ABSTRACT

Though not a life-threatening condition, chronic constipation has a substantial adverse impact on health-related quality of life and is the source of a vast sum of annual healthcare expenditures. A possible contributing factor is an apparent disconnect between patient and physician views on what constitutes constipation. Patients tend to characterize constipation in descriptive, symptom-related terms, whereas physicians most often define constipation in terms of bowel movement frequency. Three subtypes of constipation have been identified: slow-transit constipation, defecatory disorders, and normal-transit constipation. The recognition of these subtypes in clinical practice can be useful in determining the most appropriate approach to treatment for an individual patient. A good medical history and physical examination form the basis for diagnosis of constipation. Laboratory assessment should be limited, and specialized testing has a role in a few patients. Current treatment options have increased in recent years and now include lifestyle changes, fiber supplementation, polyethylene glycol, lactulose, tegaserod, and lubiprostone. New agents under investigation reflect recent advances in knowledge about the underlying pathophysiologic mechanisms of constipation. Surgery rarely has a role in the treatment of constipation.

In the evaluation and management of chronic constipation, physicians’ and patients’ perspectives are shaped by the definitions they bring to the clinical setting. Patients use a variety of descriptive terms to define constipation, with straining, hard/lumpy stools, and incomplete emptying leading the list. Physicians tend to think in terms of bowel movement frequency when defining constipation. The disconnect between patient and physician perspectives can be seen in a study that showed only 13% of patients with constipation reported having fewer than 3 bowel movements weekly.

Two sets of formal criteria have been developed to define constipation. The Rome II diagnostic criteria define constipation as having at least 2 of 6 symptoms for at least 12 weeks, not necessarily consecutive, over the past year. The American College of Gastroenterology has developed a simpler and perhaps more clinically relevant definition: unsatisfactory defecation characterized by infrequent bowel movements, difficult stool passage, or both (Table 1).

Several risk factors have been associated with an increased risk for constipation, including age younger than 4 years or older than 65 years, female gender, and several concurrent diseases (ie, multiple sclerosis, dementia, or Parkinson’s disease). Other potential risk factors include low income, polypharmacy, decreased physical activity, limited education, and history of sexual abuse. Notably, low dietary fiber intake has not been linked to constipation.

Chronic constipation adversely affects quality of life (QOL). One representative review showed that patients with chronic constipation had consistently lower scores on the domains of a QOL assessment, including physical functioning, role function, social functioning, mental health, perception of health, and bodily pain.
Constipation also exacts a substantial economic toll. Each year, constipation leads to 2.5 million physician visits, $800 million in expenditures for laxatives, and tertiary care evaluation costs of $2752 per patient.

Clinical cases can help illustrate the applicability of constipation definitions to clinical practice. Cases also provide practical examples of the principles used to identify and manage patients with chronic constipation.

**CASE STUDY 1: CONSTIPATION**

A 42-year-old female patient presents with complaints of constipation, reporting that she has been bothered by symptoms since she was a teenager but that the symptoms have worsened recently. She reports having about 1 bowel movement weekly, which typically relieves symptoms of bloating, distension, and lower abdominal discomfort. The patient states that her symptoms have significantly affected her social and professional life. She has tried several nonprescription treatments for constipation, which have generally provided only temporary symptomatic relief or in the case of fiber, worsened her symptoms (Sidebar 1).

Notable aspects of the patient’s primary medical history include hypercholesterolemia, an appendectomy at age 7, and 2 normal spontaneous vaginal deliveries. She is married, has 2 children, works as a paralegal, does not smoke, and consumes 2 to 3 glasses of wine weekly. Her family history is notable for her father’s having type 2 diabetes and coronary artery disease, and the patient reports that her mother has a history of constipation that is self-treated with laxatives. The patient’s physical examination was unremarkable, and laboratory results were normal (Sidebar 2).

