Gastroesophageal Reflux

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Objectives

After completing this article, readers should be able to:

1. Delineate the difference between physiologic reflux and gastroesophageal reflux disease.
2. Describe the signs and symptoms of reflux.
3. Discuss the methods of evaluating and diagnosing reflux.
4. Use appropriate therapies for pediatric gastroesophageal reflux disease.

Introduction

Gastroesophageal reflux is a common disorder in the pediatric population. The spectrum of symptom presentation varies substantially, and the disease manifestations can differ, depending on the patient's age and health status. For example, a healthy 3-month-old infant can present with regurgitation in the absence of other symptoms. On the other hand, a 14-year-old child who has cerebral palsy may present with anemia, food refusal, and recurrent aspiration pneumonia. The first case is an example of physiologic gastroesophageal reflux (GER), the second of gastroesophageal reflux disease (GERD). The challenges in managing reflux lay in determining what is physiologic and what is pathologic.

GER is defined as the passage of gastric contents into the esophagus, which can be a normal physiologic process in many infants. GERD, on the other hand, is defined as symptoms or complications of GER. Regurgitation is defined as the passage of gastric contents into the oral pharynx. Vomiting is defined as expulsion of the refluxed gastric contents from the mouth. Rumination is a rare functional disorder characterized by voluntary, habitual regurgitation of stomach contents into the mouth for self-stimulation. The material can be rechewed and either reswallowed or brought out of the mouth. Rumination in infants may signify a psychiatric disorder or social deprivation.

GER is common in infancy. A report on its prevalence in 948 infants in Chicago revealed that 50% of infants ages 0 to 3 months regurgitated at least once daily, 67% at age 4 months, and 5% by age 12 months. (1) Thus, the majority of infants who have GER eventually "outgrow" their reflux. In children 3 to 17 years of age, the prevalence of the different symptoms of reflux range between 1.4% and 8.2%. (2) In a survey of predominantly African-American high school students, the prevalence of esophageal symptoms of GERD (heartburn, regurgitation, and dysphagia) was 33%, and the association with smoking was significant. (3)

Mechanism and Pathophysiology of Reflux

Reflux occurs because of the transient relaxation of the lower esophageal sphincter. The short infant esophagus that has limited volume and the predominantly recumbent position of infants facilitate the regurgitation of gastric contents. In addition, delayed gastric emptying and increased abdominal pressure contribute to the development of GER. Some reports of increased familial concordance for GERD symptoms, hiatal hernia, erosive esophagitis, Barrett esophagus, and esophageal adenocarcinoma propose chromosome 13 locus (13q14) as being associated with severe pediatric GERD. (4) Chromosome 9 locus has been proposed as having an association with infantile esophagitis. (5)

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Table 1. Common Presenting Symptoms of GER/GERD

Infants and Young Children

- Recurrent vomiting
- Poor weight gain
- Irritability
- Dysphagia or feeding refusal
- Asthma
- Recurrent pneumonia
- Upper airway symptoms
- Apnea or apparent life-threatening event

Older Children and Adolescents

- Regurgitation
- Heartburn and retrosternal chest pain
- Dysphagia
- Asthma or chronic cough
- Recurrent pneumonia
- Anemia and hematemesis

Manifestations of Reflux

Common presenting signs and symptoms of reflux can differ by age (Table 1). The most common manifestation of GER in infants is vomiting. Fortunately, only a small number of infants develop GERD with complications such as failure to thrive, irritability, dysphagia, odynophagia, and arching of the back during feedings. Infants who have GERD may develop apparent life-threatening events (ALTEs), reactive airway disease, recurrent aspiration pneumonia, and chronic cough. Rarely, GERD results in stereotypic repetitive stretching and arching movements that may be mistaken for atypical seizures or dystonia, a condition known as Sandifer syndrome.

In preschool-age children, GERD may present as intermittent vomiting, food refusal, or respiratory complications. Older children are more likely to have adult-type symptoms such as heartburn, regurgitation, dysphagia, or food impaction. More severe inflammation may cause chronic blood loss with anemia and hematemesis. Chronic inflammation rarely leads to the development of the premalignant condition known as Barrett esophagus.

