

Management of chronic constipation

Recommendations from a consensus panel

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Chronic constipation (CC) results in more than 2.5 million visits to physicians and almost 100,000 hospitalizations in the United States annually.¹ While patients are most concerned about symptoms such as straining, unproductive urges, a sense of incomplete evacuation, excessive time spent on the toilet, abdominal discomfort, and bloating,^{2,7} physicians focus on the frequency of bowel movements (**FIGURE 1**). Patients frequently self-medicate for CC and spend an estimated \$800 million on laxatives annually. More important, CC has a significant adverse impact on patients' health-related quality of life.⁸

In this publication, a panel of experts examine the characterization of CC, provide guidelines for diagnosis in the primary care setting, and assess the benefits and risks of management options.

Key points and recommendations

- Patients focus on the symptoms of constipation, while physicians focus on the frequency of bowel movements. (SOR: B)
- The assessment of chronic constipation includes patient history, physical examination, and bowel record. (SOR: C)
- Dietary modifications, increased fluid intake, and initiation of an exercise program are recommended for initial management of chronic constipation. (SOR: C)
- Laxatives are recommended as initial pharmacologic management of chronic constipation but generally are effective only in the short term. (SOR: B)
- Tegaserod increases the frequency of bowel movements and improves symptoms for patients with chronic idiopathic constipation. (SOR: A)

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CHARACTERIZATION

Although a single definition has not been adopted, CC is commonly described as constipation of more than 12 weeks duration that does not respond to dietary fiber or simple therapeutic measures.^{9,10} The Rome II criteria were developed to promote consistency in the diagnosis of constipation, but use is limited primarily to clinical research¹¹ (TABLE 1).

Constipation in general, as well as CC, may result from primary (no apparent external cause) or secondary causes^{12,13} (TABLE 2). Primary constipation has been classified as slow transit (eg, colonic inertia; neuromuscular dysfunction), anorectal expulsion disorder (eg, dyssynergia; obstruction), or a combination of these, as well as normal transit (ie, stool transit time is normal, however, evacuation is difficult or hard stools are present). Management approaches to secondary causes of CC include discontinuation of medications, lifestyle modifications, or improved treatment of underlying disease.

Patients focus on constipation symptoms, while physicians are concerned about BM frequency

Secondary causes should be investigated and appropriately managed. Patients with irritable bowel syndrome (IBS) have a primary complaint of abdominal pain relieved with defecation or associated with an alteration of bowel habits.¹⁴

EPIDEMIOLOGY

The epidemiology of CC is based on constipation in general, as few data exist for CC specifically. Prevalence of constipation varies between 2% and 27%, with most studies suggesting an average of about 15%.⁴ More than 5.7 million physician visits were constipation-related in 2001.¹⁵ Although women are more than 3 times as likely as men to experience constipation, in part because of menstrual cycle influences, gynecologic procedures, and disorders that influence bowel movements (eg, ovarian cancer, fibroid tumors, endometriosis, dyschezia),^{6,16} they are less likely than men to report symptoms.⁶ Children are more likely than adults to experience constipation,¹⁷ and elderly persons, who are more than twice as likely as young adults to experience constipation, are more likely to develop complications.^{18,19} This difference between

