse of diagnostic testing and as a second year fellow, under the direction of my mentor Dr. John Saltzman, I began a prospective observational study of the use of diagnostic testing in the evaluation of obscure gastrointestinal bleeding. Also during that year, I became interested in esophageal disorders, peptic disorders and Barrett's disease. At the suggestion of Dr. Saltzman, I applied to the ANMS fellowship program with the goal of improving my understanding of esophageal motility and esophageal diseases.

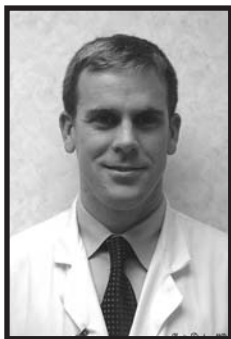
As I researched the institutions participating in this program, it was immediately clear to me that UNC was my first choice for this experience. It was both the strength of the esophageal program and the strength of the faculty overall that drew me. I was also intrigued by the program's combined approach to motility and functional GI disease for another reason: during my first year of fellowship, my continuity clinic was located at one of the satellite offices of Brigham's Women's Center. Nearly all of my patients were younger women (30-60 years) with chronic gastrointestinal complaints. Their evaluation was always negative for organic disease, and I noted I was only making half of them better with my uninspired combinations of PPIs and laxatives. I hoped that the UNC experience would teach me new skills that could benefit my patients.

As the UNC fellowship comes to a close, I can say with confidence that this has been the most enlightening experience in my nearly 10 years of medical training. It has been the greatest honor to learn from faculty whose names I had read in textbooks and who I never thought I would ever meet, let alone learn from in the one-on-one tutorial experiences that the program had set up for me. The enthusiasm of the faculty for teaching is unparalleled and the commitment to patient care is inspiring. I received not only the comprehensive education in esophageal disease from Dr. Madanick and Dr. Shaheen and the instruction in anorectal motility from Dr. Whitehead that I had come for, but also a deeper understanding of functional gastrointestinal disease and many lessons in how to communicate with and understand patients from my experience in Dr. Drossman's clinic. I believe it is this approach to doctoring that will have the greatest impact on my career in the years to come.



Jaya Agrawal, MD, MPH with Dr. Drossman

I want to convey the deepest gratitude to all of the staff, fellows and faculty who welcomed me and taught me so much, and a special thanks to Drs. Madanick, Whitehead and Drossman for designing and coordinating this incredible experience. I hope to bring this learning back to Boston to enrich the academic efforts centered around functional GI disease and to improve the lives of the patients in my clinic.



VISITING FELLOW

Kevin Dasher, MD

Johns Hopkins Medical Institutions Gastroenterology Fellow

In January 2009, I spent a month working with the UNC Functional GI & Motility Disorders group. This was under the auspices of the American Neurogastroenterology and Motility Society's Clinical Training Program, which provides financial support for GI fellows to pursue more dedicated training in functional and motility disorders than that offered by most gastroenterology fellowships. In my own training program at Johns Hopkins, I have been involved in the care of many patients with motility and functional disorders, but this has never been concentrated within a month long rotation with intensive didactic sessions, motility test interpretation, and dedicated motility and functional clinic time.

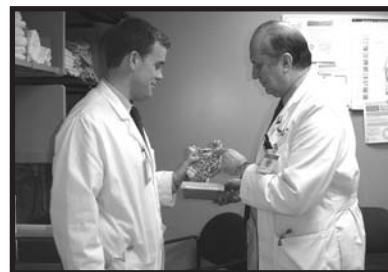
It has been estimated that at least a third of patients evaluated by gastroenterologists have underlying functional disease. Despite the ubiquity of these disorders, the majority of GI training programs do not devote considerable time to their evaluation and treatment. To become more proficient in managing these patients and conditions, I applied for and was selected to take part in a month long training program at UNC Hospital under the direction of Drs. Madanick, Drossman, and Whitehead.

From onset, the program was well orchestrated by Kirsten Nyrop and the clinical faculty. During the first week, I spent a considerable amount of time with Sheila Crawford, RN and Jill Williams, RN learning how to conduct both esophageal and anorectal motility studies. They were patient and accommodating when answering all my questions. I also spent time with Drs. Steve Weinland and Heymen through their respective work with clinical psychology and biofeedback. During my first few sessions with them, I quickly realized that caring for patients with functional disease required a team approach; a fifteen minute visit discussing anti-spasmodics or increasing fiber intake was not sufficient! This was further borne-out during my time spent in the functional GI disorders clinic with Dr. Drossman and Chris Dalton, PA. Although a 90 minute clinical visit was a novel idea to me, I now realize that this establishes the foundation for a sound physician-patient relationship, enhances patient education, and in and of itself may be therapeutic for the patient. In addition, thoughtful selection of neuromodulating drugs is just as important. Spending time with Dr. Drossman and colleagues has made me more attuned to the nuances of drug selection, with a particular focus on possible side effects.

