

# Meeting the challenge of

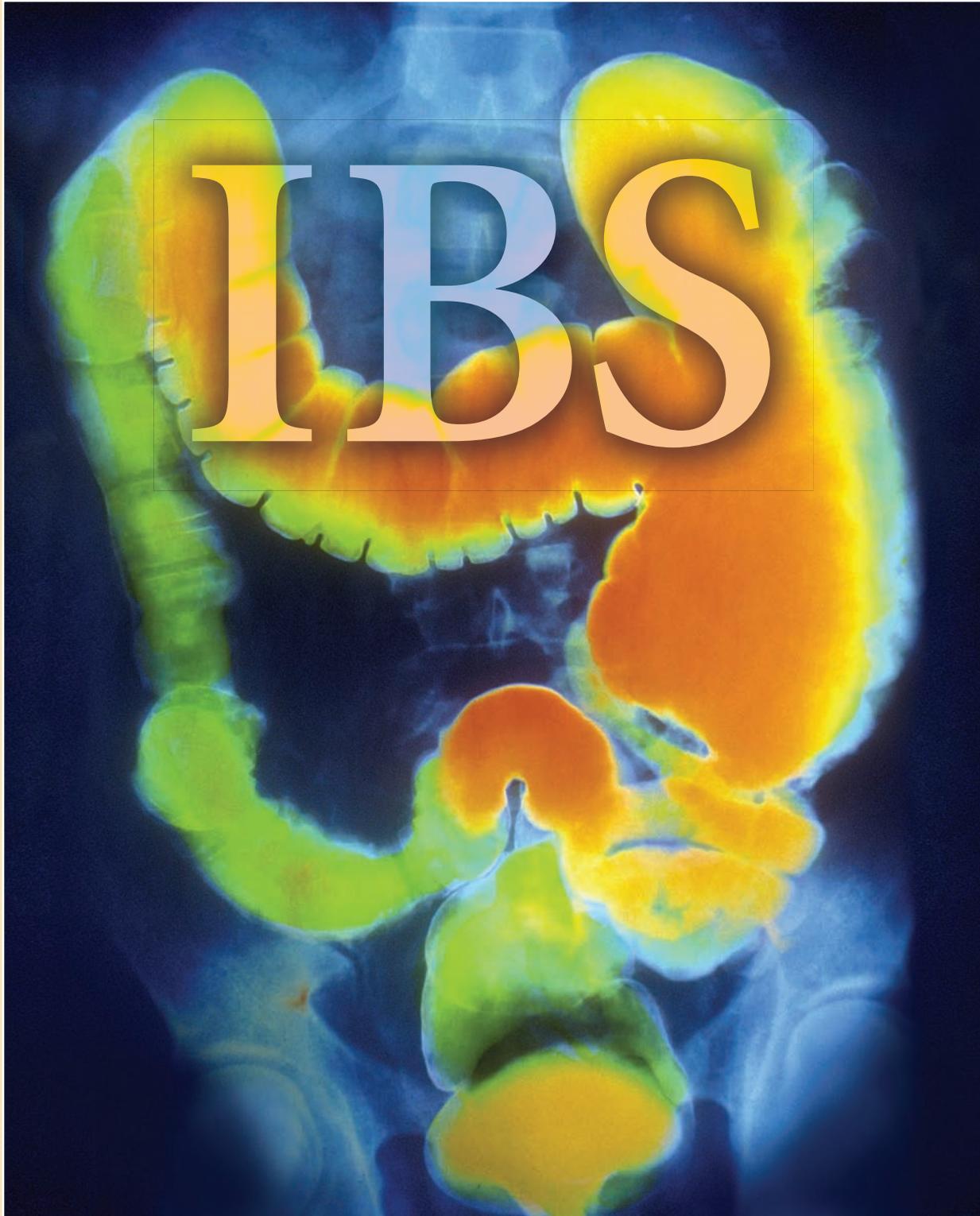


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***Abstract: Irritable bowel syndrome is frustrating and debilitating for patients, and management of this disorder is a challenge for healthcare providers. IBS is a common, functional, gastrointestinal disorder, and is often characterized by crippling symptoms without any pathologic findings.***

