Gastroesophageal Reflux

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Educational Gap

Gastroesophageal reflux (GER) is common in healthy infants, children, and adults, but when troublesome symptoms or complications occur, the patient is said to have GER disease (GERD). Clinicians should know the diagnostic techniques for distinguishing these conditions as well as recommended management.

Objectives

After completing this article, readers should be able to:

1. **Understand the differences between benign GER and GERD.**
2. **Understand other diseases and conditions that may mimic GERD.**
3. **Understand methods of diagnosing GERD.**
4. **Describe therapeutic options for the treatment of GERD (including lifestyle modifications, medical therapies, and surgical therapies).**

Introduction

Gastroesophageal reflux (GER), defined as the passage of gastric contents into the esophagus, is a normal physiologic process in healthy infants, children, and adults but may cause distress for caregivers or patients. Gastroesophageal reflux disease (GERD) is defined as the passage of gastric contents into the esophagus that results in troublesome symptoms or complications for the infant, child, or adolescent, and not for the caregiver alone. (1) Regurgitation, commonly referred to as "spitting up," is the effortless passage of gastric contents into the pharynx or mouth. Vomiting is the forceful expulsion of the gastric contents. In contrast, rumination is defined as voluntary, habitual, and effortless regurgitation of recently ingested food. Following this voluntary regurgitation, gastric contents are expulsed from the mouth or re-swallowed.

Epidemiology

GER is a common occurrence in healthy infants, children, and adults, most often in the postprandial period. Fifty percent of infants younger than 3 months of age and 67% of infants at 4 months of age will have at least one episode of regurgitation daily. (2) By 12 months of age, however, only 5% experience episodes of regurgitation. (2) Reflux symptoms (heartburn, epigastric pain, and regurgitation) affect up to 7% of school-age children and 8% of adolescents. (3) Several pediatric populations are at increased risk for the development of GERD, including patients who have neurologic impairment, obesity, lung disease (specifically cystic fibrosis), esophageal atresia, and prematurity.

Abbreviations

ALTE:	apparent life-threatening event
GER:	gastroesophageal reflux
GERD:	gastroesophageal reflux disease
H2RAs:	histamine-2 receptor antagonists
LES:	lower esophageal sphincter
MII:	multiple intraluminal impedance
PPI:	proton pump inhibitor

Pathophysiology

GER results from relaxation of the lower esophageal sphincter (LES). In healthy infants and children, relaxation of the LES is transient. In infants, gastric distention associated with large volume feeds (100–150 mL/kg per day compared to the average adult intake of 30–50 mL/kg per day) portends

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more frequent transient LES relaxations. Delayed gastric emptying also can increase the frequency of transient LES relaxations. Esophageal clearance and mucosal defense (secretions) play a significant role in prevention of esophagitis. Compromise of these functions contributes to the development of GERD. In neurologically impaired children, decreased basal LES tone also is likely to contribute to GER.

Signs and Symptoms

Infants

Regurgitation or spitting up is the most common presentation of infantile GER. Infants who have benign physiologic GER usually are described as "happy spitters." Although much less common, infants can develop GERD, with failure to thrive, feeding difficulties, arching of the back, or irritability, the most common symptom noted by caregivers (Table 1). Irritability may, in addition to GERD, be associated with other factors, including the developing nervous system in infants and exposure to tobacco smoke. Rarely, extraintestinal signs of GERD occur in infants, including apparent life-threatening events (ALTEs), wheezing, recurrent cough, aspiration pneumonia, and abnormal posturing or torticollis, known as Sandifer syndrome.

Children

In preschool and school-age children, regurgitation, vomiting, abdominal pain, and feeding difficulties are common presentations of GERD. Extraintestinal signs can include chronic cough or pneumonia and dental erosions. In older children, heartburn, regurgitation, and epigastric pain are the most common signs associated with GERD. Similarly to younger children, older youngsters may have GERD-associated chronic cough, recurrent pneumonia, and dental erosions. Severe inflammation can cause hematemesis and anemia.

Table 1. GERD Signs and Symptoms

Infants	
GI	Extraintestinal
Regurgitation	Failure to thrive
Feeding difficulties	Wheezing
Hematemesis	Stridor
	Persistent cough
	Apnea/ALTE
	Irritability
	Sandifer syndrome
Children	
GI	Extraintestinal
Heartburn	Persistent cough
Vomiting	Wheezing
Regurgitation	Laryngitis
Feeding difficulties	Stridor
Dysphagia	Chronic asthma
Chest pain	Recurrent pneumonia
Hematemesis	Dental erosions
	Anemia

Table 2. Warning Signs Necessitating Further Investigation in Infants and Children Who Have Vomiting

Bilious emesis
GI bleeding
Failure to thrive
Forceful or projectile emesis
Emesis beginning after 6 mo of age
Difficulty swallowing
History of food allergies
Fever
Diarrhea
Constipation
Abdominal pain
Hepatosplenomegaly
Lethargy
Abnormal neurologic findings
Bulging fontanelle
Anxiety or disordered eating
Suspicion of genetic or metabolic disease

Other Considerations

One of the challenges facing primary care providers is distinguishing vomiting in patients due to GER or GERD from vomiting due to other causes. Worrisome signs and symptoms in patients who have suspected GERD that may warrant further investigation are listed in Table 2. Table 3 summarizes common causes of vomiting not associated with GER or GERD. For the infant with uncomplicated reflux, reassurance by the primary care provider is appropriate. However, referral to a pediatric gastroenterologist is recommended if symptoms persist beyond 12 to 18 months of age.

