

Gastroesophageal Reflux Disease

Gastroesophageal reflux disease, commonly known as heartburn or GERD, occurs when enzymes and stomach acid escape the stomach and rise in the esophagus. Unlike the stomach, which is protected by a thick layer of mucus, the esophagus is susceptible to damage due to the strong digestive juices in the stomach and may be damaged over time. Data suggest that as many as 14 percent of Americans experience heartburn weekly and 7 percent daily.

GERD occurs when the sphincter between the stomach and esophagus is weakened and the pressure between the stomach and esophagus is uneven. If the pressure in the stomach is too high—or, conversely, the pressure in the esophagus is too low—and the sphincter is relaxed, stomach acid can flow backward, up into the esophagus. This may be experienced as a burning sensation that gradually travels upward from the stomach into the throat, along with a sour, bitter taste in the mouth. The stomach exudates can also reach the upper esophagus and trachea, causing or worsening a variety of conditions, such as asthma, chronic cough, sinusitis (swelling of the sinuses), pneumonia, and others.

A number of conditions and factors are associated with GERD (Kasper DL et al 2005):

- Side effects of certain medications
- Obesity
- Pregnancy
- Menopause
- Genetic predisposition
- Large meals
- Dietary factors
- Smoking
- Surgical damage to the lower esophageal sphincter
- Esophagitis
- Reclining after a meal

If left untreated, GERD may result in a number of complications, depending on the frequency and severity of incidents and the rate of clearance. Under normal circumstances, the stomach acid in the esophagus is cleared by the normal pumping action of the esophagus (called peristaltic action) and by saliva. If the salivary glands or peristaltic action are compromised, the GERD may be aggravated. One of the complications associated with GERD, esophagitis, or inflammation of the esophagus, can range from relatively mild with no symptoms (Bateman DN et al 2003) to erosive esophagitis that may be accompanied by bleeding and ulcers in the esophagus.

Untreated, GERD, if severe, can also cause the formation of scar tissue, or fibrosis, in the lower esophagus. If this condition progresses, it can lead to difficulty swallowing and may require medical intervention to open the narrowed passageway.

In some cases, GERD can cause cellular changes in the lower esophagus that can progress into esophageal cancer. Although this complication is relatively rare, it is important that people with GERD seek treatment and take steps to relieve their condition.

BARRETT'S ESOPHAGUS: FROM GERD TO ESOPHAGEAL CANCER

If GERD is left untreated or is very severe, the structure of the lower esophagus can be altered. When this occurs, the cell structure changes from a normal, scale-like form (squamous) to a columnar form. This condition is known as Barrett's esophagus. Although it is actually a protective mechanism because the columnar form is more of a shield against damage from strong stomach acids, Barrett's esophagus is a risk factor for esophageal cancer (Kasper DL et al 2005).

There are two common types of esophageal cancer: squamous cell and adenocarcinoma. Of these two forms, only adenocarcinoma is linked to GERD. Adenocarcinoma typically occurs in the lower third of the esophagus. The more frequent, more severe, and more long-lasting the symptoms of reflux, the greater the risk of adenocarcinoma (Lagergren J et al 1999). Over the past 25 years, incidence of adenocarcinoma has increased 350 percent faster than any other malignancy in the Western world, possibly because of the increased incidence of GERD. In the United States, however, esophageal cancer remains relatively less common than other forms of cancer (Glenn TF 2001).

DIAGNOSIS AND TREATMENT OF GERD

The diagnosis of GERD is usually made on symptoms alone—most people won't need any additional testing or procedures before they can begin therapy. If the condition does not respond to treatment, however, a number of tests may be recommended to better determine what is causing the problem (Topazian M 2005). Tests used in the context of GERD include the following:

- Barium swallow is a radiological test used if symptoms include dysphagia (difficulty in swallowing). The patient drinks a solution containing barium, which is visible under x-ray. This test allows physicians to view the esophageal lining and may reveal an ulcer or narrowed portion.
- Upper endoscopy (esophagoscopy) identifies lesions not identified by barium. A physician examines the esophagus through a flexible viewing tube. Biopsies are taken during the procedure if there is suspicion that GERD has progressed to cancer.
- Esophageal manometry determines proper functioning of the esophagus and lower esophageal sphincter. A physician passes a catheter through the nose and esophagus into the stomach. The patient drinks a small quantity of water. The catheter is slowly withdrawn while measurements are made of the peristaltic activity of the esophagus and the pressure of the lower esophageal sphincter.
- Ambulatory pH recording of the esophagus may be done over 24 hours to determine the quantity and strength of the reflux. During this test, devices are used to measure the acidity of the reflux.