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Irritable bowel syndrome (IBS) is a functional gastrointestinal (GI) disorder affecting 10% to 26% of the U.S. adult population.<sup>1</sup> Fewer than 25% of people with symptoms consistent with an IBS diagnosis seek medical attention. The condition encompasses 12% of patients seen in primary care practices and 28% of patients seen in GI practices.<sup>2</sup> IBS comprises 41% of all functional GI disorders and affects women two times more often than men.<sup>3</sup> The economic impact of IBS is approximately \$20 billion per year in the United States.<sup>4</sup>

IBS is the best studied, most common functional GI disorder, and is often characterized by debilitating symptoms without any pathologic findings.<sup>5</sup> The predominant symptoms of IBS are abdominal pain and an alteration in bowel habits with an absence of organic pathology.<sup>3</sup>

### ■ Pathophysiology

Recent research has demonstrated that the GI tract processes sensory information differently in patients who have IBS when compared to people who do not. This demonstrates that IBS is a complex disorder involving a number of different physiologic processes. Some physiologic processes include abnormalities in gut motility, altered visceral sensory function, changes in central nervous system (CNS) processing of sensory information, GI tract inflammation, altered GI flora, and food allergies and sensitivities.<sup>6</sup>

The CNS modulates various functions in the GI system including secretion, motility, and bloodflow. Signals traveling from the gut to the brain are involved in regulatory reflexes.

Perception of events in the bowel involves activation of different paths with information modulated at peripheral and CNS levels.<sup>7</sup>

In the 1970s, research resulted in antroduodenal manometry, a way to measure motility patterns in the lower portion of the stomach and the duodenum. When motion patterns in patients with IBS were measured, bursts of rhythmic contractions were noted in the small intestine; other patients exhibited prolonged contraction. Both of these patterns resulted in abdominal pain.<sup>2</sup> It was also noted that some patients with IBS exhibited an alteration in the migratory motor complex resulting in a delay or accelerated intestinal transit.<sup>6</sup>

Studies have shown that patients who have signs and symptoms of IBS are more aware of pain. They also have more pain caused by balloon distension in the rectum at significantly smaller balloon volumes than healthy subjects.<sup>7</sup>

Patients with recent infectious gastroenteritis have an increased risk of developing IBS. Although the exact mechanism is unknown, it is thought that the infectious process may have damaged the enteric nervous system (ENS) or created an immune hypersensitivity to a previously benign substance.<sup>8</sup> Serotonin, an important neurotransmitter in the ENS, is found in the GI tract. An abnormality in the serotonin levels may produce abnormal intestinal transit. A serotonin-release deficit results in constipation; a serotonin-uptake defect results in diarrhea.<sup>6</sup>

IBS has long been considered a psychosomatic disorder because there is no clear pathophysiology. Stress and

**Key words: constipation, diarrhea, functional gastrointestinal disorder, irritable bowel syndrome**

emotional events can cause GI symptoms in healthy subjects, but affect IBS patients to a greater degree.<sup>7</sup> The most common psychological signs and symptoms associated with IBS are anxiety, depression, somatization, hostility, phobias, and paranoia. Fifty percent of patients with IBS meet the criteria for a psychological diagnosis as compared to 20% of GI patients with structural disorders and 15% of control subjects.<sup>7</sup>

The introduction of functional magnetic resonance imaging gave a better understanding of the brain-gut interaction and its alteration in IBS. This imaging clearly showed the difference in cortex function in response to gut stimulation between healthy subjects and IBS patients, and provided an avenue for pharmacologic and behavioral interventions.<sup>7</sup>

Approximately one-third of patients with suspected IBS have fructose intolerance. IBS patients also have an increased incidence of lactose intolerance.<sup>9</sup> The signs and symptoms of fructose and lactose intolerance include bloating, abdominal pain, flatulence, and diarrhea, which are also found in patients with IBS. A study of 80 patients with suspected IBS demonstrated relief when they followed a fructose-restricted diet, further indicating a correlation.<sup>9</sup>

