

Gastroesophageal Reflux Disease (GERD)

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What is GERD?

Gastroesophageal reflux disease (GERD) is a chronic condition that affects approximately 19 million people in the United States. GERD may also be referred to as acid reflux disease. It occurs when the acid in your stomach backs up into your esophagus, causing a burning sensation also known as heartburn. It is normal to experience heartburn occasionally, but if you are having heartburn two or more times a week, you may have GERD.

What are the symptoms of GERD?

Not all patients experience symptoms of GERD. One of the most common symptoms of GERD is heartburn. Heartburn may present as a burning sensation in the lower chest and neck area. Other common symptoms include difficulty swallowing and a sour or bitter taste in your mouth. You may also experience a persistent cough, upset stomach, chest pain, hoarseness and asthma.

Symptoms of GERD can be worsened by triggers such as smoking, certain foods/drinks, eating too much, being overweight and lying down shortly after eating. Some foods and drinks that may trigger GERD symptoms are spicy foods, fried foods, fatty foods, citrus fruits/juices, caffeinated drinks, coffee, tea and alcohol.

How is GERD treated?

GERD is a treatable condition, but it needs to be diagnosed by a physician. If your physician diagnoses you with GERD, there are some lifestyle changes and medications that may help improve your symptoms. Lifestyle changes are usually tried first. These may include losing weight, quitting smoking, eating smaller meals, wearing looser clothing, reducing stress and raising the head of the bed while sleeping.

If lifestyle changes do not help improve your symptoms, your physician may recommend you try medication. The most common medications used to treat GERD work by either neutralizing the acid in your stomach or decreasing the amount of acid your stomach produces. Some other medications can help protect the lining of your esophagus or cause your stomach to empty faster. Many of these medications are available over-the-counter



(OTC). If your physician would like you to try an OTC medication, your local pharmacist can assist you in choosing an appropriate product. If OTC medications are not effective in controlling your symptoms, your physician may prescribe you medication to help treat your GERD.

When should I see a doctor?

If you are concerned that you may have GERD or if you experience heartburn two or more times a week, you should make an appointment to see your physician. Untreated GERD can cause serious damage to the lining of your esophagus. This damage can cause a pre-cancerous condition called Barrett's esophagus. Patients with Barrett's esophagus have an increased risk of developing esophageal cancer.

Before you visit your doctor, it is recommended that you document your symptoms for one to two weeks before your appointment. Some people call this a symptom

diary. A symptom diary should include the symptom(s) you experienced (e.g, difficulty swallowing), how long it lasted, what you were doing before the symptoms started and if it was related to any food you may have eaten. It is also helpful to include any forms of treatment you used, including medications (over-the-counter, prescription or herbals). If you used medication, it is important to document if they helped relieve the symptoms.

References

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For more information, ask your pharmacist!

This information is provided by Michigan Pharmacists Association and:

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GERD Overview

Gastroesophageal Reflux Disease (GERD) is one of the most common digestive diseases in the United States. It is estimated that 20-30 percent of Americans experience GERD symptoms at least once a month. Unfortunately, most patients treat themselves with OTC medications and do not seek medical advice. This makes it very difficult to estimate the true prevalence of GERD.

Symptoms of GERD occur due to an abnormal reflux of gastric contents into the esophagus. The presence of gastric contents in the esophagus causes damage to the esophageal mucosa. The reflux of gastric contents is usually caused by relaxation of the lower esophageal sphincter (LES). LES relaxation may be caused by increases in abdominal pressure, an atonic LES or for spontaneous reasons. Some foods and medications can decrease LES pressure and worsen GERD symptoms. Examples of foods that decrease LES pressure are fatty meals, chocolate, coffee, soda, tea and onions. Examples of medications that decrease LES pressure are anticholinergics, caffeine, ethanol, nicotine, dopamine, estrogen and progesterone.

Untreated GERD can cause serious long-term complications, including esophageal ulcerations/perforations, stricture formation and Barrett's esophagus. Patients with Barrett's esophagus have an increased risk of developing esophageal cancer.

