Last Section Update: 07/2021

Contributor(s): Maureen Williams, ND

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1 Overview

Summary and Quick Facts for Constipation

- Most people experience occasional constipation, but about 14% of adults suffer from chronic constipation.
- In this protocol you will learn about the causes of constipation and how diet and lifestyle changes can help promote regularity. This protocol will discuss the importance of intestinal microorganisms for digestive health, and how probiotic and prebiotic supplements may help relieve constipation.
- For some, constipation can often be relieved without harsh laxatives by increasing fiber and fluid intake as well as physical activity. Others require more aggressive approaches using natural interventions to evacuate the bowels.

Constipation is defined as having infrequent bowel movements, often fewer than three per week, and difficulty passing stools. Most people experience occasional constipation, but about 14% of adults suffer from chronic constipation. Many people turn to laxative medications, but these can lead to dependence and troubling side

effects.

Natural interventions can be used to help relieve constipation including effervescent magnesium and vitamin C, fiber, and probiotics.

Causes and Risk Factors

- Impaired peristalsis (wave-like contractions of the gut)
- Blockages, neurological and hormonal conditions, and medications such as opioids
- Female gender (two to three times the risk of males) and advanced age (with greatest prevalence in those older than 70)

Diagnosis

Diagnosis is based on bowel habits, symptoms, and medical history. Rome III, a set of criteria used to diagnose functional GI disorders, describes the diagnosis of chronic constipation as constipation for at least six months as well as specific symptoms for at least three months (eg, straining with at least 25% of bowel movements, **details here**).

Conventional Treatment

- Adequate fluid and fiber are first-line treatments, and regular exercise is also an important intervention
- Laxatives (osmotic and stimulant), suppositories, and enemas

Note: Chronic use of stimulant laxatives may damage the neuromuscular system of the colon, worsening constipation and leading to dependence. They may also cause potentially dangerous electrolyte and fluid imbalances, especially when combined with diuretics.

Novel and Emerging Strategies

Fecal microbiota transplantation, which involves the transfer of colonic microorganisms from a healthy donor to a symptomatic person. Five case reports of patients with chronic constipation-predominant IBS treated with fecal microbiota transplant describe immediate remission in all five cases and stable improvement in follow-up.

- **Biofeedback therapy**, where patients learn to coordinate muscular activity, is a behavioral treatment that has demonstrated superiority to laxatives in several controlled clinical trials.
- **Neurotrophin-3**, a growth factor produced by the body, may be able to combat age-related neurodegeneration in the gut, which could help relieve constipation.

Dietary and Lifestyle Considerations

- A diet containing 25 g of fiber per day resulted in increased stool frequency and decreased laxative use
- Increasing fluid intake is an effective treatment for constipation, and appears to work best together with fiber
- Prunes, kiwifruit, olive and flaxseed oil have been found to improve bowel regularity
- Increasing physical activity has been shown to successfully improve chronic constipation

Nutrients

- **Probiotics:** Probiotics containing *Bifidobacterium lactis* (*B. lactis* HN019) may shorten intestinal transit time, and *B. lactis* and *Lactobacillus casei* may have positive effects in adults with chronic constipation.
- **Magnesium and Vitamin C:** Magnesium and vitamin C have both been shown to promote bowel evacuation. Taking magnesium and vitamin C simultaneously may stimulate a bowel movement.
- **Fiber and Prebiotics:** Soluble fiber supplements keep the stool soft and easy to move and function as a prebiotic, which helps establish and maintain beneficial bacteria in the gut. Psyllium, rich in soluble fiber, has been shown to relieve constipation. Other fiber supplements include inulin, partially hydrolyzed guar gum, and glucomannan.

- **Cascara Sagrada:** The bark of the buckthorn tree, known as cascara sagrada, has traditionally been used to treat constipation. Stimulant laxatives like cascara may cause diarrhea and electrolyte loss, and so are generally recommended for short-term use only.

2 Introduction

Most people experience occasional constipation, but about 14% of adults suffer from ***chronic constipation*** (Basilisco 2013; Rao 2014; Quigley 2011; Jamshed 2011). These people often turn to **laxative** medications, but these drugs are sometimes ineffective and can cause troubling side effects such as bloating, diarrhea, and loss of bowel control. Moreover, **laxative *overuse*** may lead to ***dependence*** (Wang 2013; Leung, Rao 2011; Basilisco 2013; Pare 2014; Mayo Clinic 2014a).

For some, constipation can often be relieved *without* harsh laxatives by increasing fiber and fluid intake as well as physical activity (Rao 2014; Rush 2002; Attaluri 2011).

Others require more aggressive approaches using **natural** interventions to evacuate the bowels. These include ***effervescent magnesium and vitamin C powder***, supplemental fiber such as ***psyllium***, and ***probiotics***. Other strategies can be helpful as well: avoiding foods that can slow gut motility (eg, eggs, meat, and dairy) (UU 2015b) and eating more foods with laxative properties (eg, prunes and kiwifruit) (Rush 2002; Attaluri 2011; Rao 2014).

Many older people dismiss declining bowel function as a normal part of the aging process and learn to live with unsatisfactory evacuation. But constipation should *not* be ignored. Severe chronic constipation can lead to problematic complications like fecal impaction and fissures (Basilisco 2013; Jamshed 2011; Rogers 2013; Mayo Clinic 2012).

In this protocol you will learn about the causes of constipation and how diet and lifestyle changes can help promote regularity (Rao 2014). You will read about new insights into the ***gut-brain axis***, which links constipation to cognitive decline, mood disorders, and neurodegenerative diseases (Daulatzai 2014). This protocol will discuss the importance of intestinal microorganisms for digestive health, and how probiotic and prebiotic supplements may help relieve constipation (Quigley 2012a). You will also discover how supplements such as ***effervescent magnesium and vitamin C powder*** can help improve bowel function.

In some cases, constipation may be attributed to irritable bowel syndrome. Readers of this protocol may find additional insights in the **Irritable Bowel Syndrome** protocol.

