Gastroesophageal Reflux in Infants and Children

Series Editor:
Franklin Trimm, MD
Professor and Vice Chair of Pediatrics
Director, Pediatric Residency Program
University of South Alabama College of Medicine
Mobile, AL.

Contributors:
Erwin D. Sanchez, MD
Chief Resident
Department of Pediatrics
University of South Alabama College of Medicine
Mobile, AL.

David A. Gremse, MD
Professor and Interim Chair of Pediatrics
Director, Division of Pediatric GI/Nutrition
University of South Alabama College of Medicine
Mobile, AL.

Table of Contents

Introduction ........................................ 1
Clinical Presentation and Prognostic Features .... 1
Management ........................................ 3
Case Resolution .................................... 9
References ......................................... 9

Cover Illustration by Stacey Caiazzo
INTRODUCTION

Gastroesophageal reflux (GER) is the term used to describe the passage of gastric contents into the esophagus. GER in infants is a common, self-limited process that usually resolves by 12 months of age. Vomiting is the most common presenting symptom, occurring in 50% of all infants.\(^1\) The incidence of recurrent vomiting peaks at age 4 months, when it occurs in 67% of infants, then declines to affect only 5% to 10% of infants at age 12 months.\(^1\) Although regurgitation associated with simple GER is common in healthy infants, a smaller proportion of infants will develop complications of GER (eg, esophagitis) that produce symptoms of gastroesophageal reflux disease (GERD). The clinical presentation of normal regurgitation in infants is compared to that of GERD in infants and children in Table 1.

The prevalence of GERD, as documented by distal esophageal pH monitoring in a population of unselected infants, is estimated to be 8%.\(^2\) The severity of symptoms varies widely, from isolated regurgitation not associated with any other symptoms to irritability and persistent emesis to persistent esophagitis. The high incidence of GER during infancy results in GERD occurring in association with other problems of infancy, such as failure to thrive, persistent respiratory problems, and apnea. In some instances, GERD is causally related to these other symptoms, but in many other cases, respiratory problems and apnea occur simultaneously with GERD merely by chance.

The “GERD iceberg” has been used to compare the epidemiology and clinical presentation of GERD in adults and infants (Figure 1). The bottom of the iceberg represents the most common symptoms of mild GERD, whereas the tip represent patients with more severe disease requiring subspecialty evaluation.

CLINICAL PRESENTATION AND PROGNOSTIC FEATURES

INITIAL CASE PRESENTATION

A 2-month-old boy has excessive “spitting up” after feeding. His emesis does not contain blood or bile. He is irritable after eating and awakens frequently at night. The infant is exclusively formula-fed, he is not on any medications, and his past medical history is unremarkable. His weight is at the tenth percentile, and the results of physical examination are normal except for diaper dermatitis.

- What is the most appropriate initial work-up and management of this patient?

CLINICAL FEATURES OF GASTROESOPHAGEAL REFLUX

It is useful to distinguish the manifestations of GERD in infants (younger than 1 year) from those in children older than 1 year and adolescents. The incidence of GERD is reportedly lower in breast-fed infants compared to formula-fed infants.\(^3\) The clinical presentation of GERD in infants may include symptoms of regurgitation, coughing, choking, upper respiratory symptoms, and lower respiratory symptoms.\(^4\) Symptoms of GERD in preschool children include intermittent vomiting, abdominal pain, unexplained nighttime awakening, feeding resistance, or respiratory symptoms. Older children have a clinical presentation similar to that of adults, which may include heartburn, epigastric pain, chest pain, nocturnal pain, dysphagia, odynophagia, and water brash.

Regurgitation is the most common presentation of infantile GER\(^5\) but occurs rarely in older children and adults. The character of regurgitation varies from drooling of gastric contents to effortless emesis and occasionally to projectile vomiting.\(^5\) Infants with significant regurgitation or emesis must be evaluated for possible anatomic, metabolic, infectious, or neurologic causes.

