Constipation unplugged.

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No financial disclosures!
Learning objectives

Define and classify.
Mechanisms.
Evaluation.
Management.
Prevention.
The challenges

Self-reported constipation in older people is associated with anxiety, depression, and poor health perception, why clinical constipation in vulnerable individuals may lead to complications such as fecal impaction’s, overflow incontinence, sigmoid volvulus, and urinary retention.

Constipation is an expensive condition, with high Council meeting from laxative expenditure to Nursing time. An estimated 80% of community nurses working with older people list managing constipation, particularly disimpaction, as a part of their case load.
The challenges

Physicians tend to have a dismissive attitude about constipation and tend not to take the problem seriously. Patients are keen to find a solution but often feel that useful and empathetic advice and information are generally unavailable.

Majority of the patients have a strong imperative for self management including over-the-counter laxatives. Lifestyle modifications such as eating fruits and vegetables tend to be expensive, increased water intake can put them at risk for urinary incontinence and increasing physical activity can be challenging for those living alone or have disabilities.
Comparison of histology of stomach, small- and large intestines

- 5 feet long and 3 times more volume.
- 12 to 48 Hours.
- 3X per day to 3X per week.
- 1 liter of water each day.
- 100 trillion microbes. 24-52% of your stool weight.
• 68-year-old female with PMHx of HTN, type 2 DM, HLD, and hypothyroidism presents to the clinic with complaints of difficulty in passing bowel movements and hard lumpy stools since the past 4-5 weeks after she moved in with her son. Can this be called constipation based on the clinical definition of constipation?

A) Yes

B) No
What is constipation?
Definition

• Constipation is defined as - “a syndrome of difficulty in moving bowels, characterized as difficulty or infrequent passage or stool, hardness of stool or a feeling of incomplete evacuation, in at least 25% defecations, that may occur either in isolation or secondary to another underlying disorder.”
Definition

• The above criteria must be fulfilled for the last three months with symptom onset six months prior to diagnosis, loose stools should rarely be present without the use of laxatives, and there must be insufficient criteria for a diagnosis of irritable bowel syndrome.
Challenges with the definition

• This definition however is challenging to use clinically as everyone’s perception of a normal bowel movement is quite different.

• In the past, Bristol stool charts were used infrequently by physicians who would be keen on understanding the constipation in the patient. They have, on occasion, been replaced by pictures on the patients iPhones.
Definition

• Clinically the best way to diagnose constipation is to rely on patient’s perception. Changes in form and/or consistency along with hard stools or excessive straining should be reliable ways of diagnosing constipation.

• Although objectively hard to confirm these findings along with the need for enemas or digital in disinfection is a very useful way to collaborate the patient’s perception of difficult defecation.
Rome IV criteria
Functional constipation

• Must include 2 or more of the following:
  a. Straining during more than 25% of defecations.
  b. Lumpy or hard stools (the Bristol Stool Form Scale1-2) more than 25% of defecations.
  c. Sensation of incomplete evacuation more than 25% of defecations.
  d. Sensations of anorectal obstruction/blockage more than 25% of defecations.
  e. Manual maneuvers to facilitate more than 25% of defecations (e.g., digital evacuation, support of the pelvic floor)

• Fewer than 3 spontaneous bowel movements per week Loose stools are rarely present without the use of laxatives

• Insufficient criteria for irritable bowel syndrome
Rome IV criteria
Functional defecation disorders

• Must satisfy criteria for functional constipation.

PLUS

• During repeated attempts to defecate it must have at least two of the following:
  a) Evidence of impaired evacuation, based on balloon expulsion test or imaging.
  b) Inappropriate contraction of the pelvic floor muscles (i.e., anal sphincter or puborectalis) or than 20% relaxation of basal resting splinter pressure by manometry, imaging, or EMG.
  c) Inadequate propulsive forces assessed by manometry or imaging.
Rome IV criteria
IBS-C constipation

• 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:
  a) Related to defecation
  b) Associated with a change in frequency of stool
  c) Associated with a change in form (appearance) of stool
Constipation is:

- Reduced frequency.
- Hard stools.
- Difficulty in evacuation.
Epidemiology
Prevalence

