in the clinic

Irritable Bowel Syndrome

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**Diagnosis**

**What symptoms should prompt a clinician to consider IBS?**

Symptoms of IBS vary from person to person, but clinicians should consider IBS if abdominal discomfort or pain associated with bowel dysfunction is present. Other symptoms that suggest IBS include prominent gastrocolic reflex, alternating constipation and diarrhea, and excess gas and flatulence. Gastrointestinal symptoms that wax and wane for more than 2 years and those that are exacerbated by psychosocial stress should raise suspicion for IBS over other diagnoses.

Three general patterns of bowel symptoms are common in IBS: diarrhea-predominant, constipation-predominant, and mixed (alternating diarrhea and constipation). Determining a patient’s predominant symptom pattern can be useful in guiding management because the different subgroups respond differently to the various therapeutic options. Because an individual patient’s symptom pattern can change over time, it is debatable whether symptom pattern clearly demarcates patients with different IBS subtypes.

Certain clinical features, often called alarm features or red flag symptoms, suggest that the diagnosis is something other than IBS (2) (see Box). Alarm features include weight loss, nocturnal awakening because of gastrointestinal symptoms, blood in the stool, family history of colon cancer or inflammatory bowel disease, recent use of antibiotics, and fever.

**What are the accepted diagnostic criteria for IBS?**

History is the main diagnostic tool for IBS. There are 2 sets of symptom-based diagnostic criteria to help discriminate IBS from other disorders: the Manning criteria and the Rome criteria (Table 1). These criteria were developed for use in clinical studies, but can be helpful in clinical settings.
Manning and colleagues (3) proposed the first widely used IBS criteria in 1978 based on the symptoms listed in Table 1.

In 1989, a group of experts met in Rome and developed another set of consensus-based criteria known as the Rome criteria to assist in the diagnosis of IBS and other functional gastrointestinal disorders (4). The Rome criteria, which are also displayed in Table 1, were based on a broader array of symptoms than the Manning criteria and explicitly considered both duration and frequency of symptoms. In 1999, the same group of experts developed the Rome II criteria, a modified version of the earlier criteria intended to be more adaptable to clinical practice (5).

The group released the most recent version of the Rome criteria, Rome III, in 2006. Rome III did not change the basic diagnostic criteria for IBS but modified the time frame for symptoms and description of IBS subtyping (6). Rome III specifies that symptoms must have begun at least 6 months before the diagnosis can be established and that patients have fulfilled the Rome criteria for at least 3 months before IBS can be diagnosed. Rome III recommends that clinicians base classification of IBS symptoms as diarrhea–prominent; constipation–prominent; or mixed, based on stool consistency. Rome criteria are dynamic, and future studies are needed to confirm the validity of recent changes intended to increase the usefulness of the criteria in research and clinical settings (1).

When diagnostic criteria are satisfied; warning symptoms are absent; the history and physical examination suggest IBS; and the occult blood test, complete blood count, and erythrocyte sedimentation rate are normal, the risk for overlooking organic disease may be as low as 1% to 3%.

Even without exclusion of alarm features, the presence of at least 3 of the 6 Manning criteria has an average sensitivity of approximately 60% and specificity of approximately 80%. The criteria’s sensitivity and specificity vary by study; however, the diagnostic accuracy is known to be better in women, younger patients, and when more criteria are fulfilled (7).

<table>
<thead>
<tr>
<th>Table 1. Symptom Criteria for Irritable Bowel Syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Rome III</strong></td>
</tr>
<tr>
<td>Recurrent abdominal pain or discomfort at least 3 days per month in the past 3 months associated with 2 or more of the following:</td>
</tr>
<tr>
<td>1. Improvement with defecation</td>
</tr>
<tr>
<td>2. Onset with change in frequency of stool</td>
</tr>
<tr>
<td>3. Onset associated with a change in the form and appearance of stool</td>
</tr>
<tr>
<td><em>Criteria must be fulfilled for at least the past 3 months with symptom onset at least 6 months before diagnosis.</em></td>
</tr>
</tbody>
</table>

| **Manning** |
| Pain relief with defecation, often |
| Looser stools at pain onset, often |
| More frequent stools at pain onset, often |
| Visible abdominal distention |
| Mucus per rectum |
| Feeling of incomplete evacuation |
| *To establish IBS diagnosis, patient must meet 3 or more criteria.* |

Tolliver and coworkers showed that the Rome criteria had a positive predictive value of 98.5%—out of 196 patients, they excluded 1 case of colon cancer, 1 of colitis, and 1 of peptic ulcer (8).

Vanner and colleagues prospectively studied 95 patients who met the Rome criteria and lacked red flags and found the positive predictive value was 98% (9).

Investigators conducted interviews with a large, community-based sample of U.S. women diagnosed with IBS, and they found that Rome I was significantly more sensitive than Rome II (84% vs. 49%; P < 0.001). Only 58% of patients who had IBS according to Rome I criteria had IBS according to Rome II criteria; 17.7% did not meet the criteria for either Rome I or II (10).

What is the utility of the physical examination in diagnosing IBS?
The physical examination is usually normal in IBS, except for mild abdominal tenderness or a palpable, tender loop of colon. However, neither is sensitive or specific for IBS. Physical findings that are not associated with IBS but that are notable because they indicate the need to seek other diagnoses include fever, weight loss, lymph node enlargement, abdominal mass, and hepatosplenomegaly. The physical examination should include testing the stool for occult blood.

Which diagnostic tests are useful in diagnosing IBS?
There are no specific diagnostic tests for IBS. Tests that may be helpful for ruling out diagnoses other than IBS include endoscopy, blood tests, evaluation of stool samples, and imaging studies. Clinicians should use these tests with discretion depending on the patient’s age, history, and symptom pattern, and on the presence of alarm features for organic disease.