Because infants cannot talk, crying and irritability or arching of the back may be the only indications of esophagitis, which is diagnosed by esophagoscopy with biopsy.\(^6\) Children with esophagitis may develop an aversion to food as they begin to associate eating with pain.\(^7\) This aversion, together with the parents’ resistance to feeding infants who are repeatedly regurgitating and substantial nutrient losses resulting from emesis, all contribute to malnutrition. Although malnutrition occurs infrequently as a complication of GERD in infants, its presence is more likely to develop in infants with esophagitis. Erosive esophagitis can lead to chronic blood loss with anemia,
hematemesis, hypoalbuminemia, and melena. Other infrequent presentations of GERD in children include Sandifer’s syndrome, which is a stereotypical stretching or arching movement in response to esophageal pain that may be mistaken for atypical seizure activity.

The cause-and-effect relationship between GERD and respiratory symptoms in children is often difficult to determine. In the respiratory tract, complex reflex responses to the gastric refluxate occur in children by 3 mechanisms. First, the aspirated material may cause luminal mechanical obstruction. In addition, neurally mediated signals caused by the presence of refluxate in the local airway or distal esophagus generate afferent signals that stimulate mucus secretion, edema, and bronchial smooth muscle contraction. Finally, aspiration stimulates the chemical release of inflammatory mediators, which cause further respiratory luminal obstruction. These responses can result in signs of upper airway and lower airway obstruction. In infants, activation of laryngeal chemoreflexes associated with regurgitation of gastric contents into the pharynx may be associated with episodic prolonged apnea.

DIFFERENTIAL DIAGNOSIS

Other disorders should be considered before diagnosing a patient with GERD as the principal cause of the symptoms. The differential diagnosis includes systemic and gastrointestinal disorders. The systemic disorders include urinary tract infection; central nervous system disorders, such as hydrocephalus and meningitis; metabolic disorders, such as renal tubular acidosis, urea cycle defect, and hypocalcemia; and ingestion of drugs or toxins. Disorders affecting the gastrointestinal tract include pyloric stenosis, malrotation, milk protein allergy, peptic ulcer disease, and hepatitis.

DIAGNOSTIC STUDIES

In most cases of GER, no diagnostic studies are needed, and the diagnosis is made by history. The diagnostic tools most commonly used to diagnose or to evaluate the severity of GER are: upper gastrointestinal contrast imaging (upper GI series or barium swallow), esophageal pH monitoring, endoscopy and esophageal biopsy, esophageal manometrics, and scintigraphy.

Upper Gastrointestinal Series

The upper GI series is useful in the evaluation of GERD to screen for possible anatomic abnormalities of the upper gastrointestinal (GI) tract, including: hiatal hernia, esophageal stricture, atypical pyloric stenosis, duodenal web, or antral web. The sensitivity of barium swallow imaging in detecting GERD can be high, but it may not correlate with the severity of symptoms; many infants with mild symptoms of GER demonstrate reflux of barium into the esophagus.

Esophageal pH Monitoring

The esophageal pH probe is a thin, flexible probe with a pH-sensitive electrode that is placed in the distal esophagus. The probe can detect variations in the esophageal pH, measure the time it takes for an episode of acid reflux to be cleared and, over a given period of time, be used to record the frequency of episodes of acid reflux in the distal esophagus.

Abnormal results of esophageal pH monitoring correlate with the presence of endoscopic and histologic esophagitis in children. Pediatric patients with biopsy-proven esophagitis have abnormal results of esophageal pH monitoring in 95% of cases. However, not all pediatric patients with GER have esophagitis. Esophagitis is present in approximately 50% of children with abnormal esophageal pH monitoring results.

The North American Society for Pediatric Gastroenterology and Nutrition (NASPGN) published a statement with indications for esophageal pH monitoring in infants in 1995. Esophageal pH monitoring is useful in associating a specific time-related clinical problem with atypical symptoms of GERD in infants and children, such as chronic cough, stridor, wheezing, recurrent pneumonia, apnea, irritability, or opisthotonic posturing; and for evaluating pharmacologic or surgical therapy.

| Table 1. Clinical Presentation of Regurgitation versus GERD in Children |
|-----------------------------|-----------------------------|
| Regurgitation               | GERD                        |
| Regurgitation with normal weight gain | Regurgitation with poor weight gain |
| No irritability with or after feedings | Constant irritability |
| No significant respiratory symptoms | Lower chest pain, dysphagia, pyrosis in children |
|                               | Hematemesis and iron-deficiency anemia |
|                               | Apnea and cyanosis in infants |
|                               | Wheezing |
|                               | Recurrent pneumonia |
|                               | Cough |
|                               | Stridor |
| No neurobehavioral symptoms  | Neck tilting in infants |
|                               | Opisthotonic posturing |
|                               | Sandifer’s syndrome |