• The median prevalence is 16% in all adults.
• However, in older people, it is about 33.5% (60-101 years).
• It is greater in people who are not white, institutionalized people, and in women; the median prevalence ratio for women to men is 1.5:1.
• Laxatives are used daily by 10-18% of community dwelling older adults and 74% of nursing home residents.
Risk factors

• Increasing age
• Female sex
• Lower socioeconomic status
• Lower parental education rates
• Less self-reported physical activity
• Certain medications
• Stressful life events
• Physical and sexual abuse
• Depression
Economic impact

• 22% seek health care for constipation.
• 8 million ambulatory visits annually.
• Medical costs in excess of $230 million annually.
• Costs were 2-fold greater in women with constipation.
• 33% of total annual all-cause medical expenses - $8700 more in medical expenses.
Pathophysiology
Pathophysiology of constipation

• A substantial proportion have normal colonic transit and anorectal functions.
• Colonic motor dysfunction (i.e., STC) and impaired defecation (i.e., DD), which may occur in isolation or coexist.
• Abnormal colonic sensation and disturbances of the colonic microbiome may also contribute.
• Whereas some DDs are also associated with slow colonic transit, it is useful to consider mechanisms of STC and DDs separately.
Normal and slow transit constipation

• In normal-transit constipation, colonic motility (the way muscles contract and relax to move contents through the colon) is unaltered; stool moves through the colon at a normal rate.

• However, patients with normal-transit constipation may experience other difficulties in stool passage, for example due to harder stools.

• Normal-transit constipation is not synonymous with IBS-C because 23% of patients with IBS-C had delayed colonic transit in one study.
Normal and slow transit constipation

• In contrast, in slow-transit constipation colonic motility is decreased and bowel movements are infrequent, leading to more severe symptoms of straining and harder stools.

• Isolated STC is defined as slow colonic transit in the absence of a DD or megacolon.

• Isolated STC is regarded as a manifestation of colonic motor dysfunction and may result from inadequate caloric intake.

• Colonic inertia is defined by markedly reduced or absent responses to a meal and to a pharmacological stimulus (eg, bisacodyl or neostigmine) rather than solely by STC.
Defecatory disorders (pelvic floor dysfunction)

• The pelvic floor is a group of muscles that supports the organs within the pelvis and lower abdomen which plays an important role in defecation.

• Persons with pelvic floor dysfunction have a functional outlet obstruction, a defect in the coordination necessary for stool evacuation. This usually occurs due to the failure of the pelvic floor muscles (including the anal sphincter) to relax appropriately during evacuation efforts.

• This condition is known variously as “dyssynergic defecation,” “pelvic floor dyssynergia,” “paradoxical pelvic floor/puborectalis contraction,” “obstructed defecation,” “outlet obstruction,” or “anismus.”
Other disturbances

• Some patients may have abnormal colonic and/or rectal sensation. Increased rectal sensation is associated with abdominal pain and bloating, suggestive of irritable bowel syndrome (IBS).
• Conversely, reduced rectal sensation may explain why some patients do not experience the desire to defecate.
• Constipation is associated with alterations of the colonic mucosal microbiome independent of colonic transit; genera from Bacteroidetes are more abundant in constipated patients.
• Disturbed synthesis of bile acids, which stimulate colonic secretion when they are not absorbed in the terminal ileum, has been observed.
Classification

- Normal transit constipation
- Slow transit constipation
- Pelvic floor dysfunction or defecatory disorders
- IBS-C if pain or significant GI discomfort is present
Evaluation
Clinical evaluation

• The clinical assessment should elicit the specific symptoms of constipation, clarify which are most distressing, and assess for medications that cause constipation.

• Concerning symptoms include blood admixed with stools, a sudden change in bowel habits (especially after age 50 years), anemia, weight loss, and a family history of colon cancer.

• The timing of symptom onset (e.g., onset during childhood), dietary calorie and fiber intake, a history of abuse, and obstetric events should be recorded.

• Patients should be asked about maneuvers (e.g., straining to begin and/or to end defecation) they use to defecate.
Clinical evaluation

• Some symptoms (i.e., sense of anal blockage during defecation, need for anal digitation, or a sense of incomplete evacuation after defecation) are more suggestive of DD.

• The utility of bowel diaries and pictures of stool form (e.g., by the Bristol Stool Form Scale) for efficiently and reliably characterizing bowel habits cannot be overemphasized.

