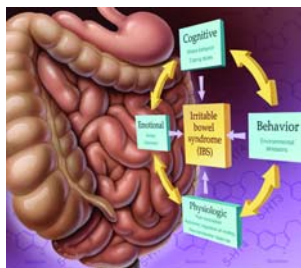


Management of Irritable Bowel Syndrome

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Irritable bowel syndrome is the most common functional disorder of the gastrointestinal tract and is frequently treated by family physicians. Despite patients' worries about the symptoms of irritable bowel syndrome, it is a benign condition. The diagnosis should be made using standard criteria after red flags that may signify organic disease have been ruled out. An effective physician-patient relationship is vital to successful management. Episodes of diarrhea are best managed with loperamide, while constipation often will respond to fiber supplements. Antispasmodics or anticholinergic agents may help relieve the abdominal pain of irritable bowel syndrome. Refractory cases are often treated with tricyclic antidepressants. Newer agents such as tegaserod and ondansetron target neurotransmitter receptors in the gastrointestinal tract. Some forms of psychologic treatment may be helpful, and gastroenterology consultation is occasionally needed to reassure the patient. Comorbid conditions such as depression or anxiety should be investigated and treated. (*Am Fam Physician* 2002;66:1867-74,1880. Copyright © 2002 American Academy of Family Physicians.)

A patient information handout on irritable bowel syndrome, written by the authors of this article, is provided on page 1880.



Irritable bowel syndrome (IBS) is a benign, chronic symptom complex of altered bowel habits and abdominal pain. It is considered a functional type of bowel disorder. That is, no organic or structural cause can be detected (using currently available diagnostic modalities) to explain its symptoms. It is the most common functional disorder of the gastrointestinal (GI) tract. Other disorders in this group include functional dyspepsia, functional anorectal pain, and noncardiac chest pain. The many forms and presentations of IBS can make the diagnosis challenging, and its functional nature can make a satisfactory treatment regimen difficult.

Epidemiology

In the United States, IBS has been reported to account for up to 3.5 million physician visits annually, at an estimated cost of \$8 billion. It remains the most common diagnosis in gastroenterologic practices.¹

See page 1856 for definitions of strength-of-evidence levels contained in this article.

The reported prevalence of patients in the general population with symptoms consistent with IBS ranges from 10 to 20 percent, and only 10 to 30 percent of those patients seek medical care.² At five-year follow-up of IBS patients, 5 percent report complete recovery and up to 30 percent report partial recovery.³

In most parts of the world, women are affected more often than men.⁴ IBS symptoms are common in adolescents and correlate with anxiety and depression in this population.⁵ Symptoms begin before 35 years of age in 50 percent of patients, and almost all report symptom onset before 50 years of age.⁴ Although IBS is seen in the elderly, new onset of symptoms after age 50 may indicate other organic pathology and warrants a more comprehensive evaluation.⁶

Etiology and Pathophysiology

The etiology of IBS remains unclear. Theories have ranged from purely psychologic to more recent proposals about postinfectious alterations in GI tract neuromuscular function. IBS may best be viewed as a biopsychosocial disorder in which altered GI motility, GI hypersensitivity, and psychosocial fac-

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The hallmark signs and symptoms of irritable bowel syndrome are abdominal pain relieved by defecation and pain associated with looser or more frequent stools.

tors all interact to predispose someone to the syndrome.

Patients with IBS have an exaggerated gastrocolic reflex, altered gastric emptying, increased small bowel contractions, and increased small intestinal transit, all of which are exacerbated by food intake or stress.⁷ However, more than 50 percent of healthy individuals report similar symptoms during increased stress.⁸ Therefore, other factors

likely play an important role in the patient who develops IBS.

One such factor may be the involvement of neurotransmitters such as serotonin, which may stimulate intestinal secretion and peristalsis in addition to visceral pain receptors via 5-HT₃ and 5-HT₄ pathways. It is at neurotransmitter receptors such as these that new and investigational therapeutic agents are targeted.