FIGURE 1
Patient versus physician description of chronic constipation

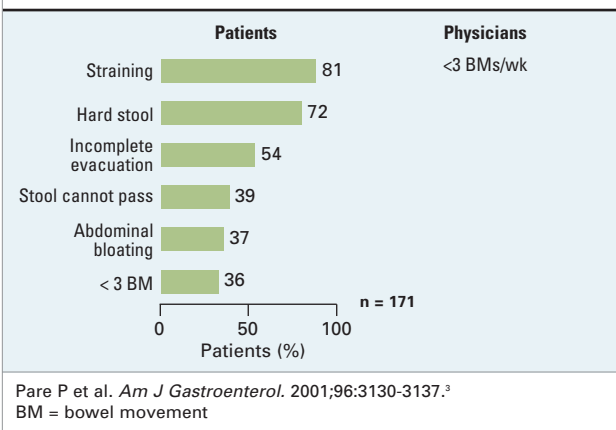


TABLE 1
Rome II diagnostic criteria

Adults
Two or more of the following for at least 12 weeks (not necessarily consecutive) in the preceding 12 months:
• Straining during >25% of bowel movements
• Lumpy or hard stools for >25% of bowel movements
• Sensation of incomplete evacuation for >25% of bowel movements
• Sensation of anorectal blockage for >25% of bowel movements
• Manual maneuvers to facilitate >25% of bowel movements (eg, digital evacuation or support of the pelvic floor)
• <3 bowel movements per week
Loose stools not present, and insufficient criteria for irritable bowel syndrome met
Infants and children
Pebble-like hard stools for a majority of bowel movements for at least 2 weeks
Firm stools ≤ 2 times per week for at least 2 weeks
No evidence of structural, endocrine, or metabolic disease

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younger and older adults may be due to the increased incidence of secondary causes of constipation in older adults.³ Other disproportionately affected groups include nonwhites,¹⁹ and those with a lower income, limited education, history of sexual abuse, symptoms of depression, or physical inactivity.²⁰

TABLE 2

Primary and secondary causes of constipation

Primary	Secondary
Functional	Connective-tissue disease
Idiopathic	Amyloidosis
Irritable bowel syndrome	Systemic sclerosis
Pelvic dyssynergia (anismus)	Lifestyle
Slow-transit constipation	Dehydration
Neuropathic	Inadequate dietary fiber
Chagas' disease	Sedentary lifestyle
Congenital anal sphincter myopathy	Voluntary suppression of defecation
Hirschsprung's disease	Medications
Hyperganglionosis	Antacids
Spinal cord injury	Anticholinergics
Obstructive	Anticonvulsants
Anal stenosis	Antidepressants
Crohn's disease	Antihistamines
Colon cancer	Antiparkinsonian drugs
Compression by tumor	Antipsychotics
Stricture	Calcium channel blockers
Gynecologic	Calcium supplements
Large rectocele	Diuretics
Pelvic relaxation	Iron supplements
	Laxatives (chronic abuse)
	Nonsteroidal anti-inflammatory drugs
	Opiates
	Metabolic/endocrine
	Diabetes mellitus
	Heavy metal poisoning
	Hypercalcemia
	Hypokalemia
	Hypothyroidism
	Hypomagnesemia
	Porphyria
	Uremia
	Neuropathic
	Autonomic neuropathy
	Multiple sclerosis
	Paraneoplastic neuropathy
	Parkinson's disease
	Psychologic
	Depression
	Eating disorders
	Situational stress

Dosh SA. *J Fam Pract.* 2002;51:555-559.¹³

Chronic constipation can be associated with medical comorbidities and complications, such as intestinal impaction and obstruction, anal fissures, hemorrhoids, volvulus, stercoral ulcers, and IBS.²¹ Quality of life is significantly impaired in patients with CC as a result of altered mental and physical functioning.^{8,22,23} The loss in productivity at work has been estimated to be more than 8 hours in a 40-hour working week.²⁴ Also, patients with CC are more likely to use health care services with an average expenditure of \$2752 per patient for additional tertiary care evaluations.¹⁰

DIAGNOSIS

The diagnosis of CC begins with a thorough medical history and physical examination (FIGURE 2, TABLE 3). A complete digital rectal exam (DRE) evaluates the anal sphincter tone and detects tenderness, sensation, obstruction, or blood. The abdomen must be carefully examined for the presence of stool. A detailed neurologic examination will exclude systemic illnesses that may cause constipation. A gynecologic exam, including rectovaginal exploration, may reveal the presence of gynecologic symptoms, for example, pain, when bearing down.

