

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.

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OPIOID USE AND IMPACT ON THE GI TRACT

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OPIOIDS: IMPACTS ON THE GI TRACT

The evidence is becoming clearer; there is a strong relationship between chronic long-standing opioid use and negative gastrointestinal symptom reporting, pain symptoms, and declining quality of life. The two most common and recognizable disorders associated with opioid use and bowel function are opioid induced constipation and narcotic bowel syndrome.

Prescription opioids are classes of narcotic medications that act on opioid receptors and are designed to reduce pain. Examples of opioids are codeine, hydrocodone, methadone, morphine, tramadol, oxycodone, and fentanyl.

In the early 2000's, there was a spike in the prescription of narcotics oxycodone and methadone, resulting in roughly a 400% increase in the sale of

these drugs. [2,5] For acute pain, opioids are used commonly, however with this class of drug, there is an increased risk for dependency, potential abuse, and the potential for neurological changes within the gut and brain.

It is very important to note that just because an individual takes opioids to manage chronic pain, they should not be automatically labeled as "drug abusers." For most, the pain is real, debilitating, and has a negative impact on their quality of life.

In December, 2016, the US House of Representatives passed the, "21 Century Cures Act," which allows the NIH to allocate 1 billion dollars to all fifty states to study opioid use, drug abuse, and expanding treatment programs. This along with ongoing research into narcotic bowel and opioid induced constipation, has the potential to help many individuals with ongoing pain and gastrointestinal symptoms.

One would not immediately assume that taking pain medications would increase your perception of pain,

On an average day in the U.S.:


 More than 650,000 opioid prescriptions dispensed¹

Figure 1. [5] Source: IMS Health National Prescription Audit, SAMHSA National Survey on Drug Use and Health, and CDC National Vital Statistic System

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

HAVE A QUESTION?

ASK THE CENTER PERSONNEL A QUESTION!

DIGEST

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ANORECTAL DISORDERS: OVERVIEW OF RECENT LECTURES BY DR. WILLIAM WHITEHEAD

In October 2016, Dr. William Whitehead traveled to Europe to present at the United European Gastroenterology Week (UEGW). As a guest lecturer, he presented on the recognition and management of common anorectal disorders. This article summarizes his lecture presented to health care providers and researchers.

What is an anorectal disorder? First, we need to identify the area of human anatomy to better understand the disorders. Anorectal disorders involve biological defects, which include defects in tissue, muscles, or nerves around the pelvic floor, rectum, and anal canal. Examples of such disorders include hemorrhoids, anal fissure, rectal prolapse, and chronic proctalgia. It will be discussed further in this article about how each disorder presents and the recommended management practices.

In the United States, symptoms associated with anorectal disorders are the 7th leading gastrointestinal symptom (about 5.75% of all GI visits) that people make appointments for at ambulatory, or walk in, clinics, which accounts for approximately 2.6 million medical visits per year.[1] More common symptoms that fall into this category are anorectal pain, itching, swelling or mass, other anorectal symptoms, and fecal incontinence.

Hemorrhoids: What is it? Of the anorectal symptoms noted, hemorrhoids were the 3rd leading diagnosis, followed by abdominal pain and gastroesophageal reflux disease (GERD).[1] Hemorrhoids are anal cushions which fill with blood. They can engorge, or grow bigger, and function as a passive barrier to stool loss. Things go wrong when there is damage to these tissues. Associated risk factors include straining and constipation, pregnancy, chronic diarrhea, rectal surgery, anal intercourse, and inflammatory bowel disease (including ulcerative colitis and Crohns disease).