Another major focus of the month was interpretation of esophageal and anorectal motility tests. Dr. Madanick and I spent a great deal of time reviewing esophageal physiology and how this is depicted by both standard manometry and pH/impedance tracings. Prior to coming to UNC, I had a modicum of experience with high-resolution manometry. However, reviewing the standard tracings and their acquisition has only enhanced my understanding of that technology. Similarly, Dr. Yolanda Scarlett patiently walked me through the acquisition and interpretation of anorectal manometry studies.

In addition to the clinical portion of the elective, Dr. Whitehead and I spent several hours reviewing the fundamentals of GI functional and motility conditions. To be able to review this material with someone who has conducted many of the original studies was invaluable.

In six months, I will complete my GI fellowship. I am currently pursuing a general gastroenterology position at an academic center and intend to incorporate motility and functional disorders into my practice. Gastroenterology is an evolving field. New technologies such as high-resolution manometry, new applications of drugs such as Seroquel for functional disease, and new insights into gut-microflora interactions serve to demystify some of the functional GI and motility disorders. Work in all of these areas is conducted at UNC and I feel fortunate to have been exposed to it during my intensive motility month and look forward to applying it as I embark on my career.



Kevin Dasher MD with Doug Drossman MD

NGM 2008

Center faculty and investigators were well-represented in presentations and posters at *Neurogastroenterology & Motility Joint International Meeting*, November 6-9, 2008 in Lucerne, Switzerland

NGM is an important forum that allows scientists and clinicians from around the world to review the tremendous progress being made in understanding gastrointestinal motor and sensory function in health and disease

Organizing Committees

Michael Fried, Chairman

ANMS: Gianrico Farrugia, Jay Pasricha

ESNM: Michael Schemann, Vincenzo Stanghellini

FBG: Douglas Drossman, Carlo DiLorenzo

INMG: Ashley Blackshaw, Roberto Dantas

Local Organizing Committee: Mark Fox, Radu Tutuian

Thursday, November 6:

Workshop

Chairpersons: **Douglas Drossman**, Michel Delvaux

WORKING TOWARDS ROME IV

Plenary Session

THE STRESS RESPONSE AND THE BOWEL

Behavioral responses and their management:

Douglas Drossman

Friday, November 7:

Parallel Sission

DIFFUSE NOXIOUS INHIBITORY CONTROLS (DNIC) ARE COMPROMISED IN PATIENTS WITH IRRITABLE BOWEL SYNDROME COMPARED TO HEALTHY CONTROLS

Steve Heyman, William E. Whitehead

Saturday, November 8:

Workshop

ROUND TABLE: THE FUTURE OF NGM

Psychosocial research: **Douglas Drossman**

POSTER PRESENTATIONS

CHRONIC CONSTIPATION: HEALTH CARE CONSULTERS VS. NON-CONSULTERS

Madhusudan Grover, Olafur Palsson, R. Levy, A. Feld, M. Von Korff, William Whitehead

TWELVE-MONTH FOLLOW-UP OF RANDOMIZED CONTROLLED TRIAL (RCT) COMPARING BIOFEEDBACK TO KEGEL EXERCISE TRAINING FOR PATIENTS WITH FECAL INCONTINENCE

Steve Heymen, William Whitehead, Yolanda Scarlett

THE EFFECT OF DAILY CONSUMPTION OF PROBIOTIC BACTERIA BIFEDOBACTERIUM LACTIS BB12 AND PREBIOTIC INULIN ON COLONIC TRANSIT TIME IN SUBJECTS WITH FUNCTIONAL BOWEL SYMPTOMS

Tamar Ringel-Kulka, Olafur Palsson, Danielle Maier, Yehuda Ringel

PRO-INFLAMMATORY IMMUNE FUNCTION IN COLONIC MUCOSA OF PATIENTS WITH DIARRHEA-PREDOMINANT IRRITABLE BOWEL SYNDROME

Yehuda Ringel, I. Carroll, B. R. Sartor

LONG-TERM GASTROINTESTINAL SYMPTOMS FOLLOWING ACUTE ENTERIC VIRAL INFECTIONS

B. Bobzien, Tamar Ringel-Kulka, M. Covington, Olafur Palsson, Yehuda Ringel



William Whitehead with wife Jan, and
Steve Heymen with wife Linda

NGM POSTERS

CHRONIC CONSTIPATION: HEALTH CARE CONSULTERS VS. NON-CONSULTERS

Madhusudan Grover, M.D.2,1, Olafur S Palsson, Psy.D.1, Marsha J Turner, M.S.1, Rona L Levy, Ph.D.4, Andrew D Feld, M.D., JD, FACP3,4, Michael Von Korff, Sc.D.3, William E Whitehead, Ph.D.1

1University of North Carolina at Chapel Hill; 2Michigan State University; 3Group Health Cooperative; 4University of Washington, Seattle.