Diagnostic Approach to GERD

History and Physical Examination

A thorough history and physical examination are central elements of the evaluation of GERD and other conditions

Table 3. Nonreflux Causes of Vomiting

- Infections
  - Sepsis
  - Meningitis
  - Gastroenteritis
  - Urinary tract infection
  - Otitis media
- Anatomic/Obstructive
  - Foreign body
  - Pyloric stenosis
  - Malrotation
  - Intussusception
  - Superior mesenteric artery syndrome
- Gastrointestinal
  - Esophagitis
    - Eosinophilic esophagitis
    - Pill esophagitis
    - Infectious esophagitis
  - Achalasia
  - Gastritis
    - Peptic ulcer disease
    - *Helicobacter pylori* infection
  - Gastroparesis
  - Cholelithiasis
  - Hepatitis
  - Pancreatitis
  - Celiac disease
  - Crohn disease
  - Eosinophilic GI disease
- Neurologic
  - Increased intracranial pressure
  - Migraine
- Respiratory
  - Posttussive emesis
  - Pneumonia
- Renal
  - Obstructive uropathy
  - Renal insufficiency
- Cardiac
  - Congestive heart failure
- Oncologic
  - Lymphoma, other solid tumors
- Drugs and alcohol consumption
- Pregnancy
- Psychologic/Behavioral
  - Overfeeding
  - Self-induced emesis
  - Rumination syndrome

that may mimic GERD. The history and examination alone may be sufficient to diagnose benign GER in a normally developed infant or young child. It is imperative to inquire about the nature of the vomiting, whether bile or blood is present in the emesis, if the child seems irritable with emesis, if emesis is forceful or projectile, or if emesis is associated with other symptoms such as fever or lethargy. Feeding history should include volume and frequency of feedings, type of formula, preparation of formula, and positioning of the infant during the feeds. A history of dysphagia or food sticking, eating slowly, cutting food into small pieces, or avoiding particular foods may be suggestive of eosinophilic esophagitis.

Past medical history should include inquiring about prematurity, neurologic problems, growth or developmental concerns, past surgeries or hospitalizations, allergies (particularly to foods), and psychological disease. Review of systems should detail respiratory complaints and ear, nose, or throat symptoms. Pertinent family history includes inquiry about gastrointestinal (GI) diseases, including GERD, and atopic disease.

Physical examination should include the patient's general appearance, measurements of weight and length, pulmonary and cardiac evaluation, abdominal examination (specifically noting the presence of abdominal distention, abdominal tenderness, bowel sounds, and hepatosplenomegaly), and a thorough neurologic assessment.

There is no symptom or constellation of symptoms that is diagnostic for GERD in infants. However, in neurologically normal older children and adolescents, the classic features (heartburn or chest pain, regurgitation, and epigastric pain) may be used to diagnose GERD. Moreover, a detailed history and examination may provide clinical clues that suggest other causes of vomiting in addition to GERD (Table 3).

Diagnostic Studies

For infants and children, history and physical examination are sufficient and further diagnostic testing is not necessary to diagnose GER. A diagnostic evaluation should be reserved for infants and children who have complications related to GERD and to evaluate for other causes of vomiting. The evaluation must be tailored to individual patients based on pertinent findings on history and examination.

EMPIRIC TRIAL OF ACID SUPPRESSION. In a neurologically intact older child (eg, older than 8 years of age) or adolescent who has classic symptoms of GERD (heartburn, regurgitation, and epigastric pain), a positive response to an empiric trial of acid suppression with a proton pump inhibitor (PPI) can be used to diagnose GERD. A 4-week trial is suggested, because 2 weeks of PPI therapy may be insufficient to treat GERD. Referral to a pediatric gastroenterologist may be indicated if a 4-week trial of PPI therapy and lifestyle changes are unsuccessful. There is no evidence, however, to support empiric treatment with PPIs in infants and young children as a way to diagnose GERD.

BARIUM CONTRAST RADIOGRAPHY. An upper GI series is a fluoroscopic examination using barium to opacify the upper GI tract (Figs 1 and 2). This test, performed by radiologists, is helpful to define the anatomy of the upper GI tract (esophagus, stomach, and small intestine). An upper GI series should be used to evaluate for anatomic

Figure 1. Esophageal stricture. Upper GI series demonstrating a tapered circumferential mid and lower esophageal stricture.