Are there different types of hemorrhoids? There are two types; internal and external hemorrhoids. Internal

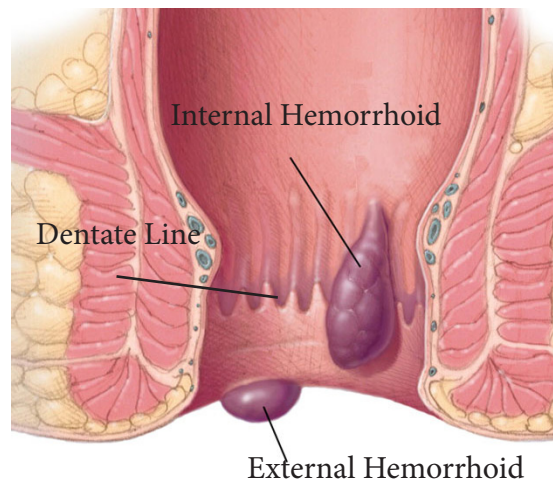


Figure 1, [2]

Internal and External Hemorrhoids

hemorrhoids occur above the dentate line and do not present with as many symptoms as external hemorrhoids because there are fewer nerve endings in that specific area. The dentate line divides the upper and lower parts of the anal canal. External hemorrhoids are typically the most bothersome to individuals. They occur below the dentate line. Symptoms associated with external hemorrhoids include pain or tenderness in the anal area and itching. There are more nerve endings below the dentate line, which is why they are more bothersome to individuals. Most people have a mix of both internal and external hemorrhoids.

What are the clinical symptoms? In most cases, there will be bright red blood associated with a bowel movement. Sometimes upon clinical examination, the hemorrhoids will prolapse, or stick out of, the anus. Less frequently, individuals will have fecal staining in their underwear. Internal hemorrhoids are given different grades, to mark the severity of the disorder, and range from 1 (least severe) to 4 (most severe). Hemorrhoidal prolapse is defined as hemorrhoid tissue that slips outside the anus.

1. Grade 1: No prolapse beyond the anus.
2. Grade 2: Occasional prolapse that can spontaneously reduce. This occurs when the hemorrhoid slips outside the anus, but retracts

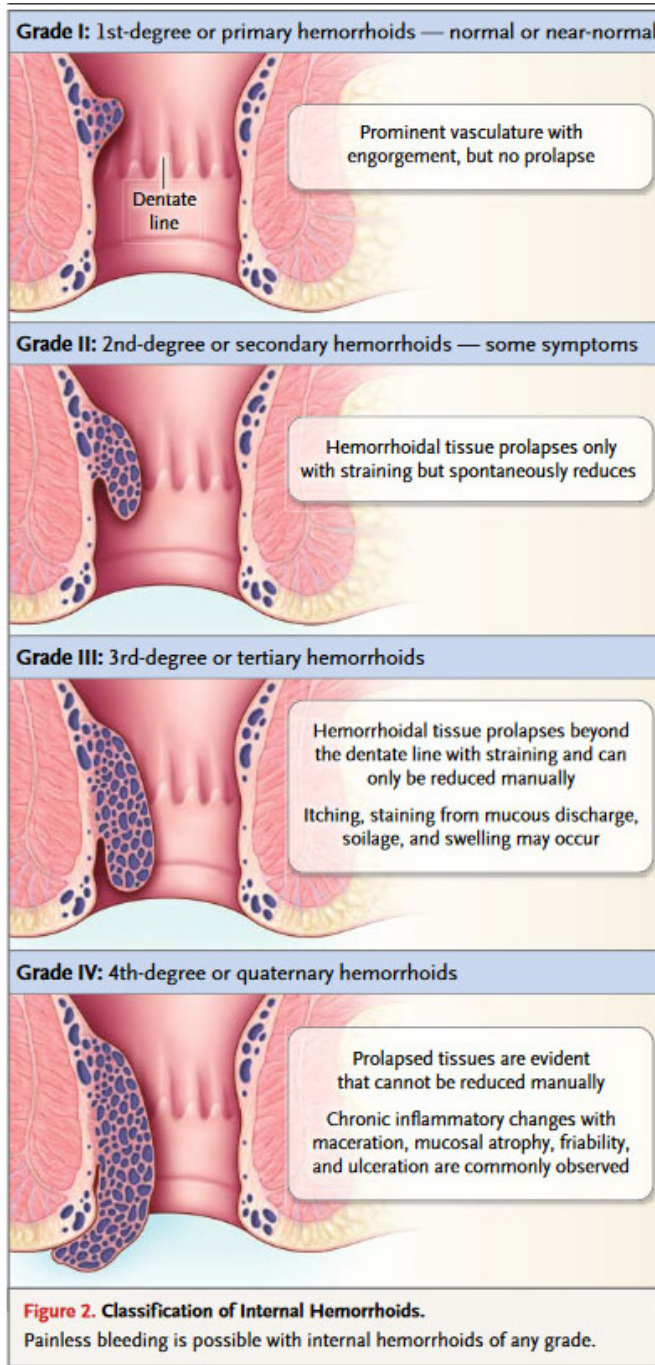


Figure 2 [3]
Grades of Hemorrhoids

spontaneously, without having to manually slip it back inside the anus.