3 Background

The large intestine, or colon, is the final major segment of the **digestive tract** (CCS 2015). Waves of muscular contractions called *peristalsis* propel fecal material through the colon (Leung, Riutta 2011). These muscular activities are coordinated by signals from the nervous system and neurohormones like histamine and serotonin (Lee 2014; Wood 2007). Colonic peristalsis is naturally strongest upon waking in the morning and after meals, and insufficient peristalsis leads to constipation (Yu 2014; Hendricks 1997).

The Gut-Brain Axis

The network of nerves that controls gut activity, known as the enteric nervous system, contains as many nerve cells as the spinal cord (Wood 2007; Daulatzai 2014). The enteric nervous system and central nervous system are functionally interdependent. In other words, dysfunction originating in the central nervous system can give rise to problems in the enteric nervous system, and dysfunction originating in the enteric system may compromise central nervous function (De Palma 2014).

This reciprocal relationship between the gastrointestinal tract and the nervous system has been called the "***gut-brain axis***" (Daulatzai 2014; O'Malley 2011; Lee 2014; De Palma 2014). Functional (primary) constipation is thought to involve gut-brain axis dysfunction (De Palma 2014). Bi-directional dysfunction of this axis also contributes to irritable bowel syndrome (Daulatzai 2014; O'Malley 2011; De Palma 2014).

Researchers have found especially strong correlations between chronic constipation and two chronic neurological diseases: Parkinson's disease and Lewy-body dementia (in which abnormal protein deposits called Lewy bodies build up in brain cells) (Idiaquez 2011; Postuma 2013; Weerkamp 2013). In one study, older individuals with a

history of chronic constipation were more than three times as likely to develop Parkinson's disease during an average 5.5 years of follow-up, and those with the most severe constipation had the greatest risk (Lin 2014). Other neurological diseases that have been correlated with constipation include restless leg syndrome (Shneyder 2013) and Alzheimer's disease (Zakrzewska-Pniewska 2012).

Inflammation is thought to underlie the connection between constipation and neurological disease. Disruptions in the gut microenvironment contribute to gastrointestinal symptoms as well as neurological problems; degradation of the gut barrier promotes systemic inflammation, which in turn promotes neuroinflammation and subsequent cognitive dysfunction (Daulatzai 2014).

4 Types of Constipation

Primary Constipation

Functional, or primary, constipation can be divided into three types: slow-transit constipation, pelvic floor dysfunction, and normal-transit constipation (Jamshed 2011).

Slow-transit constipation. In this type of constipation, motility (gut movement) is decreased, and transit time (the time it takes for food to pass from the beginning to the end of the digestive tract) is increased (Rao 2014; Jamshed 2011). Slow-transit constipation symptoms may include infrequent bowel movements, bloating, and abdominal discomfort (Jamshed 2011; Leung, Riutta 2011).

Outlet constipation, or pelvic-floor dysfunction. In this type of constipation, discoordination of the musculature of the pelvic floor results in either inappropriate anal contraction, a failure of anal relaxation, or inefficient propulsion of stool. Outlet constipation symptoms often include straining to pass stool, soft stools that do not pass easily, and discomfort in the rectum. This type of constipation is less likely to respond to traditional medical therapies (Jamshed 2011; Leung, Riutta 2011).

Normal-transit constipation. Some individuals with primary chronic constipation have neither slow transit nor an outlet problem, but rather a condition known as normal-transit constipation. Those with normal-transit constipation may even have daily bowel movements, yet describe themselves as constipated due to a persistent sense of difficult evacuation, with hard stools and abdominal bloating and discomfort. This type of constipation may be associated with elevated psychosocial distress. Normal-transit constipation is a very common type of chronic constipation (Andromanakos 2015; Jamshed 2011).

Secondary Constipation

Secondary constipation can be caused by metabolic disturbances like **hypothyroidism**; neurological problems like **Parkinson's disease**, **multiple sclerosis**, and spinal cord injuries; **celiac disease**; and diseases of the large intestine such as **colon cancer** (Rao 2014; Jamshed 2011; Leung, Riutta 2011; Volta 2011) and **diverticular disease** (Strate 2012; Boynton 2013). Several medications can cause secondary constipation as well (see Causes and Risk Factors).

Associated Conditions

Individuals with chronic constipation often have other digestive problems that involve disordered motility, such as indigestion, **gastroesophageal reflux disease**, **diverticular disease**, and **irritable bowel syndrome (IBS)** (Arora 2012; Rao 2014; Vakil 2014). In fact, the overlapping symptoms of primary constipation and constipation-predominant irritable bowel syndrome (IBS-C) make them difficult to distinguish, leading some researchers to suggest they may be the same condition (Basilisco 2013; Lee 2014; Suares 2011a). Hemorrhoids are associated with constipation as well (Ehrlich 2013).

5 Causes and Risk Factors

Causes

Primary constipation. Functional (primary) constipation has multiple possible causes.

- In *slow transit-constipation*, impaired regulation of peristalsis by the enteric nervous system and the muscles of the colon result in delayed passage of stool through the lower digestive tract. Dietary factors such as a

low-fiber diet may also contribute.

- *Normal-transit constipation* is characterized by normal peristalsis and the absence of any pathological findings, but a persistent perception of being constipated and of inadequate evacuation. There is no known cause for this type of constipation beyond its association with psychosocial stress.
- In *pelvic floor dysfunction*, there is faulty coordination of the muscles that facilitate expulsion of stool from the rectum. Psychological causes have been proposed, and physical trauma plays a role in some cases (Leung, Riutta 2011; Lembo 2003; Rao 2014; Jamshed 2011).

