

# Teaching basic gastrointestinal physiology using classic papers by Dr. Walter B. Cannon

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**Bertrand PP, Bertrand RL.** Teaching basic gastrointestinal physiology using classic papers by Dr. Walter B. Cannon. *Adv Physiol Educ* 31: 136–139, 2007; doi:10.1152/advan.00112.2006.—The movements of the gastrointestinal tract, as described by Walter B. Cannon 100 years ago, reveal much about the functions of this unique organ and how it is controlled by the body. Two classic papers by Cannon provide a rare glimpse into the hidden functions of the body and give students a great example of the scientific method in action. In this essay, we describe the basic movements and functions of the gastrointestinal tract as revealed by X-rays, contrast meals, and Cannon's careful observations. It is Cannon's experimental care and obvious interest in his subject matter that can provide your students with a taste of the excitement of discovery and insight into the processes by which experimental science moves forward.

gastrointestinal tract; motility; radiography

THE MOVEMENTS of the gastrointestinal (GI) system have been investigated for over 100 years. While many basic observations of GI function were made in these early times, the fiendish complexity of this unique organ keeps many research scientists and clinicians busy to this day. The intestine, also called the bowel by clinicians, refers to both the small and large intestines. When the stomach is included, we refer to the "GI tract." Other structures, such as the gall bladder, pancreas, esophagus, and mouth, can be included in the more general term "GI system," because they work together as an integrated unit during the response to a meal. The more popular term for these is simply "the gut."

The GI tract is the main organ for digestion and absorption of food and contributes to water balance. It has important immunological functions and is the first line of defense against food-borne pathogens. The gut has many complex behaviors that are controlled by a large number of neurons that live exclusively within the wall of the intestine. These neurons are known collectively as the enteric nervous system. The GI tract is unique among the organs of the body in having a large degree of freedom from central control. The central nervous system, by way of the sympathetic and parasympathetic nervous systems, provides overall modulation of the intestine, but it is the enteric nervous system that is responsible for the moment-to-moment functioning of the gut.

## GI Motility in Clinical Medicine

The GI tract is an extremely robust and reliable organ; nonetheless, problems can occur. One serious problem is when the normal patterns of motility (movements) in the GI tract become disordered. Once a meal has been ingested, its first

stop is the stomach. Normally, the stomach chemically, enzymatically, and mechanically digests the food until it has been broken down to the point where the small intestine can take over. Completing this process may take several hours, and the rate at which contents leave the stomach is called the "rate of gastric emptying." In conditions like diabetes, the nerves controlling the stomach can become damaged and foods take much longer to pass to the small intestine. This leads to the condition of "gastroparesis," which literally means a paralysis of the stomach, although in general there is only a slowing in the rate of gastric emptying. This may cause nausea, vomiting, weight loss, and other unpleasant symptoms.

The problems occurring in the small and large intestine are no less troublesome but are less well characterized in part because the functions of the intestine are spread out along its length. Some of the most common problems directly affecting the motility of the GI tract are obstructive diseases such as Hirschsprung's disease and functional bowel disorders such as irritable bowel syndrome. In addition to affecting motility, these disorders can also be associated with pain and other unpleasant sensations that severely reduce the quality of life for these patients. Other GI disorders can indirectly affect the motility of the GI tract. For example, viral and bacterial infections of the GI tract, gluten enteropathy (celiac disease), lactose intolerance, and inflammatory bowel diseases such as Crohn's disease and ulcerative colitis all cause frequent and painful increases in motility in addition to other insults to the GI tract.

## Background

Dr. Walter B. Cannon is one of the best known of the early American physiologists and there are many accounts of his career (2, 8, 10). Cannon was a pioneer in the field of radiology, studied shock, and discovered the role that emotions play in affecting physiological functions. These endeavors alone would be enough to remember his contributions; for example, see Randall's essay on another of Cannon's great works (11). It is, however, his earliest investigations on the GI tract that are of interest in the present essay and are, in part, what piqued Cannon's interest to study these other areas.