3. Grade 3: Prolapse where an individual can manually slip the hemorrhoid back into the anus.
4. Grade 4: Prolapse that is always outside the anus and the hemorrhoid cannot be pushed back inside the anus.

External hemorrhoids, which can also be called thrombosed (a blood clot has gotten stuck inside the hemorrhoid causing it to swell), will look like a blue

lump and are very painful.

How are hemorrhoids treated? There are several ways to treat hemorrhoids. Fiber supplements are used to prevent constipation and straining during defecation. Steroid ointments can be purchased over the counter and prescribed to help reduce inflammation. Other medications that are commonly recommended are lidocaine analgesic, vasoconstrictor, and barrier ointments. Sitz baths may also help. Sitz baths are basically comprised of a tub that is molded to fit over a toilet lid and has tubing attached to it. Warm water is used to cleanse the area of the perineum, or area between the anus and scrotum/vagina.

If conservative management does not adequately relieve symptoms of a hemorrhoid, office based procedures would be the next level of care. These type of outpatient procedures include;

1. Rubber band ligation: This procedure is as it sounds and is self-explanatory. A rubber band is used to tie off blood supply to the hemorrhoid. It is only for internal hemorrhoids.
2. Sclerotherapy: An injection into the blood vessels of the hemorrhoid which eventually causes the vessels to shrink and gradually reabsorb back into the body. This is a treatment for internal hemorrhoids.
3. Cauterization: The tissue is burned off for two primary reasons, (1) remove the problematic hemorrhoid tissue and (2) to minimize infections due to the procedure. This can be done for internal and external hemorrhoids.
4. Surgical excision: The hemorrhoid is surgically removed carefully so that no damage to the anal sphincter occurs. This can be done for internal and external hemorrhoids.
5. Staple hemorrhoidectomy: The prolapsed tissue around the internal hemorrhoid are stapled back in place to a near normal position.

Anal Fissure: What is it? Anal fissures are tears in the tissue called anoderm. The anoderm is the top layer of skin lining the anal canal. Anal fissures are diagnosed by medical history and physical examination. Anal fissures can be acute (healed after a few weeks) or they can be chronic (lasting for more than eight weeks).

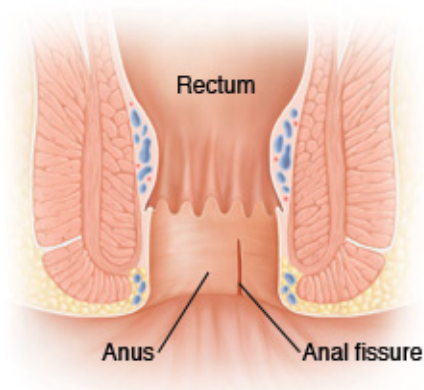


Figure 3 [5]
Anal Fissure

What are the clinical symptoms? Most individuals feel pain during and following a bowel movement and may see bright red blood on the stool as well. In cases of a chronic anal fissure, the anal sphincter may become hyper sensitive. The individual may develop skin tags near the fissure. Some individuals may describe defecation as a feeling of, “trying to pass cut glass,” or, “razor blades.” To say the least, it is a painful condition. If the fissure is chronic and does not heal, it has the potential to expose the underlying internal sphincter muscle.

How are anal fissures treated? Half of anal fissures diagnosed will heal on their own accord, along with home remedies to aid in recovery. Examples of home remedies include sitz baths, psyllium fiber or stool softeners, topical anesthetics (lidocaine), and anti-inflammatory ointments for symptom relief. It is more common to postpone surgical interventions and allow all attempts for them to heal naturally.