Differential Diagnosis of Reflux in Infants and Children

One of the challenges facing the practitioner caring for children is to distinguish vomiting due to GER or GERD from vomiting caused by other disorders. Diseases affecting a variety of systems can produce vomiting. A detailed history and physical examination can help eliminate many of these disorders. Table 2 summarizes some of the common causes of nonreflux-related emesis. Among the warning signs suggestive of nonreflux disease is bilious or forceful vomiting, which can be caused by bowel obstruction or pyloric stenosis. Other warning signals include hematemesis, hematochezia, diarrhea, abdominal tenderness or distention, onset of vomiting after 6 months of age, fever, lethargy, hepatosplenomegaly, seizures, macrocephaly, or microcephaly.

Table 2. Common Nonreflux Causes of Vomiting

Infections

- Sepsis
- Meningitis
- Urinary tract infection
- Otitis media

Obstruction

- Pyloric stenosis
- Malrotation
- Intussusception

Gastrointestinal

- Eosinophilic esophagitis
- Peptic ulcer disease
- Achalasia
- Gastroparesis
- Gastroenteritis
- Gall bladder disease
- Pancreatitis
- Celiac disease
- Pill esophagitis
- Crohn disease

Metabolic/Endocrine

- Galactosemia
- Fructose intolerance
- Urea cycle defects
- Diabetic ketoacidosis

Toxic

- Lead poisoning

Neurologic

- Hydrocephalus and shunt malfunctioning
- Subdural hematoma
- Intracranial hemorrhage
- Tumors
- Migraine

Allergic

- Dietary protein intolerance

Respiratory

- Posttussive emesis
- Pneumonia

Renal

- Obstructive uropathy
- Renal insufficiency

Cardiac

- Congestive heart failure and disease

Recreational drugs and alcohol consumption

Pregnancy

Other

- Overfeeding
- Self-induced emesis

Diagnostic Approach to GER

History and Physical Examination

A history and examination are the first and most important steps in evaluating a child who has reflux. It is important to address questions directly to a child who is

Table 3. Important Aspects in the History for Evaluating Reflux

Vomiting
• Presence of blood
• Presence of bile
• Presence of pain and irritability
• Presence of forceful emesis
• Frequency and amount of emesis
• Association with constitutional symptoms (fever, lethargy) or other gastrointestinal manifestations
Feeding History
• Frequency of feeding
• Volume of feeding
• Preparation of formula
• Change in feeding pattern
• Position and behavior of infant during feeding
• Type of feeding
Social History
• Tobacco use
• Alcohol use
Past Medical History
• Neurologic disease
• Prematurity
• Growth or developmental problems
• Past surgery and hospitalizations
• Respiratory or ear, nose, throat diseases
• Psychological factors (stressful events)
Family History
• Family history of reflux and its severity
• Other gastrointestinal diseases such as celiac disease and *Helicobacter pylori* infection
Medication History