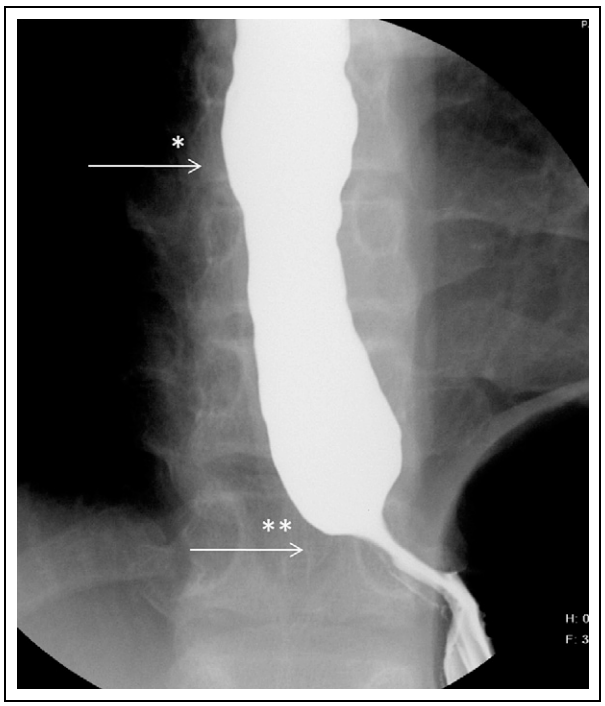

Figure 2. Achalasia. *Proximal esophageal dilation and **bird's beak appearance suggestive of achalasia.

causes of vomiting that may mimic GERD, including esophageal web or stricture, achalasia, hiatal hernia, gastric outlet obstruction (antral web or pyloric stenosis), and intestinal malrotation. It should not be used to diagnose GERD because nonpathologic reflux frequently is detected during this study.

ESOPHAGEAL PH MONITORING. Esophageal pH monitoring measures the frequency and duration of acidic esophageal reflux episodes, by using a transnasal catheter with one or more pH electrodes along the length of the catheter. A battery operated system (worn like a small purse) records output from the pH monitor, and patients and caregivers are able to input meal times and times of supine positioning for data analysis. Wireless pH monitoring may be used in older children and may be tolerated better.

Based on data extrapolated from adults, acid reflux is associated with an intraesophageal pH <4.0. The pH probe measures the total number of reflux episodes, number of reflux episodes lasting >5 minutes, duration of longest reflux episode, reflux index (percentage of study during which the pH is <4.0), and symptom index (the number of times a particular symptom associated with acid reflux occurs divided by the total number of times that particular symptom is recorded, eg, number of coughs associated with acid reflux divided by total number of cough episodes recorded). A reflux index of >6% to 12% or a symptom index >30% to 50% is considered abnormal. Using a compilation of this data, esophageal pH monitoring may be used to diagnose acid reflux. Esophageal pH monitoring is effective also for evaluating the efficacy of acid suppression therapy. In children who have a normal pH study but histologically documented esophagitis, other conditions, such as eosinophilic esophagitis, must be considered.

There are several limitations to pH monitoring. The monitor does not have the ability to measure nonacid reflux, and the results (ie, reflux index or symptom index) do not always correlate with the severity of pathologic acid reflux. For infants or children who may feed every 2 to 4 hours, it may be difficult to interpret a pH study, given that frequent feedings may buffer gastric acidity.

COMBINED MULTIPLE INTRALUMINAL IMPEDANCE AND PH MONITORING. Combined multiple intraluminal impedance (MII) and pH monitoring allows measurement of fluids, air, and solids in the esophagus, in addition to detecting nonacid and acid reflux. This technology also is able to distinguish between swallowed (antegrade) and

regurgitated (retrograde) boluses, and the technique can be used while a patient is on acid suppression therapy. This procedure also utilizes a transnasal catheter but has both pH and impedance electrodes, allowing correlation of documented symptoms (for example, cough, chest pain, or ALTE) with episodes of both acid and nonacid reflux. This capability is particularly helpful in understanding extraintestinal symptoms, with the caveat that such symptoms must occur during the course of the 24-hour study to be detected. Recent data suggest that the enhanced information provided by the MII changes management (such as medication changes, use of fundoplication, and changes in feeding regimen) in 25% of patients, compared with standard pH monitoring alone. (4)(5)

