Approach to the Patient with Chronic Constipation

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Diagnosis of Chronic Constipation
Infrequency Is Not the Most Frequent Symptom

- Straining: 81%
- Hard/lumpy stools: 72%
- Incomplete emptying: 54%
- Stool cannot be passed: 39%
- Fullness or bloating: 37%
- <3 BMs per week: 36%
- Digital maneuvers: 28%

Infrequency Is Not the Most Frequent Symptom

Rome III Criteria for Chronic Constipation

• Two or more of the following symptoms*:
  – Straining
  – Lumpy or hard stools
  – Sensation of incomplete evacuation
  – Sensation of anorectal obstruction/blockage
  – Manual maneuvers to facilitate defecation
  – < 3 BMs/week

• Loose stools are not present without laxative use

• Insufficient criteria for IBS (i.e., little abdominal pain)

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

What Is Constipation?  
A Broader Definition

• Unsatisfactory defecation characterized by infrequent stools, difficult stool passage, or both

• Difficult stool passage includes
  – Straining
  – A sense of difficulty passing stool
  – Incomplete evacuation
  – Hard/lumpy stools
  – Prolonged time to expel stool
  – Need for manual maneuvers to pass stool

Differentiating Between Chronic Constipation and IBS-C

Pathophysiology of Constipation

Chronic Idiopathic Constipation

- Normal-transit constipation
- Defecatory disorders
  - Pelvic floor dyssynergia
  - Megarectum
  - Rectocele
  - Perineal descent
- Slow-transit constipation (colonic inertia)

Normal Anorectal Physiology

At rest

When evacuating
What Is Pelvic Floor Dyssynergia?

- Paradoxical anal sphincter contraction or involuntary anal spasm (anismus) during attempted defecation
- An acquired disorder in approximately 2/3 of patients
- 1/3 of patients may have never learned the process of defecation properly (present since childhood)

Biofeedback Therapy for Pelvic Floor Dyssynergia

- Patient views pressure signals of the anal sphincter on a monitor during relaxing and squeezing to train pelvic floor muscles, emphasizing coordination
- Rapport with therapist is crucial to success
- Effects appear to be long lasting

Distinguishing Between Constipation Subtypes

- Suggestive of slow transit
  - Lack of urge
  - Decreased stool frequency

- Suggestive of defecatory disorder
  - Hard stools
  - Impaction
  - Need for digital maneuvers
  - Feelings of anal blockage
  - Severe straining
  - High anal sphincter tone at rest
  - Minimal < 1.0 cm or excessive > 3.5 cm perineal descent
  - Puborectalis muscle is tender on palpation
  - Defect in anterior wall of the rectum suggestive of a rectocele

Initial Management of Chronic Constipation

Identify predominant symptoms
- infrequent stools
- difficult stool passage, or both

Look for red flags and underlying causes

Red flags
- Appropriate diagnostic tests

No red flags
- Empiric treatment
Alarm Features That May Suggest an Underlying Cause of Constipation

- Hematochezia
- Family history of colon cancer
- Family history of IBD
- Anemia
- Positive fecal occult blood test
- “Unexplained” weight loss ≥ 10 pounds
- Severe, persistent constipation that is unresponsive to treatment
- New-onset constipation in an elderly patient
Potential Underlying Causes of Constipation

- Medications
- Mechanical obstruction
- Metabolic and endocrine disorders
- Neurological disorders
- Central nervous system disorders
- Collagen vascular and muscle disorders
- Pregnancy

Borum ML. *Prim Care* 2001;28:577.
Basic Clinical Laboratory Tests

• Complete blood count
• Thyroid function tests
  – TSH, free T4
• Measurements of
  – Calcium
  – Electrolytes
• Data do not exist to validate or define the tests that need to be performed
• American College of Gastroenterology task force does not recommend diagnostic testing in patients without alarm signs or symptoms
  – Routine colon cancer screening is recommended for all patients age ≥ 50 years (African-Americans ≥45 years)

## Advanced Diagnostic Tests

<table>
<thead>
<tr>
<th>Test</th>
<th>Use</th>
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</table>
| Anorectal manometry       | • Assesses the internal and external anal sphincters, pelvic floor, and associated nerves  
                           | • Screening test of choice for outlet obstruction                   |
| Balloon expulsion         | • Detects defecatory disorders                                      |
|                           | • Simple, office-based screening test                               |
| Defecography              | • Detects structural abnormalities of the rectum                    |
|                           | • Operator dependent, poor reliability, not widely available         |
| Colonic transit study     | • Measures rate at which fecal mass moves through colon              |

