

# Irritable bowel syndrome: Clinical review

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## Abstract

Irritable Bowel Syndrome (IBS) is a highly prevalent gastrointestinal disorder affecting over 10% of the global population. It is a condition managed mostly in primary care but can often result in referral to secondary care. The characteristic features of IBS are abdominal pain or discomfort with a change in bowel habit or defecation. Other features include bloating and abdominal distension. There is no test for diagnosing IBS and it is largely a diagnosis of exclusion. Patients are classified based on the Rome IV criteria and categorised based on the predominant symptom. The pathogenesis of IBS is understood to be multifactorial therefore the treatment options are diverse, seeking to address the IBS patient by using a holistic approach. Subsequently, therapeutic treatments are constantly evolving in an attempt to best manage the symptoms of IBS. In this review, we will aim to put a spotlight on IBS and in particular focus on the pathophysiology of IBS and how this understanding shapes how we manage IBS based on the current medical guidelines.

**Key words:** Irritable bowel syndrome, pathophysiology, diagnosis, treatment

## Background

Irritable Bowel Syndrome (IBS) is a gastrointestinal (GI) disorder that is characterised by altered bowel habits in conjunction with abdominal pain and/or bloating without structural or chemical abnormalities. IBS can severely impair quality of life and poses a significant health burden. As there is no single indicative test for IBS, and as it is a diagnosis of exclusion, diagnosing the condition can prove to be a challenge (1). Patients often present after a lengthy period since the initial symptoms develop typically with stress or dietary triggers. Psychological co-morbidities like depression often co-exist in patients with IBS which has produced many questions regarding the cause and true nature of IBS. The *New England Journal of Medicine* has in its archives dating back to the 1850s, content which alludes to the varied presentation (alternating diarrhoea and constipation) of IBS which we know now describes IBS-M (IBS-mixed variant), a mixed version of IBS. Cumming reported “The bowels are at one time constipated, another lax, in the same person. How the disease has two such different symptoms I do not profess to explain”(2).

Over time, our understanding has evolved and IBS which was once regarded an exclusively functional GI condition is now seen to be more complex. Understanding the minutiae of the possible pathophysiological theories for IBS symptoms is increasingly important because newer pharmacotherapy agents are beginning to target these previously unknown mechanisms. Altered gastrointestinal motility, visceral hypersensitivity, post infectious reactivity, brain-gut interactions, alteration in faecal micro flora, bacterial overgrowth, food sensitivity, carbohydrate malabsorption, and intestinal inflammation have been considered as possible causes in the pathophysiology of IBS (3).

## Epidemiology

The prevalence of IBS differs widely across the globe. Based on meta-analysis data of numerous study populations comprising over 250,000 subjects, the global prevalence of IBS is estimated to be over 11% (95% CI 9.8%-12.5%) with different parts of the world with different prevalent rates. Initially, studies found a low prevalence of IBS in developing countries. Recent research has found an increased prevalence in the developing nations. As economies begin to prosper, lifestyles have been found to become more Western-centric, possibly explaining this change (4, 5). In a large meta-analysis study, the prevalence of IBS in women was 67% higher when compared with men and more predominantly in the working age (95% CI 1.53-1.82) (6). The increased prevalence was predominantly found in the West and women were more likely to display symptoms suggestive of IBS-C rather than IBS-D. In the US, it is said that 3 in 10 people with IBS consult a primary care physician. This adheres to the trend of IBS in the western world. Therefore it is widely accepted that the majority of people with IBS remain undiagnosed in the community (7).

## Pathophysiology

The cause of IBS is not fully understood however many theories have been proposed over time which have guided the approaches to managing the condition. Earlier research stipulated that IBS has traditionally been regarded as a condition exclusively associated with abnormal colonic motility. This did not fully explain the spectrum of clinical presentations of IBS and this concept has developed over time in response to new evidence and ongoing research (8).

The pathophysiology of IBS is not fully understood, but certain pathogenic factors have been identified that could explain the onset or development of IBS. Growing evidence has suggested that IBS is not solely a functional disorder as once believed.

### Altered gastrointestinal motility

Early evidence from manometric and colonic transit studies revealed that patients with IBS were found to have contractions in dense clusters in the small intestine associated with symptoms like abdominal pain. Secondly, patients were found to have altered gastric transit, either too fast or too slow, resulting in diarrhoea and constipation respectively. In one study, postprandial subjects demonstrated high amplitude colonic contractions coinciding with abdominal pain suggesting a relationship with food ingestion (9).

### Visceral hypersensitivity

There is sufficient evidence to suggest that many differences exist in IBS. Experimental studies revealed that patients with IBS have been found to have increased sensitivity to balloon distension in both the upper and lower GI tracts. Further to this, IBS patients have also

been found to have a heightened sensitivity to intestinal contractions when compared with normal subjects. The exact mechanisms are not fully understood but it has been proposed that patients with IBS may exhibit a heightened pain response to visceral stimulation (10).

### Impaired gut microbiota

Several trillion microbes reside in our bowel and make up over a thousand different species. The most recognisable bacteria are Lactobacilli and Bifidobacteria (11). Such bacteria, also known as beneficial bacteria are known to have anti-inflammatory properties via an immune mediated response. Also, microbiota is thought to be essential in ensuring the homeostasis of the gut-brain axis which is regarded as a key element in the pathophysiology of IBS (12). The current assumption is that IBS patients have altered microbiota in their intestine. A study involving over one hundred IBS patients demonstrated that IBS patients had a different composition of gut microbiota. IBS patients were found to have less variety of bacteria and fewer beneficial bacteria such as Lactobacillus and Bacteroids species whilst the number of pathogenic bacteria were found to be increased (13). In IBS certain gut bacteria can generate chemicals which produce gas leading to abdominal distension. It has been suggested that an overpopulation of gas-producing bacteria in the intestine, an alteration in the gut microbiota, may account for abdominal distension in IBS patients.

### Gut-brain axis

IBS is a condition in which there is a disruption in the gut-brain axis. This axis is made up the central nervous system (CNS), the hypothalamic pituitary axis (HPA) and the enteric nervous system (ENS). Neural impulses are propagated from the gut via the vagus nerve, the spinal and the enteric nerves. The vagus nerve plays the most pivotal role in the communication between the gut and the brain. The hypothalamic pituitary axis (HPA) is also integral in this communication link because it modulates adaptive responses against stress through the production of corticosteroids alongside regulating important processes such as digestion and the immune system. Signals from CNS are transmitted by neuroendocrine neurotransmitters like serotonin to the gut to alter the behaviour of gut microbiota (14). Various neuroimaging studies on IBS patients have supported the gut-brain axis dysregulation hypothesis. Stress is thought to act on the emotional limbic system, resulting in a release of adrenocorticotrophic hormone and cortisol which then engages with the ENS resulting in symptoms like abdominal pain and loose motions (due to the induction of colonic dysmotility and visceral sensitivity). Several immune mediators are thought to be involved (e.g. IL-6 ) in this process (15).

### Dietary intolerance

One of the commonest contributing factors for troublesome symptoms in IBS is food intolerance. Patients with IBS typically report that certain foods trigger symptoms. An overwhelming majority of IBS patients report some form of food intolerance. A specific category of food known as FODMAPS (Table 1) are thought to be partly

Table 1: Dietary FODMAPs (18).

	Word that corresponds to letter in acronym	Compounds in this category	Foods that contain these compounds
<b>F</b>	Fermentable		
<b>O</b>	Oligosaccharides	Fructans, galacto-oligosaccharides	Wheat, barley, rye, onion, leek, white part of spring onion, garlic, shallots, artichokes, beetroot, fennel, peas, chicory, pistachio, cashews, legumes, lentils, and chickpeas
<b>D</b>	Disaccharides	Lactose	Milk, custard, ice cream, and yogurt
<b>M</b>	Monosaccharides	"Free fructose" (fructose in excess of glucose)	Apples, pears, mangoes, cherries, watermelon, asparagus, sugar snap peas, honey, high-fructose corn syrup
<b>A</b>	And		
<b>P</b>	Polyols	Sorbitol, mannitol, maltitol, and xylitol	Apples, pears, apricots, cherries, nectarines, peaches, plums, watermelon, mushrooms, cauliflower, artificially sweetened chewing gum and confectionery

responsible for these symptoms. These are foods that contain fermentable oligosaccharides, disaccharides, monosaccharides and polyols (16). FODMAPs cause IBS symptoms because they are fermented by gut bacteria and due to their osmotic effects. Meta-analysis data has demonstrated an improvement in symptoms and a 70% improvement in quality of life in patients who adopt a low FODMAP diet (17). Lactose containing foods and gluten rich diets have also been found to have a possible link to the pathogenesis of IBS symptoms but the evidence is not robust enough to substantiate this up to now.

### Post-infectious IBS

Acute GI infections are a predisposing factor for development of IBS. It is thought that approximately 10% of patients with IBS had a preceding infectious illness. Prospective data has shown that 3-36% of GI infections can lead to IBS symptoms (19). The cause of persistent or new bowel symptoms after an acute GI infection is uncertain, but several mechanisms have been highlighted. Enteritis may increase the risk of IBS via one of many mechanisms which include disruption of the mucosal nerves leading to

irritability, bile acid dysfunction and malabsorption, and distortion of colonic flora (20). One study looked at 19,000 patients who consumed contaminated drinking water which contained *Giardia lamblia*, norovirus and *Campylobacter jejuni* (21). The researchers noted that the risk for IBS symptoms was more profound in those with a background of anxiety and depression. This reinforces the concept of the gut-brain interaction in IBS and reaffirms the hypothesis that the pathophysiology of IBS is multifactorial.

### Genetics

Growing evidence shows that there may be genetic link to IBS. 5CN5A is a sodium channel gene mutation which is associated with abdominal pain in IBS and is thought to be a common denominator in 2% of IBS patients (22). A link between congenital sucrose isomaltase deficiency and IBS has also been considered highlighting the possibility of genes in the predisposition of IBS (23). These associations require further research but further demonstrate the ever changing understanding of the pathophysiology of IBS.

### Serotonin dysregulation

There is evidence to suggest that serotonin (5HT) is an important neurotransmitter involved in the stimulation of gut peristalsis. A function of 5HT is to enable gut motility and secretion of intestinal matter. 5HT is also thought to be pivotal in visceral sensitivity and blood flow (24). Abnormalities in the serotonin reuptake transport system have been discovered in patients with IBS. 5-HT<sub>2A</sub> receptor polymorphisms may be associated with the development of IBS. A significant association has also been found between the SS genotype of serotonin reuptake transporter polymorphism (SERT-P) and IBS-C (25). Research has also found that patients with IBS-C have an increased serotonin concentration in the colonic mucosa compared with IBS-D sufferers. Therefore there is a possible link between the impaired release of serotonin and the development IBS symptoms (26).

### Diagnosis and Assessment

Without the presence of a specific disease marker, several diagnostic criteria have been developed to standardise the diagnosis of IBS. The diagnostic criteria have developed over many years from Manning et al in 1979, to the Rome I criteria in 1994, and most notably, Rome IV criteria (2006). The current and widely used Rome IV criteria (Table 2) is the foundation upon which The National Institute for Health and Care Excellence (NICE) offers clinical recommendations in diagnosing IBS in the UK (27).

Routine diagnostic testing is not recommended in IBS as it is a diagnosis of exclusion and no specific test is available to confirm a diagnosis. It is important for clinicians to perform a detailed history and examination of patients with IBS to exclude other important differential diagnoses. Specific attention ought to be made to exclude key alarm features (Table 2) or red flags for GI malignancies.

Table 2 (1, 28)

### ROME IV CRITERIA FOR IRRITABLE BOWEL SYNDROME

Patient has recurrent abdominal pain ( $\geq 1$  day per week, on average in the previous 3 months), with an onset  $\geq 6$  months prior to diagnosis

**Abdominal pain is associated with at least two of the following three symptoms:**

- Pain related to defecation
- Change in frequency of stool
- Change in form (appearance) of stool

**Patient has none of the following warning signs (alarm features):**

- Age  $\geq 50$ yr, no previous colon cancer screening, and presence of symptoms
- Recent change in bowel habit
- Evidence of overt GI bleeding (melaena or haematochezia)
- Nocturnal pain or passage of stools
- Unintentional weight loss
- Family history of colorectal cancer or inflammatory bowel disease
- Palpable abdominal mass or lymphadenopathy
- Evidence of iron deficiency on blood testing
- Positive test for faecal occult blood

Where indicated, testing should include a complete blood count, coeliac antibodies, comprehensive metabolic profile, inflammatory markers, erythrocyte sedimentation rate or C-reactive protein, thyroid function tests and if suspected, imaging and cancer tumour markers. Stool sampling should be offered on a case by case basis paying attention to possible infective and inflammatory pathologies (28).