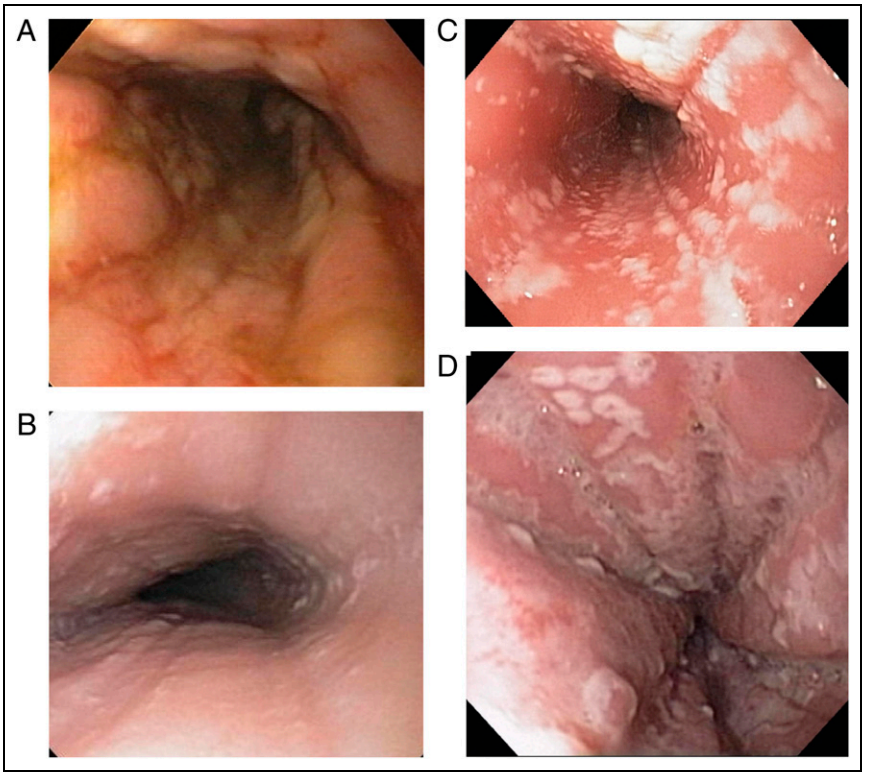

Figure 3. Causes of esophagitis. A. Erosive esophagitis: severe erythema and edema with linear ulcerations, associated with chronic GERD. (Provided courtesy of Dr Edwin de Zoeten.) B. Eosinophilic esophagitis: white plaques, linear ridging, and trachealization of the esophagus consistent with eosinophilic esophagitis. (Provided courtesy of Dr Glenn Furuta.) C. Infectious esophagitis (*Candida*): white plaques consistent with candidal esophagitis in a patient with Crohn disease. D. Infectious esophagitis (herpes simplex virus): severe ulcerations consistent with herpes simplex virus infection.

ESOPHAGEAL MANOMETRY. Esophageal manometry measures esophageal function by assessing esophageal peristalsis and upper esophageal sphincter and LES pressures. Manometry is useful in diagnosing esophageal motility disorders, such as achalasia (suboptimal relaxation of the LES). Many children who have GERD will have abnormal manometric studies because of esophageal injury or inflammation. However, manometry cannot be used to diagnose GERD or predict success with therapy because it cannot determine whether any reflux (acid or nonacid) or esophagitis is present. In addition, access to physicians skilled in pediatric esophageal manometry is limited, even among tertiary and quaternary care pediatric centers.

ENDOSCOPY WITH BIOPSY. Upper intestinal endoscopy with biopsy allows for direct visual inspection and histologic examination of the esophagus, stomach, and duodenum (Figs 3 and 4). Endoscopy allows for identification of diseases that mimic reflux, including eosinophilic esophagitis, esophageal stricture, pill esophagitis, infectious esophagitis, peptic ulcer disease, and Crohn disease. Therefore, endoscopy with biopsy may be recommended for infants and children who have unexplained refractory or recurring GERD symptoms to assess for other conditions and evaluate for long-term complications of GERD.

SCINTIGRAPHY. Commonly known as a gastric emptying scan, this technique uses formula or food labeled with ^{99}technetium to measure gastric emptying. The scan may identify esophageal reflux and aspiration, although the sensitivity (15%–59%) and specificity (83%–100%) for the diagnosis of GERD as compared with esophageal pH monitoring are poor. Therefore, scintigraphy is not recommended to diagnose or manage reflux in infants or children.

Prognosis of GER

Uncomplicated GER carries a favorable prognosis because most infants will "outgrow" regurgitation by 7 to 12 months of age. Children who have neurologic impairment, obesity, interstitial lung disease, anatomic GI

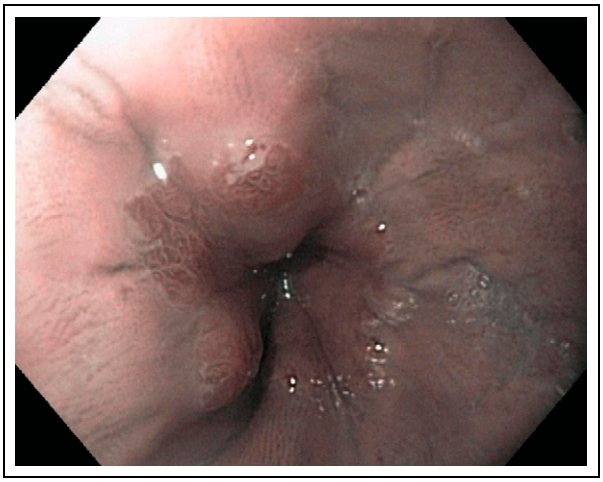

Figure 4. Complications of GERD (Barrett esophagus). Barrett esophagus seen endoscopically by narrow band imaging (note change in epithelium). (Provided courtesy of Dr Edwin de Zoeten.)

abnormalities, malrotation, hiatal hernia, and prematurity carry a higher risk for the development of GERD and its complications.