Under most circumstances, however, patients will be diagnosed based on symptoms, and lifestyle changes or medications may be prescribed. The goal of treatment is to provide relief from symptoms and allow the esophagus a chance to heal. Lifestyle changes recommended to help alleviate GERD include losing weight, avoiding fatty foods, quitting smoking and avoiding all tobacco products, sleeping with the upper portion of the body elevated, avoiding eating within three hours of bedtime, and avoiding consuming large quantities of liquids with meals.

The following common conventional medications may be used to treat GERD:

Antacids. Over-the-counter antacids are the first medications commonly used in GERD. Antacids neutralize stomach acidity, which irritates the esophageal lining during reflux. Typically, antacids are aluminum or magnesium hydroxides, calcium carbonate, or sodium bicarbonate. These antacids allow sustained neutralizing action. Examples of antacids are Maalox®, Gelusil, Mylanta®, Riopan®, Tums®, and milk of magnesia. While they are very common, antacids have side effects that should be noted, including a “rebound” affect that may actually worsen indigestion. In addition, antacids contain aluminum, a neurotoxic heavy metal that has been linked to brain diseases (Reinke CM et al 2003).

H2 blockers. H2 blockers prevent secretion of stomach acid by inhibiting the action of histamine, which is a stimulus for acid secretion. Examples of H2 blockers are cimetidine (Tagamet®), Zantac®, Axid®, and Pepcid®. Long-term use of H2 blockers is associated with side effects. Some physicians are concerned that suppressing heartburn pain with H2 receptor antagonist drugs might result in patients' not making the lifestyle changes needed to control chronic esophageal reflux. Failure to adequately control GERD can result in esophagitis and esophageal cancer (Farrow DC et al 2000; Suleiman UL et al 2000). For long-term treatment, proton pump inhibitors are often preferred by physicians.

Proton pump inhibitors. Proton pump inhibitors have dramatically altered the conventional treatment of GERD. They are effective in symptom relief, have relatively few side effects, and resolve the vast majority of mild GERD cases. They inhibit stomach acid by preventing the secretion of protons from inside the parietal cells of the stomach to the stomach cavity. Proton pump inhibitors have been found especially useful when GERD is not well controlled by H2 blockers (Vanderhoff BT et al 2002). Examples of proton pump inhibitors are Nexium®, Prilosec, and Prevacid®. It is important to note that proton pump therapy may inhibit the absorption of vitamin B12 from food but not from supplements (Ruscin JM et al 2002; ter HH et al 2001).

Although there was initial concern that the use of proton pump inhibitors could be a risk factor for atrophic gastritis and gastric cancer, newer research has shown that the use of these drugs is actually associated with a lower risk of cancer (El Serag HB et al 2004; Raj A et al 2004). In one study, proton pump inhibitor therapy appeared beneficial in the prevention of dysplasia and adenocarcinoma in 350 patients with Barrett's esophagus over a follow-up period with a median duration of 4.7 years. The investigators suggested on the basis of their results that all patients with this condition, even those with no esophagitis or symptoms, should be encouraged to continue long-term proton pump inhibitor therapy (Hillman LC et al 2004). More studies are being conducted to help us better understand the relationship between proton pump inhibitors and various forms of cancer.

In general, proton pump inhibitors have been shown to be safe and effective drugs, with few potential drug interactions, that can be used in patients on multiple medications, pregnant women, and children (Martin de Argila C 2005). There is a significant risk, however, of rebound symptoms once the proton pump inhibitors are discontinued. Studies have shown that stomach acid secretion rebounds vigorously after discontinuation of proton pump inhibitors following long-term therapy, which can lead to recurrence of symptoms. This rebound effect can last for up to 24 months although its clinical significance is unknown (Fossmark G et al 2005; Qvistad G et al 2004; Gillen D et al 2001; Farup PG et al 2001).

Baclofen. Most patients with GERD suffer from something called “transient lower esophageal sphincter relaxations,” which cause the esophageal sphincter to relax and allow stomach acid to penetrate the esophagus. One novel method of therapy involves medications that can prevent these events. Baclofen is a unique gamma-aminobutyric-B agonist that has been shown to inhibit lower esophageal sphincter relaxations, thereby preventing reflux (Wise J et al 2004). Baclofen significantly reduced the number of reflux episodes, reducing the frequency and intensity of symptoms, including pain, regurgitation, and bitter taste. The percentage of time that the esophagus was exposed to acid conditions was also significantly lower in patients taking baclofen (Ciccaglione AF et al 2003; Zhang Q et al 2002).

