

World Gastroenterology Organisation Global Guideline

# Irritable bowel syndrome: a global perspective

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## 1 Introduction

**Definition.** Irritable bowel syndrome (IBS) is a functional bowel disorder in which abdominal pain or discomfort is associated with defecation or a change in bowel habit. Bloating, distension, and disordered defecation are commonly associated features. (In some languages, the words “bloating” and “distension” may be represented by the same term.)

Irritable bowel syndrome is a relapsing functional bowel disorder defined by symptom-based diagnostic criteria, in the absence of detectable organic causes. The symptomatic array is not specific for IBS, as such symptoms may be experienced occasionally by almost every individual. To distinguish IBS from transient gut symptoms, experts have underscored the chronic and relapsing nature of IBS and have proposed diagnostic criteria based on the occurrence rate of symptoms (see the section on diagnosis below).

Some characteristics of IBS are:

- It is not known to be associated with an increased risk for the development of cancer or inflammatory bowel disease, or with increased mortality.
- It generates significant direct and indirect health-care costs.
- No pathophysiological substrate has been demonstrated in IBS.
- A transition of IBS to, and overlap with, other symptomatic gastrointestinal disorders (e.g., gastroesophageal reflux disease, dyspepsia, and functional constipation) may occur.
- The condition usually causes long-term symptoms:
  - May occur in episodes.
  - Symptoms vary and may be meal-related.
  - Symptoms interfere with daily life and social functioning in many patients.
  - Symptoms sometimes seem to develop as a consequence of a severe intestinal infection or to be precipitated by major life events, or in a period of considerable stress.

In general, there is a lack of recognition of the condition; many patients with IBS symptoms do not consult a physician and are not formally diagnosed. IBS generates significant direct and indirect health-care costs.

### IBS subclassification

According to the Rome III criteria, and on the basis of the patient’s stool characteristics:

- IBS with diarrhea (IBS-D):
  - Loose stools > 25% of the time and hard stools < 25% of the time
  - Up to one-third of cases
  - More common in men
- IBS with constipation (IBS-C):
  - Hard stools > 25% of the time and loose stools < 25% of the time
  - Up to one-third of cases
  - More common in women

- IBS with mixed bowel habits or cyclic pattern (IBS-M):
  - Both hard and soft stools > 25% of the time
  - One-third to one-half of cases

It must be remembered, however, that:

- Patients commonly transition between these subgroups.
- The symptoms of diarrhea and constipation are commonly misinterpreted in IBS patients. Thus, many IBS patients who complain of “diarrhea” are referring to the frequent passage of formed stools and, in the same patient population, “constipation” may refer to any one of a variety of complaints associated with the attempted act of defecation and not simply to infrequent bowel movements.

On clinical grounds, other subclassifications can be used:

- Based on symptoms:
  - IBS with predominant bowel dysfunction
  - IBS with predominant pain
  - IBS with predominant bloating
- Based on precipitating factors:
  - Post-infectious (PI-IBS)
  - Food-induced (meal-induced)
  - Stress-related

However, with the exception of PI-IBS, which is quite well characterized, the relevance of any of these classifications to the prognosis or response to therapy remains to be defined.

It must also be remembered that the Rome III criteria are not commonly used in clinical practice. Furthermore, cultural issues may inform symptom reporting. In India, for example, a patient who reports straining or passing hard stools is likely to complain of constipation even if he or she passes stools more than once daily.

### Global prevalence and incidence

The global picture of IBS prevalence is far from complete (Fig. 1), with no data available from several regions. In addition, comparisons of data from different regions are often problematic due to the use of different diagnostic criteria (in general, the “looser” the criteria, the higher the prevalence), as well as the influence of other factors such as population selection, inclusion or exclusion of comorbid disorders (e.g., anxiety), access to health care, and cultural influences. In Mexico, for example, the prevalence of IBS in the community using the Rome II criteria was 16%, but the figure increased to 35% among hospital patients using the same criteria. What is remarkable is that the available data suggest the prevalence is quite similar across many countries, despite substantial lifestyle differences.

- The prevalence of IBS in Europe and North America is estimated to be 10–15%. In Sweden, the most commonly cited figure is 13.5%.
- The prevalence of IBS is increasing in countries in the Asia–Pacific region, particularly in countries with developing economies. Estimates of the prevalence of IBS (using the Rome II diagnostic criteria) vary widely in the Asia–Pacific region. Studies from India show that the Rome I criteria for IBS identify more patients than the Rome II criteria. Reported prevalences include 0.82% in

Beijing, 5.7% in southern China, 6.6% in Hong Kong, 8.6% in Singapore, 14% in Pakistan, and 22.1% in Taiwan. A study in China found that the prevalence of IBS as defined by the Rome III criteria in outpatient clinics was 15.9%.

- Generally, data from South America are scarce; in Uruguay, for example, there is only one study, and the overall prevalence was 10.9% (14.8% in women and 5.4% in men); 58% with IBS-C and 17% with IBS-D. In 72% of the cases, the age of onset was < 45 years.
- Data from Africa are even more scanty. A study in a Nigerian student population based on the Rome II criteria found a 26.1% prevalence. A study among outpatients in the same country, based on the same criteria, reported a 33% prevalence.

### Other observations on IBS epidemiology

- IBS mainly occurs between the ages of 15 and 65.
- The first presentation of patients to a physician is usually in the 30–50-year-old age group.
- In some cases, symptoms may date back to childhood.
- The prevalence is greater in women—although this result is not reproduced in India, for example.
- There is a decrease in reporting frequency among older individuals.
- The estimated prevalence of IBS in children is similar to that in adults.
- Typical IBS symptoms are common in “healthy” population samples.

