Irritable bowel syndrome

Rome IV –from May 2016 of Gastroenterology

C. Functional bowel disorders

C1. Irritable bowel syndrome

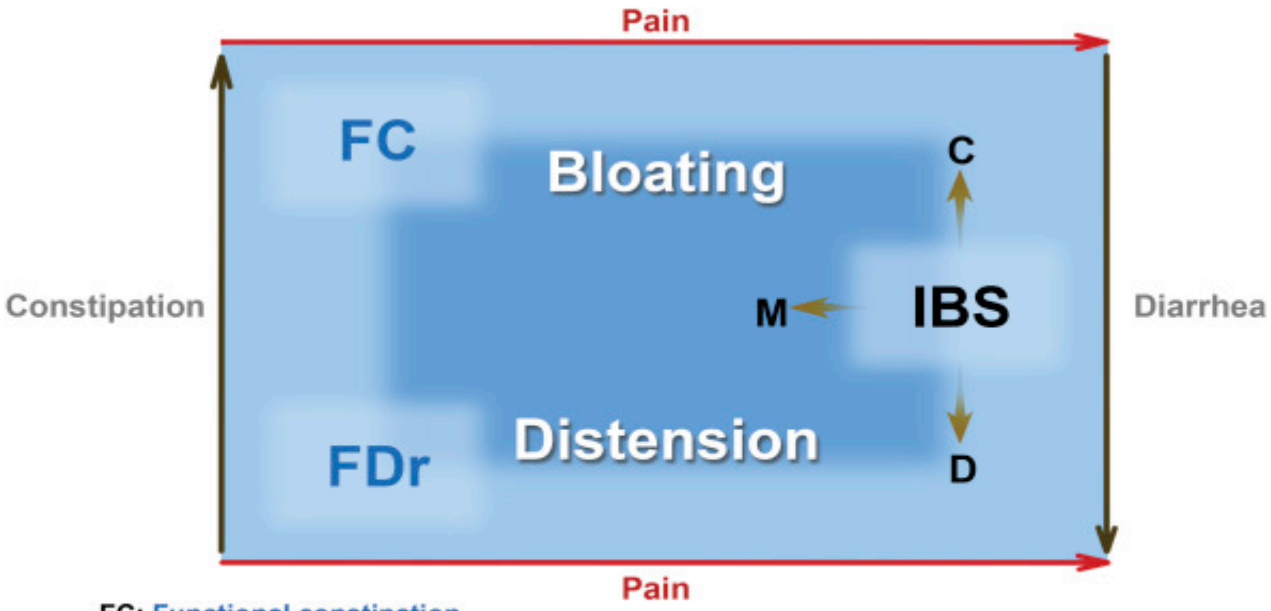
C2. Functional constipation

C3. Functional diarrhea

C4. Functional abdominal bloating/distension

C5. Unspecified functional bowel disorders

C6. Opioid-induced constipation



FC: Functional constipation
FDr: Functional diarrhea
IBS-C: Irritable bowel syndrome with predominant constipation
IBS-D: Irritable bowel syndrome with predominant diarrhea
IBS-M: Irritable bowel syndrome with predominant irregular bowel habits (mixed D/C)

Pathophysiology

- Biopsychosocial model was introduced by Engel in 1977- it postulates that there is a complex interaction between a patient's genetic composition and interactions with the environment which affect the susceptibility to disease, phenotypic expression, and patient attitudes.
- Environmental exposures in childhood (salmonella infection) can increase risk for IBS
- Family and twin studies have found a genetic component with several polymorphisms and candidate genes of a variety of functions
  - Motor function, membrane permeability, visceral sensitivity
  - There may also be epigenetic factors which affect expression

Abnormal motility

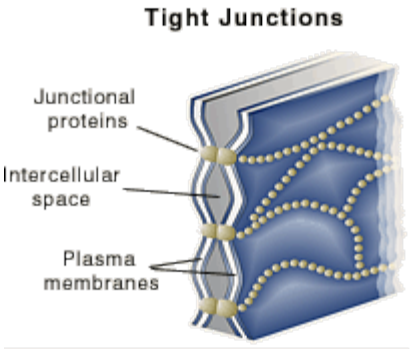
- Abnormal Motility can create nausea, vomiting, diarrhea, and abdominal pain in response to emotional or environmental stress
- These are regulated through the gut-brain axis through various efferent and afferent connections
- Those with functional gastrointestinal disorders have greater motility in response to stress

Visceral hypersensitivity

- Mayer et al in 1994 described visceral hypersensitivity in FGID patients
  - Patients with IBS were found to have a lower pain threshold with balloon distention
- Hypersensitivity and sensitization
  - Repeated balloon dilations let to a transient increase in pain intensity in normal subjects
  - In IBS patients this increased sensitivity lasted longer