FIGURE 2

Assessment of a patient with constipation

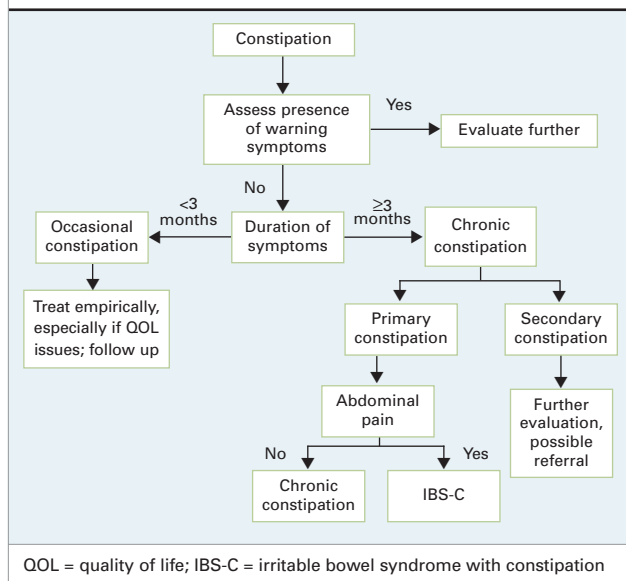


TABLE 4 lists the warning signs of secondary CC that require immediate intervention. A systematic review by Rao et al concluded that evidence to support the use of

TABLE 3

Diagnostic findings in patients with defecatory disorders

<p>History Prolonged strain to expel stool Unusual postures on the toilet to facilitate stool expulsion Support of the perineum, digitation of rectum, or posterior vaginal pressure to facilitate rectal emptying Inability to expel enema fluid Constipation after subtotal colectomy for constipation</p>
<p>Rectal examination (with patient in left lateral position) Inspection Anus pulled forward while the patient is bearing down Anal verge descends <1.0 cm or >3.5 cm (or beyond the ischial tuberosities) while the patient is bearing down Perineum balloons down while the patient is bearing down, and rectal mucosa partially prolapses through anal canal Palpation High anal-sphincter tone at rest Anal-sphincter pressure during voluntary contraction is only slightly higher than tone at rest Perineum and examining finger descend <1.0 cm or >3.5 cm while patient simulates straining during defecation Puborectalis muscle is tender on palpation through the rectal wall posteriorly, or palpation reproduces pain Defect in anterior wall of the rectum, suggestive of rectocele</p>
<p>Anorectal manometry and balloon expulsion (with patient in left lateral position) Average tone of anal sphincter at rest, >80 cm water (or >60 mm Hg) Average pressure of anal sphincter during contraction, >240 cm water (or >180 mm Hg) Failure to expel balloon</p>
<p><small>Lembo A, Camilleri M. <i>N Engl J Med.</i> 2003;349:1360-1368.⁹ Copyright © 2003. <i>The New England Journal of Medicine.</i> Used with permission.</small></p>

blood tests, radiography, or endoscopy in the routine workup of patients with constipation without alarm features is lacking. Colonic transit, anorectal manometry, and balloon expulsion tests reveal physiologic abnormalities in many selected patients with constipation, but no single test adequately defines pathophysiology.²⁵

A physician should ask questions of the patient regarding bowel habits and symptoms associated with defecation. A 7-day stool diary (TABLE 5), which includes the Bristol Stool Scale also may be helpful

TABLE 4

Warning signs of other conditions that require investigation

Evaluation	Warning sign
History	Unintended weight loss Nocturnal pain Rectal bleeding Recent change in bowel habits Pelvic pain with defecation Patient older than 50 years
Family history	Gastrointestinal cancer Inflammatory bowel disease
Physical examination	Physical abnormalities (ie, abdominal mass, rectal prolapse)
Laboratory findings	Anemia Leukocytosis Elevated erythrocyte sedimentation rate Elevated thyroid stimulating hormone Elevated white blood cell count Elevated calcium level

