

# DIGEST



UNC  
SCHOOL OF MEDICINE

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

## IN THIS ISSUE:



NEW RESEARCH INTO THE CONSERVATIVE MANAGEMENT OF ACCIDENTAL BOWEL LEAKAGE

FUNCTIONAL GASTROENTEROLOGY QUESTION AND ANSWER

BELCHING, AEROPHAGIO, AND HICCUPS: ATYPICAL SYMPTOMS OF AIR TRANSPORT

NEW PUBLICATIONS FROM THE CENTER

## BELCHING, AEROPHAGIA, AND HICCUPS: ATYPICAL SYMPTOMS OF AIR TRANSPORT JOHN PANDOLFINO, MD



*John Pandolfino, MD is a Professor in Medicine and Chief of the Division of Medicine-Gastroenterology and Hepatology at Northwestern University Feinberg School of Medicine. Dr. Pandolfino's clinical interests include esophageal disorders, swallowing disorders, gastroesophageal reflux disease (GERD), and eosinophilic esophagitis.*

Symptoms of abnormal movement of air, such as belching, aerophagia and hiccups are common problems that are typically a benign abnormality or perception of normal physiologic events. These problems usually do not have a significant risk to one's health, but are mostly associated with an interruption in the patient's quality of life.

Belching is defined as oral expulsion of air and is a very common physiologic event that

typically occurs about 30 times per day in most healthy individuals.[1,2] It can be either silent or audible and most patients who seek medical advice usually have audible belching that can interfere with conversation, eating and be embarrassing in most social environments. The most important distinction in trying to figure out why belching is abnormal is to distinguish whether it starts in the stomach (sub-gastric) or in the esophagus (supra-gastric). This distinction is very important because they have different triggers and are treated differently.

Sub-gastric belching is the classic belch that arises from gastric distention and is common after a meal to help reduce the bloated feeling of fullness.[1] The gastric distention elicits an involuntary reflex that travels via the vagus nerve into the brainstem where the active arm of the reflex sends a signal down to the lower esophageal sphincter and the diaphragm that stimulates both to relax. Once the lower esophageal sphincter and the diaphragm

[Continued on Pg 4](#)

## REACH OUT TO THE CENTER

Twitter®



@FGIFYI

E-Mail



sjeremia@  
med.unc.edu

The Digest



Print and Online

Website



[www.med.unc.edu/ibs/](http://www.med.unc.edu/ibs/)

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

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

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

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

# HAVE A QUESTION?

## ASK THE CENTER PERSONNEL A QUESTION!

# DIGEST

## Center Director

William E. Whitehead, PhD

## Center Associate Director

Yehuda Ringel, MD

## Faculty, Clinicians & Investigators

Shrikant I. Bangiwalla, PhD  
 Spencer Dorn, MD, MPH  
 Steve Heymen, PhD  
 Temitope O. Keku, PhD  
 Jane Leserman, PhD  
 Ryan Madanick, MD  
 Olafur S. Palsson, PsyD  
 Yolanda Scarlett, MD  
 Lisa Gangarosa, MD  
 Nicholas J. Shaheen, MD, MPH  
 Miranda van Tilburg, PhD  
 Danielle Maier MPAS, PA-C

## Center Coordinator

## Center Webmaster

Stefanie Twist

## Center for Functional GI & Motility Disorders

*The University of North Carolina  
 at Chapel Hill*  
 130 Mason Farm Rd.  
 CB#7080  
 Chapel Hill, NC 27599  
 (919) 843-6961  
[www.med.unc.edu/ibs](http://www.med.unc.edu/ibs)  
 Printed on 30% post-consumer  
 recycled paper

<b>Cover</b>	BELCHING, AEROPHAGIA, AND HICCUPS: ATYPICAL SYMPTOMS OF AIR TRANSPORT
<b>4</b>	CONTINUED FROM COVER
<b>6</b>	NEW RESEARCH INTO THE CONSERVATIVE MANAGEMENT OF ACCIDENTAL BOWEL LEAKAGE
<b>8</b>	FUNCTIONAL GASTROENTEROLOGY Q&A
<b>10</b>	NEW PUBLICATIONS FROM THE CENTER
<b>13</b>	UNITED EUROPEAN GASTROENTEROLOGY WEEK AND NASPGHAN RESEARCH AWARD
<b>14</b>	OPPORTUNITY TO SUPPORT THE CENTER
<b>15</b>	FACULTY AND STAFF AT THE CENTER

Opinions expressed by authors are their own and not necessarily those of the UNC Center for Functional GI and Motility Disorders. We do not guarantee or endorse any specific product or any claim made by an author and disclaim all liability relating thereto. Occasionally specific products are cited in articles or acknowledgements. However, no endorsement is intended or implied. Our intention is to focus on overall treatment or management issues or strategies.



# BELCHING, AEROPHAGIA, AND HICCUPS: ATYPICAL SYMPTOMS OF AIR TRANSPORT

## JOHN PANDOLFINO, MD

relax, the end of the esophagus can open and since the pressure in the stomach is usually higher than the esophagus, air will flow quickly into the esophagus. Once the air reaches the esophagus, it stimulates the upper esophageal sphincter to relax and this is where the air movement enters the oropharynx and makes

