Functional Bowel Disorders

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Employing a consensus approach, our working team critically considered the available evidence and multinational expert criticism, revised the Rome II diagnostic criteria for the functional bowel disorders, and updated diagnosis and treatment recommendations. Diagnosis of a functional bowel disorder (FBD) requires characteristic symptoms during the last 3 months and onset ≥6 months ago. Alarm symptoms suggest the possibility of structural disease, but do not necessarily negate a diagnosis of an FBD. Irritable bowel syndrome (IBS), functional bloating, functional constipation, and functional diarrhea are best identified by symptom-based approaches. Subtyping of IBS is controversial, and we suggest it be based on stool form, which can be aided by use of the Bristol Stool Form Scale. Diagnostic testing should be guided by the patient's age, primary symptom characteristics, and other clinical and laboratory features. Treatment of FBDs is based on an individualized evaluation, explanation, and reassurance. Alterations in diet, drug treatment aimed at predominant symptoms, and psychotherapy may be beneficial.

The functional bowel disorders (Table 1) are identified only by symptoms. Therefore, a symptom-based classification is necessary for clinical diagnosis, evidence-based management, and research. This 2006 working team is the fourth since 1989 to address the diagnosis of irritable bowel syndrome (IBS). The diagnostic criteria and management recommendations of the last 3 teams are known as Rome I, II, and III and, unlike the 1989 document, they include diagnostic criteria for functional bowel disorders (FBDs) other than IBS (see "The Road to Rome" on page 1552 in this issue).

Functional Bowel Disorders

Functional bowel disorders are functional gastrointestinal disorders with symptoms attributable to the middle or lower gastrointestinal tract. These include the IBS, functional bloating, functional constipation, functional diarrhea, and unspecified functional bowel disorder.

To separate these chronic conditions from transient gut symptoms, they must have occurred for the first time ≥6 months before the patient presents, and their presence on ≥3 days a month during the last 3 months indicates current activity. Previous diagnostic criteria presumed the absence of a structural or biochemical disorder. However, research will likely confirm that functional gut disorders manifest such findings. Moreover, IBS, functional bloating, functional constipation and functional diarrhea may have multiple etiologies.

Table 1. Functional Gastrointestinal Disorders

C. Functional bowel disorders
C1. Irritable bowel syndrome
C2. Functional bloating
C3. Functional constipation
C4. Functional diarrhea
C5. Unspecified functional bowel disorder

C1. Irritable Bowel Syndrome

Definition

IBS is a functional bowel disorder in which abdominal pain or discomfort is associated with defecation or a change in bowel habit, and with features of disordered defecation.

Epidemiology

Throughout the world, about 10%–20% of adults and adolescents have symptoms consistent with IBS, and most studies find a female predominance.[1–3] IBS symptoms come and go over time, often overlap with other functional disorders,[4] impair quality of life,[5] and result in high health care costs.[6]

C1. Diagnostic Criteria* for Irritable Bowel Syndrome

Recurrent abdominal pain or discomfort** at least 3 days per month in the last 3 months associated with *2 or more* of the following:

1. Improvement with defecation
2. Onset associated with a change in frequency of stool
3. Onset associated with a change in form (appearance) of stool

*Criteria fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis.

**Discomfort means an uncomfortable sensation not described as pain. In pathophysiology research and clinical trials, a pain/discomfort frequency of at least 2 days a week during screening evaluation for subject eligibility.

Supportive symptoms that are not part of the diagnostic criteria include abnormal stool frequency ([a] ≤3 bowel movements per week or [b] >3 bowel movements per day), abnormal stool form ([c] lumpy/hard stool or [d] loose/watery stool), [e] defecation straining, [f] urgency, or also a feeling of incomplete bowel movement, passing mucus, and bloating.

The Rome II working team suggested 2 systems for classifying patients into diarrhea-predominant and constipation-predominant subgroups based on the first 6 of these features.[7,8] The Rome II book classification based on the first 6 supportive symptoms includes: Diarrhea predominant: 1 or more of b, d, f, and none of a, c, e, or ≥2 of b, d, f, and 1 of a or e (c, hard/lumpy stool excluded); and Constipation predominant: ≥1 of a, c, e, and none of b, d, f, or ≥2 of a, c, e, and 1 of b, d, f.[7]

Both variations exclude patients with hard stools from the diarrhea subtype,[7,8] but 1 version can include patients with watery stools in the constipation subgroup.[7] Investigators have used these methods and modifications of them to select patients for treatment trials targeting a specific bowel pattern.