Endoscopy
Flexible sigmoidoscopy may be helpful in excluding colitis or obstructive lesions of the colon. However, if patients are young, fulfill the Rome criteria, and have no alarm features, a presumptive diagnosis of IBS can be made without endoscopy but should be reevaluated depending on the course of symptoms over time. Because patients with IBS have abnormally sensitive gastrointestinal tracts, they may find endoscopy more uncomfortable than do patients without this condition. Rectal and colonic balloon studies have shown hypersensitivity of the intestines in 55% to 93% of patients with IBS (11). Thus, normal endoscopy can be particularly indicative of IBS when it causes more pain than expected or when it reproduces the patient’s symptoms.

Blood Tests
A CBC and an ESR are reasonable to evaluate for anemia, elevated sedimentation rate, or leukocytosis because these findings are not compatible with IBS. Serum amylase and liver enzyme levels may be useful if pancreatic or biliary disease is suspected.

Evaluation of Stool Samples
Evaluation of stool for *Clostridium difficile* may be helpful if the patient has recently taken antibiotics. Examination of stool for ova and parasites may be helpful in patients with diarrhea-predominant symptoms, especially if travel history suggests potential exposure to parasites. In general, bacterial cultures are unlikely to be helpful in the diagnosis of chronic diarrhea. However, there is a form of IBS in which patients develop typical IBS symptoms after resolution of an acute episode of dysentery. This condition may take 6 months to resolve and can lead to chronic IBS. Factors associated with post infectious IBS include age, female sex, severity of infection, and possibly psychological predisposition. Awareness of the condition can limit the search for persistent infection.

Stool collection over a 24-hour period for quantification of volume may be helpful in patients who report large-volume or watery diarrhea. Normal stool volume is 200 mL or less per day. Volumes over 350 to 400 mL suggest etiologies other than IBS.

Measurement of fecal calprotectin in stool samples can help to identify patients with intestinal inflammation as an organic cause of symptoms mimicking IBS. In one study, the positive predictive value of fecal calprotectin for organic disease was 76% and the negative predictive value was 89% (12).

A spot or 24-hour fecal fat test can show malabsorption. Screening for celiac sprue with antigliadin and antien domysial antibodies is both sensitive and specific (13). If no fat malabsorption is detected, clinicians may still consider these antibody tests in patients with unexplained anemia or weight loss.

**Imaging Studies**

Imaging studies should be used judiciously, but the following tests may help to exclude conditions that could mimic IBS. A flat and upright abdominal radiograph during an episode of pain may show unrecognized bowel obstruction, aerophagia, or retained stool. A small bowel barium radiograph can diagnose ileal and jejunal Crohn disease, and dilatation or diverticula favoring small bowel overgrowth. Computed tomography (CT) scanning will have low yield if there are no alarm symptoms.

**What is the differential diagnosis that clinicians should consider when evaluating a patient for possible IBS?**

The differential diagnosis of a patient presenting with symptoms of IBS is extensive (Table 2). Thus, some clinicians feel obligated to perform a wide variety of diagnostic tests before attributing a patient’s symptoms to IBS. However, no definitive data support routine performance of any diagnostic tests in patients with potential IBS. Clinicians should consider symptom patterns when trying to exclude serious diagnoses that can masquerade as IBS.

**Patients with Constipation-Prominent Symptoms**

In patients with constipation, clinicians should consider partial colonic obstruction or non-IBS causes of colonic dysmotility. Nonobstructive causes of colonic symptoms may be because of dysmotility secondary to medications, neurologic disease, hypothyroidism, pelvic floor dysfunction, or colonic inertia (colon transit > 5 days). The diagnosis is not IBS if colonic dysmotility is present without pain or if there is another explanation for symptoms, such as neurologic disorder, pelvic floor disorder, or colonic inertia (transit through colon > 72 hours, with predominantly right colon delay). In patients younger than 45 years of age with mild, chronic constipation-predominant symptoms, normal CBC, and no alarm features, treatment with fiber or an osmotic laxative should be offered before additional diagnostic testing.

**Patients with Diarrhea-Predominant Symptoms**

The differential in patients with diarrhea-predominant symptoms includes inflammatory bowel disease, infection, malabsorption, and effects of medication and diet. For younger patients with mild, chronic diarrhea-predominant symptoms, clinicians should consider flexible sigmoidoscopy, CRC, and examination of stools for ova and parasites. For patient older than 45 years or those with refractory, severe, or new-onset symptoms, evaluating the entire colon may be warranted to exclude neoplasm. However, clinicians must keep in mind that non-IBS disease is unlikely if the patient satisfies...
### Table 2. Differential Diagnosis of Irritable Bowel Syndrome*