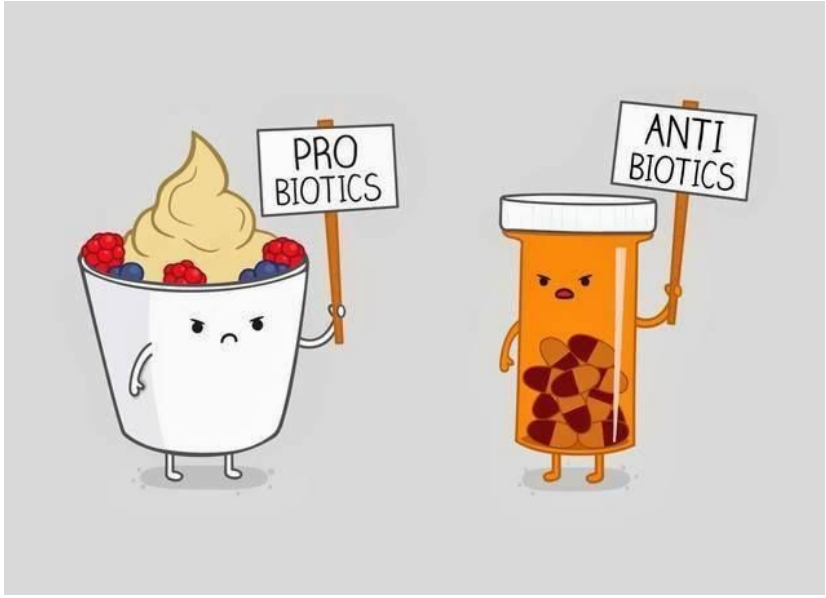
Immune dysregulation

- There is increased intestinal permeability through tight junctions. This leads to increased intraluminal antigens in the submucosal space
  - There is low grade Mast cell activation with an increase in cytokine release
  - This leads to altered sensitivity f the gut mucosa and myenteric plexus through
  - Factors that contribute include genetics, psychosocial stress, and mast cell activation
  - Enhanced by alterations in the bacterial environment or through overt infection



Microbiome

- The microbiome is shaped by host factors but influences host biology
- IBS patients have been found to have an increase in firmictus, bacteriodes, and bifidobacter
- There is decreased microbial diversity in IBS patients
- This is supported by improvement with probiotic and antibiotic use (Simmen et al gastroenterology 2013)



Nutrition

- Changes in diet such as low fermentable oligo, di and monosaccharides and polyols or gluten restriction may provide benefit though decreased osmotic effects and alterations in the gut mucosa

*99% gluten free

Brain gut axis

- Emotions can change gastric emptying and intestinal motility
- Stress can disrupt the gut brain threshold
- Enhanced motility, visceral inflammation and injury can amplify ascending pathways
  - This affects various areas of the brain leading to increased pain

IBS stratification

- How we approach the conditions should be dictated by the severity
  - Mild- 40% usually seen in PCP, no major impacts on life, treatment is mainly education, reassurance, and possibly diet changes. Medications are rarely needed
  - Moderate- 35% intermittent interruptions in activity. Treat with education, medications and a combined psychotherapy if there are underlying disorders such as anxiety and depression
  - Severe -25% often have refractory symptoms, high frequency of psychocosial comorbidities, often have unrelastic expectations of cure and prefer diagnostic interventions to treatment
    - Establish a relationship with the patient, but only order tests based on objective findings not patient desires.
    - Shift responsibility to the patient- offer options
    - Change focus from treatment to management of a chronic disease
    - Treat underlying psychosocial issues (patients are often hesitant to receive treatment due to stigma associated with depression)

