Clinical manifestations and diagnosis of irritable bowel syndrome in adults

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Literature review current through: **Sep 2023.**
This topic last updated: **Jul 20, 2022.**

INTRODUCTION

Irritable bowel syndrome (IBS) is a functional disorder of the gastrointestinal tract characterized by chronic abdominal pain and altered bowel habits. However, only a small percentage of those affected seek medical attention [1-5]. Approximately 40 percent of individuals who meet diagnostic criteria for IBS do not have a formal diagnosis [6]. IBS is associated with increased health care costs and is the second highest cause of work absenteeism [7,8]. In the United States, IBS accounts for 25 to 50 percent of all referrals to gastroenterologists [9]. This topic will review the clinical manifestations and diagnosis of IBS. The pathophysiology and management of IBS are discussed in detail separately. (See "Pathophysiology of irritable bowel syndrome" and "Treatment of irritable bowel syndrome in adults".)

EPIDEMIOLOGY

Prevalence — The prevalence of irritable bowel syndrome (IBS) in North America estimated from population-based studies is approximately 10 to 15 percent [1,2,10-14]. In a meta-analysis that included eight international studies, the pooled prevalence of IBS was estimated to be 11 percent, with wide variation by geographic region [15]. The prevalence of IBS was 25 percent lower in those aged over 50 years as compared with those who were younger (OR, 0.75; 95% CI, 0.62-0.92) [14]. The overall prevalence of IBS in females was higher as compared with males

(odds ratio 1.67 [95% CI 1.53–1.82]) [16]. This relative difference reflects an absolute difference in prevalence of approximately 5 percent between the sexes, with a prevalence in females and males of 14 and 9 percent, respectively. Females may be more likely to have constipation-predominant IBS as compared with males [16].

Associated conditions — IBS is associated with other conditions including fibromyalgia, chronic fatigue syndrome (also known as systemic exertion intolerance disease), gastroesophageal reflux disease, functional dyspepsia, non-cardiac chest pain, and psychiatric disorders including major depression, anxiety, and somatization [17-21]. (See "Pathophysiology of irritable bowel syndrome", section on 'Psychosocial dysfunction'.)

CLINICAL MANIFESTATIONS

Irritable bowel syndrome (IBS) is characterized by chronic abdominal pain and altered bowel habits [17].

Chronic abdominal pain — Abdominal pain in IBS is usually described as a cramping sensation with variable intensity and periodic exacerbations. The location and character of the pain can vary widely [17,22]. The severity of the pain may range from mild to severe. The pain is frequently related to defecation. While in some patients abdominal pain is relieved with defecation, some patients report worsening of pain with defecation [23]. Emotional stress and meals may exacerbate the pain. Patients with IBS also frequently report abdominal bloating and increased gas production in the form of flatulence or belching.

Altered bowel habits — Symptoms of IBS include diarrhea, constipation, alternating diarrhea and constipation, or normal bowel habits alternating with either diarrhea and/or constipation.

Diarrhea — Diarrhea is usually characterized as frequent loose stools of small to moderate volume. Bowel movements generally occur during waking hours, most often in the morning or after meals. Most bowel movements are preceded by lower abdominal cramping pain, urgency, and a sensation of incomplete evacuation or tenesmus. Approximately one-half of all patients with IBS complain of mucus discharge with stools [24]. Large volume diarrhea, bloody stools, nocturnal diarrhea, and greasy stools are not associated with IBS.

Constipation — Stools are often hard and may be described as pellet-shaped. Patients may also experience tenesmus even when the rectum is empty.

DIAGNOSIS

Overview of diagnostic approach — Irritable bowel syndrome (IBS) should be suspected in patients with chronic abdominal pain and altered bowel habits (constipation and/or diarrhea). A clinical diagnosis of IBS requires the fulfillment of symptom-based diagnostic criteria and a limited evaluation to exclude underlying organic disease [25,26]. (See 'Diagnostic criteria' below and 'Initial evaluation' below.)

Diagnostic criteria — In the absence of a biologic disease marker, several symptom-based criteria have been proposed to standardize the diagnosis of IBS. The most widely used among them are the Rome IV criteria.

