IBS: Constipation

Richard N. Redinger, M.D.
Professor of Medicine
Functional Bowel Disorders

- Functional bowel disorders are best understood as a biopsychosocial model of the pathophysiology of illness or disease.

- Rather than having a structural organic basis, they represent altered gut physiology via the brain/gut axis that translates neurotransmitter function into clinical symptoms.
Functional Bowel Disorders

- Psychosocial factors include life stresses particularly early life experiences with psychologic stress that affect coping capability and inadequate social support.

- Physiologic alterations with genetic and environmental influences impact gut motility and its sensation, inflammation and altered bacterial flora causing immune modulation that are associated with enhanced visceral sensitivity. CNS modulation of gut function also have linkages to emotional and cognitive areas that have behavioral consequences.
A. **Functional esophageal disorders**  
   A1. Functional heartburn  
   A2. Functional chest pain of presumed esophageal origin  
   A3. Functional dysphagia  
   A4. Globus  
B. **Functional gastroduodenal disorders**  
   B1. Functional dyspepsia  
      B1a. Postprandial distress syndrome  
      B1b. Epigastric pain syndrome  
   B2. Belching disorders  
      B2a. Aerophagia  
      B2b. Unspecified excessive belching  
   B3. Nausea and vomiting disorders  
      B3a. Chronic idiopathic nausea  
      B3b. Functional vomiting  
      B3c. Cyclic vomiting syndrome  
   B4. Rumination syndrome in adults
Rome III Functional Gastrointestinal Disorders

C. Functional bowel disorders
   C1. Irritable bowel syndrome
   C2. Functional bloating
   C3. Functional constipation
   C4. Functional diarrhea
   C5. Unspecified functional bowel disorder

D. Functional abdominal pain syndrome

E. Functional gallbladder and Sphincter of Oddi (SO) disorders
   E1. Functional gallbladder disorder
   E2. Functional biliary SO disorder
   E3. Functional pancreatic SO disorder

F. Functional anorectal disorders
   F1. Functional fecal incontinence
   F2. Functional anorectal pain
      F2a. Chronic proctalgia
         F2a1. Levator ani syndrome
         F2a2. Unspecified functional anorectal pain
      F2b. Proctalgia fugax
   F3. Functional defecation disorders
      F3a. Dyssynergic defecation
      F3b. Inadequate defecatory propulsion
Qualifications for Symptom Based Criteria

1. Coexisting disease(s) must be excluded
   i.e., no evidence of inflammation, anatomy, metabolic or neoplastic abnormalities
2. Symptoms from one domain may overlap with various other GI functional bowel disorders
3. Symptoms must exist for 6 months prior to diagnosis and be active for 3 months
4. Diagnostic categories do not include psychosocial criteria but are seen more commonly in referred versus primary care practices
5. Criteria are determined by clinical consensus and existing evidence
Functional Gastrointestinal Disorders

Table 1.

C. Functional bowel disorders
   C1. Irritable bowel syndrome*
   C2. Functional bloating
   C3. Functional constipation*
   C4. Functional diarrhea
   C5. Unspecified functional bowel disorder
Irritable Bowel Syndrome

Definition:

*IBS is a functional bowel disorder in which abdominal pain or discomfort is associated with defecation or a change in bowel habit, and with features of disordered defecation.*
Epidemiology

Throughout the world, about 10%-20% of adults and adolescents have symptoms consistent with IBS, and most studies find a female predominance. IBS symptoms come and go over time, often overlap with other functional disorders, impair quality of life, and result in high health care costs.
Diagnostic criteria* for IBS

Recurrent abdominal pain or discomfort** at least 3 days per month in the last 3 months associated with 2 or more of the following:

1. Improvement with defecation
2. Onset associated with a change in frequency of stool
3. Onset associated with a change in form (appearance) of stool

