INTRODUCTION

The Irritable Bowel Syndrome (IBS) is a chronic gastrointestinal (GI) condition characterized by abdominal pain, bloating and disturbed defecation. IBS is one of a group of functional GI disorders in which abnormalities in motility, visceral sensation, and psychosocial factors interplay to cause symptoms. Over the past two decades, the scientific energy directed towards IBS has significantly enhanced our understanding of the epidemiology, clinical impact, pathophysiology, and management of this condition.

The prevalence of IBS in the United States and Britain is estimated to be 14%–24% in women and 5%–19% in men (1). IBS is responsible for 2.4–3.5 million physician visits per year and accounts for 12% of primary care visits and 28% of gastroenterological practice making it the most common reason for GI referral in the United States (2). Estimates of the total direct costs of IBS indicate that $1.3–8 billion are spent yearly in the United States on the condition (3–5).

Multiple guidelines regarding the diagnosis and treatment of IBS have been published and are undergoing continuous revision. The most recent clinical practice guideline for IBS published by the American Gastroenterological Association advocated a stepwise diagnostic approach which included the taking of an appropriate history, various laboratory tests, and colonic visualization to exclude organic diseases (6). This manuscript will review the available evidence addressing the diagnosis of IBS, as well as highlight the difficulties inherent to diagnosing a condition without definitive laboratory, radiologic, or endoscopic markers.

DIAGNOSIS OF IRRITABLE BOWEL SYNDROME

Multiple entities are associated with abdominal pain and irregular bowel habits (Table 1) including IBS, GI

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malignancies, endocrinologic disorders, inflammatory bowel diseases (IBD), enteric infections, and malabsorption syndromes. Historically, the diagnosis of IBS has been predicated upon the exclusion of organic GI disease. It is this approach that is the basis for most clinical guidelines regarding the diagnosis of IBS. As there are no reliable biochemical or structural markers for this condition, the diagnosis of IBS has relied upon the patient’s description of his/her abdominal and defecatory symptoms. Multiple symptom-based criteria for the diagnosis of IBS (Table 2) have been developed and include the Manning, Rome I, and Rome II criteria (7–9).

The Rome I and Rome II criteria, developed by multinational working groups, provide a structured framework for the selection of patients for inclusion in diagnostic and therapeutic trials of IBS (8–9). The Rome II definition for IBS requires at least 12 weeks (which need not be consecutive), in the preceding 12 months, of abdominal discomfort or pain that is accompanied by at least two of the following three symptoms: the abdominal discomfort or pain is a) relieved with defecation, b) associated with a change in the frequency of defecation, and/or c) associated with a change in the form or appearance of the stool. A critical adjunct to the use of symptom-based criteria is the exclusion of “alarm symptoms” or “red flags.” Such symptoms and signs include age >50 years old, unexplained weight loss, progressive or unrelenting pain, a family history of colon cancer, evidence of GI bleeding, or stool characteristics such as fasting, nocturnal or large volume (300 mL/day) diarrhea. The presence of such findings should alert the clinician to the need for a more extensive diagnostic evaluation to exclude an organic cause for the patient’s complaints. The exclusion of alarm symptoms should be part of the standard evaluation of patients with abdominal and defecatory symptoms, but their absence serves more to support rather than to establish the diagnosis of IBS.

### VALIDATION OF SYMPTOM-BASED DIAGNOSTIC CRITERIA

Of the commonly used symptom-based criteria for the diagnosis of IBS, the Manning criteria have been the most extensively studied. The positive predictive value (PPV) of the Manning criteria for the diagnosis of IBS has ranged between 65%–75%, depending upon the number of symptoms present and the number of symptoms included for analysis (in the original Manning study, four of six criteria reached statistical significance as predictors of IBS, while two others

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Table 2
Symptom-Based Criteria for the Diagnosis of IBS

<table>
<thead>
<tr>
<th>Manning Criteria</th>
<th>Rome Criteria</th>
<th>Rome II Criteria</th>
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<tbody>
<tr>
<td>Abdominal pain relieved by defecation</td>
<td>At least 12 weeks of continuous or recurrent symptoms of the following:</td>
<td>At least 12 weeks, which need not be consecutive, in the preceding 12 months of abdominal discomfort or pain that has two of the three features:</td>
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<tr>
<td>Looser stools with the onset of pain</td>
<td>Abdominal pain or discomfort: (1) relieved with defecation, or (2) associated with a change in frequency of stool, or (3) associated with a change in consistency of stool</td>
<td>Relieved with defecation and/or</td>
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<tr>
<td>More frequent stools with the onset of pain</td>
<td>Two or more of the following, at least on one fourth of occasions or days: (1) Altered stool frequency, or (2) Altered stool form, or (3) Altered stool passage, or (4) Passage of mucous, or (5) Bloating or feeling of abdominal distention</td>
<td>Onset associated with a change in frequency of stool and/or</td>
</tr>
<tr>
<td>Abdominal distension</td>
<td></td>
<td>Onset associated with a change in form (appearance) of stool.</td>
</tr>
<tr>
<td>Passage of mucus in stools</td>
<td></td>
<td></td>
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<tr>
<td>Sensation of incomplete evacuation</td>
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approached statistical significance). Studies suggest that the Manning criteria may better differentiate between IBS patients and healthy controls as opposed to patients with organic GI diseases. There is also evidence to suggest that the Manning criteria may only be valid in females with IBS.

In an attempt to build upon the strengths, while limiting the weaknesses of the Manning criteria, the Rome I criteria were developed largely through expert consensus. The Rome I criteria have been less extensively studied than the Manning criteria. In one trial that evaluated the diagnostic accuracy of the Rome I criteria in the absence of “red flag” symptoms, the sensitivity was 65%, specificity 100%, and PPV 98% in distinguishing between IBS and organic disease (11). The Rome II criteria have not been formally validated, but have been compared to the Manning and Rome I criteria in a number of studies. These studies have reported reasonably good agreement between the different symptom-based criteria with kappa values of about 0.70 (12–14). From these studies it appears that the Rome II criteria may be less sensitive than the Manning or Rome I criteria. This may be at least in part related to the rather restrictive temporal pain requirement of Rome II. A recent study found that lib-
eralizing the temporal pain requirement significantly improves the sensitivity of Rome II (15). What does all this mean to the clinician? If a patient fulfills the Rome II criteria and there are no alarm symptoms, the clinician can feel assured of the diagnosis of IBS. On the other hand, failure to fulfill the Rome II criteria does not definitively exclude a functional etiology as the basis for a patient’s complaints.

THE IMPLICATIONS OF MAKING A POSITIVE DIAGNOSIS OF IBS

It is important for patients and physicians to feel confident about the diagnosis of IBS. It is clear that a lack of confidence regarding this diagnosis influences the ordering of diagnostic tests and empiric therapies which in many cases are unnecessary. The study by Vanner et al, determined that once the diagnosis of IBS was established through application of the Rome I criteria and the absence of “red flag” symptoms, it did not require change through two years of subsequent follow-up (11). A similar analysis by Owens and colleagues demonstrated the stability of the diagnosis of IBS (based upon retrospective application of the Rome I criteria) over a 30-year period of follow-up (16). Thus, once the diagnosis of IBS is established through the application of symptom-based criteria and the exclusion of “alarm or red flag” symptoms, the clinician can feel confident about the accuracy and durability of the diagnosis. Armed with a confident diagnosis, the clinician has an opportunity to decrease health care utilization and associated costs by avoiding potentially unnecessary diagnostic tests.

REVIEW OF DIAGNOSTIC TESTING IN IBS

The American Gastroenterological Association (AGA) practice guidelines for IBS recommend that a physical examination be performed in patients with suspected IBS, primarily to help rule out organic disease. The presence of abdominal pain on palpation is common in patients with IBS. Unfortunately, this finding is nonspecific in the absence of severe localizing tenderness, an abdominal mass, or hernia. Perhaps the most important element of the physical examination, particularly in patients with defecatory complaints, is the digital rectal examination. In addition to checking for the presence of fecal occult blood, an evaluation for sphincter dysfunction, pelvic floor dysfunction, or rectal prolapse can be undertaken. The guidelines further recommend the performance of a complete blood count (CBC), erythrocyte sedimentation rate (ESR), serum chemistries, stool examination for ova and parasites (O&P), and fecal occult blood testing (FOBT). Colonic visualization with flexible sigmoidoscopy, barium enema, or colonoscopy (if the patient is older than 50 years of age) is also recommended (6). Other experts recommend the use of hydrogen breath tests and thyroid function testing to rule out lactose malabsorption and thyroid dysfunction, respectively (17,18). The degree to which these additional tests add to the diagnostic certainty of IBS, as established by validated symptom-based criteria such as the Manning or Rome I/II criteria, is unknown.

Clinicians should consider several issues when deciding if a diagnostic test is needed. First, they should consider the pre-test probability of the disorder based upon the known prevalence of the disorder in patients with specific symptoms. If the pre-test probability of a disorder is very low, then further diagnostic tests may not be necessary (19). Second, clinicians should consider the accuracy (e.g., sensitivity, specificity, positive and negative predictive value) of the diagnostic test if the pre-test probability of a disorder is high enough to warrant investigation. In an effort to delineate the utility of diagnostic tests commonly obtained as part of the evaluation of IBS, a literature search of trials investigating various testing modalities in patients positively diagnosed with IBS (based upon explicit fulfillment of symptom based criteria) was undertaken (Table 3).

Structural Colonic Evaluations

Several studies (20–23) have systematically evaluated the structure of the colon in patients with suspected IBS. Hamm examined flexible sigmoidoscopy, colonoscopy, or barium enema in patients fulfilling the Rome I criteria (20). Of the 306 patients evaluated, four were given alternative diagnoses (3 IBD, 1 colonic obstruction) which may have been responsible for their GI symptoms. Tolliver performed a similar analysis in 196 patients with suspected IBS (21). Of
the 42 abnormalities identified, only two patients were found to have organic diseases (1 IBD, 1 cancer) that could have been potential causes of GI symptoms. The remainder of the abnormalities in these patients consisted of benign polyps, diverticulosis, hemorrhoids, lipomata, and melanosis coli.

MacIntosh evaluated flexible sigmoidoscopy in patients with suspected IBS and in non-IBS controls (22). Among the IBS cohort, 84% fulfilled the Rome I criteria, while only 5% of the controls fulfilled the Rome I criteria. No patients with IBS were given alternative diagnoses based upon results of their flexible sigmoidoscopy. Francis and colleagues evaluated 125 patients who fulfilled the Rome I criteria with flexible sigmoidoscopy, barium enema, or colonoscopy (23). No organic gastrointestinal disorders were identified and no patients were given alternative diagnoses to explain their gastrointestinal symptoms as a result of these examinations.

Only one study has evaluated the use of rectal biopsies as part of the evaluation of IBS (22). No patients from among a group of 89 patients with suspected IBS or 59 non-IBS controls had rectal biopsy findings that resulted in an alternative or additional organic GI diagnosis.

### Laboratory Evaluations

Several reports (20,21,24) have examined the use of commonly recommended laboratory tests such as CBC, serum chemistries, and fecal occult blood testing (FOBT) as part of the diagnostic evaluation of IBS. In the trial by Tolliver, CBC and serum chemistries were performed in 196 patients with suspected IBS (21). In no patient did the results of the CBC lead to an alternative diagnosis of organic GI disease. Serum chemistries were abnormal in two patients (1.0%). Both subjects had abnormal liver associated enzymes of unknown eti-
ology, so it is unclear whether or not they were the consequence of an alternative GI diagnosis.

Sanders and colleagues evaluated the use of CBC and serum chemistries in 300 patients who fulfilled the Rome II criteria for IBS (24). They identified five patients (1.67%) who had organic GI disease. One patient was anemic and later found to have celiac disease and two patients had abnormal liver associated enzymes that were attributed to excess alcohol intake. Two patients with elevated CRP, one also with an elevated ESR, were found to have inflammatory bowel disease. These investigators also performed antigliadin antibody (IgA and IgG) and endomysial antibody (EMA) testing. Upper endoscopy and duodenal biopsies were performed in those with positive antibody tests. Sixty-six patients (22%) with suspected IBS had positive antibody tests and 14 (4.67%) had histologic evidence of celiac disease compared to two (0.67%) gender-matched, asymptomatic controls. The effect of a gluten-free diet upon the GI symptoms of patients diagnosed with celiac disease was not reported in this study. In addition, this single study was reported from a referral setting in a relatively homogeneous population. Another recent study in a small group of patients with suspected IBS and negative serological tests for celiac disease identified immunological markers for celiac disease in duodenal aspirates (25). The results of these interesting studies require replication in the US prior to recommending routine testing for celiac disease in IBS patients.

The study by Tolliver also examined the use of FOBT in patients with suspected IBS (21). Fifteen out of 183 patients (8.2%) had a positive FOBT and subsequently underwent full colonoscopic examination. Four of the 15 with positive FOBT, or 2.2% of the original cohort, had structural abnormalities identified during colonoscopy which were not felt to provide an explanation for the patients’ IBS symptoms.

Two studies have evaluated the role of TSH as part of the evaluation of IBS. Hamm tested TSH in over 1200 patients fulfilling the Rome I criteria and identified 67 patients (6%), with abnormalities (20). It was not clear whether these thyroid abnormalities were responsible for the patients’ GI symptoms since symptom response following correction of thyroid function was not reported. Tolliver identified 1 of 171 patients (0.6%) with an abnormal TSH (21). The nature of the thyroid dysfunction was not reported, nor was the impact of therapy upon GI symptoms. It is important to put this data in perspective as thyroid function test abnormalities are common in the general population with a reported prevalence of 5%–9% (26).

**Stool Analysis for Ova and Parasites (O&P)**

Two trials have evaluated the results of stool O&P examination in patients with suspected IBS. Hamm found that 19 of 1154 patients (1.7%) had evidence of an intestinal pathogen on stool O&P examination. Of these 19 subjects, eight (0.69%) were colonized with *Blastocystis hominis*, a relatively common finding of unclear clinical significance (20). Clinical outcomes following eradication of the identified pathogens were not reported. Likewise, Tolliver performed stool O&P examinations in 170 patients with suspected IBS and found no subjects with enteric infection (21).

**Hydrogen Breath Testing**

The prevalence of lactose malabsorption is estimated to be approximately 25% in western countries and as high as 75% in those of African or Asian descent (27,28). Two trials have reported the results of hydrogen breath testing for lactose malabsorption in patients with suspected IBS (20,21). One trial found that 23% (256/1122) of patients demonstrated impaired lactose absorption on the basis of lactose hydrogen breath testing (20). Response to a lactose free diet was not reported, so it is impossible to determine whether the lactose malabsorption was responsible for the patient’s GI symptoms. In another study, 186 patients with suspected IBS were evaluated with lactose hydrogen breath testing (21). These investigators found a similar prevalence of lactose malabsorption with 25.8% (48/186) having abnormal test results. In a subsequent publication, reflecting three years of follow-up, these investigators demonstrated that patients with IBS and lactose malabsorption who were placed on a lactose restricted diet did not differ with regards to their GI symptoms when compared to IBS patients without evidence of lactose malabsorption (29).

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Pimentel performed lactulose hydrogen breath testing in 202 patients fulfilling the Rome I criteria referred for evaluation of possible small intestinal bacterial overgrowth (SIBO) (30). Seventy-eight percent (157/202) had abnormal breath test results and were treated with a 10-day course of antibiotics. Forty-seven of 157 patients (29.9%) with an abnormal breath test result were restudied after antibiotic therapy and 25 (53.2%) had a negative follow-up study. Twelve patients (48%) with SIBO eradication, compared to four patients (18.2%) with evidence of persistent SIBO, achieved symptom improvement. The results of this study should be viewed with caution given a number of serious methodological flaws including a biased study population, lack of blinding, use of a test that is neither sensitive or specific for SIBO, and follow-up testing in fewer than half of the study cohort. Recently, the same investigators have reported that treatment of SIBO in patients with suspected IBS (unknown diagnostic criteria) with neomycin resulted in significant improvements in composite IBS symptoms and bowel habits (31). The potential role of bacterial overgrowth in the subset of patients with suspected SIBO deserves further study.

**Imaging Studies**

Francis and colleagues evaluated the role of abdominal ultrasound in 125 patients (100 women, 25 men) with suspected IBS by the Rome I criteria (23). Twenty percent of women and 8% of men had an abnormality on ultrasound examination. Ten percent of women had pelvic abnormalities, the majority of which were gynecologic in origin. The prevalence of hepatobiliary abnormalities was similar in women and men (10% and 8%, respectively). Importantly, the identification of an anatomic abnormality on ultrasound did not lead to additional therapeutic measures in any patient, nor were the authors able to correlate any of the abnormalities identified to the patients’ GI symptoms. These investigators concluded that abdominal ultrasound in patients fulfilling a symptom-based diagnosis of IBS was unnecessary and may actually be counterproductive since the identification of trivial anatomic abnormalities could conceivably lead to unnecessary patient concern and additional, more invasive tests or procedures.

### Table 4

<table>
<thead>
<tr>
<th>Organic GI Disease</th>
<th>IBS Patients (Pre-test probability)</th>
<th>General Population (Prevalence)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colitis/IBD</td>
<td>0.51–0.98%</td>
<td>0.3–1.2%</td>
</tr>
<tr>
<td>Colorectal Cancer</td>
<td>0–0.51%</td>
<td>4–6%</td>
</tr>
<tr>
<td>Celiac disease</td>
<td>4.67%</td>
<td>0.25–0.5%</td>
</tr>
<tr>
<td>Gastrointestinal Infection</td>
<td>0–1.7%</td>
<td>N/A</td>
</tr>
<tr>
<td>Thyroid dysfunction</td>
<td>6%</td>
<td>5–9%</td>
</tr>
<tr>
<td>Lactose Malabsorption</td>
<td>22–26%</td>
<td>25%</td>
</tr>
</tbody>
</table>

**CONCLUSION**

Patients that fulfill accepted symptom-based criteria and do not have warning signs can be confidently diagnosed with IBS. Based upon review of the available literature, it appears that the diagnostic tests currently recommended to evaluate patients with suspected IBS are no more likely to identify significant organic GI disease than would be expected in the general population (Table 4). One possible exception may be celiac disease based upon a single study from the UK. The role of SIBO as a cause of symptoms in a subset of patients with IBS also deserves further study. Several caveats should be considered when interpreting this data. Due to their design, many of the trials that did identify organic disease in patients with suspected IBS were unable to confirm that the identified conditions were responsible for patients’ GI symptoms. In addition, nearly all of the available studies were from secondary or tertiary referral centers, so to generalize these results to patients in primary care remains unclear. From a pragmatic standpoint, the clinician often uses diagnostic testing to provide reassurance to the patient as much as to actually rule out organic disease. Other factors including concerns about the medical-legal ramifications of “missing” a diagnosis also influence the ordering of diagnostic tests. It may be both unrealistic and unnecessary to recommend a rou-
tine series of diagnostic tests in patients with a heterogeneous group of disorders like IBS. However, before being able to draw this conclusion, we need data from well designed clinical trials to help us to decide upon the most appropriate evaluation for patients with suspected IBS.

References
14. Martin P, Badia X, Balboa A, et al. Irritable bowel syndrome prevalence varies enormously depending upon the employed diagnostic criteria: comparison of Rome II versus previous crite-