- **Rome IV criteria for IBS** – According to the Rome IV criteria, IBS is defined as recurrent abdominal pain, on average, at least one day per week in the last three months, associated with two or more of the following criteria [17,25]:
  - Related to defecation
  - Associated with a change in stool frequency
  - Associated with a change in stool form (appearance)
- **IBS subtypes** – Subtypes of IBS are recognized based on the patient's reported predominant bowel habit on days with abnormal bowel movements. The Bristol stool form scale (BSFS) should be used to record stool consistency [27]. Subtypes can only confidently be established when the patient is evaluated off medications used to treat bowel habit abnormalities. IBS subtypes are defined for clinical practice as follows:
  - **IBS with predominant constipation** – Patient reports that abnormal bowel movements are usually constipation (type 1 and 2 in the BSFS)
  - **IBS with predominant diarrhea** – Patient reports that abnormal bowel movements are usually diarrhea (type 6 and 7 in the BSFS)
  - **IBS with mixed bowel habits** – Patient reports that abnormal bowel movements are usually both constipation and diarrhea (more than one-fourth of all the abnormal bowel movements were constipation and more than one-fourth were diarrhea)
  - **IBS unclassified** – Patients who meet diagnostic criteria for IBS but cannot be accurately categorized into one of the other three subtypes.
- **Other criteria** – The Manning criteria include relief of pain with bowel movements, looser and more frequent stools with onset of pain, passage of mucus, and a sense of incomplete emptying (table 1) [24]. There have been conflicting data regarding the predictive ability of the Manning criteria [28-30]. The Kruis criteria are less frequently used in clinical

practice [31,32]. A number of studies have assessed the accuracy of the Rome and Manning criteria in a variety of practice settings [33-36]. As a result, some investigators continue to use the Manning criteria or a combination of both. No symptom-based criteria have ideal accuracy for diagnosing IBS; however, the Manning and Kruis criteria perform at least as well as the Rome I criteria [10].

Initial evaluation

History and physical examination — The medical history serves to identify clinical manifestations of IBS as well as identify other possible causes of similar symptoms. The BSFS should be used to record stool consistency [27]. We perform a thorough history with particular attention to the symptoms that are concerning for organic disease. The history should include exposure to a variety of medications that can cause similar symptoms (table 2 and table 3). A subgroup of patients report an acute viral or bacterial gastroenteritis prior to the onset of IBS symptoms. Family history assessment should include the presence of inflammatory bowel disease, colorectal cancer, and celiac disease. The physical examination is usually normal in patients with IBS. However, patients may have mild abdominal tenderness to palpation. In patients with constipation a rectal examination may be useful in identifying dyssynergic defecation [37]. (See "Etiology and evaluation of chronic constipation in adults", section on 'Physical examination' and 'Additional evaluation based on the presence of alarm features' below.)

Laboratory testing — There is no definitive diagnostic laboratory test for IBS. The purpose of laboratory testing is primarily to exclude an alternative diagnosis.

- In all patients with suspected IBS, we perform a complete blood count.
- In patients with diarrhea, we perform the following [26,38]:
  - Fecal calprotectin or fecal lactoferrin
  - Stool testing for giardia (antigen detection or nucleic acid amplification assay)
  - Serologic testing for celiac disease
  - C-reactive protein levels, only if fecal calprotectin and fecal lactoferrin cannot be performed

A fecal calprotectin above a threshold level of 50 mcg/g had a pooled sensitivity and specificity for IBD of 81 and 87 percent, respectively [26]. Lactoferrin threshold values above the threshold range of 4.0 to 7.25 mg/g have a sensitivity and specificity for IBD of 79 and 93 percent, respectively. In a meta-analysis, patients with IBS symptoms and a CRP level of ≤0.5 or calprotectin level of ≤40µg/g, there was a ≤1 percent probability of IBD [26,39].

Data to support testing for celiac disease are conflicting. In a meta-analysis of 14 studies that included 4204 individuals, of whom 2278 (54 percent) met diagnostic criteria for IBS, 4 percent of patients had celiac disease [40]. However, almost all the studies included in this analysis were conducted outside the United States. A prospective multicenter study performed in the United States compared the prevalence of abnormal celiac antibodies and biopsy proven celiac disease in patients with non-constipated IBS to that of healthy controls. Although more than 7 percent of non-constipated IBS patients had celiac disease associated antibodies suggesting gluten sensitivity, the prevalence of biopsy proven celiac disease was similar to controls [41]. (See "Epidemiology, pathogenesis, and clinical manifestations of celiac disease in adults" and "Diagnosis of celiac disease in adults", section on 'Serologic evaluation'.)

