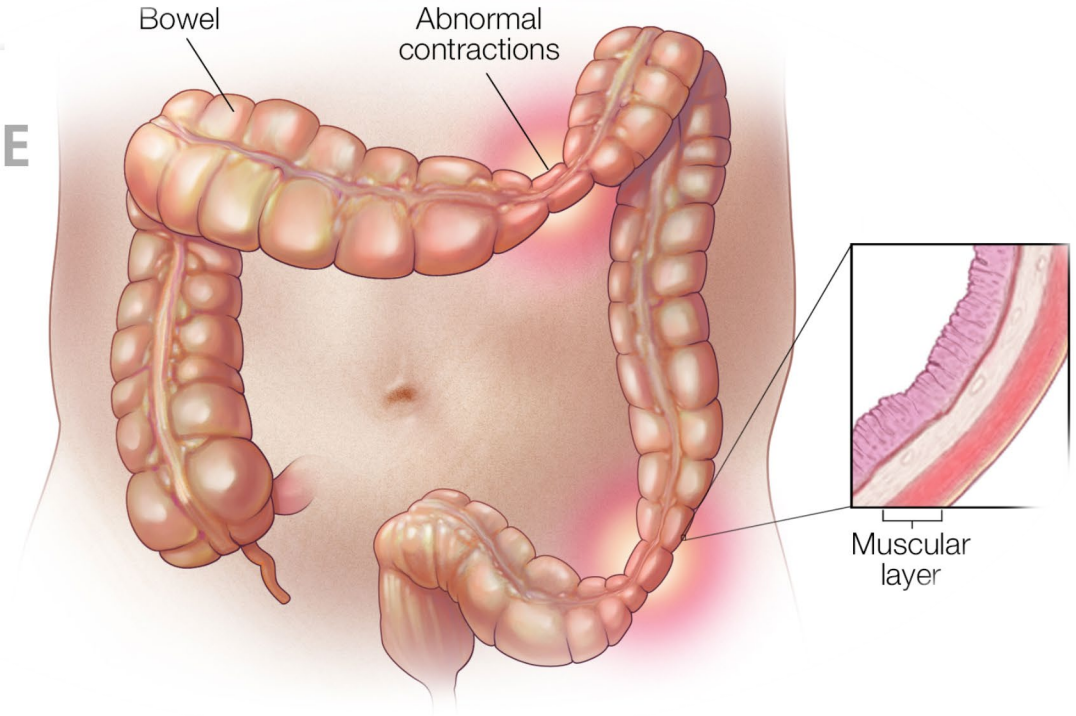

Irritable Bowel Syndrome

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Disclosure

- Sandy Zuo, Pharm. D.
- Potential conflicts of interest – None
- Sponsorships – None
- Proprietary information or results of ongoing research may be subject to different interpretations
- Speaker's presentation is educational in nature and indicates agreement to abide by the non-commercialism guidelines provided

Objectives

- Define the difference between irritable bowel disease (IBD) and irritable bowel syndrome (IBS)
- Define the pathophysiology of IBS and the different types of IBS
- List non-pharmacological and pharmacological treatment plans to manage and treat IBS
- List and recognize ADRs associated with IBS treatment

Pre-Test Assessment Questions

1. What is the difference between IBS and IBD?
   a. IBS and IBD have different clinical symptoms
   b. IBS causes inflammation, while IBD does not
   c. IBD causes inflammation, while IBS does not
2. IBS can be classified into _____ subtypes.
   a. 1
   b. 2
   c. 3
   d. 4
   e. 5

Epidemiology

- Irritable bowel syndrome, IBS, is a GI disorder often characterized by altered bowel habits, associated with abdominal discomfort or pain
- Affects 9 – 23 % of the population worldwide
- Comprise of ~12% of patients that seek healthcare in primary care practices, and often exhibit poorer quality of life

IBD or IBS?

- Both disease states present with similar symptoms: abdominal pain, bloating, gas and either constipation or diarrhea
- Main difference: IBS does NOT cause inflammation, unlike IBD

Pathophysiology of IBS

- Traditionally thought of as a condition with visceral hypersensitivity, leading to abdominal discomfort or pain, and GI motor disturbances
- However, this does not explain the wide range of presentation type
- Possible etiologies: psychological disturbances, serotonin dysregulation, bacterial overgrowth, central dysregulation, genetics
- Bottomline: No one knows!