■ **Structural diseases versus functional disorders**

Modern medicine focuses on structural or organic diseases to the exclusion of functional disorders. Structural diseases have a basis in the structure or anatomy of a body system, and structural diseases of the GI system include ulcers, inflammation, infection, and cancer.<sup>5</sup>

Functional disorders are based on how the system works, have no clear pathophysiologic cause, and usually do not result in system abnormalities (see *Common characteristics*

*of functional syndromes*). They affect most body systems, and include fibromyalgia (FM), chronic fatigue syndrome, interstitial cystitis, and chronic pelvic pain.<sup>5</sup> Functional disorders of the GI system include motility disorders in which the nerves and muscles of the GI tract do not function normally, and others in which patients experience hypersensitivity to pain.<sup>5</sup> It is not uncommon for patients to have more than one functional disorder. The most common functional disorder that coexists with IBS is FM.<sup>5</sup>

When diagnosing a functional disorder of the GI system, the following criteria must be met: symptoms should have occurred within the last 3 months, and the symptom onset should be at least 6 months prior to diagnosis.<sup>10</sup> Diagnostic tests are designed to identify structural problems, not functional disorders. Therefore, most diagnostic tests performed on patients with IBS are normal.<sup>5</sup>

IBS has no apparent physiologic mechanism. It is viewed as a biopsychosocial disorder resulting from an interaction between factors such as visceral hyperalgesia, genetic and environmental factors, infection, inflammation, gut motility, and psychological factors.<sup>7</sup> For this reason, establishing an IBS diagnosis depends on establishing a symptom complex.

■ **IBS subtypes**

The four subtypes of IBS include irritable bowel syndrome-diarrhea (IBS-D), irritable bowel syndrome-constipation (IBS-C), irritable bowel syndrome-mixed (IBS-M), and unsubtyped IBS.<sup>8</sup>

*IBS-D* is a condition where at least 25% of the time a patient has frequent, loose stools of small and medium volumes, not accompanied by abdominal discomfort at least 75% of the time. Stools produced by patients with IBS-D are a 6-7 on the Bristol Stool Form Scale, a tool used to characterize stool patterns.<sup>7</sup> Hard and lumpy stools occur less than 25% of the time. Bowel movements occur during waking hours, in the morning, or after meals. Most are preceded by urgency followed by a feeling of incomplete evacuation. Nocturnal diarrhea, bloody stools, dehydration, or weight loss are not features of IBS.<sup>11</sup>

*IBS-C* can last days to months with interludes of diarrhea or normal bowel function. Stool is hard and pellet shaped in 25% of bowel movements or a 1-2 on the Bristol Stool Form Scale (stools are either separate, hard lumps like nuts that are difficult to pass or sausage-shaped, but lumpy). Loose, mushy, or watery stools occur less than 25% of the time. Patients commonly experience a feeling of incomplete evacuation even when the rectum is empty.<sup>12</sup>

*IBS-M* is characterized by bowel movements that are hard and lumpy 25% of the time and 25% loose and mushy.<sup>13</sup> Stools are normal 50% of the time.

**Common characteristics of functional syndromes<sup>5</sup>**

1. No objective test results supporting an organic diagnosis
2. Diagnosis based on subjective report by the patient
3. Excessive utilization of healthcare services. IBS leads healthcare expenditure among GI diagnoses
4. Predominantly females—approximately 70%
5. Stress increases signs and symptoms
6. Psychosocial variable
7. Impaired quality of life
8. Impaired quality of sleep
9. Impaired sensory processing of the brain from the affected system
10. Healthcare provider/patient relationship is central to the treatment
11. Various functional disorders have similar treatment approaches regardless of the body system involved.

*Unsubtyped IBS* means the patient has insufficient abnormality of stool consistency to fit the definitions of IBS-D, IBS-C, or IBS-M.<sup>14</sup>

It should be noted that 75% of patients with IBS change subtypes within a year of initial diagnosis. Twenty-nine percent switch between IBS-C and IBS-D.<sup>3</sup>

### ■ Symptoms of IBS

Patients with IBS present with a symptom complex of chronic or intermittent abdominal pain and changes in stool consistency and frequency.<sup>8</sup> While normal defecation patterns range from three bowel movements per week to three bowel movements per day, there is an alteration of this pattern in patients with IBS.

