



Zelmac™ Learning System: Module 2

Learning Objectives

Overview of Gastrointestinal Disorders

Learning Objectives

- Recognize that a variety of GI conditions can cause symptoms similar to those present in IBS, making exclusion of other diseases essential
- Learn that GI disorders are classified as either organic or functional according to whether a specific, identifiable structural or biochemical cause is present or not present, respectively
- Recognize that IBS occurs worldwide, not just in Western cultures
- Understand the prevalence of IBS in different patient populations
- Describe the major mechanisms that have been proposed to explain IBS
- Outline the factors that may trigger or exacerbate IBS symptoms
- Name the characteristic GI and non-GI symptoms of IBS
- Become familiar with the different diagnostic criteria that have been established
- Understand the different laboratory and other tests that doctors use to distinguish between diseases

Overview of Gastrointestinal Disorders

Introduction

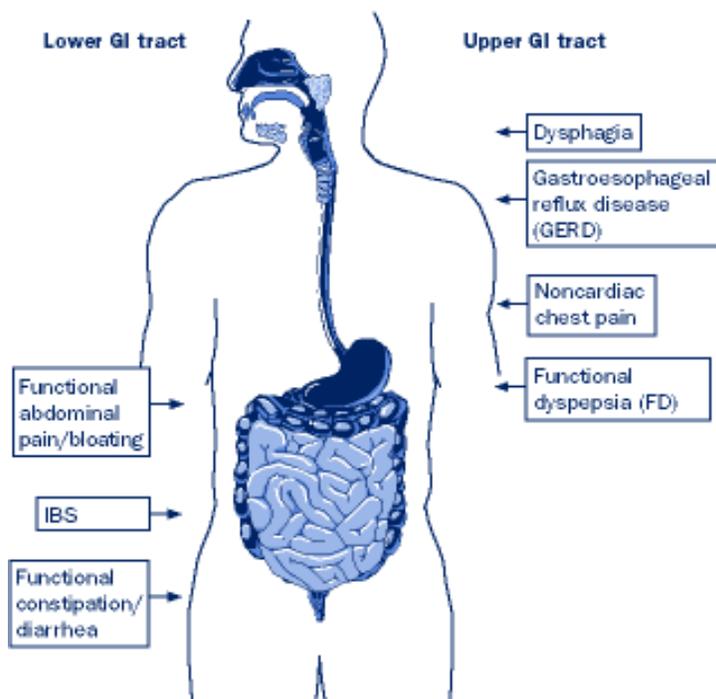
Gastrointestinal disorders are either organic or functional. Organic diseases are those that can be identified by structural or biochemical changes or abnormalities. Functional disorders, on the other hand, are those that cause symptoms and may seem to affect the function of an organ, yet the organ shows no sign of disease on examination (Figure 2.1).³ As a result, xrays, blood tests, and endoscopies can have essentially normal results. It is very important to understand this difference because the

Functional Disorders

Functional GI disorders can affect any part of the GI tract, including the esophagus, stomach, and intestines. They are disorders of function (how the GI tract works), not structural or biochemical abnormalities

distinction between the two forms the basis for how physicians classify and diagnose GI disorders.

Figure 2.1. Functional Gastrointestinal Disorders



The symptoms for different GI disorders can often be very similar, making accurate diagnosis difficult. For example, several conditions cause diarrhea, abdominal pain, or vomiting. This chapter contains descriptions of some of the more common disorders and their relationships to irritable bowel syndrome (IBS).

Inflammatory Bowel Disease: The Major Class of Organic GI Disorders

Inflammatory bowel disease (IBD) is a general term that includes both **ulcerative colitis** and **Crohn's disease**, each disease demonstrating specific biochemical and structural features. The causes of IBD are unknown. Ulcerative colitis is an inflammatory disease of the large and/or small intestine. Crohn's disease is an inflammation that extends into the deeper layers of the intestinal wall, affecting any part of the gastrointestinal tract from the mouth to the anus.

Ulcerative Colitis

In ulcerative colitis, a chronic inflammation, ulcers form in the inner lining, or mucosa, of the colon or rectum. The lining of the intestine takes on a cobblestone appearance, and the walls become thick and narrowed in places. Although the exact cause is unknown, episodes may occur after respiratory infections or stress. Ulcerative colitis is primarily found in the 15- to 30-year-old and 50- to 70-year-old age groups. Approximately 10% of people with this disease have a family history of ulcerative colitis.⁴

In serious cases, patients may have diarrhea between 10 and 25 times per day, which may contain blood and/or pus. Accompanying symptoms include abdominal pain and cramping that usually subsides following a bowel movement, audible intestinal sounds (borborygmus), fever, weight loss, dehydration, foul-smelling stools, rectal bleeding, and pain when passing stools (tenesmus). Additional symptoms that may be associated with ulcerative colitis are nausea and vomiting, joint pain, and gastrointestinal bleeding.

Crohn's Disease

Crohn's disease is an incurable and sometimes debilitating inflammation of the bowel. The inflammation occurs most often in the ileum and the first part of the large intestine (cecum) known as the ileocecal region. Although theories abound with regard to the cause of Crohn's disease, none has yet been proven. People with Crohn's disease tend to have abnormalities of the immune system, but it is unclear whether these abnormalities are the cause or result of the disease. Inflammation frequently occurs at the site where the small intestine joins the large intestine but may occur along any part of the digestive tract. The entire intestinal wall thickens, unlike ulcerative colitis, which affects only the mucosa, and deep **ulcers** and **fistulas** (channels) may form.

Symptoms of Crohn's disease include persistent, recurrent crampy abdominal pain; low-grade fever; diarrhea interspersed with normal bowel movements or constipation; loss of appetite;

Outlook for Ulcerative Colitis

Surgical removal of the colon is the only cure for this disease. However, the disease varies in severity. Patients can go into remission after a single attack, while others suffer with a chronic, persistent condition.

weight loss; an abdominal mass that can be felt, borborygmus; clubbing of the fingers and toes; blood passed in stools; foul-smelling stools; and tenesmus. Other, possibly-related symptoms are joint pain, incontinence, swollen gums, constipation, abdominal fullness, and gaseousness.

Crohn's disease may occur at any age but most commonly affects adolescents and young adults. Risk factors may include a family history of the disease or those of Jewish and Northern European ancestry. People with Crohn's disease have an increased risk of small bowel of colorectal carcinoma.⁴

Gastrointestinal Tract Infections

Viral, bacterial, or parasitic infections are also categorized as organic, inflammatory disorders. Symptoms and signs may include prolonged diarrhea accompanied by fever, nausea or vomiting, or a variety of other nonspecific symptoms. When prolonged bouts of diarrhea cannot be explained, and if these bouts occur with other intestinal symptoms, laboratory blood tests are generally performed to determine whether infection is present. Stool samples to find **parasites** or eggs in the stool, can quickly rule out parasitic infestations, such as giardiasis, trichomoniasis, and amebiasis. Stool cultures can also help to rule out bacterial infection.

