

Understanding the Human Gut and the Enteric Nervous System (ENS)

In order to understand food intolerance, it is helpful to understand the gut, its structure (anatomy), and how it works. One thing that makes this more difficult is the use of multiple words for the same thing. For instance, the gut is also the gastrointestinal tract, the digestive tract and the alimentary tract, the esophagus is the gullet or food pipe, the intestine is the bowel, feces are stools or bowel movements or sh**!

The main job the gut has is to take in food, break that food down so that energy and nutrients can be extracted, and then expel the remaining waste. This sounds easy, but it really is quite a complex process because the gut has to also protect the body from exposure to things that are toxic or otherwise not good for it. The following information is provided to help understand that complexity.

The Structure of the Gut

THE BASIC STRUCTURE OF THE GUT

It is easiest to think of the gut as a hollow tube that runs from the mouth to the anus.

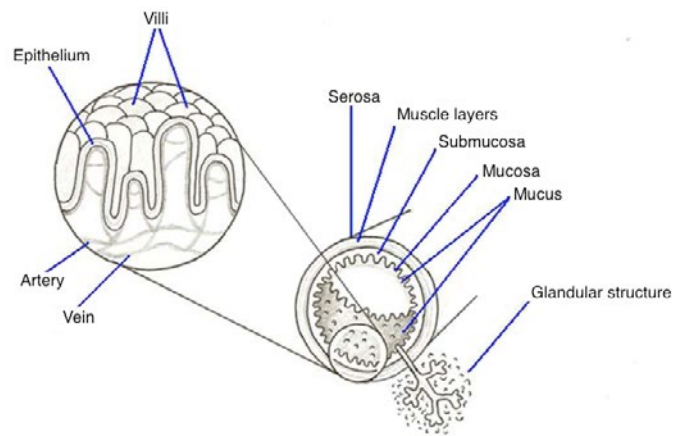


FIGURE 1 The basic structure of the gut. It is a hollow tube made up of various layers.

As shown in Figure 1, above, if you slice the tube and look at it from one end, you will see that is made up of:

- **a lumen**, which is the central part that holds the cocktail of contents, and
- **a wall**, which has several parts:
 - **The mucosa:** This is the gut lining. It has a layer of cells called the epithelium, which acts as the skin of the gut. A layer of mucus (slime) overlies the epithelium. This acts as a lubricant and helps protect the epithelium.
 - **The submucosa:** This is the tissue beneath the mucosa through which the blood and lymph vessels bring nutrients and cells to and from the wall.
 - **Muscles** have an important role: to mix and move the contents of the lumen.
 - **Nerves:** A complex nervous system called the enteric nervous system (ENS) is embedded within all the layers of the wall of the gut. Its job is to sense what is in the gut and to coordinate the muscle movements so that mixing and moving of contents through the gut proceeds in an ordered way,

- **Sources of secretions:** The wall also provides enzymes, secretions, and liquids in order to assist in the digestion of food in the lumen. These secretions may come from the cells lining the epithelium, or from specialized glandular structures that are attached to the gut. Some of these structures are organs in their own right, such as the pancreas, the liver, and gall bladder, while others are simply small glands in the wall of the gut. All these structures have their own passageways, called ducts into the lumen (the pancreatic duct, the bile duct).
- **The serosa:** This is a smooth lining of cells on the outside of the gut.

THE SPECIALIZED STRUCTURES OF THE GUT

The hollow tube that is the gut is made up of many parts in various sections, each performing different specialized functions. The sections have special muscular structures called sphincters between them to control what goes through to the next section and to ensure contents flow only one way. Because movement of the contents of the gut is generally only in one direction (from the mouth toward the anus), the proper function of any part is somewhat dependent upon the function of the part that precedes it. This will become obvious as each structure is described below. The parts are all shown in the diagram below (Figure 2). The parts of the gut within the abdomen are very long and stretch for at least 25 feet (8 meters)! How they are all packed into the abdominal space is shown in Figure 3 (page 7).