Table 2. Subtyping IBS by Predominant Stool Pattern

1. IBS with constipation (IBS-C)—hard or lumpy stools[a] ≥25% and loose (mushy) or watery stools[b] <25% of bowel movements.[c]
2. IBS with diarrhea (IBS-D)—loose (mushy) or watery stools[b] ≥25% and hard or lumpy stool[a] <25% of bowel movements.[c]
3. Mixed IBS (IBS-M)—hard or lumpy stools[a] ≥25% and loose (mushy) or watery stools[b] ≥25% of bowel movements.[c]
4. Unsubtyped IBS—insufficient abnormality of stool consistency to meet criteria for IBS-C, D, or M.[c]

Note. To subtype patients according to bowel habit for research or clinical trials, the following subsclassification may be used (see Figure 1). The validity and stability of such subtypes over time is unknown and should be the subject of future research.
[a]Bristol Stool Form Scale 1–2 (separate hard lumps like nuts [difficult to pass] or sausage shaped but lumpy).
[b]Bristol Stool Form Scale 6–7 (fluffy pieces with ragged edges, a mushy stool or watery, no solid pieces, entirely liquid).
[c]In the absence of use of antidiarrheals or laxatives

Patient reports of "diarrhea" and "constipation" may mislead physicians. The stool may be solid, though defecation is frequent (pseudodiarrhea).[9] Conversely, straining to defecate may occur with soft or watery stools. Some patients feel constipated because they have unproductive urges to defecate or feelings of incomplete evacuation that prompt them to strain after passing stool. The need for accurate symptom description is corroborated by reports of straining, urgency, and incomplete evacuation across the spectrum of stool form.[10,11] In subgroups identified by cluster analysis[12] or symptoms,[13] most patients have a stool frequency within the normal range regardless of bowel pattern. However, stool form (from watery to hard) reflects intestinal transit time.[9]

Therefore, assuming no use of antidiarrheals or laxatives, we propose the system shown in Table 2. Researchers and practitioners should consider using the Bristol Stool Form Scale (Table 3)[9] to identify constipation as types 1 and 2 and diarrhea as types 6 and 7.

Figure 1 describes the 4 possible bowel pattern subtypes at a particular point in time. Individuals with neither diarrhea nor constipation by these characteristics have unsubtyped IBS. Researchers have classified subjects not fitting the IBS with diarrhea (IBS-D) or IBS with constipation (IBS-C) subtypes as having either mixed IBS (IBS-M)[14] or alternating IBS (IBS-A),[15,16] or have con-

Table 3. The Bristol Stool Form Scale

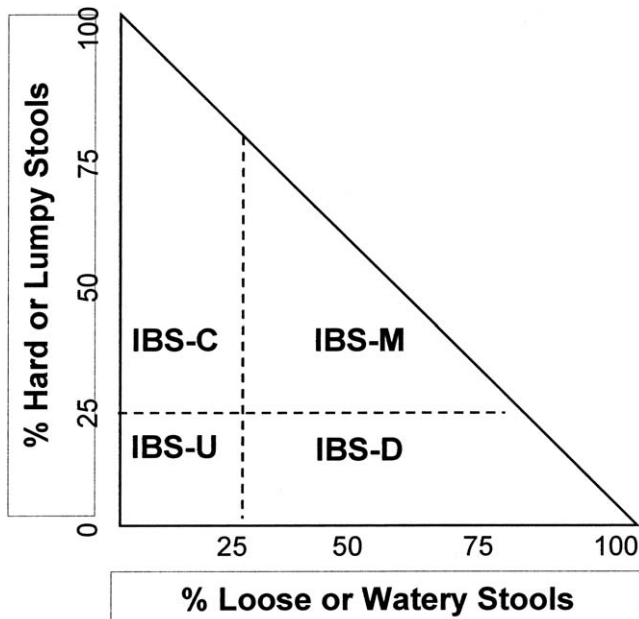| Type	Description
1	Separate hard lumps like nuts (difficult to pass)
2	Sausage shaped but lumpy
3	Like a sausage but with cracks on its surface
4	Like a sausage or snake, smooth and soft
5	Soft blobs with clear-cut edges (passed easily)
6	Fluffy pieces with ragged edges, a mushy stool
7	Watery, no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

Figure 1. Two-dimensional display of the 4 possible IBS subtypes according to bowel form at a particular point in time. IBS-C, IBS with constipation; IBS-D, IBS with diarrhea; IBS-M, mixed IBS; IBS-U, un-subtyped IBS.

sidered these terms synonymous.[13] We prefer *IBS-M* for individuals with both diarrhea and constipation ≥25% of bowel movements. Whereas this classification is a useful way of describing individuals at presentation, their bowel habits often vary over time, and we propose the term *IBS-A* for such cases.