If conservative self-management does not work to heal the chronic anal fissure, a provider might suggest topical nitroglycerine ointment, topical calcium channel blocker, or pneumatic balloon dilation. If surgery is needed, a lateral internal sphincterotomy, which is a longitudinal incision into the internal anal sphincter, is done to reduce pressure on the anal canal. However, there are draw backs with this procedure because it increases the risk for fecal incontinence.

Rectal Prolapse: What is it? Rectal prolapse is when intestinal tissue slips outside the anus. There are two types of rectal prolapse, mucosal only and full thickness. Mucosal prolapse is also called partial-thickness prolapse. This is when the rectal mucosa is no longer held in place inside your body and slips down into the anal canal when having a bowel movement. Full thickness prolapse occurs when the entire rectal wall is no longer supported inside your body and slips outside the anus. Prolapse can occur spontaneously or can be associated with straining on the toilet. Health care researchers are unsure exactly what causes rectal prolapse, but they know that the tissue affixing the rectum and intestine to other organs begins to fail and is starts to slip outside the anus.

What are the clinical symptoms? Individuals with rectal prolapse have decreased urge sensations when they are about to have a bowel movement and feel as if they can't completely move their bowels. They also complain of a sensation of bulging from the anus and say they feel similar to hemorrhoids. Individuals with rectal prolapse also have a greater risk of having diagnosis of constipation and/or fecal incontinence. Rectal prolapse is more common in women than it is men.

How is rectal prolapse treated? There are few conservative treatments for rectal prolapse. A majority of treatments require surgery. After surgery, the risk of recurrence is small. The most common approaches to abdominal surgical interventions are;

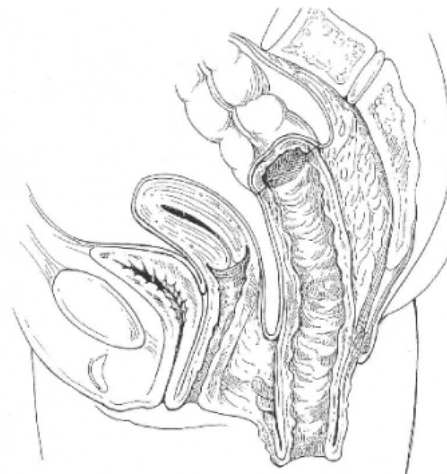


Figure 3 [4]
Rectal Prolapse

1. Reduction of the perianal hernia.
2. Fixation of the rectum to the coccyx.
3. Reduction of redundant bowel.
4. Operation to tighten the anus.
5. Resecting, or removing, the prolapsed bowel.

Levator Ani Syndrome (AKA: Chronic Proctalgia):

What is it? Levator Ani Syndrome or chronic proctalgia is described as chronic or recurring rectal pain or aching.

What are the clinical symptoms? The pain or aching sensations associated with chronic proctalgia usually last about twenty minutes or longer. Some individuals have reported the pain or aching sensations to last hours and that they were more comfortable standing than sitting. On a digital rectal exam, a majority of individuals experience tenderness when the levator muscles are probed.

As debilitating as this condition may sound, less than half of individuals with this condition speak with their physician about available treatments. The medical community believes that this condition is caused due to chronic tension, or muscle spasms, on the pelvic floor muscles.

How is chronic proctalgia treated? There are several conservative treatment options for chronic proctalgia. Most of the treatment options are designed to relieve the pain by relaxing the pelvic floor muscles. Treatments include:

1. Biofeedback
2. Electrogalvanic stimulation
3. Massage or physical therapy
4. Botulinum toxin (Botox)

One of the predictive features of who would benefit from biofeedback therapy were tenderness on digital exam and an inability to relax the anal canal when straining or evacuate a water filled balloon.



Figure 4
Digital rectal exam showing
location of levator muscles.

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Written by Stefanie Twist

Original lecture by Dr. Whitehead was delivered at United European Gastroenterology Week in Vienna Austria, October 28 - November 1, 2016.