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

**Discomfort means an uncomfortable sensation not described as pain. In pathophysiology research and clinical trials, a pain/discomfort frequency of at least 2 days a week during screening evaluation for subject eligibility.
Subtyping IBS by Predominant Stool Pattern

1. IBS with constipation (IBS-C) – hard or lumpy stools ≥25% and loose (mushy) or watery stools <25% of bowel movements.
2. IBS with diarrhea (IBS-D) – loose (mushy) or watery stools ≥25% and hard or lumpy stool < 25% of BMs.
3. Mixed IBS (IBS-M) – hard or lumpy stools ≥25% and loose (mushy) or watery stools ≥25% of bowel movements.
4. Unsubtyped IBS – insufficient abnormality of stool consistency to meet criteria for IBS-C, D, or M.
The Bristol Stool Form Scale

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</tr>
<tr>
<td></td>
<td>Type 7</td>
<td>Watery, no solid pieces</td>
<td>Entirely liquid</td>
</tr>
</tbody>
</table>

Clinical Evaluation

Diagnosis depends on careful interpretation of the temporal relationships of pain/discomfort, bowel habit, and stool characteristics. Pain/discomfort related to defecation is likely to be of bowel origin, whereas that associated with exercise, movement, urination, or menstruation usually has a different cause. Fever, gastrointestinal bleeding, weight loss, anemia, abdominal mass, and other “alarm” symptoms or signs are not due to IBS, but may accompany it.
Clinical Evaluation

In women, so-called pelvic pain, worsening of IBS symptoms during menstruation, and dyspareunia or other gynecologic symptoms may obscure the diagnosis. Incorrect symptom attribution can lead to hospitalization and surgery, especially cholecystectomy, appendectomy, and hysterectomy. The recognition and evaluation of bowel dysfunction in patients with “pelvic” or abdominal pain may reduce unnecessary surgery.
Clinical Evaluation

- Heartburn, fibromyalgia, headache, backache, genitourinary symptoms, and others are often associated with IBS, but are not useful in diagnosing it.

- Few tests are required for patients who have typical IBS symptoms and no alarm features. Unnecessary investigations may be costly and even harmful.
Investigations

- Few tests are necessary for patients with typical IBS symptoms and no alarm features. Tests are based on patients' age, duration and severity, psychosocial factors, alarm symptoms and FH colon cancers.
- Fiberoptic sigmoidoscopy or colonoscopy to r/o organic disease
- Stool Examination
- R/O celiac diseases based on clinical features
- Assess QOL, daily Fx, personality, life stresses.
Physiologic Features

IBS is best viewed as an interaction of important biological and psychosocial factors. Altered motility, visceral hyperalgesia, disturbance of brain-gut interaction, abnormal central processing, autonomic and hormonal events, genetic and environmental factors, postinfectious sequels, and psychosocial disturbance are variably involved, depending on the individual.
Psychosocial Features

Psychological disturbance, especially in referred patients, includes psychiatric disorders (eg, panic disorder, generalized anxiety disorder, mood disorder, and posttraumatic stress disorder), sleep disturbance, and dysfunctional coping. A history of childhood abuse is common. Although stressful life events sometimes correlate with symptom exacerbation, the nature of the link between psychosocial factors and IBS is unclear.
## Treatment