Introduction: Chronic constipation (CC) is a common problem in U.S. adults accounting for significant health care burden and costs in the form of physician visits, diagnostic investigations, and medications. In addition, CC significantly impairs an individual's quality of life (QOL), and that impairment is correlated with the number of constipation symptoms present. It is not clear whether the well-being of individuals with CC who do not consult is significantly affected by this problem.

Methods: 1,100 adults enrolled in a large West Coast U.S. HMO who made a clinic visit between Sep. 1 and Dec. 31, 2005, and received a clinical diagnosis of constipation (ICD-9 code: 564.0X) and 1,700 age and gender matched subjects without that diagnosis in the past 5 years were invited to participate. A mail survey was completed which included demographics, Rome III IBS and constipation modules, PAC (Patient assessment of constipation)-QoL and Short Form (SF)-12 QoL questionnaires, and the Brief Symptom Inventory of psychological symptoms.

Results: 676 constipation consultants (mean age 66.1 years, 68.5% female) and 1031 comparison subjects (mean age 66.4 years, 68.0% female) completed the survey (60% overall response). 76.9% of the consulting sample and 40.3% of the comparison sample met Rome III CC criteria. The prevalence of undiagnosed CC in this sample was therefore 40.3% (416/1031). Compared to consultants, the non-consulters had higher SF-12 physical composite QoL scores (Mean+S.D: 43.3+13.2 vs. 39.6+13.3; $p<.0001$), and less constipation-related QoL impairment on the PAC-QoL (35.8 + 19.0 vs. 46.8 + 19.6; $p<.0001$) and its four subscales (physical discomfort, psychosocial discomfort, worries & concerns, and dissatisfaction), indicating a significantly greater constipation-related QoL impairment. A higher percentage of CC consultants vs. CC non-consulters reported problems with productivity while working and with other regular daily activities due to constipation (49.2% vs. 30.2%, $p<.0001$). In multiple logistic regression analysis, only three subscales of the PAC-QoL, made independent significant contributions to predicting consulting behavior. A significantly higher number of CC consultants perceived "medication side effects" (36.5% vs. 25.7%, $p<0.01$) and "aging" (28.3% vs. 20.7%, $p<0.01$) to be causes of their constipation. In contrast, "changes in routine" as a perceived cause of constipation trended higher amongst the CC non-consulters (25.2% vs. 20.0%, $p=0.056$). A significantly higher number of CC consultants were using medications or other methods to manage their constipation (58.2% vs. 32.7%, $p<0.01$). There was a significantly higher use of prescription and OTC laxatives, enemas, fiber supplements, herbal medicines, alternative therapies and exercise amongst CC consultants compared to CC non-consulters.

Conclusions: Forty percent of patients are dealing with CC without consulting health care providers about it. These individuals had made on average more than 40 outpatient visits for other health problems over the past five years. CC non-consulters have significantly poorer QoL and more psychological symptoms compared to individuals without bowel problems. Whether patients consult doctors about CC is unrelated to demographic or psychological characteristics, but is related to constipation frequency, amount of associated abdominal pain and bloating, and impact on life functioning. Only the impact of CC on QoL makes a significant independent contribution to explaining consulting behavior.

NGM POSTERS

LONG-TERM GASTROINTESTINAL SYMPTOMS FOLLOWING ACUTE ENTERIC VIRAL INFECTIONS

Brian Bobzien,¹ Tamar Ringel-Kulka, MD, MPH² Mary Covington, MD³ Olafur S Palsson, PhD⁴ Yehuda Ringel, MD⁴
 School of Medicine, ²School of Public Health, ³Campus Health Services, ⁴Division of Gastroenterology and Hepatology,
 The University of North Carolina at Chapel Hill, Chapel Hill, NC, United States

Background: Post-infectious (PI) Irritable bowel syndrome (IBS) relates to patients in whom IBS symptoms develop after acute episode of gastroenteritis. It is estimated that the development of IBS is linked to acute bacterial gastroenteritis in approximately 15% (range from 4%-30%) of patients. However, most of the published data on PI-IBS has been derived from outbreaks of foodborne bacterial pathogens (*Campylobacter*, *Escherichia coli*, *Salmonella*, and *Shigella*) and only one previously reported study linked the condition to enteric viral infection despite the fact that viruses are the most common cause of food-borne outbreaks.

Aim: To examine the cumulative incidence of IBS among subjects with a documented history of an episode of acute enteric Norovirus infection.