Psychosocial factors also play an important role in the development of IBS and may be the most important factors in terms of who manifests IBS and how severe it becomes.⁹ For example, traumatic life events such as a history of physical or sexual abuse have been shown to correlate with the development of IBS and the severity of its symptoms.¹⁰ Studies have repeatedly shown a higher incidence of anxiety, hypochondriasis, and depression in IBS patients.¹¹ A multicomponent model (Figure 1) has been proposed that shows the

Multicomponent Model of Irritable Bowel Syndrome

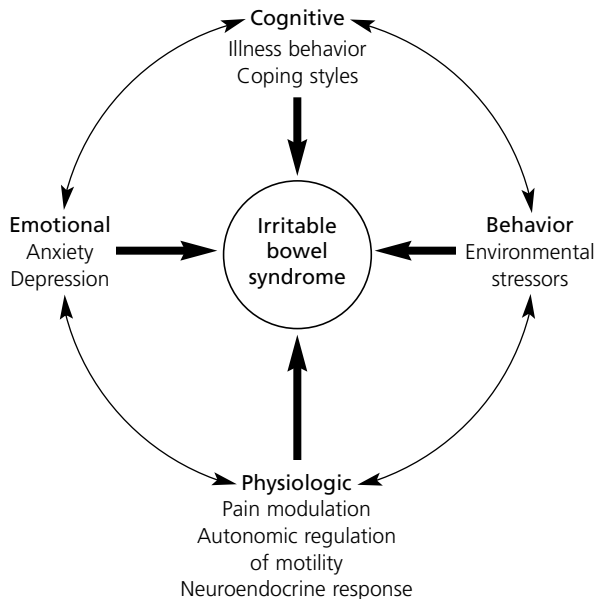


FIGURE 1. Multicomponent model of irritable bowel syndrome (IBS). Development of IBS symptoms can be explained by the interrelation of cognitive, behavior, emotional, and physiologic components.

Adapted with permission from Mayer EA. Emerging disease model for functional gastrointestinal disorders. *Am J Med* 1999;107(5A):13S.

TABLE 1
Rome I Criteria

At least three months of continuous or recurrent symptoms of abdominal pain that is:
Relieved by defecation
and/or
Associated with a change in stool consistency
and/or
Associated with a change in frequency of stool
Plus two or more of the following greater than 25 percent of the time:
Altered stool frequency (more than three per day or less than three per week)
Altered stool form (lumpy, hard or watery, loose)
Altered stool passage (straining, urgency, or incomplete evacuation)
Passage of mucus
Bloating or feeling of abdominal distention

Adapted with permission from Vanner SJ, Depew WT, Paterson WG, DaCosta LR, Groll AG, Simon JB, et al. Predictive value of the Rome criteria for diagnosing the irritable bowel syndrome. *Am J Gastroenterol* 1999;94:2912-7.

TABLE 2
Rome II Criteria

12 or more weeks of continuous or recurrent abdominal pain or discomfort
Plus at least two of the following:
Relieved by defecation
and/or
Associated with change in frequency of stool
and/or
Associated with a change in form (appearance) of stool

Adapted with permission from Drossman DA, Corazzari E, Talley NJ, Thompson WG, Whitehead WE. Rome II: the functional gastrointestinal disorders: a multinational consensus. Gut 1999; 45(suppl 2):1-81.

relationship of psychosocial (cognitive, behavior, emotional) and physiologic components of IBS.⁷

Clinical Presentation

Abdominal pain relieved by defecation and pain associated with looser or more frequent stools are the hallmark signs and symptoms of IBS. Patients also may experience diarrhea, constipation, alternating diarrhea and constipation, mucus in stools, dyspepsia, atypical chest pain, bloating, and gas. Symptoms are typically worse at times of increased stress.