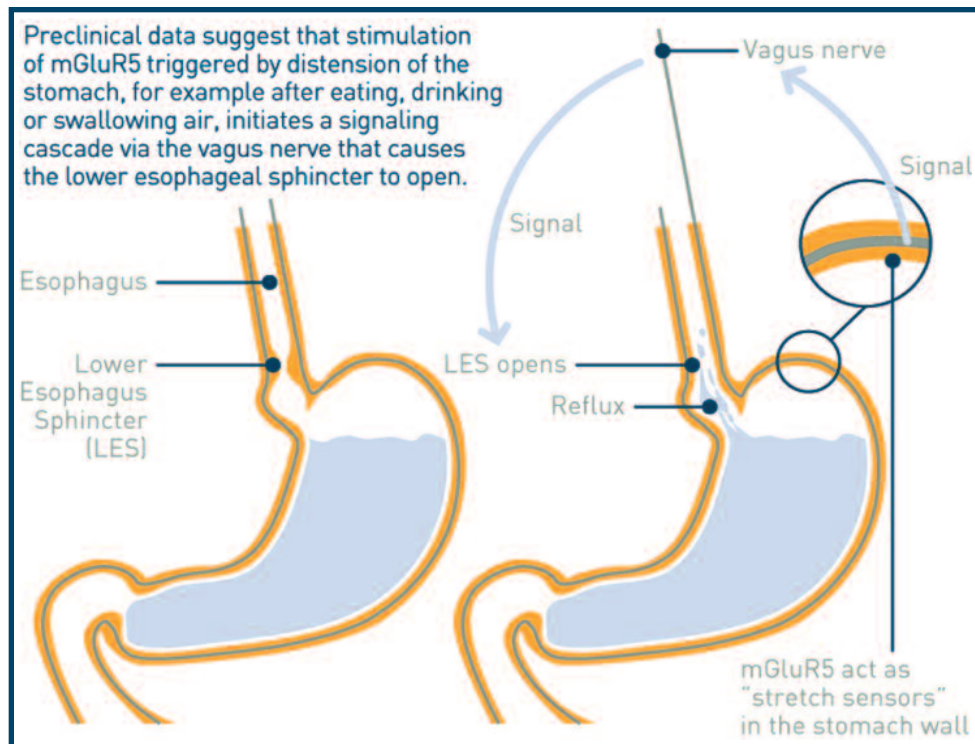
Symptoms

The most common symptom of GERD is heartburn. Other symptoms include excess salivation, belching and regurgitation. Patients experiencing GERD symptoms two times a week or more should be referred to their primary care physician for further evaluation.

Alarming symptoms may be associated with complications of GERD (i.e., Barrett's esophagus, esophageal cancer). These include pain or difficulty when swallowing, choking, blood in the stool or vomit and unexplained weight loss. If a patient has any of these symptoms, they should contact their primary care physician.

Treatment

All patients with heartburn or GERD should be counseled on lifestyle modifications, including elevating the head of the bed, decreasing fat intake, avoiding precipitating foods, losing weight, smoking cessation and not lying



down within three hours of eating. Patients with mild heartburn may get some relief with OTC medications including antacids, H₂-receptor antagonists (H₂RAs) and proton pump inhibitors (PPIs). Patients should be counseled to seek medical advice if their symptoms are not relieved within two weeks.

Patients with GERD should be treated with prescription strength acid-suppression therapy. Proton pump inhibitors are the most effective at relieving symptoms and healing the esophageal mucosa. H₂RAs are less effective than PPIs, but may be useful at controlling symptoms in patients with mild GERD. Although PPIs are generally dosed once-daily, twice-daily dosing is recommended in patients who have an inadequate response to once-daily dosing. Patients unresponsive to twice-daily dosing of PPIs may have GERD that is refractory to acid-suppression therapy. These patients may require surgical interventions and should be referred to their primary care physician for further evaluation.

Patients with GERD frequently have their symptoms return after therapy has been discontinued. Maintenance therapy is often necessary, and patients may require long-term or lifetime therapy. If PPIs are proven to be effective, it is recommended that the PPI be used long-term after it has been titrated to the lowest effective dose. Less than daily dosing of PPIs are not

recommended for maintenance therapy. Patients using H₂RAs for maintenance therapy are more likely to have recurrent episodes.

In the Pipeline

Addex Pharmaceuticals is currently trialing a new drug (ADX10059) with a novel mechanism of action for the treatment of GERD. ADX10059 is a reflux inhibitor aimed at treating the cause of GERD. It is currently undergoing Phase IIb trials with expected completion by the end of 2009. Pre-clinical data suggests that stimulation of the metabotropic glutamate receptor 5 (mGluR5) initiates a signaling cascade that causes the LES to open. In normal individuals this cascade occurs after eating or drinking to prevent the stomach from becoming distended and allowing air to escape. In patients with GERD, it is believed that an increase in mGluR5 causes the LES to open more frequently allowing gastric contents to reflux into the esophagus. ADX10059 is a mGluR5 inhibitor that may help restore normal function to the LES. It is believed that mGluR5 may also play a role in several other diseases including migraines, Parkinson's disease levodopa induced dyskinesia (PD-LID) and general anxiety disorder.

Graphic used from www.addexpharma.com/key-indications/gerd/mglur5-gerd/.

References available upon request