At the turn of the last century, the movements of the intestine in the intact animal were almost a complete mystery. Cannon has stated that "For centuries the priests and the butchers, who watched the entrails of their sacrificed victims, knew as much as the physicians about the mechanical factors of digestion" (3). In his studies, Cannon laid to rest many beliefs and misplaced commonsense about the GI tract. He also settled several controversies that were raging in the literature

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between physiologists of the time. The problem then, and indeed now, is that exposing the intestine, either during surgery or in the course of collecting tissue for an experiment, causes massive release of inflammatory agents and a profound change in the behavior of the intestine. Cannon recognized that simply refining and repeating these sorts of experiments would never settle the controversies. What was needed was a new kind of experiment where the GI tract was not exposed to trauma but its movements could still be observed.

X-rays, or Röntgen rays as they were also called, were discovered in 1895 by Wilhelm Röntgen, for which he won the first Nobel prize in 1901. In 1896, just a year after they were discovered, Cannon began using X-rays to image the esophagus during swallowing. One of Cannon's biggest innovations was to use X-rays to image the stomach and intestine in the intact animal (that is, *in vivo*) during digestion. This innovation is the basis of the fluoroscopic monitoring techniques used today, and Cannon's work laid the foundations for our current understanding of GI motility.

Cannon made many tracings and pictures so that the contents of the GI tract could be tracked every 30 min. To this, he added his own personal observations and stop watch measurements as he watched the contents when they moved too quickly to trace. In addition, Cannon made use of a versatile and nontoxic contrast agent. A contrast agent is a substance ingested by an animal or patient that absorbs the X-rays and is referred to as opaque to X-rays or "radioopaque." The soft tissues of the abdomen are mostly transparent to X-rays; thus, the contrast agent allows the movements of the intestinal contents to be visualized and followed in time during continuous or periodic illumination with X-rays. One previous study (9) had used mercury, a metal that is liquid at room temperature and is also opaque to X-rays but which is also terrifically toxic and causes severe GI dysfunction. Cannon found that a mixture containing bismuth could also block X-rays but caused little or no adverse effects on the animals he studied. He used bismuth subnitrate, which is similar to the active ingredient of stomach-soothing Pepto-Bismol (which contains bismuth subsalicylate). Today, clinicians still sometimes give a mixture of barium salts to patients to image food either transiting along the intestine or leaving the stomach. Because X-rays are intrinsically harmful, many modern techniques are now used in an attempt to gain similar information, but safely and with a wider range of consistency in the meal. For example, scintigraphy-based breath tests, magnetic resonance imaging, and single-photon emission computerized tomography imaging are all relatively modern techniques used to study the GI tract (1).

### The Papers

The two papers of note in the present essay by Cannon are "The movements of the intestine studied by means of the Rontgen rays" (4) and "The movements of the stomach studied by means of the Rontgen rays" (5). Not only are these two classic papers by Cannon very useful in teaching the basic movements of the stomach (5) and intestine (4), but they are also excellent examples of the scientific method in process. The papers were written in a way that nonspecialists and students can appreciate. Cannon clearly describes the problems he encountered and the solutions that he devised. Students should be encouraged to read the papers all the way through as they would a story or narrative. One exception is that, as was

common at the time, the summary of the paper is at the end rather than the beginning. Reading the summary first may help your students to grasp the many topics covered in the papers. The papers mainly discuss the two- and three-dimensional movements of a complex system; thus, no one figure accurately captures these dynamics. The diagrams drawn by Cannon to illustrate his findings can, however, be used to summarize the major movements of the GI tract that he observed.

For simplicity, only the data presented in Cannon's classic paper on the stomach (5) are summarized here. His later work on the intestine (4) used the same techniques and has further insights into the methods and problems he encountered. This second paper should be used as a supplement to the first paper.

First, Cannon was interested in revealing the normal movements of digestion. Previous studies had looked at digestion through fistulas (where some of the stomach is attached to the abdominal wall and, as such, is not free to move) or in isolated organs (where the blood and hormone supply have been cut off). His solution to these problems was to use the nontoxic contrast agent bismuth and X-rays to image the movement of the contents but not the soft tissues of the GI tract. The disposition of the soft tissues was then inferred from the position and movement of the contents. Figure 1 shows one of Cannon's tracings from early in digestion and an outline of the stomach with the anatomy labeled.

