IBS: CONSTANT, INTERMITTENT AND EVERYTHING IN BETWEEN
By: John W. Biery, Jr. APRN, AGPCNP-BC
Tri-State Gastroenterology Associates

IBS: WHY DOES IT MATTER?
 It has been stated that “the patient’s would give up 10-15 years of life expectancy for an instant cure of the disease”
 It affects 7-16% of the United States population and is most common in women in younger adults.
 Direct call us of IBS in the United States alone have been “estimated, conservatively, at more than $1 billion.”

IBS: OBJECTIVES
 Define IBS including phenotypes, causes, pathways and diagnostic criteria
 Infectious, autoimmune, psychosocial, brain-gut vs gut-brain
 Rome 3 v. 4, Manning criterion
 Discuss various treatment modalities
 Discuss emerging thoughts, research in diagnosis and treatment of IBS

IBS: WHAT THE HECK IS IT?
 Differing schools of thought.
 In the past IBS was proposed to be a diagnosis of exclusion. Unfortunately, studies showed that operating this way led to unnecessary testing, and thus cost, as well as declining quality of life measures (IBS 2017).
 Functional disorder (aka may or may not exhibit histopathological abnormalities to explain symptoms) that, often times takes time to tease it out, given no worrisome factors exist (will discuss later).
 Can involve abdominal pain, diarrhea, constipation, bloating, abdominal distention, nausea/vomiting, all, multiple or one. Can also occur on spectrum. (will discuss diagnostic criteria later)
 Significant impact to quality of life measures sandwiched between time of diagnosis, response to treatment and finding “new baseline.”
 Can take as long as 10 years, in some cases (up to date), and patients have been surveyed preferring to give 10 years of their life to improve the quality diminished by IBS (IBS 2017). THINK ABOUT THAT!

IBS: WHAT THE HECK IS IT?
 Represents up to 30% of referrals to gastroenterology (uptodate)
 Two main modalities thought to be causative
 Brain-gut (50%) - Psychological factors (i.e. anxiety, depression, somatisation [essentially recurrent symptoms without discernible organic cause])
 Gut-brain (50%) - Abnormal stress response
 Post-infectious
 Tie with celiac disease, poor absorption of CHO
 Food allergies
 Bile acid malabsorption
ROME CRITERIA GRADE IV

- Recurrent abdominal pain
  - > 1 day a week in previous 3 months
  - Onset >6 months prior to diagnosis
- Abdominal pain associated with 2/3 symptoms
  - Pain related to defecation
  - Change in frequency of stool
  - Change in form (appearance) of stool

BRISTOL STOOL SCALE

MANNING CRITERIA

Manning criteria for the diagnosis of irritable syndrome bowel:

- Pain relieved with defecation
- More frequent stools at the onset of pain
- Looser stools at the onset of pain
- Visible abdominal distention
- Passage of mucus
- Sensation of incomplete evacuation

* The likelihood of irritable bowel syndrome is proportional to the number of Manning criteria that are present.

EXAMPLE #1

Nicole is a 47YOF with PMH HTN, HLD, Anxiety. She has been having performance issues with her job and has noted breakthrough issues with episodic diarrhea. Previously she would have 1 bm daily to every other day and normally formed character. She notes now 2-3 episodes, often times shortly after eating or with acute stress. Bristol 6-7. No recent abx, exposures that she is aware. She, also, has noted some rectal bleeding, bright red on toilet tissue and in the commode. She denies any appetite changes, abdominal pain, pertinent family history, or UGI complaints. Her VSS, afebrile. What is the next best step?

- A) Digital rectal exam
- B) CBC, Inflammatory markers
- C) Start prep h suppositories
- D) Referral to GI
- E) All of the above

ALARM SYMPTOMS

- > 50YOA without previous CRC screening with presence of symptoms
- Recent change in bowel habit
- Evidence of overt GIB
- Nocturnal pain or passage of stool
- Overt GIB (melena or hematochezia)
- Unintentional Weight Loss
- FH CRCa or IBD
- Palpable abdominal mass, LAD
- IDA
- Fecal occult blood
IBS ETIOLOGY: POST-INFECTIOUS
- After acute gastroenteritis, up to 20% of patients have persistent IBS symptoms (abd pain, diarrhea, bloating)
- Multiple theories:
  - Idiopathic bile acid malabsorption leading to IBS-D type symptoms
  - Increased enteroendocrine cells leading to increased serotonin levels -> increased GI motility and visceral hypersensitivity (aka pain and diarrhea)
  - ABx use
- Sevenfold risk increase following A.G.E. (Advances, 2016)
  - Risk factors: Young, prolonged fever, anxiety/depression and increased length of illness (upToDate post-infectious IBS)

