Ministry of Defence

Synopsis of Causation

Irritable Bowel Syndrome

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Disclaimer

This synopsis has been completed by medical practitioners. It is based on a literature search at the standard of a textbook of medicine and generalist review articles. It is not intended to be a meta-analysis of the literature on the condition specified.

Every effort has been taken to ensure that the information contained in the synopsis is accurate and consistent with current knowledge and practice and to do this the synopsis has been subject to an external validation process by consultants in a relevant specialty nominated by the Royal Society of Medicine.

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1. Definition

1.1. Irritable bowel syndrome (IBS) is a chronic gastrointestinal disorder characterised by symptoms of abdominal pain, bloating, and bowel dysfunction. IBS is classified as one of the functional gastrointestinal disorders and is one of the most common conditions encountered in general medical practice and gastroenterology clinics. It is estimated that functional bowel disorders constitute around 30% of medical gastroenterology practice.

1.2. Despite the lack of significant mortality, IBS impacts negatively on patients' quality of life to the extent that many individuals find that their personal and social functioning is substantially impaired. The condition also has a marked financial impact, based on direct medical costs, decreased work productivity, and increased work absenteeism.

1.3. In the absence of any specific diagnostic test for IBS, several sets of symptom-based criteria have been developed to define the condition. Up to now, this approach has found greater application in the selection of subjects for clinical trials than in routine clinical practice. Among the commonly used criteria, the Manning criteria were first published in 1976 and represent the only set to have been validated in clinical practice. However, they demonstrate a positive predictive value of only 65-75%. Consequently, there have been a number of versions of the Rome criteria, initially developed in 1988 by the Working Committee for the XIII International Congress of Gastroenterology. The most recent version, Rome II was published in 1999, and the Rome III consensus is under development.[1] Using the definition employed by the Rome II criteria, IBS can be diagnosed on the basis of the following:

At least 12 weeks, which need not be consecutive, in the preceding 12 months, of abdominal discomfort or pain that has two out of three of these features:

1. Relieved with defaecation; and/or
2. Onset associated with a change in frequency of stool; and/or
3. Onset associated with a change in form (appearance) of the stool

1.4. Three subtypes of IBS have been recognised, namely diarrhoea-predominant, constipation-predominant, and alternating bowel habits. IBS is characterised by fluctuation of symptoms, sometimes between the different subtypes, and by periods of symptom remission.

1.5. In addition to the three subtypes described above, a variant of functional bowel disorder is encountered in patients who suffer from functional abdominal pain but who do not satisfy the strict terms of the Rome criteria. In practice, it is difficult to separate this group of patients into a distinct entity, given the degree of crossover of symptoms. Consequently, following investigation, these patients tend to be diagnosed as having IBS and treated accordingly.

1.6. In the developed world, IBS is 2-3 times more common in women than men. The condition is more common in younger rather than older adults and may indeed present from the teenage years onwards. Estimates of prevalence of IBS have generally ranged around 10%. Studies based on the Manning criteria tend to report higher prevalence than those based on the Rome criteria.[2] The prevalence rates in Asian studies have been generally lower than those reported in European and US studies. Recently published prevalence studies have included the following:

- a large study conducted over eight European countries found a prevalence of IBS of 11.5%, with 9.6% reporting current symptoms[3]

- a UK community-based survey, reported prevalence of IBS of 10.5%. The prevalence was 14.0% in women and 6.6% in men[4]
- a large US survey reported prevalence of IBS of 7%. Around half had consulted a physician for irritable bowel syndrome symptoms in the previous year, but over 90% had used an over-the-counter medication for IBS (e.g. antidiarrhoeal, laxative, antacid, or analgesic)[5]

1.7. It is thought that only around one-quarter to one-half of patients who have symptoms suggestive of IBS proceed to seek medical advice.[5,6] Thus, in addition to investigating potential causative or exacerbating features, research into IBS has also been directed at identifying factors that influence health care-seeking.

1.8. Symptom patterns may change over time creating an overlap between IBS, functional dyspepsia and gastro-oesophageal reflux disease.

2. Clinical features

2.1. In the absence of alarm features, clinicians are able to adopt a positive approach to making a diagnosis of IBS and the process should not be viewed inevitably as a diagnosis of exclusion. Bowel-related symptoms of IBS, which are typically episodic, include the following:[7]

- abdominal pain or discomfort
- abdominal bloating or distension
- disordered bowel habit, either diarrhoea, constipation, or alternating diarrhoea and constipation
- change in form of the stool e.g. loose, watery, or pellet-like

2.2. Symptoms affecting other areas of the body are also frequent, including:

- nausea
- low back pain
- thigh pain
- tiredness
- urinary symptoms e.g. frequency, urgency, and urge incontinence
- gynaecological symptoms e.g. dysmenorrhoea, dyspareunia

2.3. Patients referred to secondary and tertiary care tend to report severe symptoms. In such cases, severe pain may be present, at times equated by women to the pain of childbirth. In constipation predominant IBS, bowel movements may be separated by many days or even weeks. Diarrhoea predominant IBS may be characterised by extreme urgency or faecal incontinence.

2.4. Suicidal ideation has been reported, with critical issues being identified as feelings of hopelessness related to symptom severity, interference with life, and inadequacy of treatment.[8] Co-morbid anxiety or depression may also be diagnosed.

2.5. Examination is essentially normal although some tenderness may be elicited in the lower abdomen to either the right or left side. The sigmoid colon containing faeces can often be felt through the abdominal wall. Some patients experience generalised bloating with an increase of girth that is normally absent upon waking in the morning. On examination there is generalised tenderness but no palpable dilated loops of bowel.

2.6. Investigations can often be kept to a minimum. Examination of the colon to exclude colorectal cancer is especially indicated in patients who exhibit any alarm features ("red flag" signs) such as age over 50 years, particularly if symptoms are of recent onset, rectal bleeding, weight loss, and family history of cancer. IBS also needs to be distinguished from organic disorders such as inflammatory bowel disease (ulcerative colitis and Crohn's disease), diverticular disease, lactose intolerance, and coeliac disease. For patients who present with diarrhoea predominant features, sigmoidoscopy and biopsy are warranted to exclude organic disease even in the absence of alarm features.

3. Aetiology

3.1. IBS is a multifactorial condition and the precise aetiology remains uncertain. Potential causes that have been investigated include genetic predisposition, diet, gastrointestinal infection, and psychological factors, including psychosocial stressors and life events. Gene-environment interactions that are presently unknown are likely to be relevant. The diversity of proposed aetiological factors is fully consistent with a **biopsychosocial model** of the disorder. In this view, psychosocial factors may weigh heavily for some patients with IBS whereas, in other patients with similar symptoms, physiological influences may predominate.

3.2. No single conceptual model can explain all cases of the condition and more than one mechanism may operate in any one patient. The outcome for each individual, whether measured in terms of health care visits, quality of life impairment, or pain intensity, is a result of the interacting effects of intestinal physiology, the central and enteric nervous systems, and perceptual, cognitive, emotional, and behavioural aspects that are characteristic of the patient.[9] A number of hypotheses have been put forward in an attempt to explain the various mechanisms involved:

3.2.1. **Motility**: Abnormal gastrointestinal motor function is generally believed to play a significant role in IBS.[10] Gut spasm or other abnormal contractile activities may produce pain and discomfort. Patterns of contractile and electrical activity have been identified in the distal colon of patients with IBS that are not necessarily abnormal but appear exaggerated.[11] Recent studies have suggested that distension may be related to a disturbance in gas transport leading to gas retention.[12]

3.2.2. **Inflammation**: Histological and immunohistological studies have identified signs of an inflammatory response and immune activation in a subset of patients who suffer from IBS, lending support to the hypothesis that the condition may have an inflammatory component. It has been suggested that inflammatory changes in the intestinal mucosa could represent a response to initial bacterial infection in susceptible individuals, furthermore that such susceptibility may be genetically determined and related to a relative deficiency of anti-inflammatory cytokines. However, it should be noted that findings of low-grade inflammation and immune activation in the large intestine are not confined to patients with a history of overt infection.[13] An alternative explanation for the development of low-grade inflammation suggests that it may arise as an abnormal response to normal gut bacterial flora or a contained response to changes in the flora.[12]

3.2.3. **Bacterial flora**: it remains a contentious issue as to whether or not IBS is accompanied by qualitative and/or quantitative changes in the bacterial flora of the gut. Positive findings in this regard have been reported in some studies but have failed to be replicated in others. Reports of a beneficial effect derived from treatment with certain probiotics (see para 4.4) lend support to the argument that the gut flora may play a role in IBS.

3.2.4. **Visceral sensation**: The symptoms of IBS have been linked to visceral hypersensitivity and visceral hyperalgesia. The latter term describes a phenomenon that appears highly specific to IBS in which pain is felt as a result of stimuli that are normally pain free. However, as visceral sensation is normal in some patients who suffer from IBS, it is accepted that this hypothesis cannot provide a complete explanation for the condition.[12]

3.2.5. **Brain-gut axis:** It is now assumed that symptoms of IBS are mediated by the brain-gut axis, which consists of three parts - the enteric nervous system, the autonomic nervous system, and the central nervous system (spinal cord, brain).[10] The enteric nervous system functions semi-independently, but information is also relayed to the brain via the autonomic nervous system. At the brain level, incoming information is processed, and affective and cognitive dimensions are added to it, including emotional and behavioural responses to abnormal sensations. Finally, the brain sends information back to the gut to influence its function, again via the autonomic nervous system.[14] Thus bi-directional communication takes place between the central nervous system and the enteric nervous system, both in health and disease. This model provides the framework for the reciprocal interaction between biological, psychological and social factors in IBS. Various CNS- and gut-directed stressors may produce dysfunction in the brain-gut axis. One theory proposes that the central nervous system is hypervigilant in IBS and records an exaggerated, inappropriate, or aberrant perception of visceral events. There is also evidence for an important interaction between emotions and visceral function occurring at the brain level. Advanced imaging techniques have demonstrated abnormalities in brain activation in patients with IBS as compared to controls, notably in the **anterior cingulate cortex**, an area of the brain that may be capable of generating visceral symptoms in response to emotionally laden ideas, memories, and stimuli.[11]

3.2.6. **Neurotransmitter imbalance:** Researchers have identified a number of neurotransmitters such as serotonin and noradrenaline that may play an important role in IBS. Attention has focused mainly on **serotonin** (5-HT), which is found extensively in the gastrointestinal tract as well as in the brain. It is considered that serotonin forms a vital link in the brain-gut axis. Serotonin has been shown to be involved in three major actions in the gut

- mediating intestinal motility
- mediating intestinal secretion
- modulating perception in the bowels

Alterations in key elements of serotonin signalling have been demonstrated in patients with IBS.[15] (See also para 3.4.2)

3.3. Several specific aetiological factors have been linked to the development and perpetuation of IBS. A distinction may be made between risk factors (e.g. genetics, personality development, abuse in early life), trigger factors (e.g. psychosocial stressors in adult life, infection) and perpetuating factors (e.g. coping style and anxiety).[14] However, in considering the aetiological factors listed below, it should be understood that, for many individuals with IBS, no cause can be identified.

3.4. **Genetic and familial factors**: Several twin and familial aggregation studies in IBS have been consistent with either a genetic or a social learning hypothesis, and it is possible that both play a role. A study of twins has found that the concordance of IBS is significantly higher in monozygotic twins (17%) than in dizygotic twins (8%). However, a history of IBS in either parent was a stronger predictor of IBS for one of a dizygotic pair of twins than was the presence of IBS in the other twin. These findings provide support for a limited genetic component in IBS whilst suggesting that learning within the family environment is of at least equal importance.[16] A familial aggregation study has reported an increased frequency of IBS in the first-degree relatives of IBS patients compared with relatives of controls (17% vs. 7%), providing further support for a genetic or intrafamilial environmental component.[17] Several potential genetic markers have now been investigated in IBS including the following:

3.4.1. **Cytokines:** The production of cytokines is under genetic control, and some are pro-

inflammatory while others have anti-inflammatory properties. Results from a UK study suggest that at least some patients with IBS may be genetically predisposed to produce lower amounts of the anti-inflammatory cytokine known as interleukin 10. It has been suggested that a resultant imbalance of cytokines may compromise the inflammatory response in some individuals, providing an explanation for the observation that gastrointestinal infections can sometimes trigger the symptoms of IBS (see also para 3.7.2).[18] However, contradictory results were obtained from a study in the Netherlands.[19]

3.4.2. **Serotonin transporter gene**: Serotonin plays an important role in intestinal peristalsis and secretion, as well as in sensory signalling in the brain-gut axis (see para 3.2.6). A specific protein called the serotonin reuptake transporter (SERT) mediates removal of serotonin from its sites of activity, thus terminating serotonin action. It is thought that SERT dysfunction may contribute both to behavioural and functional gut disorders.[19] Several studies have looked for an association between SERT polymorphisms and IBS and have reported apparently contradictory findings. One US study, which investigated nine different polymorphisms of the SERT gene, found one that had appeared to have a significant association with diarrhoea-predominant IBS in women.[20] More work is required to clarify the role of SERT polymorphisms.

3.4.3. There is potential for polymorphisms of the genes encoding for α2-adrenoreceptors to lead to enhanced release of noradrenaline. Two such polymorphisms have been linked to constipation-predominant IBS but the precise significance of these findings is unclear.[19]

3.5. **Psychiatric illness and psychological factors**: The biopsychosocial model maintains that symptom manifestations in IBS and consequent consulting behaviour are influenced at least in part by psychological processes. A number of psychological and social variables have been linked to the predisposition, precipitation, and perpetuation of IBS. However, it is important to recognise that psychosocial features are prominent in only a subset of patients with IBS.

3.5.1. **Psychiatric co-morbidity**: It is recognised that, among those individuals who have symptoms of IBS, treatment is sought by less than half. Of those who do seek treatment, 50% to 90% have psychiatric disorders, such as depression, generalised anxiety disorder, panic disorder, post-traumatic stress disorder, and social phobia.[21] In this regard, patients with IBS demonstrate more psychiatric co-morbidity than observed in comparison groups of general medical patients or patients with organic gastrointestinal disorders such as inflammatory bowel disease. However, it remains conceivable that the data is influenced to a significant extent by patterns of health care-seeking behaviour (see section 3.5.4) and that the figures overestimate the role of psychiatric co-morbidity in IBS patients in the community as a whole.[2] Indeed, in a community study of a cohort of young adults from New Zealand, IBS did not appear to be significantly related to any psychiatric disorder.[22]

3.5.2. **Somatisation** can be defined as a psychological or behavioural trait, seen as the propensity to experience and report bodily (i.e. somatic) symptoms, to misattribute them to disease, and to seek medical attention for them. Several studies have reported excess somatisation tendency in patients with IBS. This finding may also help to explain the elevated rates of non-gastrointestinal symptoms (e.g. musculoskeletal complaints, urinary symptoms, and fatigue) that are found in IBS patients. Brain imaging studies have suggested that the tendency to report visceral and somatic symptoms may relate to amplification of incoming non-noxious signals to emotional pain centres, such amplification being enhanced by psychological distress.[9]

3.5.3. **Personality characteristics:** IBS has been linked to elevated levels of **neuroticism**, a stable personality trait that is partly genetically determined and causes individuals to identify life experiences as personally threatening to them. **Catastrophising** is a dysfunctional cognitive trait that has been found to be elevated in patients with IBS, contributing to an extreme degree of distress, a morbid sense of pessimism and helplessness to affect a change.[9]

3.5.4. **Illness behaviour and health care-seeking**: Evidence suggests that IBS patients tend to have a lower than normal threshold for experiencing illnesses as distressing and acting in response by health care seeking. Patients with IBS who seek medical attention are more likely than those who do not consult to exhibit psychiatric symptoms, psychological distress, maladaptive coping strategies, and somatisation. Compared to control subjects, patients with IBS appear to display more general anxiety about their health, as demonstrated by the finding that they make more healthcare visits for reasons that are unrelated to the gastrointestinal tract. Patients with IBS who seek treatment are more likely than healthy control subjects to report poor health in childhood, greater parental attention to illness, and school absence as a result of sickness. These influences may have fostered a greater attention to illness and a pattern of health care-seeking that persists later in life.

3.5.5. Other factors that have been associated with an increased likelihood of physician consultation include:

- older age
- female gender
- longer duration of symptoms
- abdominal pain as a prominent symptom

3.6. **Psychosocial stressors and life events:** It is generally accepted that both trauma in childhood and chronic severe stress in adult life can cause long-lasting, potentially irreversible changes in the stress response system.[14]

3.6.1. Several studies have reported high rates of **sexual and physical abuse** (notably childhood sexual abuse) in patients who consult with IBS. In one study, a history of sexual abuse was reported by 32% of IBS patients at a gastroenterology clinic in France as compared to 14% for patients with organic digestive diseases.[23]

3.6.2. **Chronic highly threatening stressors** may trigger the onset and/or exacerbations of IBS symptoms. Highly threatening life events, such as bereavement, break-up of an intimate relationship, and job loss, precede the onset of IBS more frequently than they precede organic gastrointestinal illness. A chronic threat that such events will occur can prove equally distressing. Major changes of a positive nature, such as marriage or the birth of a child, can also trigger IBS in susceptible people. A study of 117 outpatients has investigated the relationship of IBS symptom intensity to chronic stressor situations of at least six months duration.[24] The stressors involved included divorce, relationship difficulties, serious illness (of self or other), lawsuits, business failures, housing difficulties, and forced redundancies. The presence of one or more highly threatening chronic difficulty contributed significantly to the long-term prediction of symptom intensity. Almost all of the variance within individuals in symptom intensity was explained by the severity of chronic threat during the prior six months or more. No patient with continued exposure to even one chronic highly threatening stressor improved clinically (by 50%) over the 16-month study period; all patients who improved did so in the absence of such a stressor.

3.6.3. In contrast, an increase in commonplace daily sources of stress (termed "hassles" by one set of researchers) does not appear to exacerbate symptoms.[25,26]

3.6.4. A rating exercise using a Life Experiences Survey has demonstrated that patients with IBS are more likely than those with peptic ulcer disease to report life events as negative.[27]

3.6.5. Individuals with IBS, irrespective of whether they seek medical help, report more loss, separation, and familial disruption both during childhood and in adult life than do control subjects.[28]

3.7. **Infection:** Several studies have reported an increased incidence of IBS in the months following an episode of acute bacterial **gastroenteritis.** There is no evidence of persistent infection and it is thought that gastroenteritis could be one of several triggers that may precipitate inflammation-based IBS in susceptible individuals. The risk of developing IBS following an episode of gastroenteritis is in the order of 4%-23%.[12] A cohort study has reported that individuals who have suffered an episode of bacteriologically confirmed gastroenteritis are 10 times more likely to be diagnosed with IBS in the following year as compared to the general population.[29] Post-infectious IBS is most commonly diarrhoea-predominant.

3.7.1. In practice, the diagnosis of post-infectious IBS is often based solely on the patient's history. An increased risk of developing IBS following gastroenteritis is associated with:

- female gender
- more severe initial infection: post-infectious IBS is more likely to develop in patients who are hospitalised than in those treated at home. The risk of developing post-infectious IBS is 6 times greater in patients who initially had diarrhoea for 15-21 days as compared to those whose diarrhoea resolved within a week[30]
- prominent psychosocial factors operating at the time of, or prior to, the acute illness (see section 3.7.3).

3.7.2. **Post-infectious inflammatory changes** in the gastrointestinal mucosa have been detected including low-grade lymphocytic infiltration and an increase in mast cells.[31] One study assessed the expression of interleukin 1ß (IL-1ß), a cytokine that acts as an important modulator of the inflammatory process. Both during and three months after acute infection, the expression of IL-1ß was increased in rectal biopsies taken from patients with post-infectious IBS, as compared to controls who returned to normal bowel habits following the episode of gastroenteritis.[13] In another study, rectal biopsy showed that cell counts of serotonin-containing enterochromaffin cells were higher in patients with post-infectious IBS, as compared to healthy volunteers and to controls who were asymptomatic following an episode of gastroenteritis. Anxiety, depression, and fatigue were also significantly increased in the patients with post-infectious IBS as compared to the control group.[32]

3.7.3. **Psychosocial factors in post-infectious IBS:** Prospective studies have been reported involving patients admitted to hospital with a diagnosis of acute gastroenteritis. Higher scores for bodily preoccupation, anxiety, somatisation, and neurotic trait were recorded at the time of the initial illness in those who went on to develop post-infectious IBS as compared to those who reverted to normal bowel function following infection. Life event scores were also elevated in the group of patients who developed post-infectious IBS. The life event score was defined as the total number of life events experienced during the 12 months leading up to the acute episode of gastroenteritis. Events were of a

varied nature ranging from a minor illness and a holiday to bereavement and a relationship breakdown. Rectal biopsy specimens taken during the acute illness phase showed a chronic inflammatory response in both groups, but follow-up biopsy taken 3-6 months later demonstrated persistence of chronic inflammatory changes only in the group of patients in whom post-infectious IBS had developed. This combination of pathological and psychological findings lends support to the hypothesis that psychological factors exert an effect by enhancing biological changes, thus contributing to the expression of symptoms.[33,34]

3.8. **Diet:** Many patients consider that their symptoms worsen after meals. However, in most cases no clear relationship can be demonstrated between symptoms and the ingestion of any particular type of food. Nevertheless, around 60% of patients with IBS believe that they have some form of dietary intolerance or allergy and frequently try exclusion diets.[35] It is important to take a dietary history, partly to ensure that patients have not adopted an extreme diet that, contrary to their own expectations, may have exacerbated their symptoms.

3.8.1. A diet that is high in **fibre** may increase faecal bulk and ease symptoms in some patients. Conversely, some patients who increase their intake of fibre report a marked deterioration in symptoms of bloating, pain and disordered bowel habit, especially when using insoluble cereal fibre e.g. wheat bran.

3.8.2. Food items that have been shown to exacerbate IBS symptoms in some patients include coffee and other caffeine containing products, dietary fat, and sugar substitutes such as sorbitol or fructose.

3.8.3. There is scant evidence to support true IgE mediated dietary allergy (i.e. classical allergy to foods such as nuts and shellfish) as a significant factor in IBS. However, this mechanism may be relevant in a subgroup of patients with a history of atopy.[35]

3.8.4. IgG antibodies to food are common in the general population and have usually been considered to be consistent with normal function. However, there is some preliminary evidence to suggest that, where IgG antibodies to particular foods are detected in patients with IBS, there may be a role for the elimination of the specific dietary component involved. The most common foods identified in this category have been yeast, milk, eggs, wheat, barley, peas, cashew nuts, and almonds.[36]

3.9. **Other factors**

3.9.1. **Drugs:** Antibiotics, particularly erythromycin, and non-steroidal anti-inflammatory drugs (NSAIDs) can exacerbate the symptoms of IBS.

3.9.2. **Abdominal or pelvic surgery** can trigger or exacerbate the symptoms of IBS. Surgical trauma to the pelvis may sensitise adjacent organs and studies have shown that hysterectomy is associated with an increase in rectal and bladder sensitivity.[11]

4. Prognosis

4.1. IBS should be regarded as a lifelong condition. Only 5% of patients reporting IBS are symptom-free at 5 years of follow-up. Moreover, up to 45% of patients with IBS report a change in symptom pattern over time, fulfilling criteria for other functional gastrointestinal disorders such as functional dyspepsia or gastro-oesophageal reflux.[2] Patients can expect to have symptoms intermittently, especially when exposed to exacerbating factors.

4.2. Although patients may respond to education about the condition and symptomatic measures, the treatment of IBS often proves problematical. Many individuals with symptoms of IBS do not seek medical attention or have stopped consulting because of disillusionment with current treatment options. Thus less than half of patients with IBS are taking prescribed medication.[4]

4.3. Best results are achieved by adopting an approach that is specifically tailored to the needs of the individual. The optimum environment in which to deal with the many issues raised by IBS is provided by a lengthy, slow-paced, empathetic consultation conducted by an experienced physician. In the secondary care setting, the aim should be to dispel any belief that the patient may hold that the condition is so serious that it requires continuing hospital input and instead produce an action plan that facilitates discharge back to primary care. A combination of measures may be required focusing on the relief of the most debilitating symptom(s) whilst addressing any adverse psychological features and chronic highly threatening stressors that may be present. Consequently, a joint consultation involving a clinical psychologist may be beneficial. The subset of IBS patients with prominent psychosocial features tend to respond poorly to standard medical treatment and to have the most severe and disabling symptoms unless the psychosocial factors are addressed effectively.[9]

4.4. Treatment options in current use include the following:

- Bulking agents: soluble fibre may ease symptoms and relieve constipation. In contrast, insoluble fibre e.g. wheat bran may relieve constipation but does not appear to ease global symptoms
- Elimination diets: best carried out under the supervision of a dietician. Any food that is suspected of causing problems should be excluded from the diet for at least one month before the effects are reviewed
- Antispasmodics: either anticholinergics (e.g. hyoscine) or smooth muscle relaxants (e.g. mebeverine and peppermint oil)
- Antidiarrhoeals for diarrhoea predominant IBS
- Laxatives for constipation predominant IBS
- Tricyclic antidepressants: may be beneficial by virtue of either an anticholinergic effect on the gut and/or a mood-modifying action on state of mind. There is less evidence to support the use of antidepressants in the selective serotonin reuptake inhibitor (SSRI) class
- Psychological treatments; positive outcomes have been reported from trials involving cognitive behavioural therapy, psychotherapy, hypnotherapy, and relaxation training respectively
- Probiotics (“friendly bacteria”): Given the potential involvement of infection and inflammation in at least some cases of IBS, probiotics may have a role by virtue of exerting an anti-inflammatory effect. Different probiotic strains can have different

therapeutic activities. The *Bifodobacterium infantis* strain has shown particular promise but further research is required.

- The gut flora may also be modulated by the use of prebiotics. These are non-digestible food ingredients (carbohydrates) that can benefit the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon
- A type 4 serotonin receptor (5-HT_4) agonist for constipation predominant IBS has been licensed in several countries including the US. A type 3 serotonin receptor (5-HT_3) antagonist is available in the US for diarrhoea predominant IBS, but has been linked to cases of ischaemic colitis. These new treatments are not currently licensed in the UK
- Polymodal therapy may be prescribed, using combinations of treatments drawn from the above list e.g. pre- and pro-biotics combined with a tricyclic antidepressant
- Doctors may also guide their patients to seek information from helpful literature and web sites

4.5. Co-morbid psychiatric conditions, where present, should be treated as appropriate

4.6. Symptoms of IBS may cause diagnostic confusion and lead to unnecessary surgical treatment. Abdominal and pelvic surgery, including cholecystectomy, hysterectomy, and appendicectomy is more likely to be performed in patients with IBS as compared to controls.[37] A recent study reported that 11% of IBS patients had undergone abdominal surgery secondary to IBS symptoms.[5]

5. Summary

5.1. Irritable bowel syndrome (IBS) is a chronic, functional gastrointestinal disorder characterised by recurrent episodes of abdominal pain and altered bowel habit including diarrhoea or constipation. The condition is common and patients often find that their quality of life is substantially impaired.

5.2. IBS is a multifactorial condition and the precise aetiology remains uncertain. Different combinations of factors are likely to operate in any single individual. The underlying mechanisms involved include genetic predisposition, abnormal intestinal motility, inflammation, visceral hypersensitivity, dysfunction of the brain-gut axis, and neurotransmitter imbalance.

5.3. Psychosocial features are prominent in a subset of patients with IBS. A history of sexual or physical abuse is relatively common. Psychiatric co-morbidity is common in those who seek treatment. Chronic highly threatening stressors may trigger the onset and/or exacerbations of IBS symptoms. In contrast, commonplace daily sources of stress do not appear to generate symptoms.

5.4. The incidence of IBS is increased following bacterial gastroenteritis. IBS develops more commonly after severe initial infections and in those cases in which prominent psychosocial factors were operating at the time of, or prior to, the acute illness.

5.5. IBS should be regarded as a lifelong condition. Patients can expect to have symptoms intermittently, especially when exposed to exacerbating factors.

5.6. There are varied treatment options with no single clear therapy. Patients may respond to combination therapy.

5.7. Structured, informative, empathetic and unhurried consultation with a positive diagnosis can lead to improved symptom control.

6. Related Synopses

Stress (mental and physical) and Physical Disease

Depression

Generalised Anxiety State

Colorectal Cancer

7. Glossary

anterior cingulate cortex	An area of the brain involved in a wide range of autonomic functions, including regulation of heart rate and blood pressure, as well as cognitive functions such as reward anticipation, decision-making, empathy, and emotion.
atopy	Allergic reaction with strong family tendencies.
autonomic nervous system	The part of the nervous system that controls functions automatically without voluntary control, such as control of heartbeat and gland secretions.
concordance studies	Research to identify agreement in the types of data that occur in natural pairs. A pair of twins is *concordant* if both are affected or both are unaffected, but *discordant* if one of them only is affected.
coeliac disease	A disease characterised by atrophy of the villi (processes that serve to increase the absorbing surface of the small intestine). Caused by gluten sensitivity and leads to impaired absorption of nutrients.
cytokines	Proteins that act as intercellular mediators. They differ from classical hormones in that they are produced by a number of tissue or cell types, rather than specialist glands.
dizygotic twins	Twins derived from two separate eggs.
dyspareunia	Painful sexual intercourse.
enteric nervous system	An independent nervous system that controls and co-ordinates motility, blood flow, and secretion to meet the digestive needs of the individual.
histological	Pertaining to the study of cells and tissue at the microscopic level.
Immunoglobulin E (IgE)	One of five classes of immunoglobulin (specific protein substances involved in the body's immune response to infections, foreign substances etc). IgE is associated with immediate type allergic reactions.
Immunoglobulin G (IgG)	One of five classes of immunoglobulin. IgG antibodies are predominant in serum and are active against bacteria, fungi, viruses, and foreign particles.
immunohistological	Histological (*q.v.*) study of immunoreactive cells.
ischaemic colitis	Decreased blood flow to the colon, which may damage the bowel and cause symptoms of fever, pain, and bloody diarrhoea.

lymphocytes	Circulating white blood cells that are associated with functions conferring immunity. Hence: *lymphocytic*.
mast cells	Cells found in connective tissue and mucosa *(q.v.)* that release histamine, heparin, and serotonin *(q.v.)* in response to injury or inflammation.
monozygotic twins	Twins that are derived from a single egg.
mucosa	Also known as mucous membrane; a membrane that lines a body cavity and that is covered in mucous, a smooth, slimy fluid composed of secretions, white blood cells, desquamated cells, and various salts.
noradrenaline	A neurotransmitter (substance that transmits nerve impulses from one nerve cell to another) and hormone produced and secreted by the adrenal glands.
peristalsis	The worm-like movement by which a tubular organ such as the digestive tract propels its contents.
polymorphism	The presence of several distinct forms of a gene or phenotypic trait within a population with frequencies greater than 1%.
serotonin (5-hydroxytryptamine)	A neurotransmitter (substance that transmits nerve impulses from one nerve cell to another) and hormone. Present in the brain, digestive tract, and platelets.
sigmoid colon	The final portion of the colon, connecting to the descending colon above and the rectum below.
somatisation	The conversion of anxiety into physical symptoms.
visceral	Pertaining to the viscera, i.e. the organs situated in one of the great cavities of the body. Most commonly applied to the organs within the abdominal cavity.

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