(available at www.aboutconstipation.org/bristol.html).²⁶ The diary allows assessment of baseline bowel habits and treatment efficacy. Patients should record dietary habits including fluid intake, amount and frequency of exercise, and use of over-the-counter medication.²⁷ Further studies and possible referral to a gastroenterologist may be needed if patients have warning signs or CC that does not resolve with therapy (TABLE 6).²⁸

PHARMACOLOGIC AND NONPHARMACOLOGIC MANAGEMENT

Management generally includes both nonpharmacologic and pharmacologic measures. Goals of management include improving symptoms, restoring normal bowel function, increasing colonic transit if abnormal, and facilitating defecation.

Although diet, fluid, and exercise are widely believed to positively influence fecal elimination, few data support these interventions. Fluid does not shorten colon transit time or determine stool bulk. Dietary fiber promotes bloating and flatulence and may harden feces. Exercise has not shown to be a benefit in CC.²⁹⁻³² Nonetheless, the consensus panel recommends that management should start with a healthy lifestyle, particularly because of the risk-lowering potential for various diseases.³³ Refined and processed foods should be avoided because fiber generally is removed during

TABLE 5

Seven-day stool diary

Date							
Time of bowel movement							
Straining (yes/no)							
Feeling of incomplete evacuation (yes/no)							
Stool consistency (1–7, from Bristol Stool Scale)							
Urge (yes/no)							
Digital maneuvers (yes/no)							
Drug therapies (including over-the-counter drugs)							
Comments (include other symptoms)							

preparation. Foods with little or no fiber, such as ice cream, cheese, and meat, should be avoided. Caffeine- and alcohol-containing liquids increase renal elimination of fluids and should be avoided; although coffee may stimulate colonic motility.³⁴

Other nonpharmacologic therapies include surgery, biofeedback, and acupuncture. Surgical removal of the colon may be an option for persons with severe symptoms caused by colonic inertia, although benefits must be weighed against possible complications such as abdominal pain and diarrhea.¹⁷ Biofeedback to retrain the muscles that control release of bowel movements may be useful in patients with CC caused by anorectal dysfunction.³⁵

Pharmacologic options include laxatives, prokinetic drugs, and other therapies.

Laxatives

Laxatives offer various modes of action. Bulking agents, such as natural and synthetic fiber (bran, psyllium, methylcellulose, and calcium polycarbophil), draw water into the intestine, increase stool weight, and soften stool consistency. Most fiber supplements (with the exception of pectin) must be taken with 8 fluid ounces of water or constipation may worsen, thereby potentially causing serious complications. These agents act solely to increase bowel movement frequency; however, benefits decline with time.^{36,37} Wheat bran, the most studied natural fiber,³⁸ is ineffective in patients with slow transit constipation or dyssynergia, and may be effective in patients with normal transit constipation.³⁹ If patients

do not respond to fiber therapy, stool softeners have been used as combination therapy. While safe and well tolerated, bulking agents may interfere with absorption of some drugs. Side effects include choking (if not taken with sufficient water), abdominal pain, and bloating. Those containing psyllium have been associated with rare reactions such as anaphylaxis, asthma, and other allergic conditions.

Stool softeners (eg, docusate sodium), or emollient laxatives, are surface-active agents with emulsifying and detergent properties. They allow water to interact with fecal mass for a softer stool. Alone, they do not increase the number of stools and, therefore, are ineffective for the treatment of CC.⁴⁰ Although stool softeners generally are used in combination with other therapies, no evidence suggests that this is an effective approach. Stool softeners are safe and well tolerated, although docusates have been associated with an increased risk of hepatotoxicity by enhancing the liver's uptake of hepatotoxic drugs.⁴¹

Osmotic laxatives include saline, magnesium, polyethylene glycol (PEG 3350), and lactulose. Saline and magnesium laxatives draw water into the colon for easier passage of stool. Although little of the sodium, phosphate, or magnesium contained in these products is absorbed from the colon, these levels must be closely monitored in patients with renal dysfunction. Sodium-containing osmotic laxatives should be avoided in patients with renal dysfunction, congestive heart failure, or high blood pressure. A chemically inert polymer lacking the sodium contained in PEG electrolyte solutions,