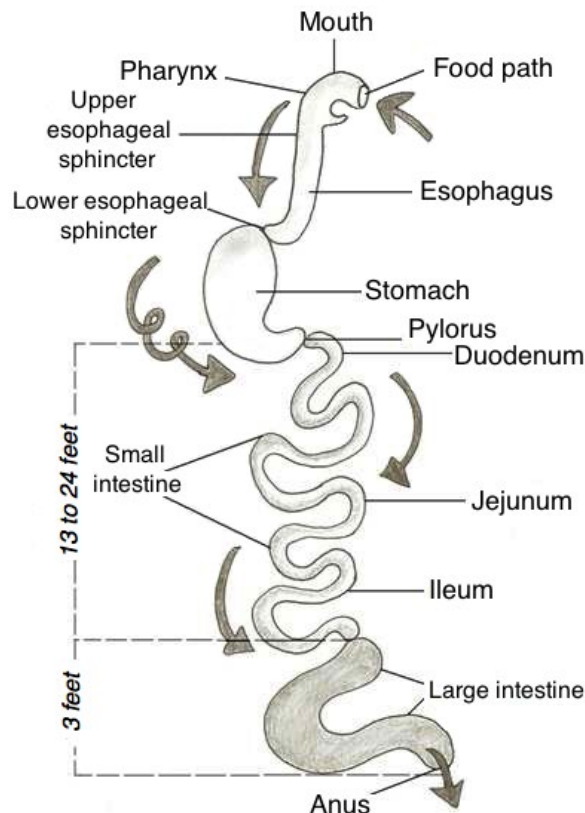


FIGURE 2 The parts of the gut stretched out. The length of the small intestine and the large intestine is also shown.

The mouth

The mouth is the part with which you will be most familiar. Food begins its journey of digestion here. There are some highly specialized structures in the mouth that all have important roles. They include tongue, teeth, and salivary glands.

- **Tongue:** The lining (epithelium) of the tongue has lots of taste buds in it that connect to the nervous system of the gut so that it can tell our brain whether the food is salty, sweet, sour, or bitter. Most of the tongue is a big muscle that helps move food around the mouth. A chewed mouthful of food is called a bolus.
- **Teeth** are specialized structures essential for good chewing of food.
- **Salivary glands** produce liquid that contain enzymes and minerals to make our food moist and to start digestion.

The nervous system of the mouth is very complex and sophisticated. It needs to be, to enable us to swallow—something most of us do without really even thinking about it! The first step is for the tongue to move the food bolus to the back of the mouth (the pharynx) and then to the esophagus. When the epiglottis (the “punching bag” that hangs at the back of our mouth) is stimulated by the passing of this food bolus, the upper esophageal sphincter must relax and the opening to the lungs must close off to prevent food from going down the “wrong way.”

The esophagus

The esophagus is—just as the colloquial term for it, food pipe, suggests—a pipe that takes food from the mouth to the stomach. It does this by coordinated muscle movement called peristalsis. Because of peristalsis, we can swallow the contents of the mouth even if we are standing upside down! Gravity plays no part in the movement of food down it. Once the food has traveled from the mouth into the stomach, it should stay there and not reflux back up. The sphincter around the end of the esophagus (the lower esophageal sphincter) ensures that travel in the esophageal lumen is mostly a one-way event. Problems can arise when the muscles do not coordinate well because the nervous system of the esophagus goes “out of tune.” Normally, occasional reflux of gastric contents does occur, but this is rapidly cleared by peristalsis. However, conditions such as gastroesophageal reflux disease can be caused by excessive reflux of stomach contents (acid).

The stomach

The stomach is a J-shaped pouch that has the important function of storing a big meal and holding it up while the early processing of food occurs. Its muscular wall is very good at mixing its contents. When the time is right, it permits small amounts of the pulverized semiliquid contents (known as chyme) to be released to the next part of the gut, the first part of the small bowel. This requires the pyloric sphincter to relax. Chewed food that entered the stomach as a semisolid lump then becomes semiliquid due to the churning and the large amounts of liquid being secreted by the stomach lining. This liquid is very acidic, which is important to help break down solid material and to reduce the bacterial content of the food (almost sterilizing it). The stomach also secretes enzymes that break down proteins.

The length of time that the food contents remain in the stomach varies. Liquids empty from the stomach faster than solids; this makes sense because there is less to break down. Fatty meals slow down the rate of emptying. Fat content of the meal is sensed by the gut, which secretes hormones to slow the emptying process down.

When food is in the stomach, the stomach expands. The expansion is called distension. Distension of the stomach is sensed by the nerves in the stomach. This information is then processed by the nervous system within the gut wall and contributes to the complex process of emptying and mixing the contents. Sensing the distension also leads to messages being sent to the brain. These messages are a big part of how it is that we feel “full.” If the stomach empties quickly, you may feel hungry faster. Conversely, if you have a fatty meal, your stomach stays full for longer and keeps you feeling fuller for longer. That is why a meal of greasy fish and chips will keep you satisfied for hours, whereas you will feel hungry again after a large, but low-fat salad.