Managing Crohn's

There is no cure for Crohn's disease. Treatment goals include controlling inflammation, relieving symptoms, and correcting nutritional deficiencies.

Table 2.1. Summary of Primary Organic Gastrointestinal Disorders

Organic Gastrointestinal Disorder	Symptoms/Characteristics
<i>Inflammatory bowel disease</i>	
Ulcerative colitis	<p>Chronic, diffuse superficial inflammation of the mucosal lining of the large intestine</p> <p>Abdominal pain and cramping that usually subsides following a bowel movement, audible intestinal sounds, fever, weight loss, dehydration, foul-smelling stools, rectal bleeding, and pain when passing stools</p> <p>May also be accompanied by nausea and vomiting, joint pain, and GI bleeding</p>
Crohn's disease	<p>Chronic but episodic inflammation of the entire intestinal wall; deep ulcers and fistulas</p> <p>Crampy abdominal pain, low-grade fever, diarrhea</p>

	interspersed with normal bowel movement or constipation, loss of appetite, weight loss, audible intestinal sounds, an abdominal mass that can be felt, foul-smelling stool, bloody stools, and pain when passing stool.
	May also be accompanied by joint pain, incontinence, swollen gums, constipation, abdominal fullness, and gaseousness.

<i>Gastrointestinal tract infections and infestations</i>	Prolonged diarrhea of unknown cause
	May be accompanied by a fever, nausea and vomiting, or a variety of nonspecific symptoms
	Requires laboratory and stool samples for exclusion

Motility-Related Functional Disorders of the Upper GI Tract

Disorders such as irritable bowel syndrome have no structural or biochemical cause. They are disorders of function, not structural or biochemical abnormalities. In functional GI disorders, the normal motility or movement (peristalsis) is abnormal. Muscular spasms can cause pain, and the contractions can be fast or very slow. Functional motility-related disorders are classified according to their location (upper GI tract or lower GI tract), symptoms, and general characteristics. Such disorders may be related to one or more interruptions of pathways involving the release of the neurotransmitters **serotonin** or **acetylcholine**.

Dysphagia

Dysphagia or difficulty swallowing may be related to an organic disease resulting from an **esophageal stricture** or a result of pressure on the esophagus by an organ, gland, abscess, or tumor, **gastroesophageal reflux disease (GERD)**, a bacterial or viral infection, herpes **stomatitis**, a side effect of chemotherapy or radiation treatment, or ingestion of a **caustic** substance.

Functional dysphagia, however, is not the result of an esophageal stricture and can be classified as either low or high. High dysphagia is difficulty with initial swallowing, whereas low dysphagia is the sensation of food not going down correctly and is often accompanied by chest pain. Swallowing difficulty may be constant or intermittent.



Dysphagia may result from spontaneous, **non-propagated esophageal spasms** that produce ring-like contractions in the esophagus (corkscrew esophagus). This may be due to abnormal neuronal control of the esophageal muscle. Esophageal spasm is largely unresponsive to treatment, and its prognosis is variable.⁵ Functional dysphagia may also be related to an emotional or anxiety disorder (**globus hystericus**).

Gastroesophageal Reflux Disease (GERD)

Gastroesophageal reflux disease (GERD), also known as **peptic esophagitis**, is a digestive disease affecting the lower esophageal sphincter (the muscle that connects the esophagus with the stomach). Most of us occasionally experience heartburn or acid indigestion caused by GERD. However, some people suffer from GERD due to a condition called a **hiatal hernia**. In this case, the opening in the diaphragm becomes abnormally large, allowing the upper part of the stomach to protrude into the chest. Stomach contents are retained above the opening (which acts as an additional sphincter) and can then easily reflux back upward into the esophagus.⁷ GERD is considered a distinct disease when the regurgitation occurs frequently enough to cause pain and damage to the mucosal lining of the esophagus.

GERD has been described as “food coming back into my mouth” or as “leaving a bitter taste in my mouth.” Accompanying symptoms include heartburn or acid indigestion, a burning chest pain that radiates up from the breastbone to the level of the jaw. In addition to heartburn, many people experience belching, regurgitation of food, nausea and vomiting, a sore throat, and hoarseness or a change in voice. In these severe cases, symptoms may also include vomiting of blood, coughing or wheezing, or weight loss.

The symptoms of GERD are often worse after meals or certain foods such as chocolate, peppermint, coffee, alcohol, and fatty or spicy foods.⁶ Reportedly, symptoms are also worse when a patient is lying down or bending over. Finally, symptoms may be particularly troublesome during the night, and are typically increased by obesity and during pregnancy.⁷

Treating GERD includes reducing reflux and subsequent damage to the esophageal lining and eliminating foods and drinks that can weaken the sphincter or irritate the mucosa. Other treatment measures include weight reduction, dietary changes (including avoiding alcohol and tobacco), avoiding lying down right after meals, sleeping with the head of the bed elevated, and taking

How Common is GERD?

Statistics from the US Department of Health and Human Services indicated that about 7 million people in the US suffer from GERD

medications and vitamins with plenty of water. Mild cases generally respond to over-the-counter antacids.⁶

Long-term complications of GERD include **esophagitis**, with esophageal bleeding and ulcers that may produce chronic scarring and a narrowing or stricture of the esophagus, and **Barrett's esophagus** (columnar metaplasia), which may increase the risk of esophageal cancer.

Noncardiac Chest Pain

Noncardiac chest pain may be mistaken for cardiac pain because it may feel similar in intensity and location, but it is not associated with heart problems. Exercise does not exacerbate this type of pain, unlike that of heart disease, and in many patients, the pain has no obvious cause. Patients may often also have nonspecific esophageal motor disorders or **hypertensive peristalsis**.

Nonulcerative Dyspepsia (Functional Dyspepsia)

Nonulcerative dyspepsia (NUD), or functional dyspepsia, is a vague term for a collection of symptoms including the following:

- Belching
- Bloating
- Abdominal distention
- Upper abdominal pain (usually after meals)

The absence of detectable abnormalities of the intestine is mandatory for the diagnosis of functional dyspepsia.

Motility-related Functional Disorders of the Lower GI Tract

Irritable Bowel Syndrome (IBS)

Classic **irritable bowel syndrome (IBS)** is a common condition—a functional disorder characterized by recurrent abdominal pain and discomfort accompanied by alterations in bowel function, diarrhea, constipation, or a combination of both, typically over months or years. Abdominal pain, often due to spasms, may cause sharp pain or dull pain. The exact symptoms differ between patients and may change over time in an individual patient (see Chapter 5). IBS has been termed a **syndrome** because it includes a set of symptoms that appear together with

Drugs for GERD?