Cannon's experimental setup was simple. He placed a calm cat on its back in a stretcher and secured it there. The source of the X-rays was placed behind the cat, and a fluorescent screen was placed in front of the cat. The X-rays passed through the cat and, when they reached the screen, caused a visible emission of light. More X-rays caused a brighter light and fewer X-rays caused a dimmer light. The varying degrees to which the X-rays were blocked by the body of the cat thus formed the image on the screen. The contrast agent, as explained above, absorbed many of the X-rays; thus, these areas were dark or

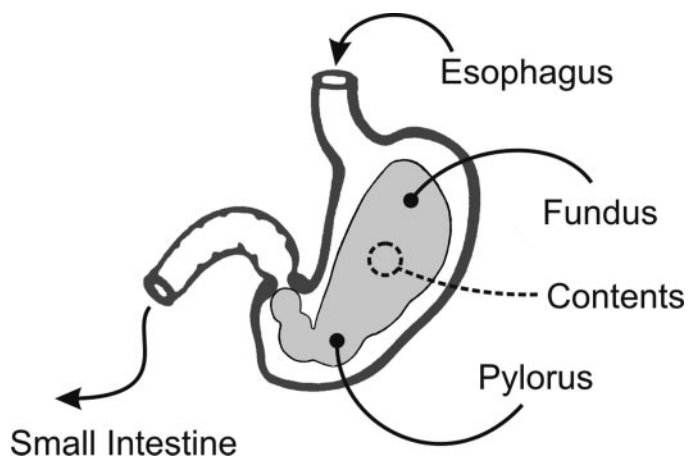


Fig. 1. Illustration of the stomach and the major anatomical components. The main body of the stomach with the attached esophagus and small intestine is shown. The gray area in the middle of the stomach is a tracing from Cannon's experiments and is labeled "contents." The contents represent the shadow cast by the radioopaque bismuth meal given to the experimental animal about an hour previously. The top and bottom of the stomach are labeled for the two major divisions of the stomach, the fundus and the pylorus, which are discussed in Cannon's paper (5). The upper fundic region includes the cardiac region and the corpus (or body) of the stomach (not shown). The lower pyloric region can be divided into the antral part (near the small intestine) and the preantral part (near the fundus) (not shown).

“shadows” on the screen. Cannon placed thin paper over the fluorescent screen and traced the outlines of these dark areas. One of the important controls Cannon used during these experiments was to take pictures using a film camera (radiographs) of key experiments to show that the tracings he made accurately represented what was on the fluorescent screen.

Second, Cannon’s observations of the stomach during digestion showed clearly that it is composed of two physiologically separate components: the fundus and the pylorus. The fundic region of the stomach is an active reservoir. It receives food from the esophagus, holds the food while salivary enzymes continue to digest it, and then periodically pushes the food into the pyloric region of the stomach. Cannon showed that little or no mixing takes place in the fundus by using three separate experimental protocols. First, in *experiment 1*, he used little starch balls mixed with contrast agent and observed that they did not move relative to each other. Second, in *experiment 2*, he fed the animal bread with the contrast agent, then without the contrast agent, and then again with the contrast agent, producing layers of contrast in the stomach. While the pyloric region quickly became a homogenous shade of gray, the fundic portion kept its layered pattern for over an hour. Finally, in *experiment 3*, when samples were taken from the fundus after an alkaline meal, Cannon observed that the surface pH of the food was now acidic due to gastric juices, but the inner part was still alkaline, indicating that no mixing had taken place within the fundus.

The pylorus receives food from the fundus, mixes it with gastric secretions, and pushes it toward the pyloric sphincter. This is shown in Fig. 2, where tracings from 5.5 h of observations are shown. The mixing in the pylorus is composed of waves of contraction. In Fig. 2, these contractions, frozen in time, are shown, forming the rounded areas of content in the pyloric region near the pyloric sphincter and the start of the small intestine (on the *left*). Cannon’s measurements showed that a wave passes every 10 s, thoroughly mixing the food (see *experiment 2* above). This was too fast to make accurate tracings, but not too fast for Cannon to carefully observe and

time the waves. He found that digestion in this area took many hours to be completed. In Fig. 2, after almost 6 h, most of the meal has finally been pushed into the small intestine. The process of the stomach moving food into the small intestine is now called “gastric emptying.” Importantly, Cannon noticed that the rate of gastric emptying varied for different kinds of meals. Bread and milk left the stomach before a salmon meal (4). He followed up these observations with another classic paper that looked at gastric emptying in depth (6).