• By contrast, self-reported stool frequency is unreliable and does not predict colonic transit.

• In constipated patients, laxatives can predispose to alternating constipation and diarrhea, which may lead to a misdiagnosis of IBS.
Testing
Question

Based on American College of Gastroenterology guidelines, which of the following blood test has more utility in the management of constipation compared to others?

1) CBC
2) TSH
3) Serum calcium
4) Serum fasting glucose
Diagnostic tests

• A complete blood cell count may be useful for diagnosis.
• The diagnostic utility and cost-effectiveness of fasting serum glucose, sensitive thyroid-stimulating hormone, and calcium measurements is very low.
• Colonoscopy to identify colon cancer is required only in patients with concerning clinical features or constipation refractory to medical management, and for patients who have not had an age-appropriate colon cancer screening.
• A rectal balloon expulsion test and anorectal manometry should be performed in constipated patients who do not respond to a high-fiber diet and nonprescription laxatives.
Rectal balloon expulsion test

- This test measures the time required for a patient to evacuate a water-filled balloon in the seated position; the normal value depends on the technique and is generally less than 1 minute.

- Although the test is highly sensitive and specific for identifying DD, the results may be falsely normal in patients with pelvic laxity, for example, because in one study more than 90% of patients with a large rectocele, enterocele, peritoneocele, and/or sigmoidocele had a normal balloon expulsion test result.

- In these patients, the normal result on the balloon expulsion test may not reflect normal anorectal functions.
Balloon filled with 50 mL water

Anal canal closed

Polyethylene catheter

3-way stopcock → to pressure transducers

Normal < 60 seconds

Patient sits on toilet

Patient tries to expel balloon
Anorectal manometry

• In addition to high resting anal pressure, manometry may reveal a reduced rectoanal gradient during evacuation.

• However, even among healthy controls, the rectoanal gradient (ie, rectal-anal pressure) during evacuation can be negative, for example, up to −55 mm Hg in asymptomatic women.

• This feature is counterintuitive because a positive gradient is necessary for normal evacuation. This limits the utility of the rectoanal gradient during evacuation for diagnosing DD.

• Anal resting pressure, anal pressure during evacuation greater than the 90th percentile, rectal pressure, anal relaxation, or rectoanal gradient less than the 10th percentile value in sex-matched controls) suggest a DD.
Defecography

- Defecography is generally used when the results of anorectal manometry do not concur with the clinical impression and/or when anatomic abnormalities (e.g., a clinically important rectocele) are suspected.

- The most relevant findings in DD include inadequate or excessive perineal descent or widening of the anorectal angle during defecation.

- Other features include internal rectal intussusception, solitary rectal ulcers, rectoceles, and rectal prolapse. If the vagina and small intestine are opacified, enteroceles, bladder, and uterovaginal prolapse are also visible.

- In some cases magnetic resonance defecography is preferable for visualizing the bony landmarks, which are necessary for measuring pelvic floor motion.
Defecography

Representative examples of normal and abnormal anorectal evacuation recorded with magnetic resonance imaging (top row) and high-resolution manometry (bottom row).
Colon transit

• Before the test, medications that slow or accelerate colonic transit should be discontinued.
• The most common and cost-effective approach is to use radiopaque markers (SITZMARK, Konsyl Pharmaceuticals, Inc).
• The “Hinton technique” entails ingestion of a capsule containing 24 radiopaque markers. Normally, an abdominal x-ray taken 5 days later reveals less than 5 markers remaining in the colon.
• Alternatively (ie, “Metcalf technique”), a capsule containing 24 radiopaque markers is ingested on days 1, 2, and 3. More than 68 remaining markers combined on days 4 and 7 reflect slow colonic transit.
Colonic manometry and barostat testing

• This test is used selectively in patients with medically refractory STC who are being considered for colectomy at specialized centers.
Putting it together

Colonic problems -

Outlet problems -
Treatment
• You establish that the patient has constipation that has not been treated for it. What would be the best initial treatment for her?
A) Addition of wheat bran for breakfast daily
B) Taking prune juice as needed
C) Increasing water intake and moderate exercise
D) Start senna and/or miralax
Adjunctive approaches

