Classic diseases revisited

The irritable bowel syndrome

Carol Y Francis, PJ Whorwell

Summary

Irritable bowel syndrome is a common disorder varying in severity from trivial to incapacitating. The pathophysiology and epidemiology are gradually being unravelled and it is now becoming apparent just how poor the quality of life of some of these patients can be. It is no longer acceptable practice to diagnose the condition and discharge the patient on a high fibre diet, particularly as the latter can often make the situation worse. Although hard to treat, worthwhile responses can be achieved by careful targeting of therapy to the many different facets of the disorder.

Keywords: irritable bowel syndrome

IBS: most common symptoms

- abdominal pain or discomfort (any site)
- abnormal bowel habit
- abdominal distension
- feelings of incomplete evacuation
- mucus per rectum

Box 1

IBS: prevalence

- 15% - 20% of Western population
- female: male ratio 2.5:1
- up to 50% attending gastrointestinal clinic
- also common in third world

Box 2

Department of Medicine,
University Hospital of South
Manchester,
Nell Lane, West Didsbury,
Manchester M20 2LR, UK
CY Francis
PJ Whorwell

Irritable bowel syndrome (IBS) is a functional disorder of the gut, characterised by abdominal pain, abdominal distension and some abnormality of bowel habit (box 1). It is extremely common (box 2), affects females more than males and recent reports suggest that it is just as common in the third world as in developed countries.¹ IBS remains a challenging condition to treat as there are no diagnostic tests and, until recently, little has been known about the underlying pathophysiology. However, important developments are taking place which hopefully will lead to better management of the condition. One recent milestone has been the introduction of guidelines allowing a more confident diagnosis of IBS to be made and this has been useful both in the clinical and research setting. Furthermore, the pathophysiology of the disorder is now becoming more clearly understood, suggesting that it may reflect a combination of disordered motor function and visceral sensation.

The concept that IBS is a purely psychosomatic condition is now not tenable, although psychological factors have an important role to play in disease exacerbation and perpetuation. It is probably best to consider the disorder as multifactorial in origin, with psychopathology being just one of many contributing factors.

Signs and symptoms

ABDOMINAL PAIN

Apart from a small subgroup of patients presenting with painless diarrhoea, IBS patients commonly complain of pain of varying severity. It is usually intermittent or colicky and is occasionally so severe that some women may even equate its intensity to that of labour pains. It is now appreciated that pain can arise from both the large and small bowel and indeed may be felt at just about any site within the abdomen.² Continuous abdominal pain is sometimes observed and is more common in patients exhibiting psychopathology. This particular form of IBS is extremely hard to treat and often has a poor prognosis.

ABDOMINAL DISTENSION

Abdominal distension is an intriguing symptom that is poorly understood and which on occasions can be extremely prominent. Patients may find it a very intrusive feature of their disorder whilst members of the medical profession are inclined to dismiss it as being trivial. It is usually at its mildest in the morning, worsening as the day progresses such that some patients have to loosen clothing or even change to a larger size. It has been suggested that this complaint may be an artefact but studies utilising computed tomography have confirmed that distension is a real and measurable feature.³ It also appears to be unrelated to intraluminal gas^{4,5} and as yet no convincing explanation has been advocated, although an abnormality of tone coupled with enhanced visceral sensitivity is possible.

DISTURBED DEFECATION

This varies from diarrhoea in which patients complain of frequent loose motions often worse on first rising in the morning to constipation which can either mean straining frequently to pass small pellet-like stools or only passing stools infrequently (fewer than three stools per week). It is not uncommon for patients who frequently open their bowels only to pass hard pellets to be erroneously classified as having diarrhoea. This is because only the numerical frequency of bowel action has been taken into account rather than a detailed enquiry about stool consistency being made. This is a very important practical point as it may result in constipated patients being given inappropriate treatment with antidiarrhoeals.