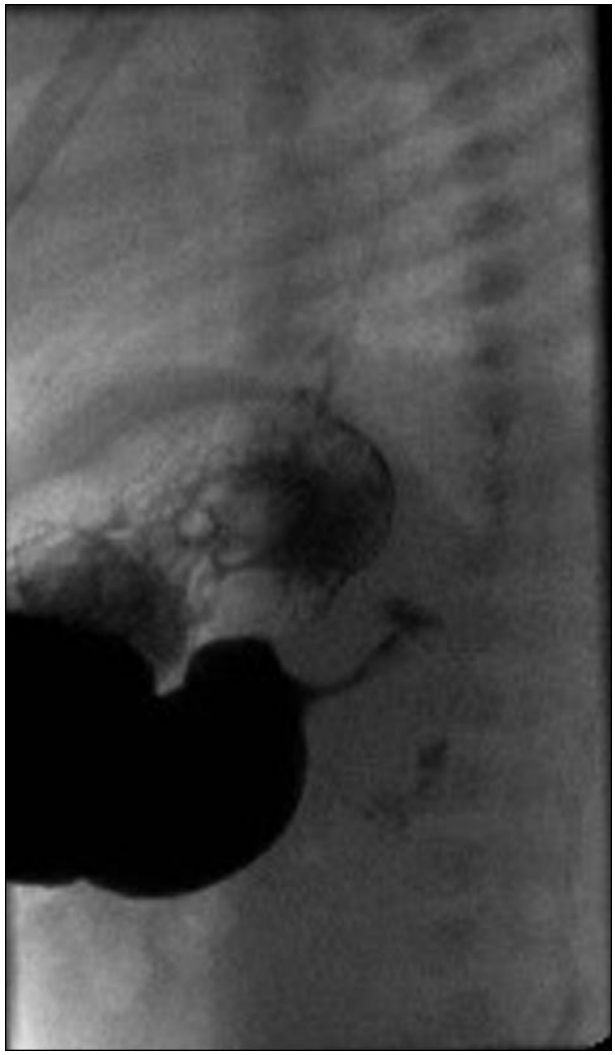

Figure 1. Upper gastrointestinal radiographic series in a 4-month-old boy who has vomiting and failure to thrive shows delay in gastric emptying and an elongated pyloric channel consistent with pyloric stenosis.

able to communicate. Important elements of the history are listed in Table 3. These findings can help to delineate reflux disease or point to nonreflux conditions.

Diagnostic Studies

For most infants and children who have GER, a history and physical examination are sufficient to diagnose nonpathologic GER reliably. Diagnostic testing should be saved for the child who has complications or when the diagnosis of GERD is in question. The decision to select a specific diagnostic test is based on the clinical question that needs to be answered. For example, a child suspected of having esophagitis needs esophageal biopsies, whereas a child who has pulmonary symptoms and no clinical GERD symptoms may benefit from a pH probe study.

CONTRAST RADIOGRAPHS. The upper gastrointestinal (UGI) series is a common modality for evaluating the UGI tract. A positive contrast agent, such as barium, is used to opacify the UGI tract, and fluoroscopic and radiographic images are obtained, yielding both functional and structural information. Examples of conditions that can be identified on UGI imaging are malrotation, esophageal or antral webs, pyloric stenosis, and a congenital band around the lower esophagus known as a Schatzki ring, which is associated with hiatal hernia (Figs.

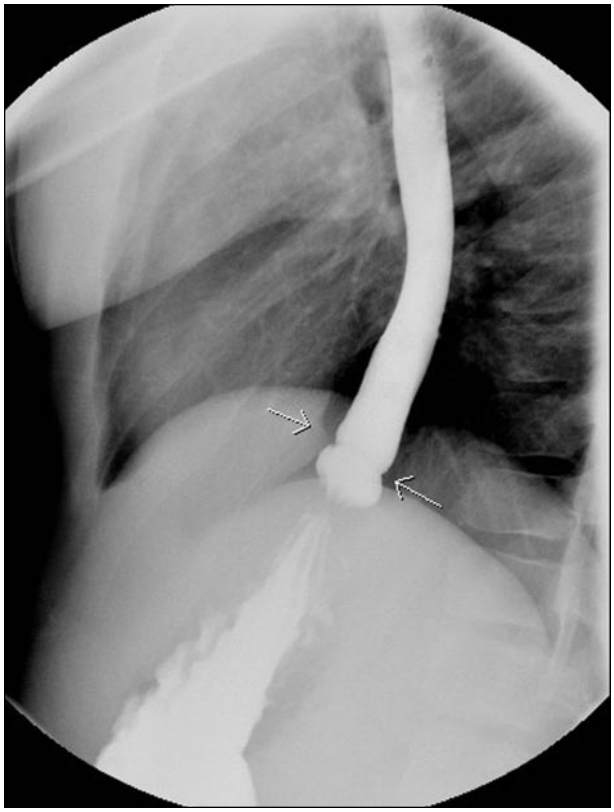

Figure 2. A 12-year-old boy who has dysphagia has an indentation in the distal esophagus (arrows) consistent with a Schatzki ring, a congenital lower esophageal ring associated with hiatal hernia.

1 and 2). In general, UGI contrast studies cannot discriminate between physiologic and nonphysiologic reflux.

ESOPHAGEAL pH MONITORING. Esophageal pH monitoring measures the frequency and duration of acid reflux episodes into the esophagus through transnasal placement of microelectrodes that continuously sense the presence of acid. This is used widely as an index of esophageal acid exposure and can be useful in determining the presence of a temporal association between acid reflux and frequently occurring symptoms and for assessing the adequacy of dosage of histamine-2 receptor antagonists (H2RAs) or proton pump inhibitors (PPIs) in children whose GERD symptoms are not improving. The reproducibility of the reflux index for this test ranges from 69% to 85%, and it cannot detect nonacidic reflux. If apnea is suspected, simultaneous correlation with respiratory efforts and chest wall movement is necessary.