Rationale for Changes in the Diagnostic Criteria

The symptom criteria are useful for clinical practice, epidemiologic surveys, pathophysiology research, and therapeutic trials. The symptom frequencies suggested for the FBDs are arbitrary and may need to be modified for different purposes. Epidemiologists should explore several frequencies to understand their significance. In therapeutic trials, the higher the symptom frequency threshold for subject enrollment, the larger the potential treatment effect and the smaller the number of subjects that may be needed to show a significant difference. However, such patients may be less likely to achieve satisfactory relief, and such studies are less applicable to the general population. Hence, enrollment symptom criteria are critical. The recommended threshold for pain or discomfort of ≥2 days a week for pathophysiology studies and clinical trials is reported by a majority of IBS patients.[16] About three fourths of patients who rated their pain as at least moderate (not ignorable, but without affect on lifestyle) also had pain ≥2 days a week.[17] Because relief of pain/discomfort with defecation may be incomplete,[11] *improved* with defecation replaces *relieved*.

The Rome II subtyping using multiple criteria were complex and difficult to use in practice. We therefore simplified them by using only the most reliable criterion, stool form. Current evidence indicates that bowel pattern subtyping is best done according to stool form rather than bowel frequency,[9–13,18] particularly IBS-M[15]; however, we emphasize that bowel pattern subtypes are highly unstable. In a patient population with approximately 33% prevalence rates of IBS-D, IBS-C, and IBS-M, 75% of patients change subtypes and 29% switch between IBS-C and IBS-D over 1 year.[14] Other investigators report the IBS-M subtype in about 50% of referred patients according to 3 sets of criteria,[15] and IBS-M is the most prevalent group in primary care.[16] In addition, a majority of patients have rapidly fluctuating symptoms lasting from <1 hour to <1 week.[15,16] Therefore, the rate of documented bowel pattern change is a function of the data collection frequency, and there are insufficient data upon which to recommend a time period for defining IBS-A. In drug studies on patients subtyped by stool form, investigators may want to assess pharmacologic effects on stool frequency, straining, urgency, and incomplete evacuation as well as stool form. Although the committee recommends a change in subtyping from the multisymptom Rome II classification to one based on stool form only, there are insufficient data to exclude either classification at this time. Further validation studies are needed.

Because of the characteristic symptom instability, we prefer the terms *IBS with constipation* and *IBS with diarrhea* instead of *constipation-* and *diarrhea-predominant IBS*. In this categorical system, many people whose features place them close to a subtype boundary change pattern without a major change in pathophysiology. Moreover, the heterogeneity and variable natural history of IBS significantly limit clinical trials of motility-active drugs and drug therapy in practice. In both research and practice, it may be desirable to base drug use on a stronger bowel pattern predominance than the requirements of this system.

Clinical Evaluation

Diagnosis depends on careful interpretation of the temporal relationships of pain/discomfort, bowel habit, and stool characteristics. Pain/discomfort related to defecation is likely to be of bowel origin, whereas that associated with exercise, movement, urination, or menstruation usually has a different cause. Fever, gastrointestinal bleeding, weight loss, anemia, abdominal mass, and other "alarm" symptoms or signs are not due to IBS, but may accompany it.

In women, so-called pelvic pain,[19] worsening of IBS symptoms during menstruation,[20] and dyspareunia or other gynecologic symptoms may obscure the diagnosis.

Incorrect symptom attribution can lead to hospitalization and surgery, especially cholecystectomy, appendectomy, and hysterectomy.[21] The recognition and evaluation of bowel dysfunction in patients with "pelvic" or abdominal pain may reduce unnecessary surgery.

Heartburn, fibromyalgia, headache, backache, genitourinary symptoms, and others are often associated with IBS, but are not useful in diagnosing it. These symptoms increase as the severity of IBS increases and may be associated with psychological factors.[4] Obviously, a common disorder such as IBS may coexist with organic gastrointestinal disease. There are no discriminating physical signs of IBS, but abdominal tenderness may be present. Tensing the abdominal wall increases local tenderness associated with abdominal wall pain, whereas it lessens visceral tenderness by protecting the abdominal organs (Carnett test).[22]