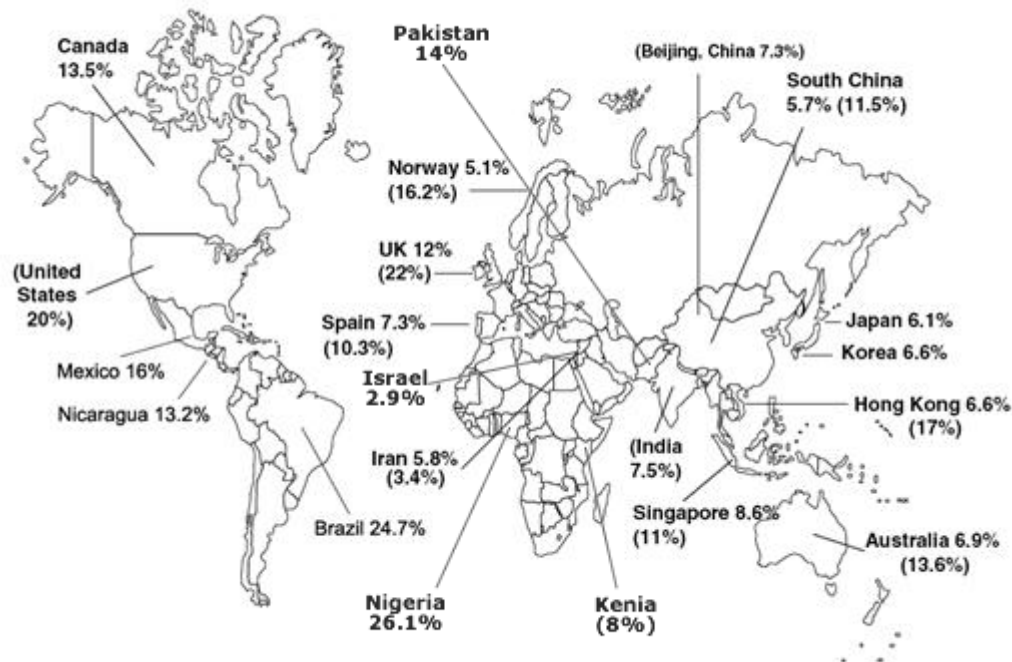


Fig. 1 World map of IBS prevalence (2000–2004) based on the Rome II and III criteria, with figures for the Manning criteria in brackets where available. Adapted from *Neurogastroenterol Motil* 2005;17:317–24.

## IBS demographics and different presenting features between East and West

- As in the case of prevalence data, global information on presenting features also varies and comparisons of studies based on community data, outpatient clinic data, and hospital statistics are fraught with difficulties.
- Typical IBS symptoms are common in healthy population samples, but the majority of sufferers with IBS are not actually medically diagnosed. This may explain apparent differences between countries in the reported prevalence. Most studies only count diagnosed IBS and not community prevalence.
- A study in China showed that the prevalence of IBS in south China was higher than that reported in Beijing, but lower than that reported in Western countries.
- Some studies in non-Western countries indicate:
  - A lack of female predominance (possibly due to differences in access and health care-seeking behaviors). In south China, for example, the male-to-female ratio is only 1 : 1.25 (in comparison with 1 : 2 in western Europe).
  - A close association between marked distress and IBS in men, in a manner similar to that found in women in Western studies.
  - Greater frequency of upper abdominal pain.
  - Lower impact of defecatory symptoms on a patient's daily life (not evident in China or Mexico).
- Several studies suggest that among Afro-Caribbean Americans, in comparison with white individuals:
  - The stool frequency is lower.
  - The prevalence of constipation is higher.
- In Latin America, constipation predominance is more frequent than diarrhea predominance.
- Stool frequency appears to be greater in the Indian community as a whole—99% passed stools once or more per day.
- In Mexico, 70% of patients have anxiety, 46% depression, and 40% both.
- In Mexico, IBS incurs a high economic impact due to a high use of medical resources.
- Clinical overlap between functional dyspepsia and IBS, defined according to the Rome III criteria, is very common in China.
- Psychological distress, life events, and negative coping style may play important roles in the pathogenesis of IBS. These factors may also influence the individual's illness behavior and clinical outcome.

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## 2 Diagnosis of IBS

### Clinical history

In assessing the patient with IBS, it is important not only to consider the primary presenting symptoms, but also to identify precipitating factors and other associated gastrointestinal and extragastrointestinal symptoms. It is vital also to seek and directly question for the presence of alarm symptoms. The history is critical and involves both the identification of those features regarded as typical of IBS and the recognition of “red flags” that suggest alternative diagnoses. Accordingly, the patient should be asked about the following (features marked with an asterisk \* are compatible with IBS):

- The pattern of abdominal pain or discomfort:
  - Chronic duration\*
  - Type of pain: intermittent\* or continuous
  - Previous pain episodes\*
  - Location of pain. In some individuals, pain may be well-localized (to the lower quadrant of the abdomen, for example), while in others the pain location tends to move around
  - Relief with defecation or passing of flatus\*
  - Nocturnal pain is unusual and is considered a warning sign
- Other abdominal symptoms:
  - Bloating
  - Distension
  - Borborygmi
  - Flatulence