**Sidebar 1. Medication Taken Previously by Patient with Constipation**

- She has tried several over-the-counter and prescription preparations for constipation, including:
  - Fiber (i.e., diet, psyllium/methylcellulose)
  - Magnesium hydroxide
  - Senna
  - Sodium phosphate enemas
  - Lactulose
  - Bisacodyl
- These agents gave her temporary relief or in the case of fiber, worsened her symptoms

**Sidebar 2. Physical Examination and Laboratory Results of Patient with Constipation**

- Physical Examination
  - Unremarkable. Rectal examination was significant for lack of rectal scars, no external hemorrhoids or fissures. Normal resting tone with appropriate relaxation of the pelvic floor on simulated bear down. No stool was present in the rectal vault. A small rectocele was noted.
- Laboratory Results
  - Normal thyroid-stimulating hormone, complete blood count, glucose, calcium, magnesium, and phosphorus.

**CONSTIPATION SUBTYPES**

A reasonable question regarding this patient relates to the need and potential value of categorizing the patient by clinical subtype of constipation. A majority of patients with constipation have normal-transit constipation. Between 25% and 33% of patients have a defecatory disorder, about 15% have slow-transit constipation, and the remaining patients have constipation that is characterized by an overlap of the subtypes.

**Slow-transit constipation.** This subtype is characterized by impaired phasic colonic motor activity, diminished gastrocolic responses, a decrease in the number
and quality of interstitial cells of Cajal, and neuropathy associated with altered release of neurotransmitters. The condition has a strong female predominance. Patients rarely report an urge to defecate, and bloating is a prominent feature.12

Defecatory disorder. This subtype is most often associated with an inability to coordinate abdominal, rectoanal, and pelvic floor muscles during defecation (pelvic dyssynergia). In short, the patient is unable to relax the anal sphincter. The condition often represents an acquired behavioral disorder, and common features include frequent straining and/or the need for digital manipulation and incomplete evacuation. On rectal examination, the patient may have a high resting pressure, and on bear-down descent may be poor or very great.13

Normal-transit constipation. This condition overlaps with irritable bowel syndrome (IBS). The pathophysiology is poorly understood. The condition has an association with visceral hypersensitivity, and variable alteration in colonic motor function is observed. A comparison of constipation-predominant IBS (IBS-C) and chronic constipation is provided in the Figure.3,14

Do these clinical subtypes have relevance to the patients that physicians see in their practices? A diagnosis of pelvic dyssynergia may be helpful in identifying candidates for biofeedback therapy. However, little data exist to document the utility of these subtypes with respect to response to laxatives, although patients with slow-transit constipation and defecatory disorder are known not respond to dietary fiber as well as normal-transit patients. Subtyping probably has some utility, but intervention with dietary fiber remains the initial approach to clinical management for most patients, regardless of the underlying pathophysiology, because fiber is inexpensive and safe.

Testing
A good history and physical examination generally will exclude secondary causes of constipation. Little or no data support the utility of most laboratory tests for constipation, and therefore, the laboratory assessment should be limited. Examples of tests that may be useful in specific cases include thyroid-stimulating hormone, calcium, complete blood count, glucose, barium enema, colonoscopy, and flexible sigmoidoscopy. Most tests probably are not necessary for patients who are younger than 50 years and who do not have red flags (eg, blood in stool, anemia, or family history of colorectal cancer).15

Specialized testing for colonic transit and anorectal function has a limited role in selected patients whose symptoms are refractory to initial therapy. Anorectal manometry has a widely varying diagnostic yield of 20% to 75% for dyssynergia. Defecography detects abnormalities in 25% to 90% of cases, and the diagnostic accuracy for dyssynergia ranges between 13% and 37%. Large, well-designed, prospective studies are needed to examine the utility of these tests. Colonic transit time studies identify slow-transit constipation in 38% to 80% of cases.15 A review of the diagnostic tests for constipation is provided in Table 2.16