• Except for patients with dehydration, increased fluid intake does not treat constipation.
• There is an inverse relationship between physical activity and the severity of constipation.
• Moderate to vigorous intensive physical activity (20-60 minutes on 3-5 days per week) improve symptoms and quality of life in IBS.
• The effects of probiotics on constipation are poorly understood.
# Medical management

<table>
<thead>
<tr>
<th>Treatment, frequency</th>
<th>Dose</th>
<th>NNT (95% CI) for CC and IBS-C</th>
<th>Cost per month (2018 US $)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bulking agents: psyllium, daily</td>
<td>CC: Variable dose IBS-C: Variable dose</td>
<td>CC: 2 (1-3) IBS-C: 10 (6-33)</td>
<td>8.34</td>
<td>Start with low dose and increase gradually</td>
</tr>
<tr>
<td>Polyethylene glycol, daily</td>
<td>CC: 17 g IBS-C: NA</td>
<td>CC: 3 (2-4) IBS-C: NA</td>
<td>8.73</td>
<td>More evidence in CC than IBS-C. Improved bowel symptoms but not abdominal pain in IBS-C</td>
</tr>
<tr>
<td>Lactulose, daily</td>
<td>20 g</td>
<td>NA</td>
<td>13.28</td>
<td>Can produce bloating and distention</td>
</tr>
<tr>
<td>Bisacodyl, daily</td>
<td>CC: 10 mg IBS-C: NA</td>
<td>CC: 4 (NA) IBS-C: NA</td>
<td>5.17</td>
<td>Available as suppository, preferably administered 30 min after breakfast</td>
</tr>
</tbody>
</table>
## Medical management

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Daily Dose</th>
<th>CC (μg)</th>
<th>IBS-C</th>
<th>CC (μg)</th>
<th>IBS-C</th>
<th>CC (μg)</th>
<th>IBS-C</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Senna, daily</td>
<td>17.2-34.4 mg</td>
<td>NA</td>
<td>6.96</td>
<td>NA</td>
<td>6.96</td>
<td>NA</td>
<td>6.96</td>
<td>Widely used anthraquinone laxative</td>
</tr>
<tr>
<td>Prucalopride, daily</td>
<td>CC: 2 mg</td>
<td>CC: 6 (5-9)</td>
<td>IBS-C: NA</td>
<td>500</td>
<td>Recently approved in the United States. Available in Mexico, Canada, and Europe</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>IBS-C: NA</td>
<td>IBS-C: NA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Linaclotide, daily</td>
<td>CC: 72 or 145 μg</td>
<td>CC: 12 (6-29) (72 μg); 10 (6-19) (145 μg)</td>
<td>IBS-C: 6 (4-16) (290 μg)</td>
<td>466.47</td>
<td>Improves abdominal pain, bloating, and global IBS symptoms in IBS-C</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>IBS-C: 290 μg</td>
<td>IBS-C: 6 (4-16) (290 μg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lubiprostone, twice daily</td>
<td>CC: 24 μg</td>
<td>CC: 4 (3-6) (24 μg)</td>
<td>IBS-C: 12 (8-25) (8 μg)</td>
<td>445.32</td>
<td>Also improves abdominal bloating, discomfort, constipation severity in opioid-induced constipation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>IBS-C: 8 μg</td>
<td>IBS-C: 12 (8-25) (8 μg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Plecanatide, daily</td>
<td>CC: 3 mg or 6 mg</td>
<td>CC: 11 (8-19) (3 mg); 12 (8-23) (6 mg)</td>
<td>IBS-C: 9 (6-16) (3 mg); 9 (6-17) (6 mg)</td>
<td>466.16</td>
<td>Same as linaclotide</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>IBS-C: 3 mg or 6 mg</td>
<td>IBS-C: 9 (6-16) (3 mg); 9 (6-17) (6 mg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>
Patient with chronic idiopathic constipation

Supplement dietary fiber intake and/or OTC laxatives (Table 4)

Anorectal Manometry balloon expulsion test

- Normal
  - Treat with secretory agent (if one fails, try another)
    - Colonic transit
      - Slow
        - Slow-transit constipation
          - Options—medications, loop ileostomy, colectomy/IRA
      - Normal
        - Normal-transit constipation (? IBS)

- Inconclusive
  - Defecography
    - Normal
    - Abnormal
      - Defecatory disorder
        - Pelvic floor biofeedback therapy