Histamine (H₂) receptor antagonists, proton pump inhibitors (PPIs), and prokinetic drugs are effective in controlling severe symptoms, but they do not address the altered motility aspect of the disease.⁶ Although off label, gastrointestinal motility agents are playing a role in the management of GERD (eg, Reglan, Propulsid). Future on-label indications may expand this role further.

reasonable consistency. Research has not yet been able to determine exactly why certain people suffer from IBS. The condition commonly begins in young adulthood, sometimes even in adolescence and seems to affect more females than males.

Although abdominal pain and cramps are among the most common symptoms of IBS, pain or discomfort alone is not sufficient to diagnose IBS.⁸ However, when a bowel movement or the passage of gas temporarily relieves the pain and cramps, a physician may suspect IBS. Subtypes of this syndrome, based on the predominant bowel habit of the patients, include the following:

- Constipation-predominant IBS (C-IBS)
- Diarrhea-predominant IBS (D-IBS)
- Alternating bowel movements (alternating IBS)

There is debate, however, as to whether these classifications are misleading. Many patients experience all of these symptoms at some time.

Patients with IBS may also experience upper GI symptoms like GERD and dyspepsia and non-GI symptoms such as urologic dysfunction, fatigue, and gynecologic symptoms. Psychologic symptoms are also commonly found in IBS patients who seek treatment for their symptoms, but it is unclear whether the psychologic symptoms contribute to the IBS symptoms or whether, perhaps, the chronic symptoms of IBS cause the psychologic symptoms observed in some patients. It is important to note that there is no excess of psychologic symptoms compared with the general population, in the group of patients who do not seek treatment. According to current medical opinion, psychologic factors are thought to be triggers or factors that may worsen symptoms but are not believed to cause the symptoms of IBS. Chapter 5 contains more detailed information on the clinical presentation and diagnosis of IBS.

Functional Abdominal Bloating

Functional abdominal bloating is characterized by the following:

- Abdominal fullness or distention
- Audible bowel sounds (borborygmi) and excessive **flatus**

These symptoms must have been present (for at least 3 months) without evidence of maldigestion or malabsorption, or excessive consumption of fermentable carbohydrate such as beans or lentils.⁹

What Causes the Pain?

In IBS, increased pain sensitivity results from the increased sensitivity of the nerves. The nerves in the bowel are like a stereo playing at full volume at all times. The everyday wear and tear gets amplified and can lead to terrible cramps, diarrhea, constipation or a mixture of all three.

Chronic (Functional) Constipation

Chronic or functional constipation is characterized by the presence (for at least 3 months) of the following symptoms:

- Persistently difficult defecation
- Straining at defecation
- Hard or lumpy stools
- Sensation of incomplete defecation
- Two or fewer bowel movements per week

Chronic constipation seems to be related to factors similar to those in IBS, but unlike IBS, abdominal pain is not a diagnostic factor.⁸

Supplementary dietary fiber can increase fecal bulk, soften the stool, and may ease difficulties associated with defecation. In severe cases, however, fiber supplements worsen symptoms. Osmotic laxatives and enemas are the main treatment for severely constipated patients with slow bowel transit.

Functional Diarrhea

Functional diarrhea is the passage of formed or unformed stool along with the following:

- Three or more bowel movements per day not due to organic disease
- Increase in stool weight

Symptoms must be present for at least 3 months, and structural mucosal disorders such as malabsorption diseases (chronic pancreatic insufficiency, gluten sensitivity), inflammatory bowel diseases (Crohn's disease, ulcerative colitis), and GI tract infections and infestations must first be excluded before a physician makes a diagnosis of functional diarrhea.⁸

Changes in diet are often helpful. For example, poorly absorbed foods, such as beans and lentils, should be restricted. In persistent cases, antidiarrheal agents taken before meals can improve symptoms.⁵

Functional Abdominal Pain

Abdominal pain must meet the following requirements to be considered functional⁸:

- Frequent, recurrent, or continuous pain for at least 6 months

- Pain not associated with eating, defecation, or menstruation
- No evidence of organic disease

Most patients show deficits in daily functioning and exhibit chronic illness behavior. However, the relationship between abdominal pain and a disturbance of GI function is often difficult to establish.

Table 2.2. Summary of Functional Gastrointestinal Disorders

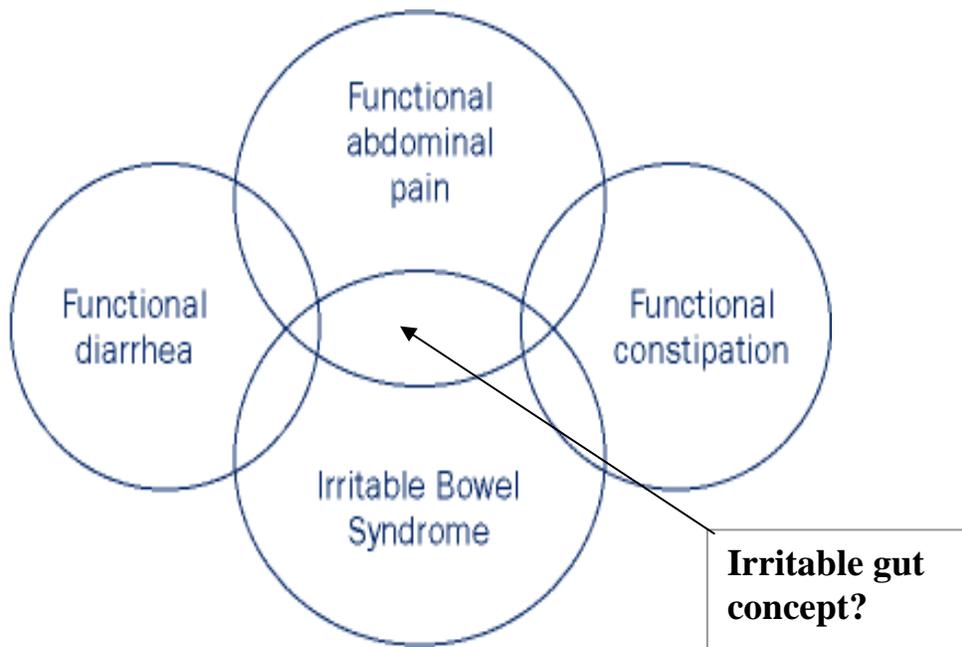
Functional Gastrointestinal Disorder	Symptoms/Characteristics
UPPER GI TRACT	
Dysphagia	<ul style="list-style-type: none"> • Difficulty with initial swallowing (high dysphagia) • Sensation of food not going down correctly (low dysphagia), often associated with chest pain • May be associated with an actual esophageal stricture
Gastroesophageal reflux disease (GERD)	<ul style="list-style-type: none"> • Regurgitation of gastric contents into the esophagus • Causes heartburn/acid indigestion and burning chest pain • Can cause belching, food regurgitation, nausea and vomiting, sore throat, and hoarseness • Worse after meals • Exacerbated by chocolate, peppermint, coffee, alcohol, and fatty or spicy foods • Worse upon lying down or bending • More frequent at nighttime
Noncardiac chest pain	<ul style="list-style-type: none"> • Resembles cardiac pain, but is not associated with heart problems • Exercise does not make the pain worse • Pain has no obvious cause, but may be due to a nonspecific motility disorder of the esophagus
Nonulcerative dyspepsia (NUD)	<ul style="list-style-type: none"> • Characterized by belching, bloating, abdominal distention, and upper abdominal pain (usually after meals)
LOWER GI TRACT	
Irritable bowel syndrome (IBS)	<ul style="list-style-type: none"> • Abdominal pain or cramps, or pain that is relieved by defecation • Associated with a change in stool frequency or consistency • May be one of three recognized subtypes: constipation-