TREATMENT ISSUES AND DECISIONS
In the clinical case described above, the patient has failed several therapies, including fiber, magnesium hydroxide, senna, phosphate enemas, lactulose, and bisacodyl. What is left for her to try? If all therapies fail, is surgery an option for the patient? Although the answers to those questions are not clear-cut, traditional medical therapies for constipation have proved to be largely ineffective. A recent review showed that 15% of patients with constipation treated medically were completely satisfied, and another 28% of patients were fairly satisfied. A majority (51%) were “not particularly” or “not at all” satisfied with their medical therapy.17

Fiber. Fiber typically is first-line treatment for most patients with chronic constipation. However, available evidence suggests fiber works only on the subgroup of patients who...
patients with normal-transit constipation. Up to 80% of patients in that subgroup report complete relief of constipation symptoms in response to fiber. In contrast, 20% to 30% of patients with defecatory disorder or slow-transit constipation report that fiber improves their symptoms, and very few patients in these 2 subgroups obtain complete relief from symptoms.18

Lifestyle changes. Though frequently recommended, lifestyle changes have a mixed record in the management of chronic constipation. With respect to exercise, for example, 1 study found that the total amount of physical activity did not differ significantly between patients with and without constipation.19 In another study, a 4-week exercise program had no effect on constipation symptoms.20 On the other hand, investigators in the Nurses Health Study found that mild or moderate exercise plus high fiber intake reduced complaints of constipation.21

Increased fluid intake, another common recommendation for treatment of constipation, is unlikely to improve constipation symptoms, except in patients who are clinically dehydrated. Several studies have shown that individuals with constipation consume amounts of water that are similar to those of people without constipation.

Polyethylene glycol (PEG). With regard to the first clinical case, the patient had not yet tried PEG, which may be an option for her. This agent is a laxative that is similar to the product used for bowel cleansing before colonoscopy but has been modified chemically for therapeutic use. In a 2-week randomized, placebo-controlled trial, PEG significantly increased the rate of treatment success and received significantly higher ratings from physicians and patients with respect to treatment effectiveness.22

Polyethylene glycol and lactulose were compared in a randomized trial involving 115 patients with chronic constipation. Treatment with PEG significantly increased stool frequency, decreased straining, and led to greater overall improvement.23 Additionally, PEG was found to be more cost effective than lactulose for treatment of chronic constipation.24

Tegaserod. The patient in the clinical case also has not tried tegaserod, which offers another therapeutic consideration for her. Two placebo-controlled trials, one European and one based in the United States, had improvement in weekly complete spontaneous bowel movements (CSBM) as their primary endpoint. In both trials, 12 weeks of treatment with tegaserod significantly improved the number of weekly CSBMs and the number of spontaneous bowel movements.25,26

Lubiprostone. Lubiprostone is a novel functional fatty acid that increases secretion by selectively activating the gastrointestinal type-2 chloride channels without altering serum levels of sodium and potassium. Phase III clinical trials with lubiprostone 24 µg twice daily showed improvement in symptoms of chronic constipation, including stool frequency, stool consistency, and straining. The US Food and Drug Administration (FDA) recently approved lubiprostone for the treatment of chronic idiopathic constipation in adult men and women.

Future options. Several therapies in development reflect new approaches to treatment of chronic constipation, including the mixed serotonin agonist/antago-

<table>
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<th>Table 2. Review of Diagnostic Tests for Constipation</th>
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<tr>
<td><strong>Anorectal manometry</strong></td>
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<td><strong>Balloon-expulsion test</strong></td>
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<td><strong>Colonic-transit study</strong></td>
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<td><strong>Defecography</strong></td>
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Data from Lembo and Camilleri.24
nist renzapride, the peripheral μ-opioid antagonist alvimopan, the neuropeptide neurotensin-3, and MML-416773 (a guanylate cyclase-C agonist).