- Abnormal
  - Suppositories/enemas Loop ileostomy
Fiber

• Soluble dietary fiber (e.g., psyllium or ispaghula) supplements reduce bowel symptoms in chronic constipation and IBS.
• Insoluble dietary fiber (e.g., wheat bran) does not.
• Soluble fiber should be considered as the first step in constipated patients, particularly in primary care.
• Beginning with a single daily dose taken with fluids and/or meals, the dose should be gradually adjusted after a 7- to 10-day period. Response may manifest over several weeks. Patients should be reminded that fiber supplements may increase gaseousness.
• Gaseousness improves over time or can be reduced by switching to a different fiber supplement.
Osmotic laxatives

- Another initial option is an osmotic agent, administered daily and supplemented, when necessary, with stimulant laxatives.

- No studies have compared osmotic and stimulant laxatives. A meta-analysis of 7 controlled studies with 1141 patients who had chronic idiopathic constipation observed that the NNT for osmotic and stimulant laxatives was 3.

- Osmotic agents (ie, polyethylene glycol [PEG]–based solutions), magnesium citrate–based products, sodium phosphate–based products, and nonabsorbable carbohydrates (ie, lactulose) draw fluid into the intestinal lumen to maintain gut isomolality, thereby increasing stool water and colon propulsion.

- The dose should be titrated to produce soft but not liquid stools.

- For PEG, there is extensive evidence, including a controlled trial lasting 6 months and retrospective studies that confirm that treatment with PEG is safe and effective for up to 24 months.
Osmotic laxatives

- Magnesium hydroxide and other salts improve stool frequency and consistency. Among 244 constipated women, a natural mineral water rich in magnesium and sulfate was safe and improved symptoms of chronic constipation over 2 weeks compared with mineral water that was low in magnesium.
- Although absorption of magnesium is limited, patients with renal disease may experience severe hypermagnesemia.
- Adverse effects of sodium phosphate–based bowel cleansing preparations include hyperphosphatemia, hypocalcemia, and hypokalemia; less than 1 in 1000 individuals have development of acute phosphate nephropathy.
Osmotic laxatives

- PEG was better than lactulose for improving stool frequency, stool consistency, and abdominal pain in a Cochrane Database review of 10 randomized trials.
- In a randomized crossover study of 30 men, lactulose and sorbitol were equally effective, but lactulose was associated with more nausea.
- Bacterial metabolism of these unabsorbed carbohydrates leads to gas production.
Stimulant laxatives

• Stimulant laxatives such as senna, bisacodyl, and sodium picosulfate induce propagated colonic contractions.
• Even long-term use is very safe; bisacodyl and sodium picosulfate have antiabsorptive and secretory effects.
• These agents may be used as rescue agents, (e.g., if patients do not have a bowel movement for 2-3 days) or more regularly if required.
• Stimulant suppositories (i.e., bisacodyl and glycerin) should be given about 30 minutes after breakfast in order to synchronize their effects with the gastrocolonic response.
• Stimulant laxatives do not appear to damage the enteric nervous system.
Intestinal secretagogues

- Secretagogues such as lubiprostone, linaclotide, and plecanatide are approved by the US Food and Drug Administration (FDA) for treating chronic constipation and IBS-C.

- These agents increase intestinal chloride secretion by activating channels on the apical (luminal) enterocyte surface.

- To maintain electroneutrality, sodium is also secreted into the intestinal lumen by other ion channels and transporters. To preserve isosmolality, water secretion follows.
Intestinal secretagogues

- Lubiprostone, a bicyclic fatty acid derivative of prostaglandin E1, primarily activates the apical type 2 chloride channels; it accelerates small intestinal and colonic transit in healthy individuals.

- In women of childbearing age, a negative pregnancy test result should be documented before starting treatment, and contraceptive measures are necessary.

- Like the heat-stable enterotoxins that cause diarrhea, linaclotide is a 14-amino acid peptide.