Third, Cannon showed that the function of the pyloric sphincter is to open infrequently to allow soft, well-digested food to pass slowly to the duodenum (the first part of the small intestine). Cannon observed that only about a third of the peristaltic waves in the pylorus were associated with movement of the contrast agent into the small intestine. Furthermore, there seemed to be no clear pattern to the activity, with Cannon in one instance observing three consecutive openings followed by eight failures to open. Cannon again used little starch balls mixed with contrast agent to show that hard food inhibits the opening of the sphincter even when well-digested food is present.

Fourth, Cannon was interested in the pathophysiology of the stomach. Vomiting, or emesis, as it is also known, is the rapid emptying of the stomach’s contents up the esophagus and through the mouth. Vomiting is an important defense mechanism that protects the body from ingested toxins. During the time of Cannon’s experiments, there was a dispute in the literature about how food is forced back up the esophagus. He showed that the movements ascribed as normal by one group were actually very similar to vomiting and that vomiting took place without any clear evidence for “antiperistalsis.” A common belief at the time was that the stomach would reverse its normal peristaltic activity and pump food from the pyloric region to the fundus and then up into esophagus. Instead, he observed that the fundus went flaccid while the pylorus was taken over by several strong waves of normal peristalsis. The stomach was then divided by a sustained contraction of the muscle around the pylorus that blocked contents from moving down into the GI tract. Finally, there followed strong contractions of the abdominal muscles and an increase in pressure on the stomach. The stomach contents, having nowhere else to go, were forced upward. Thus, the stomach contents were expelled without any sign of antiperistalsis.

Finally, Cannon’s simple observations of cat behavior during the experiment provided a clear link between emotional state and the inner functions of the body. He became conscious of the cats’ moods and surroundings during the experiment. As a careful experimenter, Cannon noticed at the start that female cats were better suited to being restrained for several hours than were male cats, who would struggle throughout the time. The female cats stayed in a tranquil mood and could be calmed easily by petting. He noted that when male cats were used or when a female cat became angry, all movements of the GI tract stopped. Another possible source of irritation tested by Cannon was the loud crackle of the X-ray generator. Somewhat unexpectedly (and luckily for Cannon), he found that the loud noises of the generator actually soothed the cats. Cannon performed several important controls to substantiate his observations. First, as a first control, he deduced that digestion does take place normally in male cats when they are unrestrained. He fed a male cat a bismuth meal but waited 90 min before

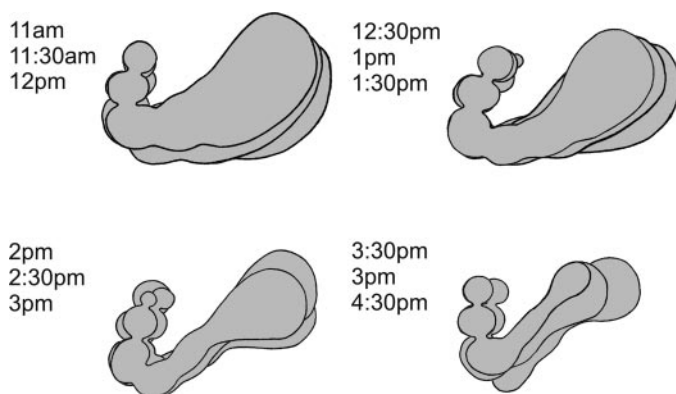


Fig. 2. The steady reduction in volume of the stomach after a meal. The composite figure shows a single experiment composed of 12 tracings, with 3 sequential tracings shown in each image (earlier traces are behind the later traces). The tracings show the outline of the contents of the stomach during digestion of a bread, milk, and bismuth meal; tracings are filled with gray to help visualize them. Each tracing was made at a 30-min interval from 11:00 AM to 4:30 PM. In each subsequent trace, the outline of the contents is reduced until around 5 h after the meal, when most of the meal has been pushed into the small intestine (on the *left*; not shown). [Adapted from Figs. 3–5 of Ref. 5.]