Few tests are required for patients who have typical IBS symptoms and no alarm features.[23,24] Unnecessary investigations may be costly and even harmful.[25] Testing is based on the patient's age, duration and severity of symptoms, psychosocial factors, alarm symptoms, and family history of gastrointestinal disease. Investigations may include a sigmoidoscopy or colonoscopy to rule out inflammation, tumors, or melanosis coli owing to regular laxative use. Stool examination for occult blood, leukocytes, or ova and parasites (eg, *Giardia*) where they are endemic may be indicated, but routine rectal biopsy and abdominal ultrasonography usually are not. Many people who report severe lactose intolerance absorb lactose normally with negligible symptoms,[26] undermining the value of documenting lactase deficiency. The discovery of diverticulosis does not change the diagnosis of IBS. Some patients with celiac sprue have IBS symptoms.[27] In IBS patients who were HLA-DQ2–positive and had intestinal antibodies to gliadin and other dietary proteins, stool frequency and intestinal IgA levels decreased after gluten restriction.[28] However, the available data suggest testing for celiac disease only if indicated by clinical features and local prevalence.[29]

A confident diagnosis that holds up over time can usually be made through careful history taking, examination, and limited laboratory and structural evaluations individualized to each patient's needs. IBS is often properly diagnosed without testing. After diagnosis, a change in the clinical features may warrant additional investigation. However, persistence and recurrence is expected, and needless investigation may undermine the patient's confidence in the diagnosis and in the physician.[25]

Physiologic Features

IBS is best viewed as an interaction of important biological and psychosocial factors. Altered motility, visceral hyperalgesia, disturbance of brain–gut interaction, abnormal central processing, autonomic and hormonal events, genetic and environmental factors, postinfectious sequels, and psychosocial disturbance are variably involved, depending on the individual.[30]

Psychosocial Features

Psychological disturbance, especially in referred patients, includes psychiatric disorders (eg, panic disorder, generalized anxiety disorder, mood disorder, and posttraumatic stress disorder), sleep disturbance, and dysfunctional coping.[31,32] A history of childhood abuse is common.[33] Although stressful life events sometimes correlate with symptom exacerbation, the nature of the link between psychosocial factors and IBS is unclear.

Treatment

Management depends on a confident diagnosis, explanation of why symptoms occur, and suggestions for coping with them. Education about healthy lifestyle behaviors, reassurance that the symptoms are not due to a life-threatening disease such as cancer, and establishment of a therapeutic relationship are essential, and patients have a greater expectation of benefit from lifestyle modification than drugs.[34] For such counseling, individual[35] or group[36] interactions are effective.

Most IBS patients present to primary care where physicians are best positioned to know their histories, personalities, and families. Specialists' patients are more likely to have severe symptoms, depression, anxiety, panic, or other complicating psychosocial disorders that require special treatment. In addition to allaying fear, physicians should uncover any unstated worries or aggravating factors. It is important to assess the patient's quality of life and level of daily functioning, personality, recent life stress (eg, divorce, bereavement, or job loss), and any psychological disturbance.

The type and severity of symptoms and the nature of associated psychosocial issues determine treatment.[30,37] Psychological factors may alter symptom perception, and the patient's reaction to the symptoms may be more important than the symptoms themselves. Most patients respond to psychological support, a strong physician–patient relationship, and multicomponent treatment approaches[38] that reduce health care utilization. The physician should be understanding, maintain patient contact, and prevent overtesting and harmful treatments. Unsatisfied patients may consult many physicians, undergo unjustified and hazardous investigation, take unproven medication, and have unneeded surgery.[21,25]

Patients should avoid nutritionally depleted diets and have regular, unhurried meals. Lactose restriction usually

Table 4. Possible Drugs for a Dominant Symptom in IBS[a]

Symptom	Drug	Dose
Diarrhea	Loperamide	2–4 mg when necessary/maximum 12 g/d
	Cholestyramine resin	4 g with meal
	Alosetron[b]	0.5–1 mg bid (for severe IBS, women)
Constipation	Psyllium husk	3.4 g bid with meals, then adjust
	Methylcellulose	2 g bid with meals, then adjust
	Calcium polycarbophil	1 g qd to qid
	Lactulose syrup	10–20 g bid
	70% sorbitol	15 mL bid
	Polyethylene glycol 3350	17 g in 8 oz water qd
	Tegaserod[c]	6 mg bid (for IBS, women)
	Magnesium hydroxide	2–4 tbsp qd
Abdominal pain	Smooth-muscle relaxant[d]	qd to qid ac
	Tricyclic antidepressants	Start 25–50 mg hs, then adjust
	Selective serotonin reuptake inhibitors	Begin small dose, increase as needed

[a]Local cost should be considered in drug choice.
[b]Available only in the U.S.
[c]Unavailable in the European Union.
[d]Selective antimuscarinic agents unavailable in the United States.

fails to improve symptoms,[39] and dietary calcium restriction may be harmful. Excessive fructose[40] and artificial sweeteners, such as sorbitol or mannitol, may cause diarrhea, bloating, cramping, or flatulence. More data are necessary before testing for IgG antibodies to certain foods can be recommended.[41] Dietary fiber for IBS is time honored, inexpensive, and safe, but poorly substantiated by clinical trials. Indeed, many patients believe bran exacerbates their symptoms,[42] and the only substantial randomized controlled trial of bran suggested it exacerbated flatulence and did not relieve pain.[43]