Patients with IBS frequently complain of bloating and abdominal distension.<sup>4</sup> Bloating and abdominal distension may reflect an increase in intestinal gas or an increased sensation to a normal amount of intestinal gas.<sup>4</sup>

The Rome III criteria and the Manning criteria organize the symptoms of IBS to establish a diagnosis of IBS.<sup>4</sup> The Rome III criteria include recurrent abdominal pain or discomfort associated with at least two of the following:

- pain relieved with defecation
- onset associated with a change in frequency of stool
- onset associated with a change in form (appearance) of stool<sup>14</sup>

Manning established six criteria to differentiate IBS from organic bowel disease as follows:

- onset of pain associated with more frequent bowel movements
- onset of pain associated with looser bowel movements
- pain relieved by defecation
- visible abdominal bloating
- sense of incomplete evacuation 25% of the time
- mucorrhea more than 25% of the time.<sup>3</sup>

Other signs and symptoms of IBS not included in the Rome III or Manning criteria are abnormal stool frequency less than or equal to three times per week or greater than three times per day; abnormal stool form—lumpy and hard, or loose and watery; straining during defecation; urgency or feelings of incomplete bowel movements; passing mucus; and bloating.<sup>3,15</sup>

### ■ Diagnosing IBS

IBS can be diagnosed by taking a careful history, general physical exam, and routine lab testing. This also reassures the patient that his or her concerns are being taken seriously and may help identify other diagnostic processes that may be present.<sup>10</sup> Additional testing can be avoided if the

patient does not have any “alarm signs or symptoms,” or symptoms that are not consistent with IBS including weight loss, severe symptoms of either unrelenting diarrhea or abdominal pain, rectal bleeding or lower GI bleeding, physical exam findings of abdominal mass, anemia, and a change in chronic symptoms or fecal soilage, or acute onset at age 50 or older or a family history of colon cancer.<sup>8,10,16</sup>

Other symptoms that should raise concern would require a broader workup and include symptoms of inflammatory bowel disease or celiac disease.<sup>8</sup>

Abdominal pain or discomfort is a required symptom for an IBS diagnosis. Abdominal pain or discomfort should be present for 6 months or longer and present for at least 3 days per month for the last 3 months. It should also be associated with defecation.<sup>14</sup> Quality of pain is different for each patient; some patients report cramps, while others experience sharp, burning pain. Location of the pain may vary, but the hallmark sign is that the pain is consistent in the individual patient.<sup>6</sup>

Typically, physical findings are normal in patients with IBS. Some patients have abdominal tenderness or firmness in the lower abdomen. Findings that are inconsistent with

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IBS include rebound tenderness or guarding, a mass in the abdomen, or a bruit. Any abnormality noted on physical exam must be explored further.<sup>6</sup>

A digital rectal exam should be performed to rule out or confirm any existing pathology. An anal fissure may be noted in patients who have been straining with constipation. The presence of a perirectal abscess may suggest Crohn's disease. Rectal tenderness is normal in patients with IBS due to pathologic mechanisms associated with the disease process.<sup>6</sup> Significant rectal tenderness, a mass or blood in the rectum, or any other abnormality warrants further evaluation.<sup>6</sup>

When the patient exhibits inconsistent signs and symptoms, there may be an organic disease process present. Weight loss is not associated with IBS and should be considered a warning sign of a more serious condition. Reports of recent travel can alert the clinician to the possibility of a bacterial or parasitic infection. An obvious bleed from the rectum or vomiting blood is another indication of a serious condition that requires further investigation.<sup>4</sup> The

### Approach to diagnosis and management of IBS<sup>7</sup>

#### Medical history

Make the patient comfortable, be nonjudgmental. Use open ended questions and obtain:

- dietary history
- medication list (including prescription and over-the-counter medications, supplements, and herbal preparations)
- psychosocial history (any pertinent psychological factors)
- family history (malignancy, inflammatory bowel disease, and celiac disease)