Methods: During the winter of 2004, there was an outbreak of Norovirus causing acute gastroenteritis linked to a dining hall at the University of North Carolina at Chapel Hill. Norovirus was identified as the causative agent by RT-PCR initially while the majority of cases were confirmed by using an epidemiological analysis according to Kaplan's criteria. Subjects were identified from the epidemiological data gathered at the UNC Campus Health Clinics at the time of the outbreak. Identified subjects were sent a questionnaire capturing demographics and prior and current general health and GI symptoms. Diagnosis of IBS was based on Rome II criteria, and the main outcome measure was the cumulative incidence of IBS in our subject population.

Results: Eighty-six subjects participated by returning the study questionnaire (mean age 25 +/- 4, 66% female, 80.2% white). Five subjects were excluded due to pre-morbid chronic GI symptoms, IBS, or pregnancy at time of the questionnaire. Of the remaining 81 subjects, 14 (17.3%) reported developing IBS symptoms within the three years after the acute infection. The prevalence of IBS in the study population increased from 4.7% prior to the acute viral infection to 18.8% following the infection. Age, gender, and vomiting during the acute illness were not identified as significant predictors for the development of the condition following the acute illness. Post viral infection IBS did not show significant preference for a specific subtype (diarrhea or constipation predominant) of IBS.

Conclusions: We provide additional epidemiological evidence for the association between acute enteric viral infection and the development of IBS. Unlike the single previous report that suggested a transient effect of viral infection, our study provides evidence for a long-term sequelae and highlights acute viral gastroenteritis as a significant risk factor for the development of IBS. Further research is needed to determine the nature of this association.

(Supported by grants T35 DK0738626, K23 DK075621, RR00046)

NGM POSTERS

12-MONTH FOLLOW-UP OF AN RCT COMPARING BIOFEEDBACK TO KEGEL EXERCISE TRAINING FOR PATIENTS WITH FECAL INCONTINENCE

Steve Heymen, PhD; Yolanda Scarlett, MD; and William E. Whitehead, PhD

UNC Center for Functional GI and Motility Disorders, University of North Carolina at Chapel Hill

Introduction: In an RCT (n= 108), biofeedback for FI was superior to Kegel exercises [76% vs. 41% reported adequate relief in an intent-to-treat (ITT) analysis, acquired at 3-month follow-up, $p < 0.001$]. Patients not completing treatment or not returning for 3-month follow-up (FU) were counted as treatment failures (n=15). Patients in both groups received identical contact time with the therapist and identical training with regard to education, medical management, behavior strategies, and Kegel exercises. The only difference in the two treatment protocols was the addition of biofeedback instrumentation to the Kegel exercise training for the biofeedback group. In addition, biofeedback patients had significantly lower scores on the Fecal Incontinence Severity Index (FISI) compared to controls ($p < 0.01$, and a trend favoring biofeedback over controls ($p = 0.09$) for FI frequency (from diary data).

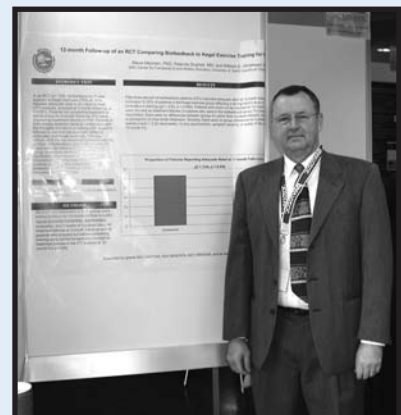
Aim: To determine the long-term benefit of biofeedback for fecal incontinence.

Methods: All treatment responders in both groups were invited to return for 12-month FU that included repeat anorectal manometry, psychometric evaluation, and 2 weeks of symptom diary. All treatment failures at 3-month follow-up and all patients who dropped out before completing training were carried forward and counted as treatment failures in the ITT analysis at 12-month FU (n=108).

Results: Fifty-three percent of biofeedback patients (53%) reported adequate relief at 12-month follow-up compared to 35% of patients in the Kegel exercise group reflecting a strong trend in favor of biofeedback training ($\chi^2 = 3.64$, $p = 0.056$). Patients who could not be reached for 12-month follow-up were counted as treatment failures (3 subjects who were in the biofeedback group). For treatment responders, there were no differences between groups for pelvic floor squeeze strength, resting tone, or perception of intra-rectal distension. Similarly, there were no group differences for numbers of FI events (mean = 0.52 days/week), or any psychometric, symptom severity, or quality of life measures at 12-month FU

Conclusions: A greater proportion of patients receiving biofeedback treatment continue to report adequate relief of fecal incontinence one year after treatment compared to patients receiving Kegel exercise training without biofeedback, although this difference was not significant. Fecal incontinence recurred in a small number of successfully treated patients, suggesting that periodic “refresher” sessions may be beneficial. This long-term follow-up data demonstrates the efficacy of biofeedback for the treatment of fecal incontinence.