GERD = gastroesophageal reflux disease.
The major disadvantage of esophageal pH monitoring is that it is unable to determine the volume of refluxate in the distal esophagus. Another limitation is that it does not detect nonacidic reflux episodes that occur postprandially in infants because the pH of breast milk and of standard milk formula is higher than 6. To enhance the sensitivity of the test, some investigators use apple juice (pH 3.5) alternating with breast milk or formula. Infants with simple regurgitation generally do not need esophageal pH monitoring.

Endoscopy and Esophageal Biopsy

Esophagoscopy with biopsy may be useful to evaluate GER that is unresponsive to medical therapy. Esophagoscopy is the most accurate test to diagnose esophagitis. This test is indicated in patients with GERD and poor weight gain, irritability, recurrent pneumonia, or hematemesis. In addition, upper endoscopy is useful to assess for other causes of abdominal pain and vomiting in pediatric patients, such as esophageal or antral webs, Crohn’s esophagitis, and eosinophilic or infectious esophagitis. Endoscopy allows direct visualization of the esophageal mucosa and biopsy to determine the severity of reflux esophagitis. Erosive esophagitis is reported less often in infants and children with GERD compared to adults with GERD. However, a normal endoscopic appearance of the esophageal mucosa in pediatric patients does not exclude histologic evidence of reflux esophagitis. Because there is poor correlation between endoscopic and histologic findings in infants and children, esophageal biopsy is recommended in pediatric endoscopy for evaluation of GERD.

Normally, eosinophils and neutrophils are not present in the esophageal epithelium of children. Basal cell hyperplasia and increased papillary length, variably accompanied by an inflammatory cellular infiltrate, are the histologic criteria for esophagitis secondary to esophageal acid exposure in children as in adults. Histopathology may help demonstrate whether an eosinophilic esophagitis is present, indicated by a markedly increased number of eosinophils (> 15 eosinophils/high-power field) in the esophageal epithelium.

Esophageal Manometry

Manometry may be used to measure the pressure of the lower esophageal sphincter tone. Manometry of the esophagus is helpful in the evaluation of patients with suspected achalasia or motility disorders of the esophagus. Manometric studies are difficult to perform in the undated infant, however, and have proven to be of little clinical use for patients with uncomplicated GERD. These studies thus remain primarily a research tool.

Scintigraphy

Scintigraphy is used to measure gastric emptying and can help record how often reflux into the esophagus occurs. It may be useful in quantitating the frequency of GER, however, it is not widely used because it is not as sensitive as an upper GI study in ruling out anatomic obstruction and does not allow the amount of ambulation or mobility that a prolonged pH probe study does in measuring the amount of reflux. Because scintigraphy provides information on rates of gastric emptying, it can be helpful in the evaluation of children with GERD who are being evaluated for surgery, to determine whether they will need to have a procedure to improve their gastric emptying at the same time.

MANAGEMENT

The evaluation and treatment of pediatric GER varies
with the predominant presenting signs and symptoms. In the infant or child with recurrent vomiting and no other significant findings to suggest another diagnosis, a thorough history and physical examination are generally sufficient to establish a diagnosis of GERD and initiate therapy. In infants, poor weight gain, excessive crying, irritability, disturbed sleep, feeding resistance, or respiratory symptoms may be indications for further diagnostic testing to rule out other possibilities before proceeding to pharmacologic treatment for GERD.

- What is the most appropriate next step in the management of the case patient?
- What medications are available for pediatric patients with GERD?

**PRINCIPLES OF CONSERVATIVE MANAGEMENT**

Conservative treatment for mild symptoms of GER involves thickened feedings and positional changes in infants, and dietary modification in children. Healthy infants who regurgitate without signs of GERD and are formula-fed may be managed by thickening feedings with up to one tablespoon of dry rice cereal per 1 oz of formula. The thickening of the feedings will reduce regurgitation and irritability. For breast-fed infants, frequent burping during feeding and upright positioning after feeding may reduce regurgitation. Smaller, more frequent feedings are recommended in older infants and children.