Surgery. In rare cases, patients with constipation may consider colectomy. Potential candidates for surgery are patients with slow-transit constipation that has proved refractory to all forms of medical therapy. A diagnosis of slow-transit constipation is essential, because those patients are the only ones who benefit from surgical intervention. Even with optimally selected patients, overall satisfaction ranges between 39% and 100% and is influenced by the type of surgery performed, presence or absence of generalized intestinal dysmotility, and the status of the pelvic floor (normal vs nonrelaxing). Abdominal pain and bloating often do not improve after surgery. Morbidity ranges between 2% and 71% in different series, and up to 28% of patients may require a permanent ileostomy.27

Case Study 1 Discussion

The patient had separate trials of PEG and tegaserod, which led to limited improvement. Combining the 2 agents resulted in more regular bowel movements and less bloating and abdominal discomfort. The patient now wants to know how long she can continue the combination therapy. Currently, only tegaserod has US FDA approval for long-term treatment of chronic constipation. PEG has approval for 2 weeks of continuous therapy for occasional constipation.

Long-term data for other agents are limited. In one recent as-yet unpublished study, open-label PEG and lactulose were evaluated for 6 months in a population of elderly (mean age 81 years) patients with constipation. Patients treated with PEG had significant improvement in stool frequency and in hard stools compared to lactulose. Both therapies did not cause significant changes in clinical parameters, including electrolytes, vitamins, iron, D-xylene, and α-1 antitrypsin.28

Case 2: Irritable Bowel Syndrome

A 42-year-old female presents with complaints of incomplete evacuation, straining, difficulty in passing small pebble-like stools, and crampy, lower abdominal discomfort. She spends 1 to 2 hours on the toilet each morning to evacuate her bowels. The symptoms have bothered her since she was in college and have significantly affected her work and social life. Assisted by a nutritionist, the patient has tried without success to alter her diet. Occasionally, she passes bright red blood from her rectum. Colonoscopy within the past year revealed only internal hemorrhoids. Pelvic ultrasound ordered by her gynecologist was normal.

The patient has tried laxatives, which induce diarrhea without relieving the constipation symptoms. A trial of fiber worsened her bloating and increased the difficulty of her evacuations. Tegaserod improved the bloating but caused diarrhea. Her primary medical history, medications, and social history are shown in Sidebar 3.

Sidebar 3: Medical History, Medications, and Social History of Patient with IBS

<table>
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<tr>
<th>Medical History</th>
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<tr>
<td>– History of ovarian cyst resection</td>
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<tr>
<td>– Gravida 1, parity 0</td>
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<tr>
<td>– Depression</td>
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<tr>
<td>– Lactose intolerance</td>
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<td>– History of chronic fatigue</td>
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<th>Medications</th>
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<tr>
<td>– Zoloft</td>
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<tr>
<th>Social History</th>
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<tbody>
<tr>
<td>– Attorney</td>
</tr>
<tr>
<td>– Does not smoke or drink excessive alcohol</td>
</tr>
<tr>
<td>– Exercises daily</td>
</tr>
<tr>
<td>– Married</td>
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IBS = irritable bowel syndrome

With respect to the patient’s family history, her mother died of breast cancer at age 56. Her father has a history of depression and coronary disease. She has a sister with a history of IBS symptoms similar to her own. The patient reports regular menses and that her bowel symptoms typically worsen immediately before menses. The patient discontinued oral contraceptives 2 years ago after a 7-year history of use.

The patient’s physical examination revealed that she weighed 154 pounds and had no obvious abnormalities. Her rectal evaluation included a negative guaiac stool test, elevated rectal tone, and poor relaxation of the pelvic floor muscles on simulated bear-down. Laboratory results included a normal thyroid-stimulating hormone, hematocrit of 34.1%, and mean corpuscular volume of 78.

Most patients with IBS do not warrant an extensive workup, particularly the use of diagnostic tests. At best
the data for diagnostic tests for IBS-C support limited testing in selected patients.29

The patient had a negative celiac antibody test. She underwent anorectal manometry, which showed an inability to pass a 60-mL water-filled balloon within 3 minutes and paradoxical contraction of the anal sphincter on bear-down.