(N.B. Distension can be measured; bloating is a subjective feeling. As defined in English, bloating and distension may not share the same pathophysiology and should not be regarded as equivalent and interchangeable terms, although in other languages they may be represented by a single word. Nor does either necessarily imply that intestinal gas production is increased.)
- Nature of the associated bowel disturbance:
  - Constipation
  - Diarrhea
  - Alternation
- Abnormalities of defecation:
  - Diarrhea for >2 weeks (N.B. One should always strive to understand exactly what the patient means by “diarrhea” and “constipation”)
  - Mucus in the feces
  - Urgency of defecation
  - Feeling of incomplete defecation (this symptom has been reported as particularly important in recent studies in Asian populations—51% in Singapore, 71% in India, 54% Taiwan)

Other information from the patient's history and important warning signs:

- Unintended weight loss
- Blood in stool
- Family history of:
  - Colorectal malignancy
  - Celiac disease
  - Inflammatory bowel disease
- Fever accompanying lower abdominal pain
- Relation to menstruation
- Relation to:
  - Drug therapy
  - Consumption of foods (especially milk), artificial sweeteners, dieting products, or alcohol
  - Visiting the (sub-)tropics
- Abnormal eating habits
  - Irregular or inadequate meals
  - Insufficient fluid intake

- Excessive fiber intake
- Obsession with dietary hygiene
- Family history of IBS. IBS clearly aggregates within families, although its genetics are poorly understood
- Nature of onset (sudden onset in relation to exposure to gastroenteritis suggests PI-IBS)

### Psychological assessment

Psychological factors have not been shown to cause or influence the onset of IBS. IBS is not a psychiatric or psychological disorder. However, psychological factors may:

- Play a role in the persistence and perceived severity of abdominal symptoms
- Contribute to impairment in the quality of life and excessive use of health-care services

For these reasons, coexisting psychological conditions are common in referral centers and may include:

- Anxiety
- Depression
- Somatization
- Hypochondriasis
- Symptom-related fears

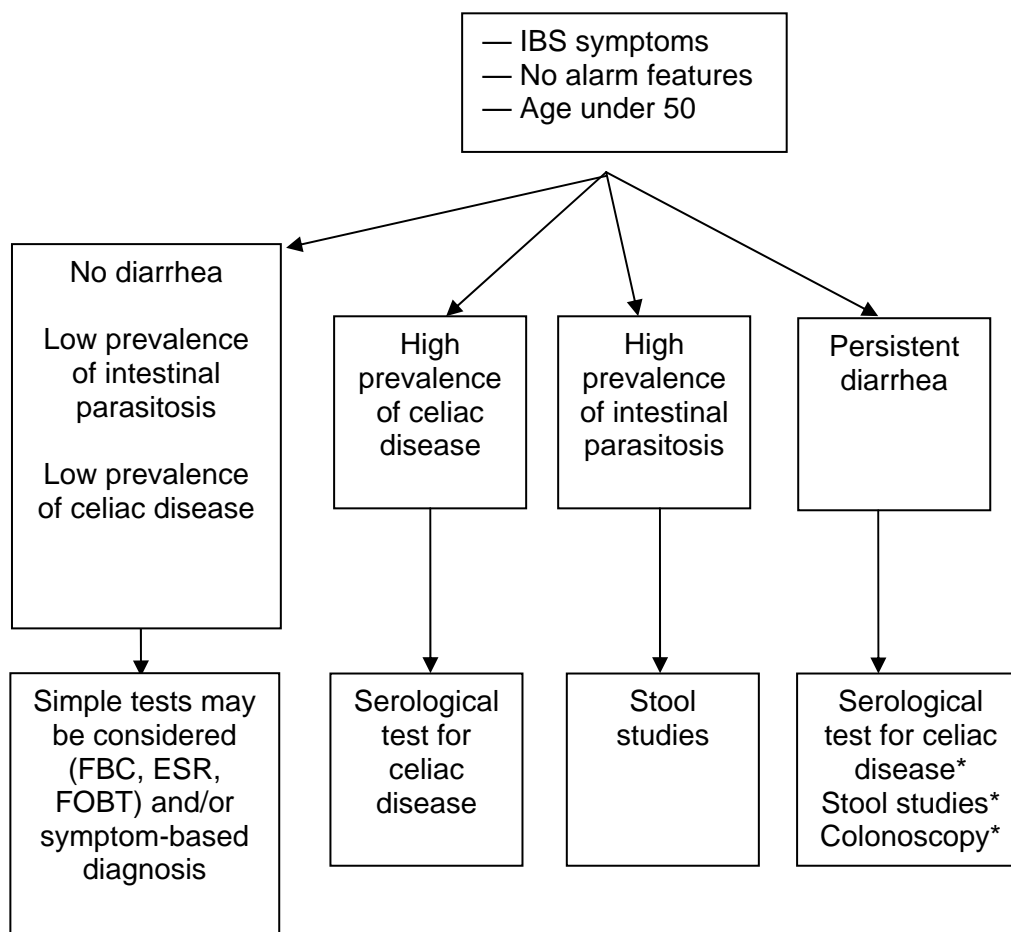
The following may be useful in providing an objective assessment of psychological features:

- Hospital Anxiety and Depression Scale (HADS). This is a simple 14-item questionnaire to measure the level of anxiety and depression.
- The Sense of Coherence (SOC) test can be used to identify patients with a low SOC who respond to cognitive behavioral therapy.
- The Patient Health Questionnaire (PHQ-15). This is a 15-item questionnaire that helps identify the presence of multiple somatic symptoms (somatization). The PHQ-15 should be validated in a given country before it is used in clinical practice in that location.

### Physical examination

- A physical examination reassures the patient and helps to detect possible organic causes.
- A general examination is carried out for signs of systemic disease.
- Abdominal examination:
  - Inspection
  - Auscultation
  - Palpation
- Examination of the perianal region:
  - Digital rectal examination

### IBS diagnostic algorithm



FBC, full blood count; FOBT, fecal occult blood test; ESR, erythrocyte sedimentation rate.