#### Obtain a list of symptoms

- Is the patient's dominant symptom abdominal pain with altered bowel function?
- Symptoms such as weight loss, rectal bleeding, fever, persistent diarrhea, anemia, nocturnal symptoms of pain and abnormal bowel habits, new onset in patients age 50 years or older will point the NP away from a diagnosis of IBS

#### Physical exam

- Perform a thorough physical exam with focus on the abdomen
- Note any specific abdominal tenderness
- Note that findings are generally normal
- Symptoms such as anemia, jaundice, organomegaly, or abdominal mass will point the NP away from a diagnosis IBS

#### Lab tests

- Complete blood count
- Chemistry panel
- Thyroid function studies
- Stool for ova and parasites and for fecal leukocytes if diarrhea is the predominant symptom
- Rule out (R/O) celiac disease by obtaining antigliadin and antiendomysial IgA antibody serologic testing

#### Invasive tests

- Invasive tests include sigmoidoscopy and colonoscopy, and testing should be performed on patients with the following criteria:
  - Age >50 years with chronic, stable symptoms
  - Age >50 years and recent onset
  - Persistent diarrhea and rectal bleeding
  - Age ≥50 years need a colonoscopy to R/O colon cancer
  - Younger patients with hematochezia, diarrhea, and weight loss need a colonoscopy as well
- Mucosal biopsy
  - Any question of inflammatory bowel disease or colitis should have a mucosal biopsy

#### Treatment plan

- Treatment is based on symptom management
- Goal of treatment is to improve patient's quality of life and relieve the patient's symptoms

#### Follow-up

- Assess the patient's response to treatment in 4 to 6 weeks

possibility of abuse should also be raised in the initial interview of the patient with IBS. A higher incidence of IBS has been found in individuals, primarily women, who have been sexually or physically abused.<sup>2</sup>

Since there are no biological markers to indicate IBS, standardization in diagnosis has been difficult. Rome III criteria and Manning criteria have been used to standardize the diagnosis.<sup>8</sup>

The initial diagnosis of IBS can be established by the presence of the following:

- symptom-based criteria, such as Rome III or Manning criteria, are met
- negative physical exam
- cost-effective set of screening studies, such as CBC with differential, thyroid function studies, and stool sent for culture, ova, and parasite or *Clostridium difficile* have been performed and negative results established.<sup>6</sup>

Because the patient's symptoms may be rooted in an organic cause, it is important to exclude any organic cause of possible IBS symptoms; however, the diagnosis should not be made only by excluding organic causes. It is important to establish a symptom complex compatible with IBS (see *Approach to diagnosis and management of IBS*).<sup>7</sup>

#### ■ Diagnostic testing

If a patient is 50 years or older, presents with symptoms that raise a concern, has not had substantial symptom improvement after appropriate treatment, or symptoms are worsening, further testing is warranted. These additional tests include routine blood work, endoscopy, abdominal or colonic imaging, stool testing for occult blood and parasites, hydrogen breath test, and antibody testing for celiac disease.<sup>8</sup>

#### Treatment plan based on severity of signs and symptoms<sup>7</sup>

Severity of signs and symptoms	Treatment plan
Mild	<ul style="list-style-type: none"> <li>• Education and reassurance</li> <li>• Simple treatment measures (such as dietary changes)</li> </ul>
Moderate	Pharmacologic therapy for <ul style="list-style-type: none"> <li>• Abnormal gut motility</li> <li>• Psychological issues</li> </ul>
Severe	<ul style="list-style-type: none"> <li>• Send patient to an IBS referral center for treatment of severe symptoms and management of psychological conditions (such as anxiety, depression)</li> </ul>

Testing for celiac disease is indicated in patients who have IBS-D or IBS-M. Studies in this subset of patients have indicated that they are at increased risk for celiac disease.<sup>17</sup>

Colonoscopy is indicated in patients 50 years and older. Any individual presenting with concerning symptoms should undergo colonoscopy immediately.<sup>17</sup> Nurse practitioners (NPs) who are not trained to perform a colonoscopy should refer the patient for an immediate colonoscopy.