What about gas in the stomach? Just about all of the gas in the stomach is swallowed air. We all swallow plenty of air; this occurs every time we swallow saliva, drinks, and food. People tend to swallow more frequently when anxious and, therefore, are likely to swallow more air. The oxygen in the air we swallow can be absorbed across the wall of the stomach and intestine and into the bloodstream. However, the major component of air is nitrogen and this is not absorbed. It has to go somewhere—it can either be belched (“burped”) or passed out via the anus (“farted”). Some people belch readily—their sphincter at the lower end of the esophagus is trained to let the gas flow the wrong way. Others seldom belch, so the gas is passed into the small intestine. Carbonated beverages introduce a lot of gas quickly and often lead to a large belch; otherwise, if belching does not relieve it, the gas can distend the stomach and/or the small intestine and cause discomfort. This will be explored further later in this document.

The small intestine

The small intestine is a very long tube, stretching 13 to 23 feet (4 to 7 meters) from the stomach to the colon. It is responsible for converting food into its simple building blocks. It converts carbohydrates into sugars, proteins into amino acids, and fats into fatty acids. It also has the very important role of absorbing all the nutrients—including vitamins, minerals, and water—present in the food just consumed. The liquid matter passes through the small intestine in only 90 minutes, so it must be very efficient at absorbing all of the building blocks and nutrients. This efficiency depends upon three important things:

1. First, food is released from the stomach to the small intestine in a regulated process to ensure that excellent mixing has occurred and that digestion has already occurred.
2. Secondly (and most importantly), the small intestine has a huge surface to enable the final thorough digestion and absorption of nutrients. The lining of the small intestine looks like a shag carpet, covered in tiny “piles” called villi. Each of those piles has itself a shag-pile lining at a microscopic level called microvilli. It is incredible to think that because of this clever structural design, the surface becomes greater than the area of a tennis court!
3. Thirdly, it is separated into three specialized sections—the duodenum, the jejunum and the ileum—which have specific tasks, as described below.

- **The duodenum:** This is the first part of the small intestine. Churned and mixed food (chyme) is released from the stomach into the duodenum, which is only about 12 inches (30 cm) long but is a very busy place. It has additional fluids entering it from the pancreas (bicarbonate and enzymes) and from the liver and gall bladder (bile). The digestive juices from the pancreas are alkaline and neutralize the very acidic chyme. This is important to prevent injury of the lining of the duodenum by acid, and to ensure that the digestive enzymes from the pancreas work properly. Bile from the gall bladder and liver is important in the absorption of fats and fat-soluble vitamins. The duodenum must also, therefore, be a good mixer of all the fluids. You can understand why the stomach only releases a certain amount of chyme at a time, so that the volumes are well balanced and mixing is successful. The

duodenum prepares the contents for the key absorptive work to be done in the next section of the digestive tract. However, the duodenum is where absorption of folic acid, iron, calcium, and zinc occurs.

- **The jejunum:** This is the region that plays the most important part in absorbing the digested products of carbohydrates, fats, and proteins, most of the vitamins and minerals, and salts and water. It is about 10 feet (3 meters) in length.
- **The ileum:** The ileum's main role is to absorb salts and water, but it can take on many of the functions of the jejunum if needed (for example, in people who have had surgery removing some jejunum). The ileum also has the important task of absorbing vitamin B12 (a vitamin important for making blood cells) and bile salts, which are sent back via the blood stream to the liver to be "recycled." The other important role of the ileum is in the immune protection of the body; it has the greatest concentration of immune cells of the whole gut and has a key role in "tasting" those molecules and bacteria that may be in the intestinal lumen. This "tasting" means that the immune system, which is present right along the gut, can protect us if any of those molecules or bacteria happen to get too close for comfort, by ensuring the presence of protection and tolerance (see below).