Secondary constipation. Causes of secondary constipation generally fall into five categories:

- **Blockages.** These include colorectal cancer, bowel stricture (narrowing), abdominal tumor pressing on the colon, and any other cause of bowel obstruction (Basilisco 2013).
- **Neurological causes.** Conditions that disrupt intestinal neuromuscular signaling can cause secondary constipation (eg, multiple sclerosis, Parkinson's disease, spinal cord injury, diabetic neuropathy, and stroke) (Basilisco 2013; Rao 2014).
- **Hormonal causes.** Endocrine conditions, such as hypothyroidism, can cause or contribute to constipation (Basilisco 2013; Rao 2014). Diabetes is associated with constipation; this is thought to be through eventual damage of enteric nerves, altered intestinal muscle contractility and function, and disrupted intestinal microbiota (Yarandi 2014).
- **Muscular causes.** For some individuals, constipation is caused by difficulty controlling the muscles of the pelvic floor and the external anal sphincter. Injury or trauma to the pelvic muscles can be responsible (Roque 2015; Leung, Riutta 2011).
- **Medications.** Medications, notably opioid pain relievers, can cause secondary constipation, particularly in the elderly. Other medications less commonly cause secondary constipation: acetaminophen (Tylenol), anticholinergics, antidepressants, antihistamines, antipsychotics, calcium-channel blockers, beta-blockers, diuretics, and non-steroidal anti-inflammatory drugs (Jamshed 2011; Rao 2014; Leung, Riutta 2011).

Risk Factors

Female gender. Women are two to three times as likely as men to have chronic constipation (Jamshed 2011; Roque 2015). This may be due to the influence of hormones on digestive function, since many women experience constipation during the luteal phase (last two weeks) of the menstrual cycle (Chu 2014; Oh 2013; Jamshed 2011). Pelvic floor injuries sustained during childbirth may be to blame in another segment of women with chronic constipation (Leung, Riutta 2011; Roque 2015).

Older age. Constipation is more common in older age, with the greatest prevalence among those 70 or older. As many as 70% of institutionalized elderly report daily use of laxatives (Leung, Riutta 2011).

6 Signs and Symptoms

The symptoms of constipation are its defining characteristics: infrequent stools, often fewer than three per week, and difficulty passing them (Basilisco 2013). People with constipation may also report abdominal bloating and discomfort, hard or lumpy stools that require straining to pass, or a sensation that there is a blockage or some other problem preventing complete emptying of the bowels (UMMC 2013a; Jamshed 2011; Mayo Clinic 2013a). Delirium, anorexia, and general functional decline may be associated with chronic constipation in the frail elderly (Jamshed 2011). Hemorrhoids, which are swollen, inflamed veins in the anal or rectal region, may occur as a result of constipation. Hemorrhoids can cause itching, bleeding, and a sensation of swelling around the anus (NIDDK 2013; Mayo Clinic 2013b).

Other complications of chronic constipation include:

- **Anal fissures** are small tears in the delicate lining of the anus (Mayo Clinic 2012).
- **Rectocele** is a bulging of the rectum toward the vaginal wall (Mayo Clinic 2014b).

- **Rectal prolapse** is a collapse and telescoping of the rectum through the anal canal (UMMC 2015b; MUSC 2015).
- **Fecal impaction** occurs when a mass of dry, hard stool becomes lodged in the rectum, usually in individuals who have been constipated for an extended period of time (UMMC 2015a).
- **Fecal incontinence** is involuntary passage of stool associated with chronic constipation. It can occur due to general anorectal muscular weakness as a result of chronic constipation, laxative use, severe hemorrhoids, rectal prolapse, or fecal impaction (UMMC 2014).
- **Acquired megacolon** is an extremely enlarged colon that can result from prolonged severe constipation and that may require surgical treatment. Acquired megacolon occurs due to weakness and collapse of chronically stretched walls of the colon (Vieira 1996; Sparberg 1990; Pereira 1987).
- **Bowel perforation** as a result of constipation is a very rare medical emergency that can cause the bowel contents to enter the abdomen (Leung, Riutta 2011; NLM 2014a).

7 Diagnosis

A diagnosis of constipation is generally based on bowel habits, duration and severity of symptoms, and medical history. A digital rectal examination may also be indicated (Rao 2014).

A specific set of criteria known as Rome III is widely used for **diagnosing functional gastrointestinal disorders**, including constipation and constipation-predominant irritable bowel syndrome (IBS-C) (Drossman 2006). According to Rome III, constipation symptoms for at least six months along with two or more of the following criteria for at least three months constitutes chronic constipation (Leung, Riutta 2011; Jamshed 2011):

- Straining with at least 25% of bowel movements
- Lumpy or hard stools at least 25% of the time
- Sensation of incomplete emptying with at least 25% of bowel movements
- Sensation of an anal or rectal blockage with at least 25% of bowel movements
- The use of hands or fingers to facilitate at least 25% of bowel movements
- Fewer than three bowel movements per week

Diagnostic tests are recommended if an underlying condition, such as hypothyroidism, may be a contributing factor. Further testing, including a complete blood count and endoscopy, may be indicated for people who have one or more “alarm features” in their history or physical exam (Rao 2014; Jamshed 2011):

- rectal bleeding
- positive occult blood (microscopic traces of blood in the stool)
- iron-deficiency anemia
- unintended weight loss of 10 pounds or more
- symptoms of obstruction
- recent onset of symptoms (especially in an older individual)
- rectal prolapse
- change in stool diameter
- family history of colon cancer
- age older than 50

8 Conventional Treatment

First-line **treatment for uncomplicated primary constipation** is to ensure adequate dietary fiber and fluid intake and physical activity level (Rao 2014; Basilisco 2013). These approaches are discussed in detail in the *Diet and Lifestyle Considerations* and *Integrative Interventions* sections.

If the diagnosis is secondary constipation, efforts should be made to treat the cause (eg, an underlying medical condition or medication side effect), but it may still be helpful for these patients to increase dietary fiber and fluids and to engage in regular physical activity (Rao 2014).

Supplemental Fiber

Methylcellulose and calcium polycarbophil. Methylcellulose and calcium polycarbophil are synthetic fibers commonly recommended to treat constipation, though there is little research into their effectiveness (Leung, Riutta 2011; Lembo 2003). Excessive gas and bloating are possible side effects of methylcellulose treatment (Rao 2014).