Drossman et al

Irritable bowel syndrome

C1. Diagnostic Criteria[a] for Irritable Bowel Syndrome

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

1.Related to defecation

2.Associated with a change in frequency of stool

3.Associated with a change in form (appearance) of stool

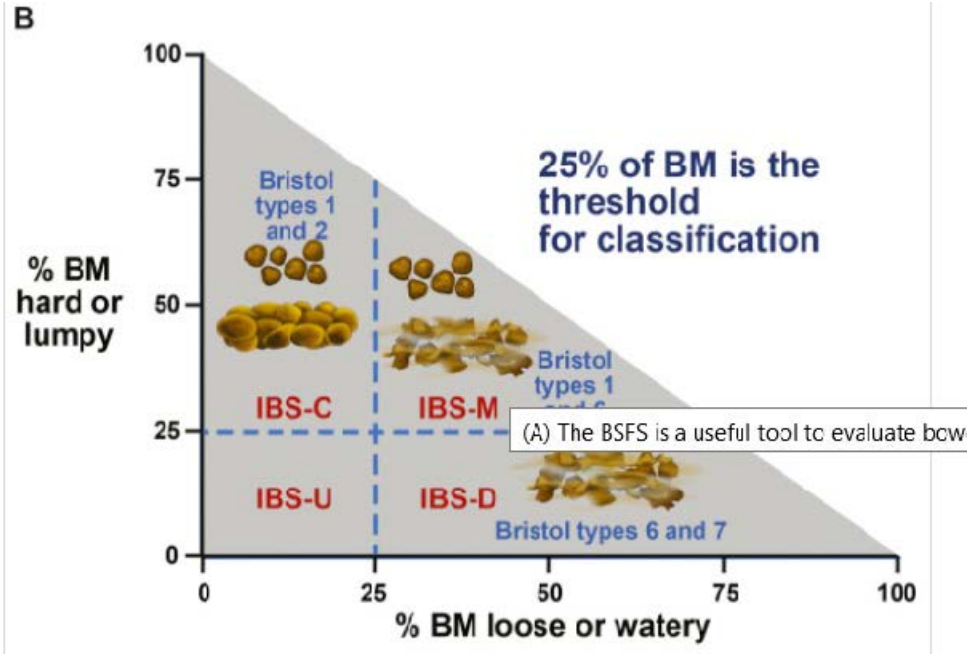
[a]Criteria fulfilled for the last 3 months with symptom onset at least 6 months before diagnosis.

Epidemiology of IBS

- prevalence 11.2% incidence of 1.35-1.5%
- Women >men, younger> older
- Often there are other comorbid conditions (migraine HA, fibromyalgia, interstitial cystitis, dyspareunia)

IBS sub classifications

IBS C > 25% of Bms are hard <25% are soft or liquid
IBS D> 25% of BMs are soft or liquid, <25% are hard
IBS M >25% are bristol 1+2 and 5+6
IBS U bowel habits cannot be classified



Initial assessment

- Thorough history, pay attention to warning signs (weight loss family history of malignancy) anemia, bleeding
  - Ask about diet (diary, wheat, caffeine, fruits, vegetables, juices, soft drinks, sugar free gum)
- Physical exam
- Directed testing CBC, inflammatory markers, fecal calprotectin (calprotectin and markers have limited utility in IBS C)
- Serologic workup for IBS D and M who fail conservative management

Treatment

- Explain the diagnosis- discuss the benign natural history, educate about the safety and utility of diagnostic tests and treatment options
- Exercise, stress reduction, attention to impaired sleep (E johannesson Am J of gastro 2011)
- Limited data about lifestyle modification
  - Dietary fiber: soluble (psyllium/spaghala) is superior to insoluble (bran) which can cause bloating (AC Ford Am J Gastro 2014)
  - Restriction of gluten showed improvement in IBS patients (J.R Biesiekierski Am J gastro 2011)
  - FODMAP (gluten elimination with FODMAP does not give any further benefits)

Pharmacotherapy is symptom based

IBS-C

Miralax- better frequency, consistency and decreased straining. No improvement in pain

Lubiprostone (amitiza)-had improvement in pain and consitpation, most common side effects were N/D

Linaclotide (linzess) – good effect in IBS-C

Sodium Chenodeoxycholic acid- pilot study showed replacement of bile salts had improvement in symptoms

Diarrhea

- Loperamide
- Bile acid sequestrants
- Rifaximin 550 mg TID x 2 weeks. Improvement in symptoms in IBS-D but response is gradually lost. The patients do respond to retreatment
- Alosetron- 5HT3 antagonist decreased pain, stool frequency, rectal urgency in women with IBS-D (rare cases of ischemic colitis) zofran also shows efficacy
- Eluxadione mu agonist/delta antagonist for IBS-D. rare sphincter of oddi dysfunction and pancreatitis in patients who drank
- TCAs, SSRI
- Antispasmodics for all IBS subtypes prevent the recurrence of symptoms
- Probiotics help with pain, bloating, flatulence
- Peppermint oil- good for abdominal pain, can cause heart burn

