

Gastroesophageal reflux disease

Gastroesophageal reflux disease (**GERD**), also known as **acid reflux**, is a long-term condition in which stomach contents rise up into the esophagus, resulting in either symptoms or complications.^{[5][6]} Symptoms include the taste of acid in the back of the mouth, heartburn, bad breath, chest pain, regurgitation, breathing problems, and wearing away of the teeth.^[5] Complications include esophagitis, esophageal stricture, and Barrett's esophagus.^[5]

Risk factors include obesity, pregnancy, smoking, hiatal hernia, and taking certain medicines.^[5] Medications involved may include antihistamines, calcium channel blockers, antidepressants and sleeping pills.^[5] Acid reflux is due to poor closure of the lower esophageal sphincter, which is at the junction between the stomach and the esophagus.^[5] Diagnosis among those who do not improve with simpler measures may involve gastroscopy, upper GI series, esophageal pH monitoring, or esophageal manometry.^[5]

Treatment options include lifestyle changes; medications; and sometimes surgery for those who do not improve with the first two measures.^[5] Lifestyle changes include not lying down for three hours after eating, raising the head of the bed, losing weight, avoiding foods which result in symptoms, and stopping smoking.^[5] Medications include antacids, H₂ receptor blockers, proton pump inhibitors, and prokinetics.^{[5][8]}

In the Western world, between 10 and 20% of the population is affected by GERD.^[8] Occasional gastroesophageal reflux without troublesome symptoms or complications is even more common.^[5] The classic symptoms of GERD were first described in 1925, when Friedenwald and Feldman commented on heartburn and its possible relationship to a hiatal hernia.^[9] In 1934 gastroenterologist Asher Winkelstein described reflux and attributed the symptoms to stomach acid.^[10]

Gastroesophageal reflux disease	
Other names	British: Gastro-oesophageal reflux disease (GORD); ^[1] gastric reflux disease, acid reflux disease, reflux, gastroesophageal reflux
	
X-ray showing radiocontrast from the stomach (white material below diaphragm) entering the esophagus (three vertical collections of white material in the mid-line of the chest) due to severe reflux	
Pronunciation	/ɡæstroʊˌspəˈdʒiːəl ˈriːflʌks / ^{[2][3][4]} GERD /ɡɜːrd /
Specialty	Gastroenterology
Symptoms	Taste of acid, heartburn, bad breath, chest pain, breathing problems ^[5]
Complications	Esophagitis, esophageal strictures, Barrett's esophagus ^[5]
Duration	Long term ^{[5][6]}
Causes	Inadequate closure of the

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	lower esophageal sphincter ^[5]
Risk factors	Obesity, pregnancy, smoking, hiatal hernia, taking certain medicines ^[5]
Diagnostic method	Gastroscopy, upper GI series, esophageal pH monitoring, esophageal manometry ^[5]
Differential diagnosis	Peptic ulcer disease, esophageal cancer, esophageal spasm, angina ^[7]
Treatment	Lifestyle changes, medications, surgery ^[5]
Medication	Antacids, H ₂ receptor blockers, proton pump inhibitors, prokinetics ^{[5][8]}
Frequency	~15% (Western populations) ^[8]

Signs and symptoms

Adults

The most common symptoms of GERD in adults are an acidic taste in the mouth, regurgitation, and heartburn.^[11] Less common symptoms include pain with swallowing/sore throat, increased salivation (also known as water brash), nausea,^[12] chest pain, and coughing.

GERD sometimes causes injury of the esophagus. These injuries may include one or more of the following:

- Reflux esophagitis – inflammation of esophageal epithelium which can cause ulcers near the junction of the stomach and esophagus
- Esophageal strictures – the persistent narrowing of the esophagus caused by reflux-induced inflammation

- Barrett's esophagus – intestinal metaplasia (changes of the epithelial cells from squamous to intestinal columnar epithelium) of the distal esophagus^[13]
- Esophageal adenocarcinoma – a form of cancer^[12]

Children

GERD may be difficult to detect in infants and children, since they cannot describe what they are feeling and indicators must be observed. Symptoms may vary from typical adult symptoms. GERD in children may cause repeated vomiting, effortless spitting up, coughing, and other respiratory problems, such as wheezing. Inconsolable crying, refusing food, crying for food and then pulling off the bottle or breast only to cry for it again, failure to gain adequate weight, bad breath, and burping are also common. Children may have one symptom or many; no single symptom is universal in all children with GERD.