In some patients, symptoms are associated with lactose intolerance. A lactose breath test (breath hydrogen test) will reveal signs that a patient has difficulty digesting lactose.<sup>17</sup>

The following blood tests can be used as diagnostic tools to identify patients with IBS:

- anti-tissue transglutaminase antibody, a major autoantigen in patients with celiac disease
- anti-*Saccharomyces cerevisiae* antibodies immunoglobulin A, which are associated with inflammatory bowel disease
- Antineutrophil cytoplasmic antibody, also associated with inflammatory bowel disease

The accuracy for establishing a diagnosis of IBS using a Prometheus test is 70%.<sup>15,18</sup>

### ■ Treatment

Goals for managing IBS include resolving individual symptoms, global symptom improvement, preventing complications, improving quality of life, and minimizing costs.<sup>17</sup> The treatment plan for IBS is based on symptom complex, functional impairment, and psychosocial difficulties affecting the course of the disease. The treatment plan can be modified based on the severity of the symptoms, and includes changes in diet, medication, alternative therapies, herbal remedies, psychotherapy, and hypnotherapy (see *Treatment plan based on severity of signs and symptoms*).<sup>7</sup>

Establishing a therapeutic relationship is one of the most important components in managing a patient with IBS. NPs should ensure the patient's understanding of the illness and address any concerns, explaining the proposed mechanisms of IBS. This validates the patient's symptoms and builds a base for therapeutic interventions, especially when reassuring the patient that symptoms of IBS are real but not life threatening. The patient should also understand the chronic nature of the syndrome, but that individuals with IBS are expected to live a normal life span. NPs should identify realistic expectations with consistent

limits and involve the patient in treatment decisions. It is crucial that the patient understands IBS can be managed, but not cured.<sup>7</sup>

Increasing dietary fiber may benefit some patients. Due to its few adverse reactions, this should be a first-line treatment for patients with IBS-C.<sup>15</sup> Some patients may experience bloating, abdominal pain, and flatulence with increased fiber. Polycarbophil compounds may produce less flatulence than psyllium compounds.<sup>19</sup> Patients should be taught to avoid legumes, which increase the risk of bloating and flatulence; caffeine, which increases anxiety and exacerbates the symptoms of IBS; and lactose or fructose, which should be avoided in patients who have difficulty digesting these sugars.<sup>19</sup>

Some symptom improvement has been noted with treatment of psychological comorbidities. Research has demonstrated positive outcomes with cognitive therapy, dynamic psychology, and hypnotherapy.<sup>19</sup> Some patients may do better than others with psychosocial treatment such as motivated patients, patients with predominantly diarrhea or pain, IBS that presents with overt psychiatric symptoms, intermittent pain that increases when the patient is stressed, and constant abdominal pain that lessens the benefit of psychotherapy or hypnotherapy.<sup>7</sup> Further research is needed to establish efficacy of psychological therapies.

Medication is used as a symptom-based management strategy aimed at relieving the most troublesome symptoms.<sup>20</sup> Commonly, patients who have constipation will receive dietary fiber; patients who have diarrhea should

***NPs should identify realistic expectations with consistent limits and involve the patient in treatment decisions.***



receive loperamide or diphenoxylate; and patients with abdominal pain should receive anticholinergics, antispasmodics, tricyclic antidepressants (off-label use), or selective serotonin reuptake inhibitors (SSRIs) for pain.<sup>7</sup>

### ■ Pharmacotherapy

Medication is used as a symptom-based management strategy aimed at relieving the most troublesome symptoms (see *Pharmacotherapy*).<sup>20</sup>

*Smooth muscle relaxants* are thought to decrease abdominal pain in patients with IBS by decreasing intestinal smooth muscle spasms. Medications such as dicyclomine and hyoscyamine relax smooth muscle spasms via anticholinergic pathways.<sup>21</sup>

