INTRODUCTION

Constipation is a common symptom, affecting up to 20% of the general population. Studies over the past decade have led to an improved understanding of the underlying pathophysiology, especially related to colonic and anorectal function. An evidence-based approach can now be used in clinical practice for the evaluation and treatment of patients with constipation. It is important to understand the symptom patterns and classification of constipation, in order to tailor therapy based on the underlying pathophysiology. This article reviews the definition and classification of constipation, along with an overview of the recommended diagnostic approach and treatment, intended for the practicing gastroenterologist.
However, patients describe a variety of symptoms to describe constipation—hard stools, small stools, straining to have a bowel movement, feeling of incomplete evacuation, and occasionally, use of digital maneuvers to assist defecation (6). The following are different classifications of constipation:

**Symptom Based Classification**

Using symptom based criteria, an international panel of experts have classified constipation into Functional Constipation and Irritable Bowel Syndrome–Constipation (IBS-C) (7). Functional Constipation has been described as a “functional bowel disorder that presents as persistently difficult, infrequent, or seemingly incomplete defecation, which do not meet IBS criteria,” with less than three bowel movements per week (7). Diagnostic criteria for Functional Constipation according to the Rome III guidelines (7,8) are shown in Table 1.

Functional constipation is further classified into slow transit constipation and functional defecation disorders (outlet obstruction) (8). Diagnostic criteria for functional defecation disorders according to Rome III guidelines are shown in Table 2. Functional defecation disorders are further classified into two categories:

- **a. Dyssynergic defecation** (paradoxical contraction or inadequate relaxation of the pelvic floor muscles during attempted defecation), and
- **b. Inadequate defecatory propulsion** (inadequate propulsive forces during attempted defecation). Diagnostic criteria for these disorders according to Rome III guidelines are shown in Table 2.

**Pathophysiology Based Classification**

Chronic constipation can be divided into three categories based on the underlying pathophysiology: a) Slow transit constipation; b) Evacuation disorders; c) Functional constipation (9–11).

**Slow Transit Constipation (STC)**

This term refers to slower than normal movement of contents from the proximal to the distal colon and rectum (12). Slow transit constipation is related to primary dysfunction of colonic smooth muscle (myopathy) or its innervation (neuropathy), or both (10). Studies have confirmed that patients with STC exhibit significantly impaired phasic colonic motor activity (13), gastro-colonic and morning waking responses, although the diurnal variation of colonic motility is preserved (10). Periodic motor activity in the rectosigmoid area is increased, serving as a brake for colonic food propulsion (14). Additionally, there is a significant decrease, not only in the number of high amplitude propagated contractions (HAPC) but also of the velocity of propagation and amplitude, leading to premature abortion of these waves in constipated patients (10,13,14).

**Evacuation Disorders**

This group includes structural abnormalities such as rectocele, rectal prolapse, intussusception, excessive perineal descent, sensory dysfunction and dyssynergic defecation. Patients with dyssynergic defecation demonstrate failure of rectoanal coordination. Based on manometric characteristics, three types of dysfunction have been recognized (15) (Figure 1). Phenotypic variability has also been described using anorectal manometry and functional pelvic MRI (16). Many patients with dyssynergic defecation also have slow transit constipation (9).

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**Table 1**

<table>
<thead>
<tr>
<th>Diagnostic Criteria for Functional Constipation*</th>
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<tbody>
<tr>
<td>1. Must include <strong>two or more</strong> of the following:</td>
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<tr>
<td>a. Straining during at least 25% of defecations</td>
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<td>b. Lumpy or hard stools at least 25% of defecations</td>
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<tr>
<td>c. Sensation of incomplete evacuation at least 25% of defecations</td>
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<tr>
<td>d. Sensation of anorectal obstruction/blockage at least 25% of defecations</td>
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<tr>
<td>e. Manual maneuvers to facilitate at least 25% of defecations (e.g. digital evacuation, support of the pelvic floor)</td>
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<tr>
<td>f. Fewer than three defecations per week</td>
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<td>2. Loose stools are rarely present without the use of laxatives</td>
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<td>3. There are insufficient criteria for IBS</td>
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*Criteria fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis
Functional Constipation

This group includes patients with chronic constipation but with normal colonic transit and pelvic floor function. Many of these patients have irritable bowel syndrome, and there have been recent insights into the underlying pathophysiology of this group of patients (17). The symptoms of constipation may arise secondary to other conditions. These include metabolic disturbances (hypercalcemia, hypothyroidism, diabetes mellitus), medications (opiates, calcium channel blockers, antipsychotics, etc), neurologic disorders (Parkinsonism, spinal cord lesions) and primary diseases of the colon (stricture, cancer, anal fissure, proctitis).