The diagnostic role of antibodies to cytolethal distending toxin B (CdtB) and vinculin requires confirmation before they can be used in the evaluation of patients with suspected IBS [42-44]. One study that evaluated anti-CdtB and anti-vinculin titers in 2375 patients with IBS diarrhea, found that patients anti-CdtB were significantly higher in IBS diarrhea as compared to patients with IBD, healthy controls, celiac disease, and IBS constipation [43]. The specificity of anti-CdtB for IBS diarrhea was 92 percent but the sensitivity was only 44 percent. Anti-vinculin had a sensitivity and specificity of 33 and 84 percent, respectively.

Other tests — In addition, we perform a limited number of studies guided by the clinical presentation. These include the following:

- Age-appropriate colorectal cancer screening in all patients.
- In IBS patients with constipation, abdominal radiograph to assess for stool accumulation and determine the severity.
- We perform physiologic testing (anorectal manometry and balloon expulsion testing) to rule out dyssynergic defecation in patients with severe constipation that is refractory to management with dietary changes and osmotic laxative therapy. (See "Etiology and evaluation of chronic constipation in adults", section on 'Dyssynergic defecation' and "Etiology and evaluation of chronic constipation in adults", section on 'Motility studies' and "Treatment of irritable bowel syndrome in adults", section on 'Constipation'.)

Additional evaluation based on the presence of alarm features — The extent of additional testing depends on the presence of alarm features. Although the presence of concerning features may identify patients more likely to have an organic disease, most patients will ultimately have a negative evaluation.

- **Alarm features** – Alarm features include [10]:

- Age of onset after age 50 years
- Rectal bleeding or melena
- Nocturnal diarrhea
- Progressive abdominal pain
- Unexplained weight loss
- Laboratory abnormalities (iron deficiency anemia, elevated C-reactive protein or fecal calprotectin/lactoferrin)
- Family history of IBD or colorectal cancer

- **Patients without alarm features** – In patients who meet diagnostic criteria for IBS and have no alarm features, we do not routinely perform any additional testing beyond the initial evaluation. This limited diagnostic approach rules out organic disease in over 95 percent of patients [45,46].

- **Patients with alarm features** – In patients with alarm features, we perform additional evaluation to exclude other causes of similar symptoms [47]. The diagnostic evaluation is based on the clinical presentation and usually includes endoscopic evaluation in all patients and imaging in selected cases. In patients with diarrhea, we perform colonoscopy to evaluate for the presence of IBD and perform biopsies to exclude microscopic colitis [48-50]. We reserve colonic imaging (eg, abdominal computed tomography scan) if there is a clinical suspicion for a structural lesion [47]. The imaging modality is guided by the clinical presentation. As an example, if pain, bloating, early satiety and constipation are of recent onset in a postmenopausal female, then we perform a pelvic imaging with an ultrasound and/or abdominal CT scan [51]. (See "Etiology and evaluation of chronic constipation in adults", section on 'Endoscopy' and "Colorectal cancer: Epidemiology, risk factors, and protective factors", section on 'Incidence'.)

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of irritable bowel syndrome (IBS) is broad. In patients with diarrhea-predominant symptoms, other important causes of chronic diarrhea include celiac disease, microscopic colitis, small intestinal bacterial overgrowth, and inflammatory bowel disease. Constipation may be secondary to organic disease, dyssynergic defecation, or slow colonic transit. While some of these alterative diagnoses are excluded during the course of evaluation in patients with suspected IBS, other diagnoses require additional diagnostic testing and need only be performed in selected patients with alarm features. Other causes of chronic diarrhea and constipation are discussed in detail separately. (See 'Initial evaluation' above and "Approach to the adult with chronic diarrhea in resource-abundant settings" and "Etiology and evaluation

of chronic constipation in adults" and 'Additional evaluation based on the presence of alarm features' above.)

DISEASE COURSE

Most patients with irritable bowel syndrome (IBS) have chronic symptoms that vary in severity over time. In a systematic review that included clinic-based IBS patients with variable long term follow-up (six months to six years), 2 to 5 percent of patients were diagnosed with an alternate gastrointestinal disease. Symptoms remained unchanged or progressed in 30 to 50 percent and 2 to 18 percent, respectively [52]. An improvement in symptoms was reported in 12 to 38 percent of patients. Patients may also experience a change in IBS subtype over time with the most frequent change being from predominant constipation or diarrhea to mixed bowel habits.