- These heat stable toxins, which are also homologues of the endogenous paracrine hormones uroguanylin in the small intestine and guanylin in the colon, act on guanylyl cyclase C, which is expressed in brush border membranes of intestinal mucosal cells from the duodenum to the rectum.
Intestinal secretagogues

- Plecanatide is a newly approved guanylyl cyclase C agonist for the treatment of both chronic constipation and IBS-C.
- Plecanatide demonstrated efficacy and safety in a randomized placebo-controlled trial of over 1300 patients with chronic constipation.
- Both 3-mg and 6-mg doses had approximately 7% more efficacy than did placebo (20% for both doses vs 12.8% for placebo; P<.004) over a 12-week trial.
- A recent systematic review and meta-analysis concluded that linaclotide and plecanatide were equally effective and safe, as might have been anticipated.
Serotonin 5-Hydroxytryptamine receptor agonists

• By stimulating serotonin 5-hydroxytryptamine 4 (5-HT₄) receptors, which are widely distributed on enteric neurons, 5-HT₄ agonists release the excitatory neurotransmitter acetylcholine and induce mucosal secretion.

• The European Agency for Evaluation of Medicinal Products approved prucalopride, a 5-HT₄ agonist, for treating chronic constipation in women in whom laxatives fail to provide adequate relief.

• It was recently approved by the FDA for treating chronic idiopathic constipation in the United States. Prucalopride is safe and does not have adverse cardiovascular effects.
Comparison

• Based on meta-analyses, systematic reviews, and the only head-to-head comparative study, therapeutic trial(s) of fiber supplementation, osmotic laxatives, and/or stimulant laxatives, which are effective, safe, and generally less expensive, should be implemented before newer agents (secretagogues, serotonin 5-HT_4 receptor agonists in Europe) are considered.

• First, the numbers in the previously mentioned table may not be strictly comparable because different studies used different end points.

• Second, except for soluble fiber, there is more evidence for efficacy in chronic constipation than in IBS-C. Although lubiprostone, linaclotide, and plecanatide have been studied in IBS-C, there are no large high-quality trials of PEG, stimulant laxatives, or prucalopride in IBS-C.
Comparison

• Third, the evidence for efficacy in chronic constipation is strong for osmotic and stimulant laxatives, which also have the most favorable cost-benefit ratios.

• Fourth, several well-designed trials demonstrate that lubiprostone, linaclotide, and plecanatide are effective for treating chronic constipation and IBS-C.

• Lastly, because lack of response to traditional agents (eg, laxatives) was not an entry criterion for the studies of the 3 secretagogues, the incremental utility of these newer agents over traditional approaches is unknown.
Opioid Induced Constipation
Opioid induced constipation

- Over the past 2 decades, the use of opiates and opioids for chronic pain has assumed epidemic proportions.
- Between 40% and 90% of patients taking opioids have constipation.
- Opioids delay GI transit, stimulate nonpropulsive motor activity, increase intestinal segmentation, and decrease electrolyte and water secretion into the gut.
- These effects work predominantly through μ-opioid receptors located in the gut as well as the central nervous system and may be difficult to overcome with most available laxatives.
- Lubiprostone is slightly better than placebo and is of similar efficacy to prucalopride
Opioid induced constipation

• A more biologically plausible approach to (OIC) is to use an effective peripheral \( \mu \)-opioid receptor antagonist.
• These drugs do not substantially counteract the benefits of pain reduction.
• For example, **naloxegol** is a pegylated derivative of naloxone that does not cross the blood-brain barrier. Two randomized, placebo-controlled trials involving 1352 patients found that naloxegol in doses of 12.5 mg or 25 mg daily were superior to placebo over a 12-week trial.
• Response rates to the 25-mg dose were considerably higher with drug vs placebo (44.4% vs 29.4%; 39.7% vs 29.3%) with a number needed to treat of 6.7 and 9.7, respectively.
Opioid induced constipation

• Similarly, in a meta-analysis, methylnaltrexone in doses of 0.15 mg/kg and 0.20 mg/kg body weight every other day when given subcutaneously and 12 mg daily when given orally, were substantially superior to placebo.

• These agents together with naloxone, naldemedine, and lubiprostone are approved for treating OIC in the United States.