Types of IBS

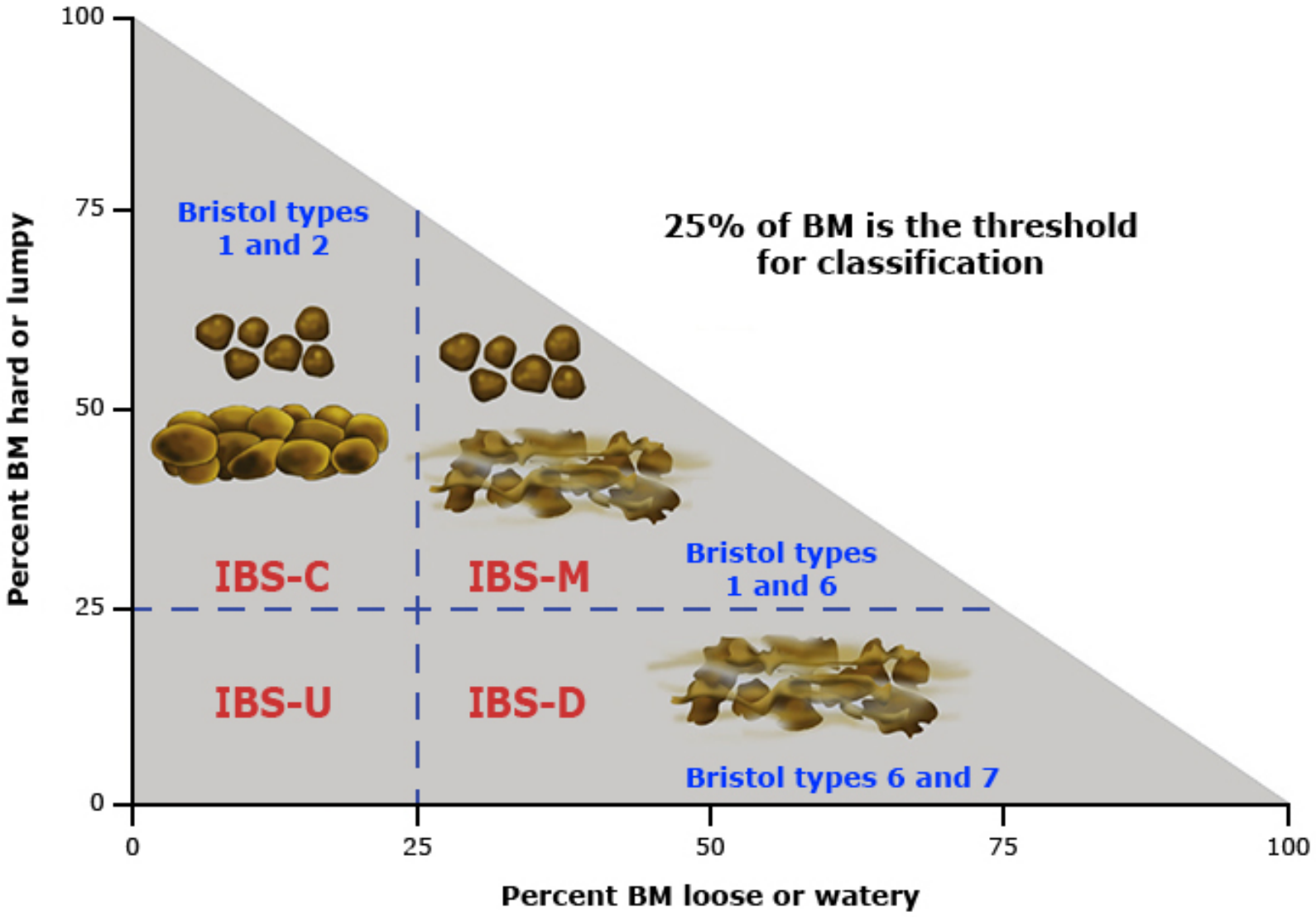
- Subtypes are based on predominant bowel habits
- Classified into **4 subtypes**: IBS with predominant constipation (IBS-C), IBS with predominant diarrhea (IBS-D), with mixed bowel habits (IBS-M), or IBS, unsubtyped
- Some patients may present with acute onset IBS that develops after an infection: fever, vomiting, diarrhea, or (+) stool culture → post-infectious IBS (IBS-PI)
- Abnormal bowel movements classified using the Bristol stool form scale