An alternative to the traditional esophageal pH monitoring employing a nasal catheter wireless system is being evaluated in older children. A small capsule containing a radio transmitter can be placed endoscopically in the distal esophagus. The capsule can monitor pH wirelessly for 48 hours. The capsule then detaches from the esophageal wall and passes through the GI tract.

ENDOSCOPY. Upper endoscopy allows macroscopic and microscopic evaluation of the esophagus and the UGI tract (Fig. 3). The severity of esophagitis can be evaluated, as can the presence of complications such as esophageal strictures or Barrett esophagus. Endoscopy allows exclusion of other conditions that mimic GERD, such as eosinophilic esophagitis, pill esophagitis, or Crohn disease. White specks have been reported as a specific esophageal finding for eosinophilic esophagitis (Fig. 4). (6) The sensitivity of white specks in the esophageal mucosa was only 30%, but the specificity was 95%. The stomach and duodenum can be evaluated for disorders such as peptic ulcer and celiac disease. Visual inspection alone may not be adequate because macroscopic diagnosis does not correlate with histologic features 50% of the time. (7) Therefore, it is useful to obtain biopsies at the time of endoscopy to detect microscopic disease and differentiate between reflux and nonreflux inflammation.

MULTICHANNEL INTRALUMINAL IMPEDANCE (MII). MII is a new technology that allows detection of reflux without measuring pH. It captures changes in the electrical impedance during the movement of a bolus between the measuring electrodes. MII allows detection of the direction of the moving bolus, thus distinguishing a swallow from a regurgitated bolus. A pH sensor is included as an additional channel. Some data are being published regarding normal impedance values for preterm infants, (8) but validated standards for different pediatric populations are still lacking. In its current state, the significance of this technology is the correlation of events, especially respiratory, with nonacid reflux.

SCINTIGRAPHY. This technology is based on the consumption of a technetium-labeled feeding. A nuclear image scan is performed to detect technetium in the GI or respiratory tract. The scan allows the measurement of gastric emptying, detects acid and nonacid reflux, and may detect aspiration in 60-minute or delayed films. The sensitivity of this test is low, ranging from 15% to 59%, but the specificity is higher at 33% to 100%.

