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Introductory Chapter: Stomach-Beyond Digestion

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<http://dx.doi.org/10.5772/intechopen.72520>

1. Introduction

The human body essentially relies on two sources to provide energy and building blocks, oxygen and food. The oxygen is taken in through the respiratory system and can be utilized almost directly for metabolic reactions, while food, after eaten, has to be sent on to a long journey of digestion before becoming utilizable nutrients to nurture the body. This heavy lifting is done by the digestive system. According to the World Health Organization (WHO), more than 6 million people on earth die of various digestive disorders every year [1], only second to heart disease (~7 million). Therefore, it is absolutely vital to understand how this system works and to take good care of it.

The human digestive system is more or less a 9-m long tube starting from the mouth and ending at the anus, plus some accessory glands including liver, pancreas, and gallbladder. The food is first chewed in the mouth, then swallowed down through the esophagus, and stays in the stomach for several hours, depending on the nature of the food and the motility of the organ, before it is sent to the small intestine to be extracted. The word *stomach* is originally derived from the Greek word *stomachos*, *stoma* meaning “mouth.” It is essentially an enlargement of the digestive tract between the esophagus and the duodenum. We also frequently use the word *gastric* when we talk about stomach-related issues, and the word *gastric* is derived from the Greek word *gaster*, meaning “belly.”

The stomach is separated from the rest of the body by two muscular rings, which keep the stomach contents contained. The lower esophageal sphincter, at the junction of the esophagus and the stomach, prevents the highly acidic gastric materials from backing up into the esophagus, otherwise esophageal damages may occur; while the pyloric sphincter, at the junction of the stomach with the duodenum, controls the amount of partially digested food to go into the duodenum, giving the small intestines enough time to absorb as much nutrients from the food as possible. The stomach sends food into the duodenum only when the intestine is not occupied.

The stomach is commonly known as a digestive organ. Although the major digestive events take place in the small intestines where multiple enzymes meet their right conditions, the process of digestion actually begins at the moment of eating. Chewing is a form of mechanical digestion, which crushes the food from big pieces into smaller ones, and the saliva contains digestive enzymes like amylase and lipase, which can break down carbohydrates and lipids. The stomach represents the second phase of digestion, which breaks down proteins into small peptides and thereby facilitates the intestinal digestion. Like the other parts of the digestive tract, the human stomach wall is structurally made of mucosa, submucosa, muscularis externa, and serosa at the histological level. The gastric mucosa consists of the simple columnar epithelium, some loose connective tissue called the lamina propria, and a thin layer of smooth muscle called the muscularis mucosae, which separate the mucosa from the submucosa beneath. At the cellular level, there are several types of secreting cells embedded within the gastric epithelium. The outermost surface of the stomach is lined with the foveolar cells, which produce alkaline mucus for shielding the epithelium from the stomach acid. The stomach has to regenerate a new layer of mucus every 2 weeks, otherwise damage to the epithelium may occur. The parietal cells, mainly found in the fundus and the stomach body, are responsible for making hydrochloric acid to sterilize the food that is brought in by the esophagus. In addition, the parietal cells also make a glycoprotein called intrinsic factor, which is required for vitamin B12 absorption. Then, the chief cells, located in the deep mucosa, produce an enzyme precursor called pepsinogen. Only in the acidic environment, this molecule can become the active enzyme pepsin for proteolysis. The production of hydrochloric acid is regulated by a hormone called gastrin, which is secreted by another type of cells called G cells. The G cells are usually located in the middle portion of the pyloric glands and are occasionally also seen in the duodenum and pancreas. All of these endocrinal cells coordinately work together for digestion. Basically, once the stomach is filled with food, the G cells start to secrete gastrin to stimulate the release of hydrochloric acid from the parietal cells and pepsinogen from the chief cells. Hydrochloric acid then converts pepsinogen into pepsin, which ultimately breaks down proteins into small peptides readily for the small intestines to absorb or to process further.

Pepsin is one of three proteases that we have for protein digestion, and the other two, trypsin and chymotrypsin, are both derived from the pancreas. When the mucous coating of the stomach is damaged by bacterial infection or drugs use, pepsin can reach the gastric epithelium and cause gastritis or ulceration. Overproduction of hydrochloric acid can also cause gastric ulcers. Zollinger-Ellison syndrome is a good example, in which ulcerations develop in the stomach due to tumor-related excessive gastrin release. Gastrin increases both the number of parietal cells and the production of hydrochloric acid [2]. As a result, the mucous layer could not deal with the overwhelming acidity and eventually gives in, then ulceration takes place.

For people who have gastroesophageal reflux disease (GERD), pepsin can be brought up into the esophagus along with the stomach acid to cause esophagitis or esophageal ulcers. If it goes up further into the larynx or pharynx, laryngitis or pharyngitis may occur. Chronic reflux is also possible to induce bronchitis or pneumonia. GERD is the most common gastrointestinal diagnosis given during office visits. In the United States, the overall costs of GERD

management exceed \$85 billion a year [3, 4]. Today, over 60% of Americans experience occasional episodes of acid reflux, and about 25% have to deal with the problem on a weekly basis [5]. Current GERD treatment primarily relies on acid-suppressive medications. However, inhibition of acid secretion can cause various digestive disorders, because hydrochloric acid is an essential element for the stomach to function normally. People who have received this type of treatment have shown multiple side effects such as diarrhea, constipation, decreased absorption of vitamins/minerals, and susceptibility to bacterial infections, bone fracture, and even elevated risk of cancer [6]. Over the years, the Food and Drug Administration of the United States has issued warnings repeatedly against this type of drugs.

In addition to digestion, the stomach can also function as a place for absorption. Although the main absorption in the human digestive system takes place in the small intestine, some small molecules nevertheless can be picked up in the stomach through its lining. This includes water, medication, amino acids, alcohol, caffeine, and some water-soluble vitamins.

The second important function of the stomach is for storage. In the animal kingdom, there is not always plenty of food available to eat or to obtain easily. Very often animals have to risk their lives to fight for a meal. Death due to starvation is very common in the wild world. During the history of evolution, animals learned to adapt this situation by developing an internal pouch to store extra food that they had acquired, so that they could stay alive for a period of time without constant hunting and eating. This structure is the stomach. In some animals, like ruminants, this organ can be very fancy and complicated. For this type of animals, every meal could be an adventure, a life-threatening event, because they usually do not possess excellent fighting skills to protect themselves against predators. Consequently, they have developed a big stomach that is able to hold a large quantity of food. For example, the stomach of a cow can retain 95 l of undigested materials. When they are in a safe place, they can regurgitate the food from the stomach and chew it more slowly and efficiently. The human stomach, on the other hand, is relatively small and can only hold up to 1 l of food. Because human beings have been more skillful survivors by nature comparing to other animals, and they do not always have to face the danger in order to feed themselves, carrying a big stomach would be a burden to them. Nevertheless, the human stomach has experienced the same path of evolution anyhow. Although they do not need to store a lot of food internally for survival, having a food pocket like the stomach has still made their lives much easier. In a modern civilized society, most people eat only 2–4 meals a day, and sometimes eating to them is not for hungry but just a social activity for pleasure. This allows them to be able to spend the rest of the day doing other things, such as listening to music, playing tennis, or walking on the beach. Even if you have to rush to work after eating, having such an internal pocket to save a big steak or a milkshake is amazing.

However, when the stomach has storage issues, the life of the patient can be problematic. For instance, for people with gastric cancer or severe gastric perforation, their stomach has to be removed partially or completely through gastrectomy, consequently, they will have to eat more frequently in order to uptake adequate nutrition. On the other hand, for people with obesity, to help them to lose weight, a gastric band may be placed around the cardia area to reduce the stomach capacity or to bypass the stomach entirely, so that they will not be able to

eat as much as they used to. However, after this kind of surgeries, a condition called dumping syndrome may develop, in which patients experience abdominal cramps or diarrhea soon after eating, especially for food containing high level of carbohydrates, because the small bowel is not made to handle the food rush without a proper preparation and regulation by the stomach [7].

Defense is another important function of the stomach that should not be overlooked. As we said at the beginning, there are two major passageways through which the human body actively takes in raw materials from the environment, oxygen through the respiratory system and food through the digestive system. As a result, these two passageways become the easiest routes for pathogens to invade our body. The Chinese has an old saying, “Illnesses are all derived from the mouth.” It tells some truth about the importance of our eating habits. During the history of evolution, the mankind has learned to cook, which has two purposes: one is to make the food easier to digest and absorb after denaturation, and the second is to kill the pathogens hidden in the food. In the modern civilized world, most people primarily live on cooked food, but sometimes we like to taste the freshness of raw materials like fresh vegetables, fruits, and even raw meat occasionally. Although these goods have already been cleaned up before sold in the market, there are still a lot of people who have no access to these modern hygienic facilities. They eat whatever harvested directly from the field or leftovers without the necessary heating-up. These life styles have accidentally turned on the green light to the pathogens. One-third of the world’s digestive fatalities is caused by diarrhea, making it the most common digestive disorder in the undeveloped regions. For instance, in Angola, diarrhea is responsible for more than 17% of the total number of annual deaths. Fortunately, our digestive system has evolved with some fantastic defense mechanisms. If the food does not taste right, we can get it out of our system by spitting or vomiting. However, our taste buds cannot always distinguish whether there are pathogens in the food. For most of the time after eaten, it is up to the stomach to deal with whatever comes next. Thankfully, we have an amazing stomach, which can function as a sterilizer by creating a highly acidic environment inside our body and keeping its acidity around pH 2.0 for most of the time. Pathogens can rarely survive through such a harsh condition [8]. That eliminates numerous risks we might have to deal with otherwise. So, we should be very careful when it comes to acid-suppressive treatment.

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