Drug therapy is directed toward the dominant symptoms[44] (Table 4). Their changeable nature[13–16] and the complex interactions between the central and enteric nervous systems circumscribe the effectiveness of specific therapies. Researchers are searching for biomarkers and genetic polymorphisms that might identify patients most likely to respond to drugs. Early therapeutic trials had significant methodological inadequacies, and deficiencies and publication bias persist[45,46] (see "Design of Treatment Trials for Functional Gastrointestinal Disorders" on page 1538 in this issue). Drugs help only some symptoms in selected patients. Loperamide may prevent diarrhea when taken before a meal or an activity that often leads to the symptom. Constipation is treated initially with dietary fiber supplementation. If response

is unsatisfactory, commercial fiber analogs may help.[47] The heterogeneous smooth-muscle relaxants are questionably beneficial for pain; trial deficiencies leave their efficacy in doubt.[48] Furthermore, their availability varies in Australia, Canada, Europe, and the United States.[44] Antidepressant drug therapy in lower than antidepressant doses may be beneficial even if there is no major psychiatric comorbidity. For example, desipramine benefits women with moderate to severe IBS who do not discontinue the drug owing to side effects,[49] and the effect appears unrelated to the drug dose.[50] Paroxetine improves the physical component of quality of life of patients with severe IBS[51] and is more effective than a high-fiber diet in improving global status.[52] The narrow therapeutic window for antidepressants suggests they be limited to patients with moderate or severe IBS.

Alosetron, a selective serotonin 5-HT$_3$ receptor antagonist, can decrease pain, urgency, stool frequency, and increase global status in women with diarrhea and IBS. Based on rigorous studies, the number needed to treat (NNT) is 7.[53] Ischemic colitis and severe obstipation led to its withdrawal, but it was reintroduced only in the United States with restricted access and a risk management program. It was efficacious and safe in a 48-week trial.[54] Well-designed studies of tegaserod, a partial 5-HT$_4$ receptor agonist, found it can improve overall status, stool frequency and form, ease of evacuation, and bloating in women with IBS and constipation. In 8 studies, the NNT for daily doses of 12 mg and 4 mg was 14 and 20, respectively,[55] and it is as effective in retreating patients as during initial therapy.[56] Published trials comparing alosetron and tegaserod with conventional anitdiarrheals and laxatives, respectively, are not available, and interpretation of NNT values calculated from older studies of these agents is compromised by trial deficiencies.

Preliminary trials of probiotics are encouraging, especially symptom improvement and normalization of the blood mononuclear cell ratio of an anti-inflammatory to a proinflammatory cytokine in patients taking *Bifidobacterium infantis*,[57] but these studies need repeating in larger numbers of patients before they can be considered established treatments. Small bowel bacterial overgrowth, as diagnosed by lactulose hydrogen breath testing is a suggested[58] but disputed[59] cause of IBS, and antibiotics provide only transient benefit[60] and risk *Clostridium difficile* infection, allergic reactions, antimicrobial resistance, and chronic functional symptoms.[61]

Cognitive–behavioral therapy, standard psychotherapy, and hypnotherapy may help selected IBS patients. Weekly cognitive–behavioral therapy for 12 weeks was better than weekly educational sessions,[49] but depressed patients did not respond; quality of life but not pain improved. Hypnotherapy, the most thoroughly evaluated psychological treat-

ment, normalizes rectal sensation,[62] and 12 sessions benefit quality of life, anxiety, and depression in refractory patients (except men with IBS and diarrhea), and the benefits last ≥5 years.[63] However, trials of psychological therapy cannot be double blind, and treatment is time consuming, costly, and often unavailable.

C2. Functional Bloating

Definition

Functional bloating is a recurrent sensation of abdominal distention that may or may not be associated with measurable distention, but is not part of another functional bowel or gastroduodenal disorder.

Epidemiology

Most of the research on bloating has dealt with subjects who also have other functional gastrointestinal disorders; up to 96% of IBS patients report this symptom. Community surveys reveal that about 10%–30% of individuals report bloating during the previous year.[64,65] It is about twice as common in women as men,[66] and is often associated with menses.[67] Typically, it worsens after meals and throughout the day and improves or disappears overnight. Abdominal inductance plethysmography confirms increased abdominal girth in some bloated IBS patients.[68]

C2. Diagnostic Criteria* for Functional Bloating

Must include *both* of the following:

1. Recurrent feeling of bloating or visible distention at least 3 days/month in 3 months
2. Insufficient criteria for a diagnosis of functional dyspepsia, IBS, or other functional GI disorder

*Criteria fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis

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Rationale for the Criteria

Because *abdominal* as a modifier of *bloating* is redundant, it was omitted. *Fullness* was also deleted, because it may imply postprandial satiety, yet bloating occurs throughout the day. Importantly, bloating overlaps with other functional disorders (eg, functional constipation, IBS, and functional dyspepsia), epidemiologic surveys and factor analyses do not convincingly demonstrate a distinct bloating group, and physiologic studies of bloating have mainly been done on patients with IBS.