Our intestines contain within them a lot of bacteria—this is a normal phenomenon. The population of bacteria is very small in the duodenum and jejunum, and slowly increases towards the end of the ileum (the terminal ileum). One reason for the low numbers in the small intestine is that there is constant and relatively rapid movement of contents through this region. The only way bacteria can get established in such a "fast-moving" environment is by sticking to the mucus that lines the epithelium. Bacteria find it easiest to stick to the epithelium of the ileum, because the rate of flow reduces there. This is because, in the jejunum, a lot of the water gushing down the gut gets absorbed into the bloodstream and tissues, so the volume gets less. It makes sense then that the "tasting area" is located in the terminal ileum. Just next door, in the large bowel, there are vast numbers of bacteria, but the ileocecal valve (the sphincter between the small and large bowel keeps them in the large bowel. This valve works like a one-way door, similar to the action of the pyloric sphincter and lower esophageal sphincter as discussed above.

The diseases that affect the small intestine are rather different from all other regions. Cancer is rare. However, food-related illnesses are common since this is the place where luminal contents truly interact with the cells and tissues in the wall of the gut, which is leakier than that of the stomach or large bowel—after all, it has to absorb lots of nutrients. The most common disease is celiac disease, which arises due to an immune reaction to gluten, a collection of proteins included in wheat, rye, barley, and possibly oats. Information about diagnosis of coeliac disease is in Chapter One of *The Complete Low-FODMAP Diet*.

The large intestine

The large intestine is also called the colon. Although it is only about 3 feet (1 meter) long, it takes anywhere from 12 hours to 2 days for contents to pass from the beginning to the end of the colon. In many people with constipation, this can be much longer. In other words, what you see in the toilet bowl might reflect what you ate a day or two before! The large bowel has an important role as a desiccator. In other words, it changes the 2 quarts (2 liters) of fluid entering it each day into neat little packages of "poop" (stools) amounting to 1 cup (200 ml) or less per day. It also deals with waste or undigested food (e.g., fiber) in partnership with the vast number of bacteria living on the mucus lining the bowel and in the contents of the large bowel.

Why do we have such a vast number of bacteria in our large bowel? First, there is food galore for them in the bowel. Food that is undigested or indigestible—such as fiber, FODMAPs, and some secreted and undigested proteins—is a feast for bacteria, so populations will flourish. Secondly, the large bowel lumen is not a rapidly-moving environment. It might help to think of the process as the contents taking a few steps forward and

occasional steps back with resultant slow progression towards the anus (as discussed above). There is plenty of time for the bacteria to multiply.

You only have to look at and smell the excreted contents of the large bowel (stools) to wonder how can they be anything but toxic or bad for you in the bowel? The truth of the matter is that our large bowel bacteria live in a harmonious relationship with us; that is, they benefit from being there and we benefit from their being there. They are our friends. We feed them with carbohydrates and proteins, and provide surfaces for them to grow happily and keep out of trouble, while they help process our waste, produce energy and important fuels for our bowel health, assist in the desiccation process, and protect us from nasty (pathogenic) bacteria that can cause disease. They also provide bulk in our feces—much of a well-formed bowel movement is bacterial mass! If you consume a diet that does not feed the bacteria (e.g., a very low-fiber diet), the bowel motions will become dry, small in quantity, and hard to pass.

The bacteria help by more than just their bulk-producing effects. They process and break down carbohydrates by fermentation. As in other fermentation (e.g., beer and wine production, bread making), gas is produced. This is mostly hydrogen, carbon dioxide, and, in some of us, methane. This will be discussed at length later. The other products of carbohydrate fermentation are short-chain fatty acids. One of these, butyrate, is the major fuel for the epithelial cells to produce energy and survive. Butyrate also protects the cells from cancerous change. This is one probable reason why a diet high in fiber may reduce our risk of bowel cancer—fiber is a major source of butyrate production, and increasing its intake will increase the amount of butyrate produced. In order to grow, bacteria need nitrogen to make proteins as part of their own structure. Bacteria obtain nitrogen from proteins that are not digested or are part of the body's secretions and, importantly, from ammonia and phenols, which are chemical compounds produced by metabolic processes in the body. Scientific evidence suggests that high levels of ammonia and phenols in the bowel promote cancer development, so the bacteria once again do us a favor by removing these products and making the bowel contents safer. If the bacteria are given too much protein to ferment, they will make gases including hydrogen sulphide (which has the smell of rotten egg gas), which is why some flatulence is smelly—a minor side effect of some excellent work!