IBS ETIOLOGY: POST-INFECTIOUS- CONTINUED
- Can persist up to 8 years following infection! (Advances, 2016)
- Must rule out persistent/recurrent infection --- if cdiff, consider repeat stool studies with lactoferrin
- More likely in patients with IBS-D, spirochete based infections (syphilis, Lyme disease etc.)- NEJOM

IBS ETIOLOGY: PSYCHOSOMATIC
- "Chicken or the egg" - remember brain-gut vs. gut brain?
- Anxiety/depression causes or caused by functional gut related issues.
- IBS has been treated, with some success, with probiotics which postulates gut-brain but improvement with Cognitive Behavioral Therapy indicates brain-gut.
- TNF thought to play a role -> increased levels of TNF found in IBS patients increase proceeding levels of anxiety -> gut-brain
- Related to Corticotropin Releasing factor in stress response increasing gut motility and visceral hypersensitivity but treatment with CRF antagonist had mixed results in mediating

IBS ETIOLOGY: CELIAC DISEASE
- Biopsy confirmed celiac disease tied to any IBS subtype (Advances 2016, nejom)
- Clinically appearing more similar to IBS-D (abd pain, diarrhea, bloating) (Advances 2016)
- All patients with any syndrome similar to IBS should have celiac serology checked (some healthcare systems offer celiac reflexive cascade that can be checked). Be mindful that gold standard is duodenal biopsy to r/o celiac's disease.

IBS ETIOLOGY: BILE ACID MALABSORPTION
- Not just in patients s/p CCE. European models (early phase) testing for malabsorption in GB present patients- NEJOM
- Causes increased intraluminal water/electrolyte secretion, increased colonic transit and stimulation of enteroendocrine cells (i.e. Serotonin) -> Diarrhea (Advances 2016)
- More often found in IBS-D subtype
- Treatment??? Thoughts? Guesses?

IBS-D
- Grade 6-7 appearing stool on BSFS (Bristol Stool Scale) (UpToDate "treatment of ibs")
- Small or moderate volume
- Daytime occurrences only (nocturnal -> abnormal)
- Pre-defecation abdominal cramping/pain/tenesmus (urgency)
  - Not abnormal to have mucus present at time of bm's
  - Over time may move between IBS-C and back again!
  - Treatment options:
    - Slow the gut, alternate reception and/or bulk the stool

*Clinical manifestations and diagnosis of irritable bowel syndrome in adults - UpToDate
IBS-C
- Broad definition, often determined by what patient “senses”
- Has more of a subjective quality
  - Infrequent bm’s (<3 bm’s weekly)
  - Hard stools/straining (grade 1-2 BSFS), scybalous stool (pallet like stools- “rabbit turds”)
  - Incomplete evacuation
  - Constellation of Abdominal discomfort, bloating, distention
  - "blockage" sensation at time of bm’s
- Overtime may move and to and from IBS-D and back again (this is more common than vice versa)
- Treatment options: liquify the stool or alternate reception within the gut

*NEJM, Uptodate “treatment of ibs”

IBS-M OR IBS-A
- Consisting of a mix of >25% constipation and >25% diarrhea. Most times constipation predominant.
- Treatment options:
  - Routine; yoga/exercise/foodmap
  - Fiber- soluble v. insoluble depending upon
  - CBT
  - Guided imagery, hypnosis
  - Peppermint oil or Slippy Elm
  - TCA’s if diarrhea, SSRIs for constipation
  - Verywellhealth.com - self care treatment of IBS, uptodate.com - treatment of IBS

IBS-D: TREATMENT
- If celiac disease
  - gluten free diet and can check celiac cascade for compliance.

IBS: TREATMENT
- FIBER
  - Soluble for diarrhea (bulk) or insoluble for constipation
  - Is the mainstay treatment for IBS-M or IBS-A
  - Does not cause constipation or diarrhea though can bulk or loosen too much to appear this way
  - Main side effect: GAS!

