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Gastroesophageal Reflux Disease: An Overview

Mayer Eckstein
Touro College

GASTROESOPHAGEAL REFLUX DISEASE: AN OVERVIEW

Mayer Eckstein

All living organisms, including humans, require nutrients in order to survive. The way our bodies absorb these nutrients is through the digestive system. This occurs when the swallowed bolus travels through the esophagus to the stomach. From the stomach it travels to the small intestine, then to the large intestine, and it is then excreted via the rectum.

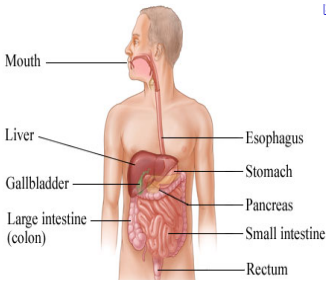

Figure 1: The Digestive System. Source: www.health.com

The question is: how does the body break down the large food particles into the nutrients we need? The answer to this is the stomach. Composed of a muscular bag, the stomach breaks down large food macromolecules. Food is released into the stomach via the lower esophageal sphincter (LES), a round muscle that controls the entrance to the stomach. Acid, released by the parietal cells of the stomach, breaks down the food into their nutrient components. The parietal cells release H^+ and Cl^- via a protein pump. These ions combine in the lumen of the stomach (otherwise they would destruct the parietal cells themselves) and form hydrochloric acid (HCl), giving the stomach a pH of ~2. The acid helps break down the food into smaller molecules. The stomach lining is protected by a mucus sheath secreted by mucus cells in the stomach lining. In addition to this, cell division replaces the stomach lining every three days (Campbell and Reece 2008).

This mixture of acid and food known as acid chyme cannot be excreted, as the acid would burn through the lining of the intestinal walls. In order to bring the pH back towards a neutral *7*, the liver and pancreas come into effect, secreting different molecules into the small intestine. The liver makes bile salts that are stored in and secreted from the gallbladder. These salts function as buffers that resist the change in pH. The pancreas secretes bicarbonate (HCO_3^-). Together, these secretions work to bring the pH level back up towards neutral (Pepitone 2010).

There are many well-known disorders associated with the digestion process, the most common of which is gastroesophageal reflux disease, more commonly known as GERD. There are six major factors that are the primary cause for GERD: impaired esophageal motility, defective mucosal defense, lower esophageal sphincter (LES) dysfunction, reflux of gastric contents, delayed gastric emptying, and hiatal hernia (DeVault and Castell 1999). Impaired esophageal motility occurs when the esophagus has trouble moving the food down and normal peristalsis does not occur. Defective mucosal defense can cause irritation to the esophagus, eliciting a burning sensation as the acid makes its way past the mucosal defense. Lower esophageal sphincter (LES) dysfunction is when the esophageal sphincter does not close properly and allows acid chyme to flow back up the esophagus. Reflux of gastric contents is similar to LES dysfunction; however, the movements and convulsions of the stomach play a major role. Delayed gastric emptying causes a back up in the stomach, which can lead to a greater chance of reflux as well as upper abdominal pain (Lewis et al. 2007). "Hiatal hernia occurs when the upper part of the stomach moves up into the chest through a small opening in the diaphragm….Some doctors believe a hiatal hernia may weaken the LES and increase the risk for gastroesophageal reflux" (Nazario 2009).

Mayer Eckstein will graduate in 2012 with a B.S. in Biology.

The symptoms of GERD vary depending on the individual. The most common adult symptoms are pyrosis, regurgitation, non-cardiac chest pain, and trouble swallowing (dysphagia).

Pyrosis, commonly referred to as heartburn, is described as a "burning, tight sensation that is felt intermittently beneath the sternum and spreads upward to the throat or jaw" (Lewis et al. 2007). Pyrosis occurs when any of the six factors that can cause GERD disrupt the normal digestive system. GERD then causes an inflammation in the chest, giving a burning sensation.

Regurgitation, another sign of GERD, usually occurs due to the buildup of undigested food near the LES. Due to the inability of digesting these food particles, the body rids itself of them by vomiting up the undigested food.

Dysphagia, or the inability to swallow, is a more complex problem then it may appear. "Patients are at a high risk of aspiration due to food or liquids going the wrong way into the lungs" (Logemann 1998). Dysphagia can also result in dehydration, malnutrition, and renal failure. Some symptoms of dysphagia include the inability to control food or saliva in the mouth, difficulty initiating a swallow, coughing, and choking. The most common symptom of dysphagia is the inability to swallow food, which the patient will describe as 'becoming stuck' or 'held up' before it either passes into the stomach or is regurgitated (Logemann 1998).

The symptoms of GERD in children are different than those of adults. Children with GERD may have any one or more of the following: colic-like symptoms, excessive vomiting, bad breath, refusal to eat, swallowing problems, excessive burping after nursing, nighttime coughing. Although most babies have the GERD symptom of mild vomiting, commonly known as 'spitting up,' most of them will outgrow it once they get a few months older and are able to sit up properly. Pediatric GERD is also a common cause of weight-gaining problems in infants (Winter 2008).

GERD can also cause some lesser common diseases. Among them are diseases such as Barrett's esophagus, esophageal ulcers, esophageal adenocarcinoma, erosion of teeth enamel, and esophageal strictures. Although these diseases are less common, their severity is not lessened by their rarity (Lewis et al. 2007).

Figure 2: Barrett's esophagus. Source: www.medscape.com

Barrett's esophagus is usually caused by chronic reflux but is also sometimes caused by ingesting a corrosive substance. The acid in the reflux damages the columnar epithelium tissue in the lower esophagus. The changed form of cells is called "premalignant," because, although they are not cancerous themselves, they significantly raise the risk of esophageal cancer. Barrett's esophagus has other symptoms that evolve from the changed tissue, including chronic heartburn, trouble swallowing (dysphagia),

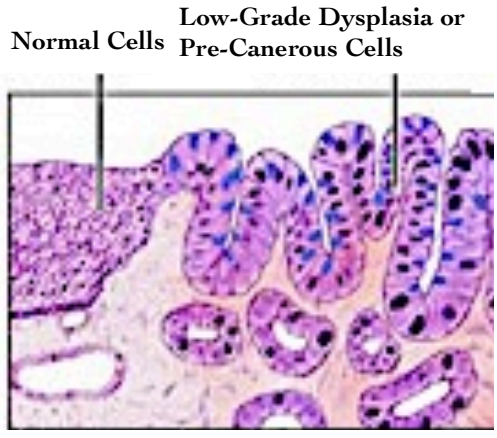

Figure 3: Change in Epithelial Tissue due to Barrett's Esophagus. Source: www.mayoclinic.com

regurgitating blood, noncardiac-related pain, and weight loss (Mayo Clinic 2011).

Another complication that GERD causes is the formation of ulcers. An ulcer is an erosion of a mucus-covered membrane and, if in a highly acidic area, can be very painful. An esophageal ulcer is a hole in the lining of the esophagus corroded by the acid chyme refluxed back up through the LES. Esophageal ulcers are usually located in the lower section of the esophagus, which is closer to the LES. Esophageal ulcers cause pain that is felt behind or just below the sternum, similar to heartburn symptoms. Chronic and severe recurrences of esophageal ulcers can cause esophageal strictures, a narrowing of the esophagus after the thicker scar tissue layer forms. Symptoms of esophageal ulcers can include heartburn, inflammation of the esophagus, the vomiting of black or bright-red-colored blood, and bloody or tarry foul-smelling stool (due to oxidized iron from hemoglobin) (Sameul 2008).

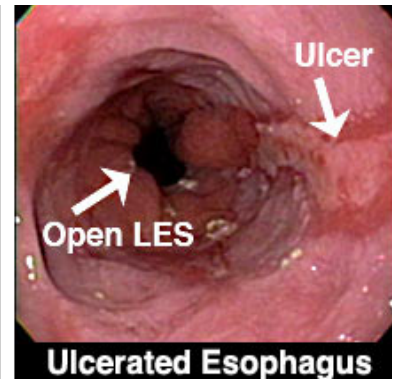

Figure 4 Esophageal Ulcer. Source: stomach-ulcer-symptoms.com

GERD can also cause esophageal adenocarcinoma, a form of esophageal cancer. Most commonly occurring in Caucasian men over the age of 60 (Chou and Gress 2006), adenocarcinoma comes from glandular cells at the junction of the esophagus and stomach, right above the LES. The most dangerous aspect of this disease is that most people diagnosed with esophageal cancer are already in the later stage of the disease. This is because significant symptoms do not usually appear until half of the inside of the esophagus is obstructed, by which point the tumor has already grown big. Because of this, in some severe cases, parts of the esophagus are removed due to the spread of the cancerous cells. Another problem of late recognition is that the cancer can spread and infect the rest of the body, spreading the disease to the entire digestive system, including the liver and pancreas. However, under chemotherapy, the tumor may shrink enough for it to be removed in a standard operating procedure. The risk of esophageal cancer is much higher for a patient with Barrett's esophagus. This is because Barrett's esophagus changes the tissue in the esophagus to a pre-malignant stage (Mayo Clinic 2011).

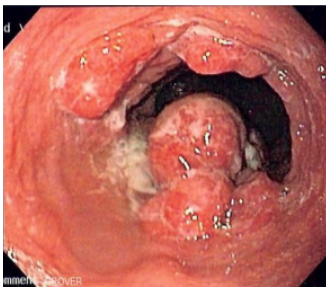

Figure 6: Esophageal Cancer Source: disease-picture.com

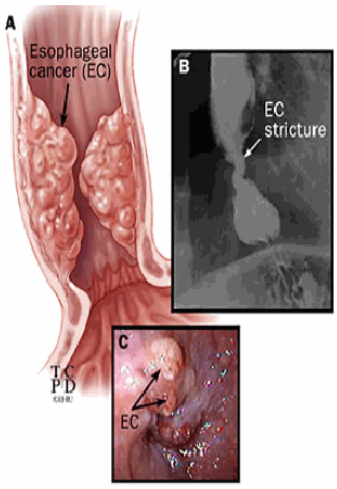

Figure 5: Esophageal cancer (A) with corresponding barium swallow x-ray (B) and endoscopic view (C). Source: disease-picture.com

The symptoms of esophageal adenocarcinoma vary greatly depending on the severity of the disease. Among the most common symptoms are: dysphagia (difficulty swallowing), odynophagia (painful swallowing), substantial weight loss (due to reduced appetite and poor nutrition), pain (usually a burning, heartburn-like feeling), husky, raspy, or hoarse sounding cough, (as a result of the tumor obstructing the airway). The presence of the tumor may disrupt normal peristalsis of the esophagus, leading to nausea, vomiting, coughing, and a

feeling of 'something stuck' in the throat. If the ability to swallow becomes too restricted, a stent can be surgically placed in the esophagus. The stent widens the esophagus, easing swallowing (Lewis et al. 2007).

Another side effect of GERD is the erosion of dental enamel. The main mineral of enamel is hydroxylapatite, which is a crystalline calcium phosphate. High acidity levels in the mouth allow bacteria to thrive and enter into the crevices of the enamel, causing cavities. GERD plays a major role in the pH level of the mouth. Usually the alkalinity of the saliva alone is enough to counter and neutralize the ingestion of acidic products. However, when a patient suffers from GERD, the acidity level in the mouth becomes much greater and overpowers the basic saliva. This usually occurs at night when the patient is sleeping in a supine position and the acid chyme is able to make it all the way back up into the oral cavity (Fried 2010).

Figure 7: Tooth Erosion. Source: www.colgate.com

The erosion of enamel is very serious because as the enamel continues to become less mineralized, it is unable to prevent the encroachment of bacteria, and the underlying dentin becomes affected as well. When dentin, which normally supports enamel, is destroyed by decay, enamel is unable to compensate for its brittleness and breaks away from the tooth easily. This leads to the complete destruction of the upper layers of the tooth, requiring either a replacement crown or a dental implant (Fried 2010).

The chronic occurrence of GERD can cause esophageal strictures. Esophageal strictures are when the esophagus narrows, making it hard to swallow. If a person suffers from GERD, the acid reflux inflames the esophagus. When the esophagus heals, scar tissue grows thick to prevent reoccurrence. This causes the tissue to pull and tighten, which can lead to difficulty swallowing. During healing, a change in texture of the esophagus also occurs. Instead of consisting of very soft tissue, the strictures cause the walls of the esophagus to harden. This can cause severe pain when swallowing (Logemann 1998).

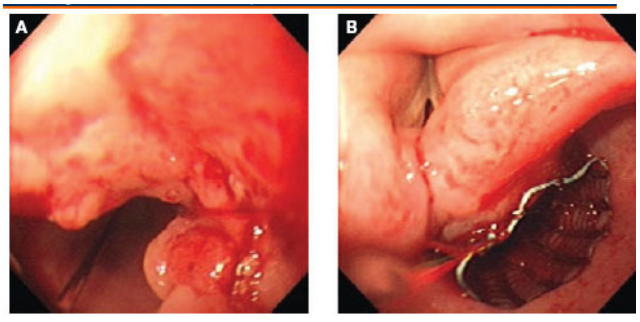

Figure 8: Esophageal Stricture. Source: www.medscape.com

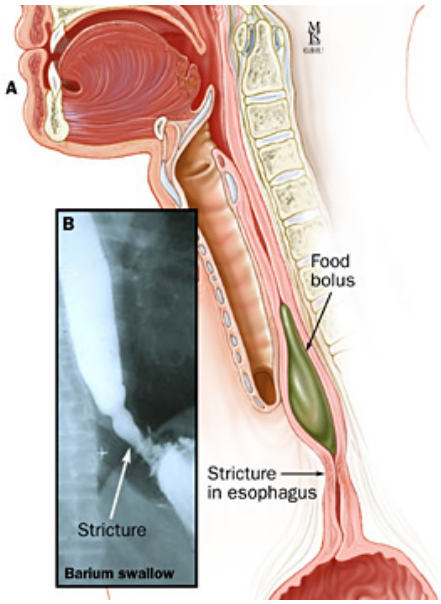

Figure 9: Esophageal Stricture.
Source: www.hopkins-gi.org

Esophageal strictures may also be cancerous. As mentioned above, (see Barrett's esophagus) the change in the tissue of the esophagus can spread and infect other cells and cause those cells to become cancerous. Symptoms of esophageal strictures include heartburn, choking, coughing, shortness of breath, frequent burping and hiccupping, a bitter or acidic taste in the mouth, pain or trouble swallowing, the vomiting of blood, and unintentional weight loss (Drugs.com 2011).

There are a few major ways in which a doctor can diagnose a patient with GERD. Among the most commonly used methods are esophageal pH monitoring, X-rays (barium swallow), esophagogastroduodenoscopy (EGD), and esophageal manometry.

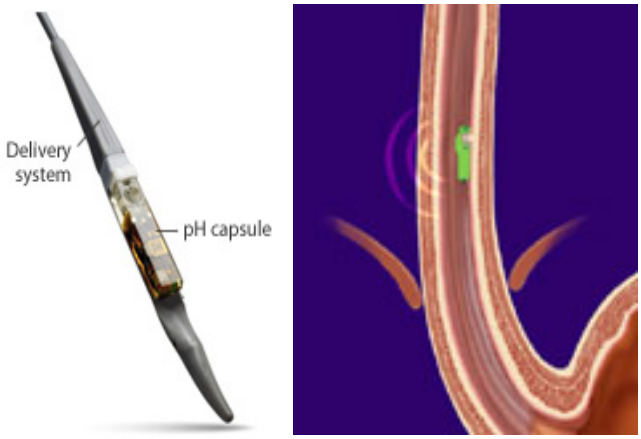

Figure 10: Esophageal pH monitor.
Source: www.givenimaging.com

Esophageal pH monitoring measures the acidity level in the esophagus. The latest technological way to test the pH involves the use of a Bravo pH monitor. The procedure of the Bravo capsule is as follows:

You will be asked to sit or lie back while the physician places the capsule into the esophagus. After the capsule is in place, suction is applied, drawing a small amount of tissue into the capsule. The capsule is then locked into place. The placement procedure is simple to perform and well tolerated by most patients. The capsule begins measuring the pH levels of the esophagus immediately, transmitting pH measurements wirelessly to a small receiver worn on your waistband or belt. The receiver houses three symptom buttons, and you will be asked to press the corresponding button when you experience heartburn, regurgitation, or chest pain during the procedure… The disposable capsule will spontaneously detach and pass naturally through a bowel movement a few days after the test (Given Imaging).

A physician may also utilize X-rays to determine if the patient has GERD. The patient is first given a radio contrasting solution that improves the visibility of internal structures. The most commonly used radio contrast for this procedure is barium sulfate. Barium sulfate is insoluble when mixed with water, and in the X-ray, reveals the internal structures in a cloudy white color. The X-ray can reveal the movement of acid chyme backing up toward the esophagus. Although barium is a heavy metal, and its water-soluble compounds can be highly toxic, the low solubility of barium sulfate protects the patient from absorbing harmful amounts and is secreted out of the body along with regular fecal matter (Lerner 2003; Fallon and Shratter 2012)

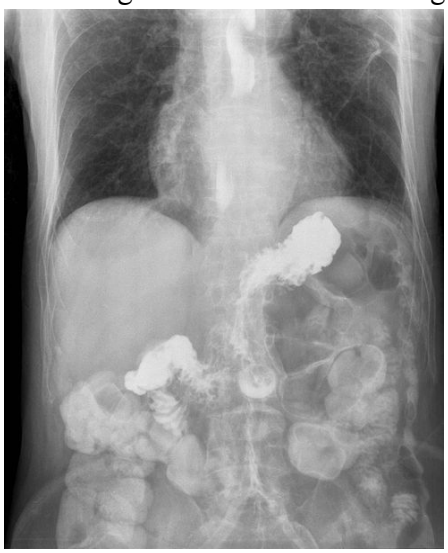

Figure 11: Barium Swallow X-Ray Source:http://en.wikibooks.org/wiki/Medical_Physiology/Gastrointestinal_Physiology#Graft_v. _Host_Disease

Another way a doctor may test for GERD is with an esophagogastroduodenoscopy (EGD). More commonly referred to as an endoscopy, it is a 15-20 minute, minimally invasive procedure that images the esophagus. Endoscopy involves passing an endoscope, a long, flexible black tube with a light and camera on the end, through the mouth to examine the esophagus, stomach, and small intestine. The camera sends a live feed to a monitor. In some cases a biopsy may be taken together with an endoscopy. The biopsy usually takes a small sampling of 1 to 3 mm of tissue from the esophagus via a forceps inserted into the endoscope. The sample is then sent to a laboratory for further histological testing. There are some possible complications with an endoscopy, such as the possibility of tearing the esophagus or stomach. However, the procedure has less than a 1 in 1000 chance of a serious complication occurring (Barrettsinfo.com).

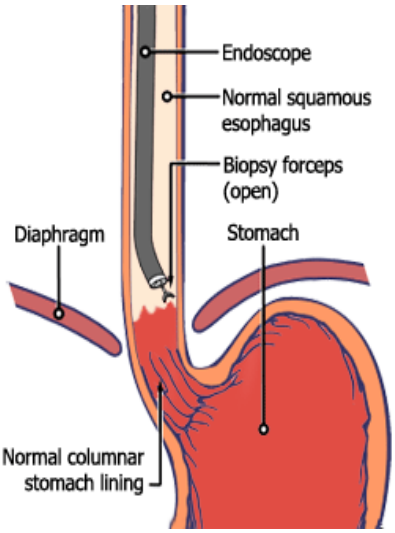

Figure 12: Endoscopy Procedure. Source: www.barrettsinfo.com

Esophageal manometry is another method for determining if a patient has GERD. A manometry is used to determine if the peristalsis of the esophagus is functioning correctly. During an esophageal manometry, a thin, pressure-sensitive tube called a catheter is passed through the mouth into the stomach. Once in place, the tube is pulled slowly back into the esophagus. When the tube is in the esophagus, the patient will be asked to swallow. The pressure of the muscle contractions are measured along several sections of the tube. The data is graphed by a computer, and the results show the peristalsis of the esophagus. Abnormal peristalsis can be a determining factor in diagnosing a patient with GERD

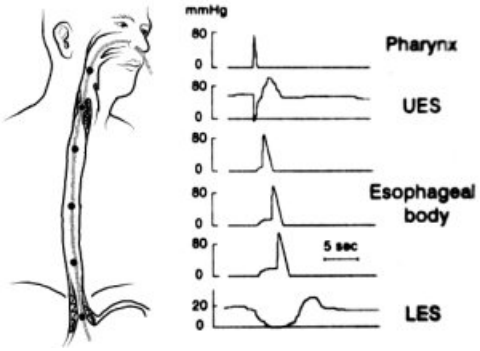

Figure 13: Esophageal Manometry Graph. Source: www.ctsnet.org

(Longstreth 2011).

There are various treatments a doctor can use to treat a patient with GERD. There are three general categories of treatments: medication, life style changes, and surgery. There are five main classes of drugs a doctor prescribes for GERD: H_2 receptor blockers, H^+ pump inhibitors, antacids, foaming agents, and prokinetics.

H_2 receptor blockers work by acting as anti-histamines at the H_2 receptors. This suppresses the acid secretion, which reduces gastric juice volume, decreasing reflux reoccurrence. A few common H_2 receptor blockers are cimetidine (Tagamet®), famotidine (Pepcid®), nizatidine (Axid®), and rantidine (Zantac®) (HealthCentral.com).

Doctors also prescribe H^+ pump inhibitors. H^+ pump inhibitors prevent the secretion of H^+ ions from the parietal cells. This slows the formation of hydrochloric acid in the lumen of the stomach, effectively raising the pH in a short period of time. H^+ pump inhibitors include esomeprazole (Nexium®), lansoprazole (Prevacid®), omeprazole (Prilosec®), pantoprazole (Prononix®), and rabeprazole (Aciphex®) (Cohen 2007; Lewis et al. 2007).

Antacids are another category of treatment used to relieve GERD. Antacids neutralize gastric acid by acting as buffers to help raise the pH, reducing acidity in the stomach. Although some antacids were found to actually raise the pH level in the stomach, all antacids reduced acidity in the lower esophagus, relieving the symptoms of GERD. Antacids also promote ulcer healing and reduce reoccurrence. There are two types of antacids: absorbable and non-absorbable. Absorbable antacids usually contain sodium bicarbonate ($NaHCO_3$) or calcium carbonate ($CaCO_3$) and undergo complete neutralization. The most common absorbable antacids are Alka-Seltzer® ($NaHCO_3$), Maalox tablets® ($CaCO_3$), and Tums® ($CaCO_3$). Among the most common non-absorbable antacids are Maalox liquid® ($Al(OH)_3$ and $Mg(OH)_2$), Mylanta® ($Al(OH)_3$), and Milk of Magnesia® ($Mg(OH)_2$). Another common antacid is Pepto-Bismol® ($C_7H_5BiO_4$) (Brown et al. 2006).

Both classes of antacids share common side effects in addition to their individual side effects. A common shared side effect is a problem with reduced acidity, which results in the inability to digest and absorb essential nutrients. Low acidity can also lead to infections; high acidity usually kills ingested bacteria, so when the pH becomes more basic, bacteria are able to survive. Too much absorbable antacid consisting of sodium (Na) can increase blood pressure as well as cause kidney disease. High levels of carbonate (CO_3) can cause kidney stones, and the high level of CO_2 output can distend and stretch the intestinal walls. Although the side effects of non-absorbable antacids are fewer, high levels of $Mg(OH)_2$ can lead to hypermagnesium, causing cardiovascular and neurological complications. An excess amount of $Al(OH)_3$ can cause formation of insoluble $Al(PO_4)$ complexes, leading to decreased phosphate levels in the blood (Decktor et al. 1995).

A doctor may also suggest the use of foaming agents to relieve GERD. Foaming agents coat the stomach and esophagus, preventing the acid chyme from reaching the mucosal layer. Common foaming agents include Gaviscon® and sucralfate (Carafate®) (NDDIC 2008).

Another treatment for GERD involves the use of prokinetics. Prokinetics are drugs that increases the frequency of contractions in the small intestine, thereby making them stronger. Prokinetics also assist in strengthening the LES, and helps empty the stomach faster. Metoclopramide (Reglan®) and bethanechol (Urecholine®) are the two most common prokinetics (Lewis et al. 2007).

Instead of drugs, or in addition to them, doctors also recommend various life style changes to prevent reoccurrences of GERD. Doctors suggest changes that lower the chance of reflux. These include, but are not limited to, eating smaller meals, sleeping with the head

raised, wearing looser clothing to relieve stomach pressure, losing weight to reduce intra-abdominal pressure, quitting smoking in order to increase the LES's competence, and avoiding foods known to cause reflux, including fatty foods, chocolate, peppermint, caffeine products, alcohol, and acid based products (NDDIC 2008; Eckstein 2012).

In the most serious of cases, when a hiatal hernia or esophageal stricture is involved, and if conservative therapy fails, surgery may be recommended. The surgery is referred to as a Nissen fundoplication. During the surgery, the upper section of the stomach is wrapped around the LES in order to strengthen it. Nissen fundoplication is a minimally invasive surgery known as a laparoscopy, which decreases complications and the overall cost of hospitalization (Lewis et al. 2007).

Endoscopic radiofrequency is another procedure used. "During this procedure a balloon-tipped four-needle catheter, called a Stretta device, delivers radiofrequency energy to the smooth muscle of the LES. The radiofrequency energy induces collagen contraction, which helps form a barrier against reflux" (Lewis et al. 2007).

GERD is a common illness, affecting about a third of the American population, according to the International Foundation for Functional Gastrointestinal Disorders (IFFGD). In most cases it is easily manageable and with proper care, reoccurrence can be prevented. In the most severe cases, GERD may cause life-threatening illnesses such as esophageal adenocarcinoma. Doctors use various methods for diagnosing and treating patients. Treatment may be as simple as life style changes or as complex as surgery. If one suspects that he or she is suffering from GERD, a competent medical doctor should be consulted.

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