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EDITORIAL

Relationship of functional gastrointestinal disorders and psychiatric disorders: Implications for treatment

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Abstract

This article revisits the links between psychopathology and functional gastrointestinal disorders such as irritable bowel syndrome (IBS), discusses the rational use of antidepressants as well as non-pharmacological approaches to the management of IBS, and suggests guidelines for the treatment of IBS based on an interdisciplinary perspective from the present state of knowledge. Relevant published literature on psychiatric disorders, especially somatization disorder, in the context of IBS, and literature providing direction for management is reviewed, and new directions are provided from findings in the literature. IBS is a heterogeneous syndrome with various potential mechanisms responsible for its clinical presentations. IBS is typically complicated with psychiatric issues, unexplained symptoms, and functional syndromes in other organ systems. Most IBS patients have multiple complaints without demonstrated cause, and that these symptoms can involve systems other than the intestine, e.g. bones and joints (fibromyalgia, temporomandibular joint syndrome), heart (non-cardiac chest pain), vascular (post-menopausal syndrome), and brain (anxiety, depression). Most IBS patients do not have psychiatric illness per se, but a range of psychoform (psychological complaints in the absence of psychiatric disorder) symptoms that accompany their somatoform (physical symptoms in the absence of medical disorder) complaints. It is not correct to label IBS patients as psychiatric patients (except those more difficult patients with true somatization disorder). One mode of treatment is unlikely to be universally effective or to resolve most symptoms. The techniques of psychotherapy or cognitive-behavioral therapy can allow IBS patients to cope more readily with their illness. Specific episodes of depressive or anxiety disorders

can be managed as appropriate for those conditions. Medications designed to improve anxiety or depression are not uniformly useful for psychiatric complaints in IBS, because the psychoform symptoms that sound similar to those seen in psychiatric disorders may not have the same significance in patients with IBS.

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Key words: Irritable bowel syndrome; Functional disorders; Gastrointestinal disease; Somatization disorder; Somatoform; Psychoform; Psychotropic medication; Psychotherapy; Symptoms; Psychiatric disorder

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INTRODUCTION

Functional medical disorders, by definition, lack objective physical, metabolic, or neurological explanations for their symptom presentations. Diagnosis of these disorders, like diagnosis of psychiatric disorders, is based entirely on subjective complaints. This may have contributed to longstanding conceptualizations of functional disorders as fundamentally psychiatric or psychological in origin, cloaking this class of disorders with a negative stigma. Although irritable bowel syndrome (IBS) may be considered an archetype among the functional gastrointestinal disorders, a wide variety of medical syndromes and disorders in many medical subspecialties are also characterized by lack of objective indicators and subjective determination of diagnosis. Non-ulcer dyspepsia, premenstrual syndrome, chronic pain syndromes, tension headaches, fibromyalgia, chronic fatigue syndrome, interstitial cystitis, reflex sympathetic dystrophy, temporomandibular joint syndrome, and various chemical and food sensitivities are examples of functional disorders in many organ systems.

Despite longstanding assumptions about psychiatric origins of functional disorders, few gastroenterologists as recently as 15 years ago used psychopharmacologic agents to treat functional gastrointestinal disorders. Clouse and Lustman^[1] observed that recognition of the utility of antidepressant agents for functional disorders, especially

IBS, precipitated a rise in the use of antidepressants in treatment of functional gastrointestinal disorders. Now, in 2007, the treatment of these disorders with antidepressants by gastroenterologists is quite common, and as many as one in eight patients with these disorders are offered psychopharmacological agents.

Recently increasing application of psychopharmacotherapy for functional gastrointestinal disorders has further confused clinicians trying to manage these poorly understood functional syndromes with historical biases toward assumptions of psychiatric origins. The use and effectiveness of antidepressants may further solidify long-held beliefs that functional gastrointestinal disorders are really psychiatric. The well-known association of psychiatric illness and functional gastrointestinal disorders further contributes to assumptions of psychopathology inherent in these disorders.

This article revisits the links between psychopathology and functional gastrointestinal disorders such as IBS and will discuss the rational use of antidepressants as well as non-pharmacological approaches such as psychotherapy and psychoeducational/behavioral approaches in the management of IBS. This article will also suggest guidelines for the treatment of IBS from an interdisciplinary (psychology, psychiatry, and gastrointestinal/internal medicine) perspective based on the present state of knowledge.

THE PSYCHIATRIC ANGLE

Psychiatric disorders are prevalent in medical practice, especially in primary care, where as many as one-third of patients may suffer from one or more current diagnosable psychiatric disorders, especially depressive and anxiety disorders^[2-5]. Among patients with functional gastrointestinal disorders, the rates of associated psychiatric disorders are even higher. In the case of IBS, 50%-90% of those seeking treatment have been found to also have comorbid lifetime psychiatric disorders, especially depressive and anxiety disorders^[6]. Somatization disorder (SD) is also highly relevant to functional gastrointestinal disease. This is not only because of documented prevalence rates of somatization disorder in 15% to 48% among IBS patient samples^[7-12], but also because of implications introduced by the presence of somatization disorder for classification and understanding of IBS and probably also other functional disorders as well.

Abnormal cytokine production has been found in association with IBS^[13], major depression^[14,15], and somatization disorder^[16]. These findings suggest a potential unifying mechanism connecting events in the nervous system (central or enteric) with IBS symptoms (e.g. fatigue, myalgia, sleep disturbance). The cytokine findings, however, have not been consistently reproducible, nor have they been correlated well with individual symptoms.

Somatization disorder, a well-validated psychiatric disorder, is the anchor of the diagnostic category of somatoform disorders^[17]. Somatization disorder shares many clinical features with IBS. Like other psychiatric disorders and functional disorders, somatization disorder lacks biological markers and is diagnosed based on subjectively reported symptoms^[18]. The diagnosis of somatization disorder is defined by patient report of

multiple subjective symptoms across multiple organ systems, often collected over time and across settings, because patients usually do not divulge all their symptoms at once to one interviewer^[11,19]. Qualifying symptoms for the diagnosis are formally defined as physical complaints that on the surface seem to represent medically based problems, but upon sufficient medical investigation defy full medical explanation^[20]. Thus, the term "somatoform" means, literally, symptoms resembling physical illness. Although somatoform symptoms have historically been considered to represent physical expression of psychological distress^[21-23], these notions are not demonstrated by empirical research, and somatization disorder and somatoform symptoms are defined without assumption of psychological mechanisms.

Somatization disorder patients complain of many medically unexplained gastrointestinal and other bodily symptoms, such as neurological, sexual, and pain symptoms, as well as psychiatric symptoms. The line between IBS and somatization disorder is further blurred by the frequent occurrence of other comorbid functional disorders in patients with IBS^[24]. Multivariate analyses suggest that comorbid functional syndromes are distinct disorders and not necessarily manifestations of one common disorder (e.g., somatization disorder), having features in common that lead to symptom reporting. Although the specific prevalence of IBS and other functional gastrointestinal disorders in patients with somatization disorder is not known, analysis of a large population study database indicated that virtually all individuals diagnosed with somatization disorder and few of those without somatization disorder acknowledged two or more medically unexplained gastrointestinal symptoms^[25].

Patients with somatization disorder often do not confine their medically unexplained symptoms to the physical domains. Most also complain of many symptoms of many psychiatric disorders they do not actually have. Patients with somatization disorder have been demonstrated to report as many as, or more, symptoms of major depression, anxiety disorders, and schizophrenia than patients who actually suffer from these disorders^[26-28]. These well documented psychiatric symptoms in these patients who do not have the psychiatric disorders associated with the symptoms they report have been termed "psychoform," in parallel to the term "somatoform" referring to symptoms suggesting bodily illness that is not present^[19,29,30].

Consistent with these symptom-reporting patterns, the medical histories of patients with somatization disorder typically reflect multiple medical and psychiatric diagnoses, often including various functional disorders^[19]. The more functional disorders a patient has, the more likely is the diagnosis of somatization disorder^[11]. When IBS or other functional disorders occur in patients with somatoform disorders, the gastrointestinal complaints are counted toward the diagnosis of SD because of the lack of objective indicators of medical illness^[20]. Patients with somatization disorder may also have many complaints of allergic reactions and medication intolerances, consult multiple physicians in many specialties, have histories of multiple failed treatments, and generally follow a difficult

course of treatment and patient-physician interactions^[19]. Patients with somatization disorder typically exhibit a pattern of symptom expression recurrently throughout most of their lives, regardless of their current mood state, unlike patients with depressive disorders, who often have medically unexplained complaints during depressive episodes but not at other times^[20]. No psychopharmacologic agent has been demonstrated to be effective in alleviating somatization disorder^[19,31], although some patients may benefit from the usual treatments for established comorbid psychiatric illnesses that are commonly associated with this disorder, such as major depression^[19,32].

THE PSYCHIATRIC-FUNCTIONAL DISORDER CONNECTION

Clinicians and researchers have observed that patients with IBS or other functional gastrointestinal disorders tend to have additional functional disorders in various other organ systems, multiple somatoform symptoms distributed across most physical categories (e.g., unexplained pain; neurological symptoms such as paralysis, imbalance, and weakness; and sexual complaints), and complaints of multiple drug allergies and sensitivities. The previously mentioned comorbid psychopathology, especially depressive and anxiety syndromes, are consistent with these patients' patterns of complaints of many types, including psychiatric. Many of these patients also engage in unusually frequent health care visits, undergo multiple diagnostic tests and surgical procedures, use many over-the-counter and prescription medications, and become refractory to treatment^[33]. Treatment of refractory functional gastrointestinal disorders has been described as difficult and frustrating^[33-35].

It is perhaps more than just coincidental that these characteristics of patients with IBS and other functional gastrointestinal disorders have many features in common with the classic features of patients with somatization disorder described earlier in this article. It has been previously hypothesized that the psychiatric comorbidity in IBS patients may reflect the inclusion of somatization disorder in IBS samples^[36,37]. North and colleagues^[11,19] further hypothesized that other clinical perceptions of IBS patients may be colored by prominent characteristics of the somatization disorder patients within their ranks. Indeed, examination of IBS patients segregated by the presence or absence of somatization disorder demonstrated that IBS patients had more abnormal illness behavior and psychiatric symptoms compared to patients with IBS alone, and patients with IBS alone were similar to a comparison group of ulcerative colitis patients on these characteristics^[11,12]. Additionally, IBS patients with somatization disorder had significantly more gastrointestinal and other symptoms, psychiatric disorders, physicians consulted, telephone calls to physicians, urgent care visits, medication changes, missed work days, benzodiazepine use, poor treatment outcomes, and treatment dissatisfaction compared to their counterparts without somatization disorder^[11]. These findings suggest one important point that IBS may be a heterogeneous

concept, namely through its frequent association with somatization disorder.

The dimensional construct of somatization outside the context of the disorder based on its name reflects a need for further explication of medically unexplained symptoms in diverse settings. Outside of somatization disorder, the concept of somatization conceptualized as a process or a behavior is poorly understood. Somatoform syndromes not meeting full criteria for somatization disorder are recognized in formal diagnostic nomenclature^[20], representing a residual category for persistent somatoform presentations lasting at least six months that do not meet somatization disorder criteria (undifferentiated somatoform disorder) and a category for unexplained physical complaints of less than six months' duration (somatoform disorder not otherwise specified). However, these diagnoses are not diagnostically validated. Thus, the field does not really know what to do with medically unexplained symptoms that are not part of somatization disorder. The symptom of low mood which we call "depression" is not synonymous with the diagnosis of major depression; depressed mood also occurs in dysthymic disorder and even in normal people and does not necessarily reflect the same processes as those occurring when this symptom is part of a major depressive episode. Similarly, "somatization" behavior outside of somatization disorder may be a very different phenomenon from behavior bearing the same name that defines somatization disorder.

Outside diagnostic constructs that characterize longstanding trait-related phenomena, the concept of somatization has come to represent state-dependent behavior in the context of psychological stress. Thus, the term "somatization" has accumulated a baggage of assumptions of psychological processes beyond the defining lack of medical explanation for the symptoms of the disorder bearing its name. It is likely that features of "somatization" observed in functional medical disorders are actually contaminated with characteristics of unrecognized cases of somatization disorder among the patients. Among patients presenting with medically unexplained symptoms who also have psychiatric illness, the likelihood of having a somatoform disorder is remarkably high^[2]. Because we do not know the etiology of medically unexplained symptoms outside validated somatoform disorders, "somatization" is a loaded term implying processes that may not apply, and thus terminology less burdened by assumptions such as "complaints without nonpsychiatric illness" may provide a more careful way to discuss these symptoms.

GENERAL APPROACH TO EFFECTIVE MANAGEMENT OF FUNCTIONAL GASTROINTESTINAL DISORDERS

IBS complaints without psychiatric illness

Many patients with IBS or other functional gastrointestinal disorders present extraordinary management problems for physicians. They absorb a great deal of time, and need more physician empathy, reassurance, explanation,

attention, and time for emotional ventilation than the average patient. Gastrointestinal symptoms may restrict their activities, change their self-image, and present a source of worry and embarrassment. The impact may be very psychological and stress-provoking. Because of these lifestyle and personal worries, psychological counseling, education and encouragement are the universal approaches with all IBS patients regardless of the level of severity and chronicity. Patients should generally be advised that they have a “medical problem” which is complex and at times difficult to treat. Patients can also be told that there may be psychological ramifications as well which can make the gastrointestinal symptoms more difficult to tolerate, and that psychiatric symptoms and disorders frequently accompany the gastrointestinal disorder.

The management of IBS calls for the best “bedside” manner of physicians as they need to approach this problem medically, yet at the same time, recognizing the psychological and psychiatric issues that so often accompany it. Being unwilling to credit the symptoms of patients with true somatic content, being dismissive of patients and calling their syndrome psychiatric (“all in your head”) or simply referring them to psychiatric professionals (without retaining the role as primary care physician) denies the complex nature of the syndrome and falsely relegates the syndrome to a failure of the patient's will. This whole issue becomes even more complex if the expertise of a mental health professional is needed. Patients are better served if they are prepared for referral to a psychiatrist or psychologist. “Let's see if psychological procedures or psychiatric medications can further improve or alleviate your symptoms in addition to your other treatments.” Treatment goals should stress solutions to these troubling symptoms and provide behavioral-cognitive strategies for coping. It is important to decide whether to focus on the pain and bowel symptoms alone, or to include other somatic and/or psychiatric symptoms in the treatment goal. This decision will depend on the patient and the presence or absence of associated symptoms, whether or not they form a diagnostic cluster for a comorbid condition. When indicated, the use of specific medications for pain (e.g. tricyclics, serotonin-selective agents, SSRIs), or bowel function (e.g. serotonergic drugs, opiates), may be useful (see section on “Psychotropic Medication”).

IBS with somatization disorder

Most IBS and other functional gastrointestinal disease can be managed with this kind of patience and logical problem-solving approaches. More refractory illness, patients with more complex and difficult courses of treatment, and patients with many psychiatric problems may require reconsideration of the potential for an underlying somatization disorder diagnosis. The diagnosis of somatization disorder can be difficult and time-consuming to document because the evidence does not present itself at a single patient appointment^[11,19]. The diagnosis may require lengthy history-taking as well as gathering considerable medical history and observation over time to develop cumulative evidence of consistent patterns of multiple symptom complaints in many

organ systems. Psychiatric consultation can sometimes facilitate this process. Because the effective management of somatization disorder hinges on recognition of the syndrome, diagnosis is the essential cornerstone of treatment^[19].

PSYCHOLOGICAL INTERVENTIONS

IBS complaints without nonpsychiatric illness

The goal of psychotherapy is not to directly change or alter specific IBS target symptoms, but rather to promote coping and problem-solving skills and enhance the patient's well being and ability to function. Behavioral and cognitive therapies are among the useful interventions. There is evidence from randomized controlled trials to suggest that psychotherapy may be as effective as serotonin-selective antidepressants for some patients and more cost-effective than antidepressant medication^[38,39].

Formal psychotherapy is best left to mental health specialists, such as clinical psychologists and psychiatrists. Cognitive/behavioral therapy developed by Aaron Beck deals with patients' irrational cognitive appraisals and assumptions that appear to underlie negative emotional states, offering counteractive strategies through rational self-talk to correct negative underlying cognitions. Generally, individuals likely to benefit from this type of therapy harbor irrational negative thoughts about themselves and tend to catastrophize interpretations of interpersonal interactions and life events.

Cognitive-behavioral therapy and problem-solving techniques provide practical assistance to dealing with life's problems. For patients suffering from IBS, what thoughts and coping skills will lead to better coping and functioning? Carrying a change of clothes, preparing for problems and developing plans for solutions help to maintain or restore a sense of control, which may improve both self-esteem and self-effectiveness. These procedures, though easy to conceive, theoretically are much harder to employ. Thus, for sufficient cognitive-behavioral and problem-solving help for recalcitrant IBS, referral to a well-trained mental health professional may be imperative.

IBS with somatization disorder

While many of the procedures described above may be helpful for IBS patients with somatization disorder, somatization disorder can be very difficult to manage and may require assistance of mental health expertise. The recommended treatment for somatization disorder revolves around orchestration of medical care by one designated gatekeeper (not necessarily a psychiatrist) whose function is to keep the patient engaged in treatment to curtail doctor-shopping and iatrogenic morbidity resulting from medically inappropriate invasive diagnostic and surgical procedures and abusable medications. While this gatekeeper logically could be a psychiatrist, not all somatization disorder patients are willing to accept a psychiatric referral, although patients who have comorbid psychiatric symptoms or disorders may be more willing to accept a psychiatric referral. After a sufficiently comprehensive medical evaluation, pursuit of further procedures should be based on objective evidence of

illness. The goal is not to cure somatization disorder, which is generally chronic and lifelong, but to divert the patient from iatrogenic harm and promote healthier functioning. Development of a solid therapeutic relationship with the somatization disorder patient provides the social leverage to assist in redirecting the patient from repetitious litanies of medical complaints to building problem-solving and coping skills to address their many interpersonal and social problems. Regular appointments with physical examinations are recommended to demonstrate physician interest in the patient's concerns and circumvent symptom production as a requisite for physician contact. Patients can be reassured that medical evaluation of their symptoms has eliminated serious and disabling disease and praised for their endurance of suffering. A management focus based on long-term follow-up rather than pursuit of further diagnostic procedures can allay patient fears, reduces medical costs, and improves patient satisfaction and well being^[12,19,40]. Some of these principles can also be helpful in management of highly symptomatic or difficult IBS patients who do not meet diagnostic criteria for somatization disorder.

PSYCHOTROPIC MEDICATION

Many patients do not respond adequately to reassurance or education because of temperament, character, or learning style. They may not respond to dietary and nutritional advice, as there is no specific dietary component that can be identified consistently in IBS patients^[41]. Finally, patients may not respond to medications for gastrointestinal symptoms, either because the symptom does not derive from the intestine itself, or because non-gastrointestinal symptoms are dominant and not influenced by drugs directed at gastrointestinal function. For these groups of patients, psychotropic medications may be helpful. The mainstay of psychopharmacotherapy in functional gastrointestinal disease is antidepressant medication. Antidepressants are not just for treatment of depression. These medications are also useful in the treatment of anxiety disorders, pain syndromes, and functional disorders, even in patients without depression.

Evidence for the utility of antidepressant medication in functional gastrointestinal disease has emerged from an increasing volume of literature providing empirical support. Randomized clinical trials, however, provide little evidence that antidepressant therapy is superior to placebo as treatment for IBS^[1]. Most of the available studies are of low or moderate quality and do not demonstrate any clear-cut advantage of antidepressant therapy. Another difficulty in assessing clinical trials of antidepressants for IBS is that most IBS patients do not require psychopharmacologic interventions because their symptoms are mild, infrequent, and only periodically troublesome. Short-term treatments, including over-the-counter preparations (e.g., laxatives, anti-diarrhea medicines, and anti-spasmodics), dietary modifications such as increased fiber, and behavioral management and encouragement, may be sufficient to manage most IBS symptoms. Antidepressant therapy is generally reserved for patients with more chronic and severe IBS.

In a meta-analysis reviewing twelve randomized placebo-controlled clinical trials, Jackson and colleagues^[42] concluded that antidepressants appear to be effective in the treatment of functional gastrointestinal disorders with a reported odds ratio exceeding 4.0. Unfortunately, however, three patients needed to be treated to improve one individual's symptoms. A Cochrane database systematic review, selecting only two studies using a dichotomous endpoint for pain relief, four using such an endpoint for global relief, and two using a continuous outcome for pain, concluded there was no evidence of an effect^[43]. In a comprehensive review of all agents for IBS, Jailwala *et al*^[44] concluded from seven double-blinded placebo-controlled and randomized studies that the evidence for global improvement using psychotropic agents is "based on a small number of studies of suboptimal quality". In their recent comprehensive review of antidepressants for functional gastrointestinal disorders, Clouse and Lustman^[1] similarly cautioned that methodological issues may have biased many of the conclusions of these studies. Many of the studies they reviewed were older and subject to criticisms of methodological designs not meeting current research standards for clinical trials.

Most studies reviewed by Clouse and Lustman used tricyclic antidepressants (primarily amitriptyline) rather than the newer antidepressant classes such as SSRIs. Studies concluding antidepressant effectiveness often used outcome measures combining IBS target symptoms with quality of life items and indicators of depression and anxiety. The studies using narrower targets for outcome measures, such as principal IBS symptoms, found fewer treatment advantages for antidepressant medications. Studies of antidepressant medications for functional gastrointestinal disease have also suffered from use of fixed dose protocols, an issue that is especially relevant for tricyclic antidepressant medications with their wide dosage range. In many of these studies, nonpsychiatric physicians (gastroenterologists and primary care providers) administered the antidepressant agents, further reducing the likelihood of demonstrating benefit from antidepressant medication. In clinical practice, doses are tailored to the patient rather than fixed, and patients are heterogeneous. Though the accumulated research suggests some beneficial effects of psychotropic medications with this population, it is difficult to make a clear judgment about their role with this population. At present, it is safest to conclude that clinical experience suggesting benefit of antidepressant medications in functional gastrointestinal disease is more persuasive than evidence from carefully executed randomized clinical trials.

How do antidepressants work?

Clouse and Lustman^[1] recently observed that gastroenterologists now routinely prescribe antidepressant medication for treatment of IBS. Talley^[45] suggested that it may be ludicrous to believe that antidepressants directly treat the underlying pathology of IBS. He noted that recent studies have demonstrated only that the older tricyclic antidepressants and the newer SSRI agents alike improve global measures of outcome such as patient satisfaction and quality of life, but do little to relieve

target IBS symptoms. In 1987, Clouse and Lustman^[46] showed in a placebo-controlled study of low-dose trazodone for patients with functional esophageal illness that trazodone reduced distress but did not improve the esophageal symptoms. Thus, patients felt better, but their gastrointestinal symptoms persisted. They likened the antidepressant approach to treatment as a “band-aid” therapy. Not intuitively, response to antidepressant medication is not predicted by the presence of a depressive or anxiety disorder^[1].

The restoration of normal intestinal motility and reduction of intestinal sensitivity to food and other irritating substances by antidepressants would be expected to be relevant to treatment of functional gastrointestinal disease. The mechanism of antidepressants considered most relevant to functional gastrointestinal disease is their modification of neurotransmitter activity. Antidepressants are powerful presynaptic blockers of serotonin and norepinephrine in the brain, improving mood and reducing pain. It is thought that neurotransmitter actions of antidepressants in the gut may also contribute to their therapeutic effects in IBS. Serotonin is found in the intestinal wall and in blood vessels, and its concentration is greatest in the enteric nervous system. Blockade of serotonin and norepinephrine in the enteric nervous system may function to reduce transmission of messages to pain centers and thereby re-establish normal brain-gut connections. Thus, serotonin could be an essential link between motility, sensation and the brain-gut connection. By increasing serotonin in both gut and brain, antidepressants could be expected to raise the threshold of gut discomfort and pain and simultaneously facilitate emotional well-being. In patient studies of functional gastrointestinal illness, however, antidepressants have not been shown to have clinically significant effects on gut physiology or individual gastrointestinal symptoms, although global well-being does improve with antidepressant therapy^[1,46].

IBS patients have elevated plasma serotonin levels, and IBS symptoms are more prominent after meals^[47]. These findings have led some workers to consider serotonin central to the pathophysiology of IBS. However, the peak increase in plasma serotonin is not well coordinated with the time when patients most often experience post-meal symptoms (60-90 min after the meal)^[48]. Other hormonal changes that occur following a meal include increased secretion of cholecystokinin (CCK), glucagon-like peptide 1 (GLP-1), and peptide YY (PYY) as well as decreased secretion of ghrelin^[49]. The degree of these changes, however, is not altered in patients with functional gastrointestinal illness compared to controls.

Clinical use of antidepressants in the treatment of functional gastrointestinal disorders

The use of antidepressants in the treatment of functional gastrointestinal disorders has been described in detail in a recent review by Clouse and Lustman^[1]. The physician should not expect these drugs to change gut motility or physiology or necessarily reduce target symptoms, but success in using these agents is best measured in terms of functioning, quality of life, well-

being, and patient satisfaction with treatment. In general, tricyclic antidepressants may convey some advantages over SSRIs for pain and for medically unexplained physical symptoms^[50,51]. Choice of antidepressant class can be aided by consideration of side effect profiles (especially anticholinergic effects, sedation, weight gain, orthostasis, and cardiac conduction problems for tricyclics and activation and gastrointestinal distress for SSRIs). To reduce side effect burden, initial doses of antidepressants should be low, e.g., 25-50 mg/d of tricyclic antidepressants, and even lower (e.g., 10 mg/d) for patients with somatization disorder. The dose should be gradually increased (by 10-15 mg/d every 5-7 d) until adequate response is achieved, sometimes requiring four weeks at psychiatric dosage. Patients least likely to have a good outcome with antidepressant therapy are those with constipation-predominant IBS, patients with objective indicators of gastrointestinal motility delay, patients with medical comorbidities exacerbated by antidepressant medications, and patients with somatization disorder^[1,39,52]. Patients with a good antidepressant response can be successfully maintained on antidepressant medications for months to years. Tapering the dosage before antidepressant withdrawal will minimize likelihood of discontinuation syndromes.

Antidepressants are generally not useful for somatization disorder, except for their utility for comorbid conditions. There is no medication specific for treatment of somatization disorder. Patients with somatization disorder generally have more adverse reactions to medications and liability for misuse of habit-forming medications.

CONCLUSION

IBS is a heterogeneous syndrome with many potential mechanisms responsible for its clinical presentations^[53]. These mechanisms appear to relate to abnormal gut motility, parallel abnormalities of enteric and/or central nervous system functioning, and even immune dysregulation. In the majority of patients, IBS is complicated by psychiatric issues and unexplained symptoms and functional syndromes in other organ systems^[1]. For these reasons, one mode of treatment is unlikely to be universally effective or to resolve most symptoms.

It has become clear in recent years that the majority of IBS patients have multiple complaints without demonstrated cause, and that these symptoms can affect systems other than the intestine, e.g. bones and joints (fibromyalgia, temporomandibular joint syndrome), heart (non-cardiac chest pain), vascular (post-menopausal syndrome), and brain (anxiety, depression). Viewed in this light, most IBS patients do not have psychiatric illness *per se*, but a range of psychoform complaints that accompany their somatoform ones. It is not correct to label them as psychiatric patients (except those more difficult patients with true somatization disorder), but it appears to be valid to utilize the techniques of psychotherapy or cognitive-behavioral therapy to allow them to cope more readily with their illness. Specific episodes of depressive

or anxiety disorder can be managed as appropriate for those conditions. It is not surprising, therefore, that drugs designed to improve anxiety or depression are not uniformly useful for psychiatric complaints in IBS, because the psychoform symptoms that sound similar to those seen in psychiatric disorders may not have the same significance in patients with IBS.

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