Bristol Stool Form Scale

Bristol Stool Chart

Type 1		Separate hard lumps, like nuts (hard to pass)
Type 2		Sausage-shaped but lumpy
Type 3		Like a sausage but with cracks on its surface
Type 4		Like a sausage or snake, smooth and soft
Type 5		Soft blobs with clear-cut edges (passed easily)
Type 6		Fluffy pieces with ragged edges, a mushy stool
Type 7		Watery, no solid pieces. **Entirely Liquid**

IBS Subtypes & Stool Consistency



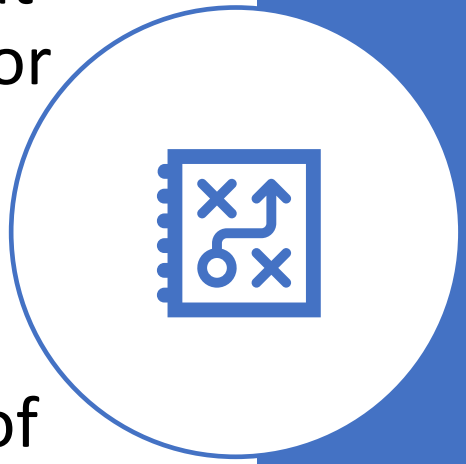
Clinical Presentation

- Common symptoms: abdominal pain, discomfort, bloating, diarrhea, constipation, fatigue
- Abdominal pain: cramping, with variable intensity/periodic exacerbations
- Approximately half of all patients with IBS complain of mucus discharge with stools

Diagnostic Criteria: ROME IV

ROME IV Criteria: Recurrent abdominal pain on average at least 1 day/week in the last 3 months, associated with 2 or more of the following criteria:

- Related to defecation
- Associated with a change in the frequency of stool
- Associated with a change in the form (appearance) of stool
- Onset >6 months prior to diagnosis



Importance of History!

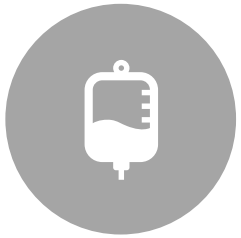
Taking a good medical history can help identify and diagnosis IBS vs. identify other possible causes of similar symptoms

Ask about medications/thorough medication reconciliation to identify medications that can cause similar symptoms

Family history: Presence of IBD? Colorectal cancer? Celiac disease?

Alarming Features

AGE OF ONSET
>50 YEARS



RECTAL BLEEDING
OR MELENA

NOCTURNAL
DIARRHEA

UNEXPLAINED
WEIGHT LOSS

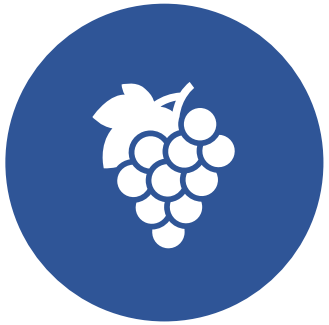
PROGRESSIVE
ABDOMINAL PAIN

Case #1

- AZ is a 42 year-old Caucasian female who presents to your clinic complaining of abdominal cramping 3x/week for the last 2 years. She feels bloated and distended most of the time, and has irregular bowel movements, ranging from 1-3 BMs/week.
- PMH: HTN, HLD, DM2
- Medications:
  - Lisinopril 40 mg daily
  - Metformin 1000 mg BID
  - Atorvastatin 40 mg daily

Based on the above presentation, which IBS subtype is AZ likely exhibiting?

Non-Pharmacological Treatment



Fiber (1st line!)

