Gastroesophageal reflux disease and heartburn

Highlights

New Research

Obesity and GERD. Increased weight in women is linked to more frequent GERD symptoms, according to the Nurses' Health Study, which included 10,545 female participants. Overweight and obese women were two to three times more likely to have frequent symptoms than women of normal weight. GERD symptoms decreased nearly 40% in women whose body mass index (BMI) dropped by more than 3.5, compared to women whose BMI remained the same.

Proton-Pump Inhibitors and Bone Fracture. Long-term use of PPIs may increase the risk of hip fractures in older adults, according to a study in the *Journal of the American Medical Association*. People taking high doses of PPIs for more than a year were 2.6 times as likely to fracture a hip as those who were not taking the drug. The authors suggested that the stomach acids blocked by PPIs may be needed to absorb calcium, or the drugs may interfere with the body's natural process of breaking down and rebuilding bones.

PPIs and H2 Blockers in Children. Otherwise healthy children who take PPI inhibitors or H2 blockers may be at increased risk for intestinal and respiratory infections, according to a study of 186 children with GERD. The rate of gastroenteritis and community-acquired pneumonia significantly increased in children who were taking these medications when researchers compared the 4 months before and after enrollment in the study.

New Approval

Proton-Pump Inhibitor Approved for Adolescents. Esomeprazole (Nexium) delayed-release capsules have been approved for use in children ages 12 - 17 for the short-term treatment of GERD. Research shows that this medication reduces heartburn symptoms in adolescents.

Introduction

Gastroesophageal reflux disease (GERD) is a condition in which acids from the stomach move backward into the esophagus (an action called reflux). *Reflux* occurs if the muscular actions in the esophagus or other protective mechanisms fail.

The hallmark symptoms of GERD are:

Heartburn: a burning sensation in the chest and throat.
Regurgitation: a sensation of acid backed up in the esophagus.

Although acid is a primary factor in damage caused by GERD, other products of the digestive tract, including pepsin and bile, can also be harmful.

Heartburn is a condition in which the acidic stomach contents back up into the esophagus, causing pain in the chest area. This reflux usually occurs because the sphincter muscle between the esophagus and stomach is weakened. Standing or sitting after a meal can help reduce the reflux that causes heartburn. Continuous irritation of the esophagus lining as in gastroesophageal reflux disease is a risk factor for the development of adenocarcinoma.

The Esophagus

The esophagus, commonly called the *food pipe*, is a narrow muscular tube about nine-and-a-half inches long. It begins below the tongue and ends at the stomach. The esophagus is narrowest at the top and bottom; it also narrows slightly in the middle. The esophagus consists of three basic layers:

An outer layer of fibrous tissue.
A middle layer containing smoother muscle.
An inner membrane, which contains numerous tiny glands.

When a person swallows food, the esophagus moves it into the stomach through the action of peristalsis, wave-like muscle contractions. In the stomach, the starch, fat, and protein in food are broken down by acid and various enzymes, notably hydrochloric acid and pepsin. The lining of the stomach has a thin layer of mucous that protects it from these fluids.

If acid and enzymes back up into the esophagus, however, its lining offers only a weak defense. The esophagus is protected using specific muscles and other factors.

The most important structure protecting the esophagus may be the *lower esophageal sphincter* (*LES*). The LES is a band of muscle around the bottom of the esophagus where it meets the stomach.

The LES opens after a person swallows to let food enter the stomach and then immediately closes to prevent regurgitation of the stomach contents, including gastric acid.

The LES maintains this pressure barrier until food is swallowed again.

If the pressure barrier is not sufficient to prevent regurgitation and acid backs-up (reflux), then peristaltic action of the esophagus serves as an additional defense mechanism and pushes the contents back down into the stomach.

Conditions Associated with GERD

Esophagitis. In most people, GERD symptoms are short-lived and occur infrequently. In about 20% of cases, however, the condition becomes chronic. When the acid causes irritation or inflammation, the condition is called *esophagitis*. If the damage becomes extensive and injures the esophagus, the disorder is known as *erosive esophagitis.*

Non-Erosive Esophageal Reflux Disease. Symptoms of gastroesophageal reflux disease can occur without any signs of inflammation or injury to the esophagus. This condition is also referred to as non-erosive esophageal reflux disease (NERD). NERD rarely progresses to full-blown GERD. Patients with NERD have no signs of inflammation or erosion in the esophagus, but they experience certain symptoms of GERD, such as burning sensations behind the breastbone for at least 3 months. Researchers suggest that nerves lying near the surface of the lining become exposed to acid that has penetrated the layers. The nerves then trigger prolonged and painful symptoms in response.

Barrett's Esophagus. A small percentage of patients with GERD may eventually develop Barrett's esophagus, a serious complication of GERD that results in precancerous changes in the tissue lining the esophagus.

Eosinophilic Esophagitis. This is a distinct disorder characterized by difficult or painful swallowing. It can occur along with GERD. The lining of the esophagus develops furrows and rings. This condition can be treated with swallowed fluticasone propionate, the active ingredient in some asthma medications.

Causes

Anyone who eats a large amount of acidic foods can have mild and temporary heartburn. This is especially true when lifting, bending over, or taking a nap after eating a large meal high in fatty, acidic foods. Persistent GERD, however, may be due to various conditions, including abnormal biologic or structural factors.

Malfunction of the Lower Esophageal Sphincter (LES) Muscles

The band of muscle tissue called the LES is responsible for closing and opening the lower end of the esophagus and is essential for maintaining a pressure barrier against contents from the stomach. It is a complex area of smooth muscles and various hormones. If it weakens and loses tone, the LES cannot close up completely after food empties into the stomach. In such cases, acid from the stomach backs up into

the esophagus. Dietary substances, drugs, and nervous system factors can weaken the LES and impair its function.

Impaired Stomach Function

A study showed that more than half of GERD patients had abnormal nerve or muscle function in the stomach. These abnormalities cause *impaired motility*, which is the inability of muscles to act spontaneously. The stomach muscles do not contract normally, which causes delays in stomach emptying, increasing the risk for acid back-up.

Abnormalities in the Esophagus

Some studies suggest that most people with atypical GERD symptoms (such as hoarseness, chronic cough, or the feeling of having a lump in the throat) may have specific abnormalities in the esophagus. (In one study, such abnormalities appeared in 73% of patients who had atypical symptoms.)

Motility Abnormalities. Problems in spontaneous muscle action (*peristalsis*) in the esophagus commonly occur in GERD, although it is not clear if such occurrences are a cause or result of long-term effects of GERD.

Adult-Ringed Esophagus. This condition is characterized by an esophagus with multiple rings and persistent trouble with swallowing (including getting food stuck in the esophagus). It occurs mostly in men.

Hiatal Hernia

The *hiatus* is a small hole in the diaphragm through which the esophagus passes into the stomach. It normally fits very snugly, but it may weaken and enlarge. When this happens, part of the stomach muscles may protrude into it, producing a condition called *hiatal hernia*. It is very common, occurring in over half of people over 60 years old, and is rarely serious. Until recent years, it was believed that most cases of persistent heartburn were caused by a hiatal hernia. Hiatal hernia may impair LES muscle function. Studies have failed to confirm evidence, however, that it is a common cause of GERD, although its presence may increase GERD symptoms in patients with both conditions.

A hiatal hernia occurs when part of the stomach protrudes up into the chest through the sheet of muscle called the diaphragm. This may result from a weakening of the surrounding tissues and may be aggravated by obesity or smoking.

Genetic Factors

Studies indicate that 31 - 43% of reflux may be hereditary. An inherited risk exists

in many cases of GERD, possibly because of inherited muscular or structural problems in the stomach or esophagus. Genetic factors may play an especially strong role in susceptibility to Barrett's esophagus, a precancerous condition caused by very severe GERD.

Asthma

At least half of people with asthma also have GERD. Some experts speculate that the coughing and sneezing accompanying asthmatic attacks cause changes in pressure in the chest that can trigger reflux. Certain asthma drugs that dilate the airways may relax the LES and contribute to GERD. On the other hand, GERD has been associated with a number of other upper respiratory problems and may be a cause of asthma, rather than a result.