### Possible Drugs for a Dominant Symptom in IBS

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Drug</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhea</td>
<td>Loperamide</td>
<td>2–4 mg when necessary/ maximum 12 g/d</td>
</tr>
<tr>
<td></td>
<td>Cholestyramine resin</td>
<td>4 g with meal</td>
</tr>
<tr>
<td></td>
<td>Alosetron&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.5–1 mg bid (for severe IBS, women)</td>
</tr>
<tr>
<td>Constipation</td>
<td>Psyllium husk</td>
<td>3.4 g bid with meals, then adjust</td>
</tr>
<tr>
<td></td>
<td>Methylcellulose</td>
<td>2 g bid with meals, then adjust</td>
</tr>
<tr>
<td></td>
<td>Calcium polycarbophil</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lactulose syrup</td>
<td>10–20 g bid</td>
</tr>
<tr>
<td></td>
<td>70% sorbitol</td>
<td>15 mL bid</td>
</tr>
<tr>
<td></td>
<td>Polyethylene glycol 3350</td>
<td>17 g in 8 oz water qd</td>
</tr>
<tr>
<td></td>
<td>Tegaserod&lt;sup&gt;c&lt;/sup&gt;</td>
<td>6 mg bid (for IBS, women)</td>
</tr>
<tr>
<td></td>
<td>Magnesium hydroxide</td>
<td>2–4 tbsp qd</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>Smooth-muscle relaxant&lt;sup&gt;d&lt;/sup&gt;</td>
<td>qd to qid ac</td>
</tr>
<tr>
<td></td>
<td>Tricyclic antidepressants</td>
<td>Start 25–50 mg hs, then adjust</td>
</tr>
<tr>
<td></td>
<td>Selective serotonin</td>
<td>Begin small dose, increase as needed</td>
</tr>
<tr>
<td></td>
<td>reuptake inhibitors</td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup> Local cost should be considered in drug choice.

<sup>b</sup> Available only in the U.S.

<sup>c</sup> Unavailable in the European Union.

<sup>d</sup> Selective antimuscarinic agents unavailable in the United States.
Treatment

- Reassurance and Education
  Regarding healthy lifestyles, behavioral Rx, provide counseling for psychosocial issues.

- Establish a Therapeutic Relationship
  Develop a strong physician-patient relationship.
  Be sympathetic, maintain patient contact, be understanding, don’t overtreat or advise harmful treatment.

- Discuss diet
  Avoid nutritional depletion, diarrheal substances (sorbitol, fructose).

- Discuss use of Probiotics
  Bifidobacterium infantis, etc

- Cognitive-Behavioral Therapy
  Standard and Hypnotherapy.
Constipation

Functional vs. Secondary
Functional Constipation

Rome III Criteria for Functional Constipation

- Two or more of the following six must be present:
  - Straining during at least 25% of defecations
  - Lumpy or hard stools in at least 25% of defecations
  - Sensation of incomplete evacuation for at least 25% of defecations
  - Sensation of anorectal obstruction/blockage for at least 25% of defecations
  - Manual maneuvers to facilitate at least 25% of defecations (e.g., digital evacuation, support of the pelvic floor)
  - Fewer than three defecations/wk
Secondary Causes

Mechanical Obstruction
- Anal stenosis
- Colorectal cancer
- Extrinsic compression
- Rectocele or sigmoidocele
- Stricture
Secondary Causes

Medications

Antacids

Anticholinergic agents (e.g., antiparkinsonian drugs, antipsychotics, antispasmodics, tricyclic antidepressants)*

Anticonvulsants (e.g., carbamazepine, phenobarbital, phenytoin)*

Antineoplastic agents (e.g., vinca derivatives)

Calcium channel blockers (e.g., verapamil)*

Diuretics (e.g., furosemide)*

5-Hydroxytryptamine, antagonists (e.g., alosetron) – off market

Iron supplements*

Nonsteroidal anti-inflammatory drugs (e.g., ibuprofen)*

Mu-opioid agonists (e.g., fentanyl, loperamide, morphine*)
Secondary Causes

Metabolic and Endocrinologic Disorders
  Diabetes mellitus*
  Heavy metal poisoning (e.g., arsenic, lead, mercury)
  Hypercalcemia*
  Hyperthyroidism
  Hypokalemia
  Hypothyroidism*
  Panhypopituitarism
  Pheochromocytoma
  Porphyria
  Pregnancy*
Secondary Causes

Neurologic and Myopathic Disorders
Amyloidosis
Autonomic neuropathy
Chagas’ disease
Dermatomyositis
Hirschsprung's Disease – complete or partial
Intestinal pseudo-obstruction
Internal neural dysplasia
Multiple sclerosis
Myopathy of colon or rectum – anal sphincter genetics
Parkinsonism
Progressive systemic sclerosis
Shy-Drager syndrome
Spinal cord injury
Stroke
Risk Factors