Probiotics

Cognitive behavioral therapy

Other options but are weak recommendations: exercise, FODMAP or gluten-free diets, peppermint oil

Peppermint Oil

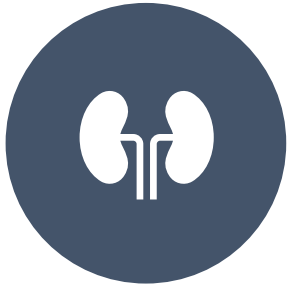
Studies suggest a benefit for peppermint oil in IBS in reducing overall symptoms

Pharmacological Therapy

- Antidepressants
  - Tricyclic Antidepressants (TCA)
  - Selective Serotonin Reuptake Inhibitor (SSRI)
- Prosecretory Agents:
  - Linaclotide
  - Plecanatide
  - Lubiprostone
- Eluxadoline
- Alosetron
- Antispasmodics

TCAs and SSRIs

TCAs improves diarrhea by slowing GI transit



SSRIs may ameliorate constipation by accelerating GI transit

TCAs and SSRIs can help relieve pain associated with IBS

Off-label use!

IBS-C Pharmacological Treatment Options

Amitriptyline (Elavil)

MoA: Inhibits reuptake of serotonin and/or norepinephrine in the CNS by inhibition of the presynaptic neuronal membrane pump

Common Dosage: 10 – 25 mg PO qHS; may gradually increase dose based on response, up to 75 mg/day

ADRs: Anticholinergic effects (urinary retention, dry mouth, ataxia), orthostatic hypotension, hyponatremia

Monitoring: Na, mental status, suicidal ideation, HR, BP, ECG in older adults w/ pre-existing cardiac disease, electrolytes

Linaclotide (Linzess)

MoA: Guanylate cyclase C agonist: ↑ Cl- and HCO3 secretion into the intestinal lumen, ↑ the speed of GI transit, reducing pain

Common Dosage: 290 mcg PO qAC

ADRs: Diarrhea, abdominal distension, flatulence, headache (HA)

Monitoring: Abdominal pain, spontaneous BM quality & frequency

Plecanatide (Trulance)

MoA: Guanylate cyclase C agonist:↑ Cl- and HCO3 secretion into the intestinal lumen, ↑ the speed of GI transit, reducing pain

Common Dosage: 3 mg PO daily

ADRs: Diarrhea, abdominal distension, flatulence, headache (HA)

Monitoring: Frequency of straining during BMs, spontaneous BM quality & frequency

Lubiprostone (Amitiza)

MoA: Activates chloride channels on the apical membrane of the GI tract to ↑intestinal fluid secretion/improve fecal transit

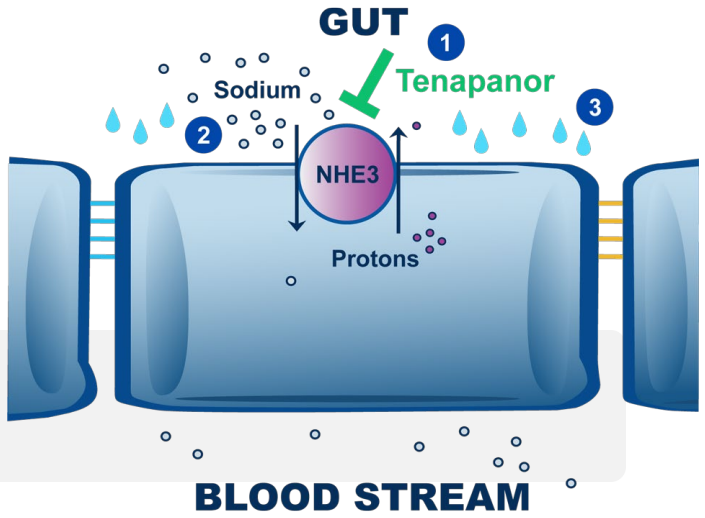
Common Dosage: Common Dosage: 8 mcg BID

ADRs: Nausea, diarrhea, HA, hypokalemia

Monitoring: GI obstruction, LFTs (prior to initiation), BP, s/sx of hypotension

For use in females only. Take w/ food & water to decrease nausea

Tenapanor (Ibsrela)