FROM THE COVER: OPIOIDS

but that is what scientists think is happening with prolonged opioid use. There is also no specific time limit to develop narcotic bowel syndrome as a result of chronic opioid use. Current literature estimates it can occur within a few weeks and is not dose dependent. [3] Pain is regulated by the central nervous system and, oddly enough, narcotics have the potential to decrease and accelerate pain perception. [2] It is suggested that the accelerated pain perception makes a person more sensitive to pain. The part of the brain thought most likely to be responsible for the increased sensitivity to pain is the dorsal horn of the spinal cord, specifically the Glial cells. [2,3,4] Chronic use of opioids can lead to a condition called hyperalgesia, which is a condition in that an individual taking opioids for the treatment of pain may develop increased sensitivity to pain. The opioid receptors eventually become tolerant to the inhibition of pain signals and may make the pain seem worse. [3]

In animal studies, the use of morphine exposure after a rat received a sciatic chronic constriction injury (CCI) significantly lengthened and increased the magnitude of the perceived pain versus rats who were given a sham operation. [4] (CCI procedures are performed to study chronic neuropathic pain and involve the animal's sciatic nerve during surgery performed under anesthesia.) The perceived pain experienced by the rats in this study was documented for months after the morphine administration had stopped.

In human studies, healthy men were followed for a period of five days to study the impacts of opioid

treatment. Researchers found adverse GI symptom reporting and delayed transit time versus placebo groups within the five day period. [1] (See Figure 2) Participants who received oxycodone had an 8% increase in their pain detection threshold, whereas the individuals randomized to receive a placebo had a 3% decrease during the same time period. The same study also reported a statistically significant ($P < 0.001$) increase in total GI transit time, cecum, and ascending colon transit time. [1] This is one of many studies that has shown that opioids increase an individual's ability to perceive pain as well as slow down intestinal motility. [1,2,3]

Medical providers hold an important role at recognizing the patient's pain and not delegitimizing their symptoms. A first point of therapy might be to remove or reduce the narcotic, but this may be adversely perceived by the patient if a plan of treatment is not explained as to why it is being done. This will avoid some perceptions from the patient that the provider thinks they are addicted, their pain isn't real, or that there is nothing else the provider can offer. [2] Medications that may help during the weaning periods are antidepressants, benzodiazepine, clonidine, constipation treatments, and psychological treatments. [2,3]

It is important that patients work closely with their doctor and do not try a new treatment plan, medications, herbs, or other interventions without consulting their health care provider first.

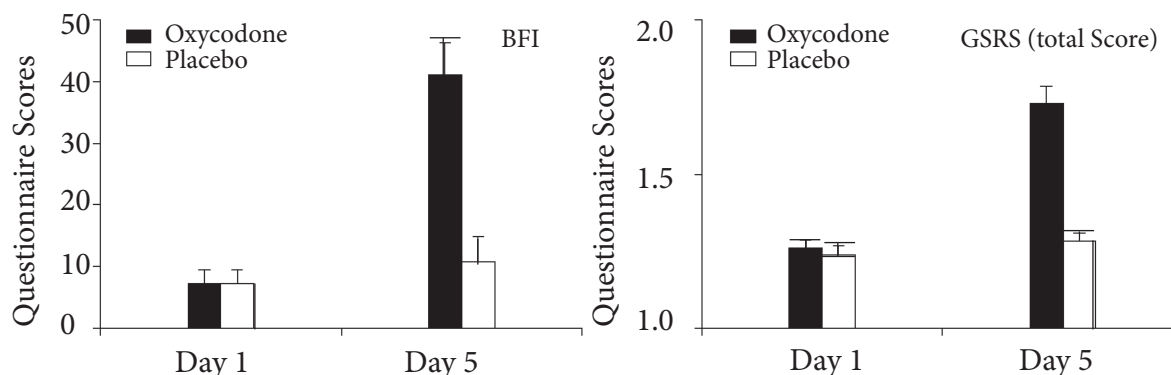


Figure 2. [1] "Bowel function index (BFI) and total gastrointestinal symptom rating scale (GSRS) results. From the left the first figure depicts the average BFI score from day 1 and day 5 for both treatments. The second figure shows total GSRS."