(Supported by grants RO1 DK57048, R24 DK067674, MO1 RR00046, and an equipment grant from Sandhill Scientific Inc.)



Steve Heymen

ACG 2008

UNC Center clinicians and researchers were represented by poster presentations at *The American College of Gastroenterology* on October 3-8, 2008 in Orlando, Florida.

The ACG Annual Scientific Meeting and Postgraduate Course is the premier GI clinical event of the year. It brings together the Postgraduate Course Directors, the ACG's Educational Affairs Committee, and the Friday Course Directors to deliver the latest clinical updates in gastroenterology and hepatology.

ACG POSTERS

THE MULTINATIONAL TRANSLATION & VALIDATION OF THE SPANISH ROME III ADULT DIAGNOSTIC QUESTIONNAIRE

Morgan D, Schmulson M, Cortes L, Squella F, Domínguez R, Rey E, Mearin F

Background: The translation and validation of the Rome III Adult Diagnostic Questionnaire (R3DQ) into Spanish is needed for the investigation of the Functional Gastrointestinal Disorders (FGIDs) in Hispanic-Latino populations, as studies are limited. Country-specific Spanish translations, locally validated, preclude multicenter studies and comparisons. The unified translation for diverse Spanish-speaking populations facilitates investigations into the epidemiology, pathophysiology, and therapy of the FGIDs.

Methods: The multinational working group includes Mexico, Spain, Chile, Central America, and the U.S. The Rome Committee translation standard is as follows: two independent forward (English to Spanish) translations, reverse translation, reconciliation, pilot, and validation.

Results: A unified Spanish Rome III instrument was developed. Eight independent Spanish to English translations were completed, two each from each region (Mexico, Spain, Chile, Central America). The translations demonstrated 70% homogeneity, and were consolidated into a unified instrument by consensus. The pilot (both clinic and population-based) is complete in each region (n=124), with mean age 41 (range 18-78). The instrument was administered by trained interviewers, with study team observation. The majority (95%) of the Spanish Rome III questions (77/81 of FGID questions) were well understood. The concepts of retching and rumination (Q33-38) and anal relaxation (Q58) were problematic. Also, 75% of health questions (Q82-Q93) were understood. Limitations included: "celiac disease" (Q89.3) which is uncommon, "black stools" (Q83) which is frequent with native foods, and "anemia" (Q85) a synonym for "fatigue". Synonyms were needed as single word substitutions in 24% of questions (22/93), given differences in literacy and socioeconomic status. Time-frequency concepts were confusing to half of the subjects, particularly "rarely", "sometimes", "often" -- where a visual analog scale was helpful.

Conclusions: The unified Spanish Rome III Adult Diagnostic Questionnaire was developed to facilitate coordinated investigations in Spain and Latin America. A single core translation of each question is feasible. The use of validated synonyms, as single word substitutions in a subset of questions, provides clarity for regional, literacy and socioeconomic differences. This approach lends itself to a software platform for each region, for either interviewer or self-administered instruments.

Funded by the Rome Foundation.

ACG POSTERS

YOGURT CONTAINING THE PROBIOTIC BACTERIA BIFIDOBACTERIUM LACTIS Bb12 AND PREBIOTIC INULIN SIGNIFICANTLY IMPROVES COLONIC TRANSIT TIME IN SUBJECTS WITH FUNCTIONAL BOWEL SYMPTOMS

Tamar Ringel-Kulka MD, MPH¹, Olafur S. Palsson, PhD², Danielle Maier MPAS, PA-C², Yehuda Ringel MD, FACG²¹ School of Public Health, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA; ²Division of Gastroenterology and Hepatology, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA

Background: Functional gastrointestinal symptoms are very common complaints in primary care and GI clinics; however, the etiology still remains unknown and effective treatments are limited. Evidence suggests that intestinal bacteria play a role in the pathophysiology of these symptoms, and that modulation of intestinal microbiota may have beneficial effect/s on the altered intestinal physiology in subjects with these symptoms.

Aim: To investigate the physiologic effect of a yogurt drink containing the probiotic bacteria *Bifidobacterium animalis ssp. lactis* Bb12 (Bb12) and the prebiotic inulin in subjects with chronic functional bowel symptoms.

Methods: Subjects with chronic functional bowel symptoms who met the Rome II criteria for IBS, or functional diarrhea, or functional constipation, or functional bloating were enrolled in a prospective double-blind, placebo-control clinical trial. Following a two-week run-in period, subjects were randomized to receive either a yogurt drink containing 5×10^9 cfu total probiotic bacteria Bb12 and inulin 1.0g (active arm) or an acidified dairy drink (placebo arm) once daily for 6-weeks. Colonic transit time (CTT) was measured following established protocol using commercially available capsules (Sitzmark capsules; Konsyl Pharmaceuticals) containing 20 identical radio-opaque rings. Subjects ingested one capsule each morning for 3 days and an abdominal X-ray was taken on the fourth day. Total and segmental colonic transit times were calculated at the end of the run-in and six-week intervention periods according to the distribution of the markers throughout the colon.