### EVALUATION OF PATIENTS WITH CONSTIPATION

A recent systematic review concluded that there is a lack of well-designed studies that have assessed the clinical utility of diagnostic procedures in adults with chronic constipation (18). The American College of Gastroenterology (ACG) Task Force recommended that the routine use of a battery of diagnostic tests should be avoided in patients with chronic constipation and that the initial approach should be empiric treatment (19). A step-wise approach to diagnosis may be

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**Table 2**

<table>
<thead>
<tr>
<th>Diagnostic Criteria for Functional Defecation Disorders *</th>
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<tr>
<td>1. The patient must satisfy diagnostic criteria for functional constipation</td>
</tr>
<tr>
<td>2. During repeated attempts to defecate must have at least two of the following:</td>
</tr>
<tr>
<td>a. Evidence of impaired evacuation, based on balloon expulsion test or imaging</td>
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<tr>
<td>b. Inappropriate contraction of the pelvic floor muscles (i.e., anal sphincter or puborectalis) or less than 20% relaxation of basal resting sphincter pressure by manometry, imaging or EMG</td>
</tr>
<tr>
<td>c. Inadequate propulsive forces assessed by manometry or imaging</td>
</tr>
</tbody>
</table>

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

**a. Dyssynergic Defecation**

Inappropriate contraction of the pelvic floor or less than 20% relaxation of basal resting sphincter pressure with adequate propulsive forces during attempted defecation

**b. Inadequate Defecatory Propulsion**

Inadequate propulsive forces with or without inappropriate contraction or less than 20% relaxation of the anal sphincter during attempted defecation

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**Figure 1.** Normal defecation pattern and the 3 subtypes of dyssynergic defecation.

a) **Normal:** note that a rise in the rectal pressure is coordinated with a drop in anal sphincter pressure or anal relaxation;

b) **Type I:** the patient can generate an adequate pushing force (rise in intra-abdominal and intrarectal pressure) along with a paradoxical increase in the anal sphincter pressure;

c) **Type II:** the patient is unable to generate an adequate pushing force (no increase in intrarectal pressure), but can exhibit a paradoxical anal contraction,

d) **Type III:** the subject can generate an adequate pushing force (increase in intrarectal pressure), but has absent or incomplete (<20%) sphincter relaxation (i.e., no decrease in anal sphincter pressure).


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beneficial and cost-effective and is commonly used in clinical practice.

**History**

Initial evaluation should always include a detailed history, including an assessment of the duration and severity of symptoms, any precipitating events, stool frequency, stool consistency (Bristol stool form scale), degree of straining during defecation, sensation of incomplete evacuation and the need for digital disimpaction of stool. Additionally, any history of ignoring stool urges changes in lifestyle, and travel should be elicited by the clinician. A dietary history should include an assessment of fiber and fluid intake and the timing of the day’s meals. Skipping breakfast may deprive the colon of the colonic propulsion that occurs during the morning waking period (20–22) and after a meal (20,23,24). History and frequency of laxative use should be reviewed. Obstetric, surgical and drug histories, along with a history of back trauma or neurological problems should be elicited.

**Physical Examination**

Physical examination should include a detailed neurological exam to evaluate for signs of neuropathy and other neurological problems. The abdomen must be examined for masses or presence of stool in the left or right lower abdominal quadrants.

The anorectal area needs to be inspected for skin excoriations, skin tags, anal fissures or hemorrhoids. Scars from previous episiotomies or obstetric tears should be noted. The perineal area should be stroked in all quadrants with a cotton bud (Q-tip) to assess sensation and the anocutaneous reflex. Stroking the perineal skin should normally activate a reflex that contracts the external anal sphincter (“anal wink”). Absence of this reflex suggests neuropathy.

Digital rectal examination (DRE) should be performed to evaluate for rectal strictures, stool in the rectal vault and heme positive stool. The anal sphincter tone should be assessed, both at rest and during squeeze. Puborectalis muscle function can be assessed during the squeeze; the muscle (which wraps around the posterior anal canal at the anorectal junction) should push the examiner’s finger anteriorly. A “bear down” maneuver needs to be performed, during which the patient attempts to simulate the act of defecation. During this maneuver, the examiner should perceive relaxation of the external anal sphincter along with perineal descent. This mechanism may be abnormal in functional defecation disorders (9).

**Blood Tests**

A complete blood count, serum electrolytes, calcium, glucose and thyroid function studies are usually performed during initial evaluation of constipation. There is, however, no evidence to support or reject the utility of these tests (18,19).