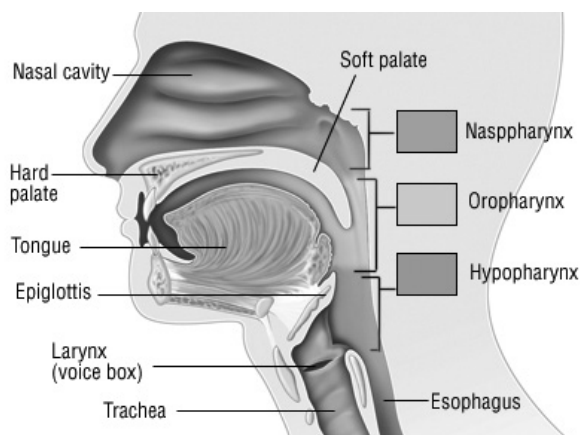


Figure 1 [4]

an audible sound. This can be isolated or associated with gastrointestinal disorders, such as GERD, slow gastric emptying, bloating and functional dyspepsia. The treatment focuses on treating the underlying disorder and occasionally medications will be used, such as baclofen, as they can block the reflex that causes belching.[2]

Supragastric belching can be differentiated from a gastric belch by presentation and history as these belches are typically much more frequent and can be stopped by asking the patient to bite down on a pencil to keep the mouth open.[1,2] These types of belches arise from air moving from the oropharynx into the esophagus during a deep breath and the air being expelled quickly from the esophagus as the upper sphincter remains open. This is a voluntary action, but patients are usually unaware that it is occurring. This is not to be confused with aerophagia (air swallowing) as the air in supragastric belching is being sucked into the esophagus as opposed to being forced into the esophagus by the swallowing mechanism. Many times it can be difficult to distinguish the causes

and techniques called impedance can help diagnose the cause by helping track the direction and flow of air through the oropharynx-esophagus-stomach. Once a supragastric belch mechanism is defined, therapy is focused on reassurance, explanation of the mechanism and behavioral modifications that will reduce the events. This can take the form of consciously keeping the mouth open when this is being triggered to therapy with a speech pathologists. [2]

Hiccups represent a unique form of air movement disorder that is associated with involuntary spasmodic contraction of the diaphragm and intercostal muscles that leads to a rapid inspiration with glottal closure. [3] The glottal closure gives rise to the classic hiccup sound and this is also believed to be associated with a vagus nerve mediated reflex arc. The vagus nerve

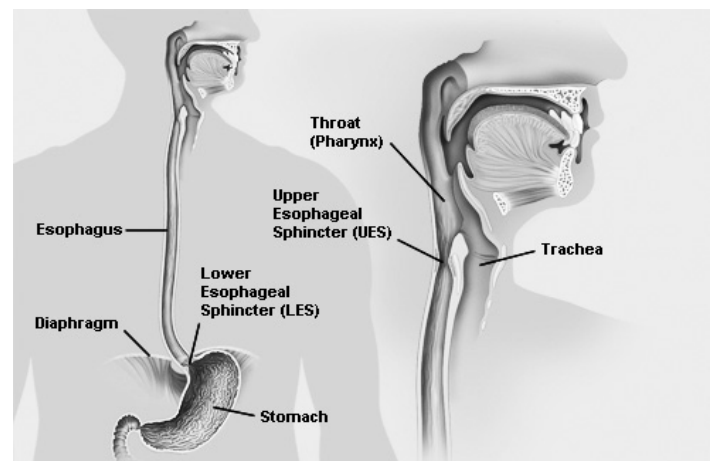
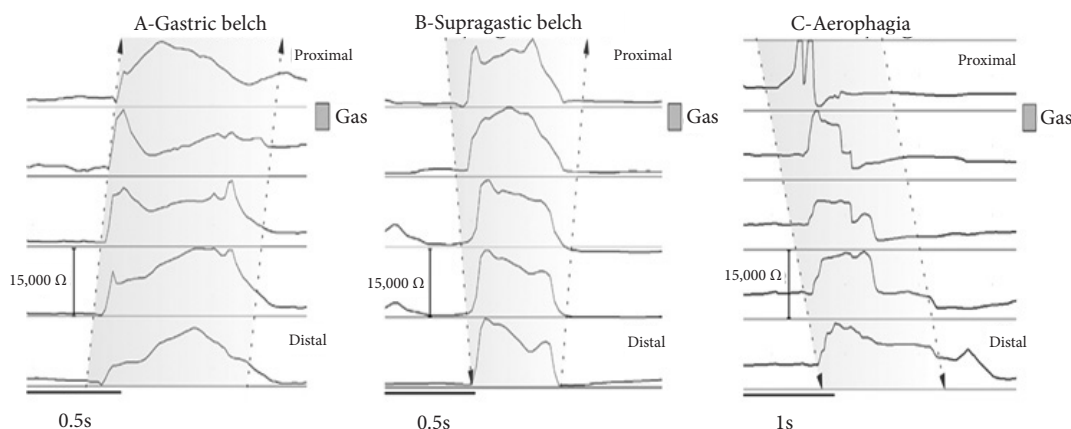


Figure 2 [5]

and phrenic nerve that supplies the diaphragm can be stimulated by a number of factors (gastric distention, temperature change, emotional stress, GI diseases, medications, CNS causes and nerve irritation). This activation sends a signal to the brainstem that then activates the diaphragm and accessory muscles of the ribcage to be activated quickly. Most patients have limited hiccups, however, they are considered intractable when they last for longer than 48 hours. Treatment focuses on identifying the underlying cause and using a combination of physical maneuvers and



*Figure 3: The impedance technique can define the presence of air by measuring impedance changes along a catheter that is placed through the nose and positioned within the esophagus and stomach. Air is identified as a sharp rise in impedance and the direction of flow can be determined by the timing of the changes in impedance (arrows). A-Gastric belching occurs with air entering the esophagus from below and leaving the esophagus through the upper sphincter. B- Supra-gastric belches enter the esophagus from above and leave immediately back through the upper sphincter. C-Aerophagia is associated with air entering the esophagus from above when the subject swallows and entering the stomach through the lower esophageal sphincter. Modified from Kessing et al, Am J of Gastroenterol 2014;109:1196-1203 with authors permission.*

medications.[3] Maneuvers that increase vagal tone or manipulate the diaphragm (bringing the knees to the chest) may interrupt the reflex arc and stop the hiccups. For patients that have severe symptoms or prolonged symptoms, medications (chlorpromazine, baclofen, Metoclopramide) can be used for 2 week trials with the medications being discontinued and weaned down to assess requirement for longer therapy. In extreme circumstances, nerve blockades and breathing pacemakers have been used to block the reflex arc; this is an extremely rare event.