**Pharmacotherapy**<sup>3,10,16,17,21</sup>

Agent	Indication	Precautions (PC), Contradictions (CI), Adverse Reactions (AR)
<b>Opioid receptor agonists / Antidiarrheals</b>		
Loperamide	IBS-D	<b>PC/CI:</b> hypersensitivity to the drugs, narrow angle glaucoma, hepatic insufficiency, advanced hepatorenal disease, pseudomembranous colitis, enterotoxigenic infection <b>AR:</b> nausea, vomiting, constipation, dry mouth, abdominal pain and distension, urine retention
Diphenoxylate	IBS-D	
<b>Smooth muscle relaxants / Anticholinergics</b>		
Dicyclomine	IBS-D, pain	<b>PC/CI:</b> hypersensitivity to the drugs, obstructive uropathy, myasthenia gravis, glaucoma, GI tract obstruction, paralytic ileus, toxic megacolon <b>AR:</b> dry mouth, dizziness, blurred vision, drowsiness, tachycardia
Hyoscyamine	IBS-D, pain	
<b>Tricyclic antidepressants</b>		
Amitriptyline	IBS-D, pain "Off label use"	<b>PC/CI:</b> hypersensitivity to the drugs, narrow angle glaucoma, in acute recovery phase following a myocardial infarction, avoid in patients taking monoamine oxidase inhibitors (MAOIs) or fluoxetine or in patients who have taken them in the last 2 weeks <b>AR:</b> drowsiness, dry mouth, blurred vision, constipation, diarrhea, dizziness, urine retention, increased heart rate, increased appetite, headache, fatigue, seizures, sexual dysfunction, light sensitivity
Imipramine	IBS-D, pain "Off label use"	
<b>Selective 5-HT<sub>3</sub> receptor antagonist</b>		
Alosetron	FDA approved for treatment of severe IBS-D in women with one or more of the following characteristics: Chronic IBS lasting over 6 months, and/or women who are unresponsive to conventional therapy.  IBS-D is considered severe if there is: <ul style="list-style-type: none"> <li>• Frequent severe abdominal pain</li> <li>• Frequent bowel urgency or incontinence or</li> <li>• Disabling or restricting daily activity</li> </ul>	<b>PC/CI:</b> hypersensitivity to the drug, history of constipation, intestinal obstruction, stricture, toxic megacolon, GI perforation, ischemic colitis, impaired intestinal blood circulation, thrombophlebitis, hypercoagulable states, Crohn's disease, ulcerative colitis, or diverticulitis <b>AR:</b> nausea, dry mouth, drowsiness, headache, diarrhea, insomnia, nervousness, decreased sexual desire or difficulty reaching orgasm, rash, weight gain. Should be discontinued immediately in patients with constipation or symptoms of ischemic colitis, reported to the provider and not resumed in these patients
<b>Chloride channel activator</b>		
Lubiprostone	FDA approved for IBS-C	<b>PC/CI:</b> hypersensitivity to the drug, severe diarrhea, history of mechanical bowel obstruction <b>AR:</b> nausea, vomiting, cough, fever, dry mouth, dizziness, insomnia, joint or back pain
<b>Bulking agents</b>		
Psyllium	IBS-C	<b>PC/CI:</b> hypersensitivity to the drugs, fecal impaction, intestinal obstruction, undiagnosed abdominal pain <b>AR:</b> abdominal fullness, bloating
Polycarbophil	IBS-C	
Methylcellulose	IBS-C	
<b>Osmotic laxatives</b>		
Polyethylene glycol	IBS-C	<b>PC/CI:</b> hypersensitivity to the drugs, known or suspicion of bowel obstruction, allergy to polyethylene glycol <b>AR:</b> nausea, flatulence, bloating
Lactulose	IBS-C	
<b>Antibiotics</b>		
Rifaximin	"Off label" use for IBS-D	<b>PC/CI:</b> hypersensitivity to the drug, pregnancy or breast feeding, antibiotic therapy, liver disease <b>AR:</b> nausea, abdominal pain, dizziness, excessive tiredness, headache, muscle tightening, joint pain. Some more serious AR that require immediate consultation with a provider: watery or bloody diarrhea (that may occur along with abdominal cramps and fever during treatment or for 2 months afterward), hives, rash, itching, difficulty breathing or swallowing, swelling of the face, throat, tongue, lips, eyes, hands, feet, ankles, or lower legs, and hoarseness