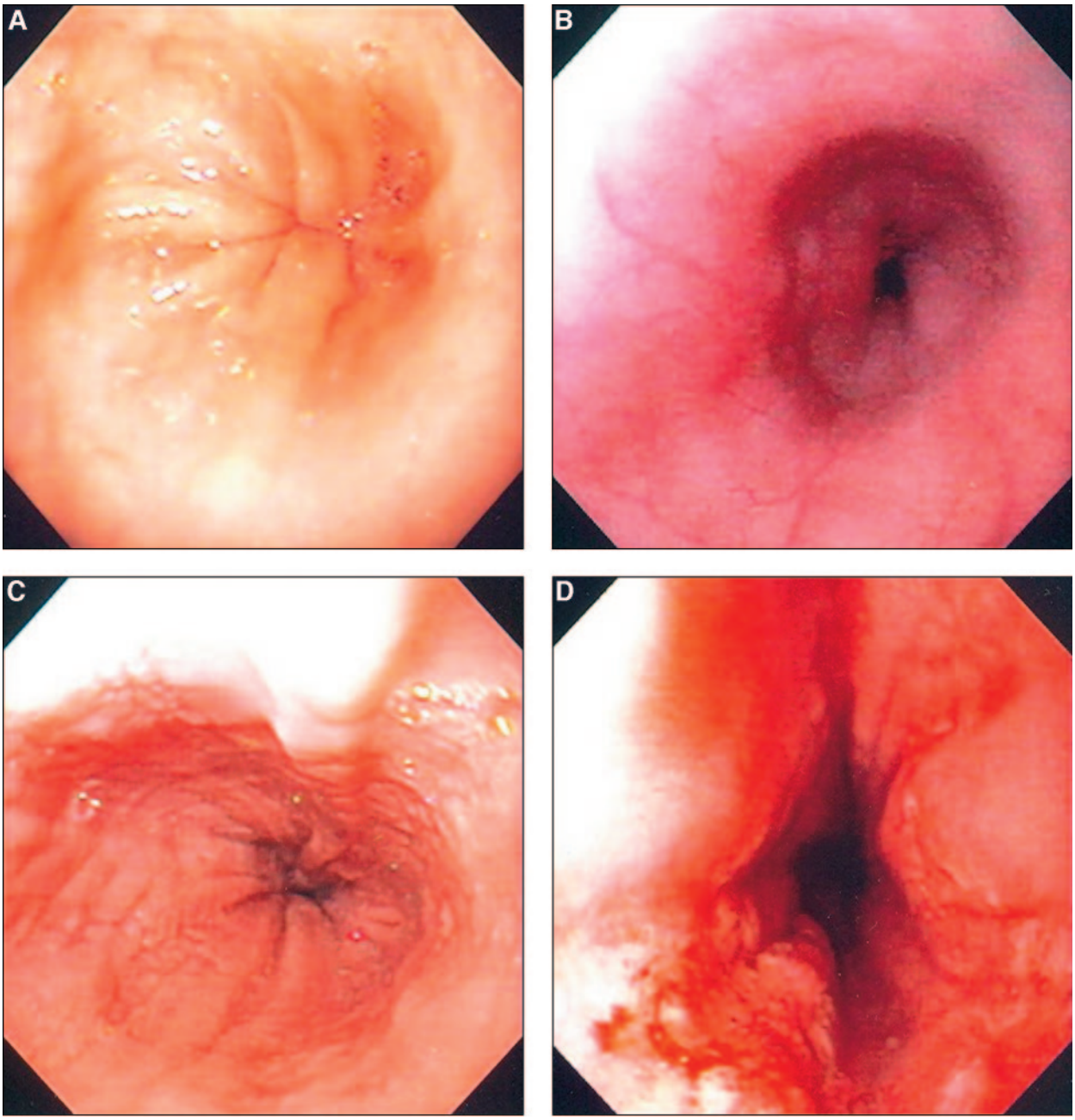

Figure 3. Endoscopic findings in GERD. A. Normal esophageal mucosa. B. Mild erythema. C. Moderate thickening and erythema of the mucosa. D. Severe erosive disease.

Complications of GERD

Complications of GERD are numerous and manifest as both esophageal and extraesophageal disorders.

Respiratory Complications

Pulmonary complications of GERD include asthma, bronchitis, apnea, ALTE, chronic cough, and recurrent aspiration pneumonia. Ear, nose, and throat complications include hoarseness, laryngitis, sinusitis, dental erosions, and recurrent otitis media. There is an increased association of such disorders in children who have GERD compared with other children. For example, a study associating asthma with GERD showed a 13.2% prevalence with reflux versus a 6.8% prevalence in children

Figure 4. White specks and longitudinal and circular markings of the esophagus in a child who has severe eosinophilic esophagitis.

who had no reflux ($P<0.0001$). (9) The same investigators found similar associations with pneumonia, sinusitis, and laryngitis. The nature of the relationship between respiratory disorders and GERD is controversial. Both GERD and asthma are common pediatric disorders that can coexist. However, studies show that GERD can be a contributing factor in patients who have asthma, especially in severe refractory cases. Other studies suggest that reflux occurs as a secondary phenomenon.

Will medical treatment of GER disease improve symptoms of asthma? Studies suggest that approximately two thirds of children who have asthma improve with reflux therapy. (10)(11)(12) Such improvement can be quantified as a reduction of dosages of bronchodilator therapy or anti-inflammatory medications, including inhaled or systemic steroids. Therefore, in a subset of patients who have asthma and reflux, medical therapy for reflux is warranted.

Chronic aspiration occurs when airway protective mechanisms fail and gastric or oral contents are seen inside the lungs. Consequently, severe pneumonia, interstitial lung disease, and pulmonary fibrosis can occur. Neurologically impaired children are at higher risk for developing reflux and aspiration.