Overall, disorders of air movement in the upper GI tract and oropharynx are common and usually associated with benign causes. Most of the time they do not require invasive testing, however, technologies such as impedance can be very helpful determining the cause of belching and may dictate therapies. The management of hiccups is typically dictated by the chronicity of the symptoms and the key aspect is to localize the trigger and utilize medications and maneuvers to block the reflex arc. It is extremely rare to require invasive treatment or chronic medical therapy for these symptoms as most will resolve on their own.

#### References:

1. Kessing et al. The pathophysiology, diagnosis and treatment of excessive belching symptoms Am J Gastroenterol 2014; 109:1196–1203
2. Bredenoord, AJ Management of belching, hiccups, and aerophagia. Clin Gastroenterol Hepatol 2013, 11(1):6-12.
3. Kahrilas PJ, Shi G. Why do we hiccup? Gut 1997; 41:712.
4. Harvard Health Guide: Epiglottitis – What is it? <http://www.drugs.com/health-guide/epiglottitis.html> Accessed 16 September 2015.
5. WebMD Digestive Disorder Health Center: Picture of the Esophagus. <http://www.webmd.com/digestive-disorders/picture-of-the-esophagus> Accessed 16 September 2015.

## NEW RESEARCH INTO THE CONSERVATIVE MANAGEMENT OF ACCIDENTAL BOWEL LEAKAGE



*Alayne D. Markland, DO, MSc is an Associate Professor of Medicine in the Division of Gerontology, Geriatrics, and Palliative Care at the University of Alabama at Birmingham (UAB) in Birmingham, Alabama. She is also a staff physician and clinician researcher at the Birmingham VA Medical Center and an investigator in the Birmingham/Atlanta Geriatric Research, Education, and Clinic Center (GRECC). Her*

*overarching goal is to enhance evidenced-based knowledge regarding the treatment of genito-urinary disorders, including urinary incontinence, fecal incontinence, and lower urinary tract symptoms in women and men. She currently is the medical director of the multidisciplinary Continence Clinic at the Birmingham VA Medical Center and practices at the National Association For Continence's Center of Excellence for Continence Care at UAB.*

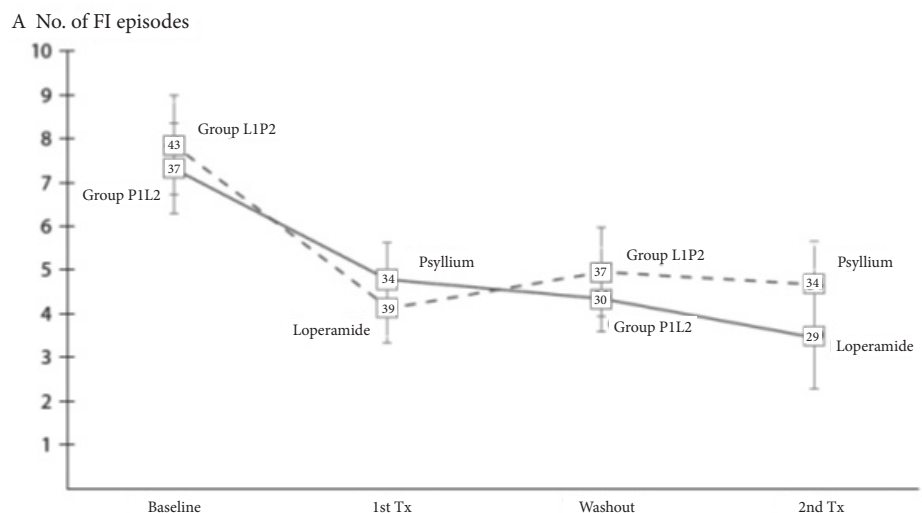
Accidental bowel leakage (ABL), also known as fecal incontinence (FI), may have a devastating impact on the quality of life both men and women. It is a very common condition, affecting 8.3% of non-institutionalized adults in the U.S. [Reference NHANES]. The most common risk factors are advancing age, diarrhea, and poor health, although constipation is a risk factor in sedentary older people and a history of obstetric trauma during childbirth is a risk factor that is unique to women. [1] The first line treatment of ABL (the treatment most physicians would try first) is collectively called conservative management. This usually includes patient education about the causes of ABL, instructions in how to perform pelvic floor exercises to strengthen sphincter muscles, and the use of medications or dietary fiber supplements to normalize stool consistency [5]. However, little information is available on whether antidiarrheal

medications or fiber supplements are effective and which is of most benefit. The aim of the new study published by Alayne Markland and colleagues was to compare these two treatments in a population of veterans with ABL.

Many people may recognize loperamide and psyllium fiber by common commercial names such as Imodium and Metamucil, respectively though there are many generic types of this medication available. Loperamide is an over-the-counter medication that is used to treat symptoms associated with loose stools and diarrhea. Psyllium fiber is an over-the-counter medication that is used to regulate stool consistency. Both constipation and diarrhea can be risk factors for ABL, though there are different reasons why each increases the risk.

The main factors tracked throughout the study were; (1) number of ABL episodes in a seven day period, (2) quality of life, and (3) side-effects of the medications.