- Risk factors for Constipation
  - Advanced age
  - Female gender
  - Low level of education
  - Low level of physical activity
  - Low socioeconomic status
  - Nonwhite ethnicity
  - Use of certain medications
Epidemiology

- Incidence – 15% Olmstead Study, non-elderly
- Prevalence – 2% - 28% variable methods, demographics
- Cost - $6.9 billion/yr, medical eval $2,252 (colonoscopy)
  - Only 4% get to gastroenterologists
Colonic Function - Physiology

- Luminal content
  - Bacteria 55%
  - Fiber 17%
  - Food residue, $H_2O$, gas

- Absorption
  - $H_2O$ Na, 1.5L-200/100 ml
  - Bowel diameter 6-5 cm

- Motor function
  1. Delays passage
  2. Mixes contents
  3. Storage (distal bowel)
  4. Propulsion: transit 35-72 hrs

- LAPCs
  - Low amplitude propagated contractions

- HAPCs
  - High amplitude propagated contractions

- Innervation
  - involuntary, ENS, Proximal colon
  - Voluntary defecation

- Myenteric plexus – excitatory
  - Transmitter substance P

- inhibitory VIP (Vasoactive Intestinal Polypeptide)

- Interstitial cells of Cajal (ICCS)
  - Intestinal pacemaker cells – provide slow wave propagation
  - Neural signaling between ENS and muscle
Colonic Function - Physiology

- Defecatory function

Physiology of defecation. Defecation requires relaxation of the puborectalis muscle with descent of the pelvic floor and straightening of the anorectal angle during straining, as well as relaxation of the internal anal sphincter. (From Lembo A, Camilleri M. Chronic constipation. N Engl J Med 2003; 349:1360-8.)
Secondary Causes

Secondary Causes of Constipation

**Mechanical Obstruction**
- Anal stenosis
- Colorectal cancer
- Extrinsic compression
- Rectocele or sigmoidcele
- Stricture

**Medications**
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**Neurologic and Myopathic Disorders**
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- Autonomic neuropathy
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- Dermatomyositis
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- Progressive systemic sclerosis
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**Pathophysiology**

**Functional Causes**

Disordered function of colon or rectum

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<th>FEATURES</th>
<th>CHARACTERISTIC FINDINGS</th>
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<td>Normal-transit constipation</td>
<td>Incomplete evacuation; abdominal pain may be present but not a predominant feature</td>
<td>Normal physiologic test results</td>
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<td>Slow-transit constipation</td>
<td>Infrequent stools (e.g., ≤1/wk); lack of urge to defecate; poor response to fiber and laxatives; generalized symptoms, including malaise and fatigue; more prevalent in young women</td>
<td>Retention in colon of &gt;20% of radiopaque markers five days after ingestion</td>
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<td>Defecatory disorders (pelvic floor dysfunction, anismus, descending perineum syndrome, rectal prolapse)</td>
<td>Frequent straining; incomplete evacuation; need for manual maneuvers to facilitate defecation</td>
<td>Abnormal balloon expulsion test and/or rectal manometry</td>
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*If severe, is called colonic inertia*
Pathophysiology
Functional Causes

Disordered function of colon or rectum
- Also called dyssynergia, obstructive defecation, outlet obstruction
  - These commonly have inappropriate contraction of anal sphincter, abnormal pelvic floor descent and deficient rectal pressure and sensation

Rome III Criteria for Functional Defecation Disorders
- The patient must satisfy diagnostic criteria for functional constipation
- During repeated attempts to defecate, the patient must have at least two of the following:
  - Evidence of impaired evacuation, based on balloon expulsion test or imaging
  - Inappropriate contraction of pelvic floor muscles (i.e., anal sphincter or puborectalis) or less than 20% relaxation of basal resting sphincter pressure by manometry, imaging, or EMG
  - Inadequate propulsive forces assessed by manometry or imaging
Pathophysiology
Functional Causes