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RESEARCH SUBJECTS NEEDED

TREATMENT STUDIES

Accidental Bowel Leakage Self Help Website (FISH)

The UNC Center for Functional GI and Motility Disorders is looking for eligible subjects to participate in the FISH Study/

Researchers in the UNC Center for Functional GI & Motility Disorders are finishing development of a complete 6 week online self-help program designed to enable individuals to reduce or get rid of accidental bowel leakage (fecal incontinence) on their own.

If you have been experiencing accidental bowel leakage, then the researchers would like your help to evaluate their new program in a research study that you can participate in entirely through your own computer.

You may be able to take part in this research study if you;

- Have experienced accidental bowel leakage at least once a week in the past 6 months.
- Are able and willing to log into a website and complete the learning tasks and answer diary questions for a few minutes each night for a six week period.
- Live in North Carolina or Virginia.
- Speak and write fluent English.

No study visits will be required. You will be reimbursed up to \$225 for completing the 6 week online self-help program.

For more information or to enroll in the study, click here to go to the online consent form: <http://bit.ly/1PFBv18> (The link is case sensitive)

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GI DISORDERS IN RETURNING VETERANS: A CALL FOR SUPPORT

Sometimes, we need a reminder that our country is currently engaged in military operations abroad and many men and women will bring home with them more than visible wounds or memories they may not want to talk about. Engagements in Afghanistan and Iraq have been responsible for the deployment of roughly 2.7 million US military personnel.[2] The psychological toll taken on these individuals often manifests itself as anxiety, stress, depression, or in more severe cases post traumatic stress disorder (PTSD). Several studies published in 2016 have sought to establish the proportion of soldiers living with this mental health conditions and how it impacts the development of functional gastrointestinal disorders (FGIDs).

Many serve and train in dangerous, stressful situations, which has been shown to increase anxiety and depression scores.[5] These hazardous conditions create high stress environments, which can be the catalyst for development of mood disorders, (such as anxiety, depression, stress, and PTSD) and functional gastrointestinal disorders.[1,5] Not all individuals deployed to a war zone develop problems thereafter, but up to 44% of returning military personnel reported experiencing difficulties after they returned.[2] These included traumatic brain injuries (TBIs), PTSD, mood disorders, substance abuse, recovering victims of sexual assault, pathogenic gastrointestinal illness, and other stressors experienced while deployed.[1,2,3,4]

These problems can be difficult to manage and may contribute to the development of secondary health-issues. Correlations have been established between individuals with anxiety, depression, and PTSD and those with FGIDs.[1,5] Compared to veterans with no mental health conditions, those that were diagnosed with PTSD, depression, or generalized anxiety disorder (GAD) were two times more likely to develop a gastrointestinal disorder, such as Irritable Bowel Syndrome (IBS), gastroesophageal reflux disease (GERD), or dyspepsia [1]. One recent review cited a 3 times increase in FGIDs in soldiers with PTSD.[1]

There are increasing avenues for treatment of mood and gastrointestinal disorders. However additional research into symptom and disorder etiology requires one major component; additional funding to implement FGID and mood disorder screenings and interventions

within the military and veteran communities. Documented delays and insufficient resources for military personnel and veterans has created low rates of utilization or availability of proven treatments. [2] A lack of education and perceived stigma, combined with an increased prevalence of mental health issues in returning veterans, represents a large problem that needs to be addressed by the military, our elected public officials and health care practitioners.

One study looked at the percentage of PTSD in veterans currently receiving mental health treatment within the Department of Veterans Affairs (VA). The researchers found that 77.2% of VA patients who were actively involved in mental health treatment screened positive for PTSD.[3] Another study examined the overall prevalence of PTSD at pre, post, and long-term deployment of soldiers. The long-term effects of deployment were assessed at a median of 7.9 years after an initial Iraq deployment. It was found that within this time frame, 25.2% of the sample suffered from deployment related PTSD symptoms.[4] With nearly a quarter of the sample reporting PTSD symptoms, it becomes evident that the prevalence within the total veteran population is undoubtedly high. Such a prevalence negatively impacts many of the individuals who serve to protect our nation.