Laxatives

Laxatives are the first-line treatment for chronic constipation that persists despite dietary and lifestyle changes (Rao 2014). Fiber supplements are sometimes referred to as bulk laxatives. There are three other categories of laxatives: stool softeners or emollients, osmotic laxatives, and stimulants (Muller-Lissner 2013; Lembo 2003; Leung, Riutta 2011). Overall, studies show laxatives increase the number of bowel movements (Muller-Lissner 2013; Pare 2014), but 28–75% of laxative users report not being satisfied with the results (Muller-Lissner 2013; Johanson 2007).

Laxatives, especially those of the stimulant variety, should not be used haphazardly or in excess, especially by those who take diuretics. Excessive laxative use in combination with diuretics can lead to potentially dangerous fluid and electrolyte imbalances (Sankar 1998). Even without diuretics, excessive laxative use—particularly stimulant laxatives—may cause electrolyte and fluid balance problems (Roerig 2010).

Stool softeners. Stool softeners, such as the commonly used docusate sodium, increase the water content of stool to facilitate elimination (Siegel 2005; Portalatin 2012). Mineral oil acts as a lubricant or emollient and is thought to facilitate easy passage of stool. Stool softeners are often the next choice of laxative when supplemental fiber is ineffective or not well tolerated (Leung, Riutta 2011), but there is little evidence demonstrating their effectiveness (Pare 2014).

Osmotic laxatives. Osmotic laxatives are unabsorbed compounds that attract water as they move through the colon (Basilisco 2013). Polyethylene glycol (PEG; Miralax), lactulose, sorbitol, glycerin, and magnesium hydroxide (Milk of Magnesia) are common osmotic laxatives, with PEG having the most evidence for increasing stool frequency and softness (Siegel 2005; Leung, Riutta 2011; Pare 2014). PEG has considerable side effects, however, including nausea, flatulence, and diarrhea, particularly in older individuals (Leung, Riutta 2011; Basilisco 2013).

Stimulant laxatives. Stimulant or irritant laxatives stimulate the enteric nerves that trigger peristalsis. They also inhibit water resorption and stimulate water secretion in the colon, keeping moisture in the stool. Bisacodyl (Dulcolax), sodium picosulfate, and senna are common stimulant laxatives. Senna is made from the pods of senna, or cassia, trees and is a source of plant chemicals called anthraquinones, which are the active component (Rama Reddy 2015; Franz 1993; Adamcewicz 2011). Both bisacodyl and senna have been shown to relieve constipation, but they frequently cause abdominal pain and diarrhea; therefore, they are best used short-term for acute constipation or long-term only in people who do not improve with other types of laxatives (Rao 2014; Roque 2015; Pashankar 2005; Connolly 1974; Basilisco 2013; Gartlehner 2007; Pare 2014; Leung, Riutta 2011). Overuse of stimulant laxatives may damage the neuromuscular system of the colon, aggravating constipation. Because many individuals attempt to remedy this problem with further use of stimulant laxatives, this condition has been referred to as “dependence” (Zhao 2012; Mayo Clinic 2014a; Mehler 2003).

Prosecretory agents. Much like stimulant laxatives, prosecretory agents cause the release of water into the intestines. Unlike osmotic laxatives, which attract and retain water molecules, prosecretory agents stimulate water flow into the intestine, reducing bowel transit time (Thomas 2015; Thayalasekeran 2013; Portalatin 2012).

There are two drugs in this category that have been approved the Food and Drug Administration (FDA): lubiprostone (Amitiza) and linaclotide (Linzess) (Thomas 2015). Clinical trials have shown that both of these medications can increase the frequency of bowel movements in individuals with chronic constipation and constipation-predominant irritable bowel syndrome (IBS-C) (Lee 2014; Liu 2011; Thayalasekeran 2013), and reduce the abdominal pain that characterizes IBS-C (Thayalasekeran 2013; Thomas 2015). However, only 20–33% of patients in these trials had beneficial responses to the medications. Side effects may also limit the usefulness of these agents: nearly 20% of those with IBS-C and 16% of those with chronic constipation treated with linaclotide developed diarrhea, both significantly higher rates than in the placebo groups. The most common side effect associated with lubiprostone treatment was nausea. Temporary shortness of breath and chest pain were rarely observed; these adverse reactions may be attributable to intestinal distention. This class of medications has also been associated with urinary tract infections, sinusitis, abdominal pain or bloating, gas, and headache, although it is not clear whether the drugs caused all of these side effects (Thomas 2015).

Suppositories and Enemas

Rectal suppositories, made with laxatives like glycerine or bisacodyl, and enemas containing saline, tap water, and even soap suds can prompt immediate bowel emptying and are generally used on an as-needed basis to treat or prevent obstruction or impaction (Portalatin 2012; Roque 2015; Rao 2014).

Surgery

Surgery is a last resort for people with severe intractable symptoms and diminished quality of life (Andromanakos 2015). Available data on the efficacy of surgical treatment is inconclusive (Lee 2014), but is unlikely to be beneficial in those with motility problems that extend to the small intestine and stomach (Rao 2014).

9 Novel and Emerging Strategies

Fecal Microbiota Transplant

The microorganisms that populate the gut, known as the microbiota, are critical to normal, healthy function of the gastrointestinal tract (Dima 2012; Choi 2015; Rossen 2015; Furnari 2012). In **fecal microbiota transplant**, the colonic microorganisms of a healthy person are transferred to a symptomatic person. A number of different fecal microbiota transplant methods are under investigation, including direct infusion of prepared fecal matter into the gastrointestinal tract and encapsulation of a highly refined preparation for oral administration. Fecal microbiota transplant is an effective treatment for recurrent *Clostridium difficile* infection, an increasingly common and difficult to treat cause of severe infectious diarrhea (Youngster 2014; Brown 2014). The potential of fecal microbiota transplantation to treat many diseases including inflammatory bowel disease, Parkinson's disease, multiple sclerosis, and metabolic syndrome is an area of active investigation (Xu 2015; Kelly 2015).