	<p>predominant, diarrhea-predominant, or alternating</p> <ul style="list-style-type: none"> • Associated with upper GI symptoms (such as gastrointestinal reflux and dyspepsia) and non-GI symptoms (such as urologic dysfunction, fatigue, and gynecologic symptoms; also psychological symptoms)
Functional abdominal bloating	<ul style="list-style-type: none"> • Abdominal fullness or distention • Audible bowel sounds and excessive flatus
Chronic (functional) constipation	<ul style="list-style-type: none"> • Persistently difficult defecation • Straining at defecation • Hard or lumpy stools • Sensation of incomplete defecation • Two or fewer bowel movements per week
Chronic (functional) diarrhea	<ul style="list-style-type: none"> • 3 or more bowel movements per day for at least 3 months • Increase in stool weight • No evidence of organic disease
Functional abdominal pain	<ul style="list-style-type: none"> • Occurrence of frequent, recurrent, or continuous pain for at least 6 months • Pain not associated with eating, defecation, or menstruation • No evidence of organic disease

Symptom Overlap in Functional GI Disorders

As illustrated in **Figure 2.2**, there is considerable overlap in the symptoms experienced by patients with various functional GI disorders. As a result, diagnosing functional GI disorders can be difficult. Gathering a careful medical history and giving a thorough physical examination are the most important factors for diagnosing IBS. If diagnostic criteria are not carefully adhered to, misdiagnosis may result, leading to inappropriate treatments.

Figure 2.2. Functional Gastrointestinal Disorders: Overlap Between Symptomatology



It is precisely this overlap of symptoms that has led some researchers to propose that these functional GI disorders are perhaps part of a larger “irritable gut” syndrome whereby a whole-body mechanism affects the entire gastrointestinal tract to varying degrees. However, this theory remains controversial.

Section ____ Summary

- Organic diseases are those that have a discernible structural or biochemical cause, while functional diseases are those for which no structural or biochemical cause can be identified. As such, the symptoms of functional diseases are thought to be due to abnormal function.
- Organic GI diseases consist primarily of the inflammatory bowel disorders—ulcerative colitis, Crohn’s disease, and gastrointestinal infections and infestations.
- Functional GI disorders may affect almost all regions of the GI tract.
- Upper GI functional disorders include dysphagia, GERD, noncardiac chest pain, and functional dyspepsia.
- Lower GI functional disorders include IBS, functional abdominal bloating, chronic constipation, functional diarrhea, and functional abdominal pain.
- Functional GI disorders primarily involve abnormalities of intestinal motility and sensitivity.
- Functional GI disorders are clinically diverse, but show overlap with respect to symptoms.
- Although it remains controversial, some have hypothesized that the functional GI disorders are part of a larger “irritable gut” syndrome.
- Many people present with more than one functional disorder.
- Psychologic factors, among other precipitating events, may trigger or make symptoms worse but are not believed to cause these functional disorders, in particular, IBS.



- When severe or prolonged, functional GI disorders can be the cause of significant distress and discomfort.

Epidemiology of IBS

Introduction

Irritable bowel syndrome (IBS) is a worldwide problem. It is second only to the common cold as the most frequent reason for work and education absenteeism. Despite the relatively high frequency of IBS in clinical practice, data on the epidemiology of this disorder are limited. This is probably caused, in part, by the lack of an agreed upon definition of IBS. National databases use different definitions, producing data comparisons, though efforts are underway to standardize and better characterize this disease. Community-based studies provide some indication of the magnitude of the prevalence of IBS, and a number of these studies are described in this chapter.

IBS: What's in a Name?

Over the years, IBS has been called many different names—colitis, mucous colitis, spastic colon, spastic bowel, and functional bowel disease. Most of these names are inaccurate. For example, colitis, a much more serious disorder, means inflammation of the large intestine or colon, and IBS does not cause inflammation.

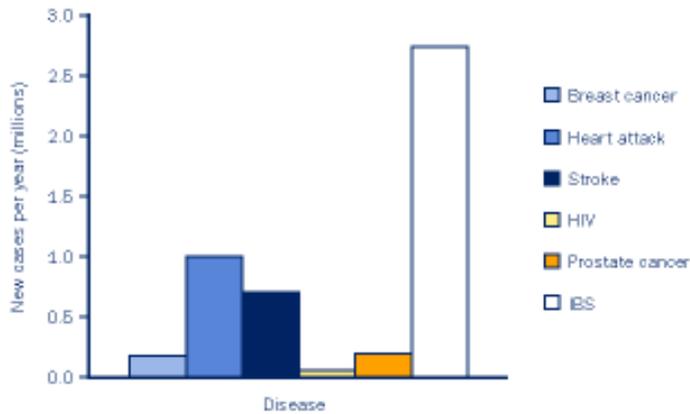
Incidence and Prevalence: US vs Worldwide

When determining the scope of the problem, two terms are generally used: **incidence** and **prevalence**. Incidence is the rate of occurrence, especially of new cases, of a disease in a population over a period of time. Prevalence is the total number of disease cases in a given population at a specific time.

Of the functional bowel disorders, IBS is the most common, affecting approximately 15% to 20% of the Western world at any time.^{10,11} The lifetime prevalence of the syndrome may be much higher; a figure of 40% has been reported. However, these figures may be considerably lower when using strict diagnostic criteria, such as the Rome II criteria.