Complications of GERD

Esophageal Complications

Esophagitis, Barrett esophagus (presence of intestinal metaplasia in the esophagus; Fig 4), strictures, and adenocarcinoma have been reported as consequences of severe GERD. Esophagitis (esophageal inflammation) can occur following chronic esophageal acid exposure and must be diagnosed by upper endoscopy and histology. Barrett esophagus (presence of intestinal metaplasia in the esophagus) can lead to the development of esophageal adenocarcinoma. Barrett esophagus is extremely rare in the pediatric population; it is present in <0.25% of children undergoing endoscopy. The condition is associated with older age (adolescence) and the presence of hiatal hernia. Of adults with Barrett esophagus, only 1% to 3% progress to adenocarcinoma. Esophageal strictures also are rare in children but have been reported in 5% of children who have chronic untreated GERD, so aggressive treatment of GERD is warranted.

Extraintestinal Complications

RESPIRATORY SYMPTOMS. GERD is associated frequently with asthma in pediatric patients. Proposed mechanisms include aspiration of gastric contents leading to airway hyperresponsiveness and inflammation and vagally mediated bronchial or laryngeal spasm. The effect of asthma on the severity of GERD has not been well studied. Although GERD has been associated with asthma, it is not clear whether GERD contributes to asthma or if GERD is a secondary phenomenon resulting from decreased LES tone as a result of negative intrathoracic pressure from chronic hyperinflation of the lung and displacement of the LES into the chest. (6) Patients who have difficult-to-control asthma, nocturnal asthma symptoms, or reflux symptoms (heartburn, regurgitation) may benefit from esophageal pH/impedance monitoring and reflux therapy if appropriate.

Recurrent pneumonia is another potential complication of reflux, caused by aspiration of gastric contents. GERD may contribute also to exacerbations of interstitial lung diseases such as idiopathic pulmonary fibrosis or cystic fibrosis because these diseases can result in impaired airway protective mechanisms, which would normally protect the lung against aspirated gastric contents.

Several strategies have been postulated to predict which patients who have respiratory disease will respond to medical or surgical antireflux treatment. Lipid-laden alveolar macrophages on bronchoscopy have poor specificity and sensitivity to detect reflux-related respiratory disease. Sputum pepsin concentrations are elevated in both controls and patients who have reflux because healthy individuals can aspirate small amounts of gastric contents normally. In addition, normal pH/impedance studies cannot rule out reflux as a cause for pneumonia. Therefore, currently no test exists to predict response to medical or surgical therapy. Consultation with a pediatric gastroenterologist may be indicated if persistent GERD is suspected in a patient who has difficult-to-control asthma or interstitial lung disease. Medical therapy, gastrojejunal feeding, and antireflux surgery may be options for patients who have respiratory complications of GERD, depending on the patient's clinical course and the severity of lung disease.

UPPER AIRWAY SYMPTOMS. Descriptive studies have postulated a link between reflux and upper airway symptoms such as hoarseness or chronic cough, as well as laryngoscopic findings such as upper airway edema, erythema, cobblestoning, and granulomas. Data are insufficient to recommend standard methods of diagnosis and management of these findings in children. Medications used to treat reflux are unlikely to improve these symptoms in children.

DENTAL CARIES. GERD may be associated with dental caries in children. Other factors, however, such as consumption of juice, bulimia nervosa, and racial or genetic

factors also may contribute to the development of caries. In addition, GERD may lead to the loss of tooth enamel. Although there are no standard recommendations for diagnosis and management of GERD in patients who have caries, care providers should perform a careful oral examination in children who have known GERD.

ALTES. It is unclear if a relationship exists between GERD and ALTE. Combined pH monitoring and MII studies have revealed an association between reflux and short episodes of nonpathologic apnea, likely representing normal protection of the airway during regurgitation. Although it is unlikely that GERD is contributing to pathologic apnea in most infants who experience an ALTE, infants who have a true ALTE obviously associated with vomiting or regurgitation may be considered for antireflux surgery. There are no data demonstrating efficacy of medical or surgical therapy in patients who have ALTE.

Treatment

Lifestyle Modifications

INFANTS. Lifestyle modifications include changes in nutrition, feeding practices, and positioning. Large volume feeds can promote regurgitation in infants due to gastric distention and an increase in transient LES relaxation. Restricting volume, however, can result in insufficient energy intake. Thus, increasing the caloric concentration or density of feedings while decreasing the total volume of the feedings may decrease GER. For example, an infant who takes 32 oz of standard 20 kcal/oz infant formula, giving 640 calories per day, may be changed to 27 oz/day of 24 kcal/oz formula or 24 oz/day of 26 kcal/oz formula.

Alternatively, adding rice cereal to formula or human milk may decrease the amount of regurgitation by thickening the formula. Rice cereal will also increase the caloric density of the formula (1 tbsp per 2 oz of 20 kcal/oz formula will increase caloric density to 27 kcal/oz). A higher flow nipple may be required to accommodate the increased consistency of the formula. Antiregurgitant formulas (ie, formulas thickened with carob bean gum or other starches) have not been proven to decrease regurgitation when compared with standard infant formula or formula mixed with rice cereal.

Changing the type of formula does not positively affect GER symptoms. A casein hydrosylate or amino acid formula would, however, be of benefit to infants who have cow milk or soy protein allergy. Thus, primary care providers may consider a 2-week trial of a casein hydrosylate or amino acid formula in infants who have had persistent vomiting or regurgitation and poor weight gain for >4 weeks. It is important to use the new formula for at least 2 weeks before making additional changes because symptoms of allergy (such as vomiting) may take several days to improve while the GI mucosa heals. If poor weight gain and vomiting persist, consultation with a pediatric gastroenterologist may be helpful.