<table>
<thead>
<tr>
<th>Disease</th>
<th>Clinical Characteristics</th>
<th>Diagnostic Strategy</th>
</tr>
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<tbody>
<tr>
<td><strong>Constipation-predominant symptoms</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Strictures due to inflammatory bowel disease, diverticulitis, ischemia, or cancer</td>
<td>Obstipation</td>
<td>Colonoscopy vs. barium enema and flexible sigmoidoscopy</td>
</tr>
<tr>
<td>Colonic inertia</td>
<td>Very infrequent bowel movements</td>
<td>Sitzmark transit study</td>
</tr>
<tr>
<td>Pelvic floor dysfunction†</td>
<td>Straining, self-digation</td>
<td>Rectal examination, balloon expulsion study, anorectal manometry, defecography</td>
</tr>
<tr>
<td>Neurologic disease‡</td>
<td>Concurrent Parkinson disease, autonomic dysfunction (Shy-Drager), multiple sclerosis</td>
<td>History and neurologic examination</td>
</tr>
<tr>
<td>Medication‡</td>
<td>Opiates, cholestyramine, calcium-channel blockers, anticholinergic medications</td>
<td>Medication history</td>
</tr>
<tr>
<td>Hypothyroidism‡</td>
<td>Other hypothyroid symptoms and signs</td>
<td>Serum thyroid-stimulating hormone</td>
</tr>
<tr>
<td><strong>Diarrhea-predominant symptoms</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Crohn disease</td>
<td>Diarrhea may be from inflammatory exudate, motility changes, small bowel overgrowth, or bile salt malabsorption</td>
<td>Colonoscopy, small bowel barium radiograph</td>
</tr>
<tr>
<td>Ulcerative colitis</td>
<td>Likely to have rectal bleeding</td>
<td>Colonoscopy</td>
</tr>
<tr>
<td>Microscopic colitis†</td>
<td>Generally middle-aged and older women with autoimmune disease (especially thyroiditis)</td>
<td>Colonoscopy/flexible sigmoidoscopy and biopsy</td>
</tr>
<tr>
<td>Parasites</td>
<td><em>Giardia</em> <em>lamblia</em> (stream and well water); <em>Ascaris lumbricoides, Entamoeba histolytica</em> (travel to developing world); <em>Strongyloides stercoralis</em> (travel to developing world, Kentucky, or Tennessee)</td>
<td>0 + P x 3, stool <em>Giardia</em> antigen, metronidazole trial</td>
</tr>
<tr>
<td><em>Clostridium difficile</em></td>
<td>Recent antibiotics taken</td>
<td>Stool ELISA, flexible sigmoidoscopy for pseudomembranes</td>
</tr>
<tr>
<td>Other bacteria</td>
<td>IBS after dysentery may persist for months after infection with bacteria</td>
<td>Compatible history, possible initial positive stool culture</td>
</tr>
<tr>
<td>Small bowel overgrowth</td>
<td>Due to severe small bowel dysmotility, partial obstruction, blind loop, or jejunal diverticulosis</td>
<td>Abdominal radiograph, small bowel barium radiograph, lactulose breath hydrogen test, antibiotic trial</td>
</tr>
<tr>
<td>Sprue† (gluten-sensitive enteropathy)</td>
<td>May present with diarrhea, usually steatorrhea</td>
<td>Usually steatorrhea, positive gliadin, endomysial serum antibodies; endoscopy with small bowel biopsy is gold standard</td>
</tr>
<tr>
<td>Lactose intolerance†</td>
<td>Symptoms worse with lactose consumption</td>
<td>Avoidance trial, lactose breath test</td>
</tr>
<tr>
<td>Postgastrectomy syndrome</td>
<td>Postprandial symptoms</td>
<td>History of problems worse after gastric surgery</td>
</tr>
<tr>
<td>HIV enteropathy</td>
<td>May have chronic GI infections, such as with cryptosporidium, CMV, <em>Blastocystis hominis</em>, amoeba</td>
<td>Clinical suspicion, HIV test, low CD4</td>
</tr>
<tr>
<td>Gastrointestinal endocrine tumor</td>
<td>Carcinoid, gastrinoma, VIPoma</td>
<td>Urine 5HIAA, fasting gastrin (followed by secretin stimulation test), serum VIP</td>
</tr>
<tr>
<td><strong>Pain-predominant symptoms</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aerophagia, bloating</td>
<td>Patient may be anxious (nervous air swallowing), can be exacerbated by antireflux surgery</td>
<td>Abdominal radiograph with pain</td>
</tr>
<tr>
<td>Intermittent small bowel</td>
<td>More likely with history of previous abdominal surgeries</td>
<td>Abdominal radiograph with pain, small bowel barium radiograph</td>
</tr>
</tbody>
</table>
Rome criteria and lacks alarm symptoms.

**Patients with Pain-Predominant Symptoms**
In patients with refractory, pain-predominant symptoms, a flat and upright abdominal radiograph during a pain episode can be helpful in revealing unrecognized bowel obstruction, aerophagia, or retained stool. Serum amylase and liver enzyme levels may diagnose pancreatic and biliary disease if symptoms suggest these diagnoses. CT scanning for neoplasms will have low yield if there are no alarm symptoms. Other rare conditions that may cause pain-predominant abdominal symptoms with some bowel dysfunction include intestinal angina (generally associated with weight loss and occult blood) and endometriosis (in general cyclic with menses).

Clinicians should use clinical judgment to modify these general guidelines to allow less or more evaluation.

**Under what circumstances should clinicians consider consultation with a gastroenterologist?**
Gastroenterologists often work with primary care physicians and patients to diagnose IBS and to exclude relevant disorders. Consultation is warranted in the following cases of diagnostic uncertainty: when patients do not fit Rome or Manning criteria, when patients have alarm symptoms, and when patients do not respond to initial management. Consultation is also necessary if specialized diagnostic procedures, such as endoscopy, are needed.