Development of a rectocele. A, Normal anatomy of the female pelvis. The levator plate is almost horizontal, supporting the rectum and vagina. The perineal body provides support for the lower posterior vaginal wall; above it lies the rectovaginal septum. B, Weakness of the pelvic floor leads to a more vertical levator plate. The perineal body is attenuated, which favors the formation of a rectocele. The laxity of the pelvic floor also favors rectal mucosal prolapse. (From Loder PB, Phillips RKS. Rectocele and pelvic floor weakness. In: Kamm MA, Lennard-Jones JE, editors. Constipation. Peterfield, England: Wrightson Biomedical; 1994. p 281.)
Bristol Stool Scale

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Psychosocial Disorders

- Depression
- Eating disorders
- Denied bowel movements
- Symptoms of somatization, obsessive compulsiveness and affective disorders
Clinical Assessment

History
Prolonged straining to expel stool
Assumption of unusual postures on toilet to facilitate stool expulsion
Support of perineum, digitation of rectum, or application of pressure to the posterior vaginal wall to facilitate rectal emptying
Inability to expel enema fluid
Constipation after subtotal colectomy for constipation

Rectal Examination (with patient in left lateral position)

Inspection
Anus “pulled” forward during attempts to simulate strain during defecation
Anal verge descends <1 cm or >4 cm (or beyond ischial tuberosities) during attempts to simulate straining at defecation
Perineum balloons down during straining; rectal mucosa partially prolapses through anal canal

Palpation
High anal sphincter tone at rest precludes easy entry of examining finger (in absence of a painful perianal condition such as an anal fissure)
Anal sphincter pressure during voluntary squeeze only minimally higher than anal tone at rest
Perineum and examining finger descend <1 cm or >4 cm during simulated straining at defecation
Puborectalis muscle tender to palpation through rectal wall posteriorly, or palpation reproduces pain
Palpable mucosal prolapse during straining
“Defect” in anterior wall of the rectum, suggestive of rectocele
Diagnostic Tests

1. To exclude systemic illness or structural disorders.
2. To elucidate the underlying pathophysiology process
Diagnostic Tests

- Tests to exclude systemic disease are Hb, ESR, biochemical screening tests for thyroid, Ca, glucose and to r/o inflammation, neoplasia, metabolic or other systemic disorders.

- To exclude structure disease
  - Do Ba enema, SBFT
  - Endoscopy for Δ BM, blood in stool, weight loss, fever
  - Age > 50y
  - C-Scope or flexsign
Diagnostic Tests

- Physiologic measures aided by symptom diaries
  - Do transit studies – radiopaque markers
  - Anorectal manometry
    - Pressure measures relaxation of sphincter
    - Sensation
  - EMG
  - Defecating proctogram
  - Balloon Expansion Test
Diagnostic Tests

**Anal Sphincter Pressures**

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<th>Value</th>
<th>Unit</th>
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<tr>
<td>Max. Resting sphincter</td>
<td>62</td>
<td>mm Hg</td>
</tr>
<tr>
<td>Max. Squeeze sphincter</td>
<td>81</td>
<td>mm Hg</td>
</tr>
</tbody>
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**Cough Reflex**

- Rectal pressure: 27 mm Hg
- Anal sphincter pressure: 75 mm Hg

**Attempted Defecation**

- Rectal pressure: 22 mm Hg
- Anal residual pressure: 73 mm Hg

**Recto-anal inhibitory reflex**

- Complete

**Rectal Sensation**

- Threshold for first sensation: 10 cc
- Threshold for desire to defecate: 40 cc
- Maximum tolerable volume: 60 cc