Completely upright and prone positioning are beneficial in infants with GERD. However, the risk of sudden infant death syndrome associated with sleeping prone in infants up to 12 months of age outweighs the benefits of the prone positioning in the management of GERD. Seated positioning should be discouraged because it provokes reflux by increasing intra-abdominal pressure. Semi-supine positioning in an infant carrier or car seat exacerbates GER and should be avoided when possible, especially after feeding. Holding the infant in a head-elevated position by placing the infant's head on the shoulder for 20 to 30 minutes after feeding before laying the infant in the supine position may reduce postprandial GER, but there are no controlled studies evaluating this technique.

Parents should be assured that most infants with mild GERD respond well to conservative management and that the symptom of recurrent vomiting resolves in nearly all infants. The prognosis of infants with GERD is excellent; it is estimated that GERD persists into childhood in fewer than 5% of infants who have GERD.

In older children and adolescents, as in adults, lifestyle changes may be beneficial in the management of GERD. These include dietary modifications, weight loss in overweight patients, avoidance of alcohol, and cessation of smoking. However, limited data are available regarding the benefits of lifestyle changes in pediatric patients with GERD. Studies in adults support dietary modification by avoidance of caffeine, chocolate, and spicy foods that cause symptoms of GERD; these recommendations are incorporated in the management of GERD in children and adolescents, as well.

**PHARMACOTHERAPEUTIC AGENTS FOR PEDIATRIC GERD**

A variety of pharmacologic agents are available for pediatric patients in whom conservative measures are not sufficient. The two major classes of pharmacologic agents for treatment of GERD are prokinetic agents and acid suppressants (Table 2). Acid suppressants are typically used when esophagitis is suspected or demonstrated. In patients without evidence of esophagitis, prokinetic medications traditionally have been used prior to trying acid suppression therapy. However, recent evidence has shown that acid suppressants may be more effective than prokinetic agents in the management of GERD and thus are being used in patients with GERD with or without evidence of esophagitis.

**Prokinetic Agents**

Prokinetic agents decrease reflux by improving contractility of the body of the esophagus, increasing lower esophageal sphincter pressure, and increasing the rate of gastric emptying. Until recently, metoclopramide and cisapride were the most widely prescribed agents used in pediatric GERD. However, cisapride is no longer commercially available in the United States for safety reasons and the efficacy of metoclopramide in pediatric patients has not been proven, and thus neither agent is widely used currently.

Cisapride was shown to be effective in decreasing symptoms and improving results of esophageal pH monitoring in 6 controlled pediatric trials. However, cisapride was withdrawn from the market in the United States because of the potential of serious cardiac arrhythmias, some fatal. These adverse effects have generally occurred in the context of excessive dosing, concomitant use of other drugs metabolized by the hepatic cytochrome P-450 3A4 isoenzyme, or in patients predisposed to arrhythmias. Cisapride is now available in the United States from the manufacturer only through a limited access clinical research protocol; however, it remains commercially available in many countries around the world.

The clinical efficacy of metoclopramide in pediatric GERD was equivocal in 4 controlled trials. Furthermore, adverse effects have been reported in 11% to 34% of
patients treated with metoclopramide. Drowsiness and restlessness are the most common adverse effects, but the most troublesome is the extrapyramidal reaction that seems to occur more frequently in children than in adults. This is an acute dystonic reaction that manifests as neck pain and rigidity, trismus, and oculogyric crisis.26 Strict limitation of dosage is important to prevent these adverse effects, and even the recommended doses must sometimes be reduced in children because of irritability and sleep disturbances. Some experts believe that because the drug is relatively ineffective, the potential adverse reactions outweigh the benefits of treatment.26

**Acid Suppressants**

The main classes of acid suppressants are antacids, histamine2 receptor antagonists (H2RAs) and proton pump inhibitors (PPIs). The principles of using these medicaments in the treatment of pediatric GERD are similar to those in adults, other than the need to prescribe weight-adjusted doses and the need to consider the form of the drug prescribed (ie, for ease of ingestion in infants and children). Dosage ranges for drugs commonly prescribed for pediatric GERD are listed in Table 2.