Of the estimated 4 million babies born in the US each year, up to 35% of them may have difficulties with reflux in the first few months of their lives, known as 'spitting up'.^[14] One theory for this is the "fourth trimester theory" which notes most animals are born with significant mobility, but humans are relatively helpless at birth, and suggests there may have once been a fourth trimester, but children began to be born earlier, evolutionarily, to accommodate the development of larger heads and brains and allow them to pass through the birth canal and this leaves them with partially undeveloped digestive systems.

Most children will outgrow their reflux by their first birthday. However, a small but significant number of them will not outgrow the condition. This is particularly true when a family history of GERD is present.

Barrett's esophagus

GERD may lead to Barrett's esophagus, a type of intestinal metaplasia,^[13] which is in turn a precursor condition for esophageal cancer. The risk of progression from Barrett's to dysplasia is uncertain, but is estimated at about 20% of cases.^[15] Due to the risk of chronic heartburn progressing to Barrett's, EGD every five years is recommended for people with chronic heartburn, or who take drugs for chronic GERD.^[16]

Causes

GERD is caused by a failure of the lower esophageal sphincter. In healthy patients, the "angle of His"—the angle at which the esophagus enters the stomach—creates a valve that prevents duodenal bile, enzymes, and stomach acid from traveling back into the esophagus where they can cause burning and inflammation of sensitive esophageal tissue.

Factors that can contribute to GERD:

- Hiatal hernia, which increases the likelihood of GERD due to mechanical and motility factors.^{[17][18]}
- Obesity: increasing body mass index is associated with more severe GERD.^[19] In a large series of 2,000 patients with symptomatic reflux disease, it has been shown that 13% of changes in esophageal acid exposure is attributable to changes in body mass index.^[20]
- Zollinger-Ellison syndrome, which can be present with increased gastric acidity due to gastrin production.
- A high blood calcium level, which can increase gastrin production, leading to increased acidity.

- Scleroderma and systemic sclerosis, which can feature esophageal dysmotility.
- The use of medicines such as prednisolone.
- Visceroptosis or Glénard syndrome, in which the stomach has sunk in the abdomen upsetting the motility and acid secretion of the stomach.

GERD has been linked to a variety of respiratory and laryngeal complaints such as laryngitis, chronic cough, pulmonary fibrosis, earache, and asthma, even when not clinically apparent. These atypical manifestations of GERD are commonly referred to as laryngopharyngeal reflux (LPR) or as extraesophageal reflux disease (EERD).

Factors that have been linked with GERD, but not conclusively:

- Obstructive sleep apnea^{[21][22]}
- Gallstones, which can impede the flow of bile into the duodenum, which can affect the ability to neutralize gastric acid

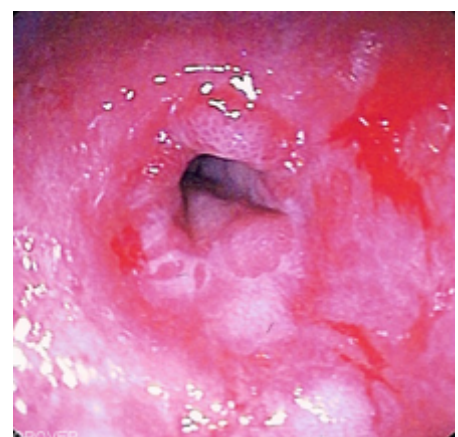
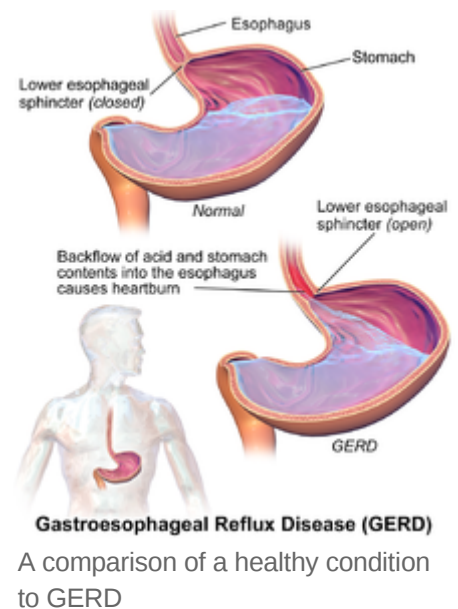
In 1999, a review of existing studies found that, on average, 40% of GERD patients also had *H. pylori* infection.^[23] The eradication of *H. pylori* can lead to an increase in acid secretion,^[24] leading to the question of whether *H. pylori*-infected GERD patients are any different than non-infected GERD patients. A double-blind study, reported in 2004, found no clinically significant difference between these two types of patients with regard to the subjective or objective measures of disease severity.^[25]