*Antidepressants* have been found to be beneficial in patients with refractory symptoms.<sup>22</sup> Antidepressant drugs are especially helpful in patients with depression or an anxiety disorder.<sup>20</sup>

*Tricyclic antidepressants and SSRIs* affect visceral afferent activity in the GI tract, which help improve abdominal pain. The use of tricyclic antidepressants and SSRIs in management of IBS is considered off-label use. Comprehensive research on the use of these medications in IBS treatment determined that:

- 60% of patients seen with IBS in referral have some psychological issue such as depression, anxiety, personality disorder, or stress.
- Tricyclic antidepressants and SSRIs may change visceral sensitivity and motor activity.
- Both tricyclic antidepressants and SSRIs have some effect on the regulation of pain.<sup>22</sup>

*Antidiarrheals* reduce stool frequency and improve stool consistency. Accelerated intestinal transit time may contribute to symptoms associated with IBS-D. Patients placed on these medications need to be watched closely to avoid constipation or worsening abdominal pain.<sup>21</sup>

*5-HT<sub>3</sub> modulator* (alosetron) is indicated only for women with severe IBS-D. Women who are treated with 5-HT<sub>3</sub> modulators experience decreased visceral pain perception. Numerous studies have shown a decrease in abdominal pain and discomfort as well, although constipation is an adverse reaction.<sup>20</sup> If constipation occurs, the drug must be stopped.

Severe gastrointestinal adverse reactions such as ischemic colitis can occur when taking alosetron. As a result, a prescribing program was implemented to help reduce these risks. This program requires providers who prescribe alosetron to enroll and confirm whether or not they understand and are aware of the benefits and risks of alosetron. Additionally, patients are required to read and sign an acknowledgement form confirming understanding of the risks associated with this medication.<sup>7,19</sup>

*Chloride channel activator/sodium channel blockers* were subjected to a four-week, randomized, multicenter trial in patients with chronic diarrhea. This study demonstrated improvement in stool consistency, straining, and constipation severity.<sup>9</sup>

*Antibiotics.* Rifaximin (Xifaxan) is an antibiotic currently approved by the U.S. FDA for patients with travelers' diarrhea and hepatic encephalopathy. Two Phase III studies, which involved 1,260 male or female patients with nonconstipation IBS, compared rifaximin to placebo. The rifaximin group showed adequate relief of IBS symptoms of bloating,

abdominal pain, and loose watery stools. Results indicated that rifaximin 550 mg taken three times a day for 14 days achieved global relief of symptoms.<sup>23</sup> In March 2011, Salix Pharmaceuticals, manufacturer of rifaximin, confirmed that the FDA is requesting more information on retreatment of refractory symptoms following treatment with rifaximin. Since the efficacy and safety in retreatment was not addressed in prior studies, additional clinical trials are needed.<sup>24</sup>

#### ■ Over-the-counter remedies

Probiotics have shown promising results such as decreased symptom severity and decreased serum inflammatory markers when used for 5 to 6 months. Probiotics also reduce inflammatory mediators in patients with IBS. Studies suggest that manipulating the gut flora may be a promising modality for treatment of IBS.<sup>8</sup>

Certain herbal therapeutic agents, such as peppermint, have been used in patients with IBS. These agents act to relax smooth muscle. In a randomized, double-blind,

*Probiotics have been shown to decrease symptom severity and serum inflammatory markers when used for 5 to 6 months.*



placebo-controlled trial, 50% of patients obtained relief of IBS symptoms using these herbal remedies.<sup>9</sup>

Carmint, an herbal supplement that contains coriander, lemon, and mint, is known for its antispasmodic and sedative properties. One randomized trial showed that treatment with carmint for 8 weeks significantly improved severity and frequency of abdominal pain and discomfort.<sup>9</sup>

#### ■ Effective management

Functional syndromes are challenging for healthcare providers. With education, compassion, and flexibility, healthcare providers can manage IBS effectively. By helping the patient make dietary changes and exploring alternative therapies, herbal remedies, and medications, NPs can ensure positive outcomes. 

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