The study was designed as a crossover study with a washout, meaning that patients were randomly assigned to start one type of treatment, stop the treatment for a short period (to allow the medication to “wash out” of their system), and then started



*Figure legend: The dotted line represents patients who first tried loperamide and then took psyllium after a washout period. The solid line shows patients who first tried psyllium and then took loperamide. Numbers in boxes show the number of patients available for analysis. The average frequency of ABL episodes and the standard error of the mean are shown for these two groups of patients.*

the second phase of the study which included the alternative treatment to see if there was any differences in how the medication affected their ABL symptoms.

Forty-three participants received loperamide as their first treatment and thirty-seven received psyllium fiber. The order of treatments was randomly assigned. The study results (see Figure) showed that patients receiving loperamide as their first treatment had significant reductions from 8 ABL episodes per week during baseline to 4 episodes at the end of treatment, and participants treated with psyllium as their first treatment also showed significant reductions from 7 ABL episodes per week to 5 episodes at the end of treatment (See Figure). However, there were no statistically significant differences between loperamide and psyllium in the magnitude of improvement in ABL episodes despite a trend for larger improvements in the loperamide group. Quality of life scores improved significantly for the loperamide treated patients but not for the psyllium treated patients from baseline to the end of the first treatment period, but again there were no statistically significant differences between the magnitude of improvement in quality of life between loperamide and psyllium.

The frequency of ABL episodes did not return to baseline levels following the washout (discontinuation of loperamide or psyllium for two weeks) as shown in the Figure, and there was no statistically significant improvement for either treatment in the second treatment period.

The most common adverse events (side-effects) for loperamide were constipation and abdominal pain while the most common side-effect for psyllium fiber was diarrhea.[1] One participant died while taking loperamide; cause of death was not specified in the report.

Medication adherence was excellent for both treatments: in the first part of the study, patients adhered to the study regimen 97-100% of the time, and in for the second part of the study, adherence was 80-96%.[1] Adherence did not significantly affect the outcome of the study.

To measure the participant's overall quality of life, the Modified Manchester Health Questionnaire (MMHQ) was administered following both treatments. The MMHQ is a validated questionnaire that identifies the overall impact ABL has on an individual's quality of life.[1,3] There are 31 questions having a response scale of 1 (never) to 5 (always) for each question. The responses to these questions are added together and

then transformed to a 0-100 scale in which a higher score is representative of increasingly severe ABL and a larger impact on the participant's quality of life. Participants who began loperamide initially had a lower MMHQ scores than those assigned to the psyllium fiber first, but when quality of life was reassessed after the second treatment, there were no significant differences between the two groups.[1] Also, within both groups, there were no significant differences between treatments in the participants' perceptions of satisfaction or improvement.

A diagnosis of ABL increases the probability that a provider might refer a patient to an assisted living community or skilled nursing facility, which is why it is important to identify and manage this condition as early as possible.[4] The article brings home the point that both loperamide and psyllium fiber should be considered as part of primary care conservative management protocol.[1] Assisting a patient to manage their ABL while they are still able to reside in their home not only can improve the patient's quality of life, but proper management can reduce overall health care costs and delay admission to an assisted living or skilled nursing facility.[4]

## References

1. Markland AD, Burgio KL, Whitehead WE, Richter HE, Wilcox CM, Redden DT, Beasley TM, Goode PS. Loperamide versus psyllium fiber for treatment of fecal incontinence: The fecal incontinence prescription (RX) management (FIRM) randomized clinical trial. *Diseases of the Colon and Rectum*; 58(10): 983-93
2. Whitehead WE, Borrud L, Goode PS, et al. Fecal Incontinence in US adults: epidemiology and risk factors. *Gastroenterology*. 2009; 137: 512-517.
3. Kwon S, Visco AG, Fitzgerald MP, Ye W, Whitehead WE; Pelvic Floor Disorders Network (PFDN). Validity and reliability of the Modified Manchester Health Questionnaire in assessing patients with fecal incontinence. *Dis Colon Rectum*. 2005 Feb;48(2):323-31
4. Grover M, Busby-Whitehead J, Palmer MH, Heymen S, Palsson OS, Goode PS, Turner M, Whitehead WE. Survey of geriatricians on the effect of fecal incontinence on nursing home referral. *J Am Geriatr Soc*. 2010 Jun;58(6):1058-62.
5. Whitehead WE, Rao SS, Lowry A, Nagle D, Varma M, Bitar KN, Bharucha AE, Hamilton FA. Treatment of fecal incontinence: state of the science summary for the National Institute of Diabetes and Digestive and Kidney Diseases workshop. *Am J Gastroenterol*. 2015 Jan;110(1):138-46

Written by Stefanie Twist and William Whitehead

## FUNCTIONAL GI QUESTION AND ANSWER

This section of the Digest is specifically for patient submitted questions that are answered by UNC faculty, gastroenterologists, or external experts in their respective fields. If you have a question you would like to be answered, please submit them us!

E-Mail: sjeremia@med.unc.edu  
 Twitter: @FGIFYI  
 Mail: 4161-G Bioinformatics Building  
 ATTN: Stefanie Twist, CB#7080  
 130 Mason Farm Rd  
 Chapel Hill NC 27599

### Patient Question:

Is there any problem with taking 1 to 3 tablets of Imodium daily for IBS-D?

### Answer from Sarina Pasricha, MD:

Irritable bowel syndrome is defined by the Rome criteria as recurrent abdominal pain or discomfort at least three days/month in the last three months associated with two or more of the following: 1. Improvement with defecation (bowel movements) 2. Onset of symptoms associated with a change in frequency of stool 3. Onset associated with a change in form (appearance) of stool. Irritable bowel syndrome with diarrhea (IBS-D) is defined as loose, mushy, or watery stools for at least 25% of bowel movements and hard or lumpy stools less than 25% of bowel movements (1). Treatment is often directed toward symptoms.