The most widely accepted diagnostic criteria for IBS are the Rome Criteria. The Rome I criteria (*Table 1*)¹² require the presence of at least two supportive features in addition to the main criteria. The Rome II criteria (*Table 2*)¹³ base the diagnosis on the presence of two of the three main criteria without the need of additional supportive criteria.¹⁴ The presence of any red flags (*Table 3*)^{6,13} should alert the physician to an alternate diagnosis. For treatment purposes, the following symptom-guided categories are useful: pain-predominant, diarrhea-predominant, or constipation-predominant. Constipation may alternate with diarrhea in

A strong physician-patient relationship is paramount in an effective management strategy for irritable bowel syndrome.

some IBS patients. *Table 4* lists some pharmacotherapeutic options based on predominant symptoms.

Management

EFFECTIVE THERAPEUTIC RELATIONSHIP

A strong physician-patient relationship is paramount in an effective management strategy for IBS. A good physician-patient relationship has also been shown to reduce repetitive office visits.¹⁶ The patient may need to be reassured repeatedly of the positive diagnosis, and specific patient concerns and fears will need to be addressed. The patient needs to be confidently told that there is no serious disease and there is no increased risk of complications (such as cancer) from IBS. A previous article¹⁷ in *American Family Physician* outlines specific points in the development of an effective therapeutic relationship with patients who have IBS.

TABLE 3
Red Flags in Evaluating for Irritable Bowel Syndrome

Anemia
Family history of colon cancer or inflammatory bowel disease
Fever
Heme-positive stools
New or recent onset in patient older than 50 years
Nocturnal symptoms
Palpable abdominal or rectal mass
Persistent diarrhea or severe constipation
Recent antibiotic use
Rectal bleeding
Weight loss

Information from references 6 and 13.

DIETARY RECOMMENDATIONS

While no specific dietary advice has been shown in trials to be efficacious, many authors advocate having patients limit alcohol, caffeine, sorbitol, and fat intake.⁶ Lactose should be eliminated only in those with proven lactase deficiency. If a patient believes a particular dietary substance is exacerbating the symptoms, then a trial of eliminating that substance is warranted. However, in general, there is no association between IBS and food intolerance.

PAIN-PREDOMINANT IBS

Jailwala and colleagues¹⁸ recently published a systematic review of randomized controlled trials (RCTs) of pharmacotherapy for IBS, in which 28 high-quality trials reporting outcomes of global improvement or IBS-specific symptom improvement were identified. [Evidence level A, systematic review of RCTs] Trials using bulking agents (various fiber products), smooth-muscle relaxants (e.g., cimetropium [not marketing a brand name yet]), pro-

TABLE 4
Medications Used in the Management of Irritable Bowel Syndrome

<i>Predominant symptom</i>	<i>Medications</i>	<i>Dosage</i>	<i>AFP level of evidence</i>	<i>Comment</i>
Diarrhea	Loperamide (Imodium)	2 to 4 mg up to four times a day	Level A	Use as needed or prophylactically in times of anticipated stress
	Cholestyramine (Questran)	4 g one to six times a day	Level C	Second-line agent
	Alosetron (Lotronex)	1 mg per day titrated to two times a day if tolerated	Level A	Restricted use in female patients only
Constipation	Fiber	Start low and titrate up to 20 to 30 g a day	Level A	May worsen bloating
	Osmotic laxative	Magnesium citrate, lactulose, or polyethylene glycol dosed as appropriate	Level C	
Abdominal pain	Antispasmodics and anticholinergics (e.g., dicyclomine [Bentyl], hyoscyamine [Levsin])	Dicyclomine, 10 to 20 mg, two to four times a day	Level B	Used as needed only
	Tricyclic antidepressant (e.g., amitriptyline [Elavil])	Start amitriptyline, 10 to 25 mg at bedtime or twice daily, or desipramine (Norpramin), 50 mg three times a day	Level A	Needs to be given daily, not as needed, therefore generally reserved for patients with more severe pain
	Tegaserod (Zelnorm)			FDA approved for short-term treatment of women
Gas or bloating	Simethicone (Mylanta)	40 to 125 mg up to four times a day as needed		Anecdotal evidence only
Comorbid depression or anxiety	Antidepressants or anxiolytics as indicated	Dose as appropriate		Treating depression has been shown to improve bowel symptoms ¹⁵

FDA = U.S. Food and Drug Administration.

kinetic agents (e.g., cisapride [Propulsid]), loperamide (Imodium), and psychotropic agents (e.g., amitriptyline [Elavil]) were included. From this analysis, the authors concluded that smooth-muscle relaxants are beneficial for the abdominal pain of IBS. However, none of the smooth-muscle relaxants used in the high-quality trials are approved by the U.S. Food and Drug Administration (FDA) for use in the United States.