**Rectal Compliance (after correcting for intrinsic balloon wall compliance)**

<table>
<thead>
<tr>
<th>Volume/Pressure</th>
<th>cc / mmHg</th>
</tr>
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<tbody>
<tr>
<td>20 / 19</td>
<td></td>
</tr>
<tr>
<td>30 / 29</td>
<td></td>
</tr>
<tr>
<td>40 / 33</td>
<td></td>
</tr>
<tr>
<td>60 / 37</td>
<td></td>
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**Normal Values (Mean, 95% confidence interval)**

<table>
<thead>
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<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td></td>
</tr>
<tr>
<td>72 (64-80)</td>
<td></td>
</tr>
<tr>
<td>193 (175-211)</td>
<td></td>
</tr>
<tr>
<td>66 (51-81)</td>
<td></td>
</tr>
<tr>
<td>154 (138-170)</td>
<td></td>
</tr>
<tr>
<td>62 (51-73)</td>
<td></td>
</tr>
<tr>
<td>106 (89-123)</td>
<td></td>
</tr>
<tr>
<td>68 (58-78)</td>
<td></td>
</tr>
<tr>
<td>49 (35-63)</td>
<td></td>
</tr>
<tr>
<td>40 (32-48)</td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td></td>
</tr>
<tr>
<td>65 (56-74)</td>
<td></td>
</tr>
<tr>
<td>143 (124-162)</td>
<td></td>
</tr>
</tbody>
</table>

**IMPRESSION:**
Resting anal canal pressures were normal. Patient has low squeeze pressures. Cough reflex was impaired with low anal pressures. Attempted defecation was consistent with type 2 dyssynergic defecation (impaired generation of rectal pressure with paradoxical increase of anal sphincter pressure). There was normal sensation in the rectal vault but tolerance was impaired. Recto-anal inhibitory reflex was complete. Rectal compliance was diminished (less distensible). Consistent with weak external anal sphincter.

**COMMENTS:**
Patient was given instructions for Kegel exercises and bowel management program. Need clinical correlation for impaired tolerance to rectal distension and “stiff” rectum.
Algorithm for the evaluation and treatment of severe constipation.
Treatment

Chronic constipation

Fecal impaction

NO

Remove constipating medications (if possible)
Increase fluid intake
Increase activity or exercise
Increase fiber intake (20–30 g/day)
Timed toilet training

YES

Manual disimpaction
Enemas and/or suppositories
Bowel regimen to prevent recurrence

Milk of magnesia
Lactulose
Sorbitol
Senna compounds
Bisacodyl

Effective

YES

Continue regimen

NO

Polyethylene glycol (PEG)

Effective

YES

Continue regimen

NO

Lubiprostone
Biofeedback therapy (dyssynergic defecation)
Alvimopan methylxanthine (opioid-induced constipation)

Treatment algorithm for the management of chronic constipation in the elderly.
**Treatment**

General measures – Reassurance, lifestyle changes, psychological support, fluids, dietary and fiber changes.

<table>
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<tr>
<th>AGENT</th>
<th>STARTING DAILY DOSE (G)</th>
<th>COMMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methylcellulose</td>
<td>4-6</td>
<td>Semisynthetic cellulose fiber that is relatively resistant to colonic bacterial degradation and tends to cause less bloating and flatus than psyllium</td>
</tr>
<tr>
<td>Psyllium</td>
<td>4-6</td>
<td>Made from ground seed husk of the ispaghula plant; forms a gel when mixed with water, so an ample amount of water should be taken with psyllium to avoid intestinal obstruction; undergoes bacterial degradation, which may contribute to side effects of bloating and flatus; allergic reactions such as anaphylaxis and asthma have been reported but are rare</td>
</tr>
<tr>
<td>Polycarbophil</td>
<td>4-6</td>
<td>Synthetic fiber made of polymer of acrylic acid, which is resistant to bacterial degradation</td>
</tr>
<tr>
<td>Guar gum</td>
<td>3-6</td>
<td>Soluble fiber extracted from seeds of the leguminous shrub <em>Cyamopsis tetragonoloba</em></td>
</tr>
</tbody>
</table>
## Treatment