TABLE 6

Colorectal studies used in the diagnosis of chronic constipation

Colorectal study	Examples	Use
Radiographic studies	Barium enema x-ray study	Assess for obstruction, abnormalities. Indicator of colonic transit.
Colonic transit studies	Sitz marker study	Objectively confirm infrequent defecation and prolonged colonic transit time. Patients with abnormal results are best referred to a gastroenterologist.
Visual study	Colonoscopy, sigmoidoscopy	Observe for physical abnormalities; irritable bowel syndrome
Balloon expulsion test		Can be used as a screening test of inability to defecate. Inability to expel the balloon suggests anismus or pelvic floor dysfunction.
Defecography		Can reveal abnormalities such as intussusception, rectocele, and enterocele. Corroborates results of other tests.
Anorectal manometry		Assesses for anismus or pelvic floor dyssynergia; screening test for Hirschsprung's disease. No controlled clinical trials validating use.
Electromyography		Demonstrates innervation and function of the pelvic floor muscles. Assesses paradoxical puborectalis contraction and preparation for performing biofeedback training.
Rectal biopsy		Diagnosis of Hirschsprung's disease and neuropathies (neuronal intranuclear inclusion disease and neuronal intestinal dysplasia).

PEG 3350 is highly soluble and not readily absorbed, but it can cause diarrhea.⁴² In a multicenter, randomized, comparative trial of PEG 3350 and lactulose, patients in the PEG 3350 group had a higher number of stools and a lower median daily score for straining at

stool than patients in the lactulose group. Overall, greater improvement in adults has been demonstrated following 4 weeks of treatment with PEG 3350, 13 g to 39 g per day, compared with lactulose, 10 g to 30 g per day.⁴³ Clinical tolerance was similar in the 2 groups, with no serious adverse events and no significant change in laboratory tests reported. Similar results have been observed in children following 8 weeks of therapy. Both PEG 3350 and lactulose were effective in significantly increasing stool frequency, while PEG 3350 causes less abdominal pain, pain at defecation, and straining at defecation. Children, however, preferred the taste of lactulose.^{44,45}

Stimulant laxatives (eg, bisacodyl, senna, cascara sagrada, casanthranol) cause rhythmic intestinal muscle contractions. Efficacy of agents is similar and dose-dependent. Recent data indicate that stimulant laxatives are ineffective in the treatment of CC.⁴⁶ The members of this consensus panel believe that combining stimulant laxatives with fiber and/or surfactants may provide better relief. High doses may cause liquid stool or diarrhea, which may result in severe metabolic disturbances. Other side effects include severe cramps, dehydration, and malnutrition with chronic use. Chronic, long-term use of stimulant laxatives is commonly believed to result in "cathartic colon," although no data support this.⁴¹ There is a theoretic concern of hepatotoxicity since sennosides are converted into rhein anthro, which is structurally similar to dantron, a laxative well known to be hepatotoxic.⁴¹ Chronic use of these laxatives can cause melanosis coli, a darkening of the intestinal lining due to the accumulation of melanin.

Prokinetic agents

Tegaserod is the only prokinetic medication currently available that has shown benefit in treating patients with CC. Another prokinetic agent, cisapride, was withdrawn from the US market because of cardiac side effects (eg, torsades de pointes) and the drug-interaction profile. Not normally considered a prokinetic agent, erythromycin has been shown to cause an indirect contractile effect on colonic circular muscle taken from the colon of patients with CC.^{47,48}