NUTRIENTS TO NEUTRALIZE GERD

The most common over-the-counter medications used to treat heartburn and GERD are antacids that contain calcium compounds, such as calcium carbonate. These products dissolve in stomach acid, freeing the calcium compounds to neutralize the extra acid (Collings KL et al 2002). While there are a few nutrients that may help with GERD, Life Extension's focus is on preventing GERD from progressing to esophageal cancer by suggesting supplements as adjuvant therapy and lifestyle changes that have been shown to help alleviate the condition. The following nutrients can be considered to help alleviate the symptoms of GERD:

Licorice extract. Deglycyrrhized licorice has been shown to protect the stomach of mice and rats by enhancing the mucosal defense mechanism (Yano S et al 1989). Mucus coats and protects the lining of the stomach and esophagus (van Marle J et al 1981). Licorice-derived compounds have the effect of raising the local concentration of prostaglandins that promote mucous secretion and cell proliferation in the stomach, leading to healing of ulcers (Baker ME 1994).

Digestive aids. Extract of radish has been shown in numerous studies to enhance motility throughout the digestive tract, which would result in faster emptying of the stomach (Jeong SI et al 2005; Gilani AH et al 2004; Jung KY et al 2000).

Nutritional Approaches to Avoid Esophageal Cancer

Because of the rapid increase in adenocarcinoma of the esophagus, a number of studies have been launched to uncover risk factors and possible strategies to reduce the risk of esophageal cancer. Diets high in cholesterol, saturated fat, and total fat have been shown to increase cancer risk, while an increased intake of fiber, vitamin C, beta-carotene, and folate has been found to reduce risk of esophageal cancer (Mayne ST et al 2002,2001).

Fruits, vegetables, and fiber also have protective effects against adenocarcinoma (Chen H et al 2002a; Wolfgarten E et al 2001). Vegetables and fruits can protect against cancer because of their phytochemicals (plant chemicals) (Steinmetz KA et al 1991).

Healthy levels of vitamin A, beta-carotene, vitamins C and E, and selenium are associated with lower incidence of adenocarcinoma (Blot WJ et al 1993; Bollschweiler E et al 2002; Zheng W et al 1995). Antioxidant nutrients protect against cancer by neutralizing free radicals before they can harm tissue (Oh TY et al 2001). Antioxidants can stimulate cancer suppressor genes and inhibit blood vessel formation (angiogenesis) in tumors (Shklar G 1998).

Many studies have shown that vitamins C, E, and beta-carotene significantly reduce the risk of adenocarcinoma and squamous cell cancer (Blot WJ et al 1993; Bollschweiler E et al 2002; Taylor PR et al 1994; Terry P et al 2000; Zheng W et al 1995). Other studies have shown that folic acid, niacin, and riboflavin intake may have a protective effect (Chen H et al 2002b; Franceschi S et al 2000; Siassi F et al 2000).

Selenium is an essential trace element with a protective effect against many cancers. Adequacy of selenium in humans, as measured by serum selenium levels, appears to be related to susceptibility to esophageal cancer (Mark SD et al 2000; Rudolph RE et al 2003). Selenium and vitamin E act in concert to protect cell membranes (Scott ML 1986).

Green tea. Particularly in Asia, a relationship exists between green tea consumption and protection against esophageal cancer, an effect due to polyphenols, a natural antioxidant compound found in tea plants. Green tea consumption had a significant protective effect in preventing esophageal cancer in nonsmokers and people who did not drink (Gao YT et al 1994). Other studies have found a protective effect of green tea against esophageal cancer (Bushman JL 1998; Cheng KK et al 1996). Part of green tea's beneficial effects may be due to its high content of GABA. Like the prescription drug baclofen, which is a GABA agonist, green tea may help stimulate contraction of the lower esophageal sphincter.

LIFESTYLE CHANGES

One review study found evidence to suggest that as many as 20 percent of people who suffer from GERD may find relief from lifestyle changes alone (DeVault KR 1996).

- **Weight reduction.** Obesity increases pressure on the abdomen and stomach, which can increase pressure on the lower

esophageal sphincter and cause reflux (Nilsson M et al 2003,2004).