Nonrespiratory Complications

Chronic esophageal exposure to acid can result in inflammation and subsequent development of reflux esophagitis, esophageal strictures, Barrett esophagus, and adenocarcinoma. In severe chronic cases, UGI bleeding and anemia may develop. Children who are neurologically impaired are at greater risk for developing such complications. Barrett esophagus and esophageal adenocarcinoma rarely develop in the pediatric age group. In addition to neurologic impairment, other risk factors for long-term complications of GERD include lifestyle factors such as obesity, size and gestational age at birth, and repaired esophageal atresia. Adult studies correlate body mass index not only with severity of symptoms such as heartburn, erosive esophagitis, and hiatal hernia, but with severe complications such as Barrett esophagus and cancer.

GERD in the Neurologically Impaired

GERD occurs more frequently in neurologically impaired children, whose reflux often is resistant to standard medical therapy and frequently requires surgical correction through fundoplication. Moreover, such children are at higher risk for developing complications related to their surgery, with higher rates of additional operations. A report by Del Giudice and associates (13) showed a high prevalence of GERD-related disease in children who had cerebral palsy. Symptomatic GI disease was seen in as many as 92% of the children. Swallowing disorder and dysfunction of oral and pharyngeal phases was found in 93% of patients. Vomiting, regurgitation, and abdominal pain occurred in 33% of patients, and chronic pulmonary aspiration occurred in about 40%. Interestingly, 91% of those patients studied had reflux on pH probe study or biopsy-proven esophagitis, and almost 67% had a significant delay in emptying (by scintigraphic gastric emptying studies).

Prognosis

GER in infants carries a favorable prognosis because most children tend to "outgrow" their reflux symptoms by 12 months of age. Children who have neurologic impairment, prematurity, obesity, esophageal atresia, or a strong family history of severe complicated GERD are at higher risk for developing complications and carry a poorer prognosis compared with infants who have physiologic reflux.

Treatment

Management Strategies

The goal of treating children who have GERD is to eliminate symptoms, heal the esophagitis, and manage and prevent complications. In physiologic reflux, reassur-

ing the family may be the only intervention necessary for this usually self-limited condition.

The rationale for empiric therapy in adults who have GERD is widely accepted. Empiric treatment trials with omeprazole have been reported for treating cough, heartburn, noncardiac chest pain, and dyspepsia in adult patients. In pediatric patients, the decision to proceed to empiric therapy has not been validated for any symptom presentation. However, when presenting symptoms are typical, the diagnosis can be based on the history, and additional diagnostic investigation is unlikely to affect the prognosis or management. If pharmacotherapy is warranted, most patients respond to treatment with acid suppression. Therefore, a therapeutic trial may be cost-effective. Currently, PPIs help many patients who have severe GERD.

A prompt diagnostic evaluation is indicated for patients presenting initially with unusual or serious complications, including emesis, failure to thrive, dysphagia, or severe respiratory complications. Diagnostic investigation is warranted when patients either do not respond to therapy or have an unusual course. No single test is appropriate for all patients suspected of having GERD. Which test to order depends on the clinical presentation and the questions the clinician would like to have answered.

The natural history of physiologic reflux in most infants is resolution as lower esophageal sphincter function matures.

Lifestyle changes can be helpful for children who have mild disease. Pharmacologic therapy is advocated for the child who has significant reflux disease, especially in the presence of complications. Because neurologically impaired children develop GERD more frequently and are more likely to develop GERD-related complications, management of these children may need to be more aggressive.

Reassurance and Lifestyle Changes

The natural history of physiologic reflux in most infants is resolution as lower esophageal sphincter function matures. Reassuring and educating the family about this disorder are keys for management. In an otherwise healthy infant, no testing or therapeutic intervention is necessary.

Infants who have GER do not benefit from changing formula protein. However, in a subset of infants who vomit due to milk protein intolerance, some authorities advocate a 2-week trial of hypoallergenic formula. Thickening the milk or formula with agents such as rice cereal does not improve GER index scores but can decrease the number of episodes of vomiting. Thickening the formula with thickening agents such as rice cereal increases the caloric density of the feedings, which may be beneficial in underweight infants who have reflux.

A number of pH probe studies have demonstrated a decrease in GERD episodes for infants placed in the prone position. However, the American Academy of Pediatrics advocates the supine position for infants to reduce the risk for sudden infant death syndrome (SIDS). Therefore, prone positioning during sleep is considered only when the risk of death due to GERD outweighs the potential increased risk of SIDS.