Results: A total of 36 (probiotic n=17; placebo n=19) subjects were enrolled. The study population consisted of 82% females, 61% whites, and mean age of 36.7 years. Baseline demographics were similar between the two groups. Total colonic transit time was significantly shortened in the active group (30.5h vs. 21.3h, $p=0.016$) and showed a trend of shortening transit time in the left (descending + rectosigmoid) colon (16.2h vs. 8.3h, $p=0.056$). No effect was noticed on CTT in the placebo arm (23.0h vs. 25.0h, $p=0.61$ for the total CTT; and 9.8h vs. 9.7h, $p=0.95$ for the left side CTT).

Conclusions: Daily supplementation of diet with yogurt containing probiotic bacteria Bb12 and inulin shortens total and left side CTT in subjects with functional bowel symptoms. In view of the current lack of effective intestinal promotility agents, this dietary intervention may be a useful addition to the management of subjects with slow transit-related functional bowel symptoms. Further studies are needed to correlate these physiologic findings with improvement in clinical symptoms.

(Supported by grants K23 DK075621, RR00046, and General Mills, Inc.)

PATIENT SYMPOSIUM 2008

The UNC Center for Functional GI & Motility Disorders hosted Patient Symposium on Saturday, October 25, 2008. The theme was Functional Gastrointestinal Disorders: New Perspectives and Treatments. The symposium was held at the William and Ida Friday Center for Continuing Education in Chapel Hill. A Q&A session followed plenary sessions, and breakout sessions ended the day. This provided the opportunity for questions and answers with the symposium faculty.

Topic Sessions

Functional GI Disorders: IBS and Functional Abdominal Pain

Douglas A. Drossman, MD

Chest Pain and Swallowing Difficulties

Ryan Madanick, MD

Constipation, Diarrhea and Bloating

Yolanda Scarlett, MD

Pelvic Floor Disorders: Fecal Incontinence and Obstructive Defecation

William E. Whitehead, PhD

Nausea and Vomiting

Joseph Zimmerman, MD

The Role of Diet in the Functional GI Disorders

William E. Heizer, MD

The Doctor-Patient Relationship

W. Grant Thompson, MD

Medical Management

Douglas A. Drossman, MD

How Can a Psychologist Help?

Stephan Weinland, PhD

Participating in a Research Study

Kim Meyer, CCRC

Biofeedback for Pelvic Floor Disorders: Constipation, Incontinence, Pain

William Whitehead, PhD

Hypnosis Treatment

Olafur Palsson, PsyD

Breakout Sessions

Ask Us About Functional GI Disorders: Gastroenterologist, Physician Assistant and Patient Advocate

Douglas A. Drossman, MD

Lynne Eckert, PA

Integrative (Complementary and Alternative) Medicine

Susan Gaylord, PhD

Psychological Treatment

Stephan Weinland, PhD

Charles Burnett, PhD

Olafur Palsson, PsyD

Good and Bad Bacteria in the Gut: Infections and Probiotics

Reuben Wong, MD

Ask Us About Functional GI Disorders: Gastroenterologist, Physician Assistant, and Psychologist

Joseph Zimmerman, MD

Lynn Eckert, PA

Stephan Weinland, PhD

Upper Gastrointestinal Symptoms and Management: Chest Pain and Dyspepsia

Ryan Madanick, MD

Reuben Wong, MD

Abdominal Pain and Constipation in Children

Miranda Van Tilburg, PhD

Understanding the Irritable Gut

W. Grant Thompson, MD

William E. Whitehead, PhD

Special Guest Speaker



W. Grant Thompson, MD, *Professor Emeritus University of Ottawa*

W. Grant Thompson, MD has presented over 200 scientific or educational reports in 5 continents and is the author of 7 highly regarded books in the field of functional GI disorders (FGIDs). Dr. Thompson is also the author of 280 scientific and lay articles dealing mainly with gastrointestinal illnesses. He serves on several international committees concerned with the classification and diagnostic criteria for the FGIDs, including his work as a Rome Foundation Board member. Dr. Thompson is retired from clinical practice, but remains active consulting in clinical trial design, medical education, medical legal work, and writing about the FGIDs.

CENTER NEWS

PATIENT CHAMPIONS HOSPITAL TOY DRIVE

By Danielle M. Bates, N.C. Children's Hospital

Emma Jane Leonard cannot remember a time before she knew North Carolina Children's Hospital. The second grader was diagnosed with gastroesophageal reflux disease as an infant and has required intermittent hospital stays most of her life. The past year has been a particular struggle for the 8-year-old and her family, as they've endured numerous diagnostic tests and three surgeries.

