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Colonic motility disorders

Bible Class, 02. December 2020

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COLONIC MOTILITY DISORDERS

- Pathophysiology
- Functional bowel disorders (Rome IV)
- Congenital aganglionic megacolon (Hirschprung disease)
- Acute colonic pseudo-obstruction (Ogilivie's syndrome)
- Anore[illegible]orders

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ENTERIC NERVOUS SYSTEM (ENS)

- Consists of:
  - Myenteric (Auerbach's) plexus
  - Submucous (Meissner's) plexus
- Motility, secretion, microcirculation and immunologic function
- > 20 neurotransmitters
  - Excitatory: acetylocholine, substance P, tachykinines
  - Inhibitory: nitric oxide, VIP, somatostatin

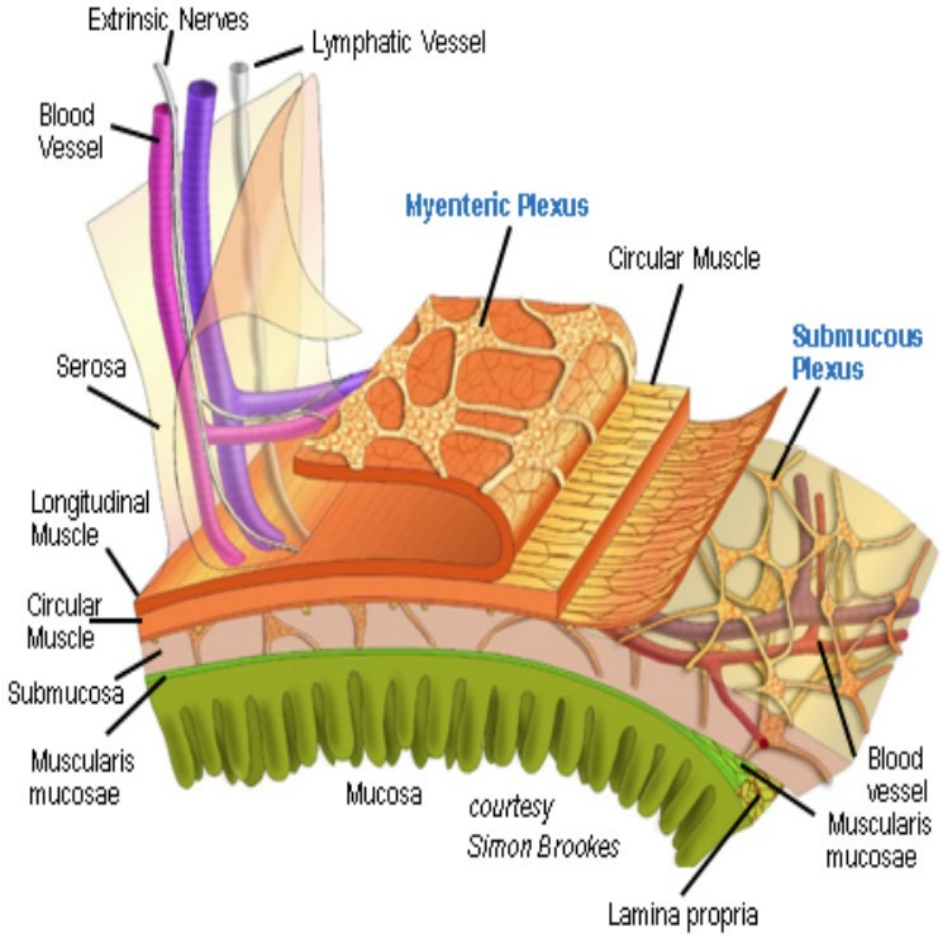

Image from: Anita Annahazi, Michael Schemann. The enteric nervous system: "A little brain in the gut". Neuroforum 2020; 26(1): 31–42

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ENTERIC VERVOUS SYSTEM (ENS)

- Indepedant network but modulated by:
  - Sympathetic
  - Parasympathetic
  - Extrinsic afferent pathways

- It may acts:
  - Directly to smooth muscle cells
  - Indirectly, through intermediate cells (endocrine cells, cells of Cajal, cells of the immune system, mast cells)

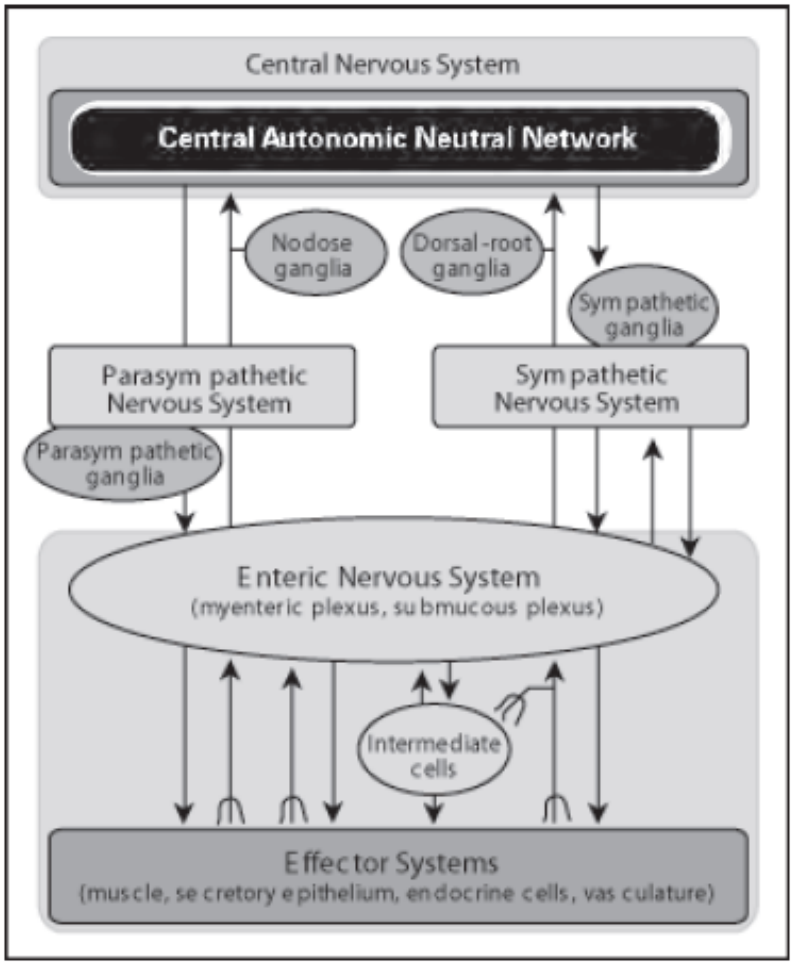

Image from: Digestive Disease Self-Education Program 8 (DDSEP 8)
by American Gastroenterological Association, Md Seth Sweetser Paperback, Published 2016

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MECHANISMS OF PERISTALSIS

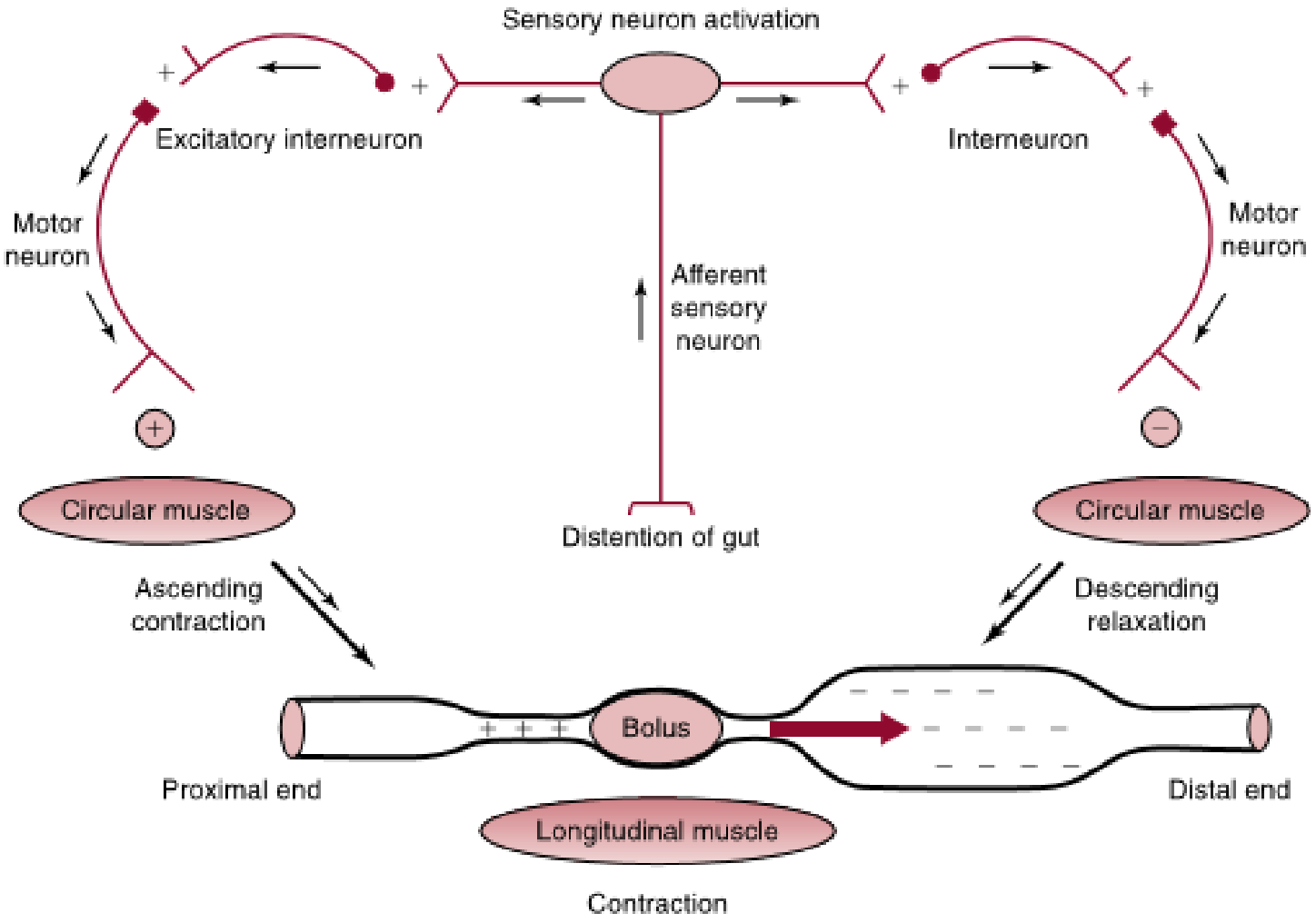

Image from: Image from: Biology of Gastrointestinal tract textbook. Chapter 1 Gastrointestinal Hormones and Neurotransmitters Rodger A. Liddle

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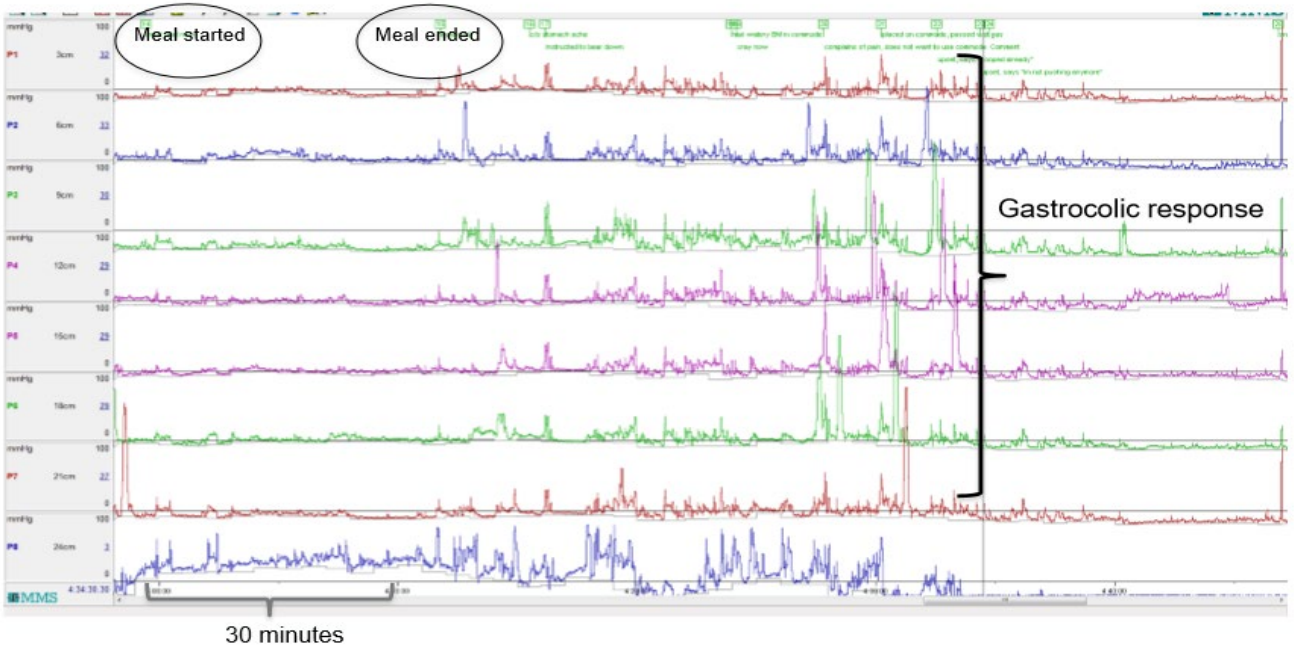
COLONIC CONTRACTILE PATTERNS

1. **Non-propagated contractions**
   - short duration (phasic) contractions
   - segmenting the colon into haustra
   - facilitate mixing, water and nutrient absorption and formation of solid stool
   - 2-4 cycles per minute

2. **Propagated contractions**
   - high amplitude propagating contractions (HAPC's); amplitude > 75 mmHg
   - propagation over at least 15 cm
   - mass movements of the colon
   - 5 - 6 times per day
   - postprandially
   - 6 a.m. – 2 p.m.

GASTROCOLIC REFLEX

- within 15-30 minutes of a meal
- stimulated by the presence of food in the stomach and duodenum
- mediated by CCK, gastrin, serotonin and neurotensin



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FUNCTIONAL BOWEL DISORDERS ROME IV

C1. Irritable bowel syndrome

C2. Functional constipation

C3. Functional diarrhea

C4. Functional abdominal bloating/distention

C5. Unspecified functional bowel disorders

C6. Opioid-induced constipation

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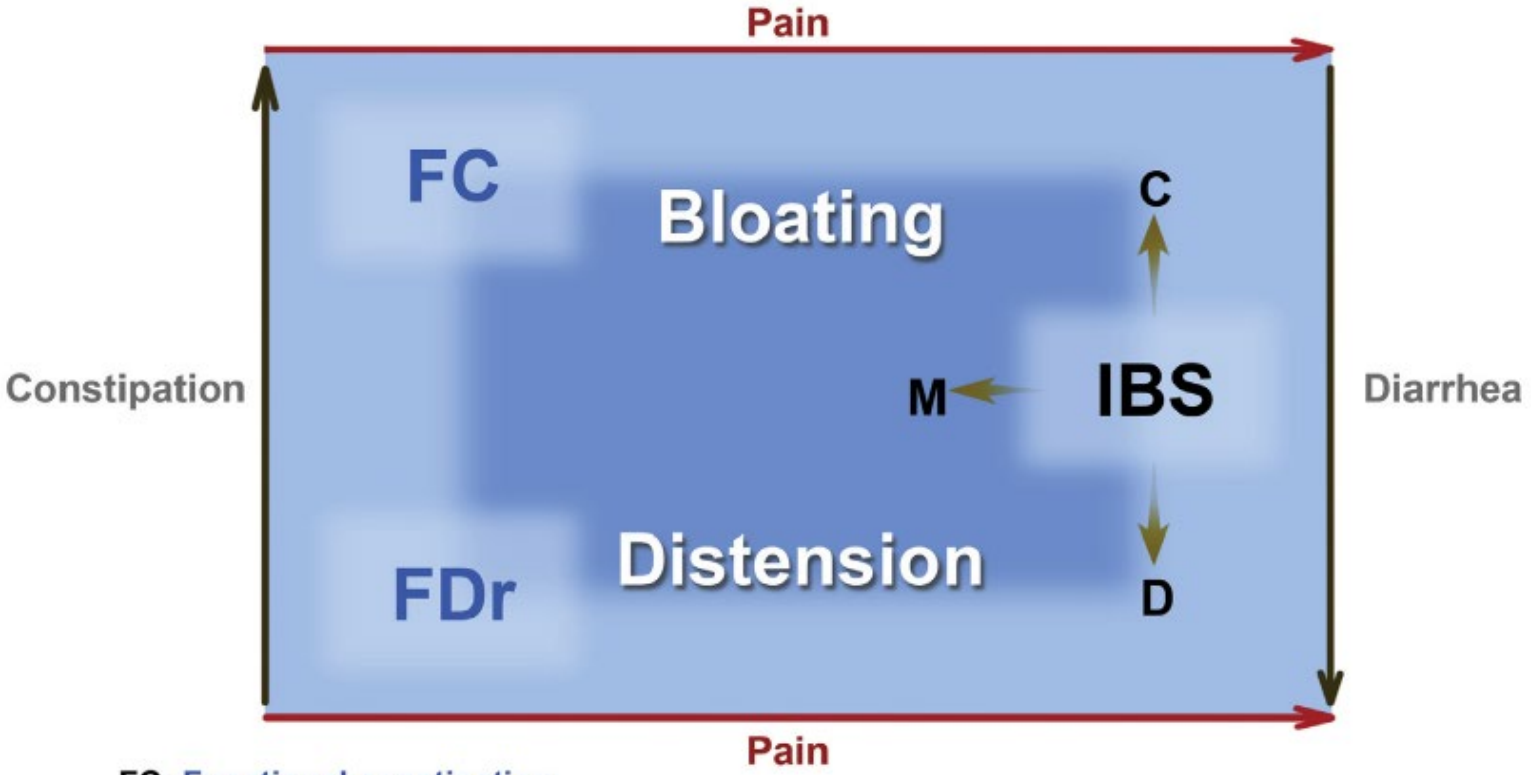
FUNCTIONAL BOWEL DISORDERS
ROME IV



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)

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C1. IRRITABLE BOWEL SYNDROME
Epidemiology

- World-wide prevalence 11.2% (9.8% - 12.8%)

Lovell RM, Ford AC. Global prevalence of and risk factorsfor irritable bowel syndrome: a meta-analysis. Clin Gastroenterol Hepatol 2012;10:712–721

- Incidence 1.35% - 1.5%
- Women > men
- Younger > older than age 50 years

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C1. IRRITABLE BOWEL SYNDROME
Diagnostic criteria

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.

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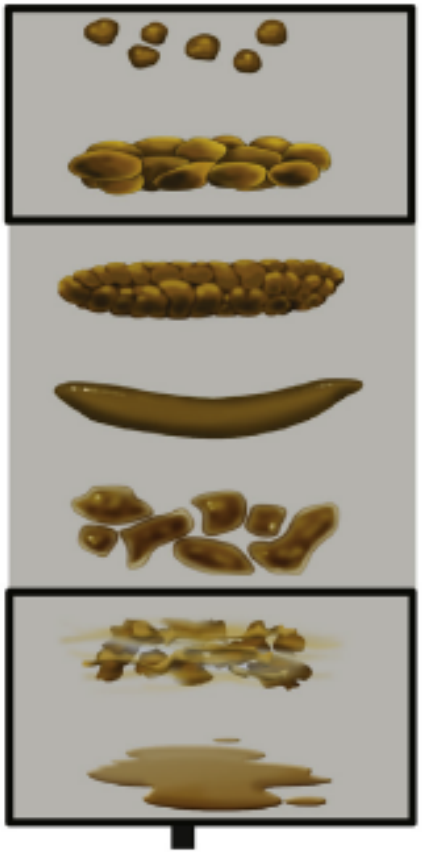
C1. IRRITABLE BOWEL SYNDROME
Bristol stool form scale (BSFS)



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 the surface
Type 4	Like a sausage or snake, smooth and soft
Type 5	Soft blobs with clear-cut edges
Type 6	Fluffy pieces with ragged edges, a mushy stool
Type 7	Watery, no solid pieces, entirely liquid

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C1. IRRITABLE BOWEL SYNDROME
Subtypes – Diagnostic criteria

IBS with predominant constipation: More than one-fourth (25%) of bowel movements with Bristol stool form types 1 or 2 and less than one-fourth (25%) of bowel movements with Bristol stool form types 6 or 7. Alternative for epidemiology or clinical practice: Patient reports that abnormal bowel movements are usually constipation (like type 1 or 2 in the picture of Bristol Stool Form Scale (BSFS), see Figure 2*A*).

IBS with predominant diarrhea (IBS-D): more than one-fourth (25%) of bowel movements with Bristol stool form types 6 or 7 and less than one-fourth (25%) of bowel movements with Bristol stool form types 1 or 2. Alternative for epidemiology or clinical practice: Patient reports that abnormal bowel movements are usually diarrhea (like type 6 or 7 in the picture of BSFS, see Figure 2*A*).

IBS with mixed bowel habits (IBS-M): more than one-fourth (25%) of bowel movements with Bristol stool form types 1 or 2 and more than one-fourth (25%) of bowel movements with Bristol stool form types 6 or 7. Alternative for epidemiology or clinical practice: Patient reports that abnormal bowel movements are usually both constipation and diarrhea (more than one-fourth of all the abnormal bowel movements were constipation and more than one-fourth were diarrhea, using picture of BSFS, see Figure 2*A*).

IBS unclassified (IBS-U): Patients who meet diagnostic criteria for IBS but whose bowel habits cannot be accurately categorized into 1 of the 3 groups above should be categorized as having IBS unclassified.

[a]IBS subtypes related to bowel habit abnormalities (IBS-C, IBS-D, and IBS-M) can only be confidently established when the patient is evaluated off medications used to treat bowel habit abnormalities.

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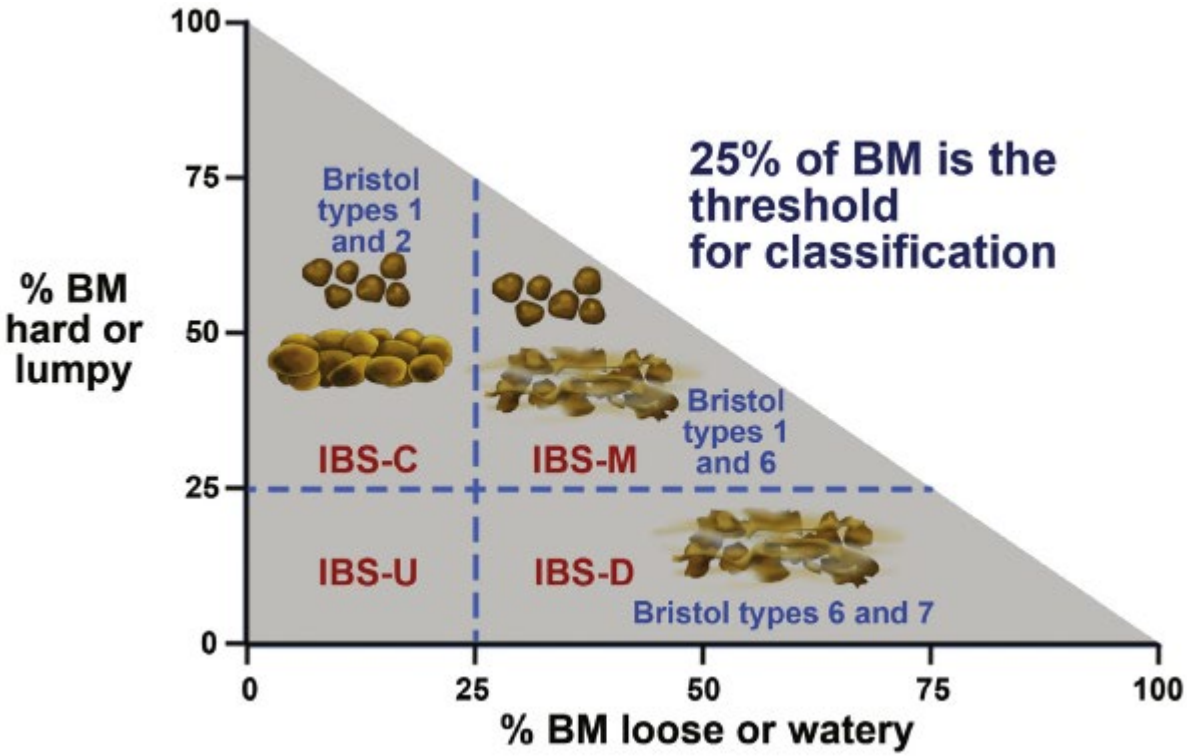
C1. IRRITABLE BOWEL SYNDROME
Subtypes



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C1. IRRITABLE BOWEL SYNDROME
Physiologic features

- Multifactorial disorder with a complex pathophysiology

- Risk factors:
  - genetic
  - enviromental
  - psychosocial

- Factors that trigger the onset:
  - prior gastroenteritis
  - food intolerances
  - chronic stress
  - diverticulitis
  - Surgery

Camilleri M, Lasch K, Zhou W. Irritable bowel syndrome: methods, mechanisms, and pathophysiology. The confluence of increased permeability, inflammation, and pain in irritable bowel syndrome. Am J Physiol Gastrointest Liver Physiol 2012;303:G775–G785

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C1. IRRITABLE BOWEL SYNDROME
Physiologic features

- The resulting pathophysiological mechanisms are variable and patient independent:
  - altered GI motility
  - visceral hyperalgesia
  - increased intestinal permeability
  - immune activation
  - altered microbiota
  - disturbances in brain – gut function

- IBS is associated with psychiatric distress, psychological disturbances, sleep disturbance

Drossman DA. Do psychosocial factors define symptom severity and patient status in irritable bowel syndrome? Am J Med 1999;107:41S–50S

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C1. IRRITABLE BOWEL SYNDROME
Clinical evaluation

1. **Clinical History**
   - Presence of alarm symptoms (rectal bleeding, unintentional weight loss, anemia, high-volume diarrhea, very frequent (> 6-10 per day) bowel movements, evidence of malnutrition) or positive family history for colorectal cancer
   - Diet: dairy products, wheat, caffeine, fruits, vegetables, juices, sweetend soft drinks, chewing gum)
   - Other symptoms:
     - GI: i.e. dyspepsia
     - Non-GI: migraine, fibromyalgia, dyspareunia
     - Exclude lactose and fructose malabsorption
   - Travel history
   - Brief psychosocial review

2. **Physical Examination**
   - Presence of ascites, abdominal mass, hepatosplenomegaly -> further evaluation
   - Anorectal examination

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C1. IRRITABLE BOWEL SYNDROME
Clinical evaluation

3. Laboratory studies

- Complete blood count (anemia? Leukocytosis?)
- CRP
- Fecal calprotectin (IBD?)
- Routine thyroid tests (if clinically warranted)
- Serologic tests for celiac disease in patients with IBS-D or IBS-M +/- upper GI-endoscopy if serologic tests are positive or clinical suspicion high
- Stool analysis (bacteria, parasites, ova)

4. Colonoscopy

- Screening if age > 50 years (> 45 for Africans)
- Alarm symptoms/signs
- Family history positive for colorectal cancer
- Persistent diarrhea (with biopsies to exclude microscopic colitis)

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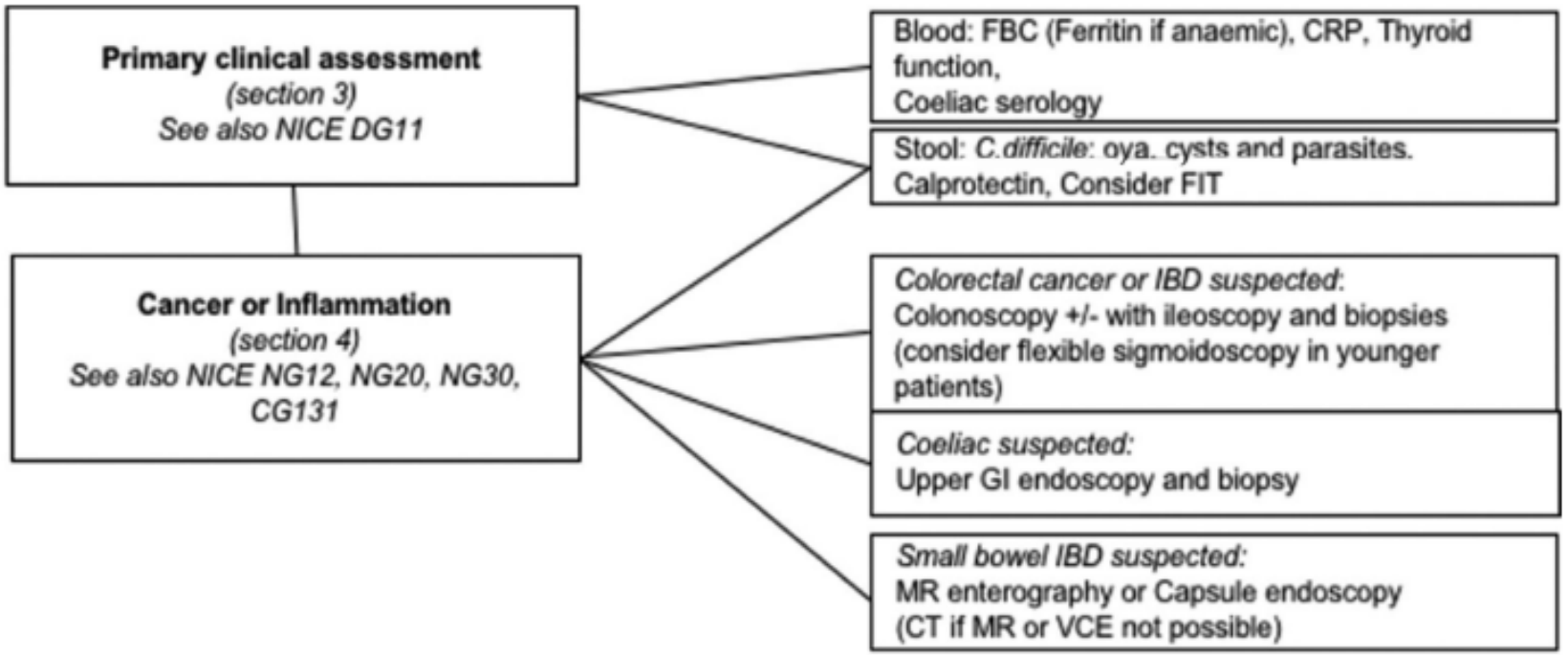
C1. IRRITABLE BOWEL SYNDROME
Clinical evaluation

Positive Diagnosis of IBS with limited laboratory studies



Consider

1) Positive diagnosis of diarrhoea-predominant irritable bowel syndrome (IBS-D) or functional diarrhoea
2) Specialist review -- especially for severe, persistent or atypical symptoms

Arasaradnam RP, et al. Gut 2018;67:1380–1399. doi:10.1136/gutjnl-2017-315909

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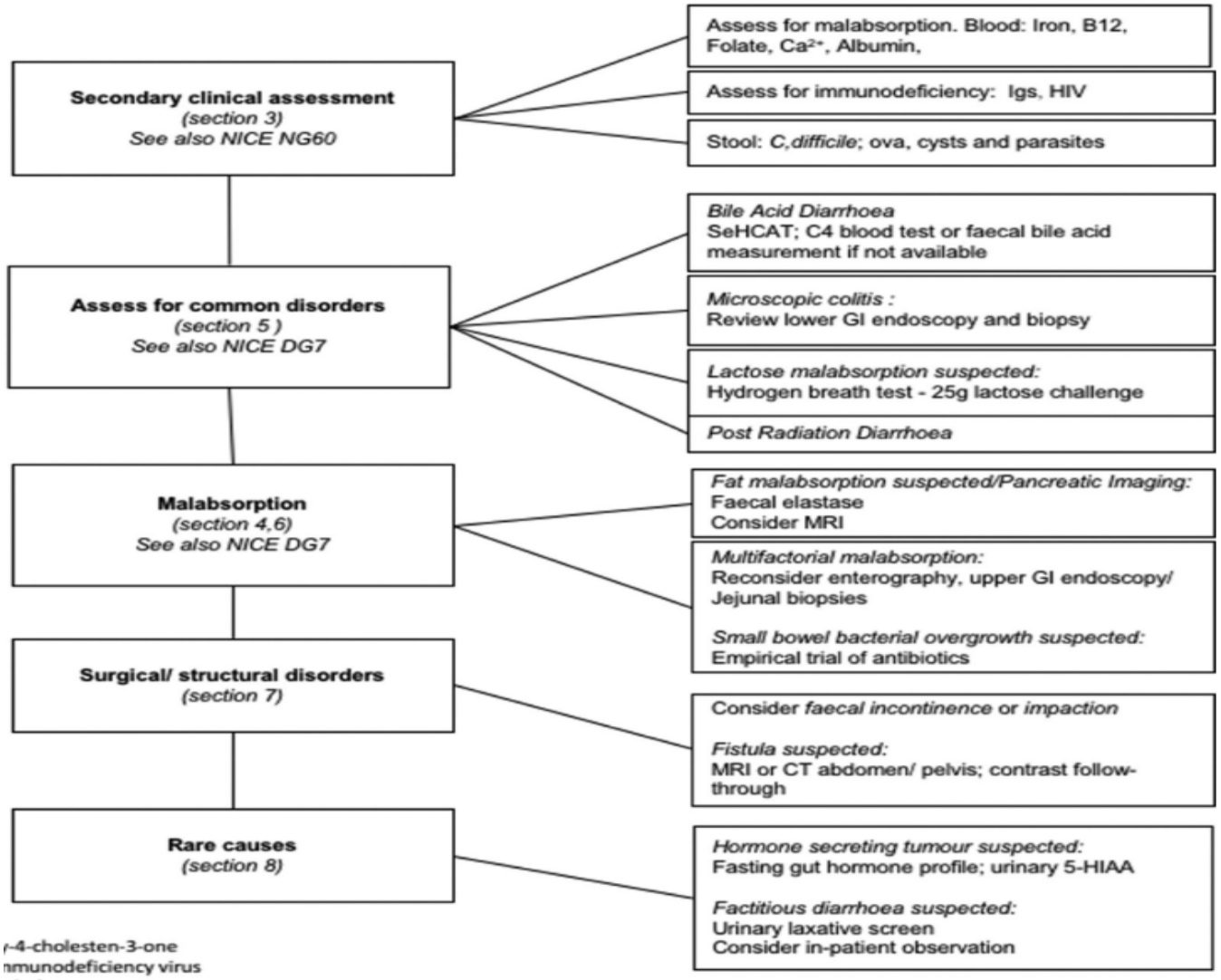
C1. IRRITABLE BOWEL SYNDROME
Clinical evaluation

Positive Diagnosis of IBS with limited laboratory studies



-4-cholesten-3-one
mmunodeficiency virus

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C1. IRRITABLE BOWEL SYNDROME
Treatment

- **Explaining the condition and providing reassurance**

- **Lifestyle modifications**
  - Exercise, stress reduction, attention to impaired sleep

- **Fiber supplementation**
  - Benefit only with soluble fiber (psyllium/ispaghula)
  - No benefit with insoluble (bran)

- **Restriction of gluten**
  - Gluten alters bowel barrier function

- **Low-FODMAP Diet**
  - Reduced fermentation and significant symptom improvement in some IBS patients

Moayyedi P, Quigley EM, Lacy BE, et al. The effect of dietary intervention on irritable bowel syndrome: a systematic review. Clin Transl Gastroenterol 2015:e107

C1. IRRITABLE BOWEL SYNDROME
Treatment

IBS-C

- **Polyethelene glycol (PEG)**
  - Improvement in stool frequency, stool consistency and in straining but not in abdominal pain or bloating

- **Lubiprostone (8 µg twice daily)**
  - Locally acting chlorid channel activator
  - Adverse events: nausea, diarrhea

- **Linaclotid (290 µg once daily)**
  - Guanylate cyclase C agonist
  - Adverse events: diarrhea

C1. IRRITABLE BOWEL SYNDROME
Treatment

IBS-D

- **Loperamide**
  - Decreases colonic transit and increases water and ion absorption
- **Bile acid sequestrants**
  - Cholestyramine, colestipol, colesevelam
  - Adverse events: bloating, abdominal discomfort
- **Probiotics**
- **Rifaximin (550 mg 3x/day over 14 days)**
- **Selective 5-HT3 antagonists**
  - Alosetron; adverse events: ischemic colitis, severe constipation
  - Ondansetron
- **Eluxadoline (100 mg twice daily)**
  - a mixed μ-receptor agonist/δ-opioid receptor antagonist
  - Adverse events: nausea, constipation, adbominal pain, sphincter of Oddi dysfunction, self-limited pancreatitis

C1. IRRITABLE BOWEL SYNDROME
Treatment

IBS: abdominal pain

- **Smooth cell antispasmodics**
  - Mebeverine, Otilonium, Dicyclomin, Trimebutine
- **Peppermint oil**

- **Antidepressants**
  a. Tricyclic antidepressants
     - Amitriptyline (10 – 50 mg once daily)
     - Desipramine (25 – 100 mg once daily)
  b. SSRIs
     - Paroxetine (10 – 40 mg once daily)
     - Sertraline (25 – 100 mg once daily)
     - Citalopram (10 – 40 mg once daily)

C1. IRRITABLE BOWEL SYNDROME
Treatment

IBS: other therapies

- **Fecal microbiota transplantation (FMT)**
  - In one study symptom reduction in 65% of patients (vs 43% in placebo) at 3 months – not sustained at 12 months

Johnsen PH, Hilpüsch F, Cavanagh JP, et al. Faecal microbiota transplantation versus placebo for moderate-to-severe irritable bowel syndrome: a double-blind, randomised, placebo-controlled, parallel-group, single-centre trial. Lancet Gastroenterol Hepatol 2018; 3:17

  - No efficacy of FMT in other studies

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C2. FUNCTIONAL CONSTIPATION
Epidemiology

- In adults prevalence rate around 14 %
  - Rates range from 1.9% to 40.1%

- Risk factors:
  - Female sex
  - Reduced caloric intake
  - Increasing age

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C2. FUNCTIONAL CONSTIPATION
Diagnostic criteria

C2. 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

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

[b]For research studies, patients meeting criteria for OIC should not be given a diagnosis of FC because it is difficult to distinguish between opioid side effects and other causes of constipation. However, clinicians recognize that these 2 conditions might overlap.

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C2. FUNCTIONAL CONSTIPATION
Categories

- **Normal-transit constipation**
- **Slow-transit constipation**
- **Defecatory or rectal evacuation disorders**

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C2. FUNCTIONAL CONSTIPATION
Physiologic features

- Multifactorial disorder with a complex pathophysiology

- Risk factors:
  - familal clustering but no data support a direct genetic cause
  - lifestyle factors in childhood (low fiber intake, low fluid intake, ignoring the call to stool)
  - absence of regular exercise

- Most FC patients do not have evidence of visceral hypersensitivity but some have rectal hyposensitivity

- Slow-Transit Subgroup:
  - autonomic dysfunction
  - morphologic changes in the myenteric and submucosal plexus
  - reduced neurotransmitter levels (VIP, NO, 5-HT)

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C2. FUNCTIONAL CONSTIPATION
Clinical evaluation

1. **Clinical History**
   - Durations of symptoms, stool constistency and frequency, degree of straining during defecation, associated symptoms as abdominal pain, bloating or distension
   - Other causes incl. drugs

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C2. FUNCTIONAL CONSTIPATION
Clinical evaluation

Causes of chronic constipation

Neurogenic disorders	Non-neurogenic disorders
Peripheral	Hypothyroidism
Diabetes mellitus	Hypokalemia
Autonomic neuropathy	Anorexia nervosa
Hirschsprung disease	Pregnancy
Chagas disease	Panhypopituitarism
Intestinal pseudoobstruction	Systemic sclerosis
Central	Myotonic dystrophy
Multiple sclerosis	**Idiopathic constipation**
Spinal cord injury	Normal colonic transit
Parkinson disease	Slow transit constipation
Irritable bowel syndrome	Dyssynergic defecation
Drugs	
See separate table	

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C2. FUNCTIONAL CONSTIPATION
Clinical evaluation

Drugs associated with constipation

Analgesics
Anticholinergics
Antihistamines
Antispasmodics
Antidepressants
Antipsychotics
Cation-containing agents
Iron supplements
Aluminum (antacids, sucralfate)
Barium
Neurally active agents
Opiates
Antihypertensives
Ganglionic blockers
Vinca alkaloids
Calcium channel blockers
5HT3 antagonists

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C2. FUNCTIONAL CONSTIPATION
Clinical evaluation

1. **Clinical History**
   - Durations of symptoms, stool constistency and frequency, degree of straining during defecation, associated symptoms as abdominal pain, bloating or distension
   - Other causes incl. drugs
   - Presence of alarm symptoms (rectal bleeding, unintentional weight loss, anemia) or positive family history for colorectal cancer

2. **Physical Examination**
   - Presence of ascites, abdominal mass, hepatosplenomegaly -> further evaluation
   - Anorectal examination (dyssynergic defecation? rectal mass?)
   - Exclude central nervous system disorders and spinal lesions

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C2. FUNCTIONAL CONSTIPATION
Clinical evaluation

3. **Laboratory studies**
   - Complete blood count (anemia? Leukocytosis?)
   - CRP
   - Fecal calprotectin
   - Routine thyroid tests
   - Serum Calcium

4. **Colonoscopy**
   - Screening if age > 50 years (> 45 for Africans)
   - Alarm symptoms/signs
   - Family history positive for colorectal cancer

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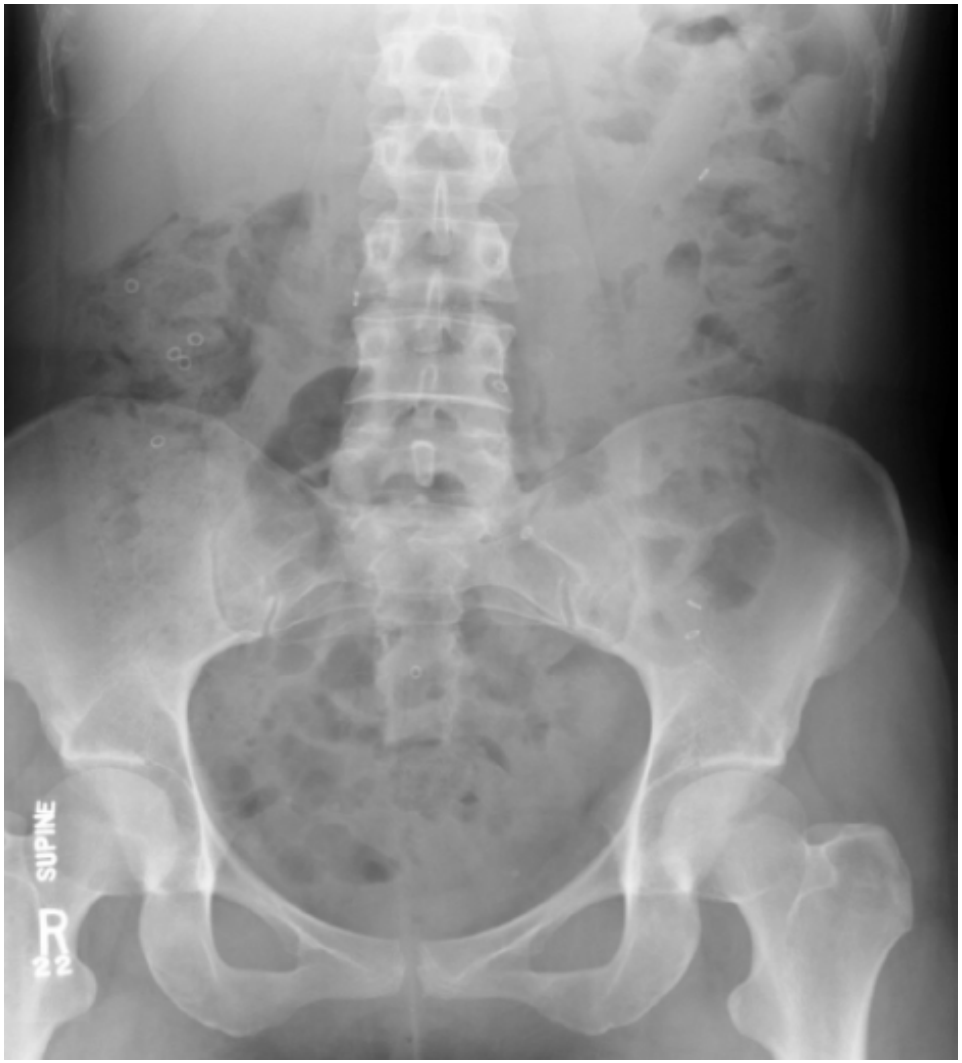
C2. FUNCTIONAL CONSTIPATION
Clinical evaluation



5. **Testing for slow colonic transit**

   - can be considered for patients who do not respond to empiric therapy
   - Radiopaque markers: inexpensive, simple, safe

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C2. FUNCTIONAL CONSTIPATION
Clinical evaluation

6. **Anorectal manometry and balloon expulsion testing**
   - to indetify dysenergic defecation

7. **Defecography**
   - to indetify anatomic etiologies
     - intussusception
     - rectocele
     - inability to relax the puborectalis or decrase the anorectal angle

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C2. FUNCTIONAL CONSTIPATION
Treatment

- **Eliminating medications that can cause/worsen constipation**

- **Lifestyle modifications**
  - exercise
  - scheduling routine bathroom time after the morning or evening meals
  - elevating the feet with a foot stool or using a toilet lower to the ground

- **Dietary modification/Fiber supplementation**
  - containing an adequate amount of fiber
  - Psyllium 20 – 30 g/day
  - Prunes
  - Hemp seed extract

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C2. FUNCTIONAL CONSTIPATION
Treatment

- **Osmotic laxatives**
  - PEG 17 – 34 g/d
  - Lactulose
  - Saline laxatives (milk of magnesia, magnesium citrate)

- **Stimulant laxatives**
  - Bisacodyl, sodium picosulfate, senna
  - Adverse events: abdominal pain, diarrhea

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C2. FUNCTIONAL CONSTIPATION
Treatment

- **Lubiprostone**
- **Linaclotide**
- **Prucalopride (1 – 4 mg once daily)**
  - 5-HT4 receptor agonists
  - Stimulates peristalsis and accelerates gastrointestinal transit
  - Improves stool frequency, stool consistency and straining
  - Adverse events: headache, nausea, diarrhea

Drug	Dose
Psyllium	Up to 30 mg/d in divided doses
PEG	17–34 g/d
Chloride channel activators	Lubiprostone, 24 μg bid
Guanylate cyclase C agonists	Linaclotide 145 μg qd
Prucalopride	2–4 mg/d

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C2. FUNCTIONAL CONSTIPATION
Treatment

- **Suppositories**
  - Glycerin, bisacodyl
- **Disimpaction**
  - Enemas
- **Biofeedback therapy**
  - for dyssynergic defecation

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C3. FUNCTIONAL DIARRHEA
Epidemiology

- Incidence and prevalence not well investigated
- Incidence estimated at 5 per 100,000 patient-years
  - Preceding gastroenteritis was a significant risk factor

Porter CK, Gormley R, Tribble DR, et al. The Incidence and gastrointestinal infectious risk of functional gastrointestinal disorders in a healthy US adult population. Am J Gastroenterol 2011;106:130–138

- Reported prevalence rates range from 1.5% to 17%

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C3. FUNCTIONAL DIARRHEA
Diagnostic criteria

C3. 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

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C3. FUNCTIONAL DIARRHEA
Physiologic features

- **No single pathophysiological abnormality can explain the cause**
  - Altered GI motility
  - Brain – gut disturbances
  - Enviromental factors
  - Prior infections
  - Psychosocial factors

- **Psychosocial features**
  - Anxiety accompanies IBS, few data specially to FDr
  - Acute stress accelerates colon transit – relevance uncertain

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C3. FUNCTIONAL DIARRHEA
Clinical evaluation

1. **Clinical History**
   - Presence of alarm symptoms (rectal bleeding, unintentional weight loss, anemia, high-volume diarrhea, very frequent (> 6-10 per day) bowel movements, evidence of malnutrition) or positive family history for colorectal cancer
   - Diet: dairy products, wheat, caffeine, fruits, vegetables, juices, sweetend soft drinks, chewing gum)
   - Travel history
   - Brief psychosocial review

2. **Physical Examination**
   - Presence of ascites, abdominal mass, hepatosplenomegaly -> further evaluation
   - Anorectal examination

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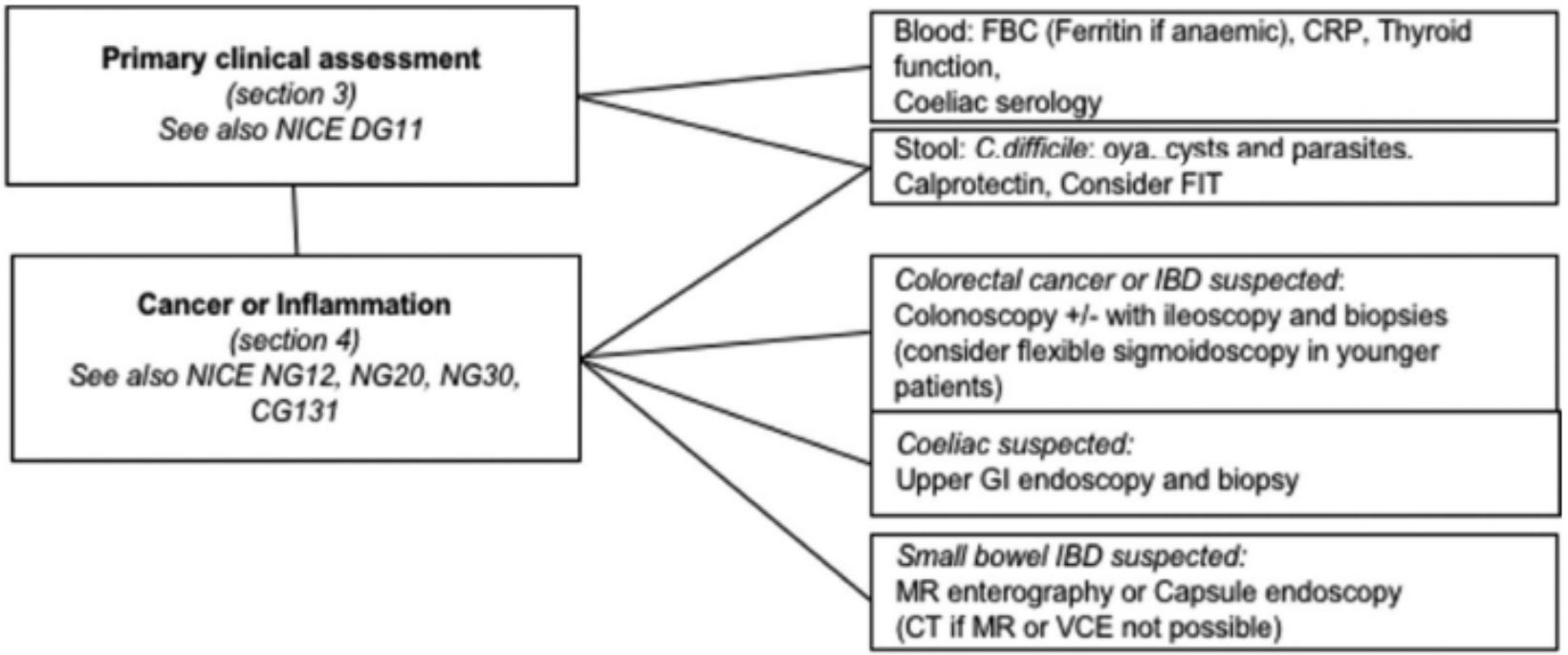
C1. IRRITABLE BOWEL SYNDROME
Clinical evaluation

Positive Diagnosis of IBS with limited laboratory studies



Consider

1) Positive diagnosis of diarrhoea-predominant irritable bowel syndrome (IBS-D) or functional diarrhoea
2) Specialist review -- especially for severe, persistent or atypical symptoms

Arasaradnam RP, et al. Gut 2018;67:1380–1399. doi:10.1136/gutjnl-2017-315909

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C1. IRRITABLE BOWEL SYNDROME
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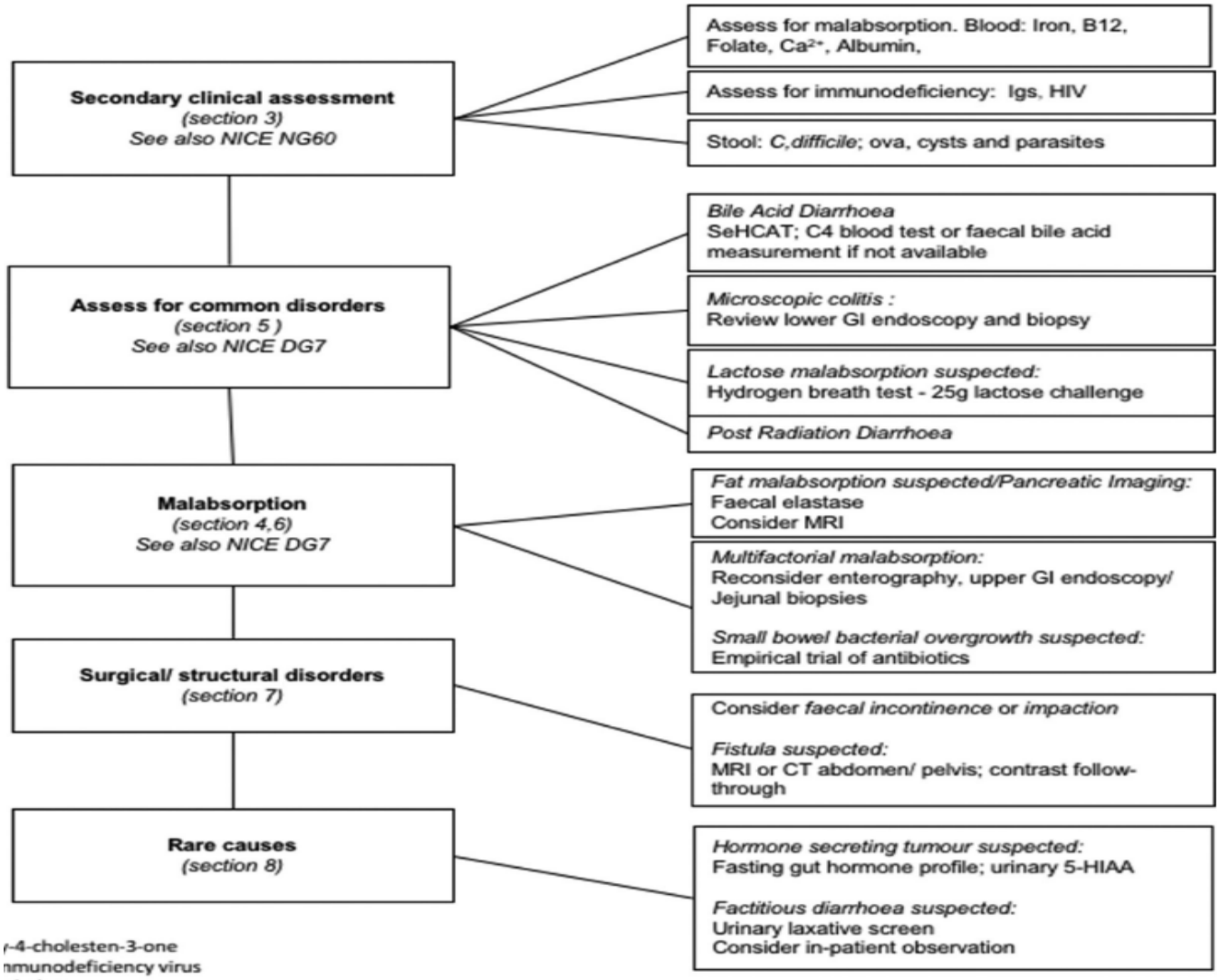

-4-cholesten-3-one
mmunodeficiency virus

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C3. FUNCTIONAL DIARRHEA
Treatment

- **Few studies for FDr – most of studies for IBS-D**

- **Loperamid**
- **Bile acid sequestrants**
  - Cholestyramine, colestipol, colesevelam
- **Probiotics**
- **Rifaximin**
- **Selective 5-HT3 antagonists** (alosetron, ondansetron)
- **Eluxadoline**

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C4. FUNCTIONAL ABDOMINAL BLOATING/DISTENTION
Epidemiology

- Prevalence 15.9% - 21%
- Women > men

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C4. FUNCTIONAL ABDOMINAL BLOATING/DISTENTION
Diagnostic criteria

C4. 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.

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C4. FUNCTIONAL ABDOMINAL BLOATING/DISTENTION
Physiologic features

- **Bloating**
  - Potential causes:
    - Visceral hypersensitivity
    - Abnormal intestinal gas transit
    - Impaired evacuation of rectal gas
    - Colonic fermentation
    - SIBO
    - Gut microbiota alteration

- **Abdominal Distention**
  - Abnormal viscerosomatic reflex involving the diaphragm and the abdominal wall muscles

    Accarino A, Perez F, Azpiroz F, et al. Abdominal distention results from caudo-ventral redistribution of contents. Gastroenterology 2009;136:1544–1551
  - Etiology of reflex unknown

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C4. FUNCTIONAL ABDOMINAL BLOATING/DISTENTION
Clinical evaluation

1. **Clinical History**
   - As IBS
   - FAB/FAD patients typically report a worsening of symptoms as day progresses, typically after meals, but allevation of symptoms overnight

2. **Physical Examination**
   - Objectivate abdominal distention
   - Signs of bowel obstruction
   - Organomegaly

3. **Testing (limited)**
   - As IBS
   - Exclude SIBO

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C4. FUNCTIONAL ABDOMINAL BLOATING/DISTENTION
Treatment

- **Simethicone**
- **Peppermint oil**
- **Lubiprostone**
- **Linaclotide**
- **Desipramine in combination with cognitive behavioural therapy**
- **Citalopram**

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C5. UNSPECIFIED BOWEL DISORDERS
Diagnostic criteria

C5. Diagnostic Criterion[a] for Unspecified Functional Bowel Disorder

Bowel symptoms not attributable to an organic etiology that do not meet criteria for IBS or functional constipation, diarrhea, or abdominal bloating/distention disorders.

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

C6. OPIOID-INDUCED CONSTIPATION
Epidemiology

- Prevalence 41% in patients with chronic non-cancer pain taking opioids

Kalso E, Edwards JE, Moore RA, et al. Opioids in chronic non-cancer pain: systematic review of efficacy and safety. Pain 2004;112:372–380

- Incidence 94% in cancer patients

Sykes NP. The relationship between opioid use and laxative use in terminally ill cancer patients. Palliat Med 1998;12:375–382

C6. OPIOID-INDUCED CONSTIPATION
Diagnostic Criteria

C6. 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

C6. OPIOID-INDUCED CONSTIPATION
Physiologic features

- The 3 classes of opioid receptors in the GI tract (μ, κ and δ) are G-protein-coupled receptors that reduce acetycholine release
  - Decrease in propulsive activity
  - Decrease in pancreatic, biliary and gastric secretions
  - Increase in anal tone

C6. OPIOID-INDUCED CONSTIPATION
Clinical evaluation

- **Clinical history**
  - Temporal relationship between constipation symptoms and opioid use?
- **Physical examination**
- **Limited laboratory tests**
- **Colonoscopy**

C6. OPIOID-INDUCED CONSTIPATION
Treatment

- **Laxatives**
- **Lubiprostone**

- **Opioid receptor antagonists**
  - **Naloxone, nalbuphine** (central active)
    - ➢ May precipitate opioid withdrawl symptoms
  - **Combination of naloxone with oxycodone**
  - **Methylnatrexone s.c.** (peripherally active)
    - ➢ 2nd line treatment in patients with chronic cancer pain
  - **Naloxegol:** oral PEGylated derivate of naloxone

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HIRSCHPRUNG DISEASE

- **Epidemiology**
  - 1 in 5000 live births
  - male:female 3:1 to 4:1

- **Pathophysiology**
  - Genetically complex disorder (RET-proto-oncogen)

  -> neutral crest cells fail to migrate during intestinal development

  -> relaxation failure of colon segment

  -> functional obstruction

  - Associated with many syndroms, especially with trisomy 21

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HIRSCHPRUNG DISEASE
Clinical features

- **Types of agangliosis**
  - **Short-segment:** rectosigmoid colon (80%)
    - **Ultra-short-segment**
  - **Long-segment:** extended proximal to rectosigmoid (15-20%)
  - **Total colonic agangliosis:** affection of the entire colon

- **Clinical presentation**
  - **Neonatal**
    - Symptoms of obstruction: emesis, abdominal distention, failure to pass meconium
    - Complications: enterocolitis, volvulus, (appendical perforation)
  - **Postnatal**
    - Chronic constipation, failure to thrive

- **Associated congenital anomalies:** genitourinary anomalies, visual and hearing impairment, congenital heart disease

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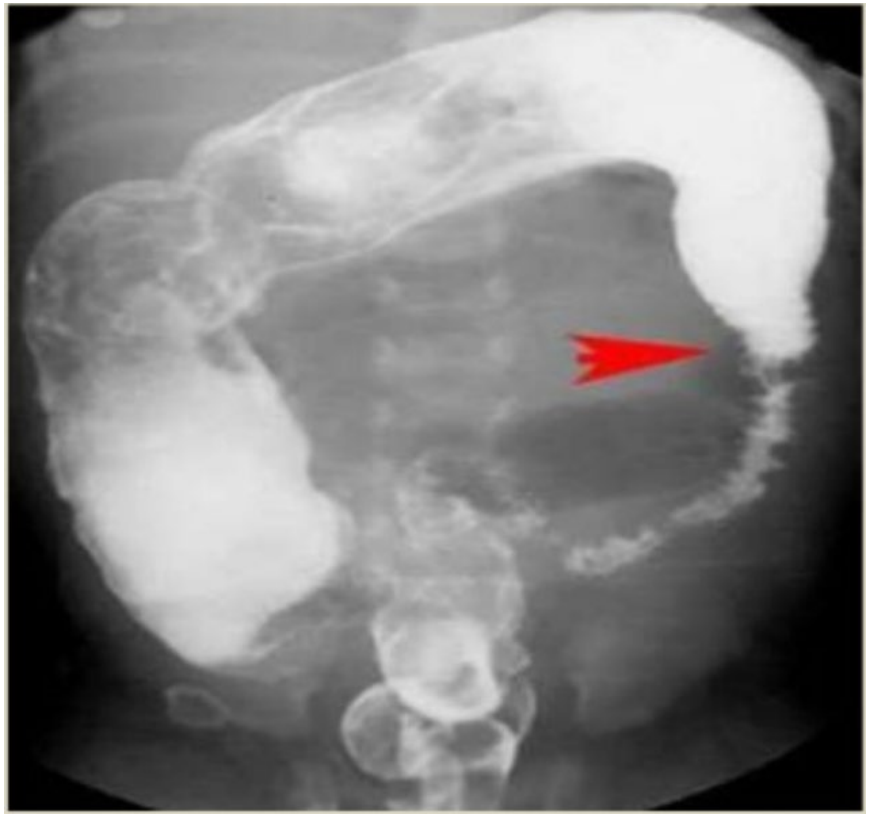
HIRSCHPRUNG DISEASE
Diagnosis

- **Barium enema**
  - Transition zone

- **Anorectal manometry**
  - Absence of rectoanal inibitory reflex

- **Suction rectal biopsy**
  - Gold standard
  - Absence of ganglion cells



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HIRSCHPRUNG DISEASE
Management - Outcome

- **Management**
  - Surgical resection of the affected segment
  - Ultra-short-segment:
    - diet, laxatives
    - Botulimun toxin injections
    - Myomectomy

- **Outcome**
  - Constipation/obstructive symptoms persist in 10-30%
  - Enterocolitis
  - Fecal incontinence
  - Urinary incontinence
  - Erectile dysfunction

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ACUTE COLONIC PSEUDO-OBSTRUCTION (OGILVIE's SYNDROME)

- **Definition**

Acute dilation of the colon in the absence of an anatomic lesion that obstructs the flow of intestinal contents

- **Etiology**

Category	Examples
Medications	Opioids, anti-cholinergics, alpha-2-adrenergic agonists, anti-psychotics, Ca^{++} channel blockers, cytotoxics, dopaminergics, epidural anesthesia
Trauma and orthopedic surgery	Fractures, hip and spine surgery
Obstetric and gynecological	Pelvic surgery especially involving spinal anesthesia; cesarian section; vaginal (normal or instrumental) delivery
Cardiothoracic surgery or disease	Cardiac surgery including transplantation; myocardial infarction, heart failure, pneumonia
Neurological diseases	Parkinsonism, stroke, dementia
Retroperitoneal diseases	Malignancy, hemorrhage
Metabolic imbalance	K^{+}, Ca^{++}, Mg^{++} imbalance; hypothyrodism
Infection	Herpes zoster

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ACUTE COLONIC PSEUDO-OBSTRUCTION (OGILVIE's SYNDROME)

- **Epidemiology**
  - Usually involves cecum and right hemicolon
  - More common in men and > 60 year old patients

- **Clinical manifestations**
  - Abdominal distention (gradually over 3 to 7 days)
  - Abdominal pain (80%)
  - Nausea, vomiting (60%)
  - Constipation and paradoxical diarrhea (40-50%)

- **Physical examination**
  - Abdomen tymbanitic but bowel sounds present
  - Aware of colonic ischemia or perforation (fever, marked abdominal tenderness, peritoneal signs)

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ACUTE COLONIC PSEUDO-OBSTRUCTION
Diagnosis

- **Diagnosis**
  - **Laboratory tests**
  - CBC, electrolytes, serum lactat
  - TSH
  - Liver, cholestatic and pancreatic enzymes
  - Stool culture (Cl. difficile)
  - **Imaging**
  - Abdominal CT scan
  - Abdominal radiographs

- **Differential Diagnosis**
  - Mechanical obstruction
  - Toxic megacolon

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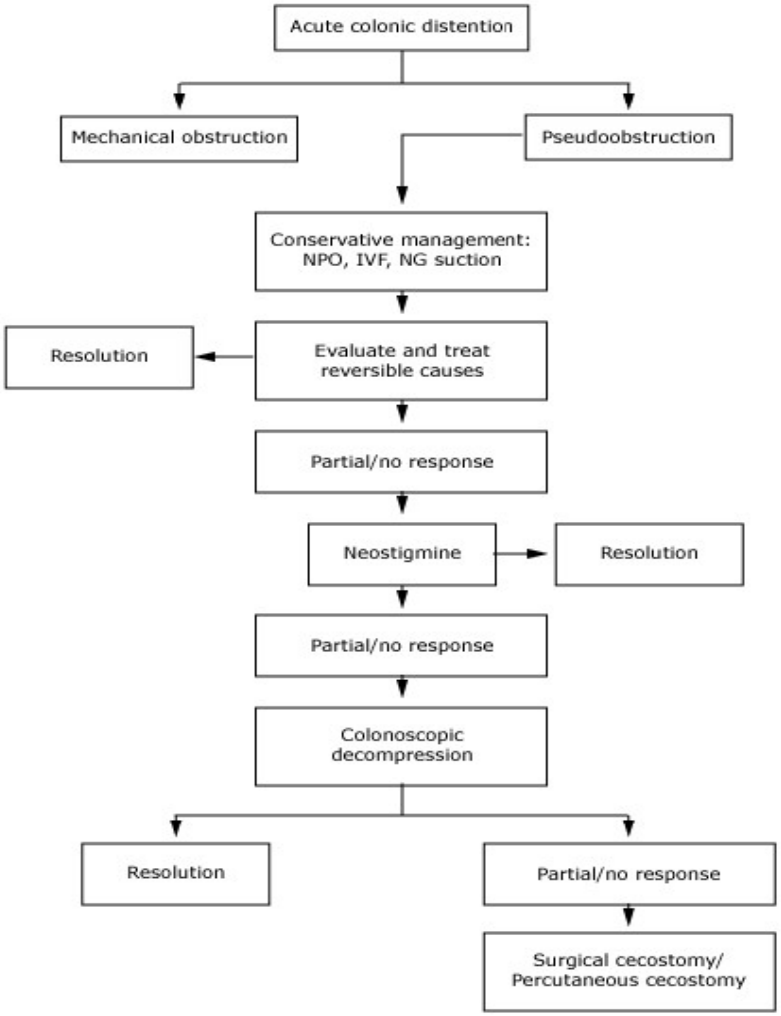
ACUTE COLONIC PSEUDO-OBSTRUCTION
Management



NPO: nothing given by mouth; IVF: intravenous fluids; NG: nasogastric.

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COLONIC BOWEL DISORDERS

Thank you for the attention

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