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**Table 2. Differential Diagnosis of Irritable Bowel Syndrome** *(continued)*

<table>
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<tr>
<th>Disease</th>
<th>Clinical Characteristics</th>
<th>Diagnostic Strategy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crohn disease</td>
<td>Small intestine or colon involvement</td>
<td>Small bowel barium radiograph colonoscopy</td>
</tr>
<tr>
<td>Acute intermittent porphyria</td>
<td>Rare; may have elevated liver enzymes and neurologic symptoms</td>
<td>Serum and urine porphyrins, especially porphobilinogen, and delta aminolevulinic acid</td>
</tr>
<tr>
<td>Ischemia</td>
<td>Intestinal angina especially in vasculopathies, food aversion, weight loss, pain 15–40 min after meals</td>
<td>Mesenteric angiogram</td>
</tr>
<tr>
<td>Chronic pancreatitis</td>
<td>Alcohol abuse, pain usually more persistent than with usual IBS</td>
<td>Abdominal radiograph for calcifications, CT scan, ERCP, endoscopic ultrasonography</td>
</tr>
<tr>
<td>Lymphoma of Gl tract</td>
<td>Generally, weight loss</td>
<td>CT scan, small bowel radiograph</td>
</tr>
<tr>
<td>Endometriosis</td>
<td>Menstrual-associated symptoms, pelvic symptoms</td>
<td>Laparoscopy</td>
</tr>
</tbody>
</table>

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*CMV = cytomegalovirus; CT = computed tomography; ELISA = enzyme-linked immunosorbent assay; ERCP = endoscopic retrograde cholangiopancreatography; GI = gastrointestinal; IBS = irritable bowel syndrome; O + P = ova and parasites; VIPoma = vasoactive intestinal peptide-producing tumor.
†Unlikely alone to cause abdominal pain.

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**Diagnosis**... Clinicians should base the diagnosis of IBS on history and physical examination, paying careful attention to fulfillment of the Rome or Manning criteria and exclusion of alarm features. Patients who fulfill the criteria and have no alarm features may need no additional testing other than a complete blood count and test for fecal occult blood to establish a presumptive diagnosis of IBS. Diagnostic testing should be judicious and focus on exclusion of specific non-IBS conditions that are consistent with the individual patient’s clinical presentation.

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**CLINICAL BOTTOM LINE**
Is dietary modification effective in the management of IBS?

Dietary modification is not proven to reduce IBS symptoms, and major exclusion diets are not recommended. However, it may be reasonable to consider dietary modification for individual cases in which specific foods seem to trigger symptoms. In addition, common-sense dietary recommendations directed at the predominant symptom can help to minimize symptoms. Clinicians should talk with patients about their dietary habits to:

- Evaluate for lactose intolerance
- Evaluate consumption of caffeine, fructose, or artificial sweeteners, all of which can have laxative effects
- Inquire about laxative-containing herbal products
- Determine whether patients with gas and bloating are drinking excess carbonated beverages, drinking with a straw, or chewing gum, all of which can lead a person to swallow too much air
- Advise against excess intake of fats, which can lead to gas retention
- Advise avoidance of certain carbohydrates, such as beans, cabbage, broccoli, and cauliflower, if they trigger symptoms. They may be difficult to digest and lead to fermentation and gas in the colon.

Inadequate dietary fiber may cause constipation, and clinicians often encourage patients with constipation-predominant IBS to increase fiber intake. Studies suggest that fiber is helpful for relief of constipation, but not for relief of pain (14, 15). Fiber is not effective for patients with diarrhea-predominant IBS and may even exacerbate symptoms. Achieving constipation relief with fiber may require high-dose therapy, which patients are often unable to tolerate.

A systematic review studied the role of bulking agents in IBS (wheat bran, corn fiber, calcium polycarbophil, ispaghula husk, and psyllium) and concluded that they were no more effective than placebo in providing global symptom relief of IBS. However, the authors deemed all of the trials inadequate because of methodological flaws or small sample size (16).

Are there nonpharmacologic interventions aside from diet that are useful in the management of IBS?

In addition to advice about diet, important nonpharmacologic aspects of IBS care include reassurance, education with advice about trigger avoidance, stress management, and exercise. Clinicians must reassure patients that their symptoms are not because of a life-threatening disorder and assist them in developing effective self-management strategies. Patients do better and use health care more efficiently when it is acknowledged that their symptoms are not imagined, that the symptoms have physiologic causes that are poorly understood but real, and that they can themselves control some symptom triggers.

In an uncontrolled study, advice about diet and exercise, stress management, and appropriate use of medications was associated with alleviation of IBS symptoms in 80% of patients (17).

Retrospective analysis of outpatient charts at a referral center showed a correlation between patient education, including discussion of psychosocial stressors, and reduced future visits (18).

It may be helpful to ask patients to complete daily diaries of symptoms, including entries for stressors, mood, events, thoughts, and diet. Clinicians should use the diary information to help patients understand the role of psychosocial stressors and to help them develop self-management strategies.
What is the role of psychotherapy in the care of patients with IBS?

Psychosocial stressors are associated with symptoms (19–21). Patients with IBS are more likely to have had early life or current trauma, including losses or abuse (22), and are more likely to have generalized anxiety disorder and worry (23). Psychological distress is associated with IBS after dysentery (24). Psychological therapy to minimize anxiety can reduce symptoms.

One randomized, controlled trial (RCT) involving patients whose symptoms had not improved with standard medical treatment for at least 6 months showed that two thirds of the patients receiving psychotherapy had less diarrhea but not less constipation; they also had less intermittent pain, but those with constant abdominal pain did not improve (25).

Other research has found that psychotherapy also results in decreased use of health care resources. So while psychotherapy has costs on the front end, it may reduce long-term medical costs (26). However, trials of psychological treatment in IBS have methodological inadequacies, mostly because of difficulties in creating a true control group or in adequately blinding trials (27). Consequently, it has not been definitively determined whether psychotherapy is any more beneficial for IBS than other interventions.

Which pharmacologic therapies are effective in IBS?

The choice of drug therapy depends on an individual’s symptoms, and effectiveness varies from patient to patient (28). Drugs used in management of patients with IBS include antispasmodics, laxatives, antidiarrheals, antidepressants, and antibiotics. IBS drugs are described in Table 3. Limited effectiveness of conventional treatment options is frustrating for patients but also common.