Diagnosis

The diagnosis of GERD is usually made when typical symptoms are present.^[26] Reflux can be present in people without symptoms and the diagnosis requires both symptoms or complications and reflux of stomach content.^[27]

Other investigations may include esophagogastroduodenoscopy (EGD). Barium swallow X-rays should not be used for diagnosis.^[26] Esophageal manometry is not recommended for use in diagnosis, being recommended only prior to surgery.^[26] Ambulatory esophageal pH monitoring may be useful in those who do not improve after PPIs and is not needed in those in whom Barrett's esophagus is seen.^[26] Investigation for *H. pylori* is not usually needed.^[26]

The current gold standard for diagnosis of GERD is esophageal pH monitoring. It is the most objective test to diagnose the reflux disease and allows monitoring GERD patients in their response to medical or surgical treatment. One practice for diagnosis of GERD is a short-term treatment with proton-pump inhibitors, with improvement in symptoms suggesting a positive diagnosis. Short-term treatment with proton-pump inhibitors may help predict abnormal 24-hr pH monitoring results among patients with symptoms suggestive of GERD.^[28]



Endoscopic image of peptic stricture, or narrowing of the esophagus near the junction with the stomach: This is a complication of chronic gastroesophageal reflux disease and can be a cause of dysphagia or difficulty swallowing.

Endoscopy

Endoscopy, the looking down into the stomach with a fibre-optic scope, is not routinely needed if the case is typical and responds to treatment.^[26] It is recommended when people either do not respond well to treatment or have alarm symptoms, including dysphagia, anemia, blood in the stool (detected chemically), wheezing, weight loss, or voice changes.^[26] Some physicians advocate either once-in-a-lifetime or 5- to 10-yearly endoscopy for people with longstanding GERD, to evaluate the possible presence of dysplasia or Barrett's esophagus.^[29]

Biopsies performed during gastroscopy may show:

- Edema and basal hyperplasia (nonspecific inflammatory changes)
- Lymphocytic inflammation (nonspecific)
- Neutrophilic inflammation (usually due to reflux or Helicobacter gastritis)
- Eosinophilic inflammation (usually due to reflux): The presence of intraepithelial eosinophils may suggest a diagnosis of eosinophilic esophagitis (EE) if eosinophils are present in high enough numbers. Less than 20 eosinophils per high-power microscopic field in the distal esophagus, in the presence of other histologic features of GERD, is more consistent with GERD than EE.^[30]
- Goblet cell intestinal metaplasia or Barrett's esophagus
- Elongation of the papillae
- Thinning of the squamous cell layer
- Dysplasia
- Carcinoma

Reflux changes may not be erosive in nature, leading to "nonerosive reflux disease".

Severity

Severity may be documented with the Johnson-DeMeester's scoring system:^[31] 0 - None 1 - Minimal - occasional episodes 2 - Moderate - medical therapy visits 3 - Severe - interfere with daily activities

Differential diagnosis

Other causes of chest pain such as heart disease should be ruled out before making the diagnosis.^[26] Another kind of acid reflux, which causes respiratory and laryngeal signs and symptoms, is called laryngopharyngeal reflux (LPR) or "extraesophageal reflux disease" (EERD). Unlike GERD, LPR rarely produces heartburn, and is sometimes called *silent reflux*.