A series of five case reports of patients with chronic constipation-predominant irritable bowel syndrome (IBS-C) treated with fecal microbiota transplant describe immediate remission in all five cases; stool frequency increased to one to two bowel movements per day without the use of laxatives. These patients were followed for 6–28 months, during which the improvement was stable (Borody 2004).

Because the FDA regards human feces as an unapproved drug, fecal microbiota transplants require FDA approval under their Investigational New Drug program, except in cases of recurrent bowel infection due to the bacterium *Clostridium difficile* (Moore 2014).

Biofeedback Therapy

Biofeedback therapy is a behavioral treatment for chronic constipation that has demonstrated superiority to laxatives in several controlled clinical trials. In biofeedback training, patients learn how to coordinate muscular activity in the pelvic floor, abdomen, and diaphragm to achieve normal and complete defecation. There are no known adverse effects of biofeedback therapy for constipation. On average, four to six 1-hour sessions, two weeks apart, are required for successful retraining, and periodic sessions to reinforce training may be of use in the long term (Rao 2011; Lee 2014; Basilisco 2013; Camilleri 2010).

Biofeedback therapy is not widely utilized, perhaps due to the shortage of skilled practitioners, as well as the labor-intensive and time-consuming nature of the therapy. There is also no consensus on biofeedback's

importance: some sources suggest it to be a last resort after other treatments have failed, while some researchers recommend it as first-line treatment (Basilisco 2013; Camilleri 2010). The ability to use home-based biofeedback training protocols, some of which are currently under investigation, may enhance the acceptance and use of this promising therapy (Rao 2011).

Sacral Nerve Stimulation

Sacral nerve stimulation involves the use of an electrical lead that is inserted through the skin and through an opening in the lowest part of the spine (the sacrum). Low voltage/low frequency electrical impulses are delivered directly to the third or fourth sacral nerve (Sharma 2013; Thomas 2013; Norderval 2011). The degree of stimulation is adjusted for each patient so it is close to the threshold at which the electrical impulse can be felt (Duelund-Jakobsen 2013; Koch 2005).

This technique has been used successfully to treat urinary retention and urinary and fecal incontinence, and has more recently been employed to treat chronic constipation. Sacral nerve stimulation appears to increase peristaltic waves in the colon and increase bowel movement frequency in people with slow-transit constipation (Thomas 2013; Sharma 2013; Norderval 2011). A study of sacral nerve stimulation enrolled 45 participants with at least one year of severe slow or normal-transit constipation and who had not responded to other treatments. Subjects were followed for a median of 28 months after implantation of a permanent sacral nerve stimulation device. Constipation scores decreased significantly and 87% of participants were considered to have achieved treatment success (Kamm 2010).

Side effects of sacral nerve stimulation include infection, pain around the stimulator, and pain in the perineum or extending down to the leg. In addition, 16–54% of people with a sacral nerve stimulator implant have needed a second surgery due to discomfort or a device malfunction, while 8–20% have had their device removed for these reasons (Norderval 2011).

Interferential Therapy

Interferential therapy, which involves the application of electrical current via electrodes taped onto the skin, has been used to treat musculoskeletal pain. For the treatment of constipation, two of the electrodes are placed on the lower back and the other two are placed opposite these on the lower abdomen, so there is an opposing pair on the front and back of the body (Queralto 2013). The electrodes emit different medium-frequency electrical currents, resulting in therapeutic stimulation where they intersect inside the body (Fuentes 2010).

In a pilot trial, 11 adults with slow-transit constipation who had been unsuccessful with other therapies used home-based devices to apply interferential therapy, one hour per day, for three months. At the end of the trial, seven of the participants had significantly increased bowel movement frequency, reduced constipation symptoms, and improved quality of life, with no adverse events (Queralto 2013). Preliminary research suggests interferential therapy may also be beneficial in individuals with irritable bowel syndrome (Coban 2012).

Medications

Prucalopride. Prucalopride (Resolor or Resotran) is a highly selective serotonin receptor activator and appears to be safer than earlier serotonergic agents for constipation. Prucalopride has been found to increase bowel movement frequency, reduce symptoms, and improve quality of life in people with chronic constipation (Tack 2015). The drug's side effects are usually short-lived and include headache, nausea, and diarrhea (Liu 2011; Shin 2014; Quigley 2012b; Thayalasekeran 2013).

Prucalopride has limited approval in Europe and Canada, where its authorized use is limited to treating women in whom laxatives have failed (Quigley 2012b; HC 2011). Prucalopride is not yet approved for use in the United States (Lee 2014).

Anti-opiates. Opiates are powerful sedative pain relievers. Examples include morphine, codeine, hydrocodone, fentanyl, and oxycodone. Constipation is a very common side effect of this class of medication (Gold Standard 2003; Coles 2007; Allouche 2014; Siemens 2015).

Naloxegol (Movantik) and methylnaltrexone (Relistor) are anti-opiates, drugs that block the effects of opiate drugs in the digestive tract but do not interfere with their pain-reducing properties. These medications can improve bowel movement frequency in people with opioid-induced constipation; their most common side effects are

nausea, diarrhea, and abdominal pain. Naloxegol and methylnaltrexone are approved for treatment of opioid-induced constipation. Alvimopan (Entereg), another anti-opiate, is approved for opioid-induced constipation but only during hospitalization. It has been associated with an increased risk of heart attack with long-term use, but more data are needed to determine if alvimopan consistently elevates heart attack risk (Corsetti 2015; FDA 2013; Siemens 2015; Watkins 2011). Naloxone (Narcan) is an anti-opiate that has been studied for the treatment of opiate-induced constipation and IBS-C (Gold Standard 2014).