Loperamide (Imodium) is one treatment option for IBS-D. Loperamide works by binding to the opioid receptor in the large intestine to decrease peristalsis (gut contractions) and slow down gut transit time. In doing so, more water is able to be absorbed in the gastrointestinal tract. Treatment dose of loperamide can vary from 2-4 mg (with a maximum of 16 mg daily). The most common side effects of loperamide are: constipation (which occurs in 1.7%-5.3% of users), dizziness (up to 1.4%), nausea (0.7%-3.2%), and abdominal cramps (0.5%-3.0%) (2). In general, loperamide use is thought to be quite safe.

### Patient Question:

Can you help guide me to some information or research about mestinon and/or total colectomy with ileostomy bag for colonic inertia?

### Answer from Sarina Pasricha, MD:

Chronic constipation affects nearly 63 million people in the United States. Symptoms of constipation include less than 3 bowel movements per week, straining, hard stools, incomplete evacuation and the inability to pass stool. The prevalence of chronic constipation increases with age and is more common in women (3). A recent study from the University of North Carolina by Dr. Anne Peery et al. showed that constipation was the 5th most common gastrointestinal diagnoses from Emergency Department visits in the United States in 2012, which was a 61% increase from 2006. Additionally, constipation was the 4th most common gastrointestinal diagnoses in the ambulatory setting in 2010 with nearly 3 million visits (4).

There are multiple causes of constipation. A thorough work up includes a colonoscopy to evaluate for an obstruction, assessment of the anorectal and pelvic floor function, as well as an evaluation of transit time. Colonic inertia is also called slow transit constipation. Diagnoses of slow transit constipation requires an evaluation of gut transit time. This can be performed with a Sitzmark study (ingestion of radio-opaque markers followed by abdominal xray) or wireless motility capsule ingestion (such as SmartPill) (5). In patients who have chronic slow transit constipation that is not responsive to medical therapy in the absence of an evacuation disorder, a colonic manometry study is often indicated (6). A colonic manometry study includes a flexible probe with pressure transducers that is placed in the colon. Using colonic manometry, patients with colonic inertia can be determined to have either a normal manometry study, a colonic myopathy (caused by significant end-organ or muscle damage), or colonic neuropathy (damage to neuronal circuitry with secondary muscle dysfunction) (6). This is important because manometry results help to guide therapeutic options. Patients with normal colonic manometry or colonic myopathy tend to respond to conservative medical management. However, patients with colonic neuropathy have only a 15% response rate

to conservative management and may benefit from a colectomy (7). Please take note that there are very few centers in the United States that are able to perform a colonic manometry study. When colonic manometry is unavailable, physicians will often treat constipation with the strongest medications that we have available as well as with behavioral modifications. If a patient continues to have constipation that is significantly affecting his or her quality of life or causing other medical problems, then a referral for colectomy is made (8).

It has been proposed that some people are constipated because of a lack of cholinergic innervation and an imbalance in the autonomic regulation of the motor function. A study in 2010 showed that treatment with pyridostigmine (mestinon), a cholinesterase inhibitor, did not improve symptoms in patients with slow transit constipation (9). In patients who have constipation from recurrent pseudo-obstruction, pyridostigmine did result in some benefit to patients. Another article published in 2013 did show improvement in colonic transit time and bowel function in patients with diabetes and chronic constipation (10). At his time there is limited information on the use of pyridostigmine for constipation, and more research needs to be conducted to better understand the utility of this medication.

If you are experiencing chronic constipation, please talk with your gastroenterologist to make sure you are being appropriately evaluated and treated.

1. Dorn SD, Morris CB, Hu Y, Toner BB, Diamant N, Whitehead WE, et al. Irritable bowel syndrome subtypes defined by Rome II and Rome III criteria are similar. *J Clin Gastroenterol.* 2009;43(3):214-20.
2. Imodium. Clinical Pharmacology. [http://www.accessdata.fda.gov/drugsatfda\\_docs/label/2005/017694s050lbl.pdf](http://www.accessdata.fda.gov/drugsatfda_docs/label/2005/017694s050lbl.pdf) Accessed Sept 28 2015.
3. Higgins PD, Johanson JF. Epidemiology of constipation in North America: a systematic review. *Am J Gastroenterol.* 2004;99(4):750-9.
4. Peery AF, Crockett SD, Barritt AS, Dellon ES, Eluri S, Gangarosa LM, et al. Burden of Gastrointestinal, Liver, and Pancreatic Diseases in the United States. *Gastroenterology.* 2015.
5. Kim ER, Rhee PL. How to interpret a functional or motility test - colon transit study. *J Neurogastroenterol Motil.* 2012;18(1):94-9.
6. Lee YY, Erdogan A, Rao SS. How to perform and assess colonic manometry and barostat study in chronic constipation. *J Neurogastroenterol Motil.* 2014;20(4):547-52.
7. Singh S, Heady S, Coss-Adame E, Rao SS. Clinical utility of colonic manometry in slow transit constipation. *Neurogastroenterol Motil.* 2013;25(6):487-95.
8. McCoy JA, Beck DE. Surgical management of colonic inertia. *Clin Colon Rectal Surg.* 2012;25(1):20-9.
9. O'Dea CJ, Brookes JH, Wattchow DA. The efficacy of treatment of patients with severe constipation or recurrent pseudo-obstruction with pyridostigmine. *Colorectal Dis.* 2010;12(6):540-8.
10. Bharucha AE, Low P, Camilleri M, Veil E, Burton D, Kudva Y, et al. A randomised controlled study of the effect of cholinesterase inhibition on colon function in patients with diabetes mellitus and constipation. *Gut.* 2013;62(5):708-15.

