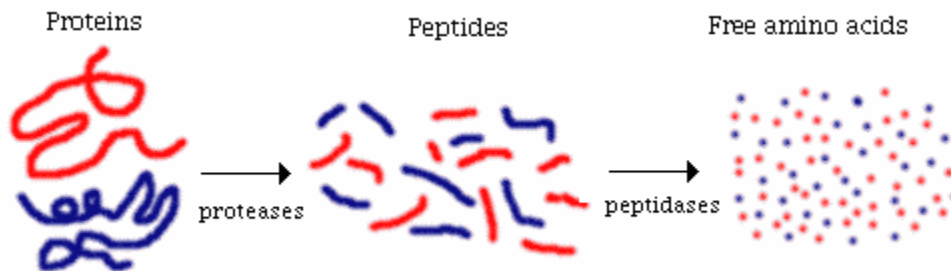


Gastrointestinal Physiology

Simply put, the digestive system is a portal for nutrients from the environment to gain access to the circulatory system. Before such transfer can occur, foodstuffs first have to be reduced to very simple molecules by a combination of mechanical and enzymatic degradation. The resulting sugars, amino acids, fatty acids and the like are then transported across the epithelium lining the intestine into blood.

Consider for a moment a Big Mac. The purpose in your eating a Big Mac, other than simple hedonism, is to assimilate the nutrients it represents and make them available to build, repair and maintain your own tissues, as well as provide energy for studying and occasional other pursuits.

At its simplest, the digestive system it is a tube running from mouth to anus. This tube is like an assembly line, or more properly, a disassembly line. Its chief goal is to break down huge macromolecules (proteins, fats and starch), which cannot be absorbed intact, into smaller molecules (amino acids, fatty acids and glucose) that can be absorbed across the wall of the tube, and into the circulatory system for dissemination around your body.



The breakdown of foodstuffs like a Big Mac is accomplished through a combination of mechanical and enzymatic processes. To accomplish this breakdown, the digestive tube requires considerable assistance from accessory digestive organs such as the salivary glands, liver and pancreas, which dump their secretions into the tube. The name "accessory" should not be taken to mean dispensable; indeed, without pancreatic enzymes you would starve to death in short order.

In many ways, the digestive system can be thought of as a well-run factory in which a large number of complex tasks are performed. The three fundamental processes that take place are:

- **Secretion:** Delivery of enzymes, mucus, ions and the like into the lumen, and hormones into blood.
- **Absorption:** Transport of water, ions and nutrients from the lumen, across the epithelium and into blood.
- **Motility:** Contractions of smooth muscle in the wall of the tube that crush, mix and propel its contents.

Each part of the digestive tube performs at least some of these tasks, and different regions of the tube have unique and important specializations.

Like any well-run factory, proper function of the digestive system requires robust control systems. Control systems must facilitate communication among different sections of the digestive tract (i.e. control on the factory floor), and between the digestive tract and the brain (i.e. between workers and management).

Control of digestive function is achieved through a combination of electrical and hormonal messages which originate either within the digestive system's own nervous and endocrine systems, as well as from the central nervous system and from endocrine organs such as the adrenal gland. Different parts of these systems are constantly talking to one another. The basic messages are along the lines of *"I just received an extraordinary load*

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of food, so I suggest you get prepared" (stomach to large intestine) or "For goodness sake, please slow down until I can catch up with what you've already given me" (small intestine to stomach).

Finally, a note about differences in digestive anatomy and physiology among animals. The digestive systems of humans, dogs, mice, horses, kangaroos and great white sharks are, to a first approximation, virtually identical. If you look more carefully however, it becomes apparent that each of these species has evolved certain digestive specializations that have allowed it to adapt to a particular diet.

These differences become particularly apparent when you compare a **carnivore** like a cat with a **herbivore** like a goat or a horse. Goats and horses evolved from ancestors that subsisted on plants and adapted parts of their digestive tracts into massive fermentation vats which enabled them efficiently utilize cellulose, the major carbohydrate of plants.

In contrast, cats evolved from animals that lived on the carcasses of other animals, and have digestive systems that reflect this history - extremely small fermentation vats and essentially no ability to utilize cellulose. Bridging the gap between carnivores and herbivores are **omnivores** like humans and pigs, whose digestive tracts attest to a historical diet that included both plants and animals. The image above shows a young omnivore in the company of herbivore and carnivore friends.

Basic Functional Anatomy of the Digestive System

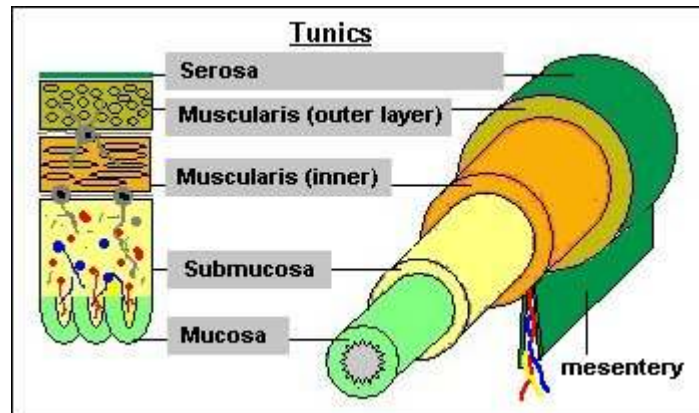
The digestive system is composed of the digestive or alimentary tube and accessory digestive organs. The basic terminology used to describe parts of the digestive system is shown below and more detailed description of each is presented in later sections.

Each of the organs of the digestive system contributes to the digestive process in several unique ways. If you were to describe their most important or predominant function, and summarize shamelessly, the list would look something like this:

- **Mouth:** Foodstuffs are broken down mechanically by chewing and saliva is added as a lubricant. In some species, saliva contains amylase, an enzyme that digests starch.
- **Esophagus:** A simple conduit between the mouth and stomach - clearly important but only marginally interesting compared to other regions of the tube.
- **Stomach:** Where the real action begins - enzymatic digestion of proteins initiated and foodstuffs reduced to liquid form.
- **Liver:** The center of metabolic activity in the body - its major role in the digestive process is to provide bile salts to the small intestine, which are critical for digestion and absorption of fats.
- **Pancreas:** Important roles as both an endocrine and exocrine organ - provides a potent mixture of digestive enzymes to the small intestine which are critical for digestion of fats, carbohydrates and protein.
- **Small Intestine:** The most exciting place to be in the entire digestive system - this is where the final stages of chemical enzymatic digestion occur and where almost all nutrients are absorbed.
- **Large Intestine:** Major differences among species in extent and importance - in all animals water is absorbed, bacterial fermentation takes place and feces are formed. In carnivores, that's about the extent of it, but in herbivores like the horse, the large intestine is huge and of critical importance for utilization of cellulose.

Microanatomy of the Digestive Tube

Remarkably diverse and specialized processes take place in different sections of the digestive tract, but there is a fundamental consistency in the architecture of the tubular digestive tract. With few exceptions, the wall of the digestive tube from the mouth to the anus is composed of **four basic layers or tunics**.



Tunica serosa is the outermost covering of the digestive tube. In most of the digestive tract (stomach and intestines) it consists of a thin layer of loose connective tissue covered by mesothelium (a type of squamous epithelium that lines body cavities); within the peritoneal cavity, this structure is also referred to as visceral peritoneum.

In the abdominal cavity, the serosa on each side of the tube fuses together to form a suspensory structure called mesentery, which houses vascular and nervous supplies to the digestive tract and is continuous with the lining of the cavity. In regions outside of the abdominal cavity where the digestive tube is essentially affixed to adjacent structures via its outer layer of connective tissue (esophagus and rectum), this tunic is referred to as *tunica adventitia* instead of tunica serosa.

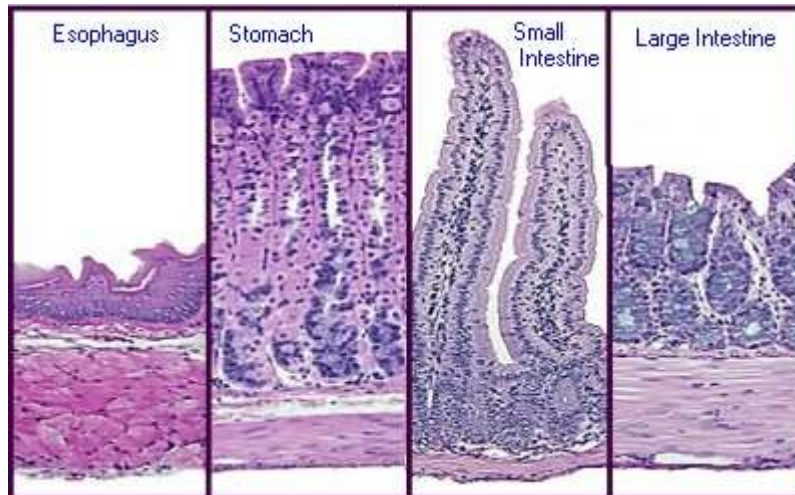
Tunica muscularis endows the digestive tube with an ability to be motile. In most of the digestive tube, this tunic consists of two thick layers of smooth muscle. Muscle fibers in the inner layer are aligned circularly, whereas those in the outer layer have a longitudinal orientation.

This combination of circular and longitudinal smooth muscle gives the tube an ability to perform complex movements that squeeze and propel ingesta in the lumen. Between the inner circular and outer longitudinal layers of smooth muscle is another critical component of the digestive tract's nervous system - the myenteric plexus.

Tunica submucosa lies immediately beneath the mucosa, and is a layer of loose to dense connective tissue containing blood and lymphatic vessels. The submucosa also contains the submucous plexus, a critical component of the digestive tract's nervous system which provides nervous control to the mucosa.

Tunica mucosa is the innermost layer of the digestive tube and lines the lumen. *Among the four tunics, the mucosa is most variable in structure and function, endowing the tube with an ability to perform diverse and specialized digestive tasks along its length.* Of critical importance in this regard are the **epithelial cells** that cover the mucosa and are thus in direct contact with the lumen. This epithelial cell sheet (*lamina epithelialis*) is distinctly different in different regions of the tract. Indeed, in most of the tract, several different cell types contribute to the epithelium, including cells dedicated to secretion, absorption or production of hormones.

These distinctive differences in architecture of the epithelium can be seen below in the micrographs of mouse digestive tube. The magnification of all four images is identical and the epithelial layer is oriented toward the top.



Beneath the epithelium, but still within the tunica mucosa is a layer - the *lamina propria* - of loose connective tissue through which course blood vessels and lymphatics that supply the epithelium. This layer also contains lymphatic nodules important to immune functions of the digestive tract. Finally, beneath the lamina propria is a thin layer of smooth muscle (*lamina muscularis mucosae*) which permits the mucosa to dynamically move and fold.

Microbial Life in the Digestive Tract

The gastrointestinal tract contains an immensely complex ecology of microorganisms. A typical person has 500 distinct species of bacteria, representing dozens of different lifestyles and capabilities. The composition and distribution of this menagerie varies with age, state of health and diet.

The number and type of bacteria in the gastrointestinal tract vary dramatically by region. In healthy individuals the stomach and proximal small intestine contain few microorganisms, largely a result of the bacteriocidal gastric acid; those that are present are aerobes and facultative anaerobes. One interesting testimonial to the effect of gastric acid to suppress bacterial populations is seen in patients with achlorhydria, a genetic condition that prevents secretion of gastric acid. Such patients, which are otherwise healthy, may have as many as 100,000,000 microorganisms per ml of stomach contents.

In contrast to the stomach and small intestine, the contents of the colon literally teem with bacteria, predominantly strict anaerobes (bacteria that survive only in environments virtually devoid of oxygen). In between extremes is a transitional zone, usually in the ileum, where moderate numbers of both aerobic and anaerobic bacteria are found.

Microbial Populations in the Digestive Tract of Normal Humans

| | Stomach | Jejunum | Ileum | Colon |
|---------------------------------|---------------------|---------------------|-----------------------------------|-------------------------------------|
| Viable bacteria per gram | 0 - 10 ³ | 0 - 10 ⁴ | 10 ⁵ - 10 ⁸ | 10 ¹⁰ - 10 ¹¹ |
| pH | 3.0 | 6.0-7.0 | 7.5 | 6.8-7.3 |

The gastrointestinal tract is sterile at birth, but colonization typically begins within a few hours of birth, starting in the small intestine and progressing caudally over a period of several days. In most circumstances, a normal flora is established by 3 to 4 weeks of age.

clear that microbial populations exert a profound effect on structure and function of the digestive system:

The morphology of the intestine of germ-free animals differs considerably from normal. The villi of the small intestine are remarkably regular, the rate of epithelial cell renewal is reduced, and the number and size of Peyer's patches is reduced.

The cecum of germ-free rats is roughly 10 times the size of that in a conventional rat.

Bacteria in the intestinal lumen metabolize a variety of sterols and steroids. For example, they can convert the bile salt cholic acid to deoxycholic acid. Small intestinal bacteria also have an active steroid metabolism.

Bacterial populations in the large intestine digest carbohydrates, proteins and lipids that escape absorption in small intestine. This fermentation, particularly of cellulose, is of critical importance for ruminants like cattle and horses which make a living by consuming plants. However, it seems that even humans and rodents derive significant benefit from the nutrients liberated by intestinal microorganisms.

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