Although prone positioning during sleep has been shown to decrease the number of regurgitation events in infants, the American Academy of Pediatrics advocates sleeping in the supine position to reduce the risk for sudden infant death syndrome.

CHILDREN AND ADOLESCENTS. For children and adolescents who have mild reflux symptoms, lifestyle changes include dietary modification (including avoidance of meals with high fat content at dinner time) and avoidance of tobacco and alcohol. For obese patients, weight loss helps. Based on data extrapolated from adult studies, children and adolescents who have GER or GERD may benefit also from avoidance of caffeine, chocolate, and spicy foods.

TRANSPYLORIC FEEDING. Nasojejunal or gastrojejunal feedings may be considered, particularly in infants who have recurrent pneumonia from aspiration and in neurologically impaired children. By providing a continuous rate of formula past the pylorus, the stomach does not fill or distend, resulting in less GER. Similar rates of pneumonia in neurologically impaired children are seen after initiation of gastrojejunal feedings compared with neurologically impaired children after antireflux surgery.

Pharmacologic Therapies

ANTACIDS. Antacids act within minutes to buffer gastric contents (Tables 4 through 6). Primarily validated in adults, antacids can be used in older children and adolescents for quick symptom relief. For optimal effect, antacids should be used after meals. Caution should be exercised when administering aluminum-containing antacids because elevated aluminum levels can cause osteopenia, rickets, microcytic anemia, and neurotoxicity. In addition, antacids may interfere with absorption and efficacy of other drugs when taken concurrently.

HISTAMINE-2 RECEPTOR ANTAGONISTS. Histamine-2 receptor antagonists (H2RAs) decrease acid production by binding to the histamine-2 receptor on the gastric parietal cell. Examples of these medications include ranitidine, famotidine, cimetidine, and nizatidine. Ranitidine reaches a peak plasma concentration 2.5 hours after ingestion in children and has a half-life of 6 hours.

Table 4. Histamine-2 Receptor Antagonists

Drug	Infant Dose	Child Dose	Adult Dose	Special Instructions	Adverse Effects
Cimetidine	Not available	Not available	≥16 y: 400–800 mg PO BID	Not recommended for children <16 y of age, reduce dose with renal insufficiency	Headache, dizziness, constipation, diarrhea, irritability, gynecomastia, rash (including Stevens-Johnson syndrome)
Famotidine	1 mo–1 y: 1 mg/kg per day PO ÷ q 12 h	1–12 y: 1 mg/kg per day PO ÷ q 12 h	≥12 y: 40–80 mg/day PO ÷ q 12 h	Reduce dose with renal insufficiency, may give with food and antacids	Headache, dizziness, constipation, diarrhea, irritability
Nizatidine	6 mo–1 y: 5–10 mg/kg per day PO ÷ q 12 h	1–12 y: 5–10 mg/kg per day PO ÷ q 12 h	≥12 y: 150 mg PO BID	Limited data for children <12 y of age, reduce dose with renal insufficiency, may give with food and antacids	Headache, dizziness, constipation, diarrhea, irritability
Ranitidine	1 mo–1 y: 4–10 mg/kg per day PO ÷ q 8–12 h	1–16 y: 4–10 mg/kg per day PO ÷ q 8–12 h	≥16 y: 150 mg PO BID	Reduce dose with renal insufficiency, may give with food and antacids	Headache, dizziness, diarrhea, constipation, irritability

BID=twice daily; PO=by mouth; q=every.

Although generally less effective than PPIs, H2RAs may be used to heal esophagitis and treat symptoms of GERD. H2RAs are considered safe for use in children and are used commonly as first-line therapy in infants. However, in some infants, H2RAs may cause irritability, head banging, and headaches. Cimetidine use is associated with gynecomastia. Tachyphylaxis has been observed with chronic H2RA use.

PROTON PUMP INHIBITORS. PPIs suppress gastric acid production by irreversibly blocking H+, K+ ATPase (commonly called the proton pump), the final step in parietal cell acid secretion. PPIs are more effective than H2RAs in blocking acid production. They must be administered on a daily basis before a meal and can take several days, once treatment is initiated, for maximal acid suppression effect. Omeprazole, lansoprazole, and esomeprazole have been approved in the United States and Europe for pediatric use. However, no PPI is approved currently for use in patients younger than 1 year of age. Yet PPI use in infants has increased dramatically in the last decade. Studies, including a recent systematic review and a placebo-controlled trial, reveal no improvement in GERD-associated symptoms in infants who have PPI use compared with placebo. (7)(8)

Generally considered safe for use in pediatrics, 12% to 14% of children will have idiosyncratic reactions to PPIs, including headache, diarrhea, constipation, and nausea. Drug-induced hypergastrinemia may occur as a result of blocking the proton pump. Acid suppression may result in abnormal intestinal flora and bacterial overgrowth. Adults on chronic PPI therapy have an increased risk for respiratory infections, bacterial gastroenteritis, and *Clostridium difficile* colitis. (9)(10) In neonates, acid suppression is associated with a higher carriage rate of *Candida* and a higher incidence of necrotizing enterocolitis. In elderly patients, vitamin B12 deficiency and an increased risk of hip fractures have been reported. The risks and benefits of long term PPI therapy should be considered, particularly in infants, in whom the studies cited above reveal no improvement of infantile GERD when compared with placebo.