Many patients will alternate between episodes of diarrhoea and constipation. Often there is associated mucus which may be quite excessive but IBS does not cause rectal bleeding and this should be investigated appropriately. Other

IBS: noncolonic symptoms
<ul style="list-style-type: none">• nausea• early satiety• dysphagia• lethargy• back pain• thigh pain• urinary frequency• urinary urgency• dyspareunia• fibromyalgia

Box 3

common symptoms are urgency of defecation and a feeling of incomplete evacuation of the rectum. Incontinence is occasionally encountered and is a particularly devastating symptom.

NONCOLONIC SYMPTOMS

Patients with IBS often suffer a whole variety of noncolonic symptoms⁶ (box 3) such as backache and lethargy which are important for a number of reasons. Firstly, they can lead to the patient being referred to the wrong specialty with a series of inappropriate and unrewarding investigations. Secondly, they may lead to the patient worrying about the possibility of coexistent disease. Thirdly, patients do not readily complain of these features for fear of being labelled as a polysymptomatic complainer and lastly, because 50% of patients with IBS actually rank a noncolonic feature of their disorder as being more intrusive than the classical symptoms of abdominal pain, distension and abnormal bowel habit.⁷ Furthermore, it has recently been shown that noncolonic symptoms may even have diagnostic potential⁸ in that they can help to substantiate the diagnosis in patients with atypical symptoms such as those presenting with abdominal pain and a normal bowel habit. The more noncolonic symptoms that are present, the more likely is the diagnosis to be IBS.⁸

The problem of inappropriate referral resulting from noncolonic symptomatology should not be underestimated. It has been shown that over 50% of women attending gynaecology clinics with abdominal pain are suffering from symptoms consistent with IBS^{9,10} and a similar figure has recently been reported in the urological setting.¹¹ Furthermore, dyspareunia is surprisingly common in women with IBS and can have a profound impact on their lives.¹²

PHYSICAL SIGNS

Although there are no pathognomonic physical signs of IBS, there are some features that are commonly observed which may aid diagnosis. Physical examination is also essential to help exclude organic disease.

Patients usually look well. Abdominal tenderness is common, varies from mild to severe and may occur at any site although it is most often observed in the left iliac fossa. Abdominal distension may be observed, particularly if the patient is seen near the end of the day. A palpable mass is sometimes felt in the right iliac fossa but characteristically on continued palpation becomes less well defined. Fielding¹³ also described a right iliac fossa squelch sign in a third of patients. Scars from previous abdominal surgery are frequently seen, particularly those of cholecystectomy, appendicectomy and various gynaecological interventions. Finally, during sigmoidoscopic examination, patients' symptoms may be reproduced and spasm of the colon can be observed.

Making a clinical diagnosis

A number of clinicians have addressed the question of how to make a positive clinical diagnosis of IBS given the constraints of a lack of diagnostic tests.^{14,15} These have been validated over the years and in 1989 by international consensus, diagnostic criteria (known as the Rome criteria, box 4¹⁶) were compiled and are now widely used both in the clinical and research setting. These criteria could represent a major step forward as long as they are updated in the light of ongoing experience.

Investigations

General practitioners should be encouraged to try and diagnose IBS confidently and positively with minimal investigation. This should be relatively easy in milder forms of the disorder but problems start to arise when patients fail to respond to the usual measures of education, reassurance and standard medication. It is at this stage, particularly if there is concern about the security of the diagnosis, that hospital referral has to be contemplated. Even in the hospital setting, investigation can often initially be limited to a full blood count, erythrocyte sedimentation rate and sigmoidoscopy. Additional tests such as biochemistry, stool culture, lactose tolerance test, thyroid function tests or jejunal biopsy may have to be contemplated. Occasionally, estimation of the daily stool weight is helpful, as values over 200 g tend to suggest a diagnosis other than IBS. In patients over the age of 45 or younger patients with a family history of cancer of the colon, breast, ovary or uterus, a colonoscopy or barium enema should be undertaken.

It is important to recognise that, because it is so common, IBS can coexist with other disorders. It has been shown, for example, that in a group of patients with ulcerative colitis in remission there is a high prevalence of IBS

The Rome criteria
Continuous or recurrent symptoms for at least three months of: <ul style="list-style-type: none">• abdominal pain, relieved with defecation, or associated with a change in frequency or consistency of stool and/or <ul style="list-style-type: none">• disturbed defecation at least 25% of the time, ie, two or more of:<ul style="list-style-type: none">– altered stool frequency– altered stool form– altered stool passage (straining or urgency, feeling of incomplete evacuation),– passage of mucus usually with <ul style="list-style-type: none">• bloating or feeling of abdominal distension

Box 4

Figure 1 Aetiology/physiology of IBS

symptoms.¹⁷ Similarly, in a patient with an established diagnosis of IBS, it is important to be alert to the fact that other disorders may supervene and the doctor should be sensitive to changes in symptom patterns or the appearance of new features.

Aetiology/pathophysiology

The cause of IBS is not known, however, the condition is highly likely to be multifactorial in origin (figure 1). There is undoubtedly a tendency for the condition to run in families, suggesting a genetic predisposition but to date no gene abnormality has been demonstrated. In the asymptomatic individual with an underlying potential for developing IBS, it is thought that some event is necessary to trigger the onset of symptoms. A number of exacerbating or triggering factors are now well recognised and include abdominal surgery, antibiotic usage, gastrointestinal infections, inappropriate diet, stress and sleep deprivation.^{18,19} It seems reasonable to assume that there may be many other precipitating factors as yet to be defined.

Traditionally, IBS has been regarded as a purely motor disorder but more recently, abnormalities of visceral sensitivity are assuming an equally important role. The notion that IBS is a purely psychological condition is probably no longer acceptable but undoubtedly, psychopathology plays an integral role in modifying the motor and visceral responses of the gut.

INTESTINAL MOTOR FUNCTION

A whole variety of motor abnormalities of both the small and large bowel have been described in patients with IBS. Unfortunately, many of these do not correlate well with clinical findings and symptoms. Perhaps one of the most consistent features is an exaggerated response to stimuli such as intravenous cholecystokinin,²⁰ balloon distension,²¹ and meals.²² High-amplitude contractions have been noted in some IBS patients during episodes of crampy abdominal pain.²² Since the heightened pressure appears before the pain it seems likely that spasm produces pain rather than vice versa. Hypermotility of the small bowel has also been found in association with pain.²

The fact that not all patients seem to display a motility disorder yet still respond to antispasmodics suggests that perception of motor events may be abnormal rather than the event itself and this forms part of the concept of visceral hypersensitivity.

VISCERAL HYPERSENSITIVITY

Ritchie¹³ was the first to show that patients with IBS report pain at lower distension volumes and/or pressures than asymptomatic controls when the rectum is distended. Over the years, interest has grown in the concept of an abnormality of visceral sensation and sensitivity in different areas of the gut has been explored. We have recently shown that the whole length of the gut is abnormally sensitive to balloon distension in a group of patients with IBS. This 'hypersensitivity' could explain symptoms such as rectal fullness, urgency, incomplete evacuation, bloating and tenderness of the sigmoid colon to palpation or internal distension. In addition, patients with IBS have also been shown to exhibit urological abnormalities²³ and this, taken in conjunction with the recently reported high incidence of fibromyalgia²⁴ suggests a more diffuse abnormality of nociception.

Hypersensitivity at the mucosal level might mean that patients sense luminal events or motor events abnormally. The mechanisms underlying the development of this hypersensitivity remains to be established, but diarrhoea can sensitise the rectum²⁵ and there is some evidence to suggest that psychological factors have a similar effect.²⁶

PSYCHOPATHOLOGY

Stress undoubtedly affects the gastrointestinal system in health, as any student prior to an exam is well aware. Nevertheless, the role of stress and psychological factors in IBS is probably overrated as only a quarter of those with symptoms of IBS present to a doctor,²⁷ and studies have shown that whilst there is a high prevalence of psychopathology among hospital IBS patients, those who do not consult have a normal psychological profile compared to the general population.²⁸ This suggests that it may be something to do with the psychopathology rather than the symptoms of IBS that make patients seek help for their gut symptoms. This might include coping capacities or illness behaviour although no clear cut relationship has so far been found with personality profile, psychiatric illness or set of stress factors. However as most studies have only been done in specialist centres on difficult cases, the

relationship between IBS and psychological factors will probably only be understood when more data are available on communities including noncomplaining subjects.