One of the most fascinating aspects of bacteria in the bowel is that the range of bacteria we have is fairly constant over time in each person, and no two people have the same range. Even if you take antibiotics that change the bacteria or flush them out with a severe colonic washout (called a colonic purge), the bacterial populations will recover and return to their usual range. How it is that this is the case is only partly understood, but we know that the range of bacteria is established early in life. This can be likened to a “club membership” being created early in life—new members are not allowed! A large amount of interest surrounds the idea that some people have a poor balance of “good” and “bad” bacteria and that this causes illnesses such as irritable bowel syndrome (IBS), or makes illnesses such as inflammatory bowel disease (IBD) harder to fix. Trying to change the “membership” has proven to be difficult. One strategy is to take bacteria that may have health-promoting benefits called probiotics. However these will only gain “temporary membership” and will only stay present if the probiotic continues to be taken. We can also take prebiotics, which are specific carbohydrates that are the preferred food of “good” bacteria. Therefore, consuming prebiotic molecules usually increases the number of good bacteria that are already members (and also dilutes the less welcome “bad” members). While this is a great theory, proof that the changes in bacteria are indeed beneficial for specific circumstances like irritable bowel syndrome is needed. This will be discussed later in this document.

The large bowel has different regions with specialized functions. Refer to Figure 3 on the following page to see a picture of these:

- The **appendix** is a wormlike structure that is attached to the first part of the large intestine (called the cecum). It is probably important for developing immune defenses in the large bowel. However, we seem to get along perfectly well if it is removed.
- The **cecum**, ascending colon, and transverse colon are all very important in the drying out of the fecal

contents.

- The **descending colon**, which is much narrower, and the sigmoid colon (so named because of its “S” shape) serve as storage containers for the waste products ready to be expelled (and they also continue the drying-out process).
- The **rectum** is the last part before the outside and it does not appreciate being full. It senses the distension and notifies our brains that we should visit a bathroom. If the contents are liquid, it becomes very impatient and must be attended to quickly (this is called urgency).
- The **anus** is the opening from which the feces is excreted out of the body from the rectum. The sphincters (specialized muscles) of the anus prevents the contents of the rectum from being released automatically. The external sphincter is under conscious control, while the internal sphincter is not. Normally, the external sphincter can be considered the “master controller.” However, if this is damaged (for instance, at childbirth), the control may not be as good and incontinence may occur. The other trigger for incontinence is when the contents are so liquid that the unconscious mechanism for defecation overrides the conscious control.

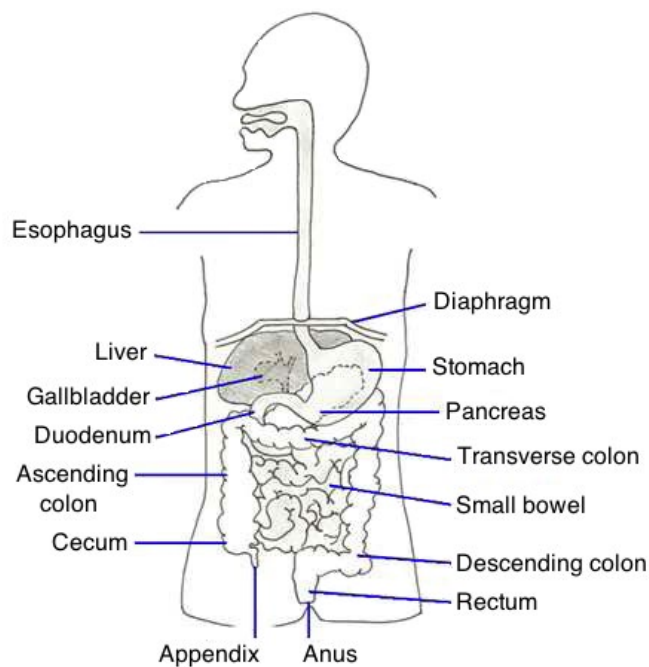


FIGURE 3 How all the parts of gut fit into the body

The Relationship between the Body and Gut Contents

The body and the contents of the gut are like a marriage—a harmonious, mutually beneficial relationship, with the potential for small episodes of disharmony and, very occasional, all-out war!

The human body is a carefully controlled environment. The temperature, water content, acidity, concentration of salts, sugar levels in the blood, and so on are controlled within very strict limits. If that control fails, bodily function is disturbed and illness can occur. This carefully controlled internal environment is in contrast to the outside environment, where we have only limited control to what we are exposed to. We all understand that our skin is an important interface between the outside world and our body's internal environment. The skin is relatively impermeable due to its thickness and coating of keratin. If it is broken or badly damaged, it becomes the site at which infection can enter the body.

