 Irritable bowel syndrome (IBS) is a functional bowel syndrome characterized by abdominal discomfort and alterations in bowel movements. Previously thought to be the result of psychological problems and stress, there is a recent focus involving the motility of the intestinal tract, autonomic system regulation, and increased visceral sensitivity. IBS is predominantly found in women, and most patients who seek treatment are between 20 and 50 years of age. Although only 10% to 30% of patients seek treatment, IBS accounts for 3.5 million office visits and is a leading cause of workforce absenteeism.

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Treatment Options for Irritable Bowel Syndrome
**Types**

There are three types of IBS that are categorized according to the severity of symptoms and the ability of symptoms to interfere with the patient’s daily functioning. The first is mild and, while symptoms do worsen with dietary intake and stress, there is no effect on the patient’s daily functioning. For intermittent IBS there is an increase in symptoms that begin to interfere with the patient’s daily functioning, a psychological component becomes apparent, and there is no correlation between symptoms and precipitating factors. The final type of IBS is continuous, in which every aspect of daily life is affected, there is a definite psychological component, and there is no identification of precipitating events.1

**Causes**

IBS causes, originally believed to be psychological, are now believed to be physiologic in origin and exacerbated by psychological stressors. Psychological components, perhaps triggers of the disorder, may include physical or emotional stress, and physical or sexual abuse. Other nonpsychological triggering factors might be lactose-containing foods, caffeine, alcohol, and fatty or spicy foods. With this in mind, the focus of treatment is directly related to the symptoms and causes or precipitating factors.1 Another cause or risk of IBS occurs after a gastrointestinal infection such as gastroenteritis, known as postinfective IBS. These patients have a low-grade inflammatory response.3

**Pathophysiology**

The pathophysiology underlying the disorder is related to altered motility and sensory abnormalities, which further leads to a dysregulation of the bowel by the central nervous system (CNS). Changes in neurotransmitters, such as serotonin, substance P, vasoactive intestinal peptide, neurotensin, cytokines, and others, contribute to visceral hypersensitivity, centrally controlling pain mechanisms, and dysregulation of the brain-gut axis. Local reflex mechanisms are responsible for the mechanical distention of the intestines that affect the emptying rate of the proximal colon, which determines overall function. Innervated intrinsic and extrinsic neurohormonal agents regulate bowel function. Inflammation and changes to the intrinsic neurotransmitters cause a bowel motor dysfunction. Extrinsic agents, such as food, stress, and endogenous hormones, can also cause a bowel motor dysfunction. Accelerated intestinal transit times or delayed colon transit time determines IBS that is either diarrhea-predominant or constipation-predominant. Because 90% of serotonin is present in the gut, pharmacologically blocking serotonin in the intestinal tract results in decreased visceral pain, transit time, and secretions, which is the current area of focus for exploring new therapeutic agents.1,2

Another area of focus still undergoing research is the alteration in intestinal flora and its importance in the pathophysiology of IBS.5

**Signs and Symptoms**

IBS is characterized by abdominal pain associated with a change in the consistency of the stool. In 2006, The Rome Foundation introduced the Rome III diagnostic criteria for IBS, which is as follows: At least 3 months with onset at least 6 months previously of recurrent abdominal pain or discomfort associated with two or more of the following:

- improvement with defecation; and/or
- onset associated with a change in frequency of stool; and/or
- onset associated with a change in form (appearance) of stool.

Discomfort is defined as an uncomfortable sensation not described as pain.5

Patients with IBS usually present with abnormal bowel habits, alternating between diarrhea and constipation, or predominantly diarrhea or predominantly constipation. Other associated symptoms include abdominal distention, bloating, gassiness, and a feeling of urgency after a meal, relieved with defecation. Any worsening of these symptoms is atypical and could be indicative of another more serious intestinal problem that would warrant further studies.1

**Diagnosis and Testing**

To diagnose and treat IBS, the healthcare provider must conduct a thorough history and physical to rule out other potential diseases. The history should include any medications the patient may be taking to rule out the possibility that symptoms may be side effects of a medication. Dietary habits must be taken into account to rule out any nutritional intolerance. Psychological stressors, acute or chronic, should also be discussed and taken into consideration. Physical examination findings may be within normal limits, though occasionally there may be some diffuse tenderness upon palpation, predominantly in the left lower quadrant, and some mild abdominal distention.1
In the absence of red flags, such as anemia, family history of colon cancer, fever, heme-positive stools, new or recent onset in patients older than 50 years of age, rectal bleeding, and weight loss, minimal diagnostic studies are necessary. Suggested studies include a complete blood count, chemistry profiles, thyroid function, and stool for occult blood, ova, and parasites. Other studies, including abdominal ultrasound, flexible sigmoidoscopy, barium enema, and colonoscopy, are not necessary in the absence of red flags, as the results will have no influence in the treatment regimen.