## RESEARCH SUBJECTS NEEDED

### Diagnostic Evaluation of Functional GI and IBS Networks (DEFINE)

The UNC Center for Functional GI and Motility Disorders is looking for eligible subjects to participate in the DEFINE study.

You may be eligible to participate if:

- You have experienced any of the following GI symptoms for at least 3-6 months without a definitive diagnosis:
  - Abdominal pain or discomfort
  - Bloating
  - Constipation
  - Diarrhea
- You have not had any definitive testing for your GI symptoms
- You are at least 18 years of age

Eligible participants may receive up to \$214 for time and travel.

Study Title: The development and validation of a blood test to identify IBS: DEFINE  
(Diagnostic Evaluation of Functional GI and IBS Networks)  
IRB #13-2900

**Principal Investigator**  
**Dr. Yehuda Ringel,**  
**MD**

### Contact Information

Charles McIendon  
919-843-1003  
[aycockmc@email.unc.edu](mailto:aycockmc@email.unc.edu)  
edu

## CAUSES OF SYMPTOMS STUDIES

## NEW PUBLICATIONS IN 2015

The Center faculty have provided vital knowledge to the advancement of patient health and quality of life as well as advancing research with publications on multiple areas of functional gastroenterology. To provide an insight into what research is currently being conducted, both at UNC Chapel Hill and collaborating with exterior institutions, below are the most recent publications and a brief summary of the findings.

Markland AD, Burgio KL, Whitehead WE, Richter HE, Wilcox CM, Redden DT, Beasley TM, Goode PS. Loperamide Versus Psyllium Fiber for Treatment of Fecal Incontinence: The Fecal Incontinence Prescription (Rx) Management (FIRM) Randomized Clinical Trial. Dis Colon Rectum. 2015 Oct;58(10):983-93

*Primary Findings: Both loperamide and psyllium fiber can effectively be used to reduce episodes of accidental bowel leakage though loperamide was associated with more adverse events, including constipation.*

De La Luz Nieto M, Wu JM, Matthews C, Whitehead WE, Markland AD. Factors associated with fecal incontinence in a nationally representative sample of diabetic women. Int Urogynecol J. 2015 Oct;26(10):1483-8.

*Primary Findings: Accidental bowel leakage impacts one in five diabetic women and is strongly correlated with women who have very frequent bowel movements. Accidental bowel leakage was also associated with advanced age, depression, poorer overall health, urinary incontinence, and defecating more than 21 times per week.*

van Tilburg MA, Claar RL, Romano JM, Langer SL, Walker LS, Whitehead WE, Abdullah B, Christie DL, Levy RL. Role of Coping With Symptoms in Depression and Disability: Comparison Between Inflammatory Bowel Disease and Abdominal Pain. J Pediatr Gastroenterol Nutr. 2015 Oct;61(4):431-6.

*Primary Findings: Patients with functional abdominal pain were more likely than patients with inflammatory bowel disease to use coping strategies such as catastrophizing, self-isolation, and behavioral disengagement. These behaviors have been linked to increased rates of depression and functional disability and it was suggested that care providers become increasingly aware of maladaptive coping behaviors.*

Kanazawa M, Nakajima S, Oshima T, Whitehead WE, Sperber AD, Palsson OS, Drossman DA, Miwa H, Fukudo S. Validity and Reliability of the Japanese Version of the Rome III Diagnostic Questionnaire for Irritable Bowel Syndrome and Functional Dyspepsia. J Neurogastroenterol Motil. 2015 Sep 2.

*Primary Findings: Translation of Rome III from English into Japanese was successful as the questionnaire was reliable and valid.*

van Tilburg MA, Rouster A, Silver D, Pellegrini G, Gao J, Hyman PE. Development and Validation of a Rome III Questionnaire for Infant and Toddler Functional Gastrointestinal Disorders. J Pediatr Gastroenterol Nutr. 2015 Aug 21

*Primary Findings: The Rome III infant and toddler questionnaire is a newly developed and content valid questionnaire that will be important to clinical care and research of infant and toddler FGIDs. In children aged 1 month to 4 years, 52% of the 332 children met criteria for a FGID by parental responses to the questionnaire.*

Eric Jelovsek J, Markland AD, Whitehead WE, Barber MD, Newman DK, Rogers RG, Dyer K, Visco A, Sung VW, Sutkin G, Meikle SF, Gantz MG; Pelvic Floor Disorders Network. Controlling anal incontinence in women by performing anal exercises with biofeedback or loperamide (CAPABLE) trial: Design and methods. Contemp Clin Trials. 2015 Aug 17. pii: S1551-7144(15)30067-7.