The precise incidence is unclear but has been estimated as approximately 1% per year (**Figure 3.1**). Currently, IBS accounts for 20% to 50% of referrals to gastroenterologists.¹²

Figure 3.1. Incidence of Selected Diseases in the USA



Functional GI disorders are the most common GI illnesses seen by primary care physicians and gastroenterologists, and IBS is the most common disease diagnosed by gastroenterologists. In the USA, IBS accounts for between 2.4 and 3.5 million physician visits every year. However, only 33% to 50% of sufferers will ever consult a doctor.¹³ In a recent survey of 854 employees of a single business in London, UK, 16.6% had symptoms of IBS, but only one-quarter of these individuals had consulted a doctor.¹²

A Danish study indicated a variation in prevalence of IBS from 5%–65% and, in the same study, incidence ranged from 1%–36%.¹⁴ Again, this variation is largely a direct result of using a number of different definitions and diagnostic criteria for IBS. At the end of the 5-year follow-up period, only 5% of subjects with IBS were completely free of all symptoms. The variation seen in the Danish study is caused mainly by differences in definition; and although symptoms often fluctuate, the overall prevalence rate is relatively constant in Western communities at approximately 15%–20%.

Worldwide Variation in Prevalence

Comparison of these data with data from other countries may, in the future, provide some indication as to whether some observations - for example, the higher prevalence of IBS observed in women in some studies - are true or are, instead, an artifact of healthcare-seeking behavior, diet, or other socio-economic factors.

Although IBS prevalence in China appears to be similar to that of Western populations, studies of IBS prevalence in Iran and Singapore indicate that prevalence is lower in these countries than in Western countries. There is no clear explanation for these observations.^{15,16}

Some studies suggest that IBS is rare in native Africans, and rates in White populations have been reported to be more than five-times higher than in Black populations.^{17,18} However, a more recent study investigating a random sample from an African population indicated that this may not be the case, and symptoms consistent with a diagnosis of IBS were very common in native Africans.¹⁹ In the developing world, symptoms of IBS may be more common in cities than in rural areas, although few studies have investigated this variation.

Prevalence by Subgroup

Gender

In many studies, women consistently present with symptoms of IBS more commonly than men; in both patient and community-based samples taken in the United States, a number of factors may be involved.²⁰ Some differences may be the result of gender differences in seeking medical advice.

To illustrate this point, on the Indian subcontinent, the reverse is true. The male:female ratio of IBS has been reported to be 4.2:1.²¹ The reason for this difference is not clear but may be explained by a combination of less available medical care and

different cultural approaches to illness. In India, men are more likely to visit physicians for treatment than women, resulting in a higher number of diagnoses in the male population.

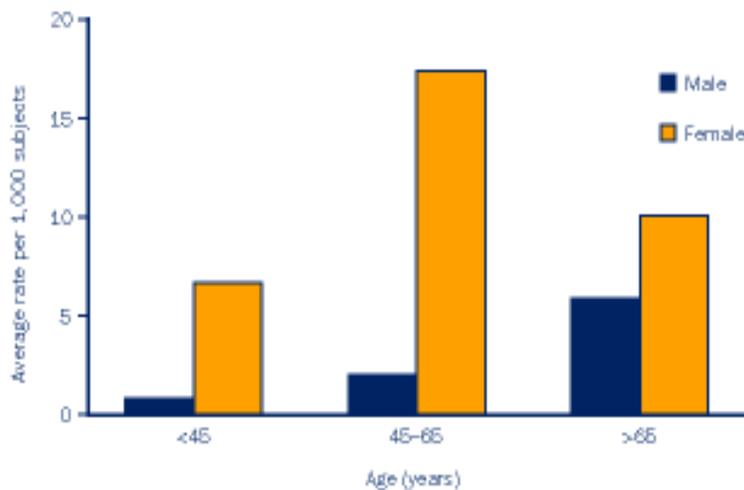
Again, the prevalence of IBS in some studies is reportedly lower in men, but this may be a reflection of the increased tendency among women to seek medical help for symptoms. However, data are lacking to conclude for certain whether disease prevalence is, indeed, higher for women.

According to the Epidemiology of Constipation (EPOC) study, the prevalence of certain subtypes of IBS and, specifically, constipation-predominant IBS, may vary according to sociodemographic features, including gender and age.²² In this study, the overall prevalence of constipation was 14.7%. By subtype, the prevalence of constipation-predominant IBS was 2.1%.

It has also been suggested that the Manning and Rome criteria (see Chapter 5) are less reliable for detecting IBS in men or that men have a poorer recall of some of the more subtle symptoms of IBS.²³ Although the frequency of pain-related **Manning symptoms** is similar among men and women with IBS, mucus, incomplete evacuation, **distention**, and **pellet stool** are less frequently observed in men.²³ The higher frequency of constipation-predominant IBS observed in the female population may be another factor contributing to the apparently increased prevalence of IBS in females.

With regard to gender, the bottom-line is that it is just not known at this time whether the incidence and prevalence of IBS is influenced by gender. The conclusion that IBS occurs more in women is unsubstantiated by the available data. The observation of a higher prevalence in women made in some studies may, in fact, be a result of more physician visits or other artifacts.

Figure 3.2. Average Rate of Self-reported IBS in the USA Classified by Age and Sex (Data from the National Health Survey, United States, 1987)¹⁸



Age

As shown in **Figure 3.2**, the average age of onset of IBS is between 20 and 29 years. IBS is most commonly diagnosed in patients aged 45–65 years, and its frequency diminishes in older patients. However, an incidence of the disease does occur in children under 12 and in teenagers. Additionally, IBS is also common in the elderly.

In Olmsted County, Minnesota, US, the prevalence of IBS among people aged 30–64 years was 17%, compared with 10.9% in those aged 65–93 years. A study of a population of 70-year-old Danish subjects showed a prevalence of 6% to 18%, depending on the definition used. Incidences were of a similar magnitude.¹⁴

IBS is also common in adolescents and children, particularly in girls with a history of recurrent abdominal pain. Symptoms of IBS

have been reported in as many as 16% of adolescents in community-based studies.²⁴⁻²⁶

Comorbid Conditions Associated With IBS

Upper GI Symptoms

Compared with non-IBS patients, patients with IBS are more likely to suffer from other functional GI disorders, particularly upper GI symptoms such as dysphagia, gastroesophageal reflux disease, and noncardiac chest pain.

Functional Somatic Symptoms

IBS patients suffer from other functional somatic symptoms as well, for example, urologic dysfunction, fatigue, and gynecologic symptoms.

Psychologic Symptoms

There may be an association between patients with IBS and psychologic symptoms, particularly depression or anxiety, phobia, somatization, and paranoia. In fact, between 40% and 60% of patients who seek medical advice for IBS symptoms have depression or anxiety, or a combination of the two. It is possible that the anxiety and depression expressed by IBS patients is a reaction to a chronic disease that has a significantly affected their daily activities.