In a study of 350 IBS patients, more than half of patients (53%) taking prescription drugs for IBS felt that they were ineffective or only somewhat effective, more than 60% reported adverse effects from these medications, and 40% of patients taking over-the-counter medications reported that they were ineffective (29).

The U.S. Food and Drug Administration (FDA) has approved only 2 drugs to treat IBS: tegaserod maleate, a 5-HT4-receptor agonist that increases intestinal motility, and alosetron hydrochloride, a 5-HT3-receptor antagonist medication that decreases abdominal sensitivity. However, tegaserod was taken off the market in March 2007 because of safety concerns, and use of alosetron has been restricted.

Antispasmodics

Antispasmodics are indicated on an as-needed basis as a first-line treatment for IBS pain. The 2 antispasmodics available in the United States, dicyclomine and hyoscyamine, block the action of acetylcholine at parasympathetic sites in secretory glands, smooth muscle, and the central nervous system. The effect is reduced contractions in the colon. The drugs are particularly helpful when taken before meals if postprandial urgency, diarrhea, and cramping are a problem. Adverse reactions increase as dose increases.

Stress management options include the following:

- Stress reduction training and relaxation therapies, such as meditation
- Counseling and support
- Regular exercise, such as walking or yoga
- Changes to the stressful situations in your life
- Adequate sleep
- Hypnotherapy

For patients who are anxious or for whom antispasmodics alone are not successful, clinicians should consider a sedative–antispasmodics combination. The risk for abuse of sedative–antispasmodics is low because of the small dose of sedatives in most formulations and because of the unpleasant anticholinergic side effects that occur with dose elevation.

A meta-analysis of 26 RCTs with antispasmodics supports their utility in the management of IBS symptoms. The study, which incorporated only trials of antispasmodics that are not approved by the FDA (cimetropium bromide, pinaverium bromide, trimetaphan, octilium bromide, and mebeverine), found that the drugs were significantly better than placebo for improving overall symptoms and pain. Patients receiving active drugs had more adverse effects (6% mean difference; \( P < 0.01 \)) than those receiving placebo, but the adverse reactions were not serious (30).

### Laxatives
Expert consensus suggests osmotic-type laxatives if fiber is unsuccessful.

<table>
<thead>
<tr>
<th>Class/Agent</th>
<th>Mechanism of Action</th>
<th>Dosing</th>
<th>Benefits</th>
<th>Side Effects</th>
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<tr>
<td>Antispasmodics</td>
<td>Reduce contractions in colon and small bowel that may produce diarrhea and cramps</td>
<td>Generally given as needed, especially before meals</td>
<td>Reduce pain</td>
<td>Dry mouth, somnolence, constipation, urine retention, diplopia; side effects usually minor</td>
<td>Effective to blunt gastrointestinal response if diarrhea/urgency or postprandial pain; first-line agents for pain</td>
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<tr>
<td>Combination antispasmodics/ sedatives</td>
<td>Additive effect of sedative to reduce GI motility</td>
<td>Generally given as needed, especially before meals</td>
<td>Useful for pain, especially if patient anxious and antispasmodics alone have failed</td>
<td>Drowsiness, additive effect with alcohol; other side effects similar to those of antispasmodics; do not take before driving or tasks requiring alertness</td>
<td>Potential for abuse minimized by anticholinergic component</td>
</tr>
<tr>
<td>Laxatives</td>
<td>Draw water into colon</td>
<td>Titrated to effect</td>
<td>Reduce distention of colon due to retained stool; PEG-based lavage solutions useful for severe constipation when a few glasses are taken at bedtime</td>
<td>Hypermagnesemia, hyperphosphatemia if renal insufficiency; can cause gas and bloating</td>
<td>Less cramping and probably safer long-term than stimulant cathartics (which may cause tachyphylaxis and &quot;cathartic colon&quot;); first-line agents after fiber in constipation-predominant IBS; avoid in IBS with gas and bloating</td>
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| Antidiarrheals | \( \mu \)-Opiate agonists have primarily gut effect to increase segmenting contractions and decrease propulsive ones | Titrated to effect | Reduce diarrhea but not pain | Can cause constipation; atropine can give dry mouth, urine retention, tachycardia | No known long-term sequelae from repeated use; loperamide has no CNS penetration; abuse of diphenoxylate prevented by combination with atropine |
| Antidepressants | Mechanism is uncertain | Lower doses than needed to treat depression | Reduce pain | Anticholinergic effects with tricyclics, diarrhea with SSRIs | Tricyclics are first-line agents in patients with pain and diarrhea, no definitive data on SSRIs |
| Antibiotics | Aims to restore normal intestinal bacteria | Rifaximin 400 mg 3 times/d for 10 days in recent trial | Symptom improvement correlates with normalization of intestinal bacteria | Antibiotic resistance; ototoxicity and CNS symptoms with neomycin | Resistance is less of a concern with rifaximin because it is not absorbed |

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</tbody>
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| Antidiarrheals | \( \mu \)-Opiate agonists have primarily gut effect to increase segmenting contractions and decrease propulsive ones | Titrated to effect | Reduce diarrhea but not pain | Can cause constipation; atropine can give dry mouth, urine retention, tachycardia | No known long-term sequelae from repeated use; loperamide has no CNS penetration; abuse of diphenoxylate prevented by combination with atropine |
| Antidepressants | Mechanism is uncertain | Lower doses than needed to treat depression | Reduce pain | Anticholinergic effects with tricyclics, diarrhea with SSRIs | Tricyclics are first-line agents in patients with pain and diarrhea, no definitive data on SSRIs |
| Antibiotics | Aims to restore normal intestinal bacteria | Rifaximin 400 mg 3 times/d for 10 days in recent trial | Symptom improvement correlates with normalization of intestinal bacteria | Antibiotic resistance; ototoxicity and CNS symptoms with neomycin | Resistance is less of a concern with rifaximin because it is not absorbed |