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Irritable bowel syndrome".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topics (see "Patient education: Irritable bowel syndrome (The Basics)")

- Beyond the Basics topics (see "Patient education: Irritable bowel syndrome (Beyond the Basics)" and "Patient education: Chronic diarrhea in adults (Beyond the Basics)")

SUMMARY AND RECOMMENDATIONS

- **Epidemiology –** Irritable bowel syndrome (IBS) is a functional disorder of the gastrointestinal tract characterized by chronic abdominal pain and altered bowel habits. The estimated prevalence of IBS globally is approximately 11 percent, with a higher prevalence in younger individuals and in females. (See 'Epidemiology' above.)

- **Clinical manifestations –** IBS is characterized by chronic abdominal pain and altered bowel habits. Abdominal pain in IBS is usually described as a cramping sensation with variable intensity and periodic exacerbations. The pain is frequently related to defecation. While in some patients abdominal pain is relieved with defecation, a substantial portion of patients report worsening of pain with defecation. Symptoms of IBS also include diarrhea, constipation, alternating diarrhea and constipation, or normal bowel habits alternating with either diarrhea and/or constipation. (See 'Altered bowel habits' above.)

- **Disease course –** Most patients with IBS have chronic symptoms that vary in severity over time. Patients may also experience a change in IBS subtype over time with the most frequent change being from predominant constipation or diarrhea to mixed bowel habits. (See 'Disease course' above.)

- **Diagnosis –** IBS should be suspected in patients with chronic abdominal pain and altered bowel habits (constipation and/or diarrhea). A clinical diagnosis of IBS requires the fulfillment of symptom-based diagnostic criteria and a limited evaluation to exclude underlying organic disease. (See 'Overview of diagnostic approach' above.)

  According to the Rome IV criteria, IBS is defined as recurrent abdominal pain, on average, at least one day per week in the last three months, associated with two or more of the following criteria (see 'Diagnostic criteria' above):

  - Related to defecation
  - Associated with a change in stool frequency
  - Associated with a change in stool form (appearance)

- **Initial evaluation –** Initial evaluation in all patients with suspected IBS includes a history and physical examination and limited testing to evaluate for the presence of alarm features concerning for organic disease. (See 'Initial evaluation' above.)

- In all patients with suspected IBS, we perform a complete blood count and age-appropriate colorectal cancer screening.
- In patients with diarrhea, we perform the following:
  - Fecal calprotectin or fecal lactoferrin
  - Stool testing for giardia
  - Serologic testing for celiac disease
  - C-reactive protein levels only if fecal calprotectin and fecal lactoferrin cannot be performed

- **Alarm features concerning for underling organic disease –** Alarm features include:
  - Age of onset after age 50 years
  - Rectal bleeding or melena
  - Nocturnal diarrhea
  - Progressive abdominal pain
  - Unexplained weight loss
  - Laboratory abnormalities (eg, iron deficiency anemia, elevated C-reactive protein or fecal calprotectin/lactoferrin)
  - Family history of inflammatory bowel disease or colorectal cancer

- **Additional evaluation based on the presence of alarm features**
  - In patients who meet diagnostic criteria for IBS and have no alarm features, we do not routinely perform any additional testing beyond the initial evaluation.
  - In patients with alarm features, we perform additional evaluation to exclude other causes of similar symptoms. The diagnostic evaluation is based on the clinical presentation and usually includes endoscopic evaluation in all patients and imaging in selected cases. (See 'Additional evaluation based on the presence of alarm features' above.)

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Topic 2630 Version 35.0

GRAPHICS

Manning criteria for the diagnosis of irritable bowel syndrome*

Pain relieved with defecation
More frequent stools at the onset of pain
Looser stools at the onset of pain
Visible abdominal distention
Passage of mucus
Sensation of incomplete evacuation

* The likelihood of irritable bowel syndrome is proportional to the number of Manning criteria that are present.