Although fiber is predominantly useful for the constipation of IBS, it may also reduce pain in IBS by reducing intracolonic pressure, though this effect has not been shown to be true in high-quality patient-oriented trials.¹⁹ The efficacy of dietary fiber therapy can be difficult to assess because the placebo response in IBS trials has been as high as 71 percent.²⁰ [Evidence level A, RCT] Fiber should be started gradually in low doses to avoid bloating.

If dietary advice and fiber supplementation do not adequately relieve abdominal pain, a short-term trial of an antispasmodic agent such as dicyclomine (Bentyl)¹⁸ or hyoscynamine (Levsin) may be tried.¹⁸ If it is effective, it can then be used as needed. Chronic use of such a drug may reduce its efficacy.¹⁹ Narcotics should be avoided.

Psychotropic agents also may benefit patients with IBS who have abdominal pain. Seven trials of psychotropic agents were included in Jailwala's systematic review.¹⁸ All seven trials showed these agents to be efficacious, but only one of these trials was considered high-quality. This trial, involving only 14 patients, showed that the tricyclic antidepressant amitriptyline yielded global improvement in patients with IBS.²¹ [Evidence level A, RCT] The use of such tricyclic antidepressants for pain relief in IBS may be effective, but their anticholinergic side effects can be troublesome. The selective serotonin reuptake inhibitors (SSRIs) have not proved to be effective agents for IBS.¹⁵

Tegaserod (Zelnorm), a 5-HT₄ agonist (of the aminoguanide indole class) that has visceral antinociceptive effects, is a newer agent that may prove useful in pain-predominant IBS. It

If dietary advice and fiber supplementation do not adequately relieve abdominal pain in irritable bowel syndrome, a short-term trial of an antispasmodic agent may be tried.

has been approved by the FDA for short-term treatment of women with IBS.^{15,22} Pain in IBS may also be mediated by opioid receptors such as mu, kappa, and delta. Several drugs that act at these receptors are under investigation.

Psychologic treatments also may be of benefit in the management of IBS, particularly in those who have associated psychiatric diagnoses or difficulty coping.²³ Psychologic treatments include cognitive-behavior therapy (e.g., stress management), dynamic psychotherapy, and hypnosis. A systematic review²⁴ of psychologic treatments for IBS found eight studies in which psychologic treatment was superior to control therapy. However, the same review²⁴ also found five studies that showed no difference. In some of the clinical trials²⁴ of psychologic treatments in IBS, psychologic improvement occurred without improvement in GI symptoms.²⁴

A recent study comparing the addition of multicomponent behavior therapy with medical treatment alone showed that the combination was significantly better at reducing IBS symptoms based on data recorded in daily symptom diaries.²⁵ [Evidence level B, uncontrolled, comparative study] The combination group also had improved overall well-being. A partial description of the components of the multicomponent behavior therapy treatment is outlined in *Table 5*.²⁵ While these components or a method of incorporating them may not be completely available to the primary care physician, the techniques employed may help the patient manage this illness.

DIARRHEA-PREDOMINANT IBS

For diarrhea-predominant IBS, 2 to 4 mg of loperamide up to four times a day can be effective.¹⁸ [Evidence level A, systematic

For diarrhea-predominant irritable bowel syndrome, loperamide (Imodium) at 2 to 4 mg up to four times a day can be effective.

review of RCTs] Loperamide slows intestinal transit, increases intestinal water absorption, and increases resting anal sphincter tone. These effects reduce the diarrhea and the sense of urgency and fecal soiling that accompany it. Loperamide is preferred to other opioid agents because it does not cross the blood-brain barrier. It can be used as needed or prophylactically during times of increased stress that may provoke symptoms (e.g., taking a test, public speaking, attending a social function, exercising).