In the same way, the lumen of the gut is the outside world and the gut's lining is the interface between it and the carefully controlled environment of the body beneath. Compared with the skin, the lining of the gut is thin and must extract things (such as nutrients) from the lumen. This opens the way for environmental toxins or other potentially harmful things to reach the body's tightly controlled environment. Likewise, proteins and other substances can leak into the lumen if the lining of the gut is not working properly. Under the very thin skin of the gut lie complex protective mechanisms that are a major part of our immune system. This system is incredibly effective at protecting us from exposure to a huge array of potentially harmful molecules.

How does our gut manage to live happily with the feces and bacterial contents of the lumen? First, each section of the gut is designed to cope with its local area conditions. The esophagus has a relatively tough lining and gets things to travel through it very quickly. The stomach's lining is able to effectively protect itself from the very acidic environment it creates via its secretions. The small intestine can quickly neutralize the acid, has a huge surface area and somewhat permeable (leaky) lining that allows rapid absorption of nutrients to occur, and moves its contents quickly along so that bacteria do not have much of a chance of staying around to cause trouble. The large bowel has a very tight, non-leaky lining, so things can sit in it for many hours, and it therefore has a very different and mutually beneficial relationship (a "happy marriage"!) with the bacteria that live there (as outlined above).

Secondly, the immune system in the wall of the gut learns what is normally present in the lumen and develops protective systems. One example is that the immune system "tastes" what is in the environment and then develops antibodies against those things. The cells that produce these antibodies then get sent to many areas of the gut where, with the cooperation of the epithelial cells, the antibodies make their way to the mucus layer. There, they can neutralize proteins or bacteria that get too close for comfort before they make it to the epithelium itself. The immune system also develops "tolerance" to certain microbes and molecules. If they get too close or are able to penetrate the barrier, the immune system deals with them quietly without getting excited.

Fortunately, most symptoms deriving from the gut are not due to the immune system reacting to contents of the gut. Food allergy and food hypersensitivity, where there is an immune reaction to food with subsequent development of gut and other symptoms, is fortunately very uncommon (see later discussion specifically on this). The symptoms are more related to the gut's "personality"—see the following section for a discussion of this.

The enteric nervous system (ENS): it's all about personality

As human beings, we are all different. One person might be fun-loving and talkative, the next a quiet, serious person, and another a worrier who sleeps poorly. This we all understand and accept.

But why are we so different? Because of interactions between individuals' innate personalities and influences from outside the brain—the environment and the rest of the body. We develop our personality during the early years of life, and it forms the “core” or baseline from which our reactions to external influences are formed. For example, how individuals react to illness can vary from a positive to negative outlook, from coping with the symptoms of the illness to becoming sullen and angry. If major life stress occurs, one individual might react by becoming introverted or depressed, while others become angry and aggressive. How a person reacts, i.e., his or her behavior and personality, is a consequence of baseline personality and how it responds to all those external influences.

The gut is no different! The gut has a personality that resides in the gut's own brain, which is better known as the enteric nervous system (ENS). Ultimately, how our gut works (whether it behaves or misbehaves) is a blend of the gut's baseline personality of how it responds to all of the external influences on the ENS. In order to understand why symptoms develop and how the gut's personality expresses itself, we need to know a bit about how the ENS works (and doesn't work).

As described in the discussion of gut structure above, there is a complex nervous system in the gut that stretches from top to bottom and is present in all those layers in the wall of the gut. A diagram of it is shown in Figure 2. The ENS senses what is going in the gut and controls gut motility (i.e., muscle activity and its coordination). It has its own memory and takes part in many reflexive actions. It is connected to the brain via the autonomic nervous system, but the ENS can function without these connections. As for the brain, the function of the ENS involves networks of nerves called neurons. When a neuron is stimulated, it sends electrical signals down its long fiber to the other end of that neuron. It communicates the electrical signal to other neurons by releasing neurotransmitters, chemicals released from the end of the nerve (e.g., serotonin). These then stimulate or inhibit the start of other neurons by binding to special receptors on their surface (like a key fitting into a lock). The neurotransmitter locking into a specific receptor can shut down (inhibit) that neuron or excite (stimulate) it. Excitation leads to electrical impulses being passed down its long fiberlike body to the end, where it will similarly communicate either with other neurons or with muscle fibers to make them contract. This is made more complex by the fact that there are many different neurotransmitters, all with their own specific receptors, and that there are many different receptors that will permit the same neurotransmitter to lock into them. Different receptors have different effects even when the same neurotransmitter is released. This then is a complex network of fibers, nerve endings, neurotransmitters, and receptors that somehow retains memory and coordinates the complex activities of the muscles of the gut.