**Defecatory Disorders**

The patient depicted by the second clinical case has symptoms suggestive of a defecatory disorder. Patients with defecatory disorders have a fairly typical presentation that includes prolonged straining to expel stool and unusual postures on the toilet to facilitate stool expulsion. To facilitate rectal emptying, they may employ support of the perineum, digitation of the rectum, or posterior vaginal pressure. Inability to expel enema fluid is common. Constipation persists after colectomy for constipation.17

The balloon-expulsion test offers an accurate means of identifying patients with pelvic floor dyssynergia. A silicone-filled stool-like device or a 4-cm balloon filled with 50 to 60 mL of water is inserted into the rectum, and the patient is asked to expel the device in privacy. Patients with normal pelvic floor function can expel the device in 1 minute or less. Inability to expel the device within 3 minutes suggests dyssynergia.30

Biofeedback effectively relieves symptoms of defecatory disorders in 69% to 78% of affected adults. The type of biofeedback (electromyography vs pressure biofeedback vs simulated defecation) does not influence the outcome. Biofeedback proved more effective in adults than in children. Whether biofeedback produces a specific benefit in patients with defecatory disorders has yet to be demonstrated conclusively, and more controlled clinical studies are needed to clarify the effects of this technique.

The success of biofeedback depends on appropriate patient selection. That point was emphasized in a recent clinical trial, in which patients with pelvic floor dyssynergia or slow-transit constipation underwent 5 weekly biofeedback sessions. After 6 months of follow-up, 71% of the patients with pelvic floor dyssynergia were satisfied with the therapy compared to 8% of the patients with slow-transit constipation.31

**Case 2 Discussion**

The patient received biofeedback therapy, which led to improvement in her symptoms of pelvic floor dyssynergia.

**Conclusions**

Patients and physicians have different criteria for defining and describing constipation. Recognizing the differences can help physicians better identify, counsel, and manage patients with constipation. At least 3 distinct subtypes of constipation have been identified. Appropriate categorization has value in clinical practice because currently available therapies are not uniformly effective across all constipation subtypes. Chronic constipation adversely affects a patient's social and personal life, and the annual cost of treating constipation approaches $1 billion for laxatives alone. Accurate identification of the specific features of chronic constipation improves the chances of treatment success and reduces the likelihood of unnecessary or inappropriate testing and therapy.

**Discussion**

*Dr Kalloo:* Do you agree with data suggesting that current therapies for constipation are not effective in 50% of patients and that only about 15% of patients find the therapies very effective?

*Dr Lembo:* I'm not sure. I think it depends on the people being queried, the type of questions being asked, and when the questions were asked. Most of these studies were done before tegaserod was launched, and I'm not sure how much PEG was being used at that point in time, or what treatments were actually tried in these patients.

*Dr Kalloo:* Amy, you mentioned something about rotating therapies. Do you do that when you notice the symptoms are starting to recur, or do you do it before that point?

*Dr Foxx-Orenstein:* I don't prescribe therapies on a rotating schedule as you might antibiotics for bacterial overgrowth, though I often recommend using some other laxative as a backup treatment if the patient's regimen fails for a time. It's very individual to the patient's needs. If a patient becomes “tolerant” to a therapy, then I recommend changing to a different class or agent or perhaps adding another treatment to the regimen.

*Dr Kalloo:* Tony, are you comfortable with tegaserod on a long-term basis?
**Dr Lembo:** It has been a remarkably safe drug, both from my personal experience in prescribing it to patients and from what I’ve seen in the literature.

**Dr Kalloo:** Then, if a patient is on it for 2 years, it’s OK?

**Dr Lembo:** In patients who have a good response to tegaserod I continue treatment for 3 to 6 months and then stop the medication to see if their symptoms recur. If their symptoms come back, then I’ll restart it.

**Dr Harris:** Sometimes for the IBS-C indication, some insurance companies will only allow patients to take it for 3 months, and then they have to stop it and restart it. I find it interesting that you stop and restart patients on therapy. Why do you do that?

**Dr Lembo:** I do it to see if they need to take the medication long term. In my experience, a small percentage of patients are able to stop tegaserod and not have their symptoms recur.

**REFERENCES**