In some patients with severe diarrhea, bile acids may lead to decreased reuptake of water from the colon.¹⁵ As such, the bile acid sequestrant, cholestyramine (Questran), may be a useful second-line agent for diarrhea-predominant IBS.²⁶ [Evidence level C, consensus opinion] In patients in whom a preceding or lingering infection is thought to be partly responsible for diarrhea-predominant symptoms, a course of empiric antibiotics or anti-giardial therapy may be warranted.²⁷ A short

TABLE 5

Selected Steps of Multicomponent Behavior Therapy for IBS

- Step 1. Provide information about IBS and normal GI functioning. Also discuss the role of stress.
- Step 2. Analyze the patient's illness in terms of symptoms, circumstances of first onset, symptom triggers, contributing factors, and consequences.
- Step 3. Teach relaxation techniques.
- Step 4. Teach patients to identify irrational thoughts regarding their GI problems.
- Step 5. Discuss ways people cope with the problems that chronic illness brings to daily life.
- Step 6. Discuss ways to manage difficulties the individual may have in social situations caused by GI problems.

IBS = irritable bowel syndrome; GI = gastrointestinal.

NOTE: For a full description of the formal techniques used, please see the original article.

*Adapted with permission from Heymann-Monnikes I, Arnold R, Florin I, Herda C, Melfsen S, Monnikes H. The combination of medical treatment plus multi-component behavioral therapy is superior to medical treatment alone in the therapy of irritable bowel syndrome. *Am J Gastroenterol* 2000;95:981-94.*

course of antibiotics may be warranted in patients with refractory diarrhea even in the absence of a preceding infection because eradication of bacterial overgrowth may decrease the diarrhea.^{15,28} [Evidence level B, uncontrolled clinical study]

Alosetron (Lotronex), a 5-HT₃ antagonist, was shown to improve pain and quality of life in diarrhea-predominant IBS in female patients.^{29,30} [Reference 29, Evidence level A, RCT] This agent was withdrawn from the market in November 2000 because of serious post-marketing events including severe constipation, ischemic colitis, and death. Recently, The FDA approved the reintroduction of alosetron for female patients with diarrhea-predominant IBS in whom conventional treat-

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ments have failed. Its use is under restricted conditions that include completion of a signed patient-physician agreement and prescription only by physicians enrolled in the Prescribing Program for Lotronex. More details can be found on the FDA Web site at www.fda.gov/cder.

Ondansetron (Zofran) is another 5-HT₃ antagonist that currently is used predominantly for management of severe nausea and vomiting. It also has been studied for use in IBS, particularly for diarrhea-predominant IBS. In a small double-blind, placebo-controlled trial,³¹ patients with IBS had firmer stools and decreased rectal pain thresholds.

CONSTIPATION-PREDOMINANT IBS

For constipation, fiber supplementation is often recommended. In dosages of 12 to 30 g per day, fiber products have been shown to accelerate colonic transit time and help relieve constipation.³² The fermentation of fiber by intestinal bacteria will produce bowel gas that may lead to distension. Fiber should be started at a low dose and titrated gradually to avoid exacerbating the pain or cramps of IBS.

The use of the prokinetic agent cisapride was not supported in a recent systematic review of the literature.¹⁸ [Evidence level A, systematic review of RCTs] Other options for constipation-predominant IBS include the osmotic laxatives such as lactulose, milk of magnesia, or polyethylene glycol solution. Newer agents are being studied. Loxiglumide (not marketing a brand name yet), a cholecystokinin-A receptor antagonist that has been studied for use in acute pancreatitis, may be a useful agent for constipation because of its effect of accelerating colonic transit.²² Tegaserod, in addition to its antinociceptive effects, also accelerates intestinal transit and appears promising for the management of constipation-predominant IBS.¹⁵

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