## Treatments

Effective counselling and patient education are important initial tools in managing IBS. Such measures can often alleviate the common anxieties and misconceptions about IBS which often act as underlying triggers for symptom relapse. This was highlighted in a study, where 52% of the enrolled patients with IBS assumed that the condition was caused by digestive enzyme deficiency, 34% assumed it required surgical intervention, and over one fifth of patients thought IBS was a precursor to cancer (29).

Patient education should be followed by practice dietary and lifestyle modification advice and evidence based medical therapies. Moderate to severer forms of IBS can be managed simultaneously with psychological therapies where considered appropriate. For some patients, a multidisciplinary approach is likely to achieve better outcomes typically involving primary care physicians, dieticians, nurse practitioners and psychologists or psychiatrists (30).

Medical treatments for IBS are currently symptomatic and there are a wide variety of approaches to management. Initial medications include antispasmodics, prokinetics and bulk-forming agents. If little clinical benefit is found, further symptomatic treatments are available. The variety of treatments available reflects the convoluted and multifaceted pathophysiology involved in the manifestation of IBS symptoms. Therefore it comes as little surprise that there is no single treatment plan that can be used for all IBS patients (31).

### Dietary and lifestyle modification

Dietary modifications have heralded successful outcomes anecdotally in the past, however new data has shown positive outcomes in study groups. The low FODMAP diet has for many patients been a beneficial dietary modification resulting in improvement and for some, resolution of IBS symptoms.

Dietary FODMAPs resulted in prolonged hydrogen production and subsequent methane production which lead to typical symptoms of IBS such as excessive gas and bloating. The combination of altered pH levels coinciding with changes to the gut microbiota are thought to contribute to changes in colonic function (32). Two studies compared the low-FODMAP diet to commonly recommended IBS diets (modified NICE guidelines). NICE and low-FODMAP diets were reported to be effective however, one study showed significantly better results in the low-FODMAP diet group, particularly with regard to pain and bloating (33).

There is insufficient evidence on the long term efficacy of FODMAP diets, however in a retrospective study, Maagaard et al highlighted the beneficial effects of the low FODMAP diet on IBS symptoms. In the study, the mean follow up time was 16 months and the majority of IBS patients in the study experienced relief of abdominal pain and bloating following adherence to low FODMAPs (34). Whilst low FODMAP diets have yielded success in patients, the underlying mechanism is not fully understood and perhaps in time with further understanding, diets may become more refined.

The challenges with low FODMAP lie in its compliance as it can be difficult to implement as routine and often requires detailed and time consuming patient education which is dependent on resource availability. Secondly, any elimination diet may be associated with nutritional deficiencies however some studies have shown little detrimental effects on nutritional status (35).

### Gluten free diet

Gluten free diets have demonstrated clinical benefit in patients without coeliac disease. A number of published studies have investigated the role of gluten in patients with IBS in recent years. Biesiekierski et al focused on patients in a double-blind, placebo-controlled, re-challenge dietary study. The significant outcome was that those patients exposed to gluten reported uncontrolled symptoms (68%), compared with patients exposed to placebo (40%) (36). Gluten reduction may be helpful in IBS, particularly if a low FODMAP diet did not provide adequate benefit.

### Fibre

There is no consensus on whether fibre intake has a favourable effect on IBS sufferers. However, given its benign nature with few side effects, it has been found to be of benefit in patients with IBS-C. Moderate efficacy was seen with constipation but studies found that pain relief was not associated with increased fibre intake (37). Fibre intake should be constantly reviewed in IBS patients, and when indicated, soluble fibre such as psyllium powder or foods high in soluble fibre such as oats are preferred (38).

### Lactose intolerance

It is important to consider lactose intolerance in patients with IBS symptoms. There is no evidence to suggest that the incidence of lactose malabsorption is higher in patients with IBS but patients with IBS and lactose intolerance have significantly more noticeable GI symptoms in response to lactose ingestion. Lactose intolerance can be diagnosed via a breath test, however a negative test does not exclude intolerance to cow's milk protein and alternative sources of milk, e.g. other mammals or soy, should be considered (39).

### Exercise

There are likely to be many processes involved for symptom relief in response to exercise. Both the physical and psychological benefits are likely to play a key role. Changes in gas transit and colonic transit due to exercise

have provided a rationale for the improved symptoms in IBS. This is supported in a paper by Villoria et al who highlighted that exercise increases gas clearance and reduced the frequency of abdominal bloating (40). Studies have demonstrated a correlation between physical activity and IBS symptom relief. Aerobic activity such as cycling has demonstrated a reduction in intestinal gas production in several studies and protects against the development of IBS according to several studies (41). Engaging in yoga as part of a study has also shown a reduction in IBS symptoms which is thought to be related to increase in sympathetic tone, which is typically reduced in IBS-D (42). Due to the increasing link between IBS and mental health conditions, exercise naturally comes under the spotlight as it has found to benefit or prevent mental health conditions. There is evidence to suggest physical activity has a positive impact on mental health, and in turn, it is assumed that this has a positive impact on IBS symptoms because of the increasingly recognisable gut-brain connection in IBS.

## Pharmacological treatment

### Antispasmodics

Antispasmodic agents can be used on an 'as required' basis when managing IBS. They offer short term relief for troublesome symptoms associated with IBS such as abdominal pain and/or bloating.

Antispasmodics work by inhibiting smooth muscle contractions in the GI tract such as mebeverine and pinaverine. There are also those that work by utilising anticholinergic or antimuscarinic properties such as those found in hyoscine and dicyclomene (43). A systemic review found that peppermint oil also helps in reducing IBS symptoms and is thought to be a calcium channel antagonist, resulting in relaxation of GI smooth muscle (44).

Despite the fact that antispasmodic medications have not shown significant clinical efficacy based on robust evidence, they are still commonly used in clinical practice. The anticholinergic side effect profile typically consisting of constipation, dry mouth and urinary retention are the most common reasons for early cessation of drug therapy (45).

### Probiotics

Probiotics are not routinely recommended in IBS however there is some evidence that probiotics improve symptoms in IBS. Preparations of the lactobacillus species are commercially available and widely consumed by patients with IBS. Trials for lactobacilli have yet to definitively prove its clinical benefit and more research is required in this field to present a stronger argument for its efficacy. Recent evidence based on studies observing the use of multi-strain probiotics (as opposed to mono-strain) has yielded improvement in symptoms for IBS patients (46). NICE guidelines have not recommended specific bacteria or named probiotic products, however 2017 guidelines summarised that they are a useful self-management option for people with IBS with little adverse effects (27).

## Medical management of IBS

### Medical treatments in IBS-C

Initial management of constipation in IBS differs in no way to conventional constipation management. The focus centres around dietary and lifestyle modification and adequate oral hydration. Dietary fibre is plentiful in a variety of foods that are also low-FODMAP such as fruits like bananas, vegetables like broccoli and seeds e.g. flaxseeds and pulses (dried seeds of legumes). Soluble fibre such as psyllium is widely available and is an inexpensive adjunct to dietary modifications. Lactulose is a typical over the counter osmotic laxative, which should be avoided in IBS due to its gas-producing and bloating effects (47). Relatively recent randomised controlled trial data has supported the role of soluble fibre in managing IBS. Analysis revealed that wheat bran, a source of insoluble fibre was found not to be of benefit. Methylcellulose is an option for patients who are unable to maintain adequate dietary fibre and it is better tolerated than bran (48). For patients with IBS-C, after a trial of soluble fibre and/or alternative constipation remedies as previously discussed, it is recommended that clinicians should consider treatment with PEG (polyethylene glycol) such as Linaclotide. Linaclotide is a synthetic guanylate cyclase C (GCC) agonist and has shown success in studies for improving IBS symptoms. It is supported strongly by the American Gastroenterological Association in the US and NICE in the UK (49).

A randomised trial involving 139 adults with IBS-C were assigned to PEG or placebo for 1 month. Patients treated with PEG compared with placebo had significantly more frequent bowel movements, improved stool consistency and less severe straining on defecation. There was little change noted with respect to the severity of bloating or abdominal pain however. Diarrhoea is the most common side effect experienced with Linaclotide which can be bothersome to most patients and is typically the cause for withdrawal of treatment (50, 51).

### Medical treatments in IBS-D

In IBS patients prone to diarrhoea, there is a typical increase in stool frequency but of normal overall volume. Loperamide, a common antidiarrhoeal can be the initial treatment of choice to be used when required. The evidence for loperamide is lacking in quality but due to its low cost and availability, it can be a useful adjunct to other therapies in countering IBS symptoms (43). An alternative to loperamide albeit with limited evidence is the use of bile acid sequestrants such as cholestyramine. The basis upon this recommendation is that in patients with IBS-D up to half of patients with functional diarrhoea and IBS-D are thought to have bile acid malabsorption (52).

Alosetron is a 5-hydroxytryptamine-3 receptor (5HT-3) antagonist. It is approved in the US for severe IBS-D in female patients in whom symptoms persist for longer than 6 months and who in those who have failed to respond to conventional treatment. Side effects of ischaemic

colitis and complications of severe constipation led to its temporary withdrawal by the Food and Drug Administration (FDA). Following a review, it was reapproved in the US under restricted conditions and starting at low dose regimes (53).

### Rifaximin

Rifaximin is an antibiotic approved by FDA that has been found to combat symptoms associated with IBS-D. It is recommended for patients who exhibit moderate/severe IBS symptoms (especially bloating) without constipation and those who fail to respond to conventional therapies. In two large RCT's, 1,260 patients with IBS received rifaximin 550mg three times a day vs placebo for 2 weeks duration and were followed up for 10 weeks. During the initial 1-month follow up phase, patients who received Rifaximin reported relief of IBS symptoms compared with placebo (41% v 32 %) (54). Rifaximin should be used in caution in patients and for an appropriate duration of time. This is because of the risk of bacterial or fungal superinfection such as *Clostridioides-difficile* associated diarrhoea and pseudomembranous colitis.

### Antidepressants in IBS

Antidepressants have been shown to relieve symptoms of IBS. Many antidepressants have analgesic properties and appear to work via their anticholinergic properties by targeting visceral hypersensitivity and central pain sensitisation (55). Tricyclic antidepressants (TCA's) and selective serotonin reuptake inhibitors (SSRI's) have both displayed some benefits in IBS patients according to studies. TCA's typically slow GI transit time, hence are used infrequently and with caution in those with IBS-C. SSRI's have been touted as a better option for IBS-C due to their recognised prokinetic effect on the small intestine. If abdominal pain persists despite initial medical treatment, NICE recommends an off-license indication of low dose TCA such as amitriptyline followed by monthly reviews to determine dose reduction. SSRI's e.g. citalopram or fluoxetine are alternatives if TCA's are not tolerated or contraindicated. TCA's and SSRI's are typically prescribed in patients who have depression. Therefore it is important to counsel patients with IBS that these drugs are used for their analgesic benefits in neuropathic pain and not for depression (56).

## Psychological therapies

Psychological therapies have been found to improve patients with IBS symptoms. Studies have indicated a correlation between psychological conditions like anxiety and depression with GI irritability leading to IBS symptoms. As the exact underlying aetiological mechanism for IBS is not fully understood but thought to involve processes within the brain and the gut, psychological therapies attempt to address the former. Therapies include cognitive behavioural therapy, relaxation training, hypnotherapy and dynamic psychotherapy (56).

Many patients report a clear pattern of GI symptoms coinciding with stress or anxiety hence it is reasonable to attempt such therapies. The majority of the trials are

limited to small sample sizes with little information on long term follow up. Despite this, many health care practitioners see it as an effective management option for patients.

## Novel treatments

There are many exciting developments in the treatment of IBS which often runs parallel to the advances made in our understanding of the pathophysiology of IBS.

Faecal microbiota transplantation (FMT) involves the transfer of faecal matter from a healthy individual into another person (via endoscope into the intestine) with the aim of treating IBS symptoms. It is based on the same premise that probiotics are used but its apparent advantages are that it allows the maturation of a greater number of bacteria and more diverse strains of bacteria in the gut. FMT has been successful in the treatment of recurrent *Clostridium difficile* infection but the exact mechanism is not fully understood. A number of studies highlight the FMT success is dependent on the characteristics of the stool donor so exciting research into seeking super donors that meet favourable profiles is a growing area of research. It is assumed that microbial diversity is a positive indicator of faecal microbiota transplant success (57, 58).

There is emerging evidence suggesting the possibility of intestinal permeability in IBS. This raises the issue of the leaky gut and some patients have been found to show elevated markers of increased immune activation and raised cytokine levels and mast cells raising the question about a different pathophysiological mechanism. This has raised the potential role of mast cell stabilisers in IBS amongst other theories. Insufficient evidence exists about this concept but this may point to newer therapeutic agents in the future (59).

## Conclusion

The role of primary care physicians in reducing the burden of IBS in the community is essential and managing patients with an individualised approach is encouraged. There are promising new developments which may present an exciting future in managing IBS. We have highlighted the growing need to understand the pathophysiological concepts in IBS so that we may understand better not only the treatments that currently exist, but also those that may arise in the future.

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