Treatment

The treatments for GERD may include food choices, lifestyle changes, medications, and possibly surgery. Initial treatment is frequently with a proton-pump inhibitor such as omeprazole.^[26] In some cases, a person with GERD symptoms can manage them by taking over-the-counter drugs.^[32] This is often safer and less expensive than taking prescription drugs.^[32] Some guidelines recommend trying to treat symptoms with an H₂ antagonist before using a proton-pump inhibitor because of cost and safety concerns.^[32]

Lifestyle changes

Certain foods may promote GERD, but most dietary interventions have little effect.^[33] Some evidence suggests that reduced sugar intake and increased fiber intake can help.^[34] Avoidance of specific foods and not eating before lying down are recommended for those having GERD symptoms.^[27] Foods that may precipitate GERD include coffee, alcohol, chocolate, fatty foods, acidic foods, and spicy foods.^[27]

Weight loss may be effective in reducing the severity and frequency of symptoms.^[35] Elevating the head of the entire bed with blocks, or using a wedge pillow that elevates the individual's shoulders and head, may inhibit GERD when lying down.^[36] Although moderate exercise may improve symptoms in people with GERD, vigorous exercise may worsen them.^[33]

Abstinence from smoking or alcohol does not appear to significantly relieve symptoms.^[35]

Medications

The primary medications used for GERD are proton-pump inhibitors, H₂ receptor blockers and antacids with or without alginic acid.^[8] The use of acid suppression therapy is a common response to GERD symptoms and many people get more of this kind of treatment than their case merits.^[37] The overuse of acid suppression is a problem because of the side effects and costs.^[37]

Proton-pump inhibitors

Proton-pump inhibitors (PPIs), such as omeprazole, are the most effective, followed by H₂ receptor blockers, such as ranitidine.^[27] If a once daily PPI is only partially effective they may be used twice a day.^[27] They should be taken one half to one hour before a meal.^[26] There is no significant difference between PPIs.^[26] When these medications are used long term, the lowest effective dose should be taken.^[27] They may also be taken only when symptoms occur in those with frequent problems.^[26] H₂ receptor blockers lead to roughly a 40% improvement.^[38]

Antacids

The evidence for antacids is weaker with a benefit of about 10% (NNT=13) while a combination of an antacid and alginic acid (such as Gaviscon) may improve symptoms 60% (NNT=4).^[38] Metoclopramide (a prokinetic) is not recommended either alone or in combination with other treatments due to concerns around adverse effects.^{[8][27]} The benefit of the prokinetic mosapride is modest.^[8]

Other agents

Sucralfate has a similar effectiveness to H₂ receptor blockers; however, sucralfate needs to be taken multiple times a day, thus limiting its use.^[8] Baclofen, an agonist of the GABA_B receptor, while effective, has similar issues of needing frequent dosing in addition to greater adverse effects compared to other medications.^[8]

Surgery

The standard surgical treatment for severe GERD is the Nissen fundoplication. In this procedure, the upper part of the stomach is wrapped around the lower esophageal sphincter to strengthen the sphincter and prevent acid reflux and to repair a hiatal hernia.^[39] It is recommended only for those who do not improve with PPIs.^[26] Quality of life is improved in the short term compared to medical therapy, but there is uncertainty in the benefits over surgery versus long-term medical management with proton pump

inhibitors.^[40] When comparing different fundoplication techniques, partial posterior fundoplication surgery is more effective than partial anterior fundoplication surgery,^[41] and partial fundoplication has better outcomes than total fundoplication.^[42]

Esophagogastric dissociation is an alternative procedure that is sometimes used to treat neurologically impaired children with GERD.^{[43][44]} Preliminary studies have shown it may have a lower failure rate^[45] and a lower incidence of recurrent reflux.^[44]