The way that the ENS senses things and drives the muscles of the gut depends upon the unique relationships between neurons, neurotransmitters, and receptors in an individual—no two people's will be alike. We all have different spectrums of neurotransmitters and receptors. Some of this is dictated by our genes: for example, some of us have genes that tell us in our development to produce lots of a certain type of neurotransmitter, whereas others produce only a small amount. How our bowels perform is determined by how this system is tuned. Given the system's complexity, it's no wonder we know so little about how to retune it when it is not tuned to our liking!

The ENS does not work in isolation. It can be influenced by neurons from the brain and spinal cord, which communicate with the neurons of the ENS in the same way (i.e., via release of neurotransmitters when the nerves are excited). Other cells that lie close by the nerve endings may also release chemicals that can affect

neurons. An example is the mast cell, which contains granules full of substances, such as histamine, that can interact with the nerve fibers. When we are allergic to something, mast cells are told to release their granules, and the histamine can then affect the nerves and the muscles to make them contract. If this happens in the bronchi (the tubes taking air to the lungs), muscles in the walls of the bronchi contract, obstructing the flow of air. This, we call asthma. Likewise, such a reaction occurring in the intestine can cause diarrhea or abdominal pain.

It is not unusual for drugs or medication we take to cause diarrhea or constipation. One way they can do this is by affecting the ENS. A very good example is codeine, a pain reliever that almost always causes constipation. Codeine binds to receptors that block muscle movements in the bowel. It is not difficult then to understand how constipation will be caused by the use of codeine.

In our diet, we may consume many substances that contain small chemicals (naturally or introduced by humans). We also break down many big molecules to small chemicals in the process of digestion. Bacteria break down additional substances in our diet (this is a normal and healthy process), but some of these substances may be chemicals that can influence the neurons of the ENS. Therefore, in the lumen of the intestine, we have many substances that might influence how our ENS performs. Fortunately, we have very efficient ways of dealing with these substances so that they find it hard to get near our neurons. Some, however, do, and may affect how the ENS performs. For example, they might:

- change the sensitivity of the nerve fibers in the bowel so that they have a lower threshold and react quickly to sensation (a condition called visceral hypersensitivity)
- lead to the release of chemicals from cells such as mast cells
- or interact with the receptors on the neurons to cause changes in how they get excited.

HOW DO WE KNOW WHAT IS GOING ON IN THE ABDOMEN?

For the ENS to work well, it needs sensory input; that is, it needs information about what is happening in the gut. This is achieved by having sensory receptors on specialized (sensory) neurons whose job it is to detect activity that has relevance to the function of the gut. The situation in the gut is very different to that in other parts of the body. Take your hand as an example. In the hand, you have sensory neurons that can detect fine touch, sharpness, and temperature. To understand this, think of being gently touched on the hand by a loved one—this is a pleasant sensation that is encouraged. In contrast, touching something very hot can cause injury, so we quickly move our hand away from such stimuli to protect ourselves from injury.

What sensations are important in the gut? It is not particularly useful for the ENS to know about fine touch or even temperature, since, for example, hot things being put into the gut have already been “screened” as they enter the mouth. It is known that taking pinch biopsies of the lining of the gut during a colonoscopy is not sensed either by the ENS or by the brain. In other words, a person having a biopsy is not aware that the pinch biopsy is occurring. What is very important in the gut, however, is its distension. The ENS has stretch receptors to detect this. So, for example, when the stomach is distended by food, the ENS directs the muscles at the outlet to the stomach to relax and the muscles in the body of the stomach to contract so that there is a controlled release of the contents of the stomach into the intestine. Similarly, distension of the large bowel leads to the ENS directing the muscles in the wall of the large bowel to contract in such a way that the contents are moved towards the anus (peristalsis). If the bowel is rapidly distended with lots of liquid, it hurries the content through the bowel, not allowing time to desiccate the contents—this leads to diarrhea, instead of the usual packages of formed stools that are released with less urgency.

To know what is going on in the gut, the brain must get information from the ENS. However, the sensory information that is rapidly processed by the ENS is also sent to the spinal cord, where further processing goes

on. Information is then sent to the brain, but it can be processed in a few areas on its way. In other words, the message that finally gets to the conscious brain will have been influenced at several levels.