PROKINETIC AGENTS. These medications are theorized to improve GER by stimulating more rapid emptying of the stomach. They may be considered in patients who show evidence of delayed gastric emptying. Metaclopramide is an effective prokinetic, but it has a significant adverse effect profile, including dystonic reactions, lethargy, irritability, gynecomastia, and permanent tardive

Table 5. **Proton Pump Inhibitors**

Drug	Infant Dose	Child Dose	Adult Dose	Special Instructions	Adverse Effects
Esomeprazole	1 mo–1 y: 0.25–1 mg/kg per day PO	1–12 y: <20 kg: 10 mg PO QD ≥20 kg: 10–20 mg PO QD	≥12 y: 20–40 mg PO QD	FDA approved for ≥1 y. Capsules should be swallowed without chewing or may be opened and sprinkled on soft food or in liquids.	Headache, diarrhea, nausea, infection
Lansoprazole	<10 wk: 0.2–0.3 mg/kg per day PO, ≥10 wk: 1–2 mg/kg PO QD	1–12 y: <30 kg: 15 mg PO QD, ≥30 kg: 30 mg PO QD	≥12 y: 30–60 mg PO QD	FDA approved for ≥1 y. Capsules should be swallowed without chewing or may be opened and sprinkled on soft food or in liquids. Disintegrating tablets should be allowed to disintegrate without chewing.	Headache, dizziness, diarrhea, nausea, infection
Omeprazole	1 mo–1 y: 0.7 mg/kg per day PO	1–16 y: 5 kg to <10 kg: 5 mg PO QD, 10 kg to ≤20 kg: 10 mg PO QD, >20 kg: 20 mg PO QD	≥16 y: 20–40 mg PO QD	FDA approved for ≥1 y. Capsules should be swallowed without chewing or capsules may be opened and granules can be sprinkled on soft food or in liquids.	Headache, dizziness, diarrhea, nausea, infection
Pantoprazole	Not available	Not available	20–40 mg PO QD	Limited data on use in children. Tablet should be swallowed without chewing.	Headache, dizziness, diarrhea, nausea, infection
Rabeprazole	Not available	≥12 y: 20 mg PO QD	≥12 y: 20 mg PO QD	FDA approved for ≥12 y. Tablet should be swallowed without chewing.	Headache, dizziness, diarrhea, nausea, infection

PO=by mouth; QD=daily.

dyskinesia. The risk of permanent tardive dyskinesia has resulted in a black box warning issued by the Food and Drug Administration (FDA). Erythromycin also may be used in patients who have delayed gastric emptying or gastroparesis. This drug, however, can cause a prolonged QT interval and should be used cautiously. Bethanechol, baclofen, and domperidone also have been used to treat delayed gastric emptying; however, each of these medications carries potential adverse effects. Thus, current guidelines do not recommend the use of prokinetic agents for treatment of GERD.

SURFACE AGENTS. Sucralfate is a surface agent, consisting of sucrose, sulfate, and aluminum. When exposed to acidic pH, it forms a gel that binds to eroded mucosa. Sucralfate has been shown in adults to improve symptoms related to ulceration. Chronic use may result in aluminum toxicity or gastric bezoar formation. Therefore, sucralfate typically is prescribed for a maximum duration of 7 to 10 days.

Surgical Therapy

FUNDOPLICATION. Fundoplication decreases GER by increasing the LES pressure and increasing the intraabdominal length of the esophagus. Recently, most fundoplication procedures have been performed

Table 6. **Antacids and Surface Agents**

Drug	Infant Dose	Child Dose	Adult Dose	Special Instructions	Adverse Effects
Antacids					
Calcium chloride	Not available	400 mg/dose PO (maximum 1,200–1,600 mg daily)	750–1,500 mg PO prn (maximum 9 g/24 h)	May use for 7–10 d. No dosing recommendations available in children ≤2.	Nausea, constipation, abdominal pain
Magnesium hydroxide	Not available	2.5–5 mL/dose PO prn up to QID	5–15 mL prn up to QID	May use for 7–10 d. No dosing recommendations available in children ≤2.	Diarrhea, abdominal pain, nausea
Surface Agents					
Sucralfate	Not available	Not available	1,000 mg PO QID	Dosing is not well established in children. Suspension is the preferred form of administration and recommended for 7–10 d.	Constipation, nausea

PO=by mouth; prn=as needed; QID=four times daily.

laparoscopically, which has decreased morbidity, length of hospital stays, and infections when compared with open fundoplication. However, both laparoscopic and open fundoplication have significant postoperative complications, including gas-bloat syndrome (a constellation of symptoms including gagging, retching, nausea, and abdominal distention resulting from altered gastric accommodation), dysphagia, and dumping syndrome (significant release of gastric contents into the duodenum, which may result in hyper- and hypoglycemia). Children at the highest risk of postoperative complications include neurologically impaired children and premature infants. (11)

