Irritable bowel syndrome (IBS) is ‘out of the closet’ and into the public domain. IBS is on news-stands throughout the world, regularly covered in health columns in daily newspapers, and weekly magazines, and also on radio and television. Why has IBS achieved such status? IBS is common, affecting 10–25% of the population, depending on geographical location, and definition. It affects men and women alike, although women more commonly seek medical advice. It is transcultural and can affect all age groups, although typically presenting in the third and fourth decades. Finally, although the condition is not associated with increased mortality, some individuals experience high morbidity with a profound impact on their ability to work or enjoy life.

IBS is the most common of the functional bowel disorders which themselves form part of a wider range of functional gastrointestinal disorders involving diverse regions of the gastrointestinal tract from pharynx to anus.\(^1,2\) IBS is a symptom complex consisting of abdominal pain associated with defaecation or a change in bowel habit, with additional features of disordered defaecation (bowel frequency or constipation) and abdominal distension. Patients also often complain of a feeling of incomplete evacuation, of increased mucus in the stool and of looser stools at the onset of pain. A number of non-colonic features have also been recognized such as nausea, vomiting, early satiety, nocturia, feeling of incomplete bladder emptying, frequency and urgency of micturition, dyspareunia and fatigue. This far-reaching and variable symptom complex has posed major problems for (i) defining patient populations included in IBS studies, (ii) developing a unifying hypothesis to explain its pathophysiology and (iii) establishing clear-cut recommendations on management. Manning et al. identified six abdominal symptoms (abdominal pain eased after bowel movement, looser stools at onset of pain, more frequent bowel movements at onset of pain, abdominal distension, mucus and incomplete evacuation) which were more frequent in IBS than in organic abdominal disease.\(^3\) These observations have been refined by a consensus panel and it is these ‘Rome Criteria’ that are now most commonly used as entry criteria for research studies in IBS.\(^1\)

The diverse symptomatology of IBS has made it difficult to propose a simple mechanistic theory of symptom production. Variation in bowel habit suggests a primary motor disorder of the gut, predominantly involving the colon.\(^4\) Motor activity in the human intestine can be studied either by measuring changes in the patterns of intestinal pressure or by measuring gut transit rates. Studies of colonic activity in the basal state have yielded conflicting results, but there is some agreement that the colon of patients with IBS is hyper-reactive, particularly to physiological stimuli such as eating a meal. In the small intestine, some studies have shown increased ‘clustered contractions’ in IBS. Other have found similar short bursts of intense activity in healthy control subjects.\(^4\) Some studies have found the periodicity of the migrating motor complex to be shorter in diarrhoea-predominant than in constipation-predominant patients or control groups, particularly because of a shorter cycle length during the daytime, but other studies have failed to confirm this. Similarly, acute stress has increased small bowel motility in some studies but inhibited it in others. Overall, motility studies in the colon and small intestine suggest no clearly reproducible abnormality that is present in all patients and that can be regarded as pathognomonic of the condition. All studies show a substantial overlap between IBS and controls, indicating that while these tests have potential value in studying pathophysiology, they cannot confirm or refute the diagnosis. Despite the difficulty in interpreting studies of intestinal motility, measures of intestinal transit have produced more concordant results, particularly with respect to the reduction in oro-caecal and whole-gut transit times in diarrhoea-predominant IBS patients.\(^4\) Overall these findings suggest that while motor abnormalities may be present in some patients with IBS, the abnormalities are not consistent, can overlap significantly with a healthy control population and do not support the view that IBS is due to an easily definable primary motor disorder of the gut.
For more than 20 years, evidence has suggested that at least some of the symptoms of IBS may be due to an alteration of gut sensation, visceral hyperalgesia.\(^5\) Hyperalgesia describes a condition in which pain threshold is reduced and/or the response to a painful stimulus is greater in magnitude and longer in duration. Since there is no obvious local cause in the gut to cause this, it has been suggested that in IBS this is due to secondary hyperalgesia associated with central hyperexcitability. Allodynia, in which pain is produced by a stimulus that does not normally produce pain, may also exist in IBS, which again may be of central origin. Increased sensitivity to distension of the rectum exists in some patients with IBS.\(^6,7\) This sensitivity is not global, since somatic pain thresholds in IBS are either normal or increased. Altered sensation may also be important in the production of other symptoms such as abdominal distension and bloating, and the feeling of incomplete evacuation. Altered visceral sensation and/or allodynia may also account for some of the non-colonic symptoms such as urinary frequency, feeling of incomplete bladder emptying, dyspareunia and possibly other gastrointestinal symptoms such as nausea and early satiety. There may also be hyperreactivity of the bronchi in IBS. The autonomic nervous system and smooth muscle are common factors in all of these non-colonic systems, which perhaps supports the view that central control/perception rather than primary multi-end-organ hyperreactivity or hypersensitivity, is the logical route to explain pathogenesis.

In many healthy individuals, emotional factors alter gut function, producing symptoms such as bowel frequency, nausea, vomiting and early satiety. Many of us can recall isolated episodes immediately prior to taking an important examination, waiting in the ‘wings’ before a theatrical performance or music recital, or before an interview. With experience, confidence and time, these responses, mediated at least in part by the autonomic nervous system, usually diminish in frequency and severity. However, in some individuals they remain prominent to the point of interfering with daily life, and may be triggered by what would be generally be regarded as ‘non-stressful’ stimuli such as going shopping or to work. These environmental stresses can also produce non-colonic symptoms such as urinary frequency. In the experimental setting, psychological stress has been shown to produce changes in motility in the small and large intestine, and some studies have suggested that responses in IBS patients are exaggerated compared to healthy controls.\(^4\) Thus, the gastrointestinal tract can respond to emotional factors both in the research laboratory and during normal daily life; this may be a factor in the production of IBS symptoms. To support this view, several studies have shown that immediately before presenting with IBS symptoms, stress scores are increased compared to healthy individuals.\(^8\) If emotional factors and stress are important in symptom production in IBS, then why does the entire population not suffer from this disorder? This may relate both to local permissive factors in the gut (and possibly other organs) or perhaps more likely, to permissive factors within the psyche itself. As far as the gut is concerned, factors such as an episode of travellers’ diarrhoea or food poisoning may provide the trigger which disrupts bowel function and heralds the start of IBS symptoms. However, in the absence of continuing evidence of intestinal infection, it is uncertain as to why chronic dysfunction continues, despite resolution of the primary insult. This perhaps brings additional logic to the argument which promotes the relevance of central processing.

Disturbance of affect has been proposed as an important determinant for IBS symptom recognition and the seeking of medical advice. Hospital-based studies have shown an excess of psychological symptoms in patients with IBS which include depression, anxiety, phobia and somatization. However, patients referred by general practitioners to hospital may not be typical IBS patients, and thus psychological profiles of IBS patients have been performed in the community. Whitehead et al. found that IBS patients in the community had a similar psychological profile to individuals without bowel symptoms,\(^10\) although in our recent studies IBS patients who had sought medical advice had significantly higher anxiety and depression scores than individuals with similar symptoms who had not consulted.\(^11\) Sixty per cent of the consulters fulfilled diagnostic criteria for major depression (50%), anxiety disorder (43%) and dysthymia (7%). The consulters judged their pain to be more severe, frequent, prolonged and disruptive to daily living than the non-consulters, but blind assessment by an investigator suggested that symptom severity was similar in the two groups, implying that perception of symptoms was important in determining whether medical advice was sought. A further questionnaire confirmed that consulters with IBS were more concerned about illness, particularly with respect to disease phobia, hypochondriacal beliefs and bodily pre-occupation.\(^12\) We pursued the affect of IBS patients further using a word-recognition memory test, to examine the way in which IBS patients view the world.\(^13\) Overall they were similar to depressed patients, although in some respects scores in this test were higher than in depressed patients, despite lower ratings on the Beck Depression Inventory. Thus, although no evidence suggests that affective disorder or indeed any other specific psychological factor is the cause of IBS, we are convinced that affect is important in interpreting
bodily symptoms, particularly if the personality structure is such that concerns about illness are already intrinsically in place. Why the gut should be the somatic target is unknown, although recent evidence suggests an overlap with groups of patients with functional symptoms in other parts of the body.

In the vast majority of patients, IBS can be diagnosed on the basis of clinical history and physical examination. IBS is not a diagnosis of exclusion in patients below the age of 45 years and providing there are no other causes for concern such as weight loss, dysphagia, rectal bleeding or iron-deficiency anaemia, then a general physical examination, rectal examination and sigmoidoscopy should suffice. If there are concerns about inflammatory bowel disease, it is helpful to check inflammatory markers (ESR, C-reactive protein, platelet count). Anti-endomysial antibodies now represent a sensitive and specific screening test for coeliac disease. In patients over the age of 45 years, the colon should be examined either by double-contrast barium enema or colonoscopy, although the latter is preferred as it enables multiple biopsies to be taken to exclude the rarer forms of colitis such as lymphocytic or collagogenous colitis, which produce persistent diarrhoea without causing macroscopic abnormalities in the colon.

The subsequent clinical outcome is often set at the first consultation. Time is required to explain possible mechanisms of symptom production, to reassure about fears of serious organic disease and to explore potential social and psychological factors which may have lead to consultation with the general practitioner and hospital referral. Therapy may be considered under two headings, (i) those treatments that are aimed specifically at the gut, so-called end-organ therapy and (ii) those that are directed predominantly at the central nervous system or central therapy.

Perhaps the most attractive end-organ therapy for IBS sufferers is that of dietary modification. Nanda et al. showed that 47% of patients with IBS responded to a systematic exclusion diet, and many identified specific foods that triggered symptoms. Over a year's follow-up, these patients remained well with dietary modification. Despite these findings, many patients seen as hospital referrals fail to respond to this approach, and require alternative management strategies. One of the most controversial issues in IBS management has been the role of dietary and other fibres. Ten years ago, virtually every patient with IBS was recommended a high-fibre diet, despite controlled clinical trial evidence which showed that its effect was not superior to placebo. Recent studies suggest that in at least 50% of patients, fibre actually makes IBS symptoms worse. The main indication for fibre in IBS is when there is associated constipation. Soluble fibre seems to be more effective and has fewer adverse effects than dietary wheat fibre. A variety of drugs are available to minimize IBS symptoms, although a critical review of controlled trials in this area concluded that there is no effective medication for the treatment of IBS. Cramping abdominal pain is sometimes helped by an anti-spasmodic, and a recent meta-analysis confirms that at least some anti-spasmodics are effective in IBS. Similarly, bowel frequency may be reduced in some patients by standard anti-diarrhoeal preparations such as loperamide. Both anti-spasmodics and anti-diarrhoeals should be used only when symptoms are present and not on a regular basis. To obtain a clinical effect, the dose of anti-spasmodic may need to be relatively high, often to the point when adverse effects are evident.

Despite the paucity of effective agents for end-organ therapy in IBS, clinical trials of central therapy have been encouraging. Hypnotherapy and psychotherapy are both of value in the management of IBS. However, expertise and facilities are not available to all patients, and use of psychotropic drugs should be considered. Affective disorder may not be clinically apparent and depression may be atypical. The classic somatic symptoms of depression may not present other than sleep disturbance and fatigue. There is little to lose from a trial of an anti-depressant, and providing adequate explanation is given as to why the drug may be of value, the majority of patients will accept this approach. Added selling points include the correction of sleep disturbance, the increase in pain threshold and therefore possible relief of abdominal pain and the potential to correct any defaecatory disorders. Our own recent studies suggest that different classes of anti-depressant have contrasting effects on bowel function. The tricylic anti-depressant imipramine, for example, slows intestinal transit and therefore may be the drug of choice for diarrhoea-predominant IBS patients, whereas paroxetine, the serotonin re-uptake inhibitor, tends to decrease intestinal transit and therefore may be more appropriate in constipated patients.

What of the future? Methods for studying intestinal motor function, visceral sensation and central control of these activities in humans are relatively primitive, and until their complex interactions can be unravelled, new insights into the mechanisms of symptom production in IBS are likely to elude us. Advances however, have been made in the investigation of visceral sensation, all of which point towards the importance of central mechanisms. The relatively new science of psychoneuroimmunology may have implications for IBS. It has been proposed that 'sub-microscopic inflammation' may exist in some functional bowel disorders, which via paracrine and neuroendocrine mechanisms, is responsible for local...
sensitization of the gut to noxious stimuli. This work remains highly speculative but may have some relevance. A variety of pharmacological approaches are being used to improve end-organ therapy in IBS, notably the development of more specific smooth-muscle relaxants. There is increasing interest in the Kappa opioid agonists, which inhibit somatic pain through a peripheral mechanism acting directly on receptors located on peripheral sensory nerve endings. They appear to be able to block the nociceptive messages, as well as inhibiting the release of sensory peptides. Serotonin also appears to have a role in mediating visceral sensation, and thus 5-HT3 and possibly 5-HT4 antagonists may have therapeutic benefit.

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References