Other Conditions Associated with GERD

Crohn's disease is a chronic ailment that causes inflammation and injury in the colon and other parts of the gastrointestinal tract, including the esophagus. Other disorders that may affect areas that can contribute to GERD include diabetes, any gastrointestinal disorder, peptic ulcers, lymphomas, and cancer.

Eradication of *Helicobacter Pylori*

Helicobacter Pylori, also called *H. pylori*, is a bacterium found in the mucous membranes and is now known to be a major cause of peptic ulcers. Antibiotics used to eradicate *H. pylori* are now accepted treatment for curing ulcers. Of some concern, however, are studies indicating that *H. Pylori* may actually protect against GERD by reducing stomach acid. Furthermore, curing ulcers by eliminating the bacteria might actually trigger GERD in some people. Studies are mixed, however, on whether patients with cured *H. Pylori* infections are at risk for GERD. An analysis of 8 studies reported no higher risk for GERD after antibiotic treatments, nor was GERD any worse in patients who already had it. Seven of the 8 studies, however, were conducted only 2 months after antibiotic treatment. Longer follow-up studies are needed to determine long-term consequences, if any.

In any case, the bacteria should be eradicated in infected patients with existing GERD who are taking ongoing acid suppressing agents. There is some evidence that the combination of *H. pylori* and chronic acid suppression in these patients can lead to atrophic gastritis, a precancerous condition in the stomach.

Over-reactive Immune Response

In some cases, the esophagus appears normal, but GERD symptoms are present. This may indicate an over-reaction of the immune system to irritants that are introduced into the esophagus. In such cases, the immune system reacts with an exaggerated (or hyper-reactive) response, triggering the release of certain factors that end up causing inflammation and possibly injury. (This event is similar to the asthmatic response in the airways.)

Drugs that Increase the Risk for GERD

NSAIDs. Nonsteroidal anti-inflammatory drugs (NSAIDs), common causes of peptic ulcers, may also cause GERD and increase severity in people who already have GERD. In a 3-year study of 25,000 people, NSAID users were twice as likely to have GERD symptoms as non-users. Symptoms did not become evident until after about 6 months of regular use. There are dozens of NSAIDs, including over-the-counter aspirin, ibuprofen (Motrin, Advil, Nuprin), and naproxen (Aleve), as well as prescription anti-inflammatory medicines. A person with GERD who takes the occasional aspirin or other NSAID will not necessarily experience adverse effects. This is especially true if there are no risk factors or indications of ulcers. Acetaminophen (Tylenol), which is NOT an NSAID, is a good alternative for those who want to relieve mild pain. It does not, however, relieve inflammation.

Other Drugs. Many other drugs can cause GERD, including but not limited to the following: calcium channel blockers (used to treat high blood pressure and angina), anticholinergics (used in drugs that treat urinary tract disorders, allergies, and glaucoma), beta adrenergic agonists (used for asthma and obstructive lung diseases), dopamine (used in Parkinson's disease), bisphosphonates (used to treat osteoporosis), sedatives, antibiotics, potassium, or iron pills.

Other Causes of GERD

Weakened peristaltic movement in the esophagus may contribute to GERD. If the mucous membrane is impaired, even a normal amount of acid can harm the esophagus. Pressure on the abdomen caused by obesity and also wearing tight clothing can contribute to acid backing up into the esophagus.

Risk Factors

GERD occurs monthly in about half of American adults. People of all ages are susceptible to GERD. Elderly people with GERD tend to have a more serious condition than younger people.

Risk Factors for Heartburn and GERD

Eating Pattern. Anyone who eats a heavy meal and subsequently lies on the back or bends over from the waist is at risk for an attack of heartburn. Anyone who snacks at bedtime is at high risk for heartburn.

Pregnancy. Pregnant women are particularly vulnerable to heartburn in their third trimester as the growing uterus puts increasing pressure on the stomach. Heartburn in such cases is often resistant to dietary interventions and even antacids.

Obesity. A number of studies suggest that obesity contributes to GERD and may increase the risk for erosive esophagitis in GERD patients. The Nurses' Health Study found that being overweight or obese significantly increased GERD symptoms in women. The higher a woman's body mass index (BMI), the study found, the more frequent were her symptoms. Women who lost weight in the study saw a decrease in their symptoms. Research suggests that the prevalence of GERD symptoms among obese patients has been underreported. Other researchers have reported that increased BMI is associated with a higher risk for cancer of the esophagus (esophageal adenocarcinoma).

Respiratory Diseases. People with asthma are at very high risk for GERD. One study indicated that patients with chronic obstructive pulmonary diseases (e.g., emphysema or chronic bronchitis) were more likely to have GERD.

Chronic obstructive pulmonary disease (COPD) refers to chronic lung disorders that result in blocked air flow in the lungs. The two main COPD disorders are

emphysema and chronic bronchitis, the most common causes of respiratory failure. Emphysema occurs when the walls between the lung's air sacs become weakened and the sacs get enlarged and filled with too much air. Damage from COPD is usually permanent and irreversible.

Smoking. Increasing evidence indicates that smoking raises the risk for GERD. Studies suggest that smoking reduces LES muscle function, increases acid secretion, impairs muscle reflexes in the throat, and damages protective mucous membranes. Smoking reduces salivation, which helps neutralize acid. Whether it is the smoke, nicotine, or both that triggers GERD is unknown. Some people who use nicotine patches to quit smoking, for example, experience heartburn, but it is not clear if it's the nicotine or stress that produces acid back-up.

Alcohol Use. Alcohol has mixed effects on GERD. It relaxes the LES muscles and, in high amounts, may irritate the mucous membrane of the esophagus. All alcoholic beverages increase stomach acid levels. A combination of heavy alcohol use and smoking increases the risk for esophageal cancer. (Small amounts of alcohol, however, may actually protect the mucosal layer.)

Risk Factors for Severe GERD

In general, overweight Caucasian males over 40 are at highest risk for complications, notably Barrett's esophagus. Others at high risk for severe symptoms, inflammation, or both include:

People who use nonsteroidal anti-inflammatory drugs (NSAIDs). Studies suggest that certain NSAID users are at higher risk for GERD, including older adults, women, alcohol and tobacco users, and patients with asthma, hiatal hernia, or obesity. One study reported that NSAIDs put people at risk for ulcers but not for erosive esophagitis or strictures. Interestingly, NSAIDs are being studied for protection *against* Barrett's esophagus.

People with hiatal hernia

Gastroesophageal Reflux Disease in Children

GERD is very common in children of all ages, but it is usually mild. Heartburn has been reported in 1.8% of 3-year-olds and in 5.2% of young people 10 - 17 years old. Children with the following conditions are at higher risk for severe GERD:

Neurologic impairments
Food allergies
Scoliosis
Cyclic vomiting
Cystic fibrosis
Problems in the lungs, ear, nose, or throat

Any medical condition affecting the digestive tract

Symptoms in Children

A physician should examine any child who has the following symptoms as soon as possible, because they may indicate complications such as anemia, failure to gain weight, or respiratory problems. Symptoms of severe GERD in infants and small children may include:

Chronic coughing
Frequent infections
Wheezing
Gasping or frequent cessation in breathing while asleep (called sleep apnea). However, one study found no association between GERD and apneas in premature infants.
Frequent vomiting in infants. About half of all infants up to 3 months old regurgitate milk at least once a day. Some simply spit up; others vomit large amounts after feedings. Vomiting in infants and older children is rarely a sign of GERD. In infants it usually resolves by age one. Severe vomiting -- particularly if it is bilious (green colored) -- always requires a doctor's visit, since it could be a symptom of severe obstruction.
Having to burp babies very frequently during and after feeding.

Babies and children may experience these symptoms without having GERD. An Australian study suggested that many infants who have normal irritability may be treated inappropriately for reflux disorders.

Complications in Infants and Children

Feeding Problems. Feeding problems may be more severe than previously thought in children with GERD. In one study, children who had GERD and problems swallowing tended to refuse food and were late in eating solids. They also cried more and reacted more negatively in general than non-GERD babies. Such behaviors negatively affected the mothers as well. These findings were supported in an earlier study which reported that children at 1 year who had GERD in infancy were no longer spitting up, but still tended to have negative dining experiences ("too slow," "upsetting"). However, these children were at no greater risk for respiratory illnesses than other 1-year-old children.

Associations with Asthma and Infections in the Upper Airways. In addition to asthma, GERD is associated with other upper airway problems, including ear infections and sinusitis. Some experts argue that the association with common childhood infections and asthma is unfounded, since GERD is normal in most children.

Dental Erosion. GERD can cause irreversible loss of tooth enamel. Based on a

2002 study, some experts suggest checking for GERD in children with dental erosions. In the study, no child *without* GERD experienced loss of tooth enamel.

Rare Complications in Infants. Although GERD is very common, the following complications are very rare and only occur in certain cases:

- Failure to thrive
- Feeding problems and severe vomiting may cause anemia
- Acid back-up may be inhaled into the airways and cause pneumonia

The infant's life may be in danger if acid reflux causes spasms in the larynx severe enough to block the airways. In fact, some experts believe this action may contribute to sudden infant death syndrome (SIDS). More research is needed to determine whether this association is valid.

Managing GERD in Infancy

Here are some hints on managing GERD in infants:

- During and after feeding, infants should be positioned vertically and burped frequently.
- If a baby with GERD is fed formula, the mother should ask the doctor how to thicken it in order to prevent splashing up from the stomach.
- Parents of infants with GERD should discuss the baby's sleeping position with their pediatrician. Experts strongly recommend that all healthy infants sleep on their backs to help prevent sudden infant death syndrome (SIDS). For babies with GERD, however, lying on the back may obstruct the airways. In one study, infants with gastroesophageal reflux who spent prolonged periods of time in infant seats, including car seats, had more reflux than those who spent waking time on their stomachs. If the physician recommends that babies with GERD sleep on their stomachs, parents should be sure that their infant's mattress is very firm, possibly tilted up at the head, and that there are no pillows. The baby's head should be turned so that the mouth and nose are completely unobstructed.
- Because food allergies may trigger GERD in children, parents may want to discuss a dietary plan with their physician that starts the child on formulas using non-allergenic proteins, and then incrementally adds other foods until symptoms are triggered.

Managing GERD in Children

The same drugs used in adults may be tried in children with chronic GERD. While some drugs are available over the counter, they should not be given to children without physician supervision.

- Milder medications, such as antacids, are used first.
- H2 blockers may be tried next. They are available over the counter and include

famotidine (Pepcid AC), cimetidine (Tagamet HB), ranitidine (Zantac 75), and nizatidine (Axid AR). The FDA has issued a warning on Pepcid AC for adults with kidney problems.

Proton-pump inhibitors (PPIs), such as omeprazole (Prilosec) and lansoprazole (Prevacid), are even more powerful agents that suppress the production of stomach acid. Delayed-release esomeprazole (Nexium) capsules have been approved for use in children ages 12 - 17 for the short-term treatment of GERD. One study found that esomeprazole (Nexium) in either a 20 or 40 mg dose once a day significantly reduced heartburn symptoms in adolescents. PPIs appear to be safe and effective even for children as young as 1 year old who fail the less intensive therapies. However, a 2006 study found that otherwise healthy children who were treated with H2 blockers and PPIs had an increased risk of developing respiratory and intestinal infections.

Surgical fundoplication involves wrapping the upper curve of the stomach (fundus) around the esophagus. The goal of this surgical technique is to strengthen the LES. Until recently, surgery was the primary treatment for children with severe complications from GERD because older drug therapies had severe side effects, were ineffective, or had not been designed for children. However, with the introduction of proton-pump inhibitor drugs, some children may be able to avoid surgery. Surgical fundoplication can be performed laparoscopically through small incisions. In one study, of 238 children from 5 months to 16 years of age who underwent laparoscopic fundoplication, all but 9 were symptom free at least 5 years after the surgery. A 2006 study found that children who underwent antireflux surgery before age 4 were less likely to be hospitalized again, or to have reflux-related events such as pneumonia and esophagitis after the surgery.

Symptoms

Heartburn. Heartburn is the primary symptom of GERD. It is a burning sensation that radiates up from the stomach to the chest and throat. Heartburn is most likely to occur in connection with the following activities:

After a heavy meal
Bending over
Lifting
Lying down, particularly on the back

According to one study, nearly three-quarters of patients with frequent GERD symptoms experience them at night. Patients with nighttime GERD also tend to experience more severe pain than those whose symptoms occur at other times. One study found that patients with nighttime pain reported levels of severity that were similar to those reported in angina and heart failure.

The severity of heartburn does not necessarily indicate actual injury in the

esophagus. For example, Barrett's esophagus, which causes precancerous changes in the esophagus, may trigger few symptoms, especially in elderly people. On the other hand, people can suffer severe heartburn without the presence of damage to the esophagus.

Dyspepsia. Up to half of GERD patients have *dyspepsia*, a syndrome consisting of the following:

- Pain and discomfort in the upper abdomen
- Fullness in the stomach
- Nausea after eating

People can have dyspepsia without having GERD.

Regurgitation. Regurgitation is the feeling of acid backing up in the throat. Sometimes acid regurgitates as far as the mouth and can be experienced as a "wet burp." Uncommonly, it may come out forcefully as vomit.

Less Common Symptoms

Many patients with GERD do not experience heartburn or regurgitation. Elderly patients with GERD often have less typical symptoms than do younger people. Instead symptoms may appear in other locations.

Chest Sensations or Pain. Patients may have the sensation that food is trapped behind the breastbone. Chest pain is a common symptom of GERD. It is very important to differentiate it from chest pain caused by heart conditions, such as angina and heart attack.

Symptoms in the Throat. Less commonly, GERD may produce symptoms that occur in the throat:

- Acid laryngitis. A condition that includes hoarseness, dry cough, the sensation of having a lump in the throat, and the need to repeatedly clear the throat.
- Trouble swallowing (*dysphagia*). In severe cases, patients may even choke or food may become trapped in the esophagus, causing severe chest pain. This may indicate a temporary spasm that narrows the tube, or it could also be an indication of serious esophageal damage or abnormalities.
- Chronic sore throat
- Persistent hiccups

Coughing and Respiratory Symptoms. Asthmatic symptoms, such as coughing and wheezing, may occur. In fact, in one study, GERD alone accounted for 41.1% of cases of chronic cough in nonsmoking patients. The incidence was even higher when GERD and asthma were combined.

Chronic Nausea and Vomiting. Nausea that persists for weeks or even months and is

not attributable to a common cause of stomach upset may be a symptom of acid reflux. In rare cases, vomiting can occur as often as once a day. All other causes of chronic nausea and vomiting should be ruled out, including ulcers, stomach cancer, obstruction, and pancreas or gallbladder disorders.

Complications

Nearly everyone has an attack of heartburn at some point in their lives. In the vast majority of cases the condition is temporary and mild, causing only transient discomfort. If patients develop persistent gastroesophageal reflux disease with frequent relapses, however, and it remains untreated, serious complications may develop over time. They can include the following:

- Erosive esophagitis (severe inflammation in the esophagus)
- Severe narrowing (*stricture*) of the esophagus
- Barrett's esophagus
- Problems in other areas, including the teeth, throat, and airways leading to the lungs

Older people are at higher risk for complications from persistent GERD. The following conditions also put individuals at risk for recurrent and serious GERD:

- The esophagus is very inflamed.
- Initial symptoms are severe.
- Symptoms persist in spite of treatments that successfully heal the esophagus.
- There are severe underlying muscular abnormalities.

Erosive Esophagitis and its Complications

Erosive esophagitis develops in chronic GERD patients when acid causes enough irritation and inflammation to produce extensive injuries in the esophagus. Some studies have suggested that overweight Caucasian males with GERD are at highest risk for this condition. In anyone, however, the longer and more severe the GERD condition, the higher the risk for erosive esophagitis.

Bleeding. In one study, bleeding occurred in more than 8% of patients with erosive esophagitis (severe inflammation of the esophagus), which is associated with GERD. In very severe cases, the patient may detect dark-colored, tarry stools (indicating the presence of blood) or may vomit blood, particularly if ulcers have developed in the esophagus. This is a sign of severe damage and requires immediate attention.

Sometimes long-term bleeding can result in iron-deficiency anemia and may even require emergency transfusions. This condition can occur without heartburn or other warning symptoms, or even obvious blood in the stools.

Barrett's Esophagus (BE) and Esophageal Cancer. In some cases, BE develops as

an advanced stage of erosive esophagitis. BE results in abnormal cellular changes in the esophagus that, in turn, put a patient at risk for esophageal cancer. There are many issues involved with BE, however, including its prevalence and true severity, that are unresolved.

Of note, GERD itself poses no significant risk for esophageal cancer. One study reported an annual incidence of 6.5 cancer cases per 10,000 people with regular GERD symptoms.

Complications of Stricture

If the esophagus becomes severely injured over time, narrowed regions called *strictures* can develop, which may impair swallowing (dysphagia). Food may even become blocked in some cases. Stretching procedures or surgery may be required to restore normal swallowing. Paradoxically, strictures may actually prevent other GERD symptoms by helping to keep acid from traveling up the esophagus.

Asthma and Other Respiratory Disorders

Asthma. Asthma and GERD often occur together. Studies report that reflux disorder coincides with 32 - 80% of asthma cases. Some theories for the causal connection between GERD and asthma are as follows:

Acid leaking from the lower esophagus in GERD stimulates the *vagus nerves*, which run through the gastrointestinal tract. These stimulated nerves trigger the nearby airways in the lung to constrict, which causes asthma symptoms.

Acid back-up that reaches the mouth may be inhaled into the airways (*aspirated*). Here, the acid triggers a reaction in the airways that causes asthma symptoms.

There is some evidence that asthma causes GERD. In contrast, some evidence suggests that GERD causes asthma. Some clinical trials report that treating GERD in patients who also have asthma reduces symptoms of both conditions. Not all such patients report improved asthma symptoms with GERD treatments, and these treatments do not appear to have much effect on actual lung function. One study suggested that this approach works in asthmatic individuals who tended to be overweight and to have severe GERD in the lower part of the esophagus.

Other Respiratory and Airway Conditions. Current studies indicate an association between GERD and various upper respiratory problems that occur in the sinuses, ear and nasal passages, and airways of the lung. People with GERD appear to have an above-average risk for chronic bronchitis, chronic sinusitis, emphysema, pulmonary fibrosis (lung scarring), and recurrent pneumonia. If a person inhales fluid from the esophagus (aspirates) into the lungs, serious pneumonia can occur. It is not yet known whether treatment of GERD would also reduce the risk for these respiratory conditions.

Dental Problems

Dental erosion (the loss of the tooth's enamel coating) is a very common problem among GERD patients, including children. It results from the acid backing up into the mouth and eroding the enamel.

Chronic Throat Conditions

An estimated 20 - 60% of patients with GERD have atypical symptoms in the throat (hoarseness, sore throat) without any significant heartburn. A failure to diagnose and treat GERD may lead to persistent throat conditions such as chronic laryngitis, hoarseness, difficulty in speaking, sore throat, cough, constant throat clearing, and granulomas (soft, pink bumps) on the vocal cords.

Sleep Apnea

GERD commonly occurs with obstructive sleep apnea, a condition in which breathing stops temporarily but repeatedly during sleep. It is not clear which condition is responsible for the other, but GERD is particularly severe when both conditions occur together. One study reported that spasms in the vocal cords caused by acid reflux may block the flow of air and cause sleep apnea in adults. On the other hand, other research suggests that the disordered breathing in sleep apnea alters pressure in the chest area and causes GERD. Both conditions may also have risk factors in common, such as sleeping on the back. Studies suggest that in such patients GERD can be markedly improved with a continuous positive airway pressure (CPAP) device, which opens the airways and is the standard treatment for severe sleep apnea.

Barrett's Esophagus

Barrett's esophagus (BE) is a serious condition in which changes occur in the cells that line the lower esophagus and cause the cells to become abnormal and precancerous. Barrett's esophagus is categorized as either long-segment or short-segment disease:

Long-segment BE occurs when abnormal cells affect 3 cm or more of the esophagus. This condition occurs in about 3 - 7% of GERD patients. It is associated with a more severe condition.

Short-segment BE affects less than 3 cm of the esophagus and is found in about 10 - 17% of GERD patients.

Risk Factors for Barrett's Esophagus

About 10% of patients with symptomatic GERD have BE. In some cases, BE develops as an advanced stage of erosive esophagitis. Some studies suggest that individuals at highest risk for BE are obese white males over the age of 50 with persistent GERD who drink alcohol. However, a number of studies have reported no relationship between alcohol use or being male and overweight with BE. Such studies have also reported no higher risk in smokers or relatives of BE patients. Only

the persistence of symptoms suggested a higher risk. Nevertheless, not all patients with BE have either esophagitis or symptoms of GERD.

The true prevalence of BE, in fact, is not entirely clear, since studies suggest that significantly more than half of people with BE have no GERD symptoms at all. BE, then, is likely to be much more prevalent and probably less harmful than is currently believed. (BE that occurs without symptoms can only be identified in clinical trials or in autopsies, so it is difficult to determine the true extent.) Some evidence suggests that the presence of specific immune factors may be involved in determining the development of BE.

Barrett's Esophagus and Cancer

The rate of esophageal cancer has been rising steadily at about 2% a year in white men. The American Cancer Society estimates that there will be 15,560 new cases of esophageal cancer and 13,940 deaths from the disease in 2007. Esophageal cancer is also very difficult to cure. The 5-year survival rate for all stages of esophageal cancer is 17% in white patients, and 12% in African-American patients. Most cases of esophageal cancer start with BE, with less than half of the cases developing with any symptoms. Of note, only a minority of BE patients develop cancer. Some evidence suggests that acid reflux may contribute to the development of cancer in BE. Researchers have speculated that exposure to extra acid in people with Barrett's esophagus produces more of an enzyme called NOX5-S, which may put stress on cells, leading to DNA damage.

Evidence suggests that asymptomatic BE is quite common in the general population, and if true, BE would pose far less of a threat than is now believed. (GERD itself poses no significant risk for esophageal cancer. One study reported an annual incidence of 6.5 cancer cases per 10,000 people with regular GERD symptoms.)

Monitoring for Barrett's Esophagus and Cancer

Barrett's esophagus is diagnosed using endoscopy, a procedure that involves inserting a tube down the throat so that the physician can view the esophagus.

Monitoring High-Risk GERD Patients. Some experts recommend a one-time screening test for BE using endoscopy in high-risk patients (such as Caucasian overweight men) with chronic GERD.

Monitoring Patients with Barrett's Esophagus for Cancer. Periodic endoscopy is recommended for detecting early cancer in patients who have been diagnosed with Barrett's esophagus. In an important 2002 study, 5-year survival was 73% in BE patients whose cancer was detected with endoscopy screening and was 0% in patients who were not regularly screened.

Treatments for Barrett's Esophagus

To date, no treatments can reverse the cellular damage done after Barrett's esophagus has developed, although some procedures are showing promise.

Medications. Some evidence suggests that a combination of proton-pump inhibitors to suppress acid, coupled with anti-inflammatory COX-2 inhibitors, might be a promising approach.

Proton-Pump Inhibitors. Some experts recommend very aggressive treatments to reduce acid reflux using high-dose proton-pump inhibitors. The standard agent has been omeprazole (Prilosec). Newer oral PPIs include lansoprazole (Prevacid), esomeprazole (Nexium), and rabeprazole (Aciphex). Even when drugs relieve symptoms completely, the condition usually recurs within months after the drugs are discontinued. In chronic cases, drugs may need to be taken throughout a patient's life. These agents provide no protection against Barrett's esophagus. Still, there is some evidence that acid reflux may contribute to the development of cancer in BE, although it is not yet known if acid blockers have any protective effects against cancer in these patients.

COX-2 (cyclooxygenase-2) inhibitors reduce inflammation and pain, as do well-known agents such as aspirin and ibuprofen, but COX-2 inhibitors may pose less of a risk for peptic ulcers and bleeding. Some early evidence suggests they may be protective against cancerous changes in patients with Barrett's esophagus. However, Vioxx and Bextra have been withdrawn from the market due to their association with an increased risk of heart attack. Celebrex remains available, but must be used with caution, especially by patients with cardiovascular risk factors. Also, research is mixed on the benefits of NSAIDs for esophageal cancer. Some studies have found that they may decrease the risk of developing or dying from esophageal cancer. However, a 2007 study indicated that a small dose of Celebrex did not prevent the progression of cancer in Barrett's esophagus patients.

Peptic ulcers may lead to emergency situations. Severe abdominal pain with or without evidence of bleeding may indicate a perforation of the ulcer through the stomach or duodenum. Vomiting of a substance that resembles coffee grounds, or the presence of black tarry stools, may indicate serious bleeding.

Procedures to Remove the Mucous Lining. Various techniques or devices have been developed to remove (ablate) the mucous lining of the esophagus. The intention is to remove early cancerous or precancerous tissue and allow regrowth of new and hopefully healthy tissue in the esophagus. Such techniques include photodynamic therapy (PDT) or laser, electrical, or heat probes.

Studies on the use of these ablation techniques combined with aggressive use of proton-pump inhibitors or surgical treatments are very encouraging. Some of these techniques may eventually even offer potential cures. At this time, they can be very effective in removing harmful tissue, although the benefits do not last in all patients.

In one study, an average of 5.6 years after anti-GERD surgery and laser treatment, only a third of patients showed no evidence of renewed precancerous cell growth. These procedures also have complications, such as possible problems swallowing, that patients should discuss with their physician.

Esophagectomy. Esophagectomy is the surgical removal of all or part of the esophagus. Patients with Barrett's esophagus, who are otherwise healthy, are candidates for this procedure if endoscopy shows developing cancer. After esophageal removal, in total or in part, a new conduit for foods and fluids must be established to replace the absent esophagus. Alternatives include the stomach, colon, and part of the small intestine called the jejunum. The stomach is the optimal choice.

Diagnosis

If a patient suffers from *chronic* heartburn, chances are good the patient also has GERD. (Occasional heartburn does not necessarily indicate the presence of GERD.) The following is the general diagnostic approach:

A physician can usually make an easy diagnosis of GERD if the patient finds relief from persistent heartburn and acid regurgitation after taking antacids for short periods.

If the diagnosis is uncertain but the physician still suspects GERD, a drug trial using a proton-pump inhibitor medication, such as omeprazole (Prilosec) identifies 80 - 90% of people with the conditions. This class of medication blocks stomach acid secretion.

Laboratory or more invasive tests, including endoscopy, may be required if the diagnosis is still uncertain, if atypical symptoms are present, if Barrett's esophagus is suspected, or if complications, such as signs of bleeding or difficulty in swallowing, are present. Some of these tests are described below.

Barium-Swallow Radiograph

A barium swallow radiograph (x-ray) is useful for identifying structural abnormalities and erosive esophagitis (severe inflammation). When taking this test, the patient drinks a solution containing barium, then x-rays are taken. This test can show stricture, active ulcer craters, hiatal hernia, erosion, or other abnormalities. The test cannot reveal mild irritation.

Upper Endoscopy

Upper endoscopy, also called *esophagogastroduodenoscopy* or *panendoscopy*, is more accurate than a barium-swallow radiograph. It is also more invasive and expensive. It is widely used in GERD, including for identifying and grading severe esophagitis, for periodic monitoring of patients with Barrett's esophagus or for screening people at high risk, or when other complications are suspected. It is also now employed as part of various surgical techniques.

Endoscopy to Diagnose GERD. Endoscopy may be performed either in a hospital or in a doctor's office:

First, the patient should eat nothing for at least 6 hours before the procedure.

The doctor administers a local anesthetic using an oral spray and an intravenous sedative to suppress the gag reflex and to relax the patient.

Next, the physician places an endoscope (a thin flexible plastic tube containing a tiny camera) into the patient's mouth and down the esophagus. The procedure does not interfere with breathing. It may be slightly uncomfortable for some patients; others are able to sleep through it.

Once the endoscope is in place, the tiny camera allows the physician to see the surface of the esophagus and to search for abnormalities, including hiatal hernia and damage to the mucous lining.

The physician performs a biopsy (the removal and microscopic examination of small tissue sections). The biopsy may detect tissue injury indicative of GERD. It may also be used to detect cancer or other conditions, such as yeast (*Candida albicans*) or viral infections (e.g., herpes simplex and cytomegalovirus). Such infections are more likely to occur in people with impaired immune systems.

Complications from the procedure are uncommon. If they occur, complications are almost always mild and typically include minor bleeding from the biopsy site or irritation where medications were injected.

If a patient has moderate-to-severe GERD symptoms and the procedure reveals injury in the esophagus, usually no further tests are needed to confirm a diagnosis. The test is not foolproof, however. A visual view misses about half of esophageal abnormalities.

Capsule Endoscopy. Capsule endoscopy was first approved for use in 2001. A new version of this pill-sized camera, renamed PillCam, was approved by the FDA in 2004. PillCam reduces the imaging time previously required by the original capsule endoscopy technique. The PillCam capsule contains tiny video cameras on both ends. After the patient swallows the capsule, a series of 2600 color pictures are transmitted to a recording device where they can be downloaded and interpreted by a doctor. A newer version of the PillCam takes 14 frames per second as opposed to the 4 frames per second of the original device. The newer PillCam is superior in visualizing the entire esophagus and in identifying GERD. The entire procedure takes 20 minutes. The capsule is naturally passed through the digestive system within 24 hours. Capsule endoscopy may provide a more attractive and less invasive alternative for patients than traditional endoscopy. However, while capsule endoscopy is useful as a screening device for diagnosing esophageal conditions such as GERD and Barrett's esophagus, traditional endoscopy is still required for gathering tissue samples or removing polyps.

PH Monitor Examination

The (ambulatory) pH monitor examination may be employed to determine acid

back-up. It is useful when endoscopy has not detected damage to the mucous lining in the esophagus, but GERD symptoms are present. pH monitoring may be used when patients have not found relief from medicine or surgery. The traditional trans-nasal catheter diagnostic procedure involved inserting a tubular probe through the nose and down to the esophagus. The tube was left in place for 24 hours. This test was irritating to the throat, and uncomfortable and awkward for most patients.

A new method, known as the Bravo pH test, uses a small capsule-sized data transmitter that is temporarily attached to the wall of the esophagus during endoscopy. The capsule records pH levels and transmits these data to a pager-sized receiver worn by the patient. Patients can continue their usual diet and activity schedule during the 24 - 48-hour monitoring period. After a few days, the capsule detaches from the esophagus, passes through the digestive tract, and is eliminated through a bowel movement.

Manometry

Manometry is a technique that measures muscular pressure. It employs a tube containing various openings, which is placed through the esophagus. As the muscular action of the esophagus exerts pressure on the tube in various locations, a computer connected to the tube measures it. It is useful for the following situations:

To determine if a GERD patient would benefit from surgery by measuring pressure exerted by the lower esophageal sphincter muscles (LES).
To detect impaired stomach motility (an inability of the muscles to contract normally), which cannot be surgically corrected with standard procedures.
To determine if impaired peristalsis or other motor abnormalities are causing chest pain in people with GERD who have these symptoms.

Other Tests

Blood and Stool Tests. Stool tests may show traces of blood that are not visible. Blood tests for anemia should be performed if bleeding is suspected.

Bernstein Test. For patients with chest pain in which the diagnosis is uncertain, a procedure called the Bernstein test may be useful, although it is rarely used. A tube is inserted through the patient's nasal passage. Then solutions of hydrochloric acid and saline are administered separately into the esophagus. If the acid infusion causes symptoms and the saline solution does not, then a diagnosis of GERD is established.

Ruling out Other Disorders

Because many illnesses share similar symptoms, careful analysis and consideration of the patient's history is key to an accurate diagnosis. The following are only a few of the conditions that could accompany or resemble GERD.

Dyspepsia. The most common disorder confused with GERD is dyspepsia, which is

defined as pain or discomfort in the upper abdomen without heartburn. Specific symptoms may include a feeling of fullness (particularly early in the meal), bloating, and nausea. Dyspepsia can be a symptom of GERD, but does not always occur with GERD. The drug metoclopramide (Reglan) helps stomach emptying and may be helpful for this condition.

Angina and Chest Pain. About 600,000 people come to emergency rooms each year with chest pains. More than 100,000 of these people are believed to actually have GERD. Chest pain from both GERD and from severe angina can occur after a heavy meal. In general, a heart problem is probably not responsible for the pain if it is worse at night and does not occur after exercise. It should be noted that the two conditions often coexist. In fact, there is some theory that in patients with coronary artery disease, acid reflux may actually trigger angina. In such cases, experts believe that acid in the esophagus may activate nerves that temporarily impair blood flow to the heart.

Asthma. Because asthma and GERD commonly occur together, physicians must be sure that each disorder is diagnosed accurately.

Other Diseases. Many gastrointestinal diseases (e.g., inflammatory bowel disease, ulcers, intestinal cancers) can cause GERD, but they are often easily identified, since they have other symptoms and affect other areas of the intestinal tract.

Treatment

Acid suppression continues to be the mainstay for treating GERD. The aim of drug therapy is to reduce the amount of acid present and improve any abnormalities in muscle function of the lower esophageal sphincter (LES), the esophagus, or the stomach.

Most cases of gastroesophageal reflux are mild and can be managed with lifestyle changes and over-the-counter medications and antacids.

Drug Treatments

Patients with moderate-to-severe symptoms that do not respond to lifestyle measures, or who are diagnosed at a late stage may be started on more or less potent agents depending on their complications at diagnosis. Experts argue, however, about the best way to initiate drug treatment for GERD in most of these patients. The two major treatment options are known as the step-up and step-down approaches:

Step-up. With a step-up drug approach the patient first tries an H2 blocker drug, which is available over the counter. These drugs include famotidine (Pepcid AC), cimetidine (Tagamet HB), ranitidine (Zantac 75), and nizatidine (Axid AR). If the condition fails to improve, therapy is "stepped up" to the more powerful proton-pump inhibitors, usually omeprazole (Prilosec).

Step-down. A step-*down* approach first uses a more potent agent, most often a

proton-pump inhibitor (PPI), such as omeprazole (Prilosec). When patients have been symptom-free for 2 months or longer, they are then "stepped down" to a half-dose. If symptoms do not recur, the drug is withdrawn. If symptoms recur, the patient is put on high-dose H2 blockers. In one study using this step-down approach, 58% of patients remained symptom-free after a year, with 27% not using any medications at all. Some physicians argue that the step-down approach should be used for most patients with moderate-to-severe GERD.

Recent guidelines indicate that PPIs should be the first drug treatment, and that these drugs should be given once a day for approximately 8 weeks. Even when symptoms are completely relieved by medication, they usually return within a few months after drug treatment has stopped. Long-term maintenance may be necessary.

If neither approach relieves symptoms, the physician should look for other conditions. Endoscopy and other tests might be used to confirm GERD and rule out other disorders. In some cases, bile, not acid, may be responsible for symptoms, so that acid-reducing or blocking agents would not be helpful. (Bile is a fluid that is present in the small intestine and gallbladder.)

Surgery

Surgery may be indicated under certain circumstances:

- If lifestyle changes and drug treatments have failed
- In patients with other medical complications
- In younger people with chronic GERD, who face a lifetime of expense and inconvenience with maintenance drug treatment

Some physicians are recommending surgery as the treatment of choice for many more patients with chronic GERD, particularly since minimally invasive surgical procedures are becoming more widely available, and since only surgery improves regurgitation. Furthermore, persistent GERD appears to be much more serious than was previously believed, and the long-term safety of acid suppression using medication is still uncertain.

Nevertheless, anti-GERD procedures have many complications and high failure rates (ranging from 30% at 5 years to 63% at 10 years) and, as with medications, current surgical procedures cannot cure GERD. About 15% of patients still require anti-GERD medications after surgery. Furthermore, about 40% of surgical patients are at risk for new symptoms after surgery (e.g., gas, bloating, trouble swallowing), with most occurring more than a year after surgery. Finally, evidence -- notably an important 2002 Swedish study -- now strongly suggests that the procedure does not reduce the risk for esophageal cancer in high-risk patients, such as those with Barrett's esophagus. New procedures may improve current results, but at this time patients should consider surgical options very carefully with both a surgeon and their primary doctor.

Prevention

People with heartburn should first try lifestyle and dietary changes. In one study, 44% of patients who experienced symptoms of gastroesophageal reflux disease (GERD) reported improvement after changing their diet. Some suggestions are the following:

Avoid or reduce consumption of foods and beverages that contain caffeine, chocolate, peppermint, spearmint, and alcohol. Both caffeinated and decaffeinated coffees increase acid secretion.

Avoid all carbonated drinks, because they increase the risk for GERD.

Although physicians often advise patients with GERD to cut down on fatty foods, many studies have found no evidence that a low-fat or high-fat meal makes any difference in symptom exacerbation. One small study, however, found that the frequency of GERD symptoms increased with a high-fat compared to a low-fat diet. Better studies are needed to confirm this. In any case, as a rule, it is always wise to avoid saturated fats (which are from animal products), and cut down on all fats if one is overweight.

Choose low-fat or skim dairy products, poultry, or fish. Increasing protein may help strengthen muscles in the muscle valve.

Consume whole-grain products rich in selenium, which may have some protective role against dangerous cell changes in Barrett's esophagus.

Eat a diet rich in fruits and vegetables, although it's best to avoid acidic vegetables and fruits (e.g., oranges, lemons, grapefruit, pineapple, tomatoes).

Patients who have trouble swallowing should avoid tough meats, vegetables with skins, doughy bread, and pasta.

Prevention of Nighttime GERD

Nearly three-quarters of patients with frequent GERD symptoms have them at night. Patients with nighttime GERD also tend to experience severe pain. It is very important to take preventive measures before going to sleep. Some suggestions for preventing acid reflux at night are as follows:

After meals, take a walk or, at the very least, remain upright.

Avoid bedtime snacks. In general, avoid eating for at least 2 hours prior to bedtime.

When going to bed, try lying on the left side rather than on the right. The stomach is located higher than the esophagus when a person sleeps on the right side, which can put pressure on the lower esophageal sphincter (LES), increasing the risk for fluid back-up.

Sleep in a tilted position to help keep acid in the stomach at night. To do this, raise the bed at an angle using 4- to 6-inch blocks at the head of the bed and use a wedge-support to elevate the top half of the body. (Extra pillows that only raise the head actually increase the risk for reflux.)

A reflux board is prescribed for use in children who have gastroesophageal reflux. A board tilts the child upward while he is lying in bed to prevent the stomach contents from going back into the esophagus and mouth, and possibly into the lungs.

Other Preventive Measures

Quitting smoking is essential.

People who are overweight should try to reduce food intake and exercise to lose weight.

People with GERD should avoid tight clothing, particularly around the abdomen.

If possible, GERD patients should avoid nonsteroidal anti-inflammatory drugs (NSAIDs), such as aspirin, ibuprofen (Motrin, Advil), or naproxen (Aleve), among others. Tylenol (acetaminophen) is a good alternative pain reliever.

Although gum chewing is commonly believed to increase the risk for GERD symptoms, one study reported it might be helpful. Because saliva helps neutralize acid and contains a number of other factors that protect the esophagus, chewing gum 30 minutes after a meal has been found to help relieve heartburn and even protect against damage caused by GERD. Chewing on anything at all can help since it stimulates saliva production.

Medications

Antacids neutralize digestive acids and are the primary drugs for mild symptoms. They are best used alone for relief of occasional and unpredictable episodes of heartburn. They all work by neutralizing the acid in the stomach. They may also stimulate the defensive systems in the stomach by increasing bicarbonate and mucous secretion. Many antacids are available without a prescription and are the first drugs recommended to relieve heartburn and mild symptoms. Despite the many brands, they all rely on various combinations of three basic ingredients: magnesium, calcium, or aluminum.

Magnesium. Magnesium salts are available in the form of magnesium carbonate, magnesium trisilicate, and most commonly, magnesium hydroxide (Milk of Magnesia). The major side effect of magnesium salts is diarrhea. Magnesium salts offered in combination products with aluminum (Mylanta and Maalox) balance the side effects of diarrhea and constipation.

Calcium. Calcium carbonate (Tums, Titralac, and Alka-2) is a potent and rapid acting antacid that can cause constipation. These antacids are actually sources of calcium. There have been rare cases of hypercalcemia (elevated levels of calcium in the blood) in people taking calcium carbonate for long periods of time. This can lead to kidney failure and is very dangerous. None of the other antacids has this side effect.

Aluminum. Aluminum salts (Amphogel, Alternagel) are also available. The most common side effect of antacids containing aluminum salts is constipation. People who take large amounts of antacids that contain aluminum may also be at risk for calcium loss, which can lead to osteoporosis.

Osteoporosis is a condition characterized by progressive loss of bone density, thinning of bone tissue, and increased vulnerability to fractures. Osteoporosis may result from disease, dietary or hormonal deficiency, or advanced age. Regular exercise and vitamin and mineral supplements can reduce and even reverse loss of bone density.

It is generally believed that liquid antacids work faster and are more potent than tablets, although evidence suggests that they all work equally well. Antacids can interact with a number of drugs in the intestines by reducing their absorption. These drugs include tetracycline, ciprofloxacin (Cipro), propranolol (Inderal), captopril (Capoten), and H2 blockers. Interactions can be avoided by taking the drugs 1 hour before or 3 hours after taking the antacid. Long-term use of nearly any antacid increases the risk for kidney stones.

H2 Blockers

H2 blockers impede acid production by blocking or antagonizing the actions of histamine, a chemical found in the body that encourages acid secretion in the stomach. They are available over the counter and provide symptom relief in about half of GERD patients. It takes 30 - 90 minutes for them to work, but the benefits last for hours. The drugs are usually taken at bedtime. Some people may need to take them twice a day.

H2 blockers inhibit acid secretion for 6 - 24 hours and are very useful for people who need persistent acid suppression. They may also prevent heartburn episodes in people who are able to predict its occurrence. In some studies, H2 blockers improved asthmatic symptoms in people who have both conditions. A 2001 study suggested, however, that they rarely provide complete symptom relief for chronic heartburn and dyspepsia and they have done little to reduce office visits to physicians for GERD.

Brands. Four H2 blockers are currently available in the U.S.:

Famotidine (Pepcid AC). Famotidine (Pepcid AC, Pepcid Oral) is the most potent H2 blocker. The most common side effect of famotidine is headache, which occurs in 4.7% of people who take it. Famotidine is virtually free of drug interactions, but the FDA has issued a warning on its use in patients with kidney problems.

Cimetidine (Tagamet, Tagamet HB). Cimetidine (Tagamet) is the oldest H2 blocker. It has few side effects; approximately 1% of people taking it will experience

mild temporary diarrhea, dizziness, rash, or headache. Cimetidine interacts with a number of commonly used medications, such as phenytoin, theophylline, and warfarin. Long-term use of excessive doses (more than 3 grams a day) may cause impotence or breast enlargement in men. These problems resolve after the drug is discontinued.

Ranitidine (Zantac, Zantac 75, Zantac Efferdose, Zantac injection, Zantac Syrup). Ranitidine (Zantac) interacts with very few drugs. In a recent study, ranitidine provided more pain relief and healed ulcers more quickly than cimetidine in people less than 60 years old, but there was no difference in older patients. A common side effect associated with ranitidine is headache, which occurs in about 3% of the people who take it.

Nizatidine Capsules (Axid AR, Axid Capsules, Nizatidine Capsules). Nizatidine (Axid) is nearly free of side effects and drug interactions. A controlled-release form is proving to help alleviate nighttime GERD symptoms.

FDA Warning for Famotidine (Pepcid AC)

Famotidine is excreted primarily by the kidney. This can pose a danger to people with kidney problems. Physicians are now being advised by the U.S. Food and Drug Administration (FDA) and Health Canada to reduce the dose and increase the time between doses in patients with kidney failure. Use of the drug in those with impaired kidney function can affect the central nervous system and may result in anxiety, depression, insomnia or drowsiness, and mental disturbances.

Drug Combinations.

Over-the-counter antacids and H2 blockers: This combination may be the best approach for many people who experience heartburn after eating. Both classes of drugs are effective in relieving GERD, but have different timing. Antacids work within a few minutes but are short-acting, while H2 blockers take longer but have long-lasting benefits. Pepcid AC combined with an antacid (calcium carbonate and magnesium) is now available as Pepcid Complete.

Proton-pump inhibitors and H2 blockers: Physicians sometimes recommend a nighttime dose of an H2 blocker for people who are taking proton-pump inhibitors twice a day. This is based on the belief that adding the H2 blocker will prevent a rise in acid reflux at night. An important 2002 study, however, reported no additional benefits from the nighttime H2 blocker. Some experts recommended an H2 blocker in patients who are on proton-pump inhibitors only to prevent breakthrough symptoms, such as before a heavy meal.

Long Term Complications. In most cases, these agents have good safety profiles and few side effects. H2 blockers can interact with other drugs, although some less so than others. In all cases, however, the physician should be made aware of any other drugs a patient is taking. More research is needed. Anyone with kidney problems

should use famotidine only under the direction of a physician.

Concerns and Limitations. Some experts are concerned that the use of acid-blocking drugs in people with peptic ulcers may mask ulcer symptoms and increase the risk for serious complications.

These agents provide no protection against Barrett's esophagus. In fact, of concern are reports that long-term acid suppression with these drugs may cause cancerous changes in the stomach in patients who are infected with *H. pylori*. Research on this question is still ongoing.

Proton-Pump Inhibitors

Proton-pump inhibitors (PPIs) suppress the production of stomach acid and work by inhibiting the molecule in the stomach glands that is responsible for acid secretion, which is called the *gastric acid pump*. According to recent guidelines, initial drug treatment should be with PPIs once daily for about 8 weeks.

The standard agent has been omeprazole (Prilosec), which is now available over the counter without a prescription. Newer prescription oral PPIs include esomeprazole (Nexium), lansoprazole (Prevacid), rabeprazole (Aciphex), and pantoprazole (Protonix).

Studies report significant relief from PPIs in most patients with heartburn. PPIs are effective for healing erosive esophagitis and may also be helpful in patients with chronic laryngitis that is suspected to be caused by GERD. The newer agents provide quicker symptom relief compared to omeprazole. However, a comparison study suggested that, to date, esomeprazole (Nexium) is the only newer oral PPI to show any significant advantage over omeprazole (Prilosec). All PPIs are more effective than the H2 blockers.

In addition to relieving most common symptoms, including heartburn, proton-pump inhibitors also have the following advantages:

They are effective in relieving chest pain and laryngitis caused by GERD.
They may also reduce acid reflux that typically occurs during strenuous exercise.

Patients with impaired esophageal muscular action are still likely to experience acid breakthrough and reflux at night. Proton-pump inhibitors also may have little or no effect on regurgitation or asthmatic symptoms. Some experts believe, however, that they should be the first drugs of choice, even for patients with milder symptoms. At this time, these drugs are recommended for the following patients:

Those with moderate symptoms that do not respond to H2 blockers
Those with severe symptoms
Those who have respiratory complications
Those who have persistent nausea

Those who have esophageal injury

These agents have no affect against non-acid reflux, such as bile back-up.

Adverse Effects. Proton-pump inhibitors may pose the following concerns:

Side effects are uncommon but may include headache, diarrhea, constipation, nausea, and itching.

Proton-pump inhibitors should be avoided by pregnant women and nursing mothers, although recent studies suggest that they do not pose an increased risk of birth defects.

They may interact with certain drugs, such as anti-seizure agents (such as phenytoin), anti-anxiety drugs (such as diazepam), and blood thinners (such as warfarin).

Long-term use of high-dose PPIs may produce vitamin B12 deficiencies, but studies are needed to confirm whether there is any significant risk. High-dose PPIs used over the long-term also may increase the risk of hip fracture in older adults, according to one study.

There is some evidence that acid reflux may contribute to the higher risk of cancer in BE, but it is not yet confirmed whether acid-blockers have any protective effects against cancer in these patients. In fact, the long-term use of proton-pump inhibitors by people with *H. pylori* may, in theory at least, reduce acid secretion enough to cause atrophic gastritis (chronic inflammation of the stomach). This condition is a risk factor for stomach cancer. To compound concerns, long-term use of PPIs may mask symptoms of stomach cancer and so delay a diagnosis. To date, however, there have been no reports of an increased risk of stomach cancer with the long-term use of these drugs.

Agents that Protect the Mucous Lining (Sucralfate)

Sucralfate (Carafate) protects the mucous lining in the gastrointestinal tract. It seems to work by sticking to an ulcer crater and protecting it from damage due to stomach acid and pepsin. It may be helpful for maintenance therapy in people with mild-to-moderate GERD. Other than constipation, which occurs in 2.2% of patients, the drug has few side effects. Sucralfate interacts with a wide variety of drugs, however, including warfarin, phenytoin, and tetracycline.

Anti-Spasm Drugs to Prevent Acid and Non-Acid Reflux

Most drugs used for GERD have no effect on non-acid reflux, such as back-up of bile. Baclofen, known as a gamma-amino butyric acid agonist, is commonly used to reduce muscle spasms. Investigators are now showing that it can reduce both acid and non-acid reflux episodes (as much as 70% in one study) and increase LES pressure, an important factor for preventing back-up.

Surgery

The standard surgical treatment for GERD is *fundoplication*. The goal of this procedure is twofold:

To increase LES pressure and, therefore, prevent acid back-up (reflux)
To repair any present hiatal hernia

There are two primary approaches:

Open Nissen fundoplication (the more invasive technique)
Laparoscopic fundoplication

In general, the overall long-term benefits of these procedures are similar. Some studies report that more than 90% of patients are free of heartburn after the operation and satisfied with their choice, even after 5 years. Fundoplication relieves GERD-induced coughs and some other respiratory symptoms in up to 85% of patients. (Its effect on asthma associated with GERD, however, is unclear.) It may enhance stomach emptying and improve peristalsis in about half of patients. (It may actually *cause* abnormal peristalsis in about 14% of patients, although in such cases the problem does not appear to be very significant.)

Still, it has other significant limitations and postoperative problems. For example, the results of one 2003 survey suggested that 18% of surgical patients still required anti-GERD medications and 38% had new symptoms (e.g., gas, bloating, trouble swallowing), with most occurring more than a year after surgery. Other studies have reported similar results. Also, fundoplication does not cure GERD. Finally, evidence from a 2002 Swedish study strongly suggests that the procedure does not reduce the risk for esophageal cancer in high-risk patients, such as those with Barrett's esophagus.

Candidates. Fundoplication is recommended for patients whose condition includes one or more of the following:

Esophagitis (inflamed esophagus)
Symptoms that persist or are recurrent in spite of anti-reflux drug treatment
Strictures
Failure to gain or maintain weight (children)

Fundoplication has little benefit for patients with impaired stomach motility (an inability of the muscles to move spontaneously).

The Open Nissen Fundoplication Procedure. Until recently, most fundoplication procedures for GERD have been the 360° Nissen fundoplication. This is called an *open* procedure because it requires wide surgical incisions.

With this procedure, the physician wraps the upper part of the stomach (*fundus*) completely around the esophagus to form a collar-like structure.

The collar places pressure on the LES and prevents stomach fluids from backing up into the esophagus.

Open fundoplication requires a 6- to 10-day hospital stay.

Laparoscopic Fundoplication. The standard invasive fundoplication procedure has been replaced in many cases by a less invasive fundoplication procedure that uses *laparoscopy*. In the operation:

Tiny incisions are made in the abdomen.

Small instruments and a tiny camera are inserted into tubes, through which the surgeon can view the region.

The surgeon creates a collar using the fundus, although the area is smaller to work with.

When performed by experienced surgeons, the procedure shows results that are equal to those of standard open fundoplication, but with faster recovery time.

Overall, laparoscopic fundoplication appears to be safe and effective in people of all ages, even babies. Laparoscopy is more difficult to perform in certain patients, including those who are obese, who have a short esophagus, or who have a history of previous surgery in the upper abdominal area. It may also be less successful in relieving atypical symptoms of GERD, including cough, abnormal chest pain, and choking. In about 8% of laparoscopies, it is necessary to convert to open surgery during the procedure because of unforeseen complications.

Other Variations. There are now a number of variants of fundoplication procedures. Examples include the following:

Toupet fundoplication employs only a partial wrap, as does a Thal fundoplication. Partial fundoplication procedures may be more effective in patients with poor or no esophageal motility (spontaneous muscle contraction). Those with normal motility may do better with the full-circle wrap.

Others use a very short and "floppy" Nissen full wrap.

Many surgeons report that such limited fundoplications result in earlier feeding and discharge from the hospital and a lower incidence of complications (trouble swallowing, gas bloating, gagging) than the full Nissan fundoplication. A British study, however, reported no significant differences in swallowing problems.

Postoperative Problems and Complications after Fundoplication. Postoperative problems can include a delay in intestinal functioning causing bloating, gagging, and vomiting. These side effects usually resolve in a few weeks. A 2003 study suggested, however, that 38% of patients develop such symptoms, and most occur more than a year after the procedures. If symptoms persist or if they start weeks or months after surgery, particularly if vomiting is present, then surgical complications are likely. Complications include the following:

An excessively wrapped fundus. This is fairly common and can cause difficulty swallowing (dysphagia), as well as gagging, gas, bloating, or an inability to burp. (A follow-up procedure that dilates the esophagus using an inflated balloon may help correct dysphagia, although it cannot treat other symptoms.)

Bowel obstruction

Wound infection

Injury to nearby organs

Respiratory complications, such as a collapsed lung. These are uncommon, particularly with laparoscopic fundoplication.

Muscle spasms after swallowing food. This can cause intense pain, and patients may require a liquid diet, sometimes for weeks. This is a rare complication in most patients, but it can be very high in children with neurologic abnormalities. Such children are already at very high risk for GERD.

Reasons for Treatment Failure. Long-term failure rates after fundoplication are 30% after 5 years and 63% after 10 years. Hiatal herniation is the most common reason for surgical failure and the need for a repeat fundoplication. Other common reasons for reoperation include breakdown, slippage, and excessive tightness of the wrap. Surgeon experience can lessen complication risks. Some studies have reported that repeat operations after open procedures occur in 9 - 30% of cases and 13% after laparoscopy. (Repeat surgery usually has good results.)

Surgical Treatments Using Endoscopy

A number of treatments that make use of endoscopy are being used or investigated for increasing LES pressure and preventing reflux, as well as for treating severe GERD and its complications.

Transoral Flexible Endoscopic Suturing. Transoral flexible endoscopic suturing (sometimes referred to as Bard's procedure) uses a tiny device at the end of the endoscope that acts like a miniature sewing machine. It places stitches in two locations near the LES, which are then tied to tighten the valve and increase pressure. There is no incision and no need for general anesthesia.

Radiofrequency. Radiofrequency energy generated from the tip of a needle (sometimes called the Stretta procedure) heats and destroys tissue in the problem spots in the LES. Either the resulting scar tissue strengthens the muscle, or the heat kills the nerves that caused the malfunction. Patients may experience some chest or stomach pain afterwards. Few serious side effects have been reported, although there have been reports of perforation, hemorrhage, and even death. A recent study reported that 81% of patients remained symptom-free for up to 3 years following the Stretta procedure.

Implants. In 2003, the FDA approved the Enteryx procedure as a treatment option for people who have persistent symptoms of GERD and who regularly take and respond to PPIs. In 2005, however, the manufacturer of Enteryx (Boston Scientific), voluntarily removed Enteryx from clinical use due to problems related to the difficult injection technique.

Techniques to Stop Bleeding. Endoscopic ablation treatment of bleeding involves using a probe passed through the endoscopic tube, which applies electricity or heat to coagulate blood and stop the bleeding.

Dilation Procedures. Strictures (abnormally narrowed regions) may need to be dilated (opened) with endoscopy. Dilation may be performed by inflating a balloon in the passageway. About 30% of patients who need this procedure require a series of dilation treatments over a long duration in order to fully open the passageway. Long-term use of proton-pump inhibitors may reduce the duration of treatments.

One study also suggested that dilation may help correct swallowing problems that can occur after fundoplication. In the study dilation improved dysphagia in 67% of the surgical patients who had experienced it.

A recent advance is the development of small-caliber upper endoscopy, which does not require sedation and can be performed in the physician's office.

Resources

http://digestive.niddk.nih.gov -- National Digestive Diseases Information Clearinghouse

www.gastro.org -- American Gastroenterological Association

www.acg.gi.org -- American College of Gastroenterology

www.asge.org -- American Society for Gastrointestinal Endoscopy

www.ssat.com -- Society for Surgery of the Alimentary Tract

www.naspgn.org -- North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition

www.reflux.org -- Pediatric/Adolescent Gastroesophageal Reflux Association

www.iffgd.org -- International Foundation for Functional Gastrointestinal

Disorders

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