INTRODUCTION

Functional gastrointestinal disorders (FGIDs) are defined by symptoms because there are no specific disease markers available and there are no structural, mechanical or biochemical abnormalities (1). The symptoms of the FGIDs are probably related to various abnormalities including increased motor reactivity, visceral hypersensitivity, as well as changes in immunologic and inflammatory function of the mucosa. There is also some alteration, although poorly understood, in the CNS-enteric nervous system regulation. Several descriptive revisions of the functional gastrointestinal disorders have taken place involving multinational work groups, most recently in the “Rome III” guidelines, in an effort to clarify this area of Gastroenterology which can be “an unsatisfying
and unproductive diagnostic adventure” for the physician and patient (2).

DEFINITION AND EPIDEMIOLOGY

Irritable Bowel Syndrome (IBS) is reviewed for the fourth time since 1989 in the new Rome III guidelines (3). Irritable Bowel Syndrome is classified as one of the Functional Bowel Disorders. IBS is characterized by abdominal pain with changes in bowel habit and disordered defecation; it is a result of dysregulation of gut motility and is not considered a psychological disorder but rather is greatly impacted by psychosocial issues. The major change in the functional bowel disorder category in Rome III is the removal of “functional abdominal pain syndrome” from functional bowel disorders to its own category. The revised criteria for IBS is shown in Table 1.

IBS is remarkably prevalent, affecting up to 10%–20% of adolescents and adults; the difference in reported prevalence is most likely a reflection of definition variation and the study designs used. In combination with functional dyspepsia, IBS is responsible for 40%–60% of referrals to outpatient gastroenterology clinics (4). Interestingly, when IBS is confidently diagnosed another cause of the patient’s symptoms is rarely found in the long-term follow-up of that patient. The actual symptoms of IBS can come and go over time and often overlap with other functional gastrointestinal disorders.

Gender differences have been studied and seem to vary. There is a prevalence in women of 14.5% compared with 7.7% in men in the US Householders study (5), with a similar 2:1(F:M) ratio reported in the National Health Interview Survey (6). In contrast, a prevalence of 12.7% vs 13.3% (women versus men) was reported in Olmstead County, Minnesota, using the original Rome criteria (7). Most studies have shown a higher prevalence in women than in men and Constipation-predominant (rather than Diarrhea-predominant) IBS is more common in women. The question of whether sex hormones play a role in the pathogenesis of IBS has also been repeatedly raised and studies have been done, with equivocal results, using an analog of gonadotropin-releasing hormone to suppress ovarian hormones. Some other interesting studies have shown a higher likelihood of men developing IBS if they have lower testosterone levels, reduced “male-trait” scores and more “nurturing traits” (8).

The prevalence of IBS does not appear to be age-related and, despite the commonly held belief that the incidence is usually highest in young to middle-aged patients, a recent review recommended consideration of IBS as a diagnosis even in the elderly with unexplained abdominal pain as the prevalence is higher in these patients than previously thought (9).

A higher prevalence of IBS in Caucasians versus African Americans has been reported but this depends on several factors including diagnostic criteria used, patterns of seeking medical care and access to medical care. One group found a significantly higher prevalence in Caucasians using standard diagnostic criteria (2). The world-wide prevalence is probably about the same; the prevalence for African Americans and His-
panic Americans as well as Japanese and Chinese populations is about the same (10).

**PATHOPHYSIOLOGY**

The abdominal pain and other symptoms associated with IBS are complex but seem to be related to a multifactorial pathophysiology which is still not completely understood and most likely involves an interplay between visceral hypersensitivity, motor dysfunction, psychosocial distress, post-infectious changes, luminal irritation and heredity as well as other newer etiologic factors which are being studied. The pathway in Table 2 was proposed by Lacy, et al (8).

**Visceral hypersensitivity** is described as the excessive sensing of stimuli such as volume or pressure. Potential sites which could mediate this hypersensitivity are at the gut level, the afferent nervous pathway or the CNS regions associated with perception of pain. Gut distention can excite mechanoreceptors and then nociceptors but it is not clear how other sensations such as fullness, discomfort or urge to defecate are communicated. Balloon inflation studies have shown that mechanical changes in the gut (especially in the recto-anal area) have the potential to excite many types of receptors in adjacent structures, such as genitouri-}

inary organs and mesentery. Other studies indicate that the visceral hypersensitivity seen in IBS is more related to changes in the central nervous system than to mechanical gut wall changes and that IBS patients also demonstrate hypervigilance and anticipation of visceral stimuli resulting in altered responses (11).

**Abnormal gut motility** has been described in IBS. The enteric nervous system (ENS) consists of the myenteric and submucosal plexuses. The ENS can function on its own (motor reflexes and secretion) but does receive input from the brain as well. Specific motility changes in IBS described in the 2002 Consensus report related to ENS function or dysfunction include (10):

1. Increased post-prandial colonic contractions
2. Fast colonic and propagated contractions in diarrhea
3. Abnormal giant migrating contractions in constipation
4. The rectosigmoid shows more symptomatic contractions in response to stimuli
5. Diarrhea-predominant IBS patients have accelerated gut transit
6. Abnormal small bowel motor patterns are seen in IBS
7. Compliance and tonic motor testing of the gut are usually normal in IBS.

It should be noted that, because of the nature of the studies, these reports are all described in small numbers of patients and whether they can be generalized to the population with IBS is unknown.

**Psychosocial factors** clearly play an important role in IBS, especially somatization (the tendency to focus on symptoms that can not be explained and to feel as though the suffering is so severe that medical attention is needed) which is more common in IBS. Only about 20% of patients with organic bowel disease present with concurrent psychological symptoms compared to 50% of those with IBS. Also, approximately 50% of IBS patients recall a particular stressful event that occurred prior to the onset of their symptoms and they are more likely to have anxiety with or without panic, phobias, post-traumatic stress disorder, depression, paranoia and hostility. A history of sexual abuse, even many years before as in childhood, should be sought as epidemiologic studies have shown a high prevalence of abuse history especially in female IBS patients with more severe symptoms (12). Nongastrointestinal and nonpsychiatric

(continued on page 21)
comorbid disorders associated with IBS include fibromyalgia (49% of these patients have IBS), TMJ syndrome (64%), chronic fatigue syndrome (51%) and chronic pelvic pain (50%) (1).

Despite all the associated psychological disorders noted above, it has been shown that IBS patients do have a heightened pain sensitivity to visceral stimulation of the brain-gut axis indicating that they have greater brain activation in response to rectal stimulation compared to normals. Most now agree that these patients have abnormal brain-gut communication as demonstrated by PET and MRI studies (13). CNS activation by visceral stimuli may also be affected by psychosocial stress (14).

Genetic factors are important in IBS; there is a 2-fold increase in IBS in monozygotic versus dyzgotic twins. It has also been shown that having a parent with IBS is an independent and stronger predictor of IBS than having a twin with IBS, suggesting that heredity seems to contribute but that social learning is at least equally important (15). Generally, there also appears to be some clustering of IBS in families and, interestingly, mothers with functional bowel disease seem to seek out medical care for their symptomatic infants more than mothers with gastric ulcer history.

Post-infectious causes of IBS were first suggested in the 1960s (16). Several subsequent prospective studies have shown that perhaps 7%–32% of patients develop IBS symptoms after an acute enteritis (17). Possible post-infectious mechanisms contributing to functional change include transient or permanent enteric nervous system injury, a change in the number or function of gut enteroendocrine and T-lymphocyte cells, a change to a chronic inflammatory state in the bowel, a sensitization of afferent pathways and possibly local tissue destruction which could result in dysmotility (8). The post-infectious group of IBS patients may have a better prognosis than those with IBS but no prior enteric infection, but post-infectious IBS-type symptoms can persist for years (6 years is often quoted); women and patients with a history of anxiety/depression appear to have a worse outcome. Salmonella infection results in the highest incidence of IBS-type symptoms of persistent bowel dysfunction; on average, reports indicate an incidence of approximately 10%. Other infectious causes include Shigella, Campylobacter, E. Coli, Giardia, Cryptococci and some viruses (39). There is also new evidence that there may be a higher frequency of IBS in patients after non-gastrointestinal infections than in controls (18).

Luminal irritation of the gut, probably caused by low-grade inflammation and immune activation, is another possible etiologic factor in IBS. This mucosal irritation is not seen endoscopically or with standard pathology techniques but inflammatory cells (such as mast cells, T lymphocytes and macrophages) have been found in the colonic and ileal mucosa of IBS patients and are felt to release inflammatory mediators which subsequently stimulate the enteric nerves resulting in “abnormal secreto-motor responses” which then affect gut motility. The mediators include nitric oxide (NO), interleukins, histamine (H) and proteases (19). Nitric oxide seems to play a role in visceral hypersensitivity even though it does not appear to be important in normal rectal sensation or tone (20). New information reveals upregulation of the expression of mRNA for H1 and H2 receptors in the IBS gut; histamine is known to enhance gastric acid production, modulate intestinal motility and cause a change in gut mucosal ion secretion (21).

Along these same lines, there is more recent interest and research into the role of food allergy in IBS. Anywhere from 20% to 65% of IBS patients believe that their symptoms may be related to certain foods. Whether this is tied in with “luminal irritation,” “infectious” etiologies or other issues is still unclear. A systematic review on this topic indicates that the gut mucosal immune system may be activated by food allergens and be associated with the development of symptoms in a subgroup of IBS patients (22).

Other factors now felt to play a causative role in IBS include abnormal movement of gas through the GI tract. There does not seem to be a difference in the amount or type of gas but in the patterns of movement, in that a large number of IBS patients have been found to retain gas which has been experimentally infused into the small bowel compared to normals and they may also have a poorer tolerance of gas in the gut. Atropine does not affect this and therefore this is most likely a sensory rather than a motor problem (23).

IBS patients seem to share similar symptoms with patients who have small bowel bacterial overgrowth.
and this has been proposed as another etiologic factor in IBS. Using Rome I criteria, a study of 202 IBS patients was done using the lactulose/hydrogen breath test. Although more studies are needed, this study found small bowel bacterial overgrowth in 78% of these IBS patients and about half had improved symptoms after antibiotic treatment if bacterial eradication was seen in follow-up testing (24). A more recent study in 2005 showed that up to 84% of IBS patients have an abnormal lactulose/hydrogen breath test (25). Lacy, et al suggest that bacterial overgrowth could provide a unifying mechanism for some of the symptoms of IBS, especially the symptoms of bloating and distention (8).

Most of the human body’s serotonin (5-hydroxytryptamine, 5-HT) is in the GI tract within enterochromaffin cells where it plays a key role in peristaltic, secretory, vasodilatory, vagal and nociceptive reflexes (26). In the enteric nervous system both sensory and motor neurons express a variety of 5-HT receptor subtypes and there appears to be a 5-HT signaling abnormality in patients with IBS (27). A study in the United Kingdom showed that patients with diarrhea-predominant IBS with post-prandial symptoms had higher levels of post-prandial plasma 5-HT than those D-IBS patients who had no increase in post-prandial symptoms; D-IBS patients also had higher platelet concentrations of 5-HT than healthy subjects (28). Two studies have shown that there are abnormalities in the serotonin reuptake transport system in IBS patients. The information about serotonin and it’s role in IBS is the basis for the use of 5-HT related medications is covered in the “Treatment” section of this article (29).

**SYMPTOMS**

The most important step in the diagnosis of IBS is listening to and reviewing the patient’s symptoms, the key feature being the presence of abdominal pain or discomfort associated with bowel dysfunction which separates IBS from functional constipation and functional diarrhea. Functional dyspepsia can cause abdominal pain but it is more likely located above the umbilicus and is not associated with changes in bowel movements.

Many medical disorders can cause a change in bowel habits along with abdominal pain or discomfort.

### Table 3

**Subtyping IBS by Predominant Stool Pattern (3)**

1. IBS with constipation (IBS-C)—hard or lumpy stools\(^a\) \(\geq\) 25% and loose (mushy) or watery stools\(^b\) <25% of bowel movements.\(^c\)
2. IBS with diarrhea (IBS-D)—loose (mushy) or watery stools\(^b\) \(\geq\) 25% and hard or lumpy stool\(^a\) <25% of bowel movements.\(^c\)
3. Mixed IBS (IBS-M)—hard or lumpy stools\(^a\) \(\geq\) 25% and loose (mushy) or watery stools\(^b\) \(\geq\) 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 subclassification may be used. 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.
- b Bristol Stool Form Scale 6–7.
- c In the absence of use of antidiarrheals or laxatives

It is imperative to first exclude “alarm” symptoms when reviewing IBS symptoms. Clues which suggest that other medical conditions may be a cause of these symptoms include weight loss, fever, anemia, occult blood in the stool, travel history to areas with endemic parasitic diseases, nighttime symptoms, new onset over age 50, family history of colon cancer or inflammatory bowel disease, arthritis or dermatitis on physical exam, signs of malabsorption and signs or symptoms of thyroid dysfunction (2). In the absence of these symptoms and evidence of a chronic condition, a focused diagnostic approach should be undertaken.

Patients with predominance of diarrhea generally have improvement in urgency and cramping after a bowel movement; some IBS patients have worsened post-prandial cramping. Those with constipation may have mucus associated with the passage of stool and complain of straining and incomplete evacuation. Fecal incontinence has been described in approximately 20% of IBS patients. The difficulty in clarifying the definition IBS, description of stools and “categorization” has been repeatedly reviewed and it is still difficult to come to a consensus. The “sub-typing” (continued on page 25)
of IBS seems to be the most descriptive and sensible; most clinicians have become comfortable using these groupings which are well outlined by Longstreth in Table 3 (3). The subtypes use stool descriptions based on the Bristol Stool Scale in Table 4 (30).

### EVALUATION AND TESTING IN IBS

In the text “Gastro-Enterology” in 1944, Bockus recommended that the diagnosis of “irritable colon” be one of exclusion only; this was the standard until the 1970’s. Even now physicians feel compelled to rule out organic disease first. The challenge for the physician in the work-up of IBS is at least in part due to the following issues well described by Drossman (31):

1. lack of positive biologic markers in IBS
2. “a diagnosis based solely on symptoms can be unsettling; clinicians struggle with the possibility of missing another diagnosis”
3. the effect and importance of psychosocial factors (not just stress, anxiety and depression but also possible true psychiatric disease) makes it difficult to develop a diagnostic approach for IBS.

The other, and perhaps more challenging, part of the evaluation is the importance of including the patient in the decision process from the beginning and having the mutual expectation of negative results of studies/tests. This makes every negative result contribute to a positive diagnosis.

After applying the Rome III criteria to a patient with abdominal pain and changes in bowel habits and then excluding “alarm” symptoms one can proceed with further evaluation to diagnose IBS which is generally based on symptoms alone. Making a “positive” diagnosis of IBS is key to the patient’s confidence and willingness to further work with the physician on symptomatic improvement. The issue then becomes one of what to do and not do in the workup. Olden describes the dilemma: “Pursuing all diagnostic possibilities via an extensive work-up can lead to unnecessary and costly testing. This futility, in turn, can subject the patient to unneeded expense, inconvenience and suffering” (2).

Table 5 provides a simplified approach to the evaluation and diagnosis of IBS. As previously noted, due to the absence of specific diagnostic tests for IBS one must investigate the symptoms (see above regarding stool changes, alarm symptoms, etc.) with the patient. Pain or discomfort related to urination, exercise, movement or menstruation rather than to bowel movements is unlikely to be from IBS (3). It should be noted that in addition to abdominal pain, bloating and stool changes, patients with IBS also frequently complain of extracolonic symptoms such as (32):

1. Low back pain
2. Lethargy
3. Nausea
4. Thigh pain
5. Urinary frequency, urgency or urge incontinence
6. Dysmenorrhea or dyspareunia
7. Heartburn

The physical examination in IBS is almost always unrevealing and normal except for some mild lower abdominal tenderness especially over the sigmoid colon. If there is evidence on exam of organomegaly, masses or bruits other appropriate investigation should ensue. A rectal exam should be done in all patients to rule out obvious pathology (mass, blood etc); mild rectal tenderness can often be found in IBS related to hypersensitivity, rectal spasm or increased tone (8).

It has not been found to be cost-effective or necessary to do routine testing in patients with suspected IBS based on symptom criteria. The following studies may be considered but their yield remains controversial. Studies such as ultrasounds, CT scans and colonic biopsies are not generally necessary or indicated (33). Testing for Celiac Sprue (CS) in D-IBS may be considered, as cur-

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**Table 4**

The Bristol Stool Form Scale (30)

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

(continued from page 22)
rent information indicates that up to 75% of patients with CS present with symptoms suggestive of IBS. At this time, an evaluation, including checking IgA anti-endomysial antibody (anti-EMA) or IgA anti-tissue transglutaminase antibody (anti-TTG) is only indicated if clinical features prompt it and the prevalence seen locally is high. The decision to test for celiac disease may be based on ethnicity (Northern European), medical history (IDDM, inflammatory arthritis), clinical syndromes such as osteoporosis, anemia and unexplained infertility, as well as on family history of CS (34).

Other medical problems which should be considered in the differential diagnosis of IBS due to a similarity in some symptoms are shown in Table 6 (35).

Clearly, it is important to make a “positive” diagnosis of IBS so that the patient is spared unnecessary treatments and surgeries. Longstreth, et al found a 3-fold higher incidence of cholecystectomy and a 2-fold higher incidence of appendectomy and hysterectomy in IBS patients; there is also a 50% higher incidence of back surgery in these patients (38).

Generally, although there are very few clinical trials assessing pretest probability and diagnostic accuracy of diagnostic studies in IBS patients there is not enough evidence to recommend the routine performance of a standardized battery of diagnostic tests in patients who meet symptom-based criteria for IBS, as noted in Table 5.
TREATMENT

Despite the frustration of diagnosis, once it is determined the patient has IBS there are modalities of therapy which may be effective for symptom relief. The consensus report from 2002 recommends the following general management plan for IBS patients (10):

1. Establish a firm diagnosis
2. Establish a caring physician-patient relationship
3. Careful reassurance (that there is no cancer and that a normal life expectancy is predicted)
4. Explanation to the patient regarding possible pathogenesis of IBS and the role of emotions, diet, etc
5. Dietary advice (see below) and avoidance of certain medications
6. Medications can be tried aiming treatment at the predominant symptom
7. Psychological treatments which are more likely to be needed in severely psychologically disturbed patients
8. To beware of unnecessary surgeries and/or alternative therapies

First, avoidance of dietary “triggers” (Table 7) specific to the patient (there is no convincing data that these particular foods result in problems so it should be individualized) can often be determined, outlined with the patient and reviewed (39).

The issue of dietary fiber remains controversial. The systematic review of trials does not show a benefit over placebo but this may be related to whether the fiber was soluble or insoluble. There is also evidence that in IBS patients with diarrhea, bloating, urgency and pain that a low fiber diet may be beneficial, which includes avoidance of brown flour/wholemeal, brown rice, pasta, nuts, certain vegetables and fruits and other grains (40). Bulk-ing agents (such as guar gum and ispaghula, see below) may have a benefit but this was shown in only 4 of 13 trials. The typical American diet contains 11–13 Gms/day; the AGA recommends 20–35 Gms/day; an empiric trial is usually recommended starting at a low dose. In terms of mechanism of action, fiber may be helpful in C-IBS by the acceleration of oro-anal transit and increase in intracolonic pressures; this can occur as a direct effect or by binding of bile salts (41). Dietary fiber is found in plants (grains, vegetables, fruits, seeds, nuts and legumes) and consists of non-digestible carbohydrates and lignin. Fiber can also be divided into soluble (often thought of as “starches”) versus insoluble (usually tough skin, peel, pods, seeds) as shown in Table 8.

Generally, the recommendation in patients with functional constipation is to increase the patient’s bran (insoluble fiber) subsequently adding more fruits and vegetables in the diet if necessary, before a trial of soluble fiber. It is not clear whether the same treatment is helpful in C-IBS patients (because insoluble fiber can cause increased bloating, visceral hypersensitivity and the likelihood of increased pain) or whether soluble fiber should be used first (41).

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Table 6
Clinical conditions with symptoms which overlap those seen in IBS

1. Chronic pelvic pain syndrome (1)
2. Pelvic floor dysfunction (dyssynergia)
3. Gynecologic surgery (may precipitate onset IBS symptoms) (36)
4. Inflammatory bowel disease
5. Slow transit constipation (37)
6. Lactose intolerance (prevalence is 30% in US adults and in IBS patients) (8)
7. Functional anorectal disorders (ex: proctalgia fugax, levator ani syndrome)
8. Intestinal pseudo-obstruction
9. Eosinophilic gastroenteritis

Table 7
Common dietary trigger foods

- caffeine (in OTC drugs, coffee, tea, chocolate, sodas and some frozen desserts)
- excess fatty food
- excess fruit, sorbitol and fructose (especially in D-IBS)
- lactose, if implicated by symptoms (up to 30% of the U.S. adults are lactose intolerant and a 10–14 day trial of avoidance may be adequate “testing” for this problem)
- beans, uncooked broccoli, cabbage and cauliflower especially if bloating or flatulence are special concerns (there are multiple other foods also)
- carbonated beverages
- certain spices
Efficacy of medications used in treating IBS is summarized in Table 9 (42).

Table 10 reviews antispasmodic medications available and the doses used (39). Studies in animals and humans have shown that antispasmodics do relax gut smooth muscle by their action on opiate receptors, cholinergic receptors or calcium channels and by their effect on enteric neurons. Peppermint oil has also been used because of its calcium channel blockade features; it is used for abdominal pain in IBS (43).

Abdominal pain can be treated with the anti-spasmodics usually best given 30-60 minutes before meals if symptoms occur related to eating.

Serotonin receptor modulating drugs are the newest therapies for IBS. Serotonin functions as a neurotransmitter of sensorimotor function in the gut. The information regarding use of Tegaserod and Alosetron is predicated on evidence-based studies with a Recommendation Grade A (Table 9). Serotonin (5-hydroxytryptamine, 5-HT), seems to be the most important neurotransmitter in the enteric nervous system in visceral (gut) sensitization. The drugs available are:

5-HT3 Receptor Antagonists: Serotonin-3 receptors are activated by serotonin that is released in response to mucosal stimulation; their activation results in increased intestinal secretion, motility and sensation. The antagonists to this pathway result in a reduced gastrocolic reflex, a slowed colonic transit time and increased colon compliance as well as diminished sensitivity of the colon to distention. The physical results of these chemical changes is a decrease in urgency and diarrhea.

Alosetron (Lotronex) is currently the only available drug in this group and is recommended in “diarrhea-predominant” IBS. In studies thus far it appears to decrease abdominal pain, decrease fecal urgency and improve quality of life in these IBS patients; constipation occurs in 22%-39% of patients. One in 700 patients were found to develop ischemic colitis (although this remains controversial) from the drug and therefore it was withdrawn and then re-introduced with strict guidelines. It was
originally recommended only for use in women with severe diarrhea-predominant IBS but recent reports show response in men also (1).

**Partial 5-HT4 Receptor Agonists:** Peristalsis is activated by stimulation of the 5-HT4 receptors resulting in an increase in gastric emptying as well as small bowel and colonic motility. These drugs are similar to the pro-kinetic drug cisapride now removed from the market. **Tegaserod (Zelnorm)** is the only FDA-approved drug for use in “constipation-predominant” IBS and seems to benefit women more than men. All four trials of tegaserod showed statistically significant improvement in global IBS scores compared with placebo. The drug does not cross the blood brain barrier; the side effect profile is good mostly involving a transient self-limited diarrhea in ~10% patients. It is FDA approved at this time for 12 weeks of therapy. It’s use should be reserved for women with “constipation-predominant IBS” who have failed other therapy (1).

**Full 5-HT4 Receptor Agonists:** This group of drugs seems promising but is still being investigated. One drug in this group is prucalopride for constipation-predominant IBS. These drugs may also be useful for gastroparesis, pseudoobstruction, dyspepsia and gerd.

Traditionally the treatment of IBS has been symptom-based as no clear underlying etiology has yet been elucidated which can be specifically diagnosed. In addition to the interventions noted above medication treatment of these patients based on the predominant symptom is shown in Table 11 (modified from reference 3).
uous symptoms as they are given as a regular regimen rather than as needed for symptoms; a trial period of at least three-to-four months is recommended before they are discontinued. Tricyclic antidepressants are better than placebo at relieving global IBS symptoms as well as abdominal pain by ameliorating the enhanced pain perception these patients have; thus the patient has an overall improved sense of well-being. Side effects can include dry mouth, constipation, bladder and sexual dysfunction and dizziness; blurred vision and drowsiness can occur but generally resolve with time (1). The most commonly used medications in this category are:

- a. desipramine (50 mg daily)
- b. nortryptiline (10 mg daily)
- c. amitryptiline (10–25 mg daily)
- d. doxepin (75 mg daily)

The first two, desipramine and nortryptiline, have less anti-cholinergic side effects and either one probably should be tried initially.

**Probiotics** are a rather new and interesting group of alternative treatment regimens. These include live, microbial supplements for example, VSL#3. One study regarding probiotics showed a statistically significant normalization of the IL-10/IL-12 ratio, i.e. a reduction of the pro-inflammatory state and a decrease in IBS symptoms except bowel movement frequency and consistency, in patients taking Bifidobacterium infantis (44). Physicians should, however, conscientiously review all non-prescription medication preparations that the patient takes by asking them to bring them to the office to be sure they are safe and non-toxic.

Recent information shows good results with the use of the nonabsorbable oral antibiotic, “Rifaximin” in IBS. A total of 87 patients were evaluated in one double-blind, randomized, placebo-controlled study at two tertiary care centers; non-placebo patients received rifaximin 400 mg three times a day for ten days. Over ten weeks of follow-up the patients who had been treated with rifaximin had a statistically significant improvement in global IBS symptoms, including bloating. This therapy, however, is not yet considered standard of care and more studies are needed (45).

Other treatments for IBS include hypnotherapy, psychological management and alternative therapies. There is now evidence that **hypnotherapy** relieves symptoms attributable to IBS (pain, bowel habits, bloating) both in the short term as well as for up to about five years. In a study of over 200 patients, 81% had continued improvement in symptoms as well as quality of life and anxiety/depression scores which was statistically significant. The patients also reported using fewer medications and seeing their physicians less frequently after hypnotherapy (46).

In terms of **psychological therapy**, Creed, et al studied 257 patients and found that abdominal pain and psychological symptoms are independently associated with the quality of life in patients with IBS. More specifically, the quality of life issues can be described as follows:

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**Table 10**

<table>
<thead>
<tr>
<th>Brand Name (generic)</th>
<th>Recommended Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Single agents</strong></td>
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</tr>
<tr>
<td>Levsin SL (hyoscyamine)</td>
<td>0.125–0.25 mg SL every 4 hours as need</td>
</tr>
<tr>
<td>Levsinex ER</td>
<td>0.375–0.75 mg PO every 12 hours</td>
</tr>
<tr>
<td>Bentyl (dicyclomine)</td>
<td>10–20 mg PO QID</td>
</tr>
<tr>
<td>Robinul (glycopyrrolate)</td>
<td>1–2 mg PO TID; maintenance 1 mg BID</td>
</tr>
<tr>
<td>Clidinium bromide</td>
<td>2.5–5.0 mg PO QID, ac and hs</td>
</tr>
<tr>
<td><strong>Combined sedative and anti-spasmodics</strong></td>
<td></td>
</tr>
<tr>
<td>Donnatral (hyoscyamine/atropine/phenobarb/scopolamine)</td>
<td>0.1 mg/0.02 mg/16.2 mg/6.5 mcg: 1–2 tabs PO QID as need</td>
</tr>
<tr>
<td>Librax (clidinium/chlordiazepoxide)</td>
<td>2.5 mg/5 mg: 1–2 caps PO QID as need</td>
</tr>
</tbody>
</table>
Psychic well being: coping with problems, confidence, usefulness, security

Physical well being: sleep, energy, pain, feeling physically well

Mood: irritability, worrying, enjoyment of life, hopefulness

Locus of control: feeling in control of life, ability to make decisions

Social/relationship: relationship with partner and family, ability to maintain friendships, feeling wanted, inferiority, enjoyment of leisure (47)

Many other groups have looked at this issue and clearly a “holistic” approach, including possible psychological intervention for severe refractory cases, benefit these patients the most. It appears that psychological help improves not only psychological/social issues but also may help productivity at work, pain and physical activity (47). A meta-analysis reviewed 32 studies, 17 of which provided appropriate data, to look at these issues; the conclusion was that “psychological treatments are, as a class of interventions, effective in reducing symptoms compared with a pooled group of control conditions.” Therapies ranged from self-help groups to behavioral psychotherapy (48). On the whole the type of psychological intervention and treatment that IBS patients need generally can be offered by the patient’s primary care physician or gastroenterologist. Recognizing that these patients experience more anxiety, panic attacks and depression than others is the first step; behavioral therapy (by an interested physician or psychologist), learning stress-management skills and treating depression (with or without medications) follows.

It is estimated that 68% of all types of patients (not just IBS) will have tried at least one Complimentary/Alternative Medication during their lifetime. IBS patients not uncommonly seek alternative treatments for their symptoms as they become discouraged with their quality of life. These remedies include peppermint oil, ginger, aloe, artichoke leaf abstract, rhubarb, Chinese and Indian herbal preparations as well as acupuncture. Herbal preparations are usually safe if used appropriately but, unfortunately, there is no quality control in

(continued on page 39)
this area; it has been shown that Chinese herbal therapy may be more helpful than placebo as far as bowel symptom scores and global improvement (49).

**Acupuncture** has shown no improvement in quality of life compared to sham treatments for IBS patients and complications can include bleeding, infection and trauma to tissue. At this time no practical recommendations can be made using any of the alternative treatments and clearly more investigation into these forms of treatment for IBS is needed.

### SUMMARY

Arriving at the diagnosis of IBS can be a relief to patients who have been having chronic and sometimes frightening symptoms for a period of time. We, as gastroenterologists, need to present IBS as a “positive diagnosis” and then we must reassure the patient that there are therapies that can be tried to manage the symptoms they experience. It is important that patients understand that this is a chronic condition and that the goal is to find a therapeutic approach which will allow the patient to gain control of symptoms when they worsen. Establishing a communicative and trusting relationship with the patient during the evaluation can better assure compliance on the patient’s part as therapies are initiated and modified. Finally, patients need to understand that the diagnosis of IBS does not protect them from other gastrointestinal conditions and new symptoms will be assessed carefully if they occur.

### References


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