According to current medical opinion, physical and psychologic symptoms are thought to trigger or exacerbate, rather than cause, IBS symptoms. Importantly, persons with IBS who do not consult a physician are psychologically similar to normal subjects. However, it is unknown whether psychologic disorders may be the etiology of IBS in some cases.

The Stress Connection

Many patients report that that stress in their lives is associated with the worsening of their symptoms, but that doesn't mean that IBS is primarily a psychological disorder. It means that stress may definitely contribute to the underlying mechanism of IBS—quite different than being a purely psychological abnormality.

Section ____ Summary

- IBS affects approximately 15% to 20% of the population worldwide.
- Accurate estimates of the incidence and prevalence of IBS are problematic because of the lack of an agreed upon definition of IBS.
- In the USA, IBS accounts for 2.4 – 3.5 million physician visits per year. However, the majority of sufferers do not consult a doctor.
- Some variation between countries exists in the prevalence of IBS, with lower rates reported in parts of Asia.
- Constipation-predominant IBS is more common in females than males, according to current surveys that have biases.
- More females than males present to their doctor with IBS symptoms.
- Onset of IBS occurs most often between 20 and 29 years of age. The condition is most common in patients aged 45 – 65 years but it affects all age groups, including children, teenagers, and the elderly.
- IBS is common in children and adolescents, and especially presents in girls as a history of recurrent abdominal pain.
- IBS appears to be associated with higher socioeconomic class and privileged childhood living conditions.

SECTION _____

Pathogenesis of IBS

Introduction

Irritable bowel syndrome is a functional disease consisting of chronic or recurrent abdominal pain associated with an abnormal bowel pattern that cannot be explained by a structural, biochemical or physical cause. Physicians are challenged in that they are managing a group of symptoms. Diagnosing IBS primarily involves the exclusion of other disorders.

Although the cause of IBS is not totally understood, advancements in the technology to assess the functioning of the gut, such as distention studies, have increased our understanding of the syndrome. Altered gastrointestinal motility and/or enhanced gastrointestinal sensitivity due to inflammation or a defect in communication between the brain and the gut (brain-gut axis) are now the predominant theories regarding possible IBS causes.

IBS is probably not a single disorder, but rather a collection of symptoms associated with a number of different pathophysiologic mechanisms. According to the prevailing diagnostic criteria, the Rome II criteria (discussed in the next chapter), IBS is characterized by abdominal discomfort or pain that is generally relieved by defecation and that may be accompanied by a change in stool frequency or consistency. It has been suggested that IBS involves both a **central** and a **peripheral** component.

Major Mechanisms

Several mechanisms have been proposed to explain IBS and other functional intestinal disorders:

The Brain Gut Interaction

It may be that the brain-gut interaction may be abnormal in persons with IBS. Visceral sensation in the gut may be related to alteration in CNS function and activation of sensory neurotransmitters. Consequently, emotional or psychological factors such as stress may influence visceral sensation and pain perception. In other words, IBS sufferers may respond differently to visceral sensation than those without IBS.

- Altered intestinal motility (gut spasm)
- Abnormal visceral sensitivity (gut sensitivity)
- Reduced ability to accommodate food material in the gastrointestinal tract (**compliance**)
- Limited intestinal inflammation due to infection

The normal movement of food material through the gastrointestinal tract depends on coordination of the peristaltic movements of the intestinal wall. In IBS, abnormal intestinal motility (peristalsis) affects the whole of the GI tract, including the esophagus and stomach, small intestine, and colon. Both reduced motility (**hypomotility**, leading to constipation) and increased motility (**hypermotility**, leading to diarrhea) have been implicated. Although there are data to support both, no clear consensus has emerged. Regardless, abnormal motility appears to be central to the development of IBS.

Altered Colonic Motility

Intuitively, IBS is often assumed to be caused by altered colonic motility because the pain of IBS frequently occurs in areas of the body in which colonic pain is usually felt. Furthermore, many characteristics of IBS suggest colonic dysfunction. In the cecum and ascending colon, mixing movements (haustral contractions) in the intestinal wall propel the fecal material slowly back and forth, but mainly toward the rectum. In the transverse and sigmoid colon, however, movement of the intestinal contents is achieved by mass movements, which occur one to three times each day. These “giant” contractions move down the colon, pushing fecal material ahead of them into the rectum and triggering the urge for a bowel movement. In IBS patients, giant contractions are thought to trigger spasms in the colon, causing abdominal pain, diarrhea, or constipation. Although this may be a plausible hypothesis, definitive evidence is lacking.

In IBS, diarrhea comes from an increased rate of passage of stool through the colon. Constipation is the result of a decreased speed of stool passing through the colon.

Altered Colonic Contractility

Some studies have demonstrated increased contractile activity in the colon in response to the presence of food. For example, following a fatty meal, the motor activity of the sigmoid colon was significantly greater in IBS patients than in normal subjects.²⁷ Most studies of intestinal motility have focused on the sigmoid colon and rectum, but few clear differences have emerged between patients with IBS and healthy subjects.²⁸

Recent evidence, using radiopaque markers to assess GI motility, suggests that patients with IBS have a significantly higher “scattering index” in the colon and faster colonic transit time than healthy controls.²⁹ Even movement backward in the colon was observed in some of these patients, indicating significant colonic contractility. Gastric- emptying time and small-intestinal transit were normal. When the transit time and scattering index were combined, the results became 65% sensitive and 96% specific for detecting IBS patients.

Altered Contractile Activity in the Small Bowel

Studies of colonic motility have, thus far, failed to provide a clear answer for the development of IBS. Other studies have focused on motility disturbances in the small bowel. Again the findings were inconsistent.²⁸ One potentially important finding was the detection of abnormal bursts of intense activity in the duodenum and ileum of IBS patients during fasting, separated by long intervals of rest. This pattern of activity, termed “discrete clustered contractions” (DCCs) is different from the migrating motor complex that is seen more commonly in healthy subjects. However, while DCCs are more common in IBS subjects than in healthy individuals, they do occur in normal subjects and in patients with both intestinal obstruction and pseudo-obstruction.³⁰ These DCCs are associated with pain in IBS about 25% of the time, but are rarely painful in non-IBS subjects.³¹

Pressure and Transit Studies Yield Inconclusive Results

Intestinal motility in IBS has also been studied using measurements of intestinal pressure (**manometric** studies) after meals. Results are conflicting, with some reporting slower transit using manometric measurements,³¹ and others reporting normal motility.²⁸

Intestinal transit studies in IBS (using barium enemas) have also been reported. In IBS with predominant diarrhea, both the transit time from mouth to cecum and the whole intestinal transit time have been shown to be reduced, although again, negative findings have been reported.²⁸

Abnormalities of sensation and/or motility are not consistent in all patients, and it is possible that the reported findings are characteristic of subgroups of patients with IBS resulting from different causes. Also, most studies describe motility and sensory abnormalities either at rest or in response to stimulation, not during the spontaneous, painful episodes. It may be that more consistent abnormalities would be apparent during such episodes.