HOW CAN THE BRAIN INFLUENCE THE GUT?

We do not have conscious control over the workings of the ENS. For instance, we cannot tell the stomach to empty its contents. Likewise, if the ENS decides that the stomach must empty its contents the wrong way (that is, vomit), we cannot consciously stop it. However, when we are asleep, the gut becomes very quiet in its activity, at least partly because of messages from the brain to the ENS. In contrast, when we are very anxious, the brain's output via the sympathetic nervous system can make the ENS "anxious," and activity can increase (for example, diarrhea may occur like before a big test or an important soccer game). In other words, the brain can influence both our perception of what is happening in the gut and also the activity or tuning of the ENS.

The best way of understanding how the brain and ENS interact is to discuss specific examples of that interaction. The normal way we learn of the need to open our bowels (i.e., feel the need to "go to the bathroom") is that the brain is told that the rectum and sigmoid colon are full and ready for emptying. The brain then directs the individual to find a toilet, get into position, and relax the muscles under the brain's control in the pelvic floor (around the anus). The ENS can ensure that the contents ("poop") are pushed by the muscles under its control through the anus to the exterior of the body. If the ENS is particularly stimulated by, for example, a large amount of very liquid contents, the brain might not get a warning early enough to ensure defecation ("pooping") is orderly and controlled, so the individual might soil themselves (be incontinent).

The sensation of bloating is another good example. How does the brain know that the abdomen at least feels distended and uncomfortable? Sensory nerves detect that the gut (whether the small intestine, the large bowel, or the stomach) is distended. These sensory neurons are excited, the message they send is processed through the ENS to reach the spinal cord, and this message is then sent up to the brain. Some people might feel mildly uncomfortable, while others might feel actual pain. This depends upon how much excitement gets sent by the nerves to the brain. Where the information ends up in the brain depends in part on the size of the signal and in part on the function of the brain itself. If the signal occurs while someone is busy doing some other activity, such as playing soccer, the brain may choose to ignore the signal. However, in a tired person at the end of the day, the brain might direct the signal to the pain center itself, and this person, who isn't distracted by any other activity, will experience significant discomfort. One person might look obviously distended (stomach "sticking out") during this sensation of bloating, while another person might not be visibly distended despite experiencing very uncomfortable bloating feelings. The main explanation for this is that the latter person has visceral hypersensitivity, so a small distension of the gut leads to great excitation of sensory neurons and a big signal going to the brain. In other words, the threshold at which the latter person's ENS tells the brain that the gut is distended is much lower than that of the former person. This concept has been observed in carefully designed research studies.

The implications of this complex interaction between the brain and the ENS are important. How readily the conscious part of the brain knows about what is happening in the gut depends upon the tuning of the ENS—i.e., its sensitivity to distension or other stimuli (increased by visceral hypersensitivity)—and how the signals are processed by the brain, which is dictated by multiple factors, including the state of mind, the environment, the presence/absence of distractions, past experiences, and how the brain itself is tuned.

CAN THE ENS BE RETUNED?

The answer is yes. In some people, after a nasty case of gastroenteritis, the ENS is retuned to make things travel through it rapidly, with resultant diarrhea. This is called postinfectious irritable bowel syndrome. How this retuning occurs is not well understood but presumably relates to some damage to the ENS from the infection itself. Also, it is well known that some people develop IBS in their twenties after having had a normal and untroubled functioning gut without any apparent severe gut illness. These are examples of where the ENS has been retuned to be disturbed. One explanation that is often suggested is that the brain is where the problem lies (a “psychosomatic” problem). Such an explanation doesn’t add up, though, because the sensory stimulation of the brain is an essential part of perceiving that things are not right in the abdomen. These stimuli would rarely originate in the brain.

An important question for anyone who has a disturbed ENS and wants it retuned is whether anyone—the person him- or herself or a health professional—can therapeutically retune the ENS to improve its function. The answer at the present time is unfortunately “no.” Drugs that change the nature of the neurotransmitters or that can block or stimulate certain receptors on the neurons have had very limited success, and some have been associated with rare side effects that have restricted their use or led to their being withdrawn from the market. There is some evidence that psychological therapies or hypnotherapy might alter the ENS, but it is not proven and the mechanism is not known. If we could understand how ENS dysfunction occurs in the first place, then we might be heading towards a real cure for IBS.