## Treatment Goals

One of the most important goals of IBS treatment is to help the patient realize that progress may be slow and is ongoing. It is necessary to create a plan outlining long-term strategies that the patient is willing to adhere to and understand. Ultimately, the goal of treatment is to utilize a multidisciplinary approach to help manage the symptoms so they do not interfere with individual daily functioning.

## Nonpharmacologic Treatment

Nonpharmacologic treatment incorporates dietary changes and lifestyle modifications. Patients need to identify particular food triggers. Common food triggers include lactose, aspartame, caffeine, alcohol, beans, cabbage, and fatty or spicy foods, and should be avoided. One method to aid in the identification of triggers is to keep a 1- to 2-week symptom diary of dietary intake, times of stress, and bowel movements and to then look for a correlation among them. Lifestyle modifications include the identification of life stressors that exacerbate the symptoms and methods to reduce them. Some techniques that might reduce stress are relaxation tapes, regular exercise, yoga, meditation, aromatherapy, hypnotherapy, and psychological counseling.

## Pharmacologic Treatment

Pharmacologic treatment is based on individual patient symptoms. Appropriate first-line medications for constipation-predominant IBS are osmotic laxatives, such as lactulose (Cephulac), magnesium citrate, and magnesium hydroxide. These exert an effect in the small intestine by drawing water into the lumen and softening the stool, and in the large intestine by producing colonic distention, which promotes peristalsis and further evacuates the bowel. These are among the few laxatives that are approved for long-term treatment. The most common adverse effects associated with their use are abdominal cramping, distention, nausea, and diarrhea. Lactulose is contraindicated in patients required to restrict galactose intake, and caution should be used when administering to patients with diabetes. Magnesium agents utilized to promote defecation are cautioned in patients with renal failure and in patients with a decreased ability to excrete magnesium due to the potential for systemic absorption.

For diarrhea-predominant IBS, loperamide (Imodium) is an appropriate first-line choice. Loperamide is an antidiarrheal that inhibits peristalsis by acting directly on intestinal mucosal nerve endings, thereby decreasing transit time; it also increases anal sphincter tone. Loperamide does not cross the blood-brain barrier into the CNS, which makes it the preferred antidiarrheal. Administration is cau-
tioned in hepatic impairment. Side effects are rare; the most common is constipation.3

An antispasmodic, dicyclomine (Bentyl), would be the best first-line option for the treatment of abdominal bloating and gas. It acts by competitively blocking acetylcholine and produces smooth muscle relaxation. Dicyclomine use is contraindicated in patients with glaucoma, pyloroduodenal stenosis, chronic obstructive pulmonary disease, cardiac dysrhythmias, impaired liver or kidney function, and myasthenia gravis. Caution should be used in patients with hypertension, hyperthyroidism, and benign prostatic hypertrophy. Common side effects include dry mouth, altered taste perception, nausea, vomiting, dysphagia, blurred vision, palpitations, and urinary hesitancy and retention.1

Another medication currently under investigation for treatment of abdominal pain associated with IBS is phloroglucinol/trimethylphloroglucinol. These antispasmodic agents act directly on smooth muscle, reducing the intensity of pain. A recent double-blind, placebo-controlled study concluded that a 1-week treatment with phloroglucinol/trimethylphloroglucinol significantly reduced the intensity of the pain associated with IBS.7

A first-line treatment for the psychological component of the disorder is a selective serotonin reuptake inhibitors (SSRIs), such as fluoxetine (Paxil) or paroxetine (Prozac). It has been suggested that antidepressants alter the patient’s pain threshold and it is unclear whether they treat a concomitant depression or associated anxiety. SSRIs produce their effect by binding to the serotonin transporter and inhibiting the reuptake of serotonin into the presynaptic neurons. Use caution when administering SSRIs to patients at high risk for suicide, with a history of seizures, diabetes, and renal or hepatic disease. SSRIs have few adverse effects; the most common are nervousness, headache, nausea, dry mouth, and insomnia.1

For second-line treatment of constipation-predominant IBS the recommendation is to continue using osmotic laxatives. For diarrhea-predominant patients, diphenoxylate with atropine is an option. It increases smooth muscle tone in the intestines, inhibits motility and propulsion, and decreases intestinal secretions. Diphenoxylate has a longer duration of action but because of its addiction potential, it is only indicated for short-term treatment. Diphenoxylate has CNS effects and is contraindicated in patients who are hypersensitive to atropine and meperidine, and patients with hepatic impairment. Common adverse effects include dry mouth, dry eyes, urinary retention, blurred vision, drowsiness, and dizziness. Additionally, atropine may aggravate glaucoma.1

Second-line treatment for abdominal bloating and gas includes antispasmodic hyoscyamine sulfate. Though exhibiting the same anticholinergic effects as dicyclomine, it has a longer duration of action. Hyoscyamine sulfate also has a similar adverse events profile and the same precautions and contraindications are in effect as with dicyclomine.1