• The peripheral μ-opioid receptor antagonist alvimopan shortens postoperative ileus but is not approved for treating OIC.
Management of DDs

- Nonstructural DDs are best managed by biofeedback-aided pelvic floor therapy, which is more effective than PEG, sham feedback, or diazepam.
- In one study, colonic transit normalized after **biofeedback therapy** in 65% of patients with disordered defecation, which suggests that pelvic floor dysfunction may delay colonic transit.
- These trials employed 5 to 6 training sessions lasting 30 to 60 minutes at 2-week intervals. The therapist's skill and experience and the patient's motivation influence the response to biofeedback therapy.
- Aided by visual or auditory feedback of anorectal and pelvic floor muscle activity, which are recorded with surface electromyographic sensors or manometry, patients are taught to increase intra-abdominal pressure and relax the pelvic floor muscles during defecation.
- Thereafter, patients learn how to expel an air-filled balloon. When rectal sensation is reduced, sensory retraining may also be provided.
Management of DDs

• Regrettably, biofeedback therapy is not widely used to manage DD, perhaps because the therapy is not widely available and/or its benefits are not widely recognized. Many therapists inappropriately teach patients with DD to strengthen the external anal sphincter rather than improve coordination between abdominal and pelvic floor motion during evacuation.

• Third-party coverage for biofeedback therapy in DD has improved and may be more accepted when using the entirely appropriate term muscle rehabilitation therapy.

• In several states, the CMS now regards biofeedback therapy as medically necessary for treating constipation due to DD.

• When insurance carriers deny approval for biofeedback therapy in patients with DD, the decision should be appealed.
Role of surgery

• Abdominal colectomy and ileorectal anastomosis is the next option in patients with medically refractory STC who do not have diffuse upper GI dysmotility or a DD. Some studies suggest that quality of life improves and is sustained over time.

• Other surgical or minimally invasive approaches for STC include antegrade colonic enemas that are administered by infusing water into the colon, either through an appendiceal conduit (Malone procedure) or indwelling cecostomy catheter (percutaneous endoscopic cecostomy [PEC]).

• Because a PEC can be performed under local anesthesia and conscious sedation, it may be preferred to colectomy in patients who have a higher surgical risk due to comorbidities. Also, a PEC is reversible. By comparison, 30% of patients have complications after the Malone procedure.

• In patients with STC, severe bloating, and/or abdominal pain, a venting ileostomy may be useful to determine if symptoms are attributable to the small intestine or colon. An ileorectal anastomosis may be inadvisable if symptoms do not improve with a venting ileostomy.
Malone procedure
Other approaches

- Sacral nerve stimulation, dividing the puborectalis muscle, and performing a postanal repair do not improve symptoms of constipation and are not FDA approved for use in the United States.
- Injection of botulinum toxin into the puborectalis muscle cannot be recommended for managing DD.
- The efficacy of the stapled transanal resection procedure, wherein staples are applied to the redundant rectal mucosa associated with rectocele and intussusception is uncertain, and the link between symptoms and actual anatomic abnormalities is tenuous.
- In one study, the $\alpha_1$-adrenergic receptor antagonist reduced anal pressure at rest and during simulated evacuation but did not improve symptoms in patients with DD.
Conclusion

- Constipation is common.
- Constipation is expensive.
- Health care providers should routinely inquire about constipation.
- Health care providers be more alert to individuals unable to communicate.
- In higher risk patients, a stepwise approach to prescribing medications should be used.
- Rectal evacuation difficulties should be specifically addressed to identify additional interventions.
References

• Bouchoucha, M., Devroede, G., Mary, F., Bon, C., Bejou, B., and Benamouzig, R. Painful or mild-pain constipation? a clinically useful alternative to classification as irritable bowel syndrome with constipation versus functional constipation. *Dig Dis Sci.* 2018; 63: 1763–1773
• Whitehead, W.E., Palsson, O.S., and Simrén, M. Biomarkers to distinguish functional constipation from irritable bowel syndrome with constipation. *Neurogastroenterol Motil.* 2016; 28: 783–792
• Bharucha, A.E. and Sharma, M. Painful and painless constipation: all roads lead to (a change in) Rome [editorial]. *Dig Dis Sci.* 2018; 63: 1671–1674
• Kinnunen, O. Study of constipation in a geriatric hospital, day hospital, old people’s home and at home. *Aging (Milano).* 1991; 3: 161–170
References


- Martin, B.C., Barghout, V., and Cerulli, A. **Direct medical costs of constipation in the United States.** *Manag Care Interface.* 2006; 19: 43–49

- Choung, R.S., Branda, M.E., Chitkara, D. et al. **Longitudinal direct medical costs associated with constipation in women.** *Aliment Pharmacol Ther.* 2011; 33: 251–260


Thank You!