IBS-D: TREATMENT
- Peppermint Oil
  - Smooth muscle relaxant
  - Available OTC
  - Inexpensive- $19/month

IBS: TREATMENT
- Rifaximin (Xifaxan)
  - Technically, an antibiotic but gut microbiome not modified and gi MOA only.
  - Best with symptoms of abd pain, bloating and diarrhea
  - Some benefit with travelers diarrhea as well
  - Can be used up to 3 dosing regimens of 550mg tid x 14 days and results moderately effective for lifetime control
  - $$$COSTLY$$$ - $1400-1900/month sans insurance
**IBS-D: TREATMENT**

Eluxadoline (Viberzi)
- Acts on multiple neuroreceptors within the gut- similar to narcotics and is schedule II.
- CONTRAINDICATED: S/P CCY, PANCREATITIS, ETOH ABUSE OR PREEXISTING PANCREATOBILIARY DISEASE
- Can be costly- a lot of times insurers classify this as end of line drug.
- Response rates roughly ¼ but anecdotally- much better
- Costly- $1076/month sans insurance

**IBS-D: TREATMENT**

Ondansetron (Zofran)
- 5HT3 improves stool consistency; No effect on abdominal pain
- multiple dosages possible
- SAFE- THEY GIVE IT TO PREGNANT WOMEN
- But not without side effect: QTc prolongation, headache, constipation
- Special note: Alosetron (Lotrenex) don’t use- > associated with ischemic colitis

**IBS-D: TREATMENT**

Amitriptyline (Elavil)
- Antidepressant, slows intestinal transit
- Multiple dosages- 10, 25, 50 (higher dosages possible would reserve these for psych)
- Side Effects: Anticholinergic side effects (sedation, dry mouth, dry eyes, anorgasmia, orthostatic hypotension)
- CHEAP

**IBS-C: TREATMENT**

- Lubiprostone (Amitiza)
  - Intestinal secretagogue (increase fluid secretion into GI tract)
  - Approved for IBS-C, CIC or OIC
  - Multiple daily dosages taken bid (8 or 24mcg)
  - Of benefit in pain relief as well
  - Main side effect: Nausea, diarrhea (duh)
  - Cost: variable- up to $350/month sans insurance

**IBS-C: TREATMENT**

- Linaclotide (Linzess)
  - Intestinal secretagogue (increase fluid secretion into GI tract) but ALSO inhibits pain fiber activity
  - Approved for CIC/IBS-C
  - 3 doses: 72, 145, 290
  - Primary side effect: Diarrhea, abd pain, headache (fluid shifting)
  - Cost: variable- $350/month sans insurance

**CBT**

- Patients have counseling sessions (either in home vs. in office) mixing education, coping mechanisms
  - Providing info on brain-gut interactions, self-monitoring with triggers and consequences
  - Muscle relaxation
  - Worry control
  - Flexible problem solving
  - Relapse prevention
- Home based therapy produced significant and sustained GI symptom improvement for patients with IBS
**FODMAP**

- Highly restrictive diet!
- Shown to adequately reduced symptoms scores ...
- BUT it cannot be proven that this is because of comprehensive Fodmap reduction or from one ingredient (e. Lactose)

**ANTISPASMODICS**

- Hyoscyamine, dicyclomine, and Donnatal (phenobarb, hyoscyamine, atropine and scopolamine)
  - Used on prn basis when anticipated stressors arise
  - Affect smooth muscle relaxation (similar MOA to peppermint oil)
  - Proven effective with abd pain, bloating, gas and urgency
  - Long-term effectiveness has not been demonstrated
  - Most times, VERY CHEAP

**PROBIOTICS**

- Controversial as many strains exist and no one strain approved for IBS (saccharomyces approved in treatment of CDAD)
- Have shown moderate improvement in some studies but magnitude of benefit and evidence of most effective strains lacking
- Cheap to VERY EXPENSIVE and rarely covered by insurance.

**FUTURE**

- Gene based studies: more common on allele 9 in females
- Fecal calprotectin for ongoing gi inflammation
- Trulance, probiotics

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**REFERENCES**


**REFERENCES CONT.**