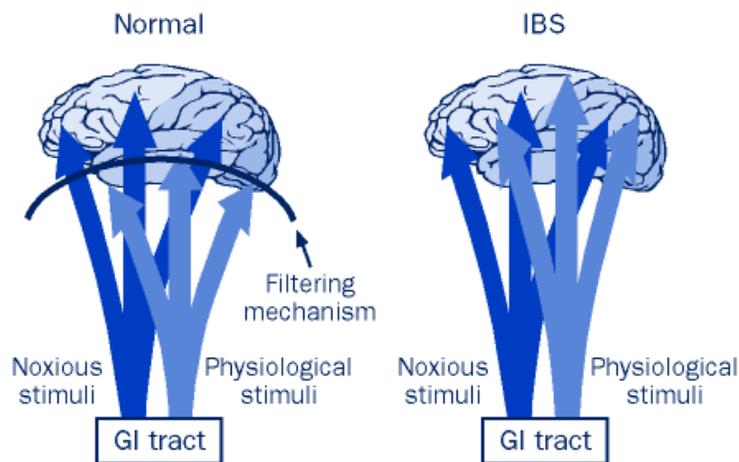
Abnormal Visceral Perception/Sensitivity

As many as two-thirds of IBS patients appear to have enhanced sensation and perception of bowel function. They can feel things in their GI tract, chest, abdomen, and rectum that others do not notice. This phenomenon is known as increased **visceral** perception/**nociception**, or **visceral hypersensitivity**.

Visceral hypersensitivity seems to be associated more with diarrhea than with constipation. Patients with visceral hypersensitivity are thought to have increased nervous sensitivity to physiologic stimuli resulting from normal events that occur in the intestine during digestion. The protective mechanism in the brain that filters out such stimuli appears to be abnormal or

absent in IBS patients. (**Figure 4.1**). As such, one theory with regard to IBS holds that IBS patients have a reduced threshold to internal (not external) pain, and, without the protective mechanism to filter out sensations from the GI tract, may experience abdominal pain and bloating from normal colonic contractions.

Figure 4.1. Visceral Hypersensitivity in IBS



In general, several studies have found that balloon distention of the rectum in IBS patients produces more discomfort, even when the balloon is inflated less, than in non-IBS patients^{32,32}; although again, other investigators have reported negative results.³⁴ Because these studies have been conducted at tertiary care referral or university centers, however, the IBS patients studied may not be representative of the IBS population, and the results from these studies may be biased.

Visceral perception in other parts of the GI tract, such as the rectum and stomach³⁵ and the large and small intestine,³⁶ may also be altered in patients with IBS. Heightened visceral perception is also found in other disorders, such as affective disorders.

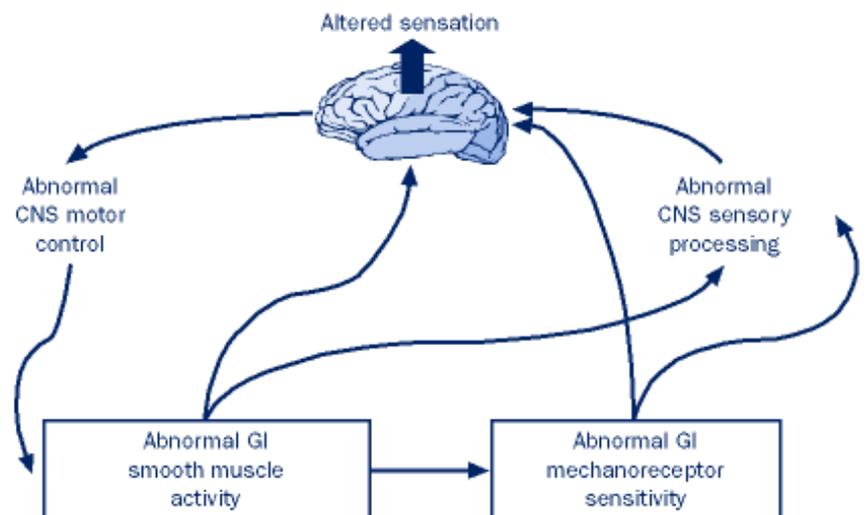
The increased sensitivity experienced by some IBS patients is not associated with a lower pain threshold because tolerance to cold or other painful stimuli is normal.^{33,37} The increased sensitivity appears to be specific to the internal organs.

Hypersensitivity

The development of hypersensitivity is not understood, but may be related to changes in the transmission of sensations to the brain. The mechanism for this hypersensitivity could be **peripheral** (abnormal responsiveness of the receptors in the intestine which respond to the mechanical stretching that occurs in the GI tract) or **central** (abnormal sensory processing by the brain) (**Figure 4.2**). In either case, hypersensitivity could explain the development of intestinal symptoms.

While increased visceral sensation in patients with IBS seems to be a component of the disorder,³⁸ it has been suggested that this is not the only defect, there being considerable overlap between sensation thresholds in IBS patients and healthy subjects.

Figure 4.2. Possible Mechanisms of Visceral Hypersensitivity



Enteric Neurotransmitters

Enteric neurotransmitters may be involved in the development of visceral hypersensitivity. Serotonin (5-hydroxytryptamine, 5-HT) is an enteric neurotransmitter that is thought to be of particular importance. Another neurotransmitter that may play an important role is acetylcholine. These will be discussed in a later chapter.

Somatization

Just as the GI tract is unusually sensitive and irritable, people with functional GI disorders often seem to have a sensitive “irritable body,” a phenomenon called **somatization**.³⁹ As such, IBS patients are more likely to also report

- Pain in the chest, abdomen, back, or pelvis
- Fatigue and low energy
- Insomnia

Reduced Compliance

The effects of distention of the intestine depend on intestinal compliance, or the degree to which the intestinal wall yields to a distending force like a balloon. This is, in turn, determined by the muscle tone of the intestinal wall. **Gastric tone** has been shown to be an important determinant of gastric sensitivity to distention.⁴⁰ The symptoms of IBS, then, may occur because the intestinal wall cannot adapt as well to different volumes of fluid and solid material in the intestines or other area of the GI tract. For example, patients with functional dyspepsia appear to relax the stomach incompletely after ingestion of a meal. This may cause increased tension in the stomach wall and stimulation of mechanoreceptors, leading to discomfort and pain.⁴¹

Limited Intestinal Inflammation

Some gastroenterologists have proposed that the primary cause of IBS is a limited intestinal inflammatory process. This is supported by the fact that a significant proportion of IBS patients has experienced past episodes of **infectious enteritis**.