PTSD alone can be a struggle to live with. Associated psychological symptoms can also contribute to the development of gastrointestinal symptoms and disorders, such as IBS, GERD, dyspepsia, and abdominal pain.[1] Currently, researchers believe stress can increase intestinal permeability, leading in increased gut neurological dysfunction and increased susceptibility to GI pathogens.[5] Changes in the enteric nervous system (nervous system in the gut) are partly due to the release of several stress effector molecules. Corticotropin-releasing hormones impair the intestinal mucosal barrier, leaving it more susceptible to bacteria and glucocorticoids can increase and change the bacteria within the mucosa.[6] Norepinephrine also disrupts the normal activity of Salmonella and E. coli bacteria.[6] With FGIDs, particularly IBS, the combined effects of these hormones act to disturb the normal composition of gut microbiota.[7]

Evidence is beginning to show that the bodies response

to stress can lead to an activation of the intestinal immune system, which leads to micro-inflammation of the epithelium of the intestines.[8] This micro-inflammation can have a negative effect on the normal bacterial balance within the digestive tract. Research is also beginning to show that upsetting the gut microbiota balance is partially responsible for the symptoms of IBS. Approximately 10% of IBS patients say their symptoms occurred after they contracted infectious diarrhea.[8-11] Infectious diarrhea can lead to an imbalance of the normal gut flora. There is also an association with the onset of IBS and the use of antibiotics.[12]

These factors support the notion that an imbalance in the intestinal microbiota composition may, directly or indirectly, interfere with the normal function of the microbiota-gut-brain axis, leading to the development of central and peripheral abnormalities of either intestinal motility or the visceral-sensory network.[8] The correlation between the release of stress related hormones, altered gut microbiota, and the onset of gastrointestinal symptoms seems to show a connection between mood disorders and the shift in the bacterial composition of the gut. However, this is the proverbial question. Which came first? The mood disorder or the gut dysbiosis? While the relationship between the brain and gut is becoming clearer, we still have many things to learn. More research is needed to further clarify this relationship.

Funding is the single most important challenge that faces implementing a functional change in the way that we research and screen for FGIDs. There are studies showing the prevalence of mental health problems in veterans [1-4], and other studies showing a link between these various issues and the onset of FGIDs [5-12], but we still do not have a large federal grant established for the study, and treatment of FGIDs in veterans. A bill titled “H.R.2311 - Functional Gastrointestinal and Motility Disorders Research Enhancement Act of 2015” was introduced into the 2015-2016 U.S. Congressional session. Not only was it a budget-neutral bill, it was also co-sponsored by a bipartisan mix of both Republicans and Democrats. Unfortunately, as the new house representatives took the oath of office, that bill has since died and needs to be reintroduced.

H.R.2311 allowed for the National Institute of Health (NIH) to “expand, intensify, and coordinate” the effort against FGIDs.[14] One critical point in this bill was the opportunity for the Department of Defense and the Department of Veterans Affairs to partner in an

effort to improve care of veterans and active-duty military personnel with FGIDs.[14] Funding for such an alliance could lead to decreasing the impact that FGIDs have on those that have given of themselves in the service of our country.

It is important to define effective screening and diagnostic procedures for these with FGIDs. Fortunately, a highly recommended screening tool, the ROME IV Criteria, is currently available. This tool uses an algorithmic approach to aide clinicians in determining an accurate diagnosis.[13] Incorporating the Rome IV screening tool can lead to an accurate diagnosis and sequentially beneficial treatment options for patients. An appropriate diagnosis could greatly improve a patient’s health status and quality of life. This screening tool is available, but a tool is only as good as the operator. Education among health care providers is needed to understand the conditions and learn when it is appropriate to refer to a gastroenterologist and/or a psychologist.

Without the public pushing the federal and state government to fuel FGID health projects, it’s unlikely that they will get the recognition or funding that is needed. Our veterans have provided an immeasurable service and thus deserve the best care available. It’s time the public voiced our demand for pro-veteran FGID legislation.

Written by Doug Emmett.

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INTERESTING NEWS FROM 2016

Not everyone has a Twitter or Facebook account and cannot see the interesting articles posted up on the Center's official social media pages. Thus, we are taking the five most interesting or important articles or events, within UNC and abroad, from 2016 and highlighting their impact on the field of understanding functional GI disorders in the Digest.