**Imaging Studies**

- **X-ray and barium enema:** A plain abdominal X-ray or abdominal obstruction series is frequently performed, although its clinical utility has not been carefully studied. This X-Ray may indicate the amount of retained stool in the colon or assess for partial obstruction. There is little evidence to support or reject its use in routine evaluation in adults with constipation. Barium enemas are also of limited clinical utility as this study cannot by itself exclude organic disease (18,19).

- **Defecography:** Defecography can provide useful information about the anatomy and can assess several parameters of anorectal function (anorectal angle at rest and during straining, perineal descent, anal diameter, indentation of the puborectalis, amount of rectal and rectocele emptying) (25,26). The technique is performed by instilling approximately 150 cc of barium paste into the rectum and recording video fluoroscopic images while the subject attempts to evacuate in the sitting position (27). However, the clinical utility of this test may be marginal because of lack of standardized technique and normal values, radiation exposure and availability of the test (13).

- **Magnetic resonance imaging:** Dynamic pelvic MRI (MR defecography) is a newer modality that can simultaneously evaluate global pelvic floor anatomy (continued on page 36)
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GI MOTILITY, A SERIES FROM THE AMS, SERIES #3

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Colonoscopy/Sigmoidoscopy

The American Society of Gastrointestinal Endoscopy (ASGE) recommends colonoscopy in patients with constipation only if they have rectal bleeding, heme-positive stool, iron deficiency anemia, weight loss, obstructive symptoms, recent onset of symptoms, rectal prolapse or change in stool caliber, and in subjects older than 50 years who have not previously had colon cancer screening (31). In younger patients, a flexible sigmoidoscopy may be sufficient to exclude distal disease. There is little evidence to support the routine use of colonoscopy in the evaluation of patients with chronic constipation without alarm symptoms (32). Often, colonoscopy is performed as part of colon cancer screening in subjects older than 50 years of age.

Physiological Testing

Patients with constipation and negative evaluations and/or a lack of response to conventional therapy need physiological testing to define the underlying pathophysiology and facilitate targeted treatment (11,18,19).

Colonic transit study:

Colonic transit can be objectively assessed using two general methods: 1) ingestion of radiopaque markers followed by x-rays of the abdomen taken at variable times, or 2) by using radioisotopes and scintigraphy (18,33).

The radio-opaque marker colonic transit study is widely available, inexpensive, and reproducible (17). The test is typically performed by administering a single capsule containing 24 plastic markers (Sitzmarks, Konsyl Pharmaceuticals, Fort Worth, Texas) on day 1 and by obtaining a plain abdominal x-ray on day 6 (18,34). Retention of >5 markers in the colon on day 6 is considered to be abnormal and indicative of slow transit constipation (Figure 2). A diffuse distribution throughout the colon may suggest slow transit throughout the entire colon (colonic inertia) whereas localization of retained markers in the left lower quadrant may suggest pelvic floor dyssynergia. The administration of multiple capsules at different days has also been used, mainly for research purposes, but the interpretation of these techniques is variable and its the validity has been questioned (18).

Figure 2A. Normal colon transit study (<5 markers on day 6).

Figure 2B. Abnormal colon transit study (>5 markers on day 6).

Example of colonic transit study: A single sitz marker capsule with 24 markers was taken on day 1 and a single X-ray was obtained on day 6 (120 hrs later). Panel A shows normal transit and Panel B shows slow colonic transit.

and dynamic motion, to evaluate for rectocele, enterocele, rectal prolapse and other pelvic floor dysfunctions (28–30). Although this technique provides excellent temporal resolution and soft tissue contrast without radiation exposure, it is limited by higher costs, lack of standardization, and availability.

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Colonic transit scintigraphy is a noninvasive method of quantitative evaluation of total and regional colonic transit (33,35). This technique involves oral administration of an isotope (111 In or 99Tc), either in a solid egg sandwich meal with water, encapsulated in a capsule together with a test meal. Anterior and posterior gamma camera images are obtained at specified time points over two to four days. Scintigraphic studies have been validated, reliable, and are reproducible for assessment of colonic transit. However, they are expensive, time consuming and are performed only in a few, tertiary care centers. Newer non-invasive technologies such as the SmartPill—a pH and pressure recording capsule that can provide an assessment of both gastric transit time (36) and colon transit time, may find wider use in the future.

Anorectal manometry: Anorectal manometry provides a comprehensive assessment of the pressure activity in the rectum and anal sphincter region together with an assessment of rectal sensation, rectoanal reflexes, and rectal compliance (37–39).