Neurotrophin-3

. Neurotrophin-3 is a growth factor produced by the body that modulates the development and function of the nervous system. Neurotrophin-3 and related compounds may be able to combat age-related neurodegeneration in the gut, which could help relieve constipation (Camilleri 2008; Chalazonitis 2004; Zhou 1996). In a randomized controlled trial, 107 subjects with chronic constipation received injections of neurotrophin-3 or placebo in one of several dosing schedules for four weeks. Compared with placebo, those who received 9 mg of neurotrophin-3 three times per week had higher stool frequency, easier bowel movement passage, and more complete bowel movements at the end of the trial (Parkman 2003). Neurotrophin-3 is not currently available for the treatment of constipation.

10 Dietary and Lifestyle Considerations

Diet and lifestyle changes are first-line therapy for chronic constipation (Rao 2014; Jamshed 2011). Increased dietary fiber and water intake and physical activity are typically recommended before laxatives or other medications (Rao 2014; Leung, Riutta 2011; Lee 2014).

Eat a High-Fiber Diet

Ninety percent of Americans do not consume the recommended daily amount of fiber. The average fiber intake for Americans is only about 16 g daily, but the suggested intake is 22 g for women over 50 and 28 g for men over 50 (USDA 2010; King 2012; Schmier 2014; Chiba 2015; McRorie 2015). Increasing fiber intake is a simple, cost-effective solution in many cases of constipation (Schmier 2014).

In a trial in 117 people with chronic constipation, a diet containing 25 g of fiber per day for two months resulted in increased stool frequency and decreased laxative use. The improvement was more pronounced in a subgroup of participants instructed to drink 2 L of mineral water per day compared with those told to drink as much water as they wanted (Anti 1998). Another preliminary trial found that eating a breakfast cereal containing 5.4 g of fiber (mainly from wheat bran) daily for two weeks had beneficial effects on bowel function in people whose regular diets included less than 15 g of fiber per day; improvements in constipation, bloating, sluggishness, and digestive discomfort were noted (Lawton 2013). Many other trials of various forms of supplemental dietary fiber have demonstrated improved bowel movement frequency and clinical benefit in constipation (Xu 2014; Yang 2012; Woo 2015; Quartarone 2013; Dahl 2003; Rao 2015).

Specific Foods to Help with Constipation

In addition to consuming plenty of dietary fiber and staying adequately hydrated, a few specific foods may improve bowel regularity.

Prunes. Prunes (dried plums) have long been used to treat constipation. It is thought that their laxative effect is in part due to their high concentration of sorbitol, a slowly digested sugar that has an osmotic effect and holds water in the intestines (Stacewicz-Sapuntzakis 2001).

Kiwifruit. Kiwifruit is a traditional laxative food. Several clinical trials have found that eating kiwifruit can relieve constipation (Rush 2002; Chan 2007; Chang 2010).

Olive and flaxseed oil. A preliminary study tested the effects of mineral oil, olive oil, and flaxseed oil in 50 dialysis patients with constipation. The participants were given one of these three oils to take daily for four weeks, at a dose of about 1 tsp per day. All three oils reduced constipation scores, with olive oil demonstrating some superiority to flaxseed oil. These results suggest edible oils might be a useful alternative to mineral oil for the treatment of constipation (Ramos 2015).

Increase Water Consumption

Increasing fluid intake is an effective treatment for constipation (Markland 2013). In addition, water and fiber appear to work best together (Anti 1998). Water restriction has been demonstrated to rapidly reduce bowel movements in healthy people (Klauser 1990), and low fluid consumption has been associated with an increased risk of chronic constipation (Markland 2013). In individuals living in nursing homes, low fluid intake is an important factor that predisposes to constipation (Robson 2000). Hydration may be an especially important consideration in those with Parkinson's disease, a condition associated with elevated risk of constipation (Ueki 2004).

High-mineral-content water may be more helpful in treating constipation than typical lower-mineral water. In a four-week study, women with chronic constipation were given 1.5 L of drinking water per day. They were divided into three groups based on the composition of the water received, which contained either 1 L, 0.5 L, or none of a high-mineral natural spring water. By week two of the study, the women whose daily water included 1 L of mineral water had better stool consistency and less use of laxatives than women in the other two groups. Response to treatment corresponded to concentrations of magnesium and sulfate in the mineral water (Dupont 2014).

Increase Physical Activity

A sedentary lifestyle is a major contributor to many chronic diseases, including constipation (Booth 2012; Sandler 1990; Khatri 2011), and a recommendation of regular exercise is part of standard management of constipation in adults (Rao 2014; Borre 2015). In a study in which experimental bed rest was imposed on healthy men for 35 days, 60% developed constipation (Iovino 2013).

Other studies have found that exercise interventions can successfully improve chronic constipation (Beradze 2011). In one such study in 43 participants with chronic constipation, 30 minutes of brisk walking twice weekly plus a daily 11-minute strength and flexibility program for 12 weeks led to significant reductions in most constipation symptoms (De Schryver 2005).

Squatting

In a study designed to determine the ideal posture for ease of defecation, 28 healthy adults adopted three different defecation postures, each for six consecutive bowel movements, and recorded the time and ease of defecation. The first posture was seated on a standard toilet; the second was seated with feet resting on a 10 cm-high footstool; and the third was squatting, using a flat container. For all of the participants, squatting was associated with the shortest time spent moving stool and the easiest sensation of bowel emptying (Sikirov 2003). According to the study authors, the straightening of the recto-anal angle that occurs with squatting is the natural posture for defecation (Sikirov 1989; Sikirov 2003).

Squatting may not be reasonable or possible for many people with constipation, especially older people. Toilet accessories that approximate the squatting position are available commercially but their usefulness has not been proven.