- **Smoking.** Smoking increases GERD symptoms. It decreases lower esophageal sphincter pressure and reduces salivary secretion (Pandolfino JE et al 2000; Smit CF et al 2001; Trudgill NJ et al 1998).
- **Fatty foods.** The relationship between dietary fat and GERD is unclear. Dietary fat is thought to delay emptying of the stomach. Reducing dietary fat is important for health in general and part of an overall strategy to reduce GERD symptoms (Colombo P et al 2002; Pehl C et al 2001; Penagini R et al 1998; Ruhl CE et al 1999).
- **Irritating foods and beverages.** These may affect some individuals, and each person's reaction may be unique. Foods that might aggravate GERD include tomatoes, garlic, onions, chocolate, peppermint, coffee, and citrus fruits. Reactions vary considerably. Monitor reactions to specific foods.
- **Meal size and frequency.** Avoid eating large meals, which can stimulate sensors that affect lower esophageal sphincter relaxation. Eat smaller meals more frequently, perhaps four or five times daily. Do not eat for at least two or three hours before bedtime.
- **Upper body elevation.** Use gravity to help keep stomach contents out of the esophagus. Elevate the upper portion of the body, including the head, at least 6 inches by raising the mattress (or entire head end of the bed frame itself) with telephone books, foam, or wood blocks. Doctors used to recommend raising the head only, but this can cause a bend at the waist and may actually increase pressure on the stomach. Elevating the entire upper body throughout the night can produce remarkable relief for GERD sufferers. Also try to lie on the left side to exert less pressure on the esophageal sphincter. A study found that sleeping on the left side is the preferred position for patients with nighttime gastroesophageal reflux (Khoury RM et al 1999).
- **Limitation of aspirin, ibuprofen, and other nonsteroidal anti-inflammatory drugs.** Nonsteroidal anti-inflammatory drugs inhibit formation of prostaglandins, thus promoting reflux. Prostaglandins inhibit gastric acid secretion and stimulate secretion of mucus and bicarbonate to minimize the effects of acid reflux.
- **Avoidance of chewing gum and hard candy.** Both chewing gum and hard candy increase the amount of swallowed oxygen and can lead to belching and reflux.

LIFE EXTENSION FOUNDATION RECOMMENDATIONS

In addition to lifestyle changes, people with GERD should consider the following supplements to help relieve symptoms and reduce the risk of esophageal cancer:

- **Life Extension Mix** (a multivitamin supplement mix rich in antioxidants)
- **Vitamin B12**—250 micrograms (mcg) daily (particularly needed with long-term acid-reduction therapy such as with H2 drugs or proton pump inhibitors)
- **Deglycyrrhizinated licorice (DGL)**—1520 milligrams (mg) daily
- **Selenium**—200 mcg daily
- **Phytofood**—1 tablespoon daily, which provides 9 mg sulforaphane to reduce DNA damage
- **Green tea extract**—1 capsule daily, which provides at least 725 mg of a 93 percent polyphenol extract
- **Digest RC**—a multiple herbal extract formulation used in Europe for more than 45 years, now available in the United States. The supplement mix works by promoting the release of bile from the liver to digest fats and proteins, in addition to other mechanisms. Although not all of Digest RC's individual components have been studied in the context of GERD, Life Extension's recommendation is based on Digest RC's ability to promote healthy digestion and stomach emptying. This will reduce the pressure in the stomach, which may make it less likely to cause episodes of GERD. Digest RC contains
 - Black radish extract: 75 mg
 - Linden bark charcoal: 75 mg
 - Artichoke extract: 47 mg
 - Calcium phosphate: 45 mg
 - Cholic acid: 40 mg
 - Peppermint: 15 mg
- **Digestive enzymes:** follow label directions

GERD SAFETY CAVEATS

An aggressive program of dietary supplementation should not be launched without the supervision of a qualified physician. Several of the nutrients suggested in this protocol may have adverse effects. These include:

Artichoke

- Do not take artichokes if you have a bile duct blockage. Artichokes can stimulate the flow of bile.

Green Tea

- Consult your doctor before taking green tea extract if you take aspirin or warfarin (Coumadin). Taking green tea extract and aspirin or warfarin can increase the risk of bleeding.
- Discontinue using green tea extract 2 weeks before any surgical procedure. Green tea extract may decrease platelet aggregation.
- Green tea extract contains caffeine, which may produce a variety of symptoms including restlessness, nausea, headache, muscle tension, sleep disturbances, and rapid heartbeat.

Licorice

- Do not take licorice extract if you have diabetes, high blood pressure, heart irregularities, abnormal muscle tension, poor kidney function, low blood potassium levels, or chronic hepatitis, cirrhosis of the liver, or any disease that impedes the flow of bile from the liver.
- Do not take licorice for more than 6 weeks in a row. High doses of licorice (more than 20 grams of licorice extract daily or 50 grams of licorice root daily) taken for extended periods may lead to excessive loss of sodium from the blood, water retention, high blood pressure, heart irregularities, fatigue, headaches, and muscle cramps.

Peppermint

- Do not take peppermint if you have a blockage in the bile ducts, gallbladder inflammation, or liver damage.

Selenium

- High doses of selenium (1000 micrograms or more daily) for prolonged periods may cause adverse reactions.
- High doses of selenium taken for prolonged periods may cause chronic selenium poisoning. Symptoms include loss of hair and nails or brittle hair and nails.
- Selenium can cause rash, breath that smells like garlic, fatigue, irritability, and nausea and vomiting.

Vitamin B12 (cyanocobalamin)

- Do not take cyanocobalamin if you have Leber's optic atrophy.

For more information see the Safety Appendix

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