The equipment needed for anorectal manometry includes four essential components: a probe, a pressure recording device (amplifier/recorder, pneumohydraulic pump, pressure transducers), a device for displaying the recording (monitor, printer or chart recorder) and a data storage facility (computer, chart recorder) (40).

Several maneuvers can be performed during anorectal manometry but the following are especially useful in the evaluation of chronic constipation (40):

a. *Resting anorectal sphincter pressure* (difference between the intrarectal pressure and the maximum anal sphincter pressure at rest).

b. *Attempted defecation* (rectal and anal sphincter responses during attempted defecation). The maneuver is used to measure the intrarectal pressure, the residual anal pressure and the percentage anal relaxation. During attempted defecation, there is normally an increase in the intrarectal pressure and a decrease in the intra-anal pressure (Figure 1). Alternatively, there may be a paradoxical increase, or absent relaxation or incomplete relaxation of the anal sphincter pressure (Figure 1) (37,38,41).

c. *Recto-anal inhibitory reflex* (presence or absence of anal sphincter relaxation during rectal balloon distension to 50 cc). This maneuver examines the integrity of the myenteric plexus between the rectum and anal canal and is typically absent in Hirschsprung’s disease (40).

d. *Rectal sensation* (first sensation, desire to defecate and maximum tolerable volume during graded rectal balloon distensions in increments of 10cc).

**Balloon expulsion test:** This test provides an assessment of an individual’s ability to expel from the rectum a simulated stool—a nonlatex balloon filled with 50 cc of warm water, placed inside the rectum. The inability to expel the balloon or the time to expel the balloon is recorded (Normal range = 10 sec-3 min, median = 50 sec) (38). This test evaluates a patient for dyssynergic defecation (40,41). Failure to expel a balloon suggests the possibility of dyssynergia. The results of this test should be interpreted alongside the results of other tests of anorectal function.

**Colonic manometry:** Ambulatory colonic manometry using solid-state probes and portable recorders provides reproducible and reliable information regarding the pathophysiology of CC (13,37). Colonic manometry may facilitate the identification of myopathy, neuropathy or normal colonic neuromuscular function on the basis of manometric patterns and neurophysiologic responses (37,42).

**TREATMENT OF CONSTIPATION**

Initial therapy often includes recommendations to patients for lifestyle modifications such as adequate hydration and non-strenuous exercise, increased natural fiber intake, and dedicated time for bowel movements, although there is only weak evidence to support these measures (43). Other initial measures include bulking agents (psyllium, methylcellulose), stool softeners (docusate sodium), stimulant laxatives (senna, bisacodyl), osmotic laxatives (milk of magnesia, lactulose, sorbitol), and polyethylene glycol (PEG). Recent systematic reviews have concluded that there is good evidence to support the use of psyllium, lactulose, polyethylene glycol (PEG) (Table 3) (19,44).
Pharmacological Therapy

Lactulose (Duphalac®, Solvay Pharmaceuticals Inc, Marietta, GA), a commonly prescribed osmotic laxative, is broken down to lactic, formic and acetic acids in the colon, increasing osmotic pressure and consequently, an increase in stool water content. The usual recommended dose is 15–45 mL (20 grams/30 mL) orally 3–4 times daily, with a maximum dose of 40 grams/day. The main side effects include bloating, diarrhea, epigastric pain, flatulence, nausea, vomiting and rarely, hypernatremia and hypokalemia (45). Three placebo controlled randomized studies have shown increased stool frequency, improved stool consistency and “success rate” with lactulose, when compared to placebo (46–48).

Polyethylene glycol (Miralax®, Braintree Laboratories, Braintree, MA; or Glycolax®, Kremers Urban, Mequon, WI) is another commonly prescribed osmotic laxative that acts by increasing luminal osmotic pressure and stool water content. The usual dose is 17 grams per day dissolved in 8 ounces of water, juice, soda, coffee, tea. The main side effects include diarrhea, flatulence, nausea, and abdominal cramps. There have been several placebo controlled randomized studies that have shown increased stool frequency and improved stool consistency with PEG, when compared to controls (49–52). Two other trials showed increased stool frequency, less
straining and improved stool consistency with PEG, when compared to lactulose (53,54).

Tegaserod (Zelnorm®, Novartis Pharmaceutical Corp, East Hanover, NJ), a serotonin 5-HT4 receptor agonist, that increases peristalsis and transit of the gastrointestinal tract, particularly of the colon. In patients with chronic constipation, data have shown greater rates of complete spontaneous bowel movement with tegaserod, as well as significant improvements in stool form and straining (55). The therapeutic benefit in responders may be sustained for over a year (56). The usual dose is 6 mg orally twice daily before meals. The main side effects include diarrhea, dizziness, and headache. Although ischemic colitis has been reported with Tegaserod use, the rate is not significantly different from the general population (57).