*CNS = central nervous system; GI = gastrointestinal; IBS = irritable bowel syndrome; PEG = polyethylene glycol; SSRIs = selective serotonin reuptake inhibitors.*
for initial therapy of constipation (31). Osmotic laxatives, like magnesium citrate or sodium phosphate, are used to rapidly empty the lower intestine and bowel. Although not usually used for long-term or repeated correction of constipation, they are considered safe and effective for severe constipation when used daily or as needed. Low-dose daily administration of another type of hyperosmotic laxative, polyethylene glycol, increases bowel frequency and decreases symptoms in chronic constipation in which fiber supplementation is not successful (32). Polyglycol is a large molecule that causes water to be retained in the stool, which softens the stool and increases the number of bowel movements.

Patients with IBS should avoid regular use of stimulant cathartics, such as senna, cascara, and phenolphthalein. Stimulant cathartics increase the risk for cramps and tachyphylaxis and may lead to a markedly slow “cathartic colon.”

**Antidiarrheals**

Nonabsorbable synthetic opioids can be useful to treat patients with diarrhea-predominant IBS. These antidiarrheal agents work by peripheral μ-opioid receptors to reduce visceral nociception viaafferent pathway inhibition. The effect is to reduce propagating contractions and to increase segmenting contractions in the bowel, which slows transit and allows more time for water absorption.

Loperamide is the first-line agent for diarrhea. It can be taken as needed or on a scheduled basis depending on the severity and frequency of symptoms. Two RCTs (33, 34) showed that loperamide is effective for diarrhea; however, it did not significantly relieve pain in either study. There are no identified safety concerns associated with repeated use of loperamide. Other opioid antidiarrheal agents are also likely to be effective. Diproxyphate hydrochloride combined with atropine sulfate is used in IBS to slow gastrointestinal transit. Diproxyphate is a constipating meperidine congener that reduces excessive gastrointestinal propulsion and motility, and atropine discourages abuse by speeding up the heart rate. Diproxyphate may exacerbate constipation.

**5-HT Antagonists**

Tegaserod, a 5-HT4-receptor agonist, was the only drug approved by the FDA for relief of abdominal discomfort, bloating, and constipation in patients with IBS (35). However, on March 30, 2007, the FDA requested that the manufacturer withdraw tegaserod from the market because of an association between use of the drug and myocardial infarction and stroke. In an analysis of over 18,000 patients, adverse cardiovascular events occurred in 13 of 11,614 patients (0.11%) receiving tegaserod compared with 1 of 7031 patients (0.01%) receiving placebo (www.fda.gov/cder/drug/advisory/tegaserod.htm).

Alosetron, a 5-HT3-receptor antagonist that can provide relief in diarrhea-predominant IBS, increases colonic compliance, reduces intestinal transit, and reduces pain and diarrhea (36). It was withdrawn from the market in 2000 because of the occurrence of serious life-threatening gastrointestinal effects and was reintroduced in 2002 with restricted availability and use. Alosetron carries a 1 in 700 risk of ischemic colitis and thus should be reserved for women with severe, refractory IBS symptoms causing significant impairment in quality of life. Prescribing physicians must register with the manufacturer (phone: 888-825-5249), and patients must sign a consent form to begin therapy. Three separate double-blind, randomized, placebo-controlled

trials have shown that alosetron for diarrhea-predominant IBS had an overall “adequate response” rate of nearly 60%. Improvement over placebo was approximately 15% (37–39).

**Antidepressants**

Antidepressants can be helpful in alleviating IBS symptoms. According to a recent meta-analysis of 12 studies, the number needed to treat for benefit in 1 person was 3.2 (40).

Clinicians should consider tricyclic antidepressants to reduce pain and diarrhea. The mechanism of action of these drugs in IBS is unclear, but it is known that they act primarily by blocking the uptake of neurotransmitters at specific presynaptic nerve endings in the central nervous system. As a result, they prevent synaptic receptor overstimulation. The benefit of tricyclics in IBS seems to be independent of the anticholinergic effects or antidepressant effects. The required dosage is less than that required for the treatment of depression. Several studies have shown benefits for tricyclic use (41–43). Tricyclics can be used in combination with antispasmodics.

Use of selective serotonin reuptake inhibitors (SSRIs) is not well-studied in patients with IBS, but early findings suggest that SSRIs can improve the quality of life in patients who have severe IBS with associated psychological stress. This may be primarily a psychological effect. Patients may also benefit from pain alleviation; however, a cohort study that associated paroxetine with improved quality of life in IBS did not find any association with alleviated abdominal pain (26).

SSRIs might be a consideration for older patients or in persons with constipation because they lack anticholinergic side effects. SSRIs may trigger episodes in patients with diarrhea-predominant IBS while being helpful for patients with constipation.

**Antibiotics**

Alterations in gut flora have been identified in patients with IBS, and some hypothesize that intestinal bacterial overgrowth may play a role in symptoms. The antibiotic neomycin has been shown to improve IBS symptoms. This effect seems to correlate with normalization of intestinal bacterial flora (44, 45). However, neomycin effectively eliminates bacterial overgrowth in only about 25% of patients (45), and side effects limit its use. Low efficacy, side effects, and concerns about antimicrobial resistance also apply to other antibiotics that have been previously investigated for treating bacterial overgrowth (46). For this reason, researchers have been seeking an antibiotic for IBS that is not systemically absorbed, has minimal adverse effects, and effectively eliminates bacterial overgrowth. One drug that meets these criteria is rifaximin.