Factors That Trigger and/or Exacerbate IBS Symptoms

A number of possible triggers or factors that appear to make IBS symptoms worse have been identified:

- Diet and other compounds that irritate or affect the lumen of the gut
- Emotional stress
- Hormones, especially the fluctuating hormones of the female menstrual cycle

The potential for abnormal intestinal function is always present in people with IBS, but it seems that a trigger must also be present for symptoms to develop. The person with IBS seems to have an intestine that is more sensitive and reactive than normal to a

wide range of compounds, and so it responds strongly to stimuli that would not affect other people. This exaggerated reaction to these stimuli can then activate or trigger pain and other symptoms. The most common triggers or exacerbators of IBS symptoms are diet and emotional stress.

Commonly cited triggers of IBS include the following:

- Foods and other dietary substances
- Drugs and medications
- Psychologic problems/stress
- Inflammation and infection
- Hormones (menstrual cycle)
- Seasonal changes

Foods and Other Dietary Substances

Gastrointestinal complaints, such as dyspepsia, heartburn, bloating, diarrhea, or constipation, are often associated with reactions to food, and many people with IBS report that their symptoms occur or become worse following a meal. Eating normally leads to colonic contractions and may result in an urge for a bowel movement within 30–60 minutes after a meal. In people with IBS, the urge may occur sooner, with cramps and diarrhea. Alternatively, some foods can trigger intestinal spasms that delay defecation, leading to constipation. Chocolate, dairy products, and alcohol are among the most common dietary triggers, although the effect of a meal is often related to the number of calories consumed, particularly in the form of fat. Animal and vegetable fat found in meat, dairy products, butter, vegetable oils and margarines, is a strong stimulus of colonic contractions. Caffeine causes loose stools in many people, but is more likely to affect those with IBS.

In some IBS patients, particularly those with predominant diarrhea, bloating, and pain, the severity of symptoms can be

linked to the consumption of certain foods. Often recommended dietary modifications include the following:

- Elimination of dairy products
- Elimination of gas-forming foods, such as **legumes**
- Supplementation of dietary fiber intake

As an initial disease management strategy, such modifications are safe and inexpensive, and they may result in a lessening of the symptoms. Dietary modifications in IBS, together with other nonpharmacologic interventions, are discussed in more detail in a later chapter. Those patients who improve on a restricted diet may be able to identify the foods that provoke symptoms when reintroduced and can control their IBS quite well in this simple way. However, food is only a trigger or exacerbator of IBS symptoms and is not a cause of IBS.

Distinguishing IBS From Food Allergy

Food “allergy” or sensitivity is occasionally confused with IBS because abdominal pain and diarrhea can accompany both problems. However, true food allergy is easily distinguishable from IBS by the presence of symptoms in other parts of the body apart from the GI tract and by a clear link between ingestion of the food and symptom development.

Medications as a Trigger of IBS Symptoms

Some medications can cause or exacerbate IBS symptoms. This is especially true of over-the-counter laxatives, which can cause cycles of diarrhea and constipation, and narcotics, which can cause abdominal cramps, constipation, bloating, slow peristalsis, and pseudo-obstruction (a condition that mimics mechanical obstruction of the GI tract). Drugs, such as calcium channel blockers and antidepressants, can also cause GI symptoms (including constipation or diarrhea).

Certain Compounds Cause an Irritated Gut

The presence of certain compounds in the lumen of the intestine may alter intestinal function, causing an “irritated gut.” These “**luminal** compounds” may include some of the products of digestion and also digestive secretions produced by the body. Several such compounds have been suggested to be of potential importance, including sugars like lactose, fructose, and sorbitol that are difficult to digest, short chain fatty acids, food allergens, and bile acids. These luminal factors probably aggravate the underlying IBS rather than being an intrinsic component of the syndrome. In IBS patients, certain of these molecules may activate chemoreceptors on the intestinal walls and initiate short (local) reflexes that locally stimulate increased contractility. Such a physiologic mechanism may help explain the role of certain types of foods as triggers of IBS symptoms.

Psychologic Factors

In healthy individuals, psychologic stress or emotional responses to stressful events can influence GI function and lead to symptoms such as pain and altered bowel function. Expressions such as “butterflies in the stomach” and “my stomach is in knots” describe sensations that are caused by stressful situations. However, the response to stress differs between individuals and, equally, the effect on the intestine may be different, depending on the state of mind and coping skills of the person.

Some evidence exists that psychiatric disease and abnormal illness behavior are more prevalent in patients with IBS than in healthy individuals,^{42,43,44} but not all studies support this conclusion.¹¹ It is equally possible that the anxiety and depression expressed by some IBS patients is really a reaction to a chronic, debilitating disease that has a significant impact on the patient's quality of life. Although patients who consult their physicians for their GI symptoms have an abnormally high frequency of psychologic problems, those IBS sufferers who do

not seek medical attention do not appear to be psychologically different from healthy subjects.⁴⁵ This was determined by comparing patients with and without IBS to other nonpatients recruited for the study.

In IBS, psychologic symptoms could trigger or make the abdominal symptoms worse or lead to a state of heightened awareness of intestinal events. Alternatively, chronic abdominal symptoms could, themselves, lead to affective disorders or disturbed perceptions. Although IBS can be made worse by psychologic problems or mental illness, and mental health counseling and stress reduction (relaxation training) can help to relieve symptoms, most physicians agree that IBS does have a definite physiologic component.

The link between psychologic stress and greater intestinal motility or contractility may relate to the neuronal control of the intestine. Intestinal sensations reach the brain via the extrinsic neurons and the spinal cord. Neuronal transmission is bidirectional, via nerve cells that connect the intestine to the brain, and via others running from the brain to the intestine. Thus, the intestine affects the brain and the brain affects the intestine (the brain–gut axis).

Many medical conditions, such as asthma and duodenal ulcer, which were originally ascribed to psychologic factors, have subsequently been recognized to be due to organic disease. Here, it is clear that psychologic factors may trigger IBS symptoms. As research continues, emerging disease models may better explain the connection between perceived psychologic stress and functional gastrointestinal disorders, including those other than IBS.⁴⁶

Hormonal Factors

A majority of young adults who present with IBS-associated constipation or idiopathic constipation are female.⁴⁷ Additionally, some women with IBS may have more severe symptoms during their menstrual periods, suggesting that reproductive hormones may aggravate IBS symptoms. Moore and colleagues⁴⁸ reviewed how gastrointestinal symptoms vary across the menstrual cycle and concluded that almost 50% of women with IBS report an increase in IBS symptoms immediately preceding and following their period. In support of this suggestion are findings that colonic muscle tone is reduced by progesterone and that constipation is common in pregnancy. Although progesterone may play a role, a recent study suggested that only a few of the apparent differences in IBS symptoms between men and women are directly related to the menstrual cycle.⁴⁹