Because of the lack of data on bloating frequency, the frequency criterion is arbitrary and may need to be modified for different purposes. Additional epidemiologic research should investigate functional bloating.

Clinical Evaluation

Bloating is distinguished from other causes of abdominal distention by its diurnal pattern. It may follow ingestion of specific foods. Excessive burping or flatus is sometimes present, but these may be unrelated to the bloating. Diarrhea, weight loss, or nutritional deficiency should prompt investigation for intestinal disease.

Physiologic Features

No unified pathophysiologic mechanism can be applied to all patients. Food intolerance, abnormal gut bacterial flora, weak abdominal musculature, and abnormal retention of fluid inside and outside the gut do not appear to be significant factors. However, studies have documented both increased intestinal gas accumulation and abnormal gas transit. Visceral hyperalgesia may be important in some patients.[68]

Psychosocial Features

No uniform psychological factors have been identified.[68]

Treatment

Although the functional bloating criteria require the absence of other disorders, most research has been done on patients who have IBS or another disorder; therefore, treatment of bloating is similar whether it is isolated or associated with another functional disorder. Most treatments are designed to reduce flatus or gut gas, which are of unproved importance in bloating, and most are of unproven efficacy. Bloating may decrease if an associated gut syndrome such as IBS or constipation is improved. If bloating is accompanied by diarrhea and worsens after ingesting dairy products, fresh fruits, or juices, further investigation or a dietary exclusion trial may be worthwhile. However, even patients with proven lactase deficiency experience little or no bloating after drinking 240 mL of milk.[26] Avoiding flatogenic foods, exercising, losing excess weight, and taking activated charcoal are safe but unproven remedies.[69,70] Data regarding the use of surfactants such as simethicone are conflicting. Antibiotics are unlikely to help, but trials of probiotics are encouraging.[71] Beano, an over-the-counter oral β-glycosidase solution, may reduce rectal passage of gas without decreasing bloating and pain.[72] Pancreatic enzymes reduce bloating, gas, and fullness during and after high-calorie, high-fat meal ingestion.[73] Tegaserod improves bloating (a secondary outcome measure) in some constipated female IBS patients.[74]

C3. Functional Constipation

Definition

Functional constipation is a functional bowel disorder that presents as persistently difficult, infrequent, or seemingly incomplete defecation, which do not meet IBS criteria.

Subjective and objective definitions of constipation include (1) straining, hard stools or scybala (hard, inspissated stool), unproductive calls ("want to but cannot"), infrequent stools, or incomplete evacuation; (2) <3 bowel movements per week, daily stool weight <35 g/day, or straining >25% of the time; and (3) prolonged whole gut or colonic transit. Stool frequency correlates poorly with colonic transit, but one can estimate gut transit using the Bristol Stool Form Scale (Table 2).[9] Usually, there is no demonstrable physiological abnormality.

Epidemiology

Constipation occurs in up to 27% of people depending on demographic factors, sampling, and definition.[75] It affects all ages and is most common in women and non-whites. In 1 survey, the prevalence was sought by 3 means: patient complaint, Rome I criteria, and transit time (using the Bristol Scale).[9,76] Approximately 8% had constipation by each definition, but only 2% were constipated by all 3. Therefore, the concept of constipation is complicated by disagreement among patients and doctors about its nature.

C3. Diagnostic Criteria* for Functional Constipation

1. Must include *2 or more* of the following:
   a. Straining during at least 25% of defecations
   b. Lumpy or hard stools in at least 25% of defecations
   c. Sensation of incomplete evacuation for at least 25% of defecations
   d. Sensation of anorectal obstruction/blockage for at least 25% of defecations
   e. Manual maneuvers to facilitate at least 25% of defecations (eg, digital evacuation, support of the pelvic floor)
   f. Fewer than 3 defecations per week
2. Loose stools are rarely present without the use of laxatives
3. There are insufficient criteria for IBS

Criteria fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis

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Rationale for Changes to Diagnostic Criteria

A required frequency of "≥25%" is substituted for ">25%" to maintain consistency with other FBD criteria. Studies using Rome II criteria yield a lower prevalence than those using Rome I criteria, because the Rome II criteria did not allow for laxative-induced loose stools,[66] an anomaly that is corrected in the Rome III criteria.