Comprehensive Lifestyle Changes

Researchers assessed a chronic constipation education program in 35 chronically constipated women. The program guidelines were: consume 25–30 g of fiber per day by eating fruits, vegetables, and whole grains; drink 1.5–2 L of fluids per day, preferring water and avoiding diuretic drinks such as alcohol; incorporate regular exercise in the form of walking, with a goal of 3.5–5 hours per week; use the toilet at the same time each day whether or not there is an urge; and use a squatting posture to promote proper defecation. After three months, measures of constipation symptoms and severity had improved significantly (Ayaz 2014).

11 Nutrients

Probiotics

The gut microbiome is increasingly recognized as a key factor in the functioning, or malfunctioning, of the entire digestive tract. **Probiotics** are supplements containing live microorganisms that are taken to improve health. Probiotics are effective in treating a wide array of digestive disorders, including chronic constipation and IBS-C (Sharifi-Rad 2020). They can also have important effects on immune and metabolic health, broadening their potential therapeutic uses to include prevention or treatment of such diverse disorders as allergies, infections,

skin disorders, heart disease, type 2 diabetes, obesity, depression, and neurological disorders (Yu 2020; Johnson 2021; Raheem 2021; Yang 2021; Zhao 2021).

Many individuals with constipation show alterations in their gut microbiome. The most consistent findings suggest those with IBS-C have fewer *Bifidobacterium* species and related bacteria in their intestinal flora (Ohkusa 2019). Probiotics, most of which contain strains of *Lactobacillus* and/or *Bifidobacterium*, may help relieve constipation through their ability to favorably influence gut microbiome composition, reduce intestinal inflammation, and promote healthy intestinal motility through their effects on the enteric nervous system (Dimidi 2020). Evidence from randomized controlled trials and meta-analyses indicates that specific probiotics can improve gut function and reduce symptoms in those with chronic constipation and IBS-C (Ohkusa 2019; Dimidi 2020; Kaminski 2020; Zhang 2020). For example, one meta-analysis that pooled findings from 15 randomized controlled trials with a combined total of 2,327 participants found mixed probiotics shortened gut transit time, increased stool frequency, improved stool consistency, and reduced bloating (Zhang 2020). Nevertheless, the optimal probiotic strains, doses, and duration of treatment have not yet been conclusively identified (Ohkusa 2019; Dimidi 2020; Kaminski 2020).

B. lactis (also called *B. animalis* subspecies *lactis*) is a probiotic species that has been widely studied and has demonstrated particular promise for treating constipation. *B. lactis* supplements may work in part by increasing numbers of endogenous colonic *Bifidobacterium* species in constipated adults, and this effect may be enhanced by the addition of a prebiotic fiber such as inulin (Tanaka 2015; Anzawa 2019).

In a randomized controlled trial in 156 subjects with functional constipation, a supplement providing 10 billion colony-forming units (CFUs) of *B. lactis* strain HN019, 10 billion CFUs of*L. acidophilus* strain NCFM, 2.5 billion CFUs of each*L. paracasei* strain Lpc-37 and two other strains of *B. lactis* per day relieved digestive discomfort better than placebo after two weeks (Airaksinen 2019). In a randomized controlled trial with 47 participants suffering from constipation symptoms and long transit time, consuming a yogurt that contained polydextrose and at least 1 billion CFUs of each *B. lactis* HN019 and *L. acidophilus* NCFM for two weeks shortened transit time and reduced constipation symptoms compared with non-probiotic yogurt (Magro 2014). Another randomized placebo-controlled trial that included 228 participants with functional constipation found *B. lactis* HN019 alone, at a dose of 10 billion CFUs per day, for 28 days increased stool frequency and reduced straining in a subgroup of those reporting three or fewer bowel movements per week at baseline (Ibarra 2018). *B. lactis* HN019 was also shown to reduce transit time and relieve symptoms compared with placebo in a trial with 100 participants whose average stool frequency at baseline was 1–3 per week. In this trial, a daily dose of 17.2 billion CFUs was more effective than 1.8 billion CFUs (Waller 2011). Eating 30 grams (one ounce) of cheese enriched with *B. lactis* daily for 30 days was also found to reduce constipation symptoms in a small controlled trial with 30 female participants (Favretto 2013). In an open trial, taking a fermented milk supplement containing a combination of *B. lactis* and *L. casei* for four weeks led to reduced constipation symptoms and decreased inflammatory cytokine levels (Wang 2020). However, not all probiotics or even all strains of *B. lactis* have been found to have beneficial effects on constipation (Dimidi 2019; Dimidi 2020), so it is important to use a probiotic with a clinically validated strain.

Magnesium

Magnesium is an age-old remedy for ameliorating constipation. In fact, magnesium sulfate, commonly known as Epsom salts, has been used for this purpose for over 350 years. Magnesium is an osmotic laxative, drawing water into the bowel, and provoking the need for elimination (Mori 2021).

In adults and children, randomized controlled trials have shown magnesium supplementation to be safe and effective for improving chronic constipation. In adults, one of these studies found that in Japanese women with mild-to-moderate chronic constipation, 500 mg of magnesium oxide taken three times daily for 28 days significantly improved the frequency of spontaneous bowel movements (SBM), colon transit time, and Bristol stool type compared with placebo. Symptoms overall and constipation-related quality of life were also significantly improved (Mori, Tomita 2019). In a three-arm study of 90 adults (the majority being female) with chronic constipation, 28 days of treatment with 1,500 mg of magnesium oxide was compared to 1,000 mg of senna or placebo. There was a significant improvement overall in the groups treated with magnesium oxide and senna (68.3% and 69.2%, respectively) compared with placebo (11.7%). Improvements in SBM and complete SBM were also significantly greater in the active treatment arms than placebo (Morishita 2021). Multiple clinical trials

in children found magnesium oxide improved constipation comparable to probiotic treatments (Bu 2007; Kubota 2020).

Because mild abdominal discomfort can occur with magnesium use, it is best to titrate or divide doses during the day. Excessive use of magnesium in individuals with constipation, particularly those with late-stage chronic kidney disease, can lead to hypermagnesemia (Mori, Suzuki 2019). Those taking additional laxatives and using magnesium in excess of 1,000 mg daily are also at greater risk of this adverse effect. In healthy individuals, the kidneys filter 2,000–2,400 mg of magnesium daily (Blaine 2015), and there is little risk associated with lower doses of magnesium for laxative purposes.

Magnesium and Vitamin C

Instead of relying on chemical laxatives, the proper nutrients taken at the right time can support soft fecal consistency and induce colonic peristaltic action without serious adverse effects (Tatsuki 2011; Farlex 2015).

There are convenient powdered formulas available that contain magnesium mixed with ascorbic acid that can induce a bowel movement relatively quickly (typically 30–90 minutes). A teaspoon or more of **vitamin C** and **magnesium** crystals will evacuate the bowel within 30–90 minutes if taken on an empty stomach with several glasses of water. One of these powdered formulas provides **4500 mg** of vitamin C and **250 mg** of magnesium in each teaspoon. The dose needs to be individually adjusted so it will not cause day-long diarrhea.

Buffered **vitamin C powders** combined with primarily **potassium** salts can work as well as **magnesium/vitamin C powders** and may be used on alternate days for those needing ongoing relief.

The suggested number of times these nutritional colon cleanses be used is about three times per week. Excess use may create tolerance and require higher dosing.

Fiber

Soluble fiber supplements absorb water and hold it in the intestines, keeping the stool soft and easy to move, and tend to create a lubricating film when exposed to water; insoluble fiber supplements add bulking particles to the stool and shorten transit time by stimulating peristalsis (Yang 2012; Suares 2011b; Eswaran 2013). Soluble fibers are generally fermentable, which means they can be digested by microbes in the intestines. This quality is referred to as “prebiotic.” Prebiotic fermentable fibers are important for establishing and maintaining healthy colonies of beneficial bacteria in the gut (Quigley 2010). Soluble fiber is present in psyllium husk, legumes, nuts, seeds, and some fruits and vegetables. Sources of insoluble fiber include wheat bran, whole grains, and vegetables (NLM 2014b).

Psyllium. The husk of the psyllium seed, a product of the *Plantago ovata* plant, is rich in soluble fiber and contains some insoluble fiber (Moreno 2003); many well-designed trials have demonstrated that **psyllium fiber** supplementation relieves constipation and irritable bowel syndrome (McRorie 1998). Psyllium has also been associated with increased stool frequency in constipated Parkinson’s disease patients (Ashraf 1997). In patients with chronic primary constipation, taking 5 g of psyllium twice daily improved stool consistency and frequency (Ashraf 1995).

In one clinical trial, 5 g of psyllium per day was shown to be superior to docusate sodium as both a stool softener and a laxative (McRorie 1998). In fact, psyllium fiber supplements are FDA-approved as laxatives. Psyllium should be taken with a full 8 oz glass of water and be accompanied by adequate fluid consumption throughout the day. It is considered best to introduce psyllium gradually (UMMC 2013b; Eswaran 2013).

Psyllium has several ancillary benefits as well, including improving the lipid profile (Komissarenko 2012; Sartore 2009), glucose metabolism (Ziai 2005; Karhunen 2010), and blood pressure control (Cicero 2007).

Other fibers. Although psyllium is one of the most common and most thoroughly studied types of supplemental fiber, several other fibers can be used to supplement dietary intake as well:

- **Inulin.** Inulin is a prebiotic soluble starch that functions as fiber in the digestive tract. Inulin is found in many plant foods, most notably in Jerusalem artichoke and chicory root, but also in more commonly eaten vegetables like onions, garlic, and asparagus (Nishimura 2015). It is considered a prebiotic fiber because of

its positive effects on colonies of beneficial bowel bacteria (Kolida 2002). A rigorous analysis of many randomized controlled trials concluded that supplemental inulin can decrease transit time, increase stool frequency, and improve stool softness in people with chronic constipation (Collado Yurrita 2014).

- **Partially hydrolyzed guar gum.** Guar gum is a product from the guar bean (*Cyamopsis tetragonoloba)*. Partially hydrolyzed guar gum is a soluble, fermentable fiber that is more palatable and less likely to cause adverse effects than whole guar gum (Lewis 1992; Slavin 2003). Preliminary research shows that supplemental guar gum helps relieve constipation symptoms in patients with constipation-predominant irritable bowel syndrome (IBS-C) (Polymeros 2014; Russo 2015; Quartarone 2013; Slavin 2003).
- **Glucomannan.** Glucomannan is a soluble, fermentable fiber found in many plants, especially the root of the konjac plant (*Amorphophallus konjac)*. It has prebiotic effects, supporting the beneficial bacteria in the large intestine (Tester 2013). Several clinical trials showed that glucomannan improved multiple measures of constipation better than placebo (Marzio 1989; Passaretti 1991; Chen 2008).
- **Pea fiber.** In a preliminary study that included 114 elderly subjects who lived in nursing homes and had constipation, the addition of 1–3 g of pea fiber powder to other foods three to four times per day for six weeks significantly increased stool frequency and decreased laxative use (Dahl 2003).
- **Flaxseed.** Flaxseed is a source of both soluble and insoluble fibers. The soluble fiber in the outer coating of the flaxseed is a mucilage that becomes slippery when wet. Mucilages, like all soluble fibers, increase moisture in stool (Kajla 2015) and are thought to have lubricating effects (Hanif Palla 2015).

Cascara Sagrada

The bark of the buckthorn tree, known as **cascara sagrada** (*Rhamnus purshiana*) (UU 2015a), has traditionally been used to treat constipation. Like senna, which is a commonly used stimulant laxative in the conventional management of constipation (Rogers 2013; Rao 2014), cascara sagrada contains anthraquinones, which stimulate peristalsis by irritating or stimulating the intestinal neuromuscular apparatus (Sigma-Aldrich 2010; NLM 2015; UU 2015a). Stimulant laxatives like cascara may cause diarrhea and electrolyte loss, and so are generally recommended for short-term use only (UMMC 2013a).

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