placing him in the X-ray generator. He saw that during the 90 min, digestion had proceeded as he observed in the female cats. Second, as a second control, he caused some female cats to become distressed by briefly blocking their breathing. He noted that at the first signs of discomfort, they were released. In this way, he was able to observe that the motility of the stomach was stopped and started again later. Finally, as a third control, Cannon was concerned that the movements of the struggling cat may have been enough to affect the stomach directly. To test this idea, he manually kneaded or palpated the stomachs of the cats and found that this did not change the motility of the stomach. Cannon later went on to investigate the role of emotions on physiological states and helped to identify the secretions of the adrenal glands as key mediators of emotions (7).

### Teaching Points

Teaching points from Cannon's papers can be summarized as follows:

1. The function of the fundus is to hold food, but not mix it, while salivary digestion continues. Cannon showed that a pH indicator failed to become mixed when sampled from the fundus. He also used multiple applications of the contrast agent at different concentrations to show that food in the fundus does not mix with food in the pylorus. Small balls mixed with contrast agent also failed to move relative to one another when in the fundus.
2. The function of the pylorus is to mix stomach contents with gastric secretions and to gradually pass the contents to the small intestine. Cannon showed that the pylorus mixes food at the rate of one peristaltic wave every 10 s. He concluded that the different motor patterns in the two regions of the stomach allow it to serve these two different functions.
3. The pyloric sphincter only opens irregularly, not with every pyloric wave of contraction. Cannon used small balls mixed with contrast agent to show that solid (undigested) food near the pyloric sphincter inhibits its opening.
4. Cannon showed that the stomach treats different foods differently. When he used a food high in fat in his later study on the intestine (5), gastric emptying was much reduced compared with a semiliquid meal of milk and bread.
5. Cannon observed that during vomiting, the fundus went flaccid while the pylorus, after several strong waves of peristalsis, was divided by a sustained contraction of the muscle around the pyloric region of the stomach. This blocked food from moving down into the GI tract during the following strong contractions of the abdominal muscles. Thus, food was expelled without any sign of antiperistalsis.
6. Cannon noted that the struggling of the cat inhibited the movements of the stomach and intestine. He showed that external manipulation of the stomach did not cause the same inhibition, thus pointing the way toward identifying an emotional influence on GI function.

### Questions for Discovery Learning

1. Describe how the image was formed that Cannon subsequently traced, what the image represented, and how Cannon controlled for movements of the cat. *Answer: the "shadow" image was formed by bismuth absorbing X-rays more than the surrounding tissue. The image seen by Cannon represented only that part of the GI tract contents*

*to which the bismuth had reached. He only took traces from the same point in respiration from an immobilized cat and made three traces of each time point to averaged them.*

2. What were some of the other basic controls that Cannon performed to ensure that "normal" digestion was observed? *Answer: he used different doses of bismuth and applied the bismuth at different times. He used different types of food. He palpated the stomach to simulate movement. He only studied calm cats.*
3. During normal digestion and during vomiting, what are the basic motor pattern of the following:
  - A. The stomach pylorus. *Answer: gentle peristalsis/strong peristalsis followed by division.*
  - B. The stomach fundus. *Answer: gentle squeezing/flaccid.*
4. What were some of the controversies in the literature that Cannon was able to settle? *Answer: was there mixing between the fundus and pylorus? What were the normal movements of the stomach? How did the pyloric sphincter function? Is there antiperistalsis during vomiting?*
5. The study of emotions on physiological function played a large role in Cannon's later research. What were some of the basic observations made by Cannon on emotional state and digestion? *Answer: digestion stopped immediately whenever the cat displayed strong emotions. The effect took time to wear off, even after the cat had calmed.*

### Summary

The careful observations of Cannon on GI motility have provided all subsequent studies with a solid foundation of understanding. These observations debunked several common misconceptions, explained disparate results in the literature, and opened up a new field of research into sympathetic reflexes. Cannon's methods are still used today, albeit with fewer or none of the harmful X-rays, to diagnose a variety of GI motility problems. It is Cannon's care and drive as an experimentalist that has helped make these papers classics. It is hoped that this care and enthusiasm can be conveyed to your students.

### ACKNOWLEDGMENTS

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