Drugs that stimulate secretion such as lubiprostone, colchicine, and misoprostol may also be useful in constipation (44). Lubiprostone (Amitiza®, Sucampo Pharmaceuticals, Betheda, MD) is a bicyclic fatty acid that selectively stimulates the type 2 chloride channels and increases intestinal chloride, sodium and water secretion. This increased fluid in the lumen secondarily promotes peristalsis of the gastrointestinal tract with an effect of promoting spontaneous bowel movements. This medication has been recently approved for the treatment of chronic constipation. The usual dose is 24 mcg orally twice daily with food. The most common adverse events include headache, nausea, diarrhea, abdominal pain, and distension. There is mixed evidence to support the use of colchicine and misoprostol.

There are several agents being investigated for use in patients with chronic constipation. Neurotrophin-3 is an agent that promotes the maturation of sensory neurons and modulates synaptic transmission at the neuromuscular junction. A 4-week, double-blind, controlled trial of s.c. injection of 9 mg of neurotrophin-3 once per week improved symptoms, in particular, stool frequency, stool consistency, and straining effort, and accelerated colonic transit in patients with slow-transit constipation (58). Another new agent, alvimopan is a peripheral mu-opioid antagonist, that has been shown to accelerate colon transit in patients on narcotic analgesics. Interestingly, it also accelerated colon transit in healthy volunteers (59), but its efficacy in patients with chronic constipation has not yet been established.

A stepwise approach is recommended in the medical treatment of constipation (12). The AGA guidelines on constipation (12) recommend a gradual increase in fiber intake, followed by milk of magnesia and stimulant laxatives if needed. Additional therapy with lactulose or PEG can be considered if there is no satisfactory clinical improvement. An alternative approach is to consider the use of newer, gut selective, FDA approved agents for chronic constipation such as Tegaserod and Lubiprostone. Several of the agents act by different mechanisms—the effects of one may complement another. Currently, however, there is no data from randomized trials supporting the use of combination therapy with any of the above agents.

Biofeedback Therapy

Biofeedback therapy uses a combination of diaphragmatic muscle training, simulated defecation, manometric or EMG guided anal sphincter and pelvic muscle relaxation, with a goal of improving recto-anal coordination, sensory awareness and correcting dyssynergia. Biofeedback is appropriate if there is pelvic floor dyssynergia on conventional anorectal manometry. Biofeedback does not appear to benefit patients with slow-transit constipation. Randomized controlled trials have shown that biofeedback therapy is superior to sham biofeedback and standard medical treatment (60)—diazepam or placebo pill (61) or continuous PEG therapy (62)—in the treatment of patients with dyssynergic defecation (63).

Surgery

In a selected group of patients with refractory chronic constipation due to slow colonic transit, subtotal colectomy with ileorectal anastomosis can significantly improve symptoms and quality of life (64,65). The main complications include small bowel obstruction and ileus (66). However, before considering surgery, it is important to establish that the neuromuscular dysfunction is confined to the colon and does not involve the stomach and small bowel (67,68). Recent evidence suggests that ambulatory colonic manometry can be very useful in identifying patients with severe colonic neuropathy, who are likely to benefit from surgery and others with more

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normal colonic function who will respond to aggressive medical management (10). Therefore, patients considering surgical therapy for chronic constipation refractory to medical therapy will need extensive evaluation, including colon transit studies, anorectal and small bowel manometry, gastric emptying studies, etc, to exclude upper gut dysmotility and/or pseudoobstruction syndrome. Surgery does not improve symptoms in patients with dyssynergic defecation unless dyssynergia has been corrected (67,68). In patients with slow colonic transit and dyssynergia, colectomy with ileostomy should be performed (69) since other procedures such as segmental resection, partial colectomy or preservation of the cecum and ileocecal valve have been shown to be associated with poor results.

CONCLUSION

This review provides the practicing gastroenterologist with an overview and a step-wise approach to the evaluation and management of chronic constipation. It is important to define and understand the various categories of constipation, based on symptoms and pathophysiology. In this era of evidence based medicine, it is possible to adopt a rational and cost-effective approach to the evaluation of constipation. Medical treatment should be tailored to the underlying etiology, based on what is known about the efficacy of various therapies. Patients who do not respond to medical treatment may need specialized evaluation for pelvic floor dysfunction and biofeedback therapy. Only rarely and in carefully selected patients, is surgical therapy needed.

Acknowledgments

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