Clinical Evaluation

The physician should clarify what the patient means by constipation. Manual maneuvers to assist defecation or straining to expel soft stools suggest anorectal dysfunction, but are diagnostically unreliable.[77] Transit time can be estimated using the Bristol Scale (Table 2).[9] Evaluation of the patient's gut symptoms, general health, psychological status, use of constipating medications, dietary fiber intake, and signs of medical illnesses (eg, hypothyroidism) should guide investigation. Physicians should perform perianal and anal examination to detect fecal impaction, anal stricture, rectal prolapse, mass, or abnormal perineal descent with straining. Laboratory tests are rarely helpful. Endoscopic evaluation of the colon may be justified for patients >50 with new symptoms or patients with alarm features or a family history of colon cancer.

If fiber supplementation fails to help or worsens the constipation, measurements of whole gut transit time may identify cases of anorectal dysfunction or colon inertia. Using radiopaque markers, measurement of whole gut transit time (primarily colon transit) is inexpensive, simple, and safe. Several methods produce similar results.[78,79] Retention of markers in the proximal or transverse colon suggests colonic dysfunction, and retention in the rectosigmoid area suggests obstructed defecation. A radioisotope technique involves less radiation than plain x-rays and may provide more information, helping to differentiate proximal colon emptying, pancolonic inertia, and dyssynergic defecation.

Physiologic Factors

Severe, intractable constipation may be due to colonic inertia or anorectal dyssynergia. These disorders may coexist, but most patients complaining of constipation have normal colonic transit and anorectal function (see "Functional Anorectal Disorders" on page 1510 in this issue).

Psychosocial Factors

No uniform psychological profile is applicable to patients with constipation; however, patients with severe

constipation and normal intestinal transit often have increased psychological distress, and depressed patients may have constipation.[80]

Treatment

Reassurance may convince some patients that failure to evacuate for 2 or 3 days is harmless. Increased fluid intake and physical exercise are unproven measures.[81] Physicians should stop or reduce any constipating medication the patient may be taking and treat depression and hypothyroidism when present. Pharmacologic therapy is not advisable until general and dietary measures are exhausted. There are few published trials of some commonly used medical therapies.[47]

The severity and nature of the symptoms guide further treatment. The indigestible matter in dietary fiber increases fecal bulk by promoting fecal water-holding capacity and bacterial proliferation. Other bulking agents include psyllium, methyl cellulose, and calcium polycarbophil. Although stimulating laxatives such as bisacodyl, sodium picosulphate, or sennosides may be tried, their effectiveness and long-term safety have not been determined by placebo-controlled trials; they were introduced in an era when high-quality trials were not performed.[82] Polyethylene glycol solution,[47] lactulose, and sorbitol[83] may be useful. Tegaserod is superior to placebo for patients with chronic constipation.[84,85] Recent studies suggest that prostaglandin analogs may be helpful.[47] Therapy of anorectal dysfunction is discussed in "Functional Anorectal Disorders" on page 1510 in this issue.

C4. Functional Diarrhea

Definition

Functional diarrhea is a continuous or recurrent syndrome characterized by the passage of loose (mushy) or watery stools without abdominal pain or discomfort.

Epidemiology

There are few studies in which functional diarrhea was specifically diagnosed as distinct from IBS-D, so it is impossible to provide a precise frequency. Unspecified diarrhea was reported by 9.6% of Minnesota residents[86] and 4.8% of people throughout the United States[87]; however, its duration and frequency are uncertain. Although a common reason for consulting a gastroenterologist, diarrhea was a presenting complaint of <2% of general practice patients.[88]

> **C4. Diagnostic Criterion* for Functional Diarrhea**
>
> **Loose (mushy) or watery stools without pain occurring in at least 75% of stools**
>
> **Criterion fulfilled for the last 3 months with symptom onset at least 6 months before diagnosis*

Rationale for the Criteria

Most people apply the term *diarrhea* to loose or watery stools. Fewer individuals relate it to increased frequency and urgency.[89] Because rapid transit increases the percentage of water in stool, stool form correlates well with transit.[9] Soft stools are 85% water, and watery stools 90% with greatly reduced stool viscosity.[90] Stool viscosity is critical because watery stool is difficult to retain, and anal contact with fluid causes extreme urgency. However, urgency alone unreliably indicates diarrhea and may be reported by individuals with hard, pelletlike stools. Thus, stool form, not frequency, defines diarrhea. How often a symptom must occur to be significant depends on its troublesomeness. Just 1 episode of fecal incontinence is a serious problem for a patient, whereas an occasional loose stool may not be.