Mild symptoms of GERD in the absence of complications may be managed by lifestyle changes for older children and adolescents. Most of the evidence is extracted from adult studies. The recommendations include weight loss for obese patients and avoidance of tobacco and alcohol. Limited pediatric evidence suggests that avoiding caffeine, chocolate, and spicy foods that provoke symptoms is beneficial.

Pharmacologic Options

ANTACIDS. Antacids, which buffer the acidic contents of the stomach, can be used for short-term therapy and relief of symptoms. Aluminum-containing antacids should be prescribed with caution in infants due to potential development of adverse effects such as neurotoxicity, anemia, and osteopenia.

H2RAs. H2RAs inhibit histamine-2 receptors on the parietal cells. Cimetidine, famotidine, nizatidine, and ranitidine are examples of drugs in this family. A number of studies demonstrate efficacy of these drugs in treating esophagitis, but the healing rate of erosive esophagitis is 60% to 70%, which is less than the healing rate for PPIs. Table 4 provides doses and adverse effects of H2RAs.

Table 4. Pediatric and Adult Doses and Adverse Effects of Histamine-2 Receptor Antagonists

Drug	Pediatric Dose	Adult Dose	Adverse Effects
Cimetidine	40 mg/kg per day divided TID	400 mg QID or 800 mg BID	Hypotension, gynecomastia, reduced hepatic metabolism of other drugs, neutropenia, agranulocytosis, and thrombocytopenia
Famotidine	1 mg/kg per day divided BID	20 to 40 mg BID	Headache, dizziness, constipation, diarrhea
Nizatidine	7 to 8 mg/kg per day divided BID/TID	150 mg BID	Headache, dizziness, constipation, diarrhea, nausea, anemia, urticaria
Ranitidine	7 to 8 mg/kg per day divided BID/TID	150 mg BID	Headache, dizziness, fatigue, irritability, rash, constipation, diarrhea, thrombocytopenia, elevated transaminases

PROKINETIC AGENTS. The primary underlying phenomenon contributing to GER is transient relaxation of the lower esophageal sphincter. Because prokinetic agents increase the tone of the sphincter, they could, theoretically, be effective drugs. However, studies have failed to demonstrate that prokinetic agents consistently reduce the frequency of reflux, suggesting that they do not affect the frequency of transient relaxations of the lower esophageal sphincter. Nevertheless, children can benefit from prokinetic therapy if gastric emptying is delayed, as evidenced by double-blind studies and randomized comparison studies for prokinetic agents such as cisapride, metoclopramide, and erythromycin.

SURFACE AGENTS. Sucralfate acts by adhering to peptic lesions, protecting the mucosal surface from the acidic or digestive enzyme effects. This agent has been shown to have similar efficacy as H2RAs in the treatment of esophagitis. Because sucralfate contains aluminum, the potential adverse effects of aluminum, especially in infants, need to be considered.

Similarly, sodium alginate forms a surface gel that decreases the regurgitation of gastric contents into the esophagus and protects the esophageal mucosa. Efficacy studies have demonstrated conflicting results. The formulation used in most published studies is not available in the United States.

PPIs. PPIs deactivate the H+, K+ATPase pumps. Their efficacy is related to their ability to maintain higher gastric pH for a prolonged period of time and suppress the meal-induced acid secretion that did not occur with H2R blockade. The use of PPIs is indicated when GERD is refractory to therapy with H2RAs. The inhibition of acid secretion in the stomach is associated with lower gastric volumes, facilitating gastric emptying and decreasing the volume of refluxed material. Omeprazole and lansoprazole are the PPIs studied most frequently in

Table 5. Pediatric and Adult Doses and Adverse Effects of Proton Pump Inhibitors

Drug	Pediatric Dose	Adult Dose	Adverse effects
Omeprazole	1.0 mg/kg per day divided bid OR 10 mg QD if weight <20kg 20 mg if weight=20 kg	20 mg QD	Headache, diarrhea, abdominal pain, nausea, rash, vitamin B12 deficiency, constipation
Lansoprazole	15 mg QD (weight <30 kg) OR 30 mg QD (>30 kg)	15 to 30 mg QD	Headache, nausea, constipation, diarrhea, abdominal pain, proteinuria, hypotension, elevated transaminase
Esomeprazole	Not available	20 to 40 mg QD	Headache, diarrhea, nausea, abdominal pain, flatulence
Pantoprazole	Not available	40 mg QD	Headache, diarrhea, nausea, abdominal pain
Rabeprazole	Not available	20 mg QD	Headache, diarrhea, nausea, abdominal pain

children. The pharmacokinetic profiles of PPIs are similar to those in adults. However, because children have higher metabolic activities than adults, they need higher doses on a per-kilogram basis (Table 5). The effective dose of PPIs ranges from 0.5 to 3.3 mg/kg per day.