### Table 2. Pediatric Doses of Drugs Used in the Treatment of GERD

<table>
<thead>
<tr>
<th>Medication</th>
<th>Recommended Dose</th>
<th>Adverse Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Prokinetic agents</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metoclopramide</td>
<td>0.1 mg/kg body weight per dose 4 times daily*</td>
<td>Restlessness, dystonia</td>
</tr>
<tr>
<td><strong>Acid neutralization/suppression agents</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antacids</td>
<td>1 mL/kg body weight per dose, 3–8 times daily*</td>
<td>Constipation, diarrhea</td>
</tr>
<tr>
<td><strong>Histamine, receptor antagonists</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cimetidine</td>
<td>20–40 mg/kg daily†</td>
<td>Headache, confusion, pancytopenia, gynecomastia</td>
</tr>
<tr>
<td>Ranitidine</td>
<td>5–10 mg/kg daily, usually given as 2 divided doses ‡</td>
<td>Headache, malaise</td>
</tr>
<tr>
<td>Famotidine</td>
<td>1.0 mg/kg daily in 2 divided doses, up to 40 mg twice daily ‡</td>
<td>Headache, malaise</td>
</tr>
<tr>
<td>Nizatidine</td>
<td>Pediatric doses not defined</td>
<td>Headache, malaise</td>
</tr>
<tr>
<td><strong>Proton pump inhibitors</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Omeprazole</td>
<td>0.7–3.3 mg/kg daily*</td>
<td>Headache, rash, diarrhea, hypergastrinemia, abdominal pain</td>
</tr>
<tr>
<td>Lansoprazole</td>
<td>For patients ≤ 30 kg: 15 mg daily; for patients &gt; 30 kg: 30 mg daily ‡</td>
<td>Headache, rash, diarrhea, hypergastrinemia, abdominal pain</td>
</tr>
<tr>
<td>Pantoprazole</td>
<td>Pediatric doses not defined</td>
<td>Headache, rash, diarrhea, hypergastrinemia, abdominal pain</td>
</tr>
<tr>
<td>Rabeprazole</td>
<td>Pediatric doses not defined</td>
<td>Headache, rash, diarrhea, hypergastrinemia, abdominal pain</td>
</tr>
</tbody>
</table>

GERD = gastroesophageal reflux disease.

†Data from Physician’s desk reference. 56th ed. Oradell (NJ): Medical Economics Co, Inc; 2002. Pages 1646, 1692, and 2152, respectively.
‡Data from Prevacid [package insert]. Lake Forest (IL): TAP Pharmaceuticals, Inc; 2002.
amount of time that the gastric pH was less than 4.29. Ranitidine (2 mg/kg 3 times daily) reduced by 90% the amount of time that the gastric pH was less than 4.29. Another study demonstrated that ranitidine 5 mg/kg per dose orally increased gastric pH for 9 to 10 hours in infants. Although there are no randomized controlled studies of ranitidine or famotidine in pediatric patients with GERD, it is believed that these drugs are at least as effective as cimetidine in children.

Proton pump inhibitors. PPIs decrease acid secretion by inhibition of H⁺-K⁺-ATPase in the gastric parietal cell canaliculus; they are more potent inhibitors of acid secretion than are H₂RAs. An open-label study of omeprazole in children revealed that a dosage range of 0.7 to 3.3 mg/kg daily was effective, based on improvement in clinical symptoms and the results of esophageal pH monitoring. Other trials of omeprazole support its efficacy in the treatment of severe esophagitis and esophagitis refractory to H₂RAs in children.

Lansoprazole has also been found to be effective in the treatment of esophagitis in children. A North American study demonstrated that lansoprazole was effective in the treatment of 66 patients ages 1 to 12 years with reflux esophagitis or GERD. The dosage range of lansoprazole is 0.7 to 4 mg/kg daily; its pharmacokinetics in children is similar to that in adults.

The use of rabeprazole, pantoprazole, and esomeprazole in children has not been well studied, although pediatric clinical trials of pantoprazole are currently being conducted.

Antacids. Antacids neutralize gastric acid by their buffering effect. They may be used as a diagnostic test in infants by relieving nonspecific symptoms such as crying. High-dose antacid therapy with magnesium hydroxide and aluminum hydroxide has been shown to be as effective as cimetidine in the treatment of esophagitis in children. However, significant aluminum absorption from antacid use can occur in infants, and may approach levels reported to cause osteopenia and neurotoxicity. As safer and more convenