

# Irritable Bowel Syndrome

---

**Irritable bowel syndrome affects the gut and causes great pain and discomfort. Modern treatments help make life easier; pharmaceutical research is exploring promising new approaches.**



## **What is irritable bowel syndrome?**

Irritable bowel syndrome (IBS) is a chronic disorder of the gut. IBS is associated with abdominal discomfort or pain, usually in the lower abdomen, and its onset is associated with a change in the frequency and form of stool. Pain and discomfort of patients are relieved by defecation. After a while, another episode of abdominal pain sets in. Symptoms can vary and sometimes seem contradictory, such as alternating diarrhoea and constipation. IBS is a multi-faceted disorder. Symptoms most probably result from a disturbance in the interaction between the gut or intestines, the brain, and the autonomic nervous system that alters regulation of bowel motility or sensory function.

There are no physical findings or diagnostic tests that definitively confirm the diagnosis of IBS. Diagnosis involves identifying certain symptoms consistent with the disorder and excluding other medical conditions with similar clinical symptoms. The Rome II Diagnostic Criteria (a system for diagnosing functional gastrointestinal disorders based on symptoms) for IBS emphasize a positive diagnosis rather than exhaustive tests to rule out other diseases. IBS is characterised by abdominal discomfort or pain that is accompanied by at least two of the following features: (i) it is relieved with defecation, and/or (ii) onset is associated with a change in frequency of stool, and/or (iii) onset is associated with a change in appearance of stool. This has to happen for at least 12 weeks or more during a 12 month period, although that does not have to be consecutive.

Exacerbations and remissions are common; symptoms tend to improve with time. IBS is a non-life-threatening condition with no serious complications. However, failure to manage symptoms can reduce quality of life, may disrupt personal or professional activities, upset emotional well-being and lead to social avoidance, anxiety and depression. The exact origin of IBS is still unknown.

### **Who does irritable bowel syndrome affect?**

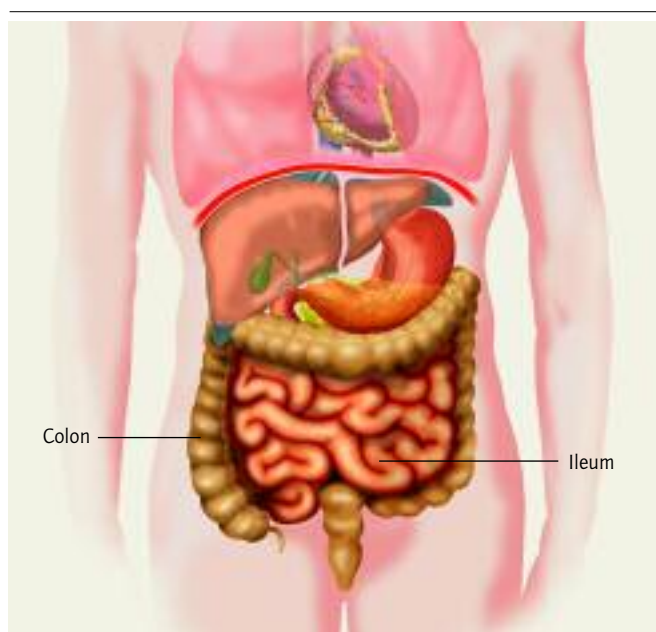
IBS is very common – about one in five people get it at some point. The prevalence of IBS in European countries varies from five to 25 per cent. Women are more commonly affected than men, leading to a male to female ratio of about 1:2. It is the most common disease diagnosed by gastroenterologists and one of the most common disorders seen by primary care physicians. Sometimes irritable bowel syndrome is referred to as spastic colon, mucous colitis, spastic colitis, nervous stomach, or irritable colon.

In 50 per cent of people, symptoms begin before the age of 35 years. Onset or recurrence is often linked to the stress of life events. But IBS is not caused by stress, and it is not a psychological or psychiatric disorder. Because of the connection between the central nervous system and the intestines, symptoms in some individuals can be exacerbated or triggered by stress. It is estimated that IBS affects some 40 million people in Europe.

### **Present treatments:**

Treatment options are available to manage IBS – whether symptoms are mild, moderate, or severe. Many patients need a treatment intermittently according to severity. Mild symptoms affect about 70 per cent of people: symptoms occur infrequently, and occasionally interfere with normal daily functioning. Moderate symptoms affect about 25 per cent of patients: symptoms occur more intensely and frequently, interfere with daily activities, and prompt awareness of what factors bring on their symptoms. Severe symptoms affect about 5 per cent of individuals with IBS: symptoms are frequent, intense, and interfere with daily functioning.

Treatment of mild cases is directed towards education, reassurance, change of lifestyle, avoiding offending foods that are thought to have been triggering symptoms in the past and occasional medication. Pharmacological therapy is best used in IBS patients with moderate to severe symptoms which do not respond to a change in diet or counselling. In the past, first line treatment has traditionally been aiming at the most bothersome symptom. However, recently introduced new therapies for IBS have been shown to treat multiple symptoms of IBS effectively.



Bulk-forming laxatives are only useful in cases where constipation predominates. Anti-diarrhoea agents that slow small and large intestinal transit time and improve consistency of stool lead to reduction in stool frequency and urgency in IBS patients. They do not lead to improvement in abdominal pain or distension. Antispasmodic medicines such as smooth muscle relaxants and antimuscarinic compounds are effective in reducing abdominal pain.

In September 2004, results of a large clinical Phase 3 study have shown that patients continue to respond to intermittent therapy with a compound which acts as partial 5-HT<sub>4</sub> agonist. Meanwhile, the product has been filed in the European Union for constipation-predominant IBS in women. With this indication, the product is already available in many countries worldwide. In the US and some other markets the compound has been approved for chronic constipation in both men and women.

### **What's in the development pipeline?**

In the past, IBS had been thought of as a functional disorder, i.e. one with no apparent anatomical or biochemical explanation. New molecules to treat IBS in late-stage development are designed to exploit the serotonin (5-HT) target.

In September 2003, results of a Phase 2 clinical study conducted in five European countries have demonstrated a benefit in patients with mixed symptoms of IBS, i.e. both diarrhoea and constipation. The new compound's effects on patients who suffer from alternating IBS symptoms are considered to be a virtue of its dual mechanism of action – the molecule is a full 5-HT<sub>4</sub> receptor agonist and also acts as a 5-HT<sub>3</sub> antagonist.

In early 2005, clinical Phase 3 trials have started with a novel chloride channel opener compound for constipation-predominant IBS. The medicine is given orally and acts to increase intestinal fluid secretion via the ClC-2 chloride ion channel in the intestinal membrane.

It is increasingly recognised that the central nervous system plays a crucial role in disorders such as IBS. Some neurological compounds have shown dual mechanisms of action that look interesting for new approaches of treatment. There is some evidence that antidepressants may provide help with pain, spasm and diarrhoea. The use of selective serotonin-reuptake-inhibitors (SSRIs) is currently being evaluated.

### **The longer-term future:**

In June 2004, investigators published findings on significant molecular alterations in serotonin function in the gut of IBS patients. Serotonin in the gut binds to 5-HT receptors on nerve cells, initiating intestinal movement. The results apparently support the assertion that disordered gastrointestinal function in IBS involves changes to the bowel. Researchers found that patients with IBS had a significant decrease in serotonin content, but no difference in serotonin release. They also had markedly reduced levels of serotonin transporting activity. This reduction is expected to decrease the capacity of epithelial cells to remove serotonin once it is released, thus increasing serotonin availability and ultimately causing abnormal bowel function.

---

#### **DISCLAIMER**

EFPIA has made all reasonable efforts to include accurate and up-to-date information in this PDF, but cannot guarantee completeness or accuracy of the information.

You must consult your doctor, or other qualified healthcare professional on any specific problem or matter covered by the information in this PDF.

The "Medicines for Mankind" publications are made available on condition that no part of the publications (including photographs) may be reproduced or abstracted without prior agreement with the European Federation of Pharmaceutical Industries and Associations (EFPIA). Under no circumstance can any of the material included in this PDF be used in promotional material and/or campaigns.

Editing Board: Dr. Robert Geursen (Chief Editor), Peter Heer, Bill Kirkness, Philippe Loewenstein, Steve Mees, Dr. Jean-Marie Muschart, Marie-Claire Pickaert (Coordinator).

Photocredits: ABPI, Allergan, AstraZeneca, EFPIA/Lander Loecx, Damian Foundation, Galderma, Hilaire Pletinckx, Roche, sanofi-aventis; Design & Production: Megaluna+Triumviraat