There will be references to the unlabeled and currently unapproved use of sodium picosulfate (limited availability in the US).

### Disclosures

All faculty, course directors, planning committee, content reviewers and others involved in content development are required to disclose any financial relationships with commercial interests. Any potential conflicts were resolved during the editorial review, prior to the beginning of the activity.

<table>
<thead>
<tr>
<th>Faculty</th>
<th>Commercial Interest Name</th>
<th>What Was Received</th>
<th>For What Role</th>
<th>For What Clinical Area/Disease State</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nimish Vakil, MD, FACP, FACG, AGAF, FASGE</td>
<td>Ironwood Pharmaceuticals</td>
<td>Consulting Fee</td>
<td>Attending advisory board</td>
<td>IBS-C</td>
</tr>
</tbody>
</table>

There will be references to the unlabeled and currently unapproved use of sodium picosulfate (limited availability in the US).

### Educational Objectives

- Identify symptoms specific to CIC to distinguish it from IBS-C.
- Diagnose CIC or IBS-C based on patients' presenting symptoms.
- Describe the Rome IV criteria for CIC and IBS-C, and demonstrate how disease severity affects patient QOL.
- Discuss the clinical guidelines for non-pharmacologic and pharmacologic options to treat patients with CIC and IBS-C.
Identifying the Patient

IBS-C vs CIC

- Pain related to bowel movements is the main differentiating feature
  - IBS-C: pain and constipation are both dominant symptoms
  - CIC: pain is not a predominant symptom and is not frequent or severe
- There is some overlap and crossover between the two conditions

Definitions – Rome IV

- IBS is a functional bowel disorder in which recurrent abdominal pain is associated with defecation or a change in bowel habits
- Criteria for a diagnosis:
  - 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
More than 25% of bowel movements are Bristol types 1 & 2 and less than 25% are types 6 & 7

OR

Patient reports that abnormal bowel movements are usually constipation

Must meet the IBS pain criteria

**Definitions – IBS-C**

**Gastroenterology 2016;150:1393-1407**

**Chronic Idiopathic Constipation**

- CIC, also know as functional constipation (FC), is a functional bowel disorder in which symptoms of difficult, infrequent, or incomplete defecation predominate.
- Patients with CIC should not meet IBS criteria, although abdominal pain and/or bloating may be present but are not predominant symptoms.
- Symptom onset should occur at least 6 months before diagnosis, and symptoms should be present during the last 3 months.

**Diagnostic Criteria for CIC**

• C2. Diagnostic Criteria for CIC
  1. 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 3 spontaneous bowel movements per week
Pathophysiology of IBS

- Environmental Contributors to IBS Symptoms
  - Early life stressors (abuse, psychosocial stressors)
  - Food intolerance
  - Antibiotics
  - Enteric infection

- Host Factors Contributing to IBS Symptoms
  - Altered pain perception
  - Altered brain-gut interaction
  - Dysbiosis
  - Increased intestinal permeability
  - Increased gut mucosal immune activation
  - Visceral hypersensitivity

Prevalence and Burden

- 35 million adults suffer from CIC
- 13 million people suffer with IBS-C
- These conditions are among the most common gastrointestinal (GI) complaints and worrisome reasons for frequent clinician visits.
- Over a 10-year period, the mean all-cause medical costs of a patient with CIC has been estimated at >$40,000.1
- IBS affects about 11% of the population globally, but only 30% of people who experience the symptoms of IBS consult physicians.2
- Approximately a third of IBS patients have the constipation-dominant subtype (IBS-C).3
- The damaging effect of IBS on health-related QOL has been found equivalent to the effects of such chronic diseases as asthma and migraine.4

AGA Survey on IBS

- Largest survey on IBS conducted by the American Gastroenterological Association
- 3200 sufferers and 300 gastroenterologists
- Results online at:
  http://ibsinamerica.gastro.org/files
  IBS_in_America_Survey_Report_2015-12-16.pdf
How Long Did it Take to Get to a Diagnosis in Patients with Chronic Constipation?

Diagnosed IBS-C

<table>
<thead>
<tr>
<th>Time Taken</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than one year</td>
<td>25</td>
</tr>
<tr>
<td>One to two years</td>
<td>30</td>
</tr>
<tr>
<td>Three to five years</td>
<td>22</td>
</tr>
<tr>
<td>Five to 10 years</td>
<td>10</td>
</tr>
<tr>
<td>More than 10 years</td>
<td>14</td>
</tr>
</tbody>
</table>

Average ~ 4 years

Evaluating the Patient with Constipation

- **Physical examination**
  - Abdominal masses
  - Distended colon
  - Rectal exam: spasm, tenderness, stool
  - Dyssynergic defecation can be diagnosed by asking the patient to bear down (sensitivity 75%, specificity 87%)

Laboratory Tests in Chronic Constipation

- CBC
- Thyroid testing is controversial
- Celiac testing more relevant for diarrhea
- A positive diagnosis can be made with a minimum of testing
Having the Constipation Conversation

Most Bothersome Symptom Reported by IBS-C Patients

Effect of IBS on Daily Life
Impact on Productivity

How many days do these symptoms interfere with your productivity?

- 10 or fewer: 44
- Between 11 and 20: 16
- More than 20: 4

Average = 9 days

How many days do these symptoms interfere with your ability to participate in a personal activity?

- 10 or fewer: 68
- Between 11 and 20: 14
- More than 20: 6

Average = 8 days

Emotions About IBS

- Frustrated: 74
- Self-conscious: 48
- Embarrassed: 39
- Fed up: 37
- Depressed: 34
- Accepting, just part of my life: 28
- Angry: 20

Average ~ 9 days

Average ~ 8 days

Emotions

- Frustrated: 74
- Self-conscious: 48
- Embarrassed: 39
- Fed up: 37
- Depressed: 34
- Accepting, just part of my life: 28
- Angry: 20

How Well Does Your Health Care Provider Understand the Burden of your Symptoms?