A second-line treatment for the psychological component of IBS is the institution of tricyclic antidepressants (TCAs) such as imipramine (Tofranil), desipramine (Norpramin), and amitriptyline. TCAs act by inhibiting the reuptake of norepinephrine and have less of an effect on serotonin. Common side effects include dry mouth, blurred vision, tachycardia, orthostatic hypotension, and electrocardiogram changes. TCAs are contraindicated in patients with cardiac conduction abnormalities and epilepsy. Though there is no difference in their effectiveness when compared to SSRIs, these agents are reserved for second-line treatment due to their increased side effects profile.1

Because of their ability to aggravate abdominal cramping and their dependency potential, the stimulant laxatives, such as bisacodyl and senna concentrates, are reserved for third-line treatment of constipation-predominant IBS. Stimulant laxatives work by producing a direct effect on the smooth muscle in the intestinal tract, increasing peristalsis and fluid accumulation, and promoting evacuation of the bowel. These agents are contraindicated in patients with appendicitis, acute surgical abdomen, fecal impaction, and intestinal obstruction. Common side effects include nausea, vomiting, and abdominal cramping.1

Surfactant laxatives, such as docusate sodium and docusate calcium only help in the prevention of constipation and are not indicated for acute treatment. These act by reducing the surface tension of the bowel contents, which allows for the incorporation of more fluid, stool softening, and easier defecation. Surfactant laxative use is contraindicated in patients with intestinal obstruction, undiagnosed abdominal pain, appendicitis, fecal impaction, or acute surgical abdomen. These agents are well tolerated with few side effects, which include mild abdominal cramping, diarrhea, and throat irritation.1

Alosetron (Lotronex) is a serotonin 5-HT3 receptor antagonist available for use and is indicated for women with
diarrhea-only IBS. In animal studies, it has been shown to decrease abdominal pain, slow colonic transit time, increase rectal tone, and increase stool consistency. Originally marketed in 2000, the Food and Drug Administration (FDA) pulled alosetron from the market due to reports of life-threatening cases of ischemic colitis. Alosetron was reintroduced with a prescriber protocol implemented by the manufacturer that requires prescribers to complete additional training.9

Another serotonin receptor antagonist, cilansetron, is undergoing clinical trials and has been granted priority review status by the FDA. Cilansetron is indicated for the treatment of diarrhea-predominant IBS and has been shown to be effective in relieving the abdominal pain and discomfort associated with the disease. Cilansetron produces an action similar to alosetron, though believed to be ten times more potent.9

Tegaserod (Zelnorm) was previously used for the treatment of women with constipation-predominant IBS. In March 2007, the manufacturer stopped selling the drug at the FDA’s request after a new safety analysis indicated an increased risk of heart attack, stroke, and worsening cardiac chest pain that can result in a heart attack in patients treated with tegaserod versus those treated with a sugar pill.10

A 5-HT3 antagonist and a 5-HT4 agonist, renzapride, is still undergoing clinical trials and has demonstrated positive results in constipation-predominant patients.11

Another alternative treatment for IBS and other gastrointestinal disorders are probiotics. Probiotics, such as Lactobacillus and Bifidobacterium, which are normally found in intestinal flora, may produce some effects on motility and the enteric nervous system.12 The mechanism of action of probiotics in IBS is still unclear but they are believed to decrease abdominal bloating and gas.13 When examining the likelihood of small-intestinal bacterial overgrowth as a contributor to IBS, treatment research has focused on nonabsorbed oral antibiotics such as rifaximin (Xifaxan) and their effectiveness on the symptoms of IBS. Rifaximin is a gut-selective antibiotic with negligible systemic absorption and a broad spectrum of activity. In a recent randomized trial, it was found that rifaximin improved IBS symptoms for up to 10 weeks after the discontinuation of the treatment.14

A complementary and alternative medicine that has been studied for use in the management of IBS is artichoke leaf extract.15 A limited study was done in patients with concomitant dyspepsia and results indicate that artichoke leaf extract reduced symptoms of IBS in patients and helped to improve patient quality of life.14 Other herbal preparations used for the treatment of abdominal pain are peppermint oil and caraway oil, though formal studies are necessary to prove their efficacy.6

## Monitoring Treatment Response

Once treatment is initiated, it is important to monitor patients for a response to therapy. There should be a follow-up appointment between 3 and 6 weeks after the original assessment and institution of therapy to evaluate progress and to alter the treatment regimen if necessary. It is important to provide continued support and to keep patients involved in their care. IBS is a challenging syndrome that requires time and patience to effectively manage the disorder. Continuous monitoring and medication adjustments for refractory symptoms are necessary to ensure an adequate therapeutic response allowing patients to function without being affected by the symptoms of the IBS.1

### REFERENCES


### ABOUT THE AUTHOR

Heidi Harmon is employed at Maine Coast Memorial Hospital, Ellsworth, Maine, and is a graduate student in the family nurse practitioner program at the University of Maine, Orono.