Like most children her age, Emma looks forward to choosing a toy from the GI Motility Lab's treasure chest after each procedure. Her usual anticipation gave way to concern this past January, however, when she saw how few toys were left in the chest. If she chose a prize for herself, there would be even fewer left—and what would happen to other kids when the toys were all gone? Her nurse, Sheila Crawford, explained that the toys were donated. Perhaps the hospital would find another donor?



Emma Jane Leonard poses with the 449 stuffed animals she donated to N.C. Children's Hospital in March



Sheila Crawford and Jill Williams
with Beanie Babies

Not satisfied with that answer, Emma decided that she would be the one to make a difference. She soon drafted a letter to all 300 of her classmates at Episcopal Day School in Southern Pines. She needed their help. Would they be willing to donate a stuffed animal to make a child at the hospital happy? Emma placed a donation box outside of the principal's office and waited to find out.

Emma returned to the hospital in March with the fruits of her labors: two suitcases and several bags, all stuffed to the brim with almost every stuffed animal imaginable—449 in all, far surpassing her original goal of 50! The Motility Lab's treasure chest overflowing, Emma asked that the extras be shared with children all over the hospital.



Jill Williams, CGRN

Jill Williams, CGRN performs diagnostic tests in the GI Motility Lab on both pediatric and adult patients. These tests are inclusive of manometry testing, pH & pH/Impedance studies, and hydrogen breath tests.

Jill relocated from Sayre, Pennsylvania where she was employed at the Guthrie HealthCare System in the GI Endoscopy Unit, and has experience with endoscopy and motility procedures.

CENTER NEWS



Drossman Research Team (from left to right): Ashley Messina, Hollie Edwards, Katherine Ballie

ONGOING STUDIES

Ashley Messina is currently working on a study looking at the effectiveness of an anti-psychotic in severe IBS cases. Currently she is coordinating a new study which utilizes a pocket PC to record the symptom experience of IBS patients, and which investigates how symptoms and bowel habits change in response to an OTC diarrhea medications. She is in the process of applying to several physician assistant programs in the area, and has recently begun work as a volunteer birth doula for UNC Birth Partners.

Hollie Edwards is a clinical research assistant, responsible for coordinating investigator-initiated projects for the Drossman group. Three current projects include the Narcotic Bowel Syndrome (NBS) study, IBS Partner study, and Digital Rectal Exam study. The aim of the NBS study is to assess patients in terms of underlying diseases, clinical features, medications, psychiatric co-morbidity, and treatment response. The IBS Partner study seeks to evaluate the affect of IBS on partners of patients, and Hollie gauges physician and medical student views utilizing The Digital Rectal Exam. The investigators for these studies include Dr. Reuben Wong (Rectal Exam and Partner Studies), and Dr. Joseph Zimmerman (Narcotic Bowel).

Katherine Ballie is a research coordinator, working on investigator-initiated research studies for the Drossman group. Current studies include the Takeda Pocket PC study, the Seroquel study for severe IBS patients, and an upcoming McNeil study which involves a pocket PC and an OTC drug. Katie works on aspects of the day-to-day protocol execution on these studies, as well as managing the contracts and grants process for her research. The investigator for these studies is Dr. Stephan Weinland.



Doug Morgan, MD

DOUG MORGAN AWARDED GATES GRANT

The Latin America consortium for the prevention of gastric cancer has received funding from the Bill & Melinda Gates Foundation, 2008-11. The consortium includes 6 countries and 4 U.S. universities. The focus in the initial phase is on the optimization of H pylori eradication regimens, assessment of gastric cancer biomarkers, and streamlining the cancer epidemiology network.

The initiatives will facilitate inclusion of the Spanish Rome III instrument and its dissemination in Latin America. Douglas Morgan, MD MPH, serves as a member of the consortium's steering committee. In addition, the UNC Gastroenterology collaborative partners in Central America are core members of the consortium: Honduras (Ricardo Dominguez MD) and Nicaragua (Rodolfo Peña MD DrPH, Loreto Cortes MD MPH).

WELCOME TO THE CENTER



Liseanne Fedor-Hammonds is a Clinical Research Specialist for Dr. Ringel and has been with UNC since 2005. She facilitates and coordinates work pertaining to investigator-initiated studies, such as inflammation and probiotics. She earned her degree at UNC-Pembroke in Business Administration, and is currently working on her Masters in the online Clinical Research program at Drexel University. In addition to school, she also enjoys spending time with her three children, Chloe, Ethan and Rylie.



