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GUT INSTINCTS: MY PERSPECTIVE

Evolution of the Diagnosis of Functional Gut Disorders: Is an Objective Positive Diagnostic Approach Within Reach?

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Irritable bowel syndrome (IBS) is a chronic painful condition that often seriously impairs life, work, and relationships.[1] Accurate diagnosis is important to save patients from unnecessary and costly investigations. Tests including colonoscopy even if negative have been documented to fail to reassure patients with IBS.[2] The Rome criteria were developed by consensus to provide diagnostic criteria for research and help clinicians make a positive diagnosis of IBS in practice rather than test and then make a diagnosis of exclusion.[3] How did these criteria come about? Are the criteria useful and used in practice? Does a positive diagnosis based on symptom assessment reassure patients? In the future, will objective testing become available to positively diagnose IBS? Let us see what the literature can tell us.

The Rome criteria arose from a landmark UK study by Grant Thompson and Ken Heaton, with the first author (a GI Fellow at the time) named Adrian Manning (and now famously referred to as the Manning criteria, which just shows you publishing even one paper as a trainee can sometimes change a field!).[4] In a clinic, a questionnaire was filled in by patients presenting with abdominal pain or bowel disturbance or both; 17–26 months after the visit all had their tests and clinical diagnoses reviewed and were then divided by the investigators into those with IBS (relevant tests negative) or organic disease. Six key questions appeared to discriminate IBS from organic gastrointestinal (GI) disease, although two items were of borderline significance (Table 1). The findings have been very widely referenced and discussed (the paper is a classic having been cited 1,449 times according to Google Scholar by March 2015). Subsequent studies provided empiric support for the initial findings and suggested the more items present, the better the discrimination.[5]

The next major piece of the puzzle was filled in by Wolfgang Kruis from Germany;[6] he showed that a limited number of symptoms and few simple non-invasive tests were useful to discriminate IBS from organic disease, although he did not include the Manning criteria is the symptom list (Table 2).

Around the same time, a leading Italian gastroenterologist Aldo Torsli set up a Working Team on IBS and he asked Grant Thompson to chair it. Following this successful process, Doug Drossman was invited to chair a new working team to address diagnostic criteria for all the functional GI disorders. A distinguished group of investigators was brought to Rome to be locked in a room to devise criteria not only for IBS but also for functional dyspepsia and other conditions, including Drossman, Thompson, and the author (although he was a very young gun at the time). A Delphi process was applied; the available evidence was reviewed and hotly debated until consensus was reached (otherwise you might never leave Rome), and it proved to be surprisingly robust. Hence was born the Rome I criteria, which have now gone through four iterations with Rome IV to be published in 2016.[3]

The current Rome III criteria[3] rely on a history of abdominal pain or discomfort then a positive reply to at least two of the three questions:

If yes:

Have you had abdominal pain or discomfort (at least 3 days per month) in the last 3 months?

(1) Is the pain improved by defecation?
(2) Is the onset of pain associated with a change in stool frequency?
(3) Is the onset of pain associated with a change in stool appearance?

The onset of symptoms should have been 6 months ago (or longer). You can see the criteria are easy to remember.

The Rome criteria were developed for research but have been recommended for clinical practice.[3] Specialists have embraced them more widely than primary care where the uptake has been low.[1] Although red flags or alarm features such as weight loss, GI bleeding, or anemia are not part of the Rome criteria as negative predictors (as Kruis pioneered), experts have suggested that the presence of such features should prompt investigation before applying a firm label, although the positive predictive value of alarm features is documented to be low (i.e., most patients with alarm features and positive Rome criteria do not have serious organic

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Table 1 Manning criteria for IBS, based on a 15 item questionnaire filled in by unselected patients referred to gastroenterology or surgery clinics with abdominal pain or a change in bowel habit or both (three or more for a positive diagnosis although thresholds have varied):

1. More frequent bowel movements associated with onset of pain
2. Looser stools associated with onset of pain
3. Pain relieved by defecation
4. Visible abdominal distension
5. Sensation of incomplete evacuation[a]
6. Mucus per rectum[a]

[a]Borderline significance in original study.

Table 2 Kruis criteria for IBS (score > 44 = IBS)

Pain, flatulence, or bowel irregularity	34
Duration of symptoms > 2 years	16
Description of abdominal pain (burning to "not so bad")	23
Alternating diarrhea and constipation	14
Red flags	
Abnormal physical findings or history pathognomonic other disease	– 47
ESR > 10 mm/h	– 13
WBC > $\times 10^9$	– 50
Anemia	– 98
History of blood in stool	–98

ESR, erythrocyte sedimentation rate; IBS, irritable bowel syndrome; WBC, white blood cell.

disease like cancer).[7] Other limitations of the Rome criteria have become apparent.[1] Positive Rome criteria do not distinguish IBS from celiac disease or microscopic colitis; celiac disease can mimic not only IBS with diarrhea but also IBS with constipation.[8] Ovarian cancer is rare but can cause IBS-like symptoms especially constipation and bloating. Inflammatory bowel disease (IBD) early in its onset is recognized to often be misdiagnosed as IBS (and IBS symptoms occur in documented IBD in remission).[9] Colon cancer is a feared misdiagnosis but in younger patients (under age 50) with no family history is rare. Bile acid malabsorption may explain one in four with IBS and diarrhea.[8] At best, current Rome III criteria identify patients with IBS with only modest sensitivity and specificity, below what many might consider best practice thresholds.[10] Even experts suggest that you can not rely on symptoms alone; a recent review recommended a few simple tests (e.g., blood count and celiac disease screening) should be ordered in patients with positive Rome criteria.[8]

Is a diagnosis by old-fashioned history taking reassuring? There is limited evidence that a positive diagnosis based on only symptoms leads to positive outcomes. For example, a positive physician–patient interaction has been linked to significantly fewer return visits for IBS.[11] However, randomized controlled trial evidence is lacking. On the other hand, colonoscopy fails by itself to reassure IBS patients based on the limited available evidence.[2]

So, if symptoms are not optimal and a diagnosis of exclusion is suboptimal, will it be possible to diagnose IBS positively by objective testing in the future? The answer here may be yes particularly as we begin to understand that IBS is not one disease but many, and the pathogenesis varies.[12] For example, infection is likely a cause in some cases, whereas others may result from dysbiosis;[13] genes likely account at least for a few.[14] Promising approaches testing stool or blood for immune activation, subtle inflammation or infection, and genes or protein products are exciting and may revolutionize our approach.[12,15,16] For example, chromogranin in stool appeared to be a possible biomarker for IBS vs. healthy controls, although this marker is also positive in celiac and other diseases.[16] Biopsy markers of disease may also change practice in the future.[17]

A positive diagnosis of IBS currently relies on you taking a good history, undertaking a targeted physical, screening for possible alarm features, and remembering the Rome criteria (and using them to make a positive diagnosis). Just do it! You willl uncommonly be wrong (and even if you are, the patient will usually be pleased with your excellent care). A positive diagnosis helps patients; even if you plan testing to rule out organic disease, advising the patient that in your opinion she or he probably has IBS will likely optimize their outcome and satisfaction with your care.

CONFLICT OF INTEREST

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