Who should be referred for specialist care?

The usual reasons for hospital referral are failure to respond to treatment or uncertainty over the diagnosis (figure 2) but other factors are worthy of consideration. Some patients certainly appear to become entrenched in their disease and in order to try and prevent such a vicious circle being established, early referral might be worth contemplating. However, in order to achieve this goal the consultant concerned should have a special interest in the disorder, or the strategy may be counterproductive. A further advantage of referral to specialised units is that motility and visceral sensitivity testing can be undertaken and it is our experience that patients find this extremely beneficial as, for the first time, they are actually having tests yielding relevant data and, on occasions, positive results.

Treatment

PATIENT EDUCATION

Like many other medical conditions, fear of the implications of a set of symptoms understandably creates much worry and anxiety. Once the diagnosis has been reliably established and the necessary investigations completed, probably the most important therapeutic measure is a careful explanation of what IBS is, with emphasis on the benign nature of the condition. It is especially important that the legitimacy of the condition is emphasised and that the patient is not told "there is nothing wrong with you". The noncolonic features of the disorder also need to be addressed, as they are often a source of great concern to the patient and some, particularly the lethargy, not immediately amenable to therapy. A number of individuals cope better with their symptoms with no further medical intervention once they have been given a sympathetic explanation. Patients need to understand that the disorder is not curable in the true sense of that word and has a tendency to fluctuate over time. However this does not mean that considerable help cannot be offered and once realistic expectations are established, coping capacities usually improve.

DIET/FIBRE

For many years, dietary fibre has been advocated as the primary line of treatment for IBS. This dogma has recently been challenged with evidence that

Figure 2 IBS flow chart

fibre, particularly that derived from wheat can actually make patients worse.²⁹ Indeed no fewer than 55% of IBS patients claim that bran makes them worse, with only 10% deriving benefit. Thus patients should be left to use bran more according to their needs.

A number of patients report that certain foods appear to exacerbate their symptoms. The problem with this observation is that the process of eating itself can bring on symptoms as well as the content of what is eaten, and this is well demonstrated by the fact that sham feeding or even thinking of food can actually promote gut motility.³⁰ Thus, distinguishing between true food intolerance and some form of heightened neurohumoral response to eating can prove extremely difficult. However, occasionally some people appear to be genuinely intolerant of certain foods and if this can be identified, can prove useful. Reports of the efficacy of exclusion diets vary considerably³¹ but when they are undertaken it is probably best to enlist the help of an interested dietitian.

CURRENT DRUG THERAPY

It is probably fair to say that there is no single drug of outstanding efficacy for the treatment of IBS and currently the best initial approach is a process of trial and error utilising combinations of antispasmodics, bulking agents or antidiarrhoeals/laxatives where appropriate.

Antispasmodics

As the abdominal pain of IBS was originally thought to be due to excessive colonic contractions, antispasmodics have become widely used in the treatment of this condition. Despite more recent evidence questioning the role of spasm, they are undoubtedly helpful in some patients, particularly when the pain is colicky and intermittent and it may be that even reducing the strength of a normal but abnormally sensed contraction is worthwhile. There are two main groups of antispasmodics—smooth muscle relaxants such as alverine and mebeverine, and anticholinergics such as dicyclomine. Patients may respond in whole or part to different preparations and it is worth trying a number over a period of time. It is also important to remember that ‘as necessary’ dosing with these drugs is sometimes preferable to continuous medication, particularly when patients have intermittent symptoms.

Antispasmodics are also worth trying for abdominal distension but this is often difficult to treat and if there is no response, peppermint oil or even a reduction of dietary fibre is worth a try.

Antidiarrhoeal agents/laxatives

Antidiarrhoeal agents such as loperamide and diphenoxylate are useful for patients whose main complaint is of frequent loose stools. The dose required varies considerably and it is often best to leave the patient to work out the optimum regime bearing in mind that PRN use is perfectly reasonable. Patients often feel quite guilty about using excessive amounts of antidiarrhoeals, so should be reassured that they are a very safe group of drugs which can be used on a long term basis without fear of serious consequences. They may also be very useful in patients suffering from urgency and incontinence.

Constipation may respond to simple stool bulking agents such as ispaghula but if these fail, lactulose is worth trying, although the latter can be nauseating and sometimes exacerbate abdominal distension. In more refractory cases, it may be necessary to resort to stronger laxatives such as sodium picosulphate. Occasionally, patients get a good response from over the counter laxatives such as senna and bisacodyl and as long as these are safe, they should not be prohibited. As with antidiarrhoeals, individual titration of the dose may be required and the patient reassured that the long-term detrimental effect of laxatives has probably been overrated.

Antidepressants

It has been suggested that the tricyclic antidepressants may have a beneficial effect in IBS which is mediated via a mechanism other than their antidepressant activity.³² This is based on the fact that patients often respond to much lower doses than those required for depression and sometimes, in contrast to their antidepressant action, response is almost immediate. Their anticholinergic activity might also contribute to their beneficial effect. They are not recommended as first line therapy and are best reserved for the more refractory patient. Sometimes, their antidiarrhoeal properties can be used to advantage but in the constipated variety of IBS, some help with bowel habit may be needed. The efficacy of the newer types of antidepressants, such as the selective serotonin re-uptake inhibitors, has yet to be evaluated.

FUTURE DRUG THERAPY

Current therapy for IBS is far from satisfactory³³ and as yet, there are no agents available which modify visceral sensitivity. This therapeutic hiatus coupled with a better understanding of the pathophysiology of IBS has led to the pharmaceutical industry taking a greater interest in developing more effective medication.

Gut-specific anticholinergics

The use of anticholinergics is often limited by their atropine-like side-effects. This problem could be minimised if more gut-specific antimuscarinics were available. This might also have the advantage that higher doses of these drugs could be used.

5-Hydroxytryptamine (serotonin) receptor antagonists

Serotonin appears to be intricately involved in the mediation of visceral sensitivity which is now known to be abnormal throughout the entire length of the gut in patients with IBS.³⁴ Preliminary data suggests that agents modifying various serotonin receptor subtypes might have therapeutic potential and a number are in development.

Cholecystokinin antagonists

Some patients are particularly intolerant of fatty foods and this is thought to be mediated through the release of cholecystokinin, a gut hormone which is known to increase intestinal motility.³⁵ Administration of exogenous cholecystokinin has been shown to reproduce the symptoms of IBS³⁶ and indeed has been suggested as a diagnostic test for the condition. These observations have led to the development of antagonists of cholecystokinin (eg, loxiglumide) which are now undergoing clinical trials.

Kappa receptor agonists

There are a number of subtypes of the opioid receptor including mu, gamma and kappa. Their anatomical distribution varies considerably with kappa receptors concentrated in the gut. It has been argued that agonists of kappa receptors might promote gut specific analgesia and preliminary data on fedotozine (a kappa agonist) has shown some beneficial effects. This approach to 'gut analgesia' is appealing as it may relieve symptoms without necessarily having to modify the underlying pathophysiology which could be different in different cases.

NON-DRUG THERAPY

Transcutaneous nerve stimulation

This treatment, based on electrical stimulation, is widely used for the treatment of pain and has been tried in patients with IBS with approximately 51% of patients showing some response.³⁷ It is worth trying where pain is a prominent feature but it should be pointed out that the other symptoms of IBS do not usually respond.

Hypnosis/psychotherapy

Despite all the measures described above, 25% of patients will remain refractory to treatment or even deteriorate. Both hypnotherapy³⁸ and psychotherapy³⁹ have been shown in clinical trials to be very useful in such patients. However, these treatments are very specialised, time consuming and unfortunately only currently provided in relatively few centres, although it is to be hoped that their availability may increase with the passage of time.

Prognosis

It is probably best to warn the patient that IBS is a long-term problem, with a tendency to exacerbations and remissions. It is surprising how much can be achieved by a process of patient education, coupled with therapeutic experimentation, advice on avoiding precipitating factors and measures to improve coping capacity. Specific negative terms such as 'incurable', 'untreatable' and 'nothing can be done for you' must on no account be used.

Conclusion

It is only just beginning to be realised how great the social impact of IBS can be, both in terms of quality of life of the individual and the economy of the community as a whole.^{40,41} For these reasons and the fact that the condition

can be so miserable for the sufferer, IBS and the related functional bowel disorders deserve to be placed much higher on the list of priorities for the research and development of new therapies.

- 1 Olubutide IO, Olawuyi F, Fasanmade AA. A study of irritable bowel syndrome diagnosed by Manning criteria in an African population. *Dig Dis Sci* 1995; 40: 983-5.
- 2 Horowitz L, Farrar JT. Intraluminal small intestinal pressure in normal patients and in patients with functional gastrointestinal disorders. *Gastroenterology* 1962; 42: 455-64.
- 3 Maxton DG, Martin DF, Whorwell PJ, Godfrey M. Abdominal distension in female patients with IBS: an investigation of possible mechanisms. *Gut* 1991; 32: 662-4.
- 4 Lasser RB, Bond JH, Levitt MD. The role of intestinal gas in functional abdominal pain. *N Engl J Med* 1975; 293: 524-6.
- 5 Maxton DG, Whorwell PJ. Abdominal distension in irritable bowel syndrome: the patient's perception. *Eur J Gastroenterol Hepatol* 1992; 4: 241-3.
- 6 Whorwell PJ, McCallm M, Creed FH, Roberts CT. Noncolonic features of irritable bowel syndrome. *Gut* 1986; 27: 37-40.
- 7 Maxton DG, Morris JA, Whorwell PJ. Ranking of symptoms by patients with irritable bowel syndrome. *BMJ* 1989; 299: 1138.
- 8 Maxton DG, Morris JA, Whorwell PJ. More accurate diagnosis of irritable bowel syndrome by the use of non colonic symptomatology. *Gut* 1991; 32: 784-6.
- 9 Prior A, Wilson K, Whorwell PJ, Farragher EB. Irritable bowel syndrome in the gynaecological clinic: a survey of 798 new referrals. *Dig Dis Sci* 1989; 34: 1820-4.
- 10 Prior A, Whorwell PJ. Gynaecological consultations in patients with irritable bowel syndrome. *Gut* 1989; 30: 996-8.
- 11 Francis CY, Duffy JN, Whorwell PJ, Morris J. High prevalence of irritable bowel syndrome in patients attending urological outpatient departments. *Gastroenterology* 1996; 110: A666 (*Dig Dis Sci* 1996; in press).
- 12 Guthrie E, Creed FH, Whorwell PJ. Severe sexual dysfunction in women with irritable bowel syndrome: a comparison with inflammatory bowel disease and duodenal ulceration. *BMJ* 1987; 295: 577-8.
- 13 Fielding JF. The irritable bowel syndrome. Part 1: clinical spectrum. *Clin Gastroenterol* 1977; 6: 607-22.
- 14 Manning AP, Thompson WG, Heaton KW, et al. Towards a positive diagnosis of the irritable bowel. *BMJ* 1978; 2: 653-4.
- 15 Holmes KM, Salter RH. Irritable bowel syndrome - a safe diagnosis. *BMJ* 1982; 285: 1533-4.
- 16 Thompson WG, Dotevall G, Drossman DA, et al. Irritable bowel syndrome: guidelines for the diagnosis. *Gastroenterology* 1989; 2: 92-5.
- 17 Isgar B, Harmen M, Kaye MD, Whorwell PJ. Symptoms of irritable bowel syndrome in ulcerative colitis in remission. *Gut* 1983; 24: 190-2.
- 18 Chaudhary NA, Truelove SC. The irritable colon. *Q J Med* 1962; 31: 307-22.
- 19 Whorwell PJ. Diagnosis and management of irritable bowel syndrome. *J R Soc Med* 1989; 82: 613-4.
- 20 Harvey RF, Read AE. Effect of cholecystokinin on colonic motility and symptoms in patients with the irritable bowel syndrome. *Lancet* 1973; ii: 1-3.
- 21 Ritchie J. Pain from distension of the pelvic colon by inflating a balloon in the irritable bowel syndrome. *Gut* 1973; 14: 125-32.
- 22 Connell AM, Jones FA, Rowlands EN. Motility of the pelvic colon. Part IV. Abdominal pain associated with colonic hypermotility after meals. *Gut* 1965; 6: 105-12.
- 23 Whorwell PJ, Lupton EW, Erduran D, Wilson K. Bladder smooth muscle abnormalities in patients with irritable bowel syndrome. *Gut* 1986; 27: 1014-7.
- 24 Veale D, Kavanagh G, Feilding JF, Fitzgerald O. Primary fibromyalgia and the irritable bowel syndrome: different expressions of a common pathogenic process. *Br J Rheumatol* 1991; 30: 220-2.
- 25 Houghton LA, Wych J, Whorwell PJ. Acute diarrhoea induces rectal sensitivity in women but not men. *Gut* 1995; 37: 270-3.
- 26 Houghton LA, Cooper P, Jackson NA, Whorwell PJ. Visceral sensation and emotion: a study using hypnosis. *Gastroenterology* 1995; 108: A3470.
- 27 Thompson WG. Irritable bowel syndrome: prevalence, prognosis and consequences. *Can Med Assoc J* 1986; 134: 111-3.
- 28 Drossman DA, Mckee DC, Sandler RS, et al. Psychological factors in the irritable bowel syndrome. A multivariate study of patients and nonpatients with irritable bowel syndrome. *Gastroenterology* 1988; 95: 701-8.
- 29 Francis CY, Whorwell PJ. Bran and irritable bowel syndrome: time for reappraisal. *Lancet* 1994; 344: 39-40.
- 30 Rogers J, Raimundo AH, Misiewicz JJ. Cephalic phase of colonic pressure response to food. *Gut* 1993; 34: 537-43.
- 31 Alun Jones V, Shorthouse M, McLaughlan P, Workman E, Hunter JO. Food intolerance: a major factor in the pathogenesis of irritable bowel syndrome. *Lancet* 1982; ii: 1115-7.
- 32 Clouse RE. Antidepressants for functional gastrointestinal syndromes. *Dig Dis Sci* 1994; 39: 2352-63.
- 33 Klein KB. Controlled treatment trials in the irritable bowel syndrome: a critique. *Gastroenterology* 1988; 95: 232-41.
- 34 Francis CY, Houghton LA, Whorwell PJ, Morris J, Bradbury J. Enhanced sensitivity of the whole gut in patients with irritable bowel syndrome (IBS). *Gastroenterology* 1995; 108: A600.
- 35 Snape WJ, Materazzo SA, Cohen S. Effect of eating and gastrointestinal hormones on human colonic myoelectrical and motor activity. *Gastroenterology* 1978; 75: 373-8.
- 36 Harvey RF, Read AE. Effect of cholecystokinin on colonic motility and symptoms in patients with the irritable bowel syndrome. *Lancet* 1973; ii: 1-3.
- 37 Sylvester K, Kendall GP, Lennard-Jones JE. Treatment of functional abdominal pain by transcutaneous electrical nerve stimulation. *BMJ* 1986; 293(6545): 481-2.
- 38 Whorwell PJ, Prior A, Farragher EB. Controlled trial of hypnotherapy in the treatment of severe refractory IBS. *Lancet* 1984; ii: 1232-3.
- 39 Creed F, Guthrie E. Psychological treatments of the irritable bowel syndrome: a review. *Gut* 1989; 30: 1601-9.
- 40 Drossman DA, Li Z, Androzzi E, et al. US householder survey of functional gastrointestinal disorders. Prevalence, sociodemography and health impact. *Dig Dis Sci* 1993; 38: 1569-80.
- 41 Houghton LA, Heyman DJ, Whorwell PJ. Symptomatology, quality of life and economic features of irritable bowel syndrome - the effect of hypnotherapy. *Aliment Pharmacol Therapeut* 1996; 10: 91-5.