In 2012 the FDA approved a device called the LINX, which consists of a series of metal beads with magnetic cores that are placed surgically around the lower esophageal sphincter, for those with severe symptoms that do not respond to other treatments. Improvement of GERD symptoms is similar to those of the Nissen fundoplication, although there is no data regarding long-term effects. Compared to Nissen fundoplication procedures, the procedure has shown a reduction in complications such as gas bloat syndrome that commonly occur.^[46] Adverse responses include difficulty swallowing, chest pain, vomiting, and nausea. Contraindications that would advise against use of the device are patients who are or may be allergic to titanium, stainless steel, nickel, or ferrous iron materials. A warning advises that the device should not be used by patients who could be exposed to, or undergo, magnetic resonance imaging (MRI) because of serious injury to the patient and damage to the device.^[47]

In those with symptoms that do not improve with PPIs surgery known as transoral incisionless fundoplication may help.^[48] Benefits may last for up to six years.^[49]

Special populations

Pregnancy

In pregnancy, dietary modifications and lifestyle changes may be attempted, but often have little effect. Calcium-based antacids are recommended if these changes are not effective. Aluminum- and magnesium hydroxide -based antacids are also safe, as is ranitidine^[50] and PPIs.^[26]

Babies

Babies may see relief with smaller, more frequent feedings, more frequent burping during feedings, holding baby in upright position 30 minutes after feedings, keep baby's head elevated while laying on the back, remove milk and soy from mothers diet or feed milk protein free formula.^[51] They may also be treated with medicines such as ranitidine or proton pump inhibitors.^[52] Proton pump inhibitors however have not been found to be effective in this population and there is a lack of evidence for safety.^[53]

Epidemiology

In Western populations, GERD affects approximately 10% to 20% of the population and 0.4% newly develop the condition.^[8] For instance, an estimated 3.4 million to 6.8 million Canadians are GERD sufferers. The prevalence rate of GERD in developed nations is also tightly linked with age, with adults aged 60 to 70 being the most commonly affected.^[54] In the United States 20% of people have symptoms in a given week and 7% every day.^[8] No data support sex predominance with regard to GERD.

History

An obsolete treatment is vagotomy ("highly selective vagotomy"), the surgical removal of vagus nerve branches that innervate the stomach lining. This treatment has been largely replaced by medication. Vagotomy by itself tended to worsen contraction of the pyloric sphincter of the stomach, and delayed stomach emptying. Historically, vagotomy was combined with pyloroplasty or gastroenterostomy to counter this problem.

Research

A number of endoscopic devices have been tested to treat chronic heartburn.

- Endocinch, puts stitches in the lower esophageal sphincter (LES) to create small pleats to help strengthen the muscle. However, long-term results were disappointing, and the device is no longer sold by Bard.^[55]
- Stretta procedure, uses electrodes to apply radio-frequency energy to the LES. A 2015 systematic review and meta-analysis in response to the systematic review (no meta-analysis) conducted by SAGES did not support the claims that Stretta was an effective treatment for GERD.^[56] A 2012 systematic review found that it improves GERD symptoms.^[57]
- NDO Surgical Plicator creates a plication, or fold, of tissue near the gastroesophageal junction, and fixates the plication with a suture-based implant. The company ceased operations in mid-2008, and the device is no longer on the market.
- Transoral incisionless fundoplication, which uses a device called Esophyx, may be effective.^[58]

See also

- Esophageal motility disorder
- Esophageal motility study

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External links

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Classification	ICD-10: K21 (http://apps.who.int/classifications/icd10/browse/2016/en#/K21) • ICD-9-CM: 530.81 (http://www.icd9data.com/getICD9Code.aspx?icd9=530.81) • OMIM: 109350 (https://omim.org/entry/109350) • MeSH: D005764 (https://www.nlm.nih.gov/cgi/mesh/2015/MB_cgi?field=uid&term=D005764) • DiseasesDB: 23596 (http://www.diseasesdatabase.com/ddb23596.htm)
External resources	MedlinePlus: 000265 (https://www.nlm.nih.gov/medlineplus/ency/article/000265.htm) • eMedicine: med/857 (https://emedicine.medscape.com/med/857-overview/ped/1177) (http://www.emedicine.com/ped/topic1177.htm#) radio/300 (http://www.emedicine.com/radio/topic300.htm#)

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