An RCT assigned 87 patients who met the Rome I criteria for IBS to receive either 400 mg of rifaximin 3 times daily for 10 days or placebo. A questionnaire was administered before treatment and 7 days after treatment. The primary outcome was global improvement in IBS. Patients were then asked to keep a weekly symptom diary for 10 weeks. Over the 10 weeks of follow-up, rifaximin resulted in greater improvement in IBS symptoms than placebo. In addition, rifaximin recipients had a lower bloating score after treatment. This preliminary, short-duration trial suggests that rifaximin improves IBS symptoms for up to 10 weeks after discontinuation of therapy (47).

**What are some possible future treatments for IBS?**

Several new drugs are being studied for the treatment of IBS. IBS therapy is moving from “symptom-based”
therapy to “hypothesis-based” therapy. Rather than treating symptoms, new IBS approaches aim to treat the underlying pathophysiology.

Trials are currently underway for treating IBS with renzapride, a 5-HT₃-receptor antagonist and a 5-HT₄-receptor agonist (48, 49). Tachykinin antagonists, like substance P and neurokinin A, might also be useful for treating IBS. Tachykinins are present in the gastrointestinal tract and are involved in such functions as gastrointestinal motility, visceral sensitization, and autonomic reaction to stress. Studies in animals and healthy humans have yielded promising results (50, 51). Neutrophins, a family of neuropeptides that includes neurtrophin-3, are also undergoing preclinical study as potential therapeutic agents for functional gastrointestinal disorders. Studies have shown that recombinant human neurtrophin-3 increased stool frequency; facilitated stool passage in patients with constipation; and accelerated gastric, small bowel, and colonic transit in healthy persons (52, 53). Antibiotics and probiotics aim to normalize intestinal bacteria.

### Is there evidence to support the effectiveness of complementary and alternative medicine treatments for IBS?

Patients with IBS frequently try nontraditional therapies, particularly if traditional approaches to treatment do not relieve their symptoms. While some patients have some relief with such therapies, data to support their use are sparse (54) (Table 4).

#### What components of care should clinicians integrate into follow-up of patients with IBS?

There are no specific data on which to base a recommendation on the frequency or the components of follow-up for patients with IBS. However, a common-sense approach includes monitoring for alarm features, progression of symptoms, and management of psychosocial stressors. The typical symptom course in IBS is chronic and fluctuating. Clinicians should consider additional diagnostic tests or referral if alarm features develop or if symptoms are refractory and persistent. Clinicians should emphasize to patients that the long-term prognosis is good. Carefully explaining the prognosis can significantly reduce patient distress.

### Table 4. Alternative and Complementary Therapies Used by Patients with Irritable Bowel Syndrome

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Proposed Action</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acupuncture</td>
<td>Relief of chronic pain</td>
<td>No definitive studies available; results of existing studies are mixed</td>
</tr>
<tr>
<td>Hypnosis</td>
<td>Relief of chronic pain</td>
<td>No definitive studies available</td>
</tr>
<tr>
<td>Peppermint oil</td>
<td>Natural antispasmodic believed to relax intestinal smooth muscle</td>
<td>Ineffective in 2 crossover trials; some effect noted in one parallel trial</td>
</tr>
<tr>
<td>Ginger</td>
<td>Natural antispasmodic believed to relax intestinal smooth muscle</td>
<td>No evidence from high-quality trials</td>
</tr>
<tr>
<td>Aloe</td>
<td>Natural antispasmodic believed to relax intestinal smooth muscle</td>
<td>No evidence from high-quality trials</td>
</tr>
<tr>
<td>Chinese herbal therapy</td>
<td>Natural antispasmodic believed to relax intestinal smooth muscle</td>
<td>Global improvement noted in 1 study</td>
</tr>
<tr>
<td>Probiotics</td>
<td>Aim to replenish the beneficial intestinal bacteria that may be lacking in patients with IBS</td>
<td>Bifidobacteria infantis showed symptom improvement in early clinical studies</td>
</tr>
</tbody>
</table>


When should clinicians consider consulting a specialist for treatment?
When management strategies are not effective, clinicians should consider consulting a gastroenterologist. Gastroenterologists may have greater knowledge of treatment options because of increased familiarity with the disorder. Clinicians should consider referral to a mental health professional for patients with refractory symptoms leading to impaired quality of life or major depression, anxiety disorder, bipolar disorder, or other serious psychological disease.

Do professional organizations offer recommendations for the care of patients with IBS?
In 2003, the American Gastroenterological Association developed clinical practice guidelines for IBS based on a comprehensive review (31).

Are there performance measures related to the care of patients with IBS?
Current proposed performance measures in the United States do not include any measures specifically related to the care of patients with IBS. However, the quality of the doctor–patient interaction is paramount in the care of patients with IBS.

A survey developed by the American Gastrointestinal Association may be useful for evaluating a patient’s satisfaction with his or her care (www.gastro.org/wmspage.cfm?parm1=3266). However, the survey has not yet been validated.

in the clinic
Tool Kit
Irritable Bowel Syndrome

www.pier.acponline.org
IBS module of PIER, an electronic decision support resource designed for rapid access to information at the point of care.

www.annals/intheclinic/tools
Download copies of the Patient Information sheet that appears on the following page for duplication and distribution to your patients.

www.gastro.org/wmspage.cfm?parm1=3266
Patient satisfaction surveys to enable the physician to quantitatively measure the patient care experience as well as physician–patient communication.
THINGS PEOPLE SHOULD KNOW
ABOUT IRRITABLE BOWEL SYNDROME

- IBS causes pain, cramping, bloating, gas, diarrhea, and constipation. Another name for the condition is spastic colitis.
- The cause of IBS is believed to be intestines that are overly sensitive to normal intestinal movement, gas, some foods, and stress.
- There is no test for IBS, so doctors make the diagnosis by carefully evaluating symptoms and excluding other conditions.
- There is no cure, but people with IBS can control symptoms by healthy diet and exercise, managing stress, avoiding things that trigger symptoms, and taking medications to treat symptoms.

Web Sites with Good Information about Irritable Bowel Syndrome

MedlinePLUS

National Institute of Diabetes and Digestive and Kidney Diseases
http://digestive.niddk.nih.gov/ddiseases/pubs/ibs_ez/

International Foundation for Functional Gastrointestinal Disorders
www.aboutibs.org/

Mayo Clinic
www.mayoclinic.com/health/irritable-bowel-syndrome/MM00461 (a short video clip that provides information about irritable bowel syndrome)

HEALTH TiPS*

Irritable bowel syndrome (IBS) is a common problem that can cause constipation, diarrhea, or both. Sometimes there is stomach pain or gas. IBS comes and goes but never goes away for good. IBS does not cause cancer.

What You Can Do:                          Things to Ask your Doctor:
Find out what makes your IBS symptoms worse
• Stress at home or work
• Some foods
Write down when your IBS symptoms happen
• Get help to deal with stress
• Stay away from too much caffeine, soda, fatty foods, and laxatives
See your doctor often to keep your IBS on track. Next doctor’s visit __________

What causes IBS?                          How can I deal with stress?
Do I need any tests?                      Do I need medicine for my IBS?
Why do I have problems if all my tests are normal?   Why doesn’t medicine always work for my IBS?
What are the side effects of my medicines for IBS?

*HEALTH TiPS are developed by the American College of Physicians Foundation and PIER and are designed to be understood by most patients.
CME Questions

1. A 24-year-old woman has a 7-month history of occasional abdominal bloating and constipation alternating with intermittent loose stools. She was well until 8 months ago, when she developed diarrhea during a trip to Mexico that was treated with ciprofloxacin. She has not had weight loss, fever, or nocturnal symptoms. Her stools are small in volume, soft, and brown and do not contain blood or mucus.

Which of the following is most likely to be the diagnosis in this patient?
A. Clostridium difficile infection
B. Helicobacter pylori infection
C. Diverticular disease
D. Postinfectious irritable bowel syndrome

2. A 25-year-old woman has a 7-month history of progressively severe constipation, generalized abdominal pain, and bloating that have affected her ability to work and handle other responsibilities. She has approximately one firm bowel movement each week. Use of over-the-counter fiber products has been ineffective. Her weight is stable, and she is otherwise healthy. Thyroid function tests and measurement of serum calcium and serum electrolyte levels are normal.

Which of the following medications is most appropriate at this time?
A. Alosetron
B. A selective serotonin reuptake inhibitor
C. A tricyclic antidepressant
D. Metronidazole
E. Polyethylene glycol

3. A 24-year-old woman is evaluated for 3-year history of oral ulcers that occur frequently, usually at times of stress, and last about 1 week. The ulcers are unrelated to rash, joint symptoms, or fever. She notes that over the past 4 months they have become larger, recur more frequently, and last longer (2 to 3 weeks). She attributes a recent 4.4-kg (10-lb) unintentional weight loss to pain while eating during outbreaks of the ulcers. Her medical history is significant for occasional abdominal pain and diarrhea that was previously diagnosed as irritable bowel syndrome. She has no history of an eating disorder, illicit drug use, blood transfusion, or any previous sexual activity. Her family history is unrevealing. On examination, she has 2 mildly tender oral ulcerations that she notes have been present for about 6 days. Results of fecal occult blood testing are positive.

What is the best next step in the management of this patient?
A. Colonoscopy
B. HIV serology
C. Hyoscyamine
D. Acyclovir
E. Biopsy of oral lesions

4. A 28-year-old man is evaluated for 6 weeks of intermittent abdominal pain relieved with bowel movements and increased frequency of bowel movements with stool that is softer and less well-formed than previously. He denies fever, upper gastrointestinal symptoms, or recent camping or travel. Physical examination is entirely normal except for some mild abdominal tenderness to deep palpation in all 4 quadrants. Stool is negative for occult blood. He has no family history of cancer or inflammatory bowel disease. He notes that the symptoms began when his wife filed for a divorce. He denies being depressed.

What is the most appropriate next step in the evaluation and management of this patient?
A. Flexible sigmoidoscopy
B. Symptom diary and follow-up visit
C. Abdominal CT scan
D. Radiographs of the abdomen
E. Reassurance

5. A 34-year-old woman with a medical history of childhood asthma and 2 normal pregnancies is evaluated for abdominal pain and bloating almost daily for the past 3 years since the birth of her youngest child. She also reports diarrhea, which she describes as 2 to 6 loose bowel movements per day, never feels like her colon is completely evacuated, and reports that stool is sometimes watery. She denies fever, weight loss, previous lactose intolerance, family history of cancer or inflammatory bowel disease, visible blood or mucus in stools, and antibiotic use. She has been prescribed dicyclomine, which provides some relief of pain but not diarrhea. Physical examination is normal. You believe that the patient most likely has irritable bowel syndrome.

Which of the following would be the most appropriate next step?
A. Colonoscopy
B. Stool cultures
C. Dietary history
D. Alosetron
E. Fluoxetine

Questions are largely from the ACP’s Medical Knowledge Self-Assessment Program (MKSAP). Go to www.annals.org/intheclinic/ to obtain up to 1.5 CME credits, to view explanations for correct answers, or to purchase the complete MKSAP program.