### Laxatives Commonly Used for Constipation

<table>
<thead>
<tr>
<th>TYPE OF LAXATIVE</th>
<th>GENERIC NAME(S)</th>
<th>DOSE</th>
<th>COMMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Osmotic Laxatives</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poorly Absorbed Ions</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Magnesium</td>
<td>Magnesium hydroxide</td>
<td>15-30 mL once or twice daily</td>
<td>Hypermagnesemia can occur in patients with renal failure and in children.</td>
</tr>
<tr>
<td></td>
<td>Magnesium citrate</td>
<td>150-300 mL every day</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Magnesium sulfate</td>
<td>15 g every day</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sodium sulfate</td>
<td>5-10 g every day</td>
<td></td>
</tr>
<tr>
<td>Sulfate</td>
<td>Sodium phosphate</td>
<td>0.5-10 mL with 12 oz of water</td>
<td>Sulfate is generally not used by itself as a laxative agent.</td>
</tr>
<tr>
<td>Phosphate</td>
<td></td>
<td></td>
<td>Hyperphosphatemia can occur, especially in patients with renal failure.</td>
</tr>
<tr>
<td>Poorly Absorbed Sugars</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disaccharides</td>
<td>Lactulose</td>
<td>15-30 mL once or twice daily</td>
<td>Gas and bloating are common side effects.</td>
</tr>
<tr>
<td>Sugar alcohols</td>
<td>Sorbitol</td>
<td>15-30 mL once or twice daily</td>
<td>Sorbitol is commonly used as a sweetener in sugar-free products. In older adults, sorbitol has an effect similar to that of lactulose but has a lower cost.</td>
</tr>
<tr>
<td></td>
<td>Mannitol</td>
<td>15-30 mL once or twice daily</td>
<td></td>
</tr>
<tr>
<td>Polyethylene glycol</td>
<td>Polyethylene glycol electrolyte</td>
<td>17-34 g once or twice daily</td>
<td>Tends to cause less bloating and cramps than other agents; tasteless and odorless, can be mixed with noncarbonated beverages. Typically used to prepare colon for diagnostic examinations and surgery; also available as powder without electrolytes for regular use (MiraLax).</td>
</tr>
</tbody>
</table>
## Treatment

<table>
<thead>
<tr>
<th>Stimulant Laxatives</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Anthraquinones</td>
<td>Cascara sagrada</td>
<td>325 mg (or 5 mL) at bedtime</td>
</tr>
<tr>
<td></td>
<td>Senna</td>
<td>1-2 7.5-mg tablets daily</td>
</tr>
<tr>
<td>Ricinoleic acid</td>
<td>Castor oil</td>
<td>15-30 mL at bedtime</td>
</tr>
<tr>
<td>Diphenylmethane Derivatives</td>
<td>Bisacodyl</td>
<td>5-10 mg at bedtime</td>
</tr>
<tr>
<td></td>
<td>Phenolphthalein</td>
<td>30-200 mg at bedtime</td>
</tr>
<tr>
<td>Stool Softeners</td>
<td>Sodium picosulfate</td>
<td>5-15 mg at bedtime</td>
</tr>
<tr>
<td>Emollients</td>
<td>Docusate sodium</td>
<td>100 mg twice daily</td>
</tr>
<tr>
<td></td>
<td>Mineral oil</td>
<td>5-15 mL at bedtime</td>
</tr>
<tr>
<td>Enemas, Suppositories</td>
<td>Phosphate enema</td>
<td>120 mL</td>
</tr>
<tr>
<td></td>
<td>Mineral oil retention enema</td>
<td>100 mL</td>
</tr>
<tr>
<td></td>
<td>Tap water enema</td>
<td>500 mL</td>
</tr>
<tr>
<td></td>
<td>Soapsuds enema</td>
<td>1500 mL</td>
</tr>
<tr>
<td></td>
<td>Glycerin suppository</td>
<td>60 g</td>
</tr>
<tr>
<td></td>
<td>Bisacodyl suppository</td>
<td>10 mg</td>
</tr>
<tr>
<td>Chloride Channel Activator</td>
<td>Lubiprostone</td>
<td>8-24 μg twice daily</td>
</tr>
</tbody>
</table>

