

Literature review

Irritable Bowel Syndrome: The Functional Medicine Approach

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Abstract: Irritable bowel syndrome (IBS) is a complex functional gastrointestinal disorder with limited success in pharmacological therapy. The functional medicine approach aims to identify the root causes and personalize diagnosis and treatment. IBS is a chronic disorder characterized by abdominal pain, altered bowel movements, and other gastrointestinal symptoms. Diagnosing the condition remains challenging due to the lack of specific biomarkers or tests, resulting in frequent misdiagnosis.

The pathogenesis of IBS involves factors such as altered gastrointestinal motility, visceral hypersensitivity, intestinal barrier disorder, stress, dietary factors, small intestinal bacterial overgrowth (SIBO), changes in intestinal flora, low-grade mucosal inflammation, and genetic predisposition. The biopsychosocial model highlights the interaction between physiological and psychological factors.

The management of IBS involves a multidimensional approach tailored to each patient. Pharmacological therapy aims to alleviate symptoms but does not cure the condition. Non-pharmacological therapies, including dietary interventions, probiotic therapy, mind therapies, exercise, and complementary therapies, play a crucial role in IBS management.

Keywords: irritable bowel syndrome, functional medicine, pathogenesis, pharmacological therapy, non-pharmacological therapy.

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Introduction

Irritable bowel syndrome (IBS) is a functional gastrointestinal disorder caused by multiple factors¹. The disease has poorly understood etiology and pathology; thus, there is a limited success of pharmacological therapy. Functional medicine looks at the conditions more broadly (in social, family, psychological, and other contexts) trying to identify the root causes, have an individual approach to diagnosis and treatment. It mixes drug therapy with complementary or alternative therapies for better clinical outcomes^{2,3}. This report summarizes the latest scientific evidence in epidemiology, etiology, pathogenesis, and treatment of the condition with a particular focus on the functional medicine approach.

Understanding IBS and its prevalence

IBS is a chronic functional gastrointestinal disorder. Although bowel symptoms predominate, other symptoms like anxiety, changes in the working of different organs may also be present. Diagnosing the condition remains a challenge due to difficulties in identifying the organic changes in the body and the lack of specific biomarkers or tests. It remains a commonly misdiagnosed condition^{1,4}.

IBS is a condition characterized by bowel discomfort, abdominal pain, altered bowel movement. It may be characterized by either frequent episodes of diarrhea or constipation. While in some individual bouts of constipation may be followed by diarrhea. Other gastrointestinal symptoms like bloating, distention, are common⁵.

The first attempts to understand the condition were made in the 19th century. However, efforts to standardize or formalize diagnostic criteria were only made in the mid-20th century. Manning first created the diagnostic criteria, which formed the basis of Rome criteria. Rome criteria for the diagnosis of IBS are now most widely accepted, and they are in their fourth iteration⁶.

Rome IV diagnostic criteria states that the onset of symptoms should be at least 6 months before the diagnosis. A person should have gastroenterological symptoms like abdominal pain at least one day in a week for the last three months, along with the association of symptoms with defecation, changes in the frequency of stool, change in the appearance of stool⁶.

Additionally, it should be noted that some patients may present with more severe signs and symptoms, related or unrelated to IBS. There are so-called “red flags” or warning signs to look for, like severe anemia, weight loss, severe bowel inflammation, family history of colorectal cancer⁶.

There have been some studies regarding the sensitivity and specificity of Rome criteria, and it seems that they are precise enough for accurate diagnosis of IBS in most cases without the need for additional investigations⁷.

Functional gastrointestinal disorders (FGIDs) are common and account for almost 40% of all the referrals to gastroenterologists⁶. Of all the recognized FGIDs, IBS is the most prevalent condition. Researchers estimate that about 11% of the population is affected by IBS globally. Females are more prone to be diagnosed with the disease. Further, there is vast variance in the prevalence of the condition between different ethnic groups and nations. This could be explained by the differences in dietary habits, environmental conditions, psychological health, and so on^{8,9}.

Pathogenesis or pathological factors in IBS

The pathogenesis of IBS is still not fully understood, that is because multiple factors perhaps cause the disease. In most people, a combination of the number of factors leads to IBS. Factors involved in the pathogenesis of the disease will differ among individuals, and thus the therapeutic approach. Some of the well-known factors predisposing or leading to the disease are genetics, environment, post-infection inflammation, altered gastric motility, altered immune response, changes in gut permeability, psychological reasons, and so on. This report looks at some of the better-known pathological factors.

GI motility disorder

Changes in GI motility is one of the essential diagnostic criteria in IBS. Such changes are present in all the patients, in some motility is increased, in others decreased, while in others there is an alternating pattern¹⁰.

It seems that one of the reasons for altered motility is the changes in serotonin (5-HT) signaling. There is reason to believe in the role of serotonin in modified gut motility, as most of it is produced by enterochromaffin cells in gut affecting both the efferent and afferent nerves. Moreover, experience from empirical drug therapy shows that drugs altering 5-HT signaling may help patients. Thus, antidepressants may help in some cases, a class of drugs that alter 5-HT signaling (tricyclic antidepressants or serotonin selective reuptake inhibitors, and other drugs)¹¹.

Visceral hypersensitivity

It is another widely accepted concept which states the gut of people living with IBS responds excessively to various stimuli. This hypersensitivity could be due to increased sensitivity of local receptors, inflammation, changes in spinal reflexes, or even alterations in the brain (due to stress or other reasons)^{12,13}.

Intestinal barrier disorder

It means altered gut permeability, or some may call it leaky gut syndrome. It is about changes or rather disruption in the tight junctions. These changes can be caused by various means like inflammation, food intolerance, visceral hypersensitivity, changes in gut flora, certain infections, and much more.

Stress and altered gut-brain interaction

Numerous studies have shown that stress is one of the major contributing factors to altered intestinal motility, permeability, and visceral hypersensitivity. Chronic worry and psychological stress may especially increase the risk of developing IBS^{14,15}. Mental stress is frequently associated with the exacerbation of the symptoms¹⁶. Stress may cause IBS in multiple ways, by altering local immune responses (altered mast cell stability and modulation of corticotrophin-releasing factor, and much more), affecting gut flora¹⁷.

In recent years role of the altered gut-brain axis, caused by chronic stress, has received a lot of attention. Stress causes changes in the hypothalamic-pituitary-adrenal (HPA) axis and autonomic nervous system responses¹⁸.

Dietary factors

Although dietary factors are not included in the diagnostic criteria, it is no secret that the kind of diet plays a vital role in the pathogenesis of any gut-related disease, and IBS is not exclusion. It is well known that dietary changes can help relieve symptoms in many cases. Further, many people living with IBS are known to report worsening of symptoms or exacerbations after a certain kind of food items.

Food allergies, intolerance, gluten intolerance, does play a role in the disease¹⁹. Diet high in fermentable oligo-, di- and monosaccharides and polyols (FODMAPs) have especially been shown to cause worsening of symptoms in IBS^{20,21}.

Studies also show that those living with IBS have some common dietary patterns like they are more probable to consume canned food, processed meat, and so on. This underlines the importance of the individual approach and the need for understanding the dietary pattern of a person living with IBS²².

Small intestinal bacterial overgrowth (SIBO)

Although IBS is not an infectious disease, nonetheless, some studies indicate improvement in IBS symptoms after antibiotic therapy²³. Some studies show the correlation between SIBO and IBS based on the correlation of results of various breathing tests and worsening or improvement of symptoms of IBS^{24,25}.

Changes in intestinal flora

Correlation between the incidence, prevalence, exacerbation, and severity of IBS and alterations in intestinal flora is yet not fully understood. Nonetheless, what studies show that intestinal flora in those living with IBS differs a lot from healthy subjects. Moreover, there are many reports of benefits from the use of various probiotics²⁶⁻²⁸.

Low-grade mucosal inflammation

It is well known that most patients living with IBS have low-grade mucosal inflammation of the gut. Moreover, there is evidence that the level of inflammation increases during exacerbation. Although the functioning of T and B lymphocytes is known to be altered, special attention has been given to the altered activity of mast cells. This low-grade inflammation may be behind leaky gut and visceral hypersensitivity²⁹.

Genetics

Although poorly understood, genetic predisposition is undoubtedly one of the major contributing factors. Some genes are now known to be associated with altered gut motility and a higher risk of developing IBS¹⁹.

Summing it up – the Biopsychosocial Model

Above mentioned are just some of the factors and mechanisms involved in disease development. It is necessary to visualize IBS as a multidimensional disorder. In most cases, it is caused by multiple reasons or even all of the above factors playing a role to a degree. The biopsychosocial model sums up the things and proposes that the disease is caused due to interaction between psychological and physiological factors, whereas genetics and early life are predisposing factors. Prolonged psychological distress leads to physiological changes in gut health and motility and vice-versa³⁰.

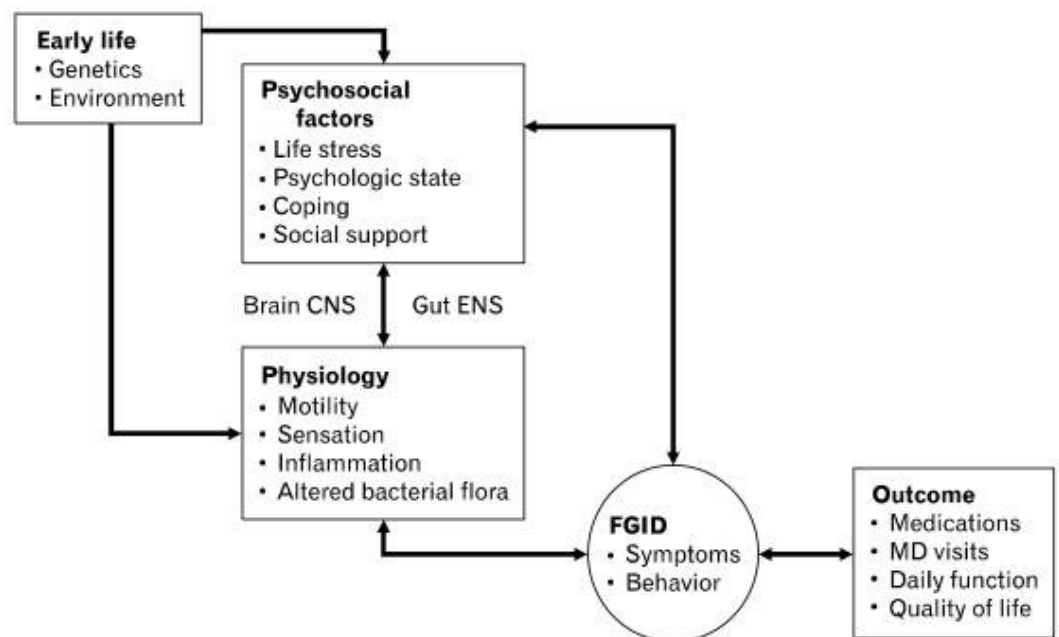


Figure 1 Biopsychosocial model of IBS (Image source: Tanaka Y, Kanazawa M, Fukudo S, Drossman DA. Biopsychosocial Model of Irritable Bowel Syndrome. *J Neurogastroenterol Motil.* 2011;17(2):131-139. doi:10.5056/jnm.2011.17.2.131)

Instrumental Diagnosis of IBS

Using Rome IV criteria, already mentioned in the article, is the primary way to diagnose the condition. However, in practice, things are more complex, and diagnosing the condition is quite challenging. Although there are no specific biomarkers for IBS, nonetheless physicians need to do several tests to exclude other organic diseases and assess the health status of the individual.



Functional medicine specialists need to pay attention to other non-intestinal symptoms, pay particular attention to the family and social history of the individual. Those living with IBS may complain about dyspepsia, nausea, unexplained heart pains. There is a need to pay special attention to the presence of other functional disorders like fibromyalgia, chronic fatigue syndrome, migraine, PTSD, mood disorders, sleep, and sexual disorders, as one or some of them may coexist with the condition³¹.

To exclude red flags or other severe disorders, physicians would frequently need to order complete blood count and chemistries, tests for inflammatory markers like erythrocyte sedimentation rate or C-reactive protein, may order specific stool tests (understanding digestive issues and excluding parasitic manifestation). Some cases may require endoscopy or colonoscopy; others may need motility studies. Serological tests may help exclude autoimmune disorders. Other tests like breathe tests may help diagnose SIBO¹².

Functional medicine specialists may frequently ask for additional tests to assess the GI effects like a test for pancreatic elastase, SCFA, F/B ratio, pathogens, tests for mycology, zonulin test, calprotectin, lactulose/mannitol. These tests help assess both the status of digestive health and the severity of leaky gut syndrome³².

Management of IBS

The multidimensional disease would certainly require multi-component therapy. Moreover, every patient would differ from another, and what worked in one may not help others. This underlines the importance of the individual approach towards each patient.

Another important thing worth understanding is that modern medicine primarily aims at the management of symptoms and cannot cure the condition. Whereas, functional medicine has a different approach as it seeks to understand the root cause of the disease and thus find a remedy that could bring prolonged remission of the condition.

Pharmacological therapy of IBS

Medical drug therapy primarily aims at alleviating the symptoms and providing relief. Most of these drugs would require prolonged treatment, as none of them seek to cure the condition. Drug therapy is primarily aimed at alternating gastrointestinal motility and secretions, manage pain, stabilize mood disorders, alter sensation³³.

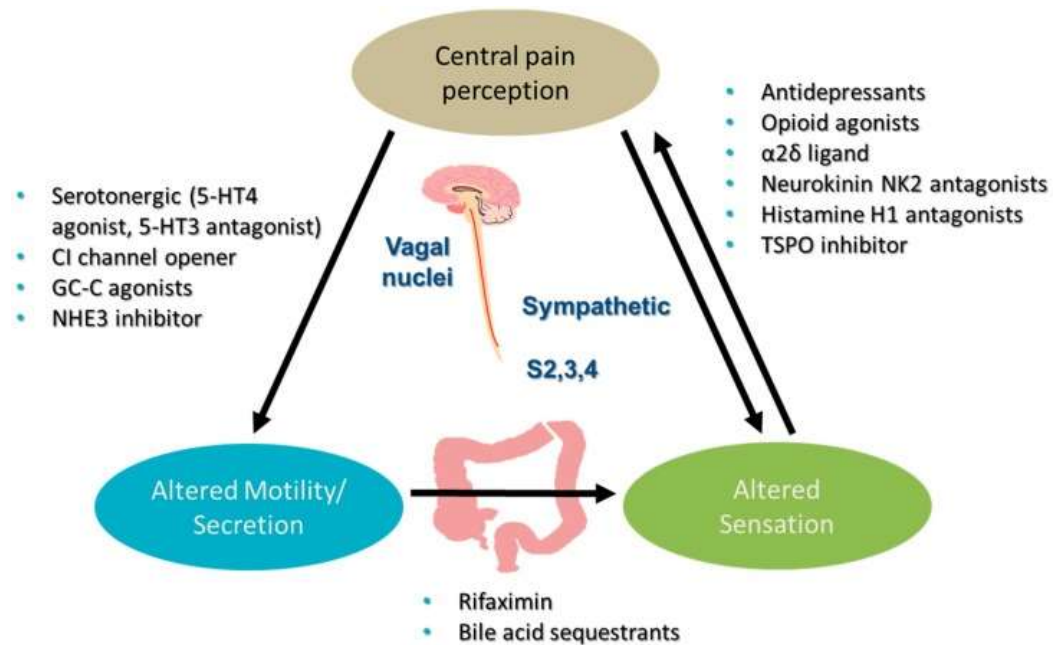


Figure 2 Pharmacological treatment of IBS (Image source: Camilleri M, Ford AC. Pharmacotherapy for Irritable Bowel Syndrome. J Clin Med. 2017;6(11). doi:10.3390/jcm6110101)

Some of the most commonly used pharmacological agents used to treat IBS are **anti-spasmodics** like otilonium bromide, dicyclomine, hyoscyamine. These medications help reduce pain, abdominal distention, and may also help normalize intestinal motility^{33,34}. Cochrane systemic review shows that these classes of drugs may help relieve pain and some other symptoms³⁵.

Bulking agents may also help in some cases; they are widely used to treat IBS due to an excellent safety profile. However, the benefit of such a treatment is not fully understood³⁵.

Antidepressants like tricyclic or selective serotonin reuptake inhibitors (SSRIs) are widely used to treat IBS as psychological disorders are common among people with IBS. Further, these drugs affect intestinal motility, secretions, and may change the response to pain stimuli. They may help reduce intestinal irritation, distention^{33,34}. Nonetheless, clinical evidence favoring their use to treat the condition is limited³⁵.

Anti-diarrheal opioids like loperamide remain widely used drugs. They are especially useful for those with diarrhea as a predominant complaint. It may not only help control stool frequency, but may also affect stool consistency, and help reduce abdominal pain^{33,34}.

Serotonin receptor (5-HT3) antagonists and serotonin receptor (5-HT4) agonists may help correct intestinal motility by either increasing or decreasing the transit time. Apart from it, these medications may reduce visceral sensitivity and pain. 5-HT3 antagonists like alosetron may reduce intestinal motility, bloating, and pain. Whereas, 5-HT4 agonists like tegaserod may increase motility. These classes of drugs have been specially approved to treat IBS, though their clinical efficacy is limited³⁴.

Other drug therapies commonly used by functional medicine practitioners are **antibiotics (like rifaximin) to treat various infections or SIBO, bile acid sequestrants, intestinal secretagogues (lubiprostone, linaclotide, or plecanatide), GABAergic agents, Histamine antagonists, mast cell stabilizers, and others**³³.

Non-pharmacological therapy of IBS

Despite the availability of a plethora of drug therapies, very few of them seem to work in most of the cases. Moreover, drug therapies are primarily aimed at symptomatic relief. Systemic reviews show that most traditional and newer drug therapies are just a little more effective than placebo. This means that **non-pharmacological treatment must be an essential part of IBS management.**

Dietary therapy may work in a number of cases since it is well-known that in many patients, symptoms of IBS worsen after prominent meals³⁶. Most dietary interventions work by restricting the intake of certain food items, and at the same time, adding specific nutrient-rich food items to the diet. Among restrictive diets, the gluten-free and low FODMAP diet are the most researched diet forms, and there is enough clinical evidence to suggest that they may work in many cases^{37,38}. Another approach is to increase the intake of dietary fiber, which can have a mild benefit in some cases. However, researchers warn that in some cases, dietary fiber may even worsen the symptoms³⁹.

Probiotic therapy is one of the well-researched fields. There is a reason to believe that manipulating gut microbiota may help in some cases as the human gut contains a tremendous amount of microbiota. Although there is no doubt that intestinal microbiota is essential for gut health, its complete role in well-being is poorly understood. Moreover, researchers are still not sure about the role of the various strains in health and disease. There are moderate evidence that different commercially available probiotic formulations may help in IBS. Probiotics may help reduce pain and severity of the disease, but the magnitude of benefit is still not evident. Nonetheless, keeping in mind the safety of the therapy, it is something worth including in the treatment-plan⁴⁰⁻⁴².

Mind or psychological therapies should be included in IBS treatment. The role of psychological factors in the disease pathogenesis is well established. Further, the efficacy of mood-altering drugs like antidepressants shows that any non-pharmacological psychotherapy may help too. There are various options available, like practicing mindfulness, yoga, tai-chi, cognitive behavior therapy, psychotherapy, bio-feedback. Functional medicine therapists must pay particular attention to family status and relations, as individuals with inter-family conflicts may have worse symptoms. Mind therapies or psychotherapies whether given in clinics or from a distance, may help reduce the severity of the condition. Moreover, these therapies are entirely free from adverse effects⁴³⁻⁴⁸.

Mechanical interventions like exercise, reflexology, massage, acupuncture may help patients feel better, reduce stress, and thus improve symptoms. These therapies also promote lifestyle changes like people doing regular exercise (biking, strength training, aerobic exercise, walking, and so on) are more probable to make a healthy lifestyle choices⁴⁹. There is a strong case in support of exercise therapy, especially considering its feasibility and numerous health benefits. Even if exercise does not help directly, it can help relieve many symptoms like constipation, mood disorders, reduce pain severity^{50,51}. Evidence in support of some complementary therapies like acupuncture is mixed with some reviews showing no benefits while others demonstrating significant improvement in symptoms^{52,53}.

Herbal therapies remain widely used for various functional disorders, especially for gastrointestinal disorders. It is estimated that about half of all the patients living with IBS would try some or another herbal remedy⁵⁴. There are numerous herbal treatments available⁴⁹, and this report looks at some of the better-known therapies.

Peppermint oil is a well-known natural remedy for digestive disorders, and it is also one of the most well-researched treatments too. It is available in various forms as oils, liquids, capsules, and so on. It is known to help with non-ulcer dyspepsia. It may be useful in relieving pain related to colonic spasms and may help relax smooth muscles. Its topical application may have a mood-elevating effect and may help with tension headaches. A systemic review of clinical data shows that it is a moderately effective therapy for short-term relief of the symptoms. However, its role in prolonged IBS therapy is unclear^{55,56}.

Turmeric extract or curcumin is the most researched herbal extract in modern times. It is known to have anti-inflammatory, antioxidant, gut microbiota modulating, anti-microbial, pain-relieving properties with extremely high safety profile. Apart from current research, it has been used in various Asian cuisines and traditional medicines to help with digestion and improve gastrointestinal health. Although, at present, there is a lack of robust clinical evidence, nonetheless, it seems to be a remedy worth using^{57,58}.

Plantago psyllium may be especially helpful for those living with constipation. It is an excellent source of fiber and thus may help with peristalsis, reduce intestinal irritation, increase secretions, normalize gut microbiota, normalize immune responses, and may also help lower cholesterol levels, blood pressure, and improve glycemic control. There is moderate clinical evidence that it may help with IBS^{59,60}.

There are numerous other well-researched herbal remedies for IBS, and discussing all of them is beyond the scope of this report. However, some of the other herbal remedies worth looking at are Aloe Vera, Artichoke, Fumaria officinalis, Hypericum perforatum, Padma Lax, and many more^{49,61}. Additionally, vitamins, minerals, and other food supplements may help too.

Conclusion

To conclude, IBS is a multi-dimensional illness requiring a multi-directional treatment approach. No single approach will work in all cases. There are numerous pharmacological and non-pharmacological therapies to choose from. However, this choice and lack of strong evidence in favor of any single treatment option make treatment tasks difficult. Nonetheless, with a broader approach towards a patient, like that proposed in functional medicine, one may identify the root causes of the disease and choose the right treatment options. When diagnosing and treating the condition, both somatic and psychological disturbances should be considered.

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