Symptom	Therapy	Dose
Diarrhea	Opioid agonists	Loperamide; 2–4 mg; when necessary
		Titrate up to 16 mg/d
	Diet	Low/no gluten; low FODMAP
	Bile salt sequestrants	cholestyramine (9 g bid–tid)
		colestipol (2 g qd–bid)
		colesevelam (625 mg qd–bid)
	Probiotics	Multiple products available
	Antibiotics	Rifaximin, 550 mg po tid × 14 d
	5-HT_3 antagonists	Alosetron (0.5–1 mg bid)
		Ondansetron (4–8 mg tid)
		Ramosetron 5 μg qd
	Mixed opioid agonists/antagonists	Eluxadoline, 100 mg bid
Constipation	Psyllium	up to 30 g/d in divided doses
	PEG	17–34 g/d
	Chloride channel activators	Lubiprostone, 8 μg bid
	Guanylate Cyclase C agonists	Linaclotide 290 μg qd
Abdominal pain	Smooth muscle antispasmodics	dicycylomine (10–20 mg qd–qid)
		Otilonium (40–80 mg bid–tid)
		Mebeverine (135 mg tid)
	Peppermint oil	Enteric-coated capsules, 250–750 mg, bid–tid
	Tricyclic antidepressants	Desipramine (25–100 mg qhs), amitriptyline (10–50 mg qhs)
	SSRIs	paroxetine (10–40 mg qd)
		sertraline (25–100 mg qd)
		citalopram (10–40 mg qd)
	Chloride channel activators	Lubiprostone 8 μg bid
	Guanylate cyclase C agonists	Linaclotide 290 μg qd
	5-HT_3 antagonists	Alosetron 0.5–1.0 mg bid

Functional constipation

Diagnostic Criteria[a] for Functional Constipation

1.Must include 2 or more of the following:[b]

- a.Straining during more than one-fourth (25%) of defecations
- b.Lumpy or hard stools (BSFS 1−2) more than one-fourth (25%) of defecations
- c.Sensation of incomplete evacuation more than one-fourth (25%) of defecations
- d.Sensation of anorectal obstruction/blockage more than one-fourth (25%) of defecations
- e.Manual maneuvers to facilitate more than one fourth (25%) of defecations (eg, digital evacuation, support of the pelvic floor)
- f.Fewer than 3 spontaneous bowel movements per week

2.Loose stools are rarely present without the use of laxatives

3.Insufficient criteria for irritable bowel syndrome

Functional constipation

- Prevalence is around 14% but with a wide range
- Risk factors female gender, increased age, reduced caloric intake
- Initial assessment should involve a thorough history and family history
- Test for slow colonic transit, dysenergic defecation in those who do not respond to conservative management
- Treatment is symptom based

Functional Diarrhea

Diagnostic Criterion[a] for Functional Diarrhea

- Loose or watery stools, without predominant abdominal pain or bothersome bloating, occurring in >25% of stools.[b]
- [a]Criterion fulfilled for the last 3 months with symptom onset at least 6 months before diagnosis
- [b]Patients meeting criteria for diarrhea-predominant IBS should be excluded

Functional Diarrhea

- Prevalence is 1.5-17%
- Exclude lactose/fructose intolerance
- Assess anal sphincter tone
- If conservative management fails consider CBC, CRP, celiac eval, stool elastase, fecal fat, colonoscopy, breath tests for malabsorption, rule out microscopic colitis
- Treat symptomatically

Functional abdominal pain/bloating

Diagnostic Criteria[a] for Functional Abdominal Bloating/Distension

Must include both of the following:

- 1.Recurrent bloating and/or distention occurring, on average, at least 1 day per week; abdominal bloating and/or distention predominates over other symptoms.[b]
- 2.There are insufficient criteria for a diagnosis of irritable bowel syndrome, functional constipation, functional diarrhea, or postprandial distress syndrome.
- [a]Criteria fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis.
- [b]Mild pain related to bloating may be present as well as minor bowel movement abnormalities.

Functional abdominal pain

- History & physical
- CBC if warning signs of anemia, SIBO testing, serologic workup if indicated
- Tx with simethicone, alpha-galactosidase (beano), peppermint oil, lubiprostone, desipramine

Opioid induced constipation

Diagnostic Criteria for Opioid-Induced Constipation

1.New, or worsening, symptoms of constipation when initiating, changing, or increasing opioid therapy that must include 2 or more of the following:

- a.Straining during more than one-fourth (25%) of defecations
- b.Lumpy or hard stools (BSFS 1−2) more than one-fourth (25%) of defecations
- c.Sensation of incomplete evacuation more than one-fourth (25%) of defecations
- d.Sensation of anorectal obstruction/blockage more than one-fourth (25%) of defecations
- e.Manual maneuvers to facilitate more than one-fourth (25%) of defecations (eg, digital evacuation, support of the pelvic floor)
- f.Fewer than three spontaneous bowel movements per week

2.Loose stools are rarely present without the use of laxatives

Opioid induced constipation

- 41% of chronic non cancer pain patients will develop it
- 94% of cancer pain patients will develop it
- History, CBC, Chem (with Calcium), KUB to assess stool burden and for fecal impaction

Treatment

- Squish and push- treat prophylactically
- 3 opioid receptors in GI tract- mu, kappa, delta
  - Subcutaneous methylnatrexone
  - Alvimopan (only approved for post operative ileus post bowel resection
  - Naloxegol: an oral PEGylated derivative of naloxone