Clinical Evaluation

The combination of abdominal pain with intermittent diarrhea and constipation is highly suggestive of IBS, and small-volume, frequent defecation is likely functional. Pseudodiarrhea[9] (frequent defecation and urgency with solid stools) is not diarrhea. A stool diary incorporating the Bristol Stool Form Scale is a useful method to verify stool form (Table 2).[9] Dietary history can disclose poorly absorbed carbohydrate intake, such as lactose by patients with hypolactasia, or "sugar-free" products containing fructose, sorbitol, or mannitol. Alcohol can cause diarrhea by impairing sodium and water absorption from the small bowel. Physical examination should seek signs of anemia or malnutrition. An abdominal mass suggests Crohn's disease in the young patient and cancer in the elderly patient. Rectal examination, colon endoscopy, and biopsy can exclude villous adenoma, microscopic colitis, and inflammatory bowel disease.

Abnormal results of blood or stool tests or other alarm features necessitate further tests. Features of malabsorption (malnutrition, weight loss, non–blood-loss anemia, or electrolyte abnormalities) should provoke the appropriate antibody tests and/or duodenal biopsy for celiac disease. Where relevant, giardiasis and tropical sprue should be excluded. Barium small bowel radiography may be necessary. Rarely, persistent diarrhea may require

tests for bile acid malabsorption or, more practically, a trial of the bile acid-binding resin cholestyramine.[91]

Physiologic Factors

Few studies have addressed the physiology of functional diarrhea. One such study found decreased nonpropagating colonic contractions and increased propagating colonic contractions.[92]

Psychosocial Factors

Psychosocial factors have also received little research attention apart from the finding of accelerated colonic transit inducible by acute stress.[93]

Treatment

Discussion of possible psychosocial factors, symptom explanation, and reassurance is important. Restriction of foods, such as those containing sorbitol or caffeine, which seem provocative, may help. Empiric antidiarrheal therapy (eg, diphenoxylate or loperimide) is usually effective, especially if taken prophylactically, such as before meals or public engagements[94] (Table 4). Alosetron slows transit and reduces the gastrocolonic response in normal volunteers and may improve diarrhea.[53] However, it is expensive and of limited availability only in the United States; there are no published, randomized, controlled trials in patients with functional diarrhea. Cholestyramine, an ion-exchange resin that binds bile acids and renders them biologically inactive, is occasionally very effective.[91] The prognosis of functional diarrhea is uncertain, but it is often self-limited.[95]

C5. Unspecified Functional Bowel Disorder

Individual symptoms discussed in the previous sections are very common in the population. These occasionally lead to medical consultation, yet are unaccompanied by other symptoms that satisfy criteria for a syndrome. Such symptoms are best classified as *unspecified*.

C5. Diagnostic Criterion* for Unspecified Functional Bowel Disorder

Bowel symptoms not attributable to an organic etiology that do not meet criteria for the previously defined categories

Criterion fulfilled for the last 3 months with symptom onset at least 6 months before diagnosis

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Future Research Directions

Development of the Rome Criteria is a continuing process, and the criteria should be updated as data allow. We suggest the following topics for research.

1. Perform long-term, longitudinal studies on patients with disorders of bowel function to better determine the natural history, specifically regarding changing severity and interchange among disorders and the predominant symptom.
2. Direct more research to patients in primary care.
3. Compare the efficacy of new drugs with that of older ones (eg, antidiarrheal agents, laxatives, and antidepressants) and placebos.
4. Study bloating with distention defined as a true increase in abdominal girth.
5. Further investigate the epidemiology of functional bloating.
6. Determine what the symptom terms (eg, *bloating* and *discomfort*) mean to patients with different disorders and whether the meanings change across cultures and countries.
7. Use unobtrusive and ambulatory, objective measures of abdominal girth to investigate the pathophysiology of distention in functional disorders and its response to drugs.
8. Investigate pharmacologic modulation of sensorimotor function and the gut microflora to identify mechanisms of bloating and/or distention.
9. Develop effective psychological treatments that can be provided by primary physicians.
10. Determine the features of colonic transit and stool water content in idiopathic diarrhea.
11. Investigate histologic changes in mucosal biopsies from patients with idiopathic diarrhea; for example, lymphocytic infiltration that does not meet criteria for lymphocytic colitis.
12. Investigate the main differences between functional diarrhea and IBS-D, including demographic features and symptom pattern and whether they require different treatments.
13. Perform repeated physiologic evaluations, including visceral sensitivity and motility, on IBS patients during periods of changing bowel habit and symptom severity.

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