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Irritable Bowel Syndrome: How Far Do You Go in the Workup?

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The diagnostic evaluation of patients with irritable bowel syndrome (IBS) can be challenging for several reasons. First, there is no biological marker for the disorder. The diagnosis is based primarily on the presence of a clustered set of symptoms relating to abdominal pain or discomfort and altered bowel habit. Second, it follows that a diagnosis based solely on symptoms can be unsettling; clinicians will struggle with the possibility of missing another diagnosis. This level of uncertainty may increase the risk of overdoing diagnostic studies, though many clinicians believe an extensive diagnostic effort justified: it seeks to satisfy the patient's request to and a specific diagnosis, as well as the physician's personal interest to ‚leave no stone unturned.' Unfortunately, this approach contributes to the disproportionately high health care costs for IBS relative to other gastrointestinal disorders as reported in one Health Maintenance Organization study.1 Finally, developing a diagnostic algorithm for IBS can be challenging given the effect of daily and life stress, and other psychosocial factors on IBS.2 Currently, the diagnostic evaluation of patients presenting with IBS symptoms has no simple standard; it is based on the art and science of medicine. Several factors can influence the decision making: (1) symptom pattern and severity will influence, for example, whether biopsies are taken for diarrhea-predominant symptoms, or ultrasound or computerized tomography (CT Scans) are done for pain and weight loss,3 (2) features such as older age on initial presentation or a family history of inflammatory bowel disease or colon cancer may lead to a more extensive (e.g., colonoscopic) evaluation, (3) a patient's pain communication style must be appraised in the light of objective screening data; this, for example, will reduce the tendency for physicians merely to order tests based on urgent requests to ‚do something' (furor medicus'),4 and finally (4), the clinical setting will influence the probability of other medical disorders; so primary care physicians more than gastroenterologists will minimize diagnostic studies, treat the symptoms of IBS and follow the patient expectantly,5 simply because the likelihood of another serious medical disease in a primary care setting is far less than in a referral practice. Efforts to consolidate these many influences on diagnostic decision making have occurred by creating specific published guidelines obtained by consensus.3,6,7 Most authors agree that an initial diagnosis of IBS should be fulfilled by: (a) meeting symptom-based diagnostic criteria, such as Rome II6,8 criteria, (b) obtaining a negative physical examination, and (c) performing a cost-effective, conservative set of screening studies. These usually include a sigmoidoscopy (or colonoscopy for patients older than 50 years), a few laboratory tests (e.g., complete blood count, stool for occult blood or ova and parasites), and additional studies if certain ‚alarm' features are found: fever, an abnormal physical examination, blood in the stool, an abnormal complete blood count or elevated sedimentation rate, significant weight loss, nocturnal symptoms that awaken the

patient, or a family history of cancer or inflammatory bowel disease.12,13 Several prospective studies now offer evidence that the proper application of such, recommendations rarely leads to a revision in diagnosis, even for patients observed over many years.6,14,15

In one study, the positive predictive value for the diagnosis of IBS using Rome I criteria and excluding ‚red flags' over 1-year follow-up was 98%.12 Of course, the gastroenterologist in referral practice may not be content to accept these probabilities without first excluding those rare conditions overlooked by routine evaluations. So how far should the gastroenterologist go in the workup of patients referred to them who typically present with IBS and have negative screening studies? One gastroenterologist recently commented to me: 'I order breath hydrogen studies and blood tests for celiac sprue on all my patients referred with IBS. No doubt this comment reflects the concern that referral gastroenterologists have an obligation to contribute additional expertise to the diagnostic effort. Recently, the breath H2 test is being requested more actively by physicians and the public alike, possibly because of media attention to a study claiming a 73% rare of bacterial overgrowth in patients with IBS referred for breath H2 testing, and a 50% improvement with antibiotic treatment.16 However, the design limitations of this study, including a high referral bias, use of an uncontrolled and unblinded treatment protocol, and only a 30% follow-up rate evaluated over a relatively short period of time, make it unlikely that clinicians in practice will also obtain such dramatic results. So although this study increases awareness of bacterial overgrowth as an entity that can mimic or exacerbate IBS, clinical experience suggests that the diagnostic yield in general gastrointestinal practice is probably much lower than reported, perhaps 10% or less.

What about celiac disease? This disorder should always be considered in evaluating IBS because the diarrhea and abdominal discomfort caused by this intestinal disease will specifically respond to a glutenfree diet. Therefore, making a diagnosis early may be cost-effective. The prevalence of celiac disease in the United States is reported to range from 1:250 to 1:1500.17 However, this is influenced by the method of assessment as well as the probability of the disorder being present in the population under study. With regard to the method of assessment, in a study set in Olmstead County,18 the reported prevalence was 1:4600, and the cases were identified by clinical and pathologic criteria. In contrast, when blood tests are used for diarrhea, the prevalence is at 1:250 or even higher,19 and in one recent study, the prevalence for women was 1:125 compared with males at 1:250.20 So, when clinically suspected, primary care physicians and specialists may now obtain anti-gliadin and anti-endomysial IgA antibody serologies. These are reasonably effective screening tests, given that the sensitivities and positive predictive values range from 90%—l00%.17 However, in populations in which the prevalence of this disorder is low, many positive serologic tests will be false positives. Therefore, because the gold standard of diagnosis requires upper endoscopy with duodenal biopsy, endoscopy is almost always needed for confirmation of the diagnosis. Recently there is considerable research being done to reduce the cost of unneeded diagnostic studies. The use of simple ‚Red Flags' or ‚Alarm Signs' based on the medical history or simple screenings and blood tests are examples. There are also more sensitive tests of intestinal inflammation Calprotectin) that can be recommended from the stool and can exclude inflammatory bowel disease (ref – Tribble). Is it possible that some simple and inexpensive tests will emerge to accurately diagnose IBS? I do not think that IBS can by diagnosed by ordering tests, either to make a unitary diagnosis, or by default by excluding other disorders. There is evidence that IBS is a heterogeneous disorder in which different physiologic sub groups contribute to the clinical expression of the syndrome. For example, there is a subgroup of patients, called ‚post-infectious IBS' who appear to respond to an enteric infection such as *cawpylobactor jejuni* with an increased inflammatory cell response.22 This is associated with activating enterochromaffin cells to produce 5HT, and CD3 cells to produce cytokines, which in turn leads to enhanced motility and lowered visceral sensation thresholds.22,23 But microscopic inflammation cannot be a diagnostic marker for IBS because it does nor typically produce pain in those who have it. All patients with active celiac disease

have microscopic inflammation, but a large proportion do not have abdominal pain, and patients with ulcerative colitis who also have microscopic inflammation when compared with patients with IBS seem

to have higher pain thresholds.24 In individuals with these disorders, there may be central nervous system counter-regulatory measures responding to the peripheral pain/inflammatory processes that increase pain thresholds. With regard to IBS, the gut-related effects of microscopic inflammation may be only one component of a dysfunctional brain-gut system. In addition, and often in response to stress, there may be a failure to activate pain inhibition systems that lead to the perception of pain and produce other symptoms that typify this disorder.25 In one prospective study of post-infectious IBS, it was found that those who retained their symptoms 3 months after an enteric infection had not only increased inflammation in the intestinal lining, but also had increased psychosocial distress at the time of the infection. Furthermore, lowered visceral pain thresholds and increased motility were present after the infection regardless of whether or not the patients retained their symptoms.26 Therefore, the microscopic inflammation and its physiologic effects on motility and sensation contribute to, but are not always sufficient for, the clinical expression of IBS pain. At least for postinfectious IBS, this provides some evidence that psychologic distress alters brain pain regulatory pathways to amplify incoming visceral signals leading to the full clinical expression of this syndrome.27,28 Recent studies using brain imaging29,30 may help us to understand the physiologic mechanisms that modulate these central nervous system responses to pain, and in the process, identify the subgroup with IBS that are more amenable to psychologic and psychopharmacological treatments.

As we continue to develop the means to assess the pathophysiological determinants of IBS symptoms, we will identify subgroups that will change our diagnostic assessment. This may even lead us to redefine what we mean by IBS. Postinfectious IBS and patients having concurrent psychosocial disturbances (among others to be determined) characterize subgroups that will be more responsive to more specific treatments. For the present, we must still make a diagnosis of IBS based on established guidelines, including symptom-based (e.g., Rome) criteria. We must also remain vigilant to identifying other relevant disorders like celiac disease that may mimic or exacerbate IBS, and will use clinical judgment (e.g., ordering anti-endomysial antibodies for patients with predominant diarrhea), rather than routinely ordering tests in all IBS patients just to exclude other disease. With careful appraisal of the historical and laboratory data and good clinical judgment, a positive diagnosis of IBS can be made in a cost-effective manner and with confidence.

References

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