*Primary Findings: This paper describes the design and methods of a multicenter trial that is being carried out by the Pelvic Floor Disorders research network. The study compares loperamide to placebo and biofeedback to a patient education intervention for treatment of moderate to severe fecal incontinence. This study uses a factorial design which allows for testing combined treatment against loperamide or biofeedback alone.*

Kiken LG, Garland EL, Bluth K, Palsson OS, Gaylord SA. From a state to a trait: Trajectories of state mindfulness in meditation during intervention predict changes in trait mindfulness. *Pers Individ Dif*. 2015 Jul 1;81:41-46

*Primary Findings: Individuals who were able to increase their state mindfulness over many sessions of meditation were more likely to increase trait mindfulness (a predisposition to be mindful in daily life) and decrease psychological distress.*

van Tilburg MA, Levy RL, Walker LS, Von Korff M, Feld LD, Garner M, Feld AD, Whitehead WE. Psychosocial mechanisms for the transmission of somatic symptoms from parents to children. *World J Gastroenterol*. 2015 May 14;21(18):5532-41

*Primary Findings: Parental reinforcement of the child's GI symptoms was not related to other illness. However, children with parents who had IBS did report more GI and non-GI symptoms, but children did not model methods of coping with the illness used by their mother. The child's psychological distress, including anxiety, depression, and somatization, was associated with the mother's psychological distress.*

Kunduru L, Kim SM, Heymen S, Whitehead WE. Factors that affect consultation and screening for fecal incontinence. *Clin Gastroenterol Hepatol*. 2015 Apr;13(4):709-16

*Primary Findings: Many patients do not have sufficient knowledge about effective and available treatments for accidental bowel leakage. Some patients choose not to discuss the condition with their physician as they believe the symptoms to be mild and if they do discuss it, prefer the physician to bring the topic up first.*

Ramsden CE1, Faurot KR, Zamora D, Palsson OS, MacIntosh BA, Gaylord S, Taha AY, Rapoport SI, Hibbeln JR, Davis JM, Mann JD. Targeted alterations in dietary n-3 and n-6 fatty acids improve life functioning and reduce psychological distress among patients with chronic headache: a secondary analysis of a randomized trial. *Pain*. 2015 Apr;156(4):587-96

*Primary Findings: Modification to participant's diets was utilized to increase Omega-3 fatty acid (n-3) consumption and decrease Omega-6 fatty acid (n-6) consumption. Pain reduction was correlated with an increase in plasma n-3 eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) and a reduction in n-6 linoleic acid (LA). This reduced physical pain and psychological distress, improved health related quality of life, and physical function in patients who had chronic headaches.*

van Tilburg MA, Hyman PE, Walker L, Rouster A, Palsson OS, Kim SM, Whitehead WE. Prevalence of functional gastrointestinal disorders in infants and toddlers. *J Pediatr*. 2015 Mar;166(3):684-9.

*Primary Findings: By adhering to the Rome criteria, it was found that 27% of infants and toddlers met the criteria for a FGID, with regurgitation as the most common in infants and functional constipation in toddlers. Infants and toddlers who met the Rome criteria were more likely than those who did not to have increased rates of medical visits, mental health visits, hospital stays, and a lower quality of life.*

Palsson OS. Hypnosis Treatment of Gastrointestinal Disorders: A Comprehensive Review of the Empirical Evidence. *Am J Clin Hypn*. 2015;58(2):134-58

*Primary Findings: Available research strongly supports hypnosis as an effective psychological tool for addressing clinical gastrointestinal symptoms and potential impacts on the central nervous system.*

Palsson OS, van Tilburg M. Hypnosis and Guided Imagery Treatment for Gastrointestinal Disorders: Experience With Scripted Protocols Developed at the University of North Carolina. *Am J Clin Hypn*. 2015;58(1):5-21.

*Primary Findings: A scripted treatment course for verbatim interventions using hypnosis had been developed at UNC and several other studies have utilized this protocol to treat patients with a wide range of disorders including: IBS, ulcerative colitis, and functional abdominal pain. Response rates in clinical trials that used this protocol range from 53% to 94% and some studies have shown that response rates can be maintained up to 12 months after the initial intervention.*

## NEW PUBLICATIONS IN 2015 CONTINUED

Bharucha AE, Dunivan G, Goode PS, Lukacz ES, Markland AD, Matthews CA, Mott L, Rogers RG, Zinsmeister AR, Whitehead WE, Rao SS, Hamilton FA. Epidemiology, pathophysiology, and classification of fecal incontinence: state of the science summary for the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) workshop. *Am J Gastroenterol*. 2015 Jan;110(1):127-36

*Primary Findings: In August 2013, the NIDDK held a state of the science workshop on fecal incontinence to define priorities for future clinical research on this disorder.*

*This article summarizes expert presentations on the current state of knowledge regarding the epidemiology, pathophysiology, diagnostic, classification, and measurement of severity and quality of life impact. It addresses gaps in knowledge and research priorities.*

Whitehead WE, Rao SS, Lowry A, Nagle D, Varma M, Bitar KN, Bharucha AE, Hamilton FA. Treatment of fecal incontinence: state of the science summary for the National Institute of Diabetes and Digestive and Kidney Diseases workshop. *Am J Gastroenterol*. 2015 Jan;110(1):138-46

*Primary Findings: This article summarizes presentations on treatments from the NIDDK state of the science workshop on fecal incontinence and addressed effectiveness and safety. Also presented was a survey of research priorities by workshop participants and other investigators not attending the workshop who have published on the treatment of fecal incontinence. The highest priority was to carry out comparative effectiveness trials on current treatments, emphasizing relative safety and cost as well as reduction in fecal incontinence severity.*

Ghoshal UC, Gwee KA, Chen M, Gong XR, Pratap N, Hou X, Syam AF, Abdullah M, Bak YT, Choi MG, Gonlachanvit S, Chua AS, Chong KM, Siah KT, Lu CL, Xiong L, Whitehead WE. Development, Translation and Validation of Enhanced Asian Rome III Questionnaires for Diagnosis of Functional Bowel Diseases in Major Asian Languages: A Rome Foundation-Asian Neurogastroenterology and Motility Association Working Team Report. *J Neurogastroenterol Motil*. 2015 Jan 1;21(1):83-92.

