Irritable Bowel Syndrome

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BRISTOL STOOL FORM SCALE

Type 1	
Type 2	
Type 3	
Type 4	
Type 5	
Type 6	
Type 7	Entirely Liquid

Type	Description
1	Separate hard lumps like nuts (difficult to pass)
2	Sausage shaped but lumpy
3	Like a sausage but with cracks on its surface
4	Like a sausage or snake, smooth and soft
5	Soft blobs with clear-cut edges (passed easily)
6	Fluffy pieces with ragged edges, a mushy stool
7	Watery, no solid pieces, ENTIRELY LIQUID

"My bowels boiled, and rested not: the days of affliction prevented me."
-Job 30:27

This is to acknowledge that Lyman E. Bilhartz, MD has disclosed no financial interests of other relationships with commercial concerns directly or indirectly related to this program. Dr. Bilhartz will be discussing off-label uses in his presentation.

Biographical Information:

Education and Training:
A native Dallasite, Dr. Bilhartz studied engineering at the University of Texas at Austin and received his MD degree from the University of Texas Southwestern Medical Center at Dallas in 1978. He completed his residency in internal medicine at the University of California, San Francisco in 1981 and remained there for a year as chief resident before returning to UT Southwestern as a fellow in gastroenterology in 1982. He was certified by the American Board of Internal Medicine in 1981 and in the subspeciality of gastroenterology in 1983. He has been a member of the faculty at UT Southwestern since 1986 where he serves as a Professor in the Department of Internal Medicine, Division of Digestive and Liver Diseases.

Clinical Interests:
Dr. Bilhartz is a full-time consulting gastroenterologist with a special interest in seeing patients with inflammatory bowel diseases (including ulcerative colitis and Crohn's disease) as well as patients with esophageal disorders and those with risk factors for colon cancer.

Cover illustration of the Bristol Stool Form Scale is from: O'Donnell LJD, Virjee J, Heaton KW. Detection of pseudodiarrhea by simple clinical assessment of intestinal transit rate. British Medical Journal 1990;300:439.

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INTRODUCTION

Irritable bowel syndrome (IBS) is the most common diagnosis made by gastroenterologists in the USA, accounting for approximately a quarter of all visits to digestive disease specialists. Even for primary care providers, IBS accounts for twelve per cent of visits, making the syndrome about as common as the common cold. Altogether, between 2.4-3.5 million patients visits per year in the USA are related to symptoms caused by the irritable bowel syndrome. The expense of managing this disorder is an estimated $8 billion in direct costs and an estimated $25 billion in indirect costs annually in the USA.

EPIDEMIOLOGY

Approximately 15% of adults in the USA report symptoms consistent with irritable bowel syndrome. The prevalence appears similar in whites and blacks but may be lower in Hispanics. Women appear to be affected three times more commonly than men, but this may reflect either a true difference in incidence or the fact that women seek medical care more frequently than men. Interestingly, the female predominance observed in the USA is not seen in other countries; for example, in India, men are three times more likely than women to report symptoms of IBS.

As a group, patients with IBS are at increased risk for other non-gastrointestinal functional disorders (eg. fibromyalgia) and miss three times as many work days than those without the disease. These persons are more likely to have behavioral and psychiatric problems than those who don't seek care.

An important aspect of these prevalence figures is that only 25% of individuals who meet the criteria for having IBS actually seek medical care. In other words, the vast majority of affected individuals never become "patients" per se; rather, they accept the symptoms as part of the aches and pains of daily living. Hence, as will be discussed, the goal of the physician is to turn "patients complaining of IBS symptoms" into individuals who chronically self-manage their IBS.

PATHOPHYSIOLOGY

Various factors have been proposed as contributing to the development of irritable bowel syndrome. Currently, no single conceptual model can explain all cases of the syndrome, but the following provides a summary of the major factors thought to be implicated in the pathogenesis.

Altered bowel motility

Alterations in contractility of the colon and small bowel have been noted in patients with irritable bowel syndrome. Physical or psychological stress and ingestion of

food may alter contractility of the colon. During fasting, the loss of the migrating motor complex has been observed in IBS patients, along with both discrete clustered contractions and prolonged propagated contractions. Pain is more frequently associated with irregular motor activity of the small bowel in patients with irritable bowel syndrome than in control subjects.

Visceral hypersensitivity

In balloon-distention studies, patients with irritable bowel syndrome experience pain and bloating at balloon volumes and pressures that are significantly lower than those that produce pain in control subjects. This observation, which has been confirmed over and over, is the single most consistent, objectively verifiable noted in IBS sufferers.

It has been postulated that sensitivity of visceral receptors is altered through recruitment of silent nociceptors in response to ischemia, distension, intraluminal contents, infection or psychiatric factors. A primary central defect of visceral pain processing has also been suggested but remains controversial. Increased excitability of the neurons in the dorsal horn of the spinal cord is postulated. There may be differences in the manner the brain modulates afferent signals from the dorsal horn neurons through the ascending pathways.

Functional MRI and positron emission tomography studies show different levels of activation in the thalamus and the anterior cingulate cortex after balloon distention of the rectum in patients with irritable bowel syndrome compared with controls. It may be that "hypervigilance" rather the true visceral hypersensitivity may be responsible for the lower pain threshold in patients with IBS.

Psychosocial factors

Stress can alter motor function in both the small and large bowel. Up to 60% of patients with irritable bowel syndrome have psychiatric symptoms such as somatization, depression and anxiety. A history of sexual and/or physical abuse in childhood predicts an increase in the severity of symptoms as an adult, but the majority of patients with IBS have no history of abuse. Exploration of this subject with the patient requires care and tact, lest the crucial physician-patient relationship be undermined.

Neurotransmitter imbalance

Various neurotransmitters including serotonin have been implicated in the pathogenesis of irritable bowel syndrome. Bear in mind that 95% of serotonin in the body is located in the GI tract, but the role(s) it plays in the regulation of gastrointestinal function is poorly understood. When serotonin is released by enterochromaffin cells, it stimulates extrinsic vagal and intrinsic enteric afferent nerve fibers resulting in intestinal secretion, peristalsis and symptoms such as nausea, vomiting, abdominal pain and bloating. There is some data to indicate that patients with irritable bowel syndrome have increased serotonin levels in plasma and the rectosigmoid colon. However, it is difficult to mechanistically explain constipation in terms of high levels of serotonin.

Infection and inflammation

There is convincing evidence that inflammation of the enteric mucosa or neural plexuses initiates or contributes to the symptoms of irritable bowel syndrome. Peripheral sensitization or hypermotility may be activated by mucosal inflammatory cytokines brought on by an acute infection in early life. A provacative theory (proposed by Gwee et al) holds that an acute infectious enteritis, occurring in a patient already afflicted by hypochondriasis or stressful life events may trigger subsequent decades of irritable bowel syndrome. To date, no single conceptual model explains all cases of the syndrome.

Hormonal influences

Hormonal influences may be important in the course of disease expression. Half of women with irritable bowel syndrome experience an increase in symptoms during the perimenstrual period.

CLINICAL PRESENTATION

Chronic abdominal pain and altered bowel habits remain the primary characteristics of the irritable bowel syndrome. The following summarizes the main clinical features of the disease:

Chronic abdominal pain

The pain is generally described as "crampy" in nature and variable in intensity. Perhaps because the words "irritable bowel" imply a minor affliction, patients with severe pain often cannot accept the diagnosis of irritable bowel syndrome since their pain is so severe. They should be reassured (or perhaps warned is a better choice) that severe, even excruciating pain is frequently seen in IBS.

The location and character of the pain can vary, but it is usually located on left side of lower abdomen. The severity ranges from mild to severe and debilitating and often is exacerbated by factors such as emotional stress or eating. Defecation often provides some relief.

Altered bowel habits

Patients may complain of any one of the following:

- diarrhea
- constipation
- alternating diarrhea and constipation
- normal bowel habits alternating with diarrhea and/or constipation

Bowel movements are often preceded by extreme urgency and may be followed by the sensation of incomplete evacuation. About 50% of patients complain of mucus discharge with stools.

Other gastrointestinal symptoms

Patients with IBS also report other GI symptoms. Gastroesophageal reflux

(GERD), early satiety, intermittent dyspepsia, nausea and non-cardiac chest pain are common. Abdominal bloating, flatulence or belching are also frequently reported.

Extraintestinal symptoms

Impaired sexual function, dysmenorrhea, dyspareunia, increased urinary frequency and urgency are symptoms that may be reported. Patients with irritable bowel syndrome are also more likely to have associated hypertension, reactive airway disease and rheumatologic syndromes (eg. fibromyalgia)

Alarm features (NOT present in IBS)

The following symptoms suggest organic disease rather than irritable bowel syndrome and warrant a more thorough evaluation:

- abdominal pain not associated with changes in bowel habit
- anemia
- family history of GI cancer (in a first degree relative, especially if age at diagnosis was less than 60 years)
- fever
- initial onset in patients aged >50 years
- occult blood in stool
- rectal bleeding
- steatorrhea
- sudden onset
- symptoms wake patient from sleep
- weight loss

Physical examination

A completely normal physical exam is the most common finding. Localized tenderness in the left lower quadrant is sometimes present and diffuse rectal tenderness or an inappropriate level of discomfort on a digital rectal exam may be present as well. Ascites, an abdominal mass or occult blood in the stool would qualify as an alarm feature and would warrant further investigation.

DIAGNOSIS

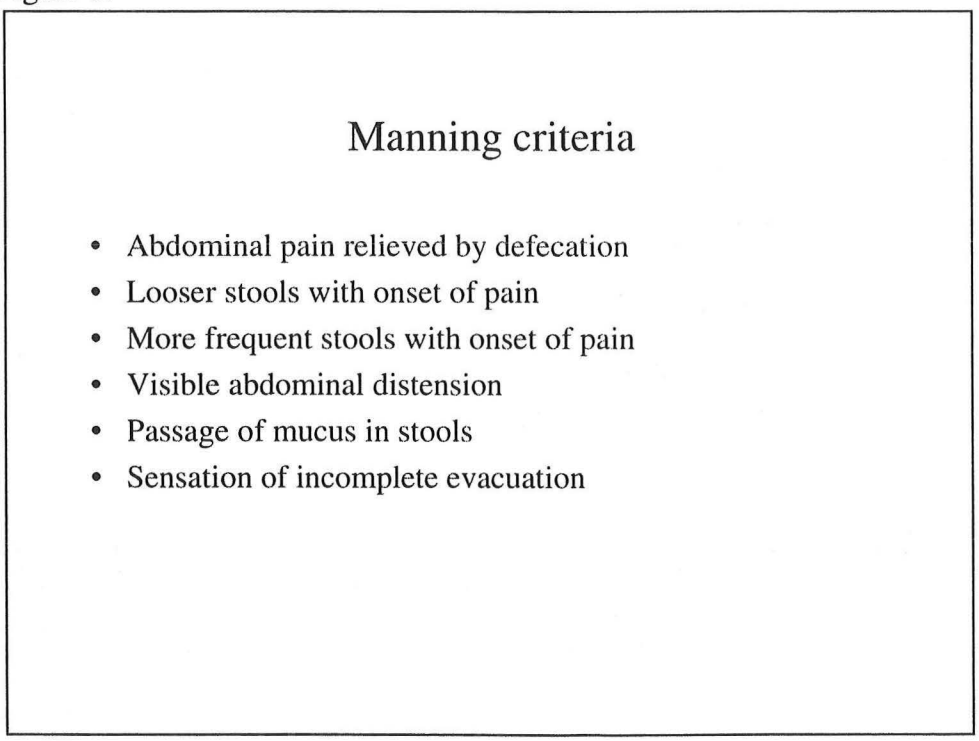
A major advance in the field of IBS investigation has been the promulgation over the past decade of diagnostic criteria which allow for a more systematic and objective means of identifying patients with the disorder. The value to clinical investigators of uniform diagnostic criteria is obvious- ascertainment bias is reduced and studies by different investigators can be better compared. A somewhat unexpected bonus to the use of diagnostic criteria has been the remarkable acceptance by patients of a "positive diagnosis" of IBS, based on having a certain number of universally recognized symptoms.

There are two fundamentally different ways to think of IBS: as a diagnosis of exclusion (meaning all *real causes* of the symptoms have been *excluded*), or, as a syndrome *defined by the presence* of specific symptoms. The former approach leads to over-testing, wasted resources, and a frustrated patient who would prefer to know what

she has, rather than a lengthy list of diseases she doesn't have. The latter approach is simpler, saves money, and allows the physician to rapidly make a positive diagnosis and to proceed directly to patient education and treatment. The risk, of course, to making a quick diagnosis of IBS based on the initial history and physical exam is that an organic disease could be overlooked and its diagnosis delayed. However, the incorporation of screening for "alarm features" goes a long way to excluding organic causes of the symptoms.

In 1978, Manning et al, using questionnaire data from 32 patients with presumed IBS and 33 patients with organic diseases of the gastrointestinal tract found that four symptoms were statistically more frequent in those with IBS. These symptoms are listed as the first four Manning criteria in Figure 1. The last two symptoms (mucous in the stools and a sensation of incomplete evacuation) were not significantly more frequent in IBS, but when added to the list, increased the discriminatory power of the criteria. Three Manning criteria should be present for the diagnosis of IBS, and the greater the number of criteria present, the greater the level of confidence there is in the diagnosis.

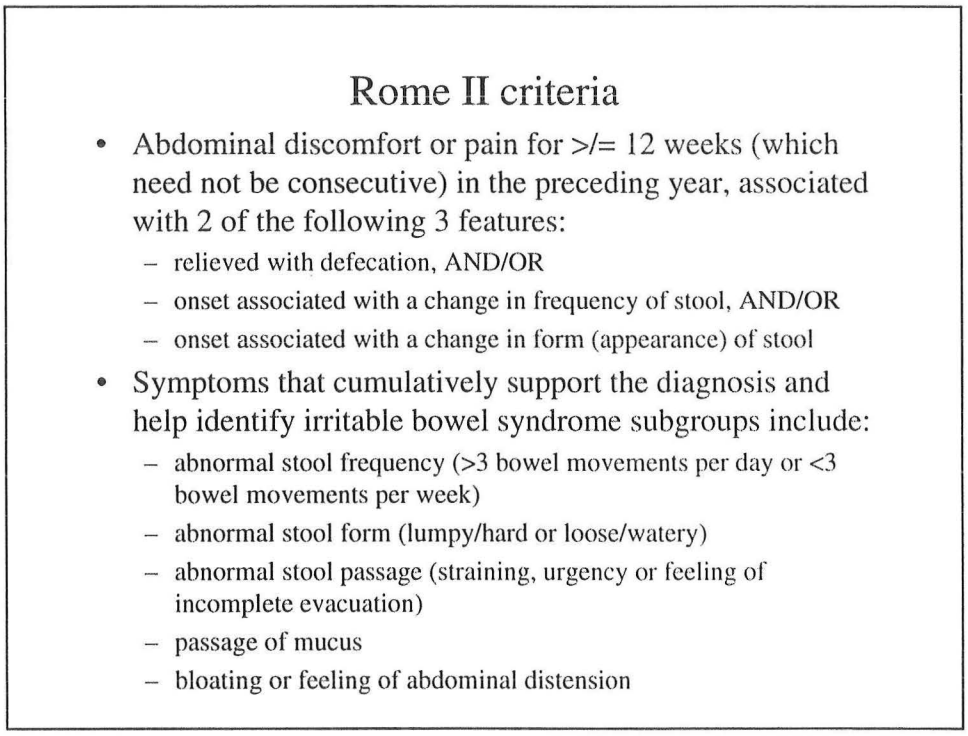
Figure 1.



Rome II criteria

In 1994, an international group of experts on the functional gastrointestinal disorders met (for the second time) in Rome and agreed upon a new set of diagnostic criteria for IBS, further refining the Manning criteria. The Rome II Criteria, as they have come to be known, are shown in Figure 2 and should always be accompanied by an asterisk explaining that the criteria apply "In the absence of structural or metabolic abnormalities to explain the symptoms".

Figure 2. *



Differential diagnosis

Despite the emphasis placed on making an early, positive diagnosis of the irritable bowel syndrome on the basis of fitting diagnostic criteria, it would be reckless to ignore the differential diagnosis of other potentially serious conditions that may present, at least in their early stages, with a similar clinical presentation. In most cases, the chronicity of the IBS symptoms, along with the absence of alarm features, makes most of the following diagnoses unlikely:

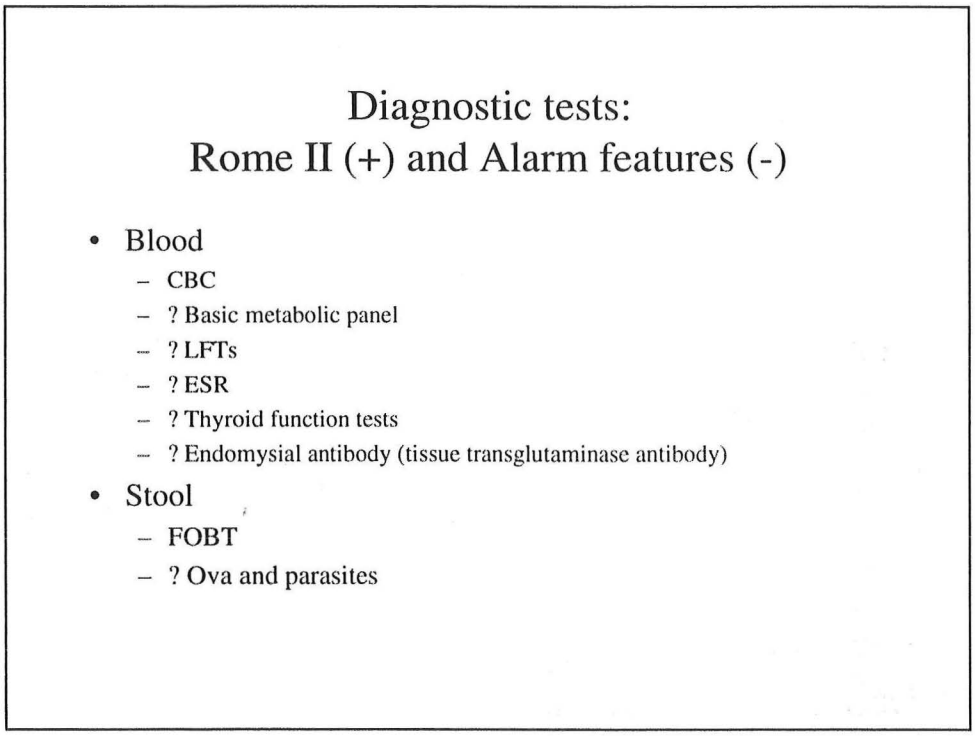
- Bowel obstruction
- Colon cancer
- Diverticulitis
- Endometriosis
- Enteric infection
- Inflammatory bowel disease
  - Ulcerative colitis
  - Crohn's disease

- Ischemic bowel
- Lactase deficiency
- Maldigestion or malabsorption

Diagnostic testing: Routine

For younger patients who meet the criteria for IBS, and who have no alarm features, a modest laboratory screening panel is proposed in Figure 3.

Figure 3.



A complete blood count (CBC) and a stool examination for occult blood should be performed in all cases. The liver and thyroid function tests may be helpful if there is any suspicion that a liver disorder is present or that the symptoms may be due to hyperthyroidism or hypothyroidism. If diarrhea is the predominant symptom, then a negative serology for the endomysial antibody makes celiac sprue unlikely and a negative stool examination for parasites makes an infectious enterocolitis unlikely.

Diagnostic testing: Symptom directed

In patients whose symptoms raise concern that an organic disease might be present, selected use of one of the following imaging studies may be helpful in excluding the disease and reassuring the patient:

- Plain abdominal films- to exclude bowel obstruction, evaluate subjective distension

- Sigmoidoscopy- to exclude colitis in diarrhea predominant IBS
- Colonoscopy- to exclude IBD and colon cancer (in older patients or those at high risk on the basis of a strong family history of colon cancer)
- Barium enema- to diagnosis severe diverticulosis, exclude colon cancer
- Small bowel series- to exclude small bowel tumors (eg. carcinoid) or Crohn's disease
- Sonography- to evaluate the biliary tract, liver and kidneys
- Abdominal CT- to evaluate the pancreas and exclude abscesses
- Diagnostic laparoscopy- to exclude endometriosis
- Lactose hydrogen breath test, Pb levels, porphyria screen...

It should be emphasized that none of these test should be considered routine (with the possible exception of a sigmoidoscopy in a patient with diarrhea predominant IBS) and that the profligate overuse of imaging studies is the major criticism of the expensive way IBS is frequently (mis)managed.

TREATMENT

A trusting physician-patient relationship is important in all aspects of medicine, but it is particularly important in managing patients with irritable bowel syndrome. IBS is a disorder with an extraordinarily high placebo response. No matter what you recommend for treatment, between 30 and 88% of your IBS patients will report improvement. Your job as a physician is to be at the high end of this placebo response and the means to achieve that goal is to have a *therapeutic* relationship with your patient.

Establish a Therapeutic Relationship

In order to establish a therapeutic relationship, the physician should:

- determine patient's understanding of the illness
- provide a comprehensive explanation of the disorder
- identify and respond to patient's concerns and expectations
- set realistic and consistent limits
- involve patient in their treatment
- establish a long-term relationship with primary care providers.

With each office visit (and you are kidding yourself if you think that IBS can be managed in a single visit), you should try and ascertain the often unstated reason for the patients visit. Ask the patient about:

- new exacerbating factors (eg. dietary change, adverse effects of new medication)
- personal concern about a serious disease
- environmental stressors (eg. major loss, abuse)
- psychiatric comorbidity (eg. depression, anxiety)
- impairment in daily function
- a hidden agenda (eg. narcotic or laxative abuse).

Patient Education

After informing the patient that, on the basis of having met the criteria, a positive diagnosis of IBS is confirmed, the following physiology lecture, supplemented by visual aids and embellished as needed, may prove helpful:

> "The intestine overreacts to a variety of stimuli such as food, hormonal changes, medication and stress."
>
> "These stimuli can produce spasm or stretching of the gut, enhanced sensitivity of nerves, or both."
>
> "This is experienced as pain, diarrhea, constipation, bloating or any combination anywhere in the abdomen."
>
> "The symptoms wax and wane, and though they may be severe, they usually gradually fade away over the years."
>
> "IBS has no association with colon cancer, colitis or any other serious condition, and will not shorten your life at all."
>
> "Let me know if you have problems, I'll work you in for a quick visit if needed, otherwise, I'd like to see you back in six weeks to see how things are going."

Dietary modifications

Generally, the type of food does not contribute to symptoms, however certain dietary substances may aggravate symptoms in some patients. These include:

- fatty foods
- beans and other gas-producing foods
- alcohol
- caffeine
- lactose (in lactase deficient individuals)
- sorbitol and fructose.

In some cases a food and symptom diary may help in identifying an aggravating item, but be prepared for the occasional obsessive patient to record and catalog every passage of flatus.

The value of a high-fiber diet or fiber supplementation is controversial. Fiber may ease symptoms in patients with predominantly constipation, but some patients experience worsening of symptoms, especially abdominal distention, bloating and flatulence. Despite the conventional wisdom that IBS can be treated with fiber supplementation, further evaluation of its efficacy is needed before definitive recommendations can be made.

Calcium polycarbophil (Equalactin™) is a synthetic, hydrophilic gel forming fiber that has the advantage of not being fermented by colonic flora. Like psyllium and

other natural fibers, it forms a semisolid gel in the gut lumen and increases the water content of the stool (thus tending to regularize stool consistency and alleviate alternating constipation and diarrhea), but it does not produce as much colonic gas.

Pharmacologic Therapy: Abdominal pain and bloating

- Consider an antispasmodic agent, particularly in patients whose symptoms are exacerbated by meals
- Anticholinergic drugs are the most frequently used (eg. oral dicyclomine or oral/sublingual hyoscyamine) although efficacy data is limited
- Consider a tricyclic antidepressant or selective serotonin reuptake inhibitor antidepressant particularly when pain is severe or frequent

Pharmacologic Therapy: Constipation

- Increased dietary fiber (25 g/day) is advocated for simple constipation although efficacy data is inconclusive
- Can also be treated with an osmotic laxative (eg. lactulose, milk of magnesia, polyethylene glycol solution)

Pharmacologic Therapy: Diarrhea

- Antidiarrheal agents (eg. loperamide) can reduce loose stools, urgency and fecal soiling
- Consider low dose tricyclic antidepressant when other measures are unsuccessful
- Consider cholestyramine in patients who have had a cholecystectomy or who may have idiopathic bile acid malabsorption.

Psychotherapy

- Psychological treatments seem to be effective in reducing:
  - anxiety and other psychological symptoms
  - abdominal pain and diarrhea (but not constipation).

- Positive response is more likely in patients who:
  - relate exacerbations of bowel symptoms to stressors
  - have more typical symptoms of irritable bowel syndrome rather than chronic pain
  - are aged <50 years
  - have lower levels of anxiety.

New Drugs

- Ondansetron
  - A 5-HT3 receptor antagonist that has produced improvement in overall status

and stool consistency in patients with predominant diarrhea but no improvement in abdominal pain and diarrhea

- Alosetron
  - A 5-HT3 receptor antagonist (withdrawn by the FDA) which was shown to reduce visceral sensitivity to rectal distension in women with diarrhea as the main symptom
- Tegaserod
  - A 5-HT4 agonist (recently approved by the FDA) which was shown to reduce visceral sensitivity to rectal distension in women with constipation as the main symptom

Experimental Drugs

- Selective GI calcium channel blockers (eg. pinaverium bromide and octylonium)
  - May reduce exaggerated motor responses

- Loxiglumide
  - A cholecystokinin A receptor antagonist which may be effective in patients with constipation
- Fedotozine
  - A kappa-opioid agonist that has shown promise as a visceral antinociceptive agent
  - Other kappa-opioid agonists are being developed

SUMMARY OF TREATMENT

1. Diagnosis is based on:
   - identification of positive symptoms consistent with the condition
   - use of symptom-based diagnostic criteria (eg Rome II and Manning criteria)
   - judicious use of diagnostic tests to exclude organic disorders.

2. Treatment is determined by nature and severity of symptoms and impact of the disease on the patient's lifestyle. It is important to:

   - establish an effective therapeutic relationship
   - provide sufficient patient education and reassurance
   - provide advice regarding dietary and lifestyle modification.

3. Direct pharmacologic therapy at the predominant symptoms.

4. Consider psychological treatments in selected patients.

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