Treatment
First-line Approaches to Treating Constipation

• Lifestyle measures
  – Increase fluid and dietary fiber intake
  – Exercise
  – Dedicated time to have a BM

• Fiber supplementation
  – Begin with 4-6 grams per day
  – Increase gradually as tolerated
  – Recommended intake is 20 to 25 grams per day


- Bran fiber
- Psyllium
- Methylcellulose
- Calcium polycarbophil
- Guar gum
# Bulking Agents and Stool Softeners

<table>
<thead>
<tr>
<th>Laxative</th>
<th>Description</th>
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<tbody>
<tr>
<td><strong>Bulking Agents</strong></td>
<td>Absorb liquids in the intestines and swell to form a soft, bulky stool, which stimulates a bowel movement</td>
</tr>
<tr>
<td></td>
<td>Psyllium appears to improve stool frequency and consistency</td>
</tr>
<tr>
<td></td>
<td>No well-designed studies to assess other bulking agents</td>
</tr>
<tr>
<td><strong>Stool Softeners</strong></td>
<td>Helps liquids mix into the stool and prevent dry, hard stool masses (eases straining rather than causing a bowel movement)</td>
</tr>
<tr>
<td></td>
<td>Appear inferior to psyllium for increasing stool frequency</td>
</tr>
<tr>
<td></td>
<td>Minimal, if any, effect on symptoms</td>
</tr>
</tbody>
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### Osmotic Laxatives
- **Polyethylene glycol (PEG)**
- **Saline laxatives**: magnesium hydroxide, magnesium citrate, sodium phosphate, sodium sulfate
- **Poorly absorbed sugars/sugar alcohols**: lactulose, sorbitol, mannitol, lactitol, glycerin suppositories

Lactulose and PEG improve stool frequency and consistency.

Insufficient data to make a recommendation about magnesium hydroxide (milk of magnesia).

### Stimulant Laxatives
- **Diphenylmethane derivatives**: bisacodyl, sodium picosulfate
- **Castor oil**
- **Anthraquinones**: senna, cascara sagrada, aloe

Insufficient data to make a recommendation (no placebo-controlled trials)

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### American College of Gastroenterology 2005 Task Force Recommendations

**Summary: Bulking Agents & Laxatives**

<table>
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<tr>
<th>Therapy</th>
<th>Recommendation</th>
<th>Grade</th>
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</thead>
<tbody>
<tr>
<td>Psyllium</td>
<td>Increases stool frequency</td>
<td>B</td>
</tr>
<tr>
<td>Stool softeners</td>
<td>May be inferior to psyllium for increasing stool frequency</td>
<td>B</td>
</tr>
<tr>
<td>PEG and lactulose</td>
<td>Improve stool frequency and consistency</td>
<td>A</td>
</tr>
</tbody>
</table>

Are Lifestyle Changes, Bulking Agents and Laxatives Satisfactory?

4680 respondents with constipation

Not completely satisfied

Completely satisfied

53%

47%

Lubiprostone: A Chloride Channel Activator

• Lubiprostone is a gastrointestinal-targeted bicyclic functional fatty acid

• Selectively activates ClC-2 chloride channels, enhancing intestinal fluid secretion and promoting motility

• Approved by the FDA for treatment of chronic idiopathic constipation in adults (24µg BID dose) and IBS-C (8µg BID dose)

SBM within 24 h of First Dose

**Phase III-1**  
Placebo: 37%  
Lubiprostone: 57%  
N=242

**Phase III-2**  
Placebo: 32%  
Lubiprostone: 63%  
N=232

* p<0.01 vs. placebo

Precautions with Lubiprostone

• Nausea is the most common side-effect and can be minimized by ingesting drug with food

• Avoid in cases with mechanical bowel obstruction, diarrhea, allergy to drug

• Pregnancy category: C
  – Check pregnancy test before initiating therapy when appropriate
  – Have patient use contraception when appropriate
Agents in the pipeline

• Linaclotide\(^1\)
  – Guanylate cyclase activator: opens CFTR channel

• Prucalopride\(^2\)
  – 5-HT\(_4\) receptor agonist

Key Points

• Chronic constipation is a common condition with multiple mechanisms

• If no red flags present, can limit diagnostic testing and start empiric treatment

• There are few high-quality studies evaluating efficacy of bulking agents, stool softeners, or stimulant laxatives in chronic constipation

• PEG, lactulose, and lubiprostone have been shown to be efficacious in treating chronic idiopathic constipation