*Primary Findings: The Rome III questionnaires were translated into Chinese, Hindi, and Telugu and often found overlapping FGIDs. Translating words describing constipation, bloating, fullness, and heartburn presented the most difficulty. Translations in Korean and Indonesian languages did not meet the sensitivity and specificity required and did not perform well.*

Dorn SD, Palsson OS, Woldeghebriel M, Fowler B, McCoy R, Weinberger M, Drossman DA. Development and pilot testing of an integrated, web-based self-management program for irritable bowel syndrome (IBS). *Neurogastroenterol Motil*. 2015 Jan;27(1):128-34.

*Primary Findings: Participants in the 12-week IBS self-management program reported that they increased their knowledge about IBS, but no significant change in quality of life or self-efficacy was noted. It has the potential to be low cost solution for deficiencies of the medical system to help patients better manage their IBS.*

## VISITING PROFESSOR TO UNC TO HOLD ROLE IN ONE OF EUROPE'S LARGEST GI MEETINGS



Magnus Simren, MD is a visiting professor from the University of Gothenberg in Sweden. Dr. Simren will be collaborating with UNC faculty and physicians at the University of North Carolina – Chapel Hill during his year sabbatical with the Center for Functional GI and Motility Disorders. The research sabbatical is supported by the Ferring Pharmaceuticals Visiting scientist fellowship.

Dr. Simren is senior researcher of the Swedish Research Council and is a board member on the Rome Foundation. He also holds the position of Chair of the United European Gastroenterology Scientific Committee, and is the Clinical Editor of Neurogastroenterology & Motility. His main

research areas include functional GI disorders, including pathogenesis and pathophysiology, new alternative treatments, quality of life of patients with GI disorders, and links between inflammation, microorganisms in the gut, and GI symptoms.

On September 3, Dr. Simren gave a lecture to UNC GI faculty, fellows, and staff on the topic of, “The Puzzle of Irritable Bowel Syndrome (IBS): Can it be solved?”

In October, UNC faculty, Drs. Whitehead and Palsson, will be joining Dr. Simren in Spain for this year's United European Gastroenterology Week (UEGW). UEGW is one of Europe's largest gastrointestinal meetings that combine major European GI societies in one meeting. Dr. Simren will be speaking at the opening plenary session and offering words of welcome to the attendees of UEGW 2015, which initiates the start of an extensive list of invited speakers and abstract presentations.

## UNC PROFESSOR AND COLLEAGUES AWARDED NASPGHAN CLINICAL PRIZE FOR THEIR RESEARCH



*Dr. Rona Levy speaking at NASPGHAN annual meeting in Washington D.C.*

Drs. Rona Levy, Miranda van Tilburg, and other contributing authors were awarded the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN) 2105 Neurogastroenterology and Motility clinical prize for the submitted abstract, “Parent-Only intervention reduces symptoms and disability in abdominal pain patients.”

Parents who participated in cognitive behavioral therapy, aimed at learning strategies to manage their child's pain,

reported a significant level of reduced symptoms in their child and reduction in missed school days for abdominal pain when compared to the control group, which just received educational support. It also showed that delivering the intervention in-person or by phone was equally effective.

The findings from this research are important as they identify a low burden, low cost method of assisting parents to reduce the symptoms of their child's abdominal pain, reduce health care utilization, and decrease the amount of school missed due to abdominal pain.

*Levy Rona L, van Tilburg MA, Langer SL, Romano JM, Mancl LA, Whitehead WE, Feld SA, Walker LS. Parent-Only intervention reduces symptoms and disability in abdominal pain patients. Journal of Pediatric Gastroenterology and Nutrition, 61(Suppl 2), S22*



## OPPORTUNITY TO SUPPORT

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

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

### CONTACT INFORMATION

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

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

- ☐ \$1,000 and above  
☐ \$500  
☐ \$100  
☐ \$50  
☐ \$ \_\_\_\_\_

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 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) 843-6961  
**Fax:** (919) 843-2793  
**www.med.unc.edu/ibs**

Make your check payable to:  
 UNC Center for Functional GI &  
 Motility Disorders

**OR:** Include the following credit card information

- ☐ Mastercard    ☐ Visa

\_\_\_\_\_ Credit card #

\_\_\_\_\_ Expiration date

\_\_\_\_\_ Signature

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.

Center Tax ID#: 56-6057-494

# FACULTY AND STAFF AT THE CENTER

## LEADERSHIP

**William E. Whitehead, PhD**

Center Director

**Yehuda Ringel, MD**

Center Associate Director  
Director, Functional GI Clinic

## CLINICAL TEAM

**Spencer Dorn, MD, MPH**

Director, GI Medicine Clinic

**Ryan Madanick, MD**

Director, GI and Hepatology  
Fellowship Program

**Yolanda Scarlett, MD**

Director, GI Motility Lab

**Lisa Gangarosa, MD**

Functional GI Services

**Robin Dever, RN**

Nurse Coordinator

**Danielle Maier, MPAS,  
PA-C**

GI Motility Services

**Jennifer Layton**

Administrative Services

## RESEARCH TEAM

**Steve Heymen, PhD**

Associate Professor of  
Medicine

**Miranda van Tilburg, PhD**

Associate Professor of  
Medicine

**Olafur Palsson, PsyD**

Professor of Medicine

**Christina Campbell**

Research Assistant

**Renuka Kelapure**

Project Manager

**Charles McLendon**

Research Coordinator

**Stefanie Twist**

Center Coordinator



THE UNIVERSITY *of* NORTH CAROLINA *at* CHAPEL HILL  
CENTER FOR FUNCTIONAL GI & MOTILITY DISOR-  
DERS  
CB 7080, Bioinformatics Building  
Chapel Hill, NC 27599-7080

Phone: (919) 966-0144  
Fax: (919) 966-8929

Nonprofit Organization  
U.S. Postage  
PAID  
Permit No. 177  
Chapel Hill, NC