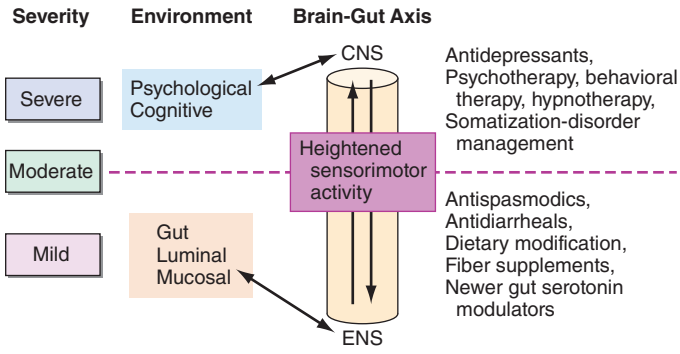

FIGURE 352-1 Therapeutic targets for irritable bowel syndrome. Patients with mild to moderate symptoms usually have intermittent symptoms that correlate with altered gut physiology. Treatments include gut-acting pharmacologic agents such as antispasmodics, antidiarrheals, fiber supplements, and gut serotonin modulators. Patients who have severe symptoms usually have constant pain and psychosocial difficulties. This group of patients is best managed with antidepressants and other psychosocial treatments. CNS, central nervous system; ENS, enteric nervous system.

associated with increased risk. The microbes involved in the initial infection are *Campylobacter*, *Salmonella*, and *Shigella*. Those patients with *Campylobacter* infection who are toxin-positive are more likely to develop postinfective IBS. Increased rectal mucosal enteroendocrine cells, T lymphocytes, and increased gut permeability are acute changes following *Campylobacter* enteritis that could persist for more than a year and may contribute to postinfective IBS.

Immune Activation and Mucosal Inflammation Some patients with IBS display persistent signs of low-grade mucosal inflammation with activated lymphocytes, mast cells, and enhanced expression of proinflammatory cytokines. These abnormalities may contribute to abnormal epithelial secretion and visceral hypersensitivity. There is increasing evidence that some members of the superfamily of transient receptor potential (TRP) cation channels such as TRPV1 (vanilloid) channels are central to the initiation and persistence of visceral hypersensitivity. Mucosal inflammation can lead to increased expression of TRPV1 in the enteric nervous system. Enhanced expression of TRPV1 channels in the sensory neurons of the gut has been observed in IBS, and such expression appears to correlate with visceral hypersensitivity and abdominal pain. Interestingly, clinical studies have also shown increased intestinal permeability in patients with IBS-D. Psychological stress and anxiety can increase the release of proinflammatory cytokine, and this in turn may alter intestinal permeability. This provides a functional link between psychological stress, immune activation, and symptom generation in patients with IBS.

Altered Gut Flora A high prevalence of small intestinal bacterial overgrowth in IBS patients has been noted based on positive lactulose hydrogen breath test. This finding, however, has been challenged by a number of other studies that found no increased incidence of bacterial overgrowth based on jejunal aspirate culture. Abnormal H_2 breath test can occur because of small-bowel rapid transit and may lead to erroneous interpretation. Hence, the role of testing for small intestinal bacterial overgrowth in IBS patients remains unclear.

Studies using culture-independent approaches such as 16S rRNA gene-based analysis found significant differences between the molecular profile of the fecal microbiota of IBS patients and that of healthy subjects. IBS patients had decreased proportions of the genera *Bifidobacterium* and *Lactobacillus* and increased ratios of Firmicutes:Bacteroidetes. It has been speculated that these changes may be related to stress and diet. A temporary reduction in lactobacilli has been reported in animal models of early-life stress. On the other hand, Firmicutes is the dominant phylum in adults consuming a diet high in animal fat and protein. However, it is still unclear whether such changes in fecal microbiota are causal, consequential, or merely the result of constipation and diarrhea. In addition, the stability of the change in the microbiota needs to be determined.

Abnormal Serotonin Pathways The serotonin (5-HT)-containing enterochromaffin cells in the colon are increased in a subset of IBS-D patients compared to healthy individuals or patients with ulcerative colitis. Furthermore, postprandial plasma 5-HT levels were significantly higher in this group of patients compared to healthy controls. Because serotonin plays an important role in the regulation of GI motility and visceral perception, the increased release of serotonin may contribute to the postprandial symptoms of these patients and provides a rationale for the use of serotonin antagonists in the treatment of this disorder.

APPROACH TO THE PATIENT: Irritable Bowel Syndrome

Because IBS is a disorder for which no pathognomonic abnormalities have been identified, its diagnosis relies on recognition of positive clinical features and elimination of other organic diseases. Symptom-based criteria have been developed for the purpose of differentiating patients with IBS from those with organic diseases. These include the Manning, Rome I, Rome II, and Rome III criteria (Table 352-1). The diagnostic values of these criteria are shown in Table 352-3. In a validation study, Rome III performed less well than either the Rome I and II criteria and all criteria studied to date showed positive predictive values of <50%, which underscores the need for developing diagnostic strategies for IBS that are more cost-effective than the current approaches. A careful history and physical examination are frequently helpful in establishing the diagnosis. Clinical features suggestive of IBS include the following: recurrence of lower abdominal pain with altered bowel habits over a period of time without progressive deterioration, onset of symptoms during periods of stress or emotional upset, absence of other systemic symptoms such as fever and weight loss, and small-volume stool without any evidence of blood.

On the other hand, the appearance of the disorder for the first time in old age, progressive course from time of onset, persistent diarrhea after a 48-h fast, and presence of nocturnal diarrhea or steatorrheal stools argue against the diagnosis of IBS.

TABLE 352-3 SENSITIVITY, SPECIFICITY, POSITIVE AND NEGATIVE PREDICTIVE VALUES, AND POSITIVE AND NEGATIVE LIKELIHOOD RATIOS FOR THE ROME AND MANNING CRITERIA FOR IRRITABLE BOWEL SYNDROME[a]

	Sensitivity, % (95% CI)	Specificity, % (95% CI)	Positive Predictive Value, % (95% CI)	Negative Predictive Value, % (95% CI)	Positive Likelihood Ratio (95% CI)	Negative Likelihood Ratio (95% CI)
Rome III criteria	17.4 (13.9–21.5)	95.6 (94.4–96.5)	49.6 (42.0–58.7)	82.1 (80.0–83.6)	3.92 (2.85–5.38)	0.86 (0.83–0.91)
Rome II criteria	23.3 (19.4–27.8)	94.5 (93.2–95.5)	51.7 (44.9–59.5)	82.9 (80.8–84.4)	4.21 (3.20–5.53)	0.81 (0.77–0.86)
Rome I criteria	24.3 (20.3–28.8)	93.9 (92.6–95.0)	50.5 (44.0–58.1)	83.0 (80.9–84.4)	4.01 (3.08–5.22)	0.81 (0.76–0.85)
Manning criteria (3 criteria)	13.7 (10.6–17.6)	97.1 (96.1–97.8)	54.1 (45.3–64.6)	81.6 (79.6–83.1)	4.66 (3.18–6.82)	0.89 (0.85–0.93)

[a]Excluding individuals reporting lower gastrointestinal alarm symptoms from the definition of irritable bowel syndrome.

Source: Adapted from AC Ford et al: Gastroenterology 145:1262, 2013.