Laverne Millikin is the Administrative Support for Dr. Whitehead's research team. Her duties include checking for messages from patients for research; checking with Dr. Whitehead on what his plans are for that day, looks for articles, updating Dr. Whitehead's "CV", making flight arrangements, and checking with Marsha Turner, the research coordinator, to see if there are things that need special attention on that particular day.



Nancy DeMaria is a clinical research assistant for Dr. Ringel. She currently works on several investigator-initiated and industry-sponsored studies focusing on inflammation, intestinal bacteria, and probiotics. She is involved in all aspects of study coordination, from submitting protocols and proposals, to recruiting and consenting subjects. She is a 2007 graduate of UNC Chapel Hill with a degree in Biology, and minors in Chemistry and Spanish. She will attend a Physician Assistant program this fall.



Nicolette DeGroot is the Media Coordinator. Working 75% of time for the Center and 25% for the Division, she designs brochures, the *Digest*, annual reports, flyers, posters and maintains the Center website. A 2006 graduate of Appalachian State University, Nicolette received a degree in Graphic Arts and Imaging Technology, with minors in Art and Sociology, and has won student print awards from the 18th Annual Gutenberg Awards and the Printing Industry of the Carolinas.

CONGRATULATIONS...

Lynne Eckert gave birth to **Brian Christopher** on November 25th, 2008. Born 4 weeks early, Brian is very healthy, at 18 inches, 5 lbs 4oz.



Research Day 2009

When: September 25-26, 2009

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

What:

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 has annually hosted a Research Day on the campus of the University of North Carolina at Chapel Hill. Although the NIH Grant will be coming to a close this summer, the Co-Directors feel strongly that the Annual Research Day is of valuable benefit and have chosen to continue hosting this informative symposium. The format will include presentations on the state-of-the-art in many areas of Gastroenterology by visiting senior scientists, followed by overviews of on-going studies involving UNC faculty and investigators.

This Symposium is open to anyone wishing to attend, but pre-registration is required. People interested in attending should contact Ceciel Rooker at cecielro@med.unc.edu.

The Rome Foundation Presents...

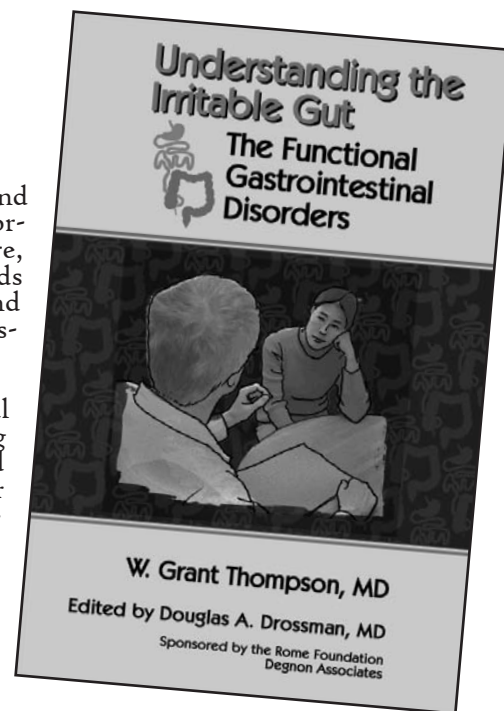
Understanding the Irritable Gut by W. Grant Thompson, MD

About the Book

The functional gastrointestinal disorders (FGIDs) can perplex doctors and patients alike. *Understanding the Irritable Gut* seeks to demystify these disorders. W. Grant Thompson, MD explains with ease and clarity the nature, prevalence, and putative causes of these disorders that affect up to two thirds of individuals worldwide. For the first time, the information developed and assembled by the Rome Foundation to identify, classify, and treat these disorders is presented in an easy-to-read, nontechnical format.

Dr. Thompson presents a general approach to the FGIDs with special emphasis on the all-important doctor/patient relationship. *Understanding the Irritable Gut* blends his professional experiences and well recognized writing talent with the information from Rome III and translates this for primary care practice. This book is a valuable resource for all nongastroenterologist health care professionals, students in the healing professions, patients seeking to be educated, and the general public.

Understanding the Irritable Gut can be purchased for \$29.95
at www.theromefoundation.org



About the Author

W. Grant Thompson, MD is Professor Emeritus (Medicine), University of Ottawa. He has presented over 200 scientific or educational reports in 5 continents and is the author of 7 highly regarded books in the field of functional GI disorders (FGIDs). Dr. Thompson is also the author of 280 scientific and lay articles dealing mainly with gastrointestinal illnesses and serves on several international committees concerned with the classification and diagnostic criteria for the FGIDs including his work as a Rome Foundation Board member. Dr. Thompson is retired from clinical practice, but remains active consulting in clinical trial design, medical education, medical legal work and writing about the FGIDs.



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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.