\* Where relevant—i.e., when there is a high prevalence of celiac disease, parasitosis, and inflammatory bowel disease or lymphocytic colitis, respectively.

### IBS diagnostic cascade

#### Level 1

- History, physical examination, exclusion of alarm symptoms, consideration of psychological factors
- Full blood count (FBC), erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP), stool studies (white blood cells, ova, parasites, occult blood)
- Thyroid function, tissue transglutaminase (TTG) antibody
- Colonoscopy and biopsy\*
- Fecal inflammation marker (e.g., calprotectin)

#### Level 2

- History, physical examination, exclusion of alarm symptoms, consideration of psychological factors
- FBC, ESR or CRP, stool studies, thyroid function
- Sigmoidoscopy\*



### Level 3

- History, physical examination, exclusion of alarm symptoms, consideration of psychological factors
- FBC, ESR, and stool examination

\* N.B. Even in “rich” countries, not all patients need colonoscopy—in particular, those with alarm symptoms and signs and those over the age of 50. The need for investigations and for sigmoidoscopy and colonoscopy, in particular, should also be dictated by the characteristics of the patient (presenting features, age, etc.) and the geographical location (i.e., whether or not in an area of high prevalence of inflammatory bowel disease, celiac disease, colon cancer, or parasitosis). One could argue, for example, that a 21-year-old woman with symptoms of IBS-D and no alarm features merits, at most, celiac serology (where appropriate).

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## 3 Evaluation of IBS

A diagnosis of IBS is usually suspected on the basis of the patient’s history and physical examination, without additional tests. Confirmation of the diagnosis of IBS requires the confident exclusion of organic disease in a manner dictated by an individual patient’s presenting features and characteristics. In many instances (e.g., in young patients with no alarm features), a secure diagnosis can be made on clinical grounds alone.

### Diagnostic criteria (Rome III)

- Onset of symptoms at least 6 months before diagnosis
- Recurrent abdominal pain or discomfort for > 3 days per month during the past 3 months
- At least two of the following features:
  - Improvement with defecation
  - Association with a change in frequency of stool
  - Association with a change in stool form

In clinical practice, whether in the setting of primary or specialist care, clinicians usually base a diagnosis of IBS on their evaluation of the whole patient (often over time) and consider a multiplicity of features that support the diagnosis (apart from pain and discomfort associated with defecation or change in stool frequency or form).

Symptoms common in IBS and supportive of the diagnosis:

- Bloating
- Abnormal stool form (hard and/or loose)
- Abnormal stool frequency (less than three times per week or over three times per day)
- Straining at defecation
- Urgency
- Feeling of incomplete evacuation
- The passage of mucus per rectum

Behavioral features helpful in recognizing IBS in general practice:

- Symptoms present for > 6 months
- Stress aggravates symptoms
- Frequent consultations for nongastrointestinal symptoms
- History of previous medically unexplained symptoms
- Aggravation after meals
- Associated anxiety and/or depression

Noncolonic complaints that often accompany IBS:

- Dyspepsia—reported in 42–87% of IBS patients
- Nausea
- Heartburn

Associated nongastrointestinal symptoms:

- Lethargy
- Backache and other muscle and joint pains
- Headache
- Urinary symptoms:
  - Nocturia
  - Frequency and urgency of micturition
  - Incomplete bladder emptying
- Dyspareunia, in women
- Insomnia
- Low tolerance to medication

### Additional tests or examinations

In the majority of cases of IBS, no additional tests or examinations are required. An effort to keep investigations to a minimum is recommended in straightforward cases of IBS, and especially in younger individuals.

- Consider additional tests or examinations if warning signs “red flags” are present:
  - Onset of symptoms after 50 years of age
  - Short history of symptoms
  - Unintended weight loss
  - Nocturnal symptoms
  - Family history of colon cancer, celiac disease, inflammatory bowel disease
  - Anemia
  - Rectal bleeding
  - Recent antibiotic use
  - Abdominal/rectal masses
  - Raised inflammatory markers
  - Fever
- Although commonly performed, full blood counts, serum biochemistry, thyroid function tests, and stool testing for occult blood and ova and parasites are indicated only if supported by clinical history and where locally relevant.
- Additional tests or examinations may also be considered if:
  - The patient has persistent symptoms or is anxious despite treatment.

— A major qualitative change in chronic symptoms has occurred. A new coexisting condition should be considered.

## Differential diagnosis

### *Celiac sprue/ gluten enteropathy*

Main symptoms and/or findings:

- Chronic diarrhea
- Failure to thrive (in children)
- Fatigue
- Estimated to affect  $\pm$  1% of all Indo-European populations
- To be considered in the differential diagnosis in regions of high prevalence

N.B.: Many patients with celiac disease do *not* have classical features and may present with “IBS-type” symptoms, including constipation. A low threshold for investigation should therefore be maintained in high-prevalence regions (those with a prevalence  $>$  1% in the general population).