Tegaserod is a partial 5-HT₄ receptor agonist indicated for the short-term treatment of women with IBS whose primary bowel symptom is constipation, as well as the treatment of chronic idiopathic constipation in

men and women younger than 65 years. Two large multicenter pivotal trials (N = 1264 and N = 1348) have evaluated patients who had at least a 6-month history of an average of fewer than 3 complete spontaneous bowel movements (CSBM) per week in chronic idiopathic constipation.^{49,50} Patients were randomized to 12 weeks of tegaserod, 2 mg or 6 mg orally bid, or placebo. The primary efficacy variable was the responder rate, which was defined as a mean increase of at least 1 CSBM per week compared with baseline during the first 4 weeks of active treatment. Tegaserod, 6 mg bid, had 14% to 18% more responders compared with placebo in the trials. In each trial, tegaserod, 6 mg bid, also significantly increased the number of CSBM and spontaneous bowel movements, as well as overall satisfaction of bowel habits over 12 weeks of treatment compared with placebo. In addition, tegaserod, 6 mg bid, produced significant improvement in stool form and several other secondary variables. Across the 2 trials, diarrhea occurred more commonly in the patients who were treated with tegaserod compared with placebo (6.6% vs. 3.0%, respectively); however, it occurred once in the majority of patients, was generally of mild-to-moderate severity, and led to discontinuation in less than 1% of patients. The long-term safety and tolerability of tegaserod in CC were demonstrated in a 13-month, single-blind study (Novartis Pharmaceutical Corporation, data on file). Serious consequences of diarrhea have been reported in a small percentage of patients in clinical trials (0.04%) and during marketed use of tegaserod.⁵¹ In the clinical trial experience with tegaserod, there have been no cases of ischemic colitis in tegaserod-using patients and 1 case of probable ischemic colitis in a placebo-using patient. In the postmarketing setting, the number of reported cases of ischemic colitis in tegaserod-using patients is lower than the background incidence of ischemic colitis in the IBS population (Novartis Pharmaceutical Corporation, data on file).

Miscellaneous

Colchicine and misoprostol also have been investigated in the management of CC. Colchicine has been shown to stimulate intestinal motility in rats and is well known to cause diarrhea in patients taking the drug for other indications.⁵² Compared with baseline, colchicine increased the frequency of bowel movements in patients with CC; however, nausea and abdominal pain also increased.⁵³

Long-term therapy with colchicine can result in a reversible myopathy or neuropathy. Misoprostol is effective for CC, but side effects observed at higher doses can be a limiting factor.^{54,55}

Other therapies generally not recommended for CC include lubricants (mineral oil, liquid paraffin), castor oil, and bethanechol. Lubricants coat the stool, enabling it to move through the intestines more easily. Long-term therapy with these agents should be avoided because of decreased absorption of fat soluble vitamins. Lubricants have been associated with aspiration pneumonia and prolonged use can result in inflammatory reactions.¹² Castor oil is a stimulant laxative that causes the accumulation of fluid in the small intestine

Most patients delay or do not seek medical care, despite the impact of CC on their quality of life

and promotes evacuation of the bowels. Castor oil has an unpleasant taste, it affects the absorption of nutrients and minerals, and is not recommended for repeated use. Bethanechol has not been studied in controlled, clinical trials. Its use is limited by side effects such as abdominal cramps, diarrhea, urinary frequency, nausea, vomiting, headache, hypertension, and blurred vision.¹²

CONCLUSION

Chronic constipation is a disorder that greatly affects patient quality of life. Nonetheless, most patients do not seek medical care because of embarrassment or wait until after trying over-the-counter medications, as the problem often is not viewed as “medical.” Patients define CC in terms of the symptoms, while physicians focus on frequency of bowel movements. Physical assessment involving a DRE and detailed patient questioning are vital to diagnosis. Although many types of pharmacologic agents have been used, very few have been shown to be effective in the management of CC. Laxatives, fiber, fluids, and exercise have not been shown to have a significant positive impact on the symptoms of CC. Conversely, newer therapies such as PEG 3350 (indicated for occasional constipation) and tegaserod (indicated for chronic idiopathic constipation) appear to be beneficial and tegaserod is well tolerated. ■

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