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Colonic motility disorders: Part 2

Bible Class, 14. July 2021

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COLONIC MOTILITY DISORDERS

- Pathophysiology

- **Functional bowel disorders (Rome IV)**
  - C1. Irritable Bowel Syndrome
  - C2. Functional Constipation
  - **C3. Functional Diarrhea**
  - **C4. Functional Abdominal Bloating/Distension**
  - **C5. Unspecified Bowel Disorders**
  - **C6. Opioid-Induced Constipation**

- **Congenital aganglionic megacolon (Hirschprung disease)**

- **Acute colonic pseudo-obstruction (Ogilivie's syndrome)**

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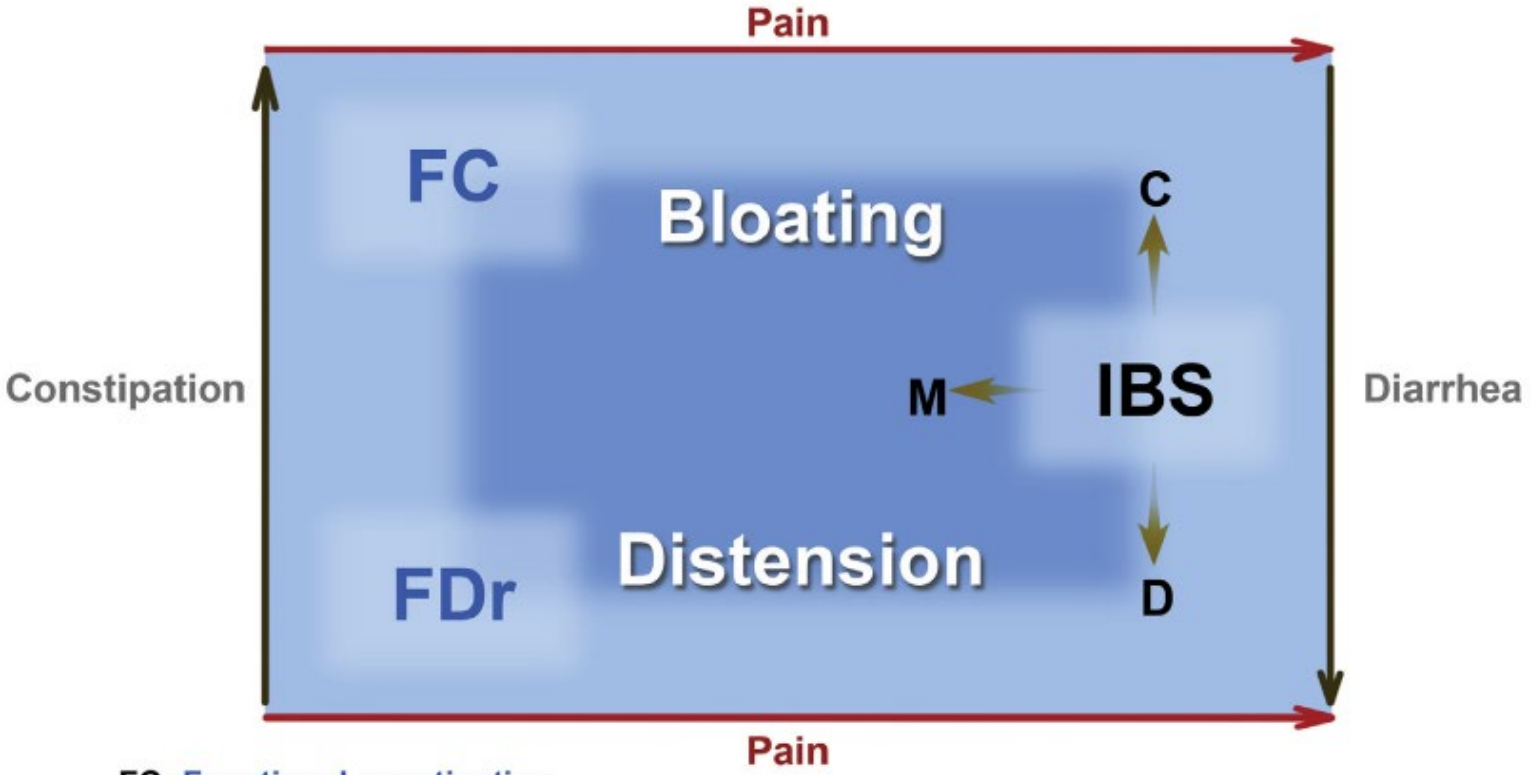
FUNCTIONAL BOWEL DISORDERS
ROME IV



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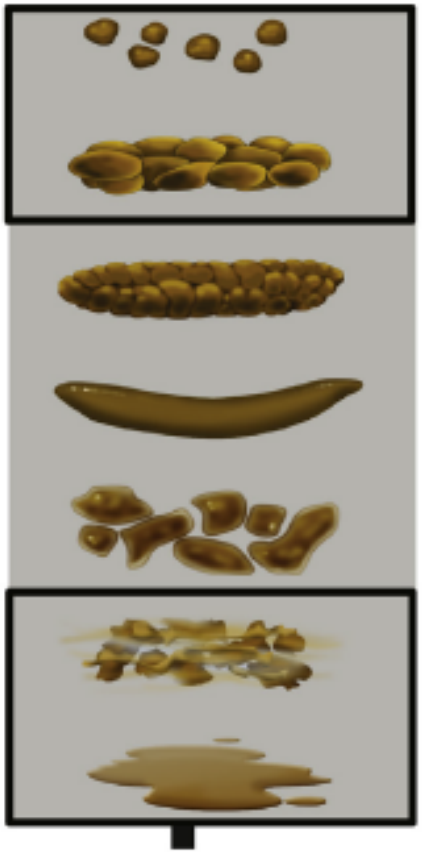
C1. IRRITABLE BOWEL SYNDROME
Bristol stool form scale (BSFS)



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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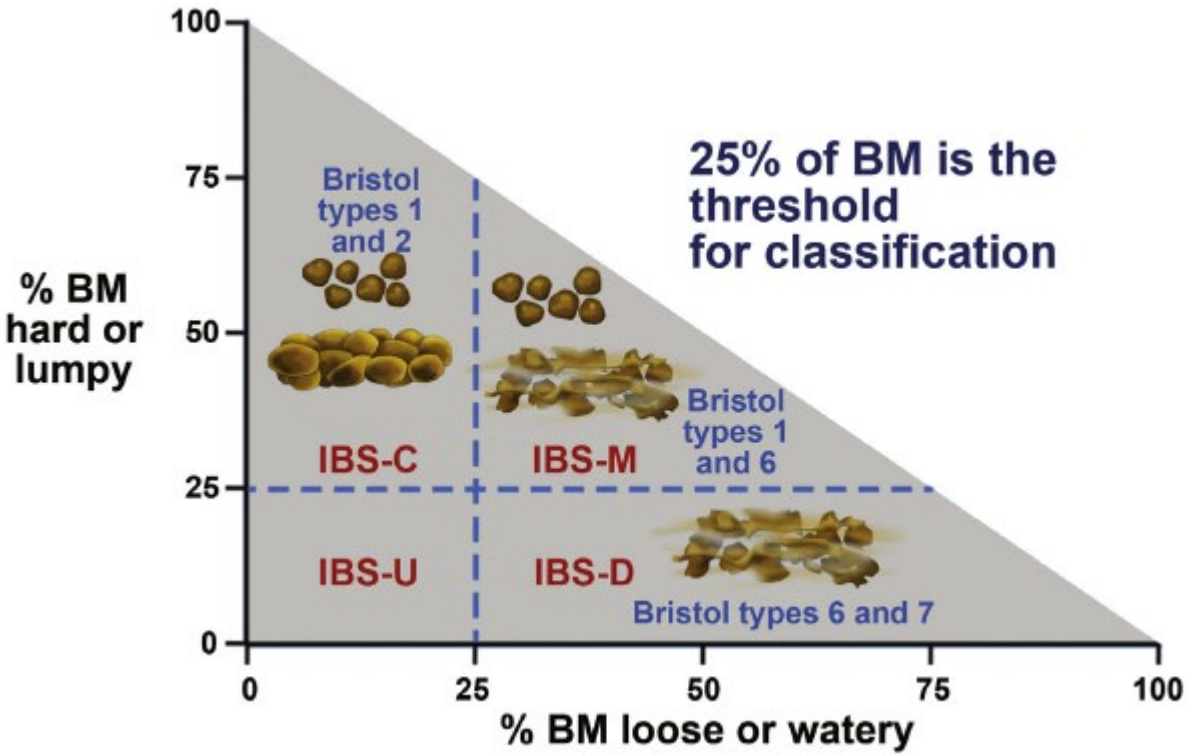
C1. IRRITABLE BOWEL SYNDROME
Subtypes



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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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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 (sphincter tone)

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C3. FUNCTIONAL DIARRHEA
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 +/- 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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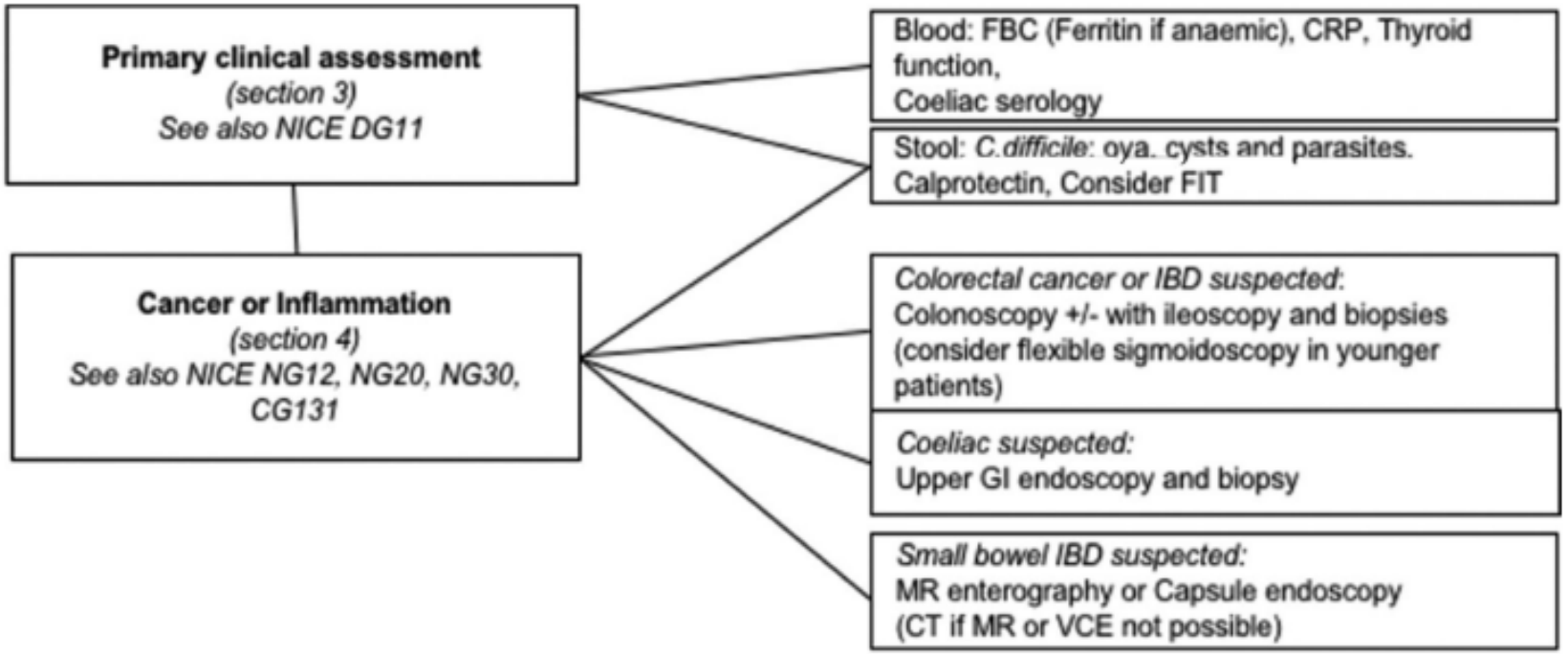
C3. FUNCTIONAL DIARRHEA
Clinical evaluation

Positive Diagnosis of IBS/functional diarrhea 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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C3. FUNCTIONAL DIARRHEA
Clinical evaluation

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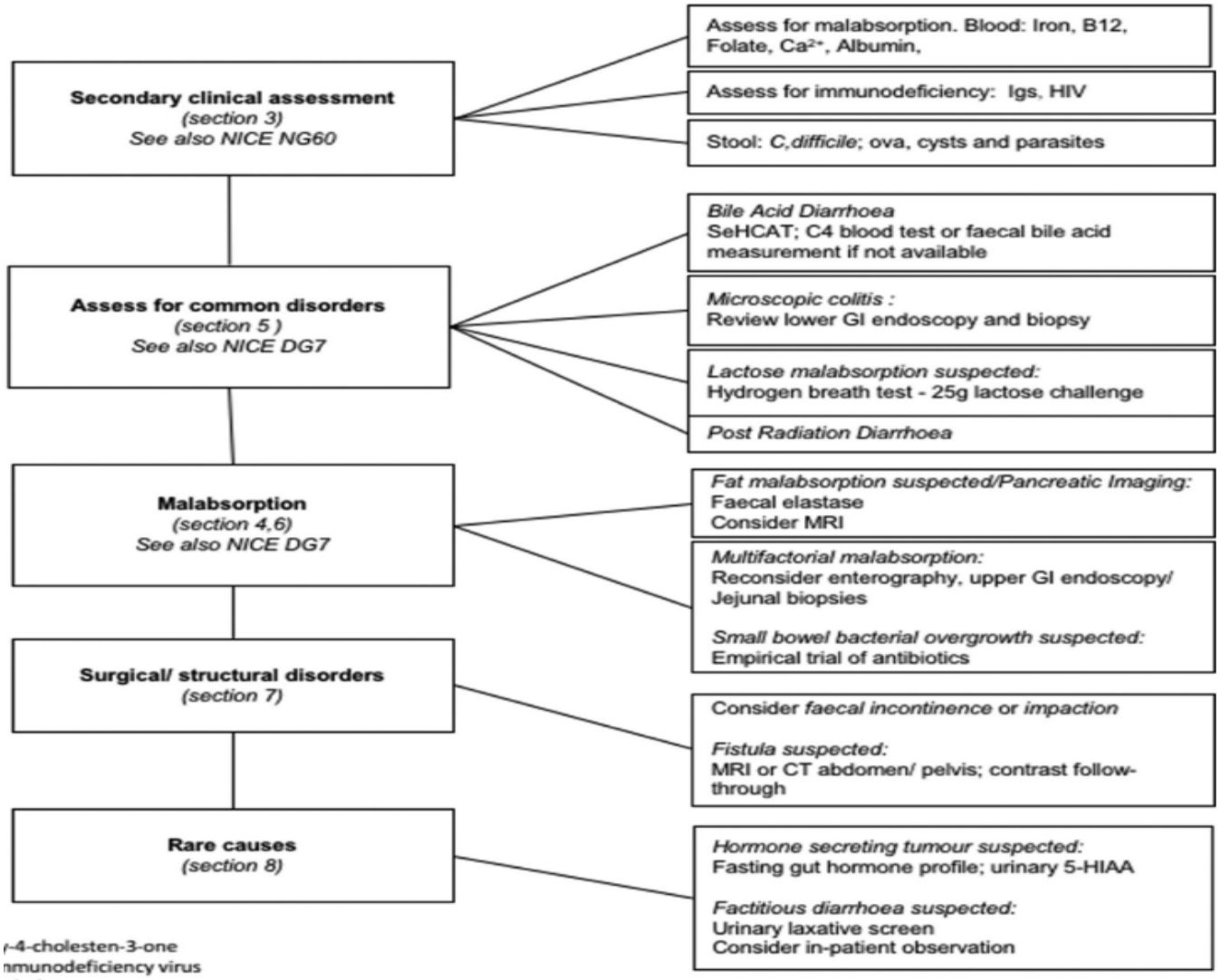

-4-cholesten-3-one
mmunodeficiency virus

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C3. FUNCTIONAL DIARRHEA
Treatment

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

- **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

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C3. FUNCTIONAL DIARRHEA
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

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C4. FUNCTIONAL ABDOMINAL BLOATING/DISTENSION
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 Distension**
  - 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/functional diarrhea
   - 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**
  - Locally acting chlorid channel activator
- **Linaclotide**
  - Guanylate cyclase C agonist
- **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 acetylocholine 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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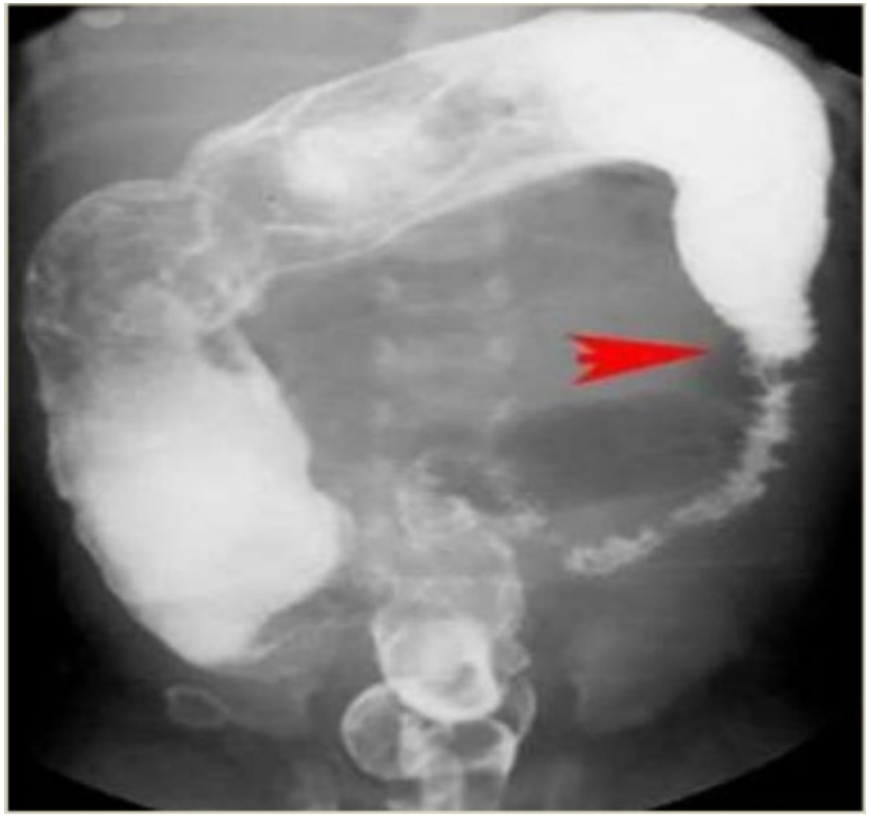
HIRSCHPRUNG DISEASE
Diagnosis

- **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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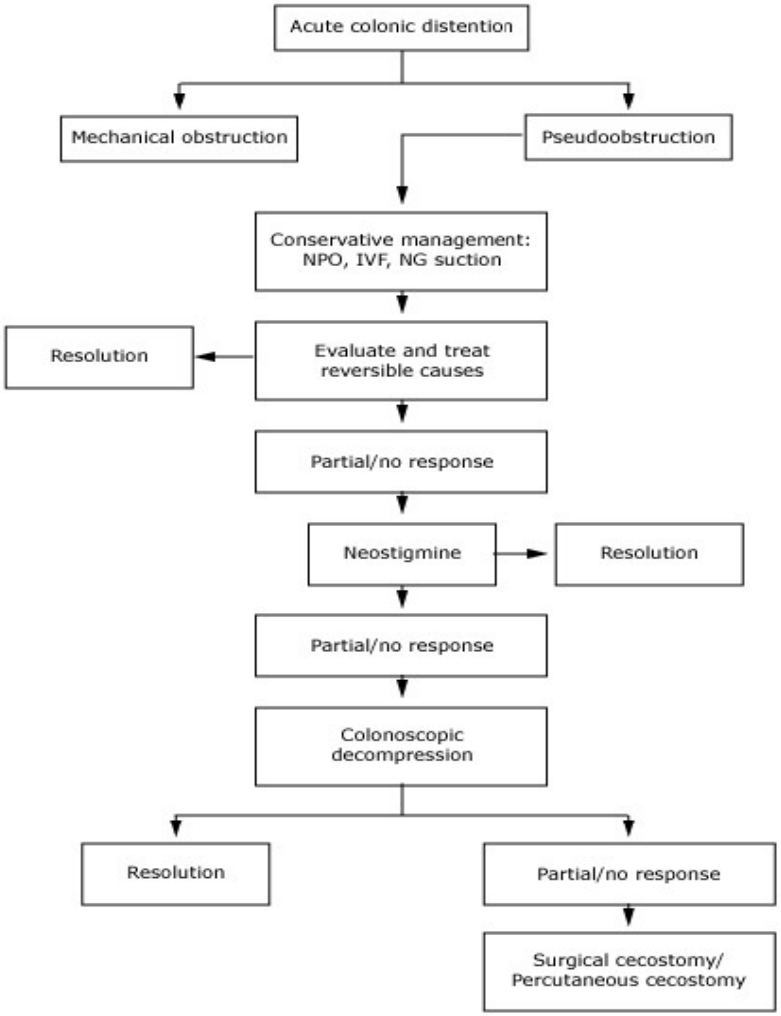
ACUTE COLONIC PSEUDO-OBSTRUCTION
Management



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

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COLONIC BOWEL DISORDERS
Part 2

Thank you for the attention

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