- Extremely: 18
- Very well: 31
- Somewhat well: 29
- Not very well: 17
- Not at all: 6

Total: 51
People with Undiagnosed Constipation Are Talking to Many People, but Not Their Doctor

IBS-C
- Diagnosed IBS-C
- Undiagnosed IBS-C

WebMD/MayoClinic: 66
Google/other search: 44
Family: 27
Friends: 25
Articles in newspapers: 16
TV: 13
Pharmaceutical/Healthcare: 14
Specific product website: 13
Facebook/Twitter/other: 10
Medical specialty society: 9
Advocacy group: 4

4 in 10 Constipated Patients Wait 3 Years or Longer Before Seeking a Diagnosis

Duration of Symptoms Before Diagnosis

Less than one year: 34
One to two years: 29
Three to five years: 17
Five to ten years: 10
More than 10 years: 11

Patients Without Diagnosis Are Often Not Asked About GI Symptoms

Has a health care professional ever asked you about gastrointestinal symptoms or regularity during an annual check-up or exam?

- Yes: 16%
- No: 71%
- Don’t remember: 13%

Did you tell your health care professional about your gastrointestinal symptoms?

- Yes: 39
- No: 40
- Don’t remember: 21
Modeling the Conversation About IBS-C and CIC

- **Speak up early**
  - Ask questions about bowel movement frequency and consistency
  - Remember that 2 of 3 patients find it more comfortable to talk about STDs than about bowel movements
- **Speak up completely**
  - Health care providers tend to move quickly past bowel symptoms
  - Elicit symptoms and impact on life with empathy
- **Speak up often**
  - It may take more than one visit to establish a conversation
  - Establish follow-up visits to follow the patient

Shared Decision Making

Evaluating the Patient: Factors Exacerbating IBS

- **Over-the-Counter**
  - Antihistamines
  - Calcium
  - Iron
  - Magnesium
  - Nonsteroidal anti-inflammatory drugs
  - Wheat bran
- **Prescription**
  - Antibiotics
  - Antidepressants
  - Antiparkinsonian drugs
  - Antipsychotics
  - Calcium-channel blockers
  - Diuretics
  - Metformin
  - Opioids
  - Sympathomimetics

JAMA. 2015;313(9):949-958.
When to Refer a Constipated Patient?

- Concerning features for organic disease
- Symptom onset after age 50
- Severe or progressively worsening symptoms
- Unexplained weight loss
- Family history of organic gastroenterological diseases, including colon cancer, celiac disease, or inflammatory bowel disease
- Rectal bleeding or melena
- Unexplained iron-deficiency anemia

JAMA. 2015;313(9):949-958.

Treatment: Fiber, Osmotic and Stimulant Laxatives

<table>
<thead>
<tr>
<th>Laxative type</th>
<th>Medications</th>
<th>Mechanism of action</th>
<th>Adverse effects</th>
<th>Level of evidence</th>
<th>Grade of recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bulk laxatives</td>
<td>Psyllium, calcium polycarbophil, methylcellulose, bran</td>
<td>Retaining water in stool, increasing stool bulk and improving consistency</td>
<td>Flatulence, bloating, abdominal distention; rarely causing mechanical obstruction of esophagus and colon</td>
<td>II</td>
<td>B/C</td>
</tr>
<tr>
<td>Osmotic laxatives</td>
<td>PEG, lactulose, sorbitol, milk of magnesia, magnesium citrate</td>
<td>Osmotic water binding</td>
<td>Bloating, flatulence, abdominal cramping; in rare instances, electrolytes disturbances</td>
<td>B/C</td>
<td></td>
</tr>
<tr>
<td>Stimulant laxatives</td>
<td>Senna, aloe, bisacodyl, sodium picosulfate</td>
<td>Increasing intestinal peristalsis by acting on myenteric nerve plexus, decreasing large intestinal water absorption</td>
<td>Abdominal discomfort, rarely electrolytes disturbance, melanosis coli</td>
<td>II</td>
<td></td>
</tr>
<tr>
<td>Stool softeners or wetting agents</td>
<td>Docusate sodium, docusate calcium</td>
<td>Promoting luminal water binding by detergent-like action, increasing stool bulk</td>
<td>Intestinal cramping; irritation of throat (liquid formulation)</td>
<td>III</td>
<td>C</td>
</tr>
</tbody>
</table>

Prebiotics, Probiotics and Diet

a) Prebiotics and symbiotics in IBS: There is insufficient evidence to recommend prebiotics or symbiotics in IBS. Recommendation: weak. Quality of evidence: very low.

b) Probiotics in IBS: Taken as a whole, probiotics improve global symptoms, bloating, and flatulence in IBS. Recommendations regarding individual species, preparations, or strains cannot be made at this time because of insufficient and conflicting data. Recommendation: weak. Quality of evidence: low.

c) FODMAPs diet plan: Used to treat IBS. Focuses on eliminating foods that contain sugars and fibers that can cause gas, abdominal pain and other symptoms. Eliminates foods that contain fermentable oligo-, di-, mono-saccharides and polys.
Flow Chart for Management in Primary Care

Approach to the Patient with Refractory or Very Severe Constipation

Take Home Messages

- Chronic constipation (IBS-C and CIC) can have a major impact on patients’ lives
- Be proactive in eliciting information
- Don’t be afraid to make a clinical diagnosis
- If lifestyle measures and PEG don’t work, move on
- Symptoms often recur and patients may need ongoing treatment and support
- Refer the patient when the symptoms are severe and fail to respond.