5. UNC hosted Magnus Simrén, MD from the University of Gothenburg, Sweden for a one year sabbatical. Dr. Simrén is one of the foremost international experts in functional gastrointestinal disorders, specifically within the areas of irritable bowel syndrome. His expertise has helped to shape many of the research protocols and publications, within UNC. He also holds roles on the Rome Board of Directors. During his time at UNC, he also was acting President for the annual United European Gastroenterology Week.

4. Publishing of American Journal of Gastroenterology's "The Negative Issue," highlighting the positive importance of reporting all research, even if it is deemed negative. This is important, as we want to know if a

new medication or therapy didn't work. That negative information can prevent someone from making the same mistake on a different research protocol or can form new criteria for treatment protocols that work more effectively. A full list of publications submitted to "The Negative Issue," can be found at <http://www.nature.com/ajg/journal/v111/n11/index.html>

3. The senate appropriations committee approved a \$2 billion dollar funding increase to the NIH and subsequently, the NIDDK, which supports funding directly related to gastrointestinal disorders. This increase also included \$261 million dollars to go towards the opioid epidemic, which is important as many individuals are currently suffering from opioid induced constipation or narcotic bowel. Added into the legislation is language that expands the gut microbiome research programs and IBS etiology and efficacy of treatments. More information on this can be found at http://www.gastro.org/news_items/2016/06/15/senate-appropriations-committee-approves-increase-for-nih-niddk

2. Introduction of Rome IV in May, 2016. This roll out of the newest diagnostic criteria has been years in the making. The last time a new diagnostic criteria was released was with Rome III in 2006. For more information about Rome IV diagnostic criteria, visit the website <http://theromefoundation.org/rome-iv/whats-new-for-rome-iv/>

1. Microbiota and the brain-gut interaction. This seems to have been the year of microbiota. So much has been discovered in relation to how our gut bacteria effects not only our gut, but how it interacts with our nervous

system and brain. In May 2016, we tweeted about the a review of emerging evidence citing post traumatic stress disorders could be prevented with the use of gut microbes. Now, this isn't a conclusive proving of theory, but it is adding to the supportive evidence that bacteria can alter our mood and personality. The full article cited can be found at <http://www.medicalnewstoday.com/articles/309600.php>

If you have an interesting mention that you feel should be added to this list, tweet out to me at @FGIFYI or Facebook me at <https://www.facebook.com/FGIFYI/>

WHERE CAN I FIND INFORMATION ON PARTICIPATING IN A CLINICAL TRIAL?

UNC Chapel Hill has a website specifically designed to match eligible research participants to openly recruiting research studies. This includes individuals who are healthy and looking to participate as a control and those with specific diseases or symptoms.

Join the Quest (<https://jointhequest.org>) helps research participants search through the open clinical trials within the University of North Carolina at Chapel Hill. The research studies vary and include surveys, drug clinical trials, device clinical trials, procedure clinical trials, medical outcome studies, and research which needs healthy volunteers, which may also be referred to as a "control."

Another resource available to patients who do not live near Chapel Hill is www.clinicaltrials.gov. This is operated under the National Institutes of Health (NIH) and has information about clinical research studies available in the United States and globally.

As with all research studies, participation is completely voluntary and you make the decision to participate. If at any time you have questions about a research

study, you can always contact the research coordinator, study investigator, or the institutional review board (IRB). You should never feel coerced or pressured to participate in a research study. You also have the right to remove yourself from the research at any time and for any reason. The research investigator also has the ability to withdraw you from a study if s/he believes that it is unsafe for you to continue to participate. After all, your health and safety is paramount.

Most studies that involve a drug, device, or procedure must report their findings to the FDA if they want their product to be approved for sale. To learn more about the FDA's role in clinical trials, visit <http://www.fda.gov/ForPatients/ClinicalTrials/ucm20041753.htm>

The Center for Functional GI and Motility Disorders has research opportunities for pediatric and adult patients and will add more throughout the year. You can find more information about these studies online at <http://www.med.unc.edu/ibs/research/research-subjects-needed>



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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.

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