Causes apoptosis of colonic epithelial cells phagocytosed by macrophages; result in lipofuscin-like pigmented condition known as pseudomelanosis coli; no definitive association established between anthraquinones and colon cancer or myenteric nerve damage (cathartic colon) Cramping is common. Has effects in small intestine and colon. Removed from U.S. market because of teratogenicity in animals. Likely has effects only on colon. Efficacy in constipation not well established. Long-term use can cause malabsorption of fat-soluble vitamins, anal seepage, and lipid pneumonia in patients predisposed to aspiration of liquids. Serious damage to rectal mucosa can result from extravasation of enema solution into the submucosa; hypertonic phosphate enemas and large-volume water or soapsuds enemas can lead to hyperphosphatemia and other electrolyte abnormalities if enema is retained; soapsuds enemas can cause colitis. Increases secretion in the intestines.
## Treatment

### Grade of Evidence for the Use of Laxatives

According to the American College of Gastroenterology Task Force on Chronic Constipation

<table>
<thead>
<tr>
<th>LAXATIVE</th>
<th>GRADE OF EVIDENCE*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bulking agents</td>
<td></td>
</tr>
<tr>
<td>Psyllium</td>
<td>B</td>
</tr>
<tr>
<td>Calcium polycarbophil</td>
<td>B</td>
</tr>
<tr>
<td>Bran</td>
<td></td>
</tr>
<tr>
<td>Stool softeners</td>
<td>B</td>
</tr>
<tr>
<td>Lubricants</td>
<td>C</td>
</tr>
<tr>
<td>Osmotic laxatives</td>
<td></td>
</tr>
<tr>
<td>PEG</td>
<td>A</td>
</tr>
<tr>
<td>Lactulose</td>
<td>A</td>
</tr>
<tr>
<td>Milk of magnesia</td>
<td>†</td>
</tr>
<tr>
<td>Stimulant laxatives</td>
<td></td>
</tr>
<tr>
<td>Prokinetic agent</td>
<td>B</td>
</tr>
<tr>
<td>Tegaserod†</td>
<td>A</td>
</tr>
<tr>
<td>Chloride channel activator</td>
<td>§</td>
</tr>
<tr>
<td>Lubiprostone</td>
<td></td>
</tr>
</tbody>
</table>

*Grade A: Based on two or more randomized controlled trials (RCTs) with adequate sample sizes and appropriate methodology. Grade B: Based on evidence from a single RCT of high quality or conflicting results from high-quality RCTs or two or more RCTs of lesser quality. Grade C: Based on noncontrolled trials or case reports.
†Insufficient data.
‡Removed from the U.S. market.
§Not yet graded.
PEG, polyethylene glycol.
Prokinetic Agents

- Tegaserid – 5HT4 agonist – Withdrawn from market
- Prucalopride – 5HT4 agonist – in clinical trials
- Peripheral Mu – opioid antagonists – methylnaltrexone to reverse narcotic bowel syndrome
- Alvimopan – for surgical ileus recovery
Other Agents

- Cholinergic agents
  - Bethanechol, neostigmine, botulinum toxin
- Newer neurotrophins
  - NGF, BDNF, neurotrophin 3
  - Linogliride – guanylate cyclase C agonist
Other Forms of Therapy

- Defecation training
- Anorectal biofeedback
- Complementary Alternative Medicine
- Sacral nerve stimulation
- Surgery – Colectomy with ileorectal anastomoses
PDF of Talk can be found here:

- https://louisville.edu/medschool/gimedicine/division-education/miscellaneous-.html