Long-term outcomes after antireflux surgery have been assessed in children and in adults. Up to 10% of all children undergoing fundoplication will have complications, and nearly 10% will require surgical revision. In addition, in neurologically normal children, there may be no improvement in the number of hospital admissions for pneumonia, respiratory distress or apnea, and failure to thrive after fundoplication. (12) Children who have neurological disorders were found to be at increased risk for admissions for pneumonia (aspiration or other), respiratory distress, and failure to thrive after fundoplication in a single study. (13) Another study revealed no change in admissions for pneumonia in children who have neurologic impairment after fundoplication. (14) These findings could be in part due to "preventative" fundoplications performed in patients (particularly those with neurologic impairment) without any evidence of GERD or misdiagnosis of GERD. Given that these studies are retrospective, prospective trials are needed to investigate long term outcomes following antireflux surgery.

Clinicians should be aware that fundoplication, particularly in neurologically impaired children, is complicated. Careful analysis of the risks and potential benefits of fundoplication should be considered before surgery. In adults, over 60% of patients continue to require acid suppression medications after fundoplication. Thus, recurrent symptoms after fundoplication are common. Investigation of recurrent reflux symptoms after fundoplication includes barium contrast radiography to determine if the fundoplication remains intact and to detect strictures, as well as pH-MII monitoring to determine the functional capacity of the fundoplication.

Fundoplication may be considered in patients who have confirmed GERD who experience severe refractory or recurrent symptoms or life-threatening complications of GERD. It is essential that primary care providers, gastroenterologists, and surgeons educate families about the significant postoperative complications associated with fundoplication before pursuing surgery. This education is even more critical in patients who have neurologic impairment because they have the highest postoperative complication rates.

Special Considerations

Children Who Have Neurologic Impairment

GERD and its complications occur more frequently in children who have neurologic impairment. The rationale for the increase in severity and complications of GERD in this population is likely due to a combination of several factors, including chronic supine positioning, swallowing dysfunction, abnormal sensory integration, constipation, abnormal muscle tone, and skeletal abnormalities. It may be difficult to diagnose GERD in neurologically impaired children, particularly those with atypical presentations, such as anxiety, dystonia, and self-injurious behaviors. In this population in particular, testing, such as barium contrast studies, pH-MII monitoring, and endoscopy may be necessary as part of the diagnostic evaluation. Medical therapies, such as long term PPI and prokinetic use, often are used to treat symptoms and esophagitis. Children who have neurologic impairment are more likely to require gastrostomy feedings to support their nutritional status. Antireflux surgery often is considered in this population; however, when compared with healthy children, neurologically impaired children have twice the risk of postoperative complications, three times the risk of death, and four times the risk of needing surgical revision. (15)

Summary

- Based on strong research evidence, (1) gastroesophageal reflux in children is a common concern for both caregivers and health-care providers.
- Based on some research evidence as well as expert consensus, (16) most infants have physiologic reflux, and reassurance and parenteral education are recommended.
- Based on some research evidence as well as expert consensus, (16) judicious use of diagnostic testing should be tailored to the history and physical examination of each patient.
- Based on strong research evidence, (7) medical treatment, including proton pump inhibitors, generally is effective in suppressing gastric acid production.
- Based on some research evidence as well as consensus, (16) antireflux surgery may be indicated in infants and children who have severe complications of reflux or symptoms resistant to therapy.

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1. The parents of a 4-month-old infant who spits up frequently but is otherwise well want to know why he does so much spitting. You explain that the most common cause of gastroesophageal reflux in children is:
   A. delayed gastric emptying.
   B. hiatal hernia.
   C. impaired esophageal peristalsis.
   D. relaxation of the lower esophageal sphincter.
   E. salivary hypersecretion.
2. A 3-month-old otherwise well infant presents with the chief complaint of regurgitating four times per day. You counsel the family that there is a 95% chance the infant will "outgrow his reflux" by what age?
   A. 6 months.
   B. 9 months.
   C. 12 months.
   D. 18 months.
   E. 24 months.
3. You suspect that a 6-month-old girl has eosinophilic esophagitis rather than gastrointestinal reflux because she manifests which symptom?
   A. apnea.
   B. dysphagia.
   C. epigastric pain.
   D. hematemesis.
   E. regurgitation.
4. You suspect that a teenage patient of yours has achalasia. Which of the following tests would be most useful in evaluation for that condition?
   A. endoscopy with biopsy.
   B. esophageal manometry.
   C. esophageal pH monitoring.
   D. MII with pH monitoring.
   E. radionuclide scintigraphy.
5. You see a 12-year-old overweight boy with heartburn and reflux symptoms in your clinic. After discussion of weight loss and lifestyle modifications, you elect to start a proton pump inhibitor (PPI). Of the following, which is a commonly reported idiosyncratic reaction to PPI therapy in children?
   A. anemia.
   B. B12 deficiency.
   C. headache.
   D. rectal bleeding.
   E. skin rash.

Gastroesophageal Reflux

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