Surgical Treatment

Antireflux surgery is indicated for children who have significant complications of GERD and have failed to respond to adequate medical therapy. Surgical treatment can be an attractive option because it can be curative, avoiding the need for long-term medication use, but the failure rates to control symptoms are high, and morbidity and occasionally death are reported in the literature. Complications related to antireflux surgery occur at higher proportions in neurologically impaired children, those who have repaired esophageal atresia, and children afflicted with chronic lung disease compared with otherwise normal children. Recognition of recurrent GERD after antireflux surgery requires a high degree of suspicion and the use of more than one test. Barium contrast studies are useful for identifying the fundoplication wrap or identifying a stricture. However, pH probe monitoring and endoscopy are required to determine the functional adequacy of the surgery in preventing acid reflux and esophagitis.

Summary

GER is a common disorder in pediatrics. Most infants develop the physiologic type and need minimal intervention because the condition typically resolves as they become older. Diagnostic testing should be tailored to the clinical concern for each child. Current medical therapy usually controls gastric acid secretion; surgical therapy is indicated for children who have significant reflux complications resistant to medical therapy. Children who are neurologically impaired are especially at risk for developing reflux and reflux-related complications.

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PIR Quiz

Quiz also available online at www.pedsinreview.org

11. Which of the following symptoms of gastroesophageal reflux is more common in older children and adolescents than in infants and young children?

    A. Apparent life-threatening event.
    B. Asthma.
    C. Failure to thrive.
    D. Hematemesis.
    E. Recurrent pneumonia.

12. A 4-month-old boy is referred to you because of recurrent periods of difficulty breathing with occasional apnea and mild cyanosis, which resolve spontaneously after 10 to 15 seconds. His mother reports that he occasionally spits up after feedings. On physical examination, he appears healthy and has gained weight well. You suspect that reflux is the cause of his symptoms. Which is the *best* test to help you confirm your suspicions?

    A. Endoscopy with stomach and esophageal biopsy.
    B. Esophageal pH monitoring and correlation with respiratory pattern.
    C. Gastric emptying nuclear scan.
    D. Multichannel intraluminal impedance test.
    E. Upper gastrointestinal radiographic series.

13. A 7-year-old boy who has recurrent asthma exacerbations is brought to the clinic by his mother, who is frustrated by his frequent symptoms. Additional history reveals that he has frequent chest pain after eating and occasionally reports regurgitation of food and an "acid taste" in his mouth. His weight is at the 40th percentile, his lungs are clear bilaterally, and the remainder of his physical examination findings are normal. You suspect that reflux may be contributing to his recurrent wheezing. Which of the following is the *most* appropriate next therapeutic intervention?

    A. Administration of antacids when he has chest pain.
    B. Avoidance of caffeine and chocolate.
    C. Daily erythromycin therapy.
    D. Daily omeprazole therapy.
    E. Daily ranitidine therapy.

14. A worried mother brings in her 5-month-old daughter because of frequent spitting up after feedings. She denies respiratory difficulty, apnea, cyanosis, or coughing with episodes, but she is frustrated because she constantly has to change the girl's clothing because of the spitting up. Her current feeding schedule includes baby foods and six bottles of cow milk formula per day. The girl's weight and height are at the 50th percentile, she appears alert and smiling, and findings on physical examination are normal. Which of the following is the *most* appropriate step in management?

    A. Advise the mother always to place the infant prone while sleeping.
    B. Discontinue all baby foods until spitting up resolves.
    C. Reassure the mother that the infant is healthy and that symptoms should resolve.
    D. Start therapy with a prokinetic agent, such as metoclopramide.
    E. Switch the infant to a soy-containing formula.

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