- FDA approved on September 12, 2019
- MoA: Sodium/hydrogen exchanger 3 inhibitor
- Common Dosage: 50 mg PO BID, prior to breakfast/dinner
- ADRs: Diarrhea (15 – 16%), dizziness (2%)
- Monitoring: Diarrhea, abdominal distension, hyperkalemia

Polyethylene Glycol 3350

- MoA: Osmotic agent: causes water retention in stool, increases stool frequency
- Common Dosage: 17 g dissolved in 120 – 240 mL of beverage daily
- ADRs: GI, diarrhea, flatulence, nausea
- Monitoring: Loose stools/diarrhea
- ACG guidelines recommend AGAINST use

Case #1 cont.

- Upon further questioning, AZ states that she has tried using wheat bran in the past before, since she read online that increasing fiber would help alleviate her symptoms.
- She has tried wheat bran for the past month, however, this has failed to help alleviate her symptoms.
- AZ is now asking for other treatment options.
- What would you recommend for her?

Case #2

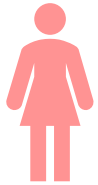
- BY is a 33-year-old male, who presents to your clinic today complaining of constipation for the past 6 months. He states that his stools are often hard and lumpy, and often has a difficult and painful time passing stool. His appetite waxes and wanes, depending on how bloated he feels. In addition, he has been feeling increasingly more fatigued. Today he is requesting for laxatives to help him go more frequently.
- PMH: Asthma on Albuterol PRN
- Labs: All WNL

What subtype of IBS is BY most likely experiencing?

What non-pharmacological options would you recommend?

IBS-D Pharmacological Treatment Options

Alosetron (Lotronex)



MoA: Potent and selective antagonist of a subtype of the serotonin 5-HT3 receptor

Common Dosage: 0.5 mg PO BID x4 weeks, may ↑ to 1 mg BID

ADRs: Abdominal distress, abdominal pain, nausea, fatigue, headache

WARNINGS: D/C immediately in patients who develop constipation, ischemic colitis

Monitoring: Constipation, rectal bleeding, bloody diarrhea

Not shown to be effective in men!

Eluxadoline (Viberzi) C-IV

MoA: Binds to mu-opioid receptors (mu, delta, kappa) to reduce abdominal pain and diarrhea

Common Dosage: 100 mg PO BID in patients w/ a gallbladder (75 mg BID if unable to tolerate 100 mg) w/ food

ADRs: Constipation, nausea, abdominal pain, rash, dizziness, URIs

WARNINGS: Pancreatitis, sphincter of Oddi spasm, CNS depression

Monitoring: Pancreatitis, new/worsening ABD pain radiating to the back, sphincter of Oddi spasms, hepatic impairment,

Dicyclomine (Bentyl)

MoA: Antispasmodic: Blocks the action of acetylcholine at parasympathetic sites in smooth muscle, secretory glands and the CNS

Common Dosage: 20 mg up to QID, recommended for PRN basis

ADRs: Dizziness (40%), xerostomia (33%), blurred vision (27%), nausea (14%)

Monitoring: Anticholinergic effects, urinary output, GI symptoms

Hyoscyamine

MoA: Antispasmodic: Blocks the action of acetylcholine at parasympathetic sites in smooth muscle, secretory glands and the CNS

Common Dosage: 0.125 – 0.25 TID – QID

ADRs: Flushing, tachycardia, ataxia, confusion, dizziness, urinary retnetion

Monitoring: Excessive dryness of eyes, nose, mouth, throat

Loperamide

MoA: Acts on circular & longitudinal intestinal muscles to inhibit peristalsis & prolong transit time, ↑ tone on anal sphincter

Common Dosage: 4 mg followed by 2 mg after each loose stool

ADR: Constipation (2 – 5%), dizziness (1%), abdominal cramps (<3%)

Monitoring: Quantity of stools, signs of CNS toxicity in patients w/ hepatic impairment

ACG guidelines suggest AGAINST using for overall sx improvement

Rifaximin (Xifaxan)

- MoA: Inhibits RNA synthesis by binding to DNA-dependent RNA polymerase
- Common Dosage: 550 mg TID x 14 days
- ADRs: Peripheral edema, dizziness, fatigue, ascites, nausea,
- Monitoring: Blood in stool, change in symptoms

Bile-Acid Sequestrants

01

Bile acid is an important factor that modulates motor, sensory and secretory functions of the intestine !

02

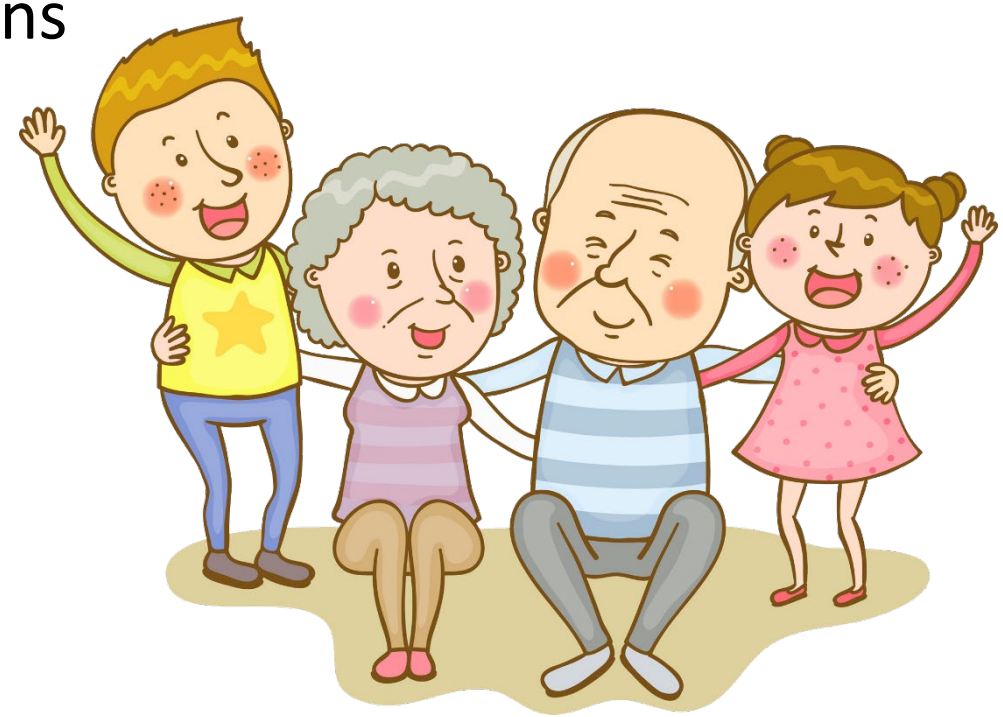
Bile acid absorption disorder occurs in up to 1/3 of patients with IBS-D

03

Suggests a role for bile-acid sequestrants: Questran, Welchol, Cholestyramine – currently not in guidelines

Special Considerations: Geriatric

- IBS sx not easily recognized, alterations in pain perception, changes in bowel pattern in the elderly are intermittent
- Caution before treating with drugs because studies have shown a strong relationship of IBS with psychiatric conditions
- Potential risks/ADRs: Falls risk, confusion, urinary retention and cardiac arrhythmias!



Case #3

CW is a 33-year-old woman referred for a second opinion. Her sx began ~6 years ago after a trip to Peru. She suffered an acute onset of nausea, vomiting, abdominal pain and diarrhea after eating at a local restaurant. She assumed it was food poisoning and was managed conservatively at the time. Since that time, she has had recurrent episodes of cramping associated with “urges”, and watery stools. 5/7 days of the week she feels bloated and distended.

- PMH: HTN
- Medications: Amlodipine 5 mg daily
- Labs: Stool O&P (-), CBC WNL, CDI (-)

Case #3

- When she saw her PCP, her PCP recommended her to try Loperamide. Although Loperamide helped improve her diarrhea, it did not relieve her sx of bloating and abdominal cramping.

What could be a possible etiology for patient's IBS?

What subtype would you classify this patient as?

How would you manage this patient's symptoms?

Pre-Test Assessment Questions

1. What is the difference between IBS and IBD?
   a. IBS and IBD have different clinical symptoms
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