Graphic 63034 Version 1.0

Medications associated with diarrhea

System targeted by drug	Type of agent	Examples
Cardiovascular	Antiarrhythmics	Digoxin Procainamide Quinidine
	Antihypertensives	ACE inhibitors Angiotensin II receptor blockers* Beta blockers Hydralazine Methyldopa
	Cholesterol-lowering agents	Clofibrate Gemfibrozil Statins
	Diuretics	Acetazolamide Ethacrynic acid Furosemide
Central nervous system	Antianxiety drugs	Alprazolam Meprobamate
	Antiparkinsonian drugs	Levodopa
	Other agents	Anticholinergic agents Fluoxetine Lithium Tacrine
Endocrine	Oral hypoglycemic agents	Metformin
	Thyroid replacement therapy	Synthroid
Gastrointestinal	Antiulcer/antacid drugs	H2RAs Magnesium-containing antacids Misoprostol Proton pump inhibitors
	Bile acids	Chenodeoxycholic acid Ursodeoxycholic acid
	Laxatives	Cathartics Lactulose Sorbitol

	Treatments for inflammatory bowel disease	5-aminosalycilates (particularly olsalazine)
Musculoskeletal	Gold salts	Auranofin
	Nonsteroidal antiinflammatory drugs	Ibuprofen Mefenamic acid Naproxen Phenylbutazone
	Treatments for periodic fever syndrome or gout	Colchicine
Other	Antibiotics¶	Amoxicillin Ampicillin Cephalosporins Clindamycin Neomycin Tetracycline
	Antineoplastic agents	Many
	Dietary	Alcohol Sugar substitutes (eg, sorbitol)
	Vitamins	Magnesium Vitamin C

ACE: angiotensin-converting enzyme; H2RA: histamine-2 receptor antagonist.

* Olmesartan has been associated with sprue-like enteropathy.

¶ Most antibiotics have been associated with diarrhea.

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Graphic 71449 Version 7.0

Drugs associated with constipation

Analgesics
Anticholinergics
Antihistamines
Antispasmodics
Antidepressants
Antipsychotics
Cation-containing agents
Iron supplements
Aluminum (antacids, sucralfate)
Barium
Neurally active agents
Opiates
Antihypertensives
Ganglionic blockers
Vinca alkaloids
Calcium channel blockers
5HT3 antagonists

Graphic 62307 Version 2.0

Contributor Disclosures

Arnold Wald, MD No relevant financial relationship(s) with ineligible companies to disclose. **Nicholas J Talley, MD, PhD** Patent Holder: Australian Provisional Patent [Diagnostic marker for functional gastrointestinal disorders]; Biomarkers of irritable bowel syndrome [Irritable bowel syndrome]; Mayo Clinic [Dysphagia questionnaire]; Mayo Clinic [Bowel Disease questionnaire]; Nepean Dyspepsia Index [Dyspepsia]; Nestec [Irritable bowel syndrome]; Singapore Provisional Patent [BDNF Tissue Repair Pathway]. Grant/Research/Clinical Trial Support: Alimetry [Gastric mapping device research collaboration]; Allakos [Gastric eosinophilic disease]; AstraZeneca [Eosinophilic gastritis, eosinophilic gastroenteritis]; Intrinsic Medicine [Bowel syndrome with constipation]; NHMRC Centre for Research Excellence in Digestive Health [NHMRC Investigator grant]. Consultant/Advisory Boards: Adelphi Values [Functional dyspepsia]; Allakos [Gastric eosinophilic disease, AK002]; AstraZeneca [Eosinophilic gastritis, eosinophilic gastroenteritis]; AusEE [Eosinophilic gut diseases]; Bayer [Inflammatory bowel syndrome]; BluMaiden [Microbiome Ad Board]; Comvita Mānuka Honey [Digestive health]; Dr Falk Pharma [Eosinophilia]; GlaxoSmithKline Australia [Educational speaker eosinophilic gut disease]; Glutagen [Celiac disease]; International Foundation for Functional Gastrointestinal Disorders [Advisory board, functional GI disorders]; Intrinsic Medicine [Human milk oligosaccharide]; IsoThrive [Esophageal microbiome]; Planet Innovation [Gas capsule, inflammatory bowel syndrome]; Progenity Inc [Intestinal capsule]; Rose Pharma [IBS]; Viscera Labs [Inflammatory bowel syndrome, diarrhea]. Other Financial Interest: Elsevier textbook royalties [Medical education]. All of the relevant financial relationships listed have been mitigated. **Shilpa Grover, MD, MPH, AGAF** No relevant financial relationship(s) with ineligible companies to disclose.

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