### *Lactose intolerance*

Main symptoms and/or findings:

- Symptoms (bloating, flatulence, diarrhea) acutely related to consumption of dairy products
- Can be identified by a lactose breath hydrogen test, after a positive milk-drinking test

### *Inflammatory bowel disease (Crohn's disease, ulcerative colitis)*

Main symptoms and/or findings:

- Significant variations in prevalence worldwide
- Diarrhea has persisted for  $>$  2 weeks
- Rectal bleeding
- Inflammatory mass, weight loss, perianal disease, fever

### *Colorectal carcinoma*

Main symptoms and/or findings:

- Older patients who develop IBS-type symptoms for the first time
- Passage of blood in the feces
- Unintended weight loss
- Pain may be obstructive in type for left-sided lesions
- Anemia or iron deficiency for right-sided lesions

### *Lymphocytic and collagenous colitis*

- Accounts for 20% of unexplained diarrhea in patients over the age of 70
- Typically painless

- Most common in middle-aged females (M : F = 1 : 15)
- Diagnosed on colonic biopsies

### *Acute diarrhea due to protozoa or bacteria*

Main symptoms and/or findings:

- Acute onset of diarrhea
- Stool examination or duodenal biopsy

A recent review on the role of intestinal protozoa in IBS concluded that “A possible role exists for protozoan parasites, such as *Blastocystis hominis* and *Dientamoeba fragilis*, in the etiology of IBS. *Dientamoeba fragilis* is known to cause IBS-like symptoms and has a propensity to cause chronic infections, but its diagnosis relies on microscopy of stained smears, which many laboratories do not perform, thereby leading to the misdiagnosis of dientamebiasis as IBS. The role of *B. hominis* as an etiological agent of IBS is inconclusive, due to contradictory reports and the controversial nature of *B. hominis* as a human pathogen. Although *Entamoeba histolytica* infections occur predominantly in developing regions of the world, clinical diagnosis of amebiasis is often difficult because symptoms of patients with IBS may closely mimic those of patients with nondysenteric amebic colitis. Clinical manifestations of *Giardia intestinalis* infection also vary from asymptomatic carriage to acute and chronic diarrhea with abdominal pain.”

While stool testing for *Giardia* and *Amoeba* is recommended in India, self-medication with imidazoles is common, rendering the results difficult to interpret.

N.B.: It is essential that all patients with IBS in relevant areas undergo parasitological investigations, in order to rule out the presence of protozoan parasites as the causative agents of the clinical features.

### *Small-intestinal bacterial overgrowth (SIBO)*

- The classical features of SIBO are those of maldigestion and malabsorption.
- Some of the symptoms of SIBO (bloating, diarrhea) may overlap with those of IBS, which has led to the suggestion that SIBO is common in IBS.
- The bulk of evidence suggests that SIBO is *not* common in IBS.

### *Diverticulitis*

The relationship between IBS and so-called “painful diverticular disease” is unclear; is painful diverticular disease no more than IBS in a patient who has diverticula? In diverticulitis, the classical symptoms and/or findings are episodic and acute to subacute during an episode, featuring:

- Left-sided abdominal pain
- Fever
- Tender inflammatory mass in the left lower quadrant

However, it is now evident that afflicted patients may have more chronic symptoms in between discrete episodes/attacks.

### *Endometriosis*

Main symptoms and/or findings:

- Cyclical lower abdominal pain
- Enlarged ovaries or nodules dorsal to the cervix (on digital vaginal examination)

### *Pelvic inflammatory disease*

Main symptoms and/or findings:

- Nonacute lower abdominal pain
- Fever
- Upward pressure pain or adnexal tenderness and swollen adnexa (on digital vaginal examination)

### *Ovarian cancer*

In women over the age of 40, ovarian cancer should be considered in the differential diagnosis. In one survey, the following symptoms were more common among women with ovarian cancer:

- Increased abdominal size
- Bloating
- Urinary urgency
- Pelvic pain

The combination of bloating, increased abdominal size, and urinary symptoms was found in 43% of women with ovarian cancer but only 8% of a control population.

### **Comorbidity with other diseases**

Patients with overlap syndromes tend to have more severe IBS.

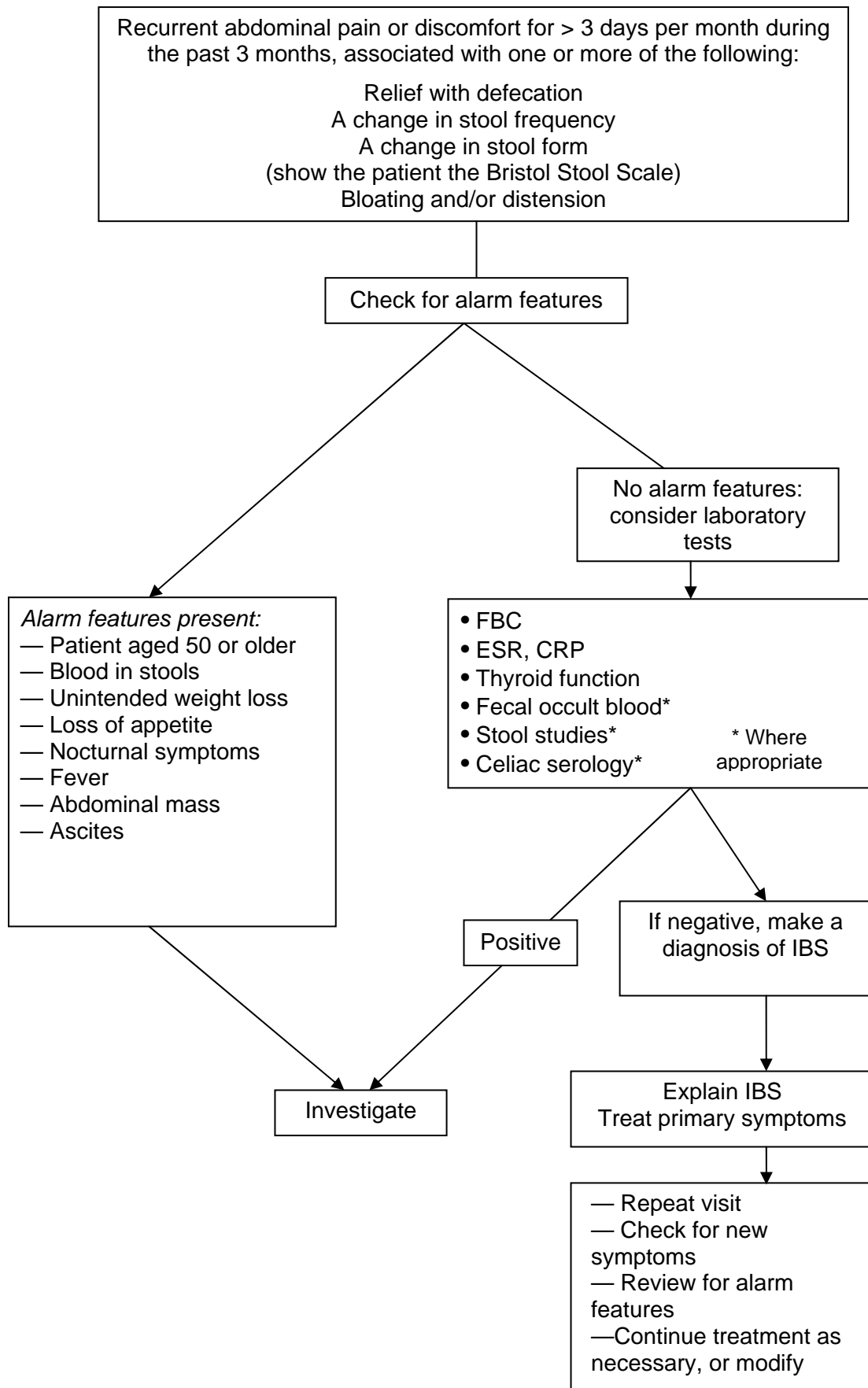
- Fibromyalgia—in 20–50% of IBS patients (although there is no evidence of this in China, for example)
- IBS is common in several other chronic pain disorders:
  - Present in 51% of patients with chronic fatigue syndrome
  - Temporomandibular joint disorder: 64%
  - Chronic pelvic pain: 50%
  - Nonulcer dyspepsia, biliary dyskinesia

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## **4 Management of IBS**

### **Introduction**

The following diagram provides a general outline of a management scheme for the patient presenting with IBS-type symptoms:



N.B.: With patient anxiety playing a key role, reassurance and education are of key importance.

Given that there is no general agreement on the cause of IBS, it comes as no surprise that no single treatment is currently regarded throughout the world as being universally applicable to the management of all IBS patients.

Given also the common association between IBS symptoms and such factors as diet, stress, and psychological factors, attention should be given to adopting measures that may alleviate, if not eliminate, such precipitants. Dietary differences between different countries and ethnic groups would be expected to have a significant influence on the prevalence of symptoms of IBS, but little information is available. The benefits, if any, of elimination diets remain to be confirmed.

Recent data on disturbances in the intestinal flora (microbiota) in IBS, as well as the suggestion mentioned above (a controversial one) that SIBO may be a factor, have spurred interest in novel approaches: probiotics, prebiotics and antibiotics. Recent meta-analyses confirm a role for probiotics in IBS, but also make it clear that the effects of probiotics in IBS, as elsewhere, are highly strain-specific. Variability and the formulation of specific strains vary dramatically around the world. For example, *Bifidobacterium infantis* 35624, which currently has the best evidence base for efficacy in IBS, is at present available only in the United States. Issues of quality control also continue to complicate recommendations in this area.

IBS patients commonly have recourse to a variety of alternative/complementary therapies throughout the world. In India (in Ayurvedic medicine) and China, for example, herbal remedies are widely available and commonly used for IBS. However, their efficacy is difficult to assess, as the concentration of active ingredients varies considerably depending on the extraction process. Few alternative therapies have been subjected to the rigors of a randomized trial in IBS.

Preliminary data on nonabsorbable antibiotics (for example,  $3 \times 400$  mg/day) are encouraging, but the trials so far have been too small for firm conclusions to be drawn.

A recent systematic review, although pointing to limitations in the trial designs in many instances, provides evidence to support the use of antidepressants (both tricyclics and selective serotonin reuptake inhibitors) in IBS. Nonpharmacological factors are often ignored, but are of paramount importance in the management of IBS. The physician–patient relationship is critical and should include attention to the following, both during the initial assessment and in the subsequent follow-up:

- Identifying and exploring the patient's concerns. A positive patient–physician relationship should be established, with the patient's symptoms and distress being accepted as real.
- Appreciating the impact of symptoms.
- Discussing the patient's anxieties related to symptoms and possible diagnoses, with the aim being to eliminate unnecessary worries.
- Identifying and helping resolve stressful factors.
- Reducing avoidance behavior. Patients may avoid activities that they fear are causing the symptoms, but avoidance behavior has a negative influence on the prognosis.
- General guidance on diet and activity: fiber-rich diets (where appropriate), regular mealtimes, the intake of sufficient fluids, and sufficient physical activity

may have (general) beneficial effects, but there is no adequate proof that these directly influence the outcome in IBS.

## Drug therapy

Throughout the world, a variety of agents are used for the treatment of individual symptoms in IBS, as follows:

- Antispasmodics for pain.
- Laxatives, fiber and bulking agents for constipation. The chloride-channel agonist lubiprostone ( $2 \times 24 \mu\text{g/day}$ ) has recently been approved by the Food and Drugs Administration (FDA) in the United States for chronic constipation and constipation-predominant IBS, but the exact role of such agents in the overall management of IBS remains to be established.
- Fiber, bulking agents and antidiarrheals for diarrhea.
- Charcoal resins, antifatulents, and other agents for bloating, distension, and flatulence.

It is important to note that the range of agents available and their formulations vary considerably between countries, and it is imperative that the prescribing physician be knowledgeable regarding the efficacy and risk profile of any agent that he or she is about to prescribe, rather than extrapolating from evidence derived from other agents in the same class or agents that have similar modes of action.

## Pain

- If an analgesic is required, paracetamol is preferred to nonsteroidal anti-inflammatory drugs (NSAIDs). Opiates are to be avoided at all costs, as dependence and addiction are a high risk in such a chronic condition. NSAIDs and opiates also have undesirable side effects on the gastrointestinal tract.
- The probiotic strain *Bifidobacterium infantis* 35624 (one capsule per day) has been shown to reduce pain, bloating, and defecatory difficulty and to normalize stool habit in IBS patients, regardless of predominant bowel habit, but is currently available only in the United States.
- Antispasmodics:
  - The availability of compounds varies tremendously throughout the world.
- Tricyclic antidepressants:
  - Amitriptyline, starting dose 10 mg/day, target dose 10–75 mg/day, at bedtime.
  - Desipramine, starting dose 10 mg/day, target dose 10–75 mg/day, at bedtime.These tend to be constipating and should be avoided among constipated patients.
- Selective serotonin reuptake inhibitors (SSRIs):
  - Paroxetine, 10–60 mg/day.
  - Citalopram, 5–20 mg/day.

## Constipation

- A fiber-rich diet or a bulk-former (e.g., psyllium) combined with sufficient intake of fluids would appear to be a logical approach in IBS, but the evidence base is not convincing and bloating and distension may be aggravated in some patients. One study in India looked at the fiber content in the diet of Indian patients with IBS and controls, and found that fiber supplementation was not required, as the



dietary content of fiber was equal to the recommended intake for patients with IBS.

- The probiotic strain *Bifidobacterium lactis* DN-173 010 has been shown to accelerate gastrointestinal transit and to increase stool frequency among IBS patients with constipation.
- Osmotic laxatives are often useful; few have been formally tested in IBS.
- Lubiprostone:
  - For the treatment of IBS with constipation in women aged 18 and over.
  - To be taken twice a day in 8- $\mu$ g doses with food and water.

### Diarrhea

- Loperamide (2 mg every morning or twice a day) is no more effective than a placebo in reducing pain, bloating, and global symptoms of IBS, but it is an effective agent for the treatment of diarrhea, reducing stool frequency and improving stool consistency.
- Alosetron, a 5-hydroxytryptamine-3 (5-HT<sub>3</sub>) receptor antagonist:
  - Indicated only for women with severe diarrhea-predominant IBS with symptoms > 6 months and no response to antidiarrheal agents.
  - May rarely cause ischemic colitis.

### Treatment of bloating and distension

- Diets that produce less gas may be helpful in some patients.
- There is no evidence to support the use of activated charcoal-containing products, “antiflatulents,” simethicone, and other agents in IBS.
- Probiotics: some specific strains, such as *Bifidobacterium lactis* DN-173 010 and the probiotic cocktail VSL#3, have clinical trial evidence of efficacy for bloating, distension, and flatulence. Others, such as *Bifidobacterium infantis* 35624, reduce bloating as well as the other cardinal symptoms of IBS.
- Antibiotic treatment with rifaximin 3  $\times$  400 mg/day has been shown to reduce bloating in some IBS patients.

### ACG Task Force on IBS recommendations

The American College of Gastroenterology (ACG) Task Force on IBS published an evidence-based systematic review on the management of IBS in January 2009 (*Am J Gastroenterol* 2009;104:S1–35). Its conclusions are summarized below.

*Antispasmodic agents, including peppermint oil.* Certain antispasmodics (hyoscine, cimetropium, pinaverium, and peppermint oil) may provide short-term relief of abdominal pain/discomfort in IBS. Evidence for long-term efficacy is not available. Evidence for safety and tolerability is limited.

*Dietary fiber, bulking agents, and laxatives.* Psyllium hydrophilic mucilloid (ispaghula husk) is moderately effective. A single study reported improvement with calcium polycarbophil. Wheat bran or corn bran is no more effective than placebo in relieving the global symptoms of IBS and cannot be recommended for routine use. Polyethylene glycol (PEG) laxative was shown to improve stool frequency, but not abdominal pain, in one small sequential study in adolescents with IBS-C.

*Antidiarrheals.* The antidiarrheal agent loperamide is no more effective than placebo in reducing pain, bloating, or global symptoms of IBS, but it is an effective agent for the treatment of diarrhea, reducing stool frequency and improving stool consistency. Randomized controlled trials comparing loperamide with other antidiarrheal agents have not been performed. Safety and tolerability data on loperamide are lacking.

*Antibiotics.* A short-term course of a nonabsorbable antibiotic is more effective than placebo for global improvement of IBS and for bloating. There are no data available to support the long-term safety and effectiveness of nonabsorbable antibiotics for the management of IBS symptoms.

*Probiotics.* In single-organism studies, lactobacilli do not appear effective for patients with IBS. Bifidobacteria and certain combinations of probiotics demonstrate some efficacy.

*5-HT<sub>3</sub>-receptor antagonists.* The 5-HT<sub>3</sub>-receptor antagonist alosetron is more effective than placebo in relieving global IBS symptoms in male and female IBS patients with diarrhea. Potentially serious side effects, including constipation and colon ischemia, occur more commonly in patients treated with alosetron in comparison with placebo. The balance of benefit and harm for alosetron is most favorable in women with severe IBS and diarrhea who have not responded to conventional therapies. The quality of evidence for the efficacy of 5-HT<sub>3</sub> antagonists in IBS is high.

*Selective C-2 chloride-channel activators.* Lubiprostone at a dosage of 8 µg twice daily is more effective than placebo in relieving global IBS symptoms in women with IBS-C.

*Antidepressant agents.* Tricyclic antidepressants (TCAs) and selective serotonin reuptake inhibitors (SSRIs) are more effective than placebo in relieving global IBS symptoms, and appear to reduce abdominal pain. There are limited data on the safety and tolerability of these agents in patients with IBS.

N.B.: The evidence base for many therapies commonly used in the management of IBS is weak, while for others it is nonexistent.

### Other treatments (including psychological)

General nonpharmacological recommendations:

- Discuss the patient's anxieties. This reduces complaints; aim to eliminate unnecessary worries.
- Aim to reduce avoidance behavior. Patients may avoid activities that they fear are causing the symptoms, but avoidance behavior has a negative influence on the prognosis.
- Discuss fear of cancer.
- Discuss and aim to resolve stressful factors.
- Regular mealtimes, the intake of sufficient fluids, and sufficient physical activity may have (general) beneficial effects, but there is no adequate proof that these influence IBS.

Apart from the general approaches described above to govern the conduct of the doctor–patient relationship in IBS, more formal psychological interventions may be

contemplated in certain circumstances and depending on the availability of appropriate resources and expertise. Such approaches may include:

- Cognitive/behavioral therapy, in group, or individual sessions
- Behavioral techniques aimed at modifying dysfunctional behaviors through:
  - Relaxation techniques
  - Contingency management (by rewarding healthy behavior)
  - Assertion training
- Hypnosis

The ACG Task Force concluded that psychological therapies, including cognitive therapy, dynamic psychotherapy, and hypnotherapy, but not relaxation therapy, are more effective than usual care in relieving global symptoms of IBS.

With regard to herbal therapies and acupuncture, the ACG Task Force concluded that the available randomized controlled trials, mostly testing unique Chinese herbal mixtures, appeared to show a benefit. It was not possible to combine these studies into a meaningful meta-analysis, however, and overall, any benefit of Chinese herbal therapy in IBS continues to be potentially confounded by the variable components used and their purity. Also, there are significant concerns about toxicity, especially liver failure, with the use of any Chinese herbal mixture. A systematic review of trials of acupuncture was inconclusive due to heterogeneous outcomes. Further research is needed before any recommendations on acupuncture or herbal therapy can be made.

## Prognosis

For most patients with IBS, symptoms are likely to persist, but not worsen. A smaller proportion will deteriorate, and some will recover completely. For example, a recent study found that while 18% of a random sample of 1021 people in the general (U.S.) population had IBS, 38% had no complaints 12–20 months later.

Factors that may negatively affect the prognosis include:

- Avoidance behavior related to IBS symptoms
- Anxiety about certain medical conditions
- Impaired function as a result of symptoms
- A long history of IBS symptoms
- Chronic ongoing life stress
- Psychiatric comorbidity

Approaches by the physician that positively affect the treatment outcome:

- Acknowledging the disease
- Educating the patient about IBS
- Reassuring the patient

## Follow-up

In mild cases, there is generally no medical need for follow-up consultations in the long term, unless:

- Symptoms persist, with considerable inconvenience or dysfunction.
- The patient is seriously worried about the condition.
- Diarrhea > 2 weeks.

- Constipation persists and does not respond to therapy.
- Warning signs for possibly serious gastrointestinal disease develop:
  - Rectal bleeding
  - Anemia
  - Unintended weight loss
  - Colon cancer in the family history
  - Fever
  - A major change in symptoms
- Beware of eating disorders developing:
  - Most patients with IBS try some form of dietary manipulation.
  - This can lead to nutritionally inadequate diets or ingestion of abnormal amounts of fruit, caffeine, dairy products, and dietary fiber.
  - The tendency to develop an eating disorder is more common in female IBS patients.

### IBS management cascade

#### Level 1

- Reassurance, dietary and lifestyle review, and counseling
- Try a quality probiotic with proven efficacy
- Symptomatic treatment of:
  - Pain with a locally available antispasmodic, for more severely affected patients add a low-dose tricyclic antidepressant or SSRI
  - Constipation with dietary measures and fiber supplementation progressing to osmotic laxatives or lactulose
  - Diarrhea with simple antidiarrheals
- Consider psychological approaches (hypnotherapy, psychotherapy, group therapy) and consultation with a dietitian, where indicated
- Add specific pharmacological agents, where approved:
  - Lubiprostone for C-IBS
  - Rifaximin for diarrhea and bloating
  - Alosetron for D-IBS

#### Level 2

- Reassurance, dietary and lifestyle review, and counseling
- Add a quality probiotic with proven efficacy
- Symptomatic treatment of:
  - Pain with a locally available antispasmodic, for more severely affected patients add a low-dose tricyclic antidepressant
  - Constipation with dietary measures and fiber supplementation
  - Diarrhea with bulking agents and simple antidiarrheals

#### Level 3

- Reassurance, dietary and lifestyle review, and counseling
- Symptomatic treatment of:
  - Pain with a locally available antispasmodic
  - Constipation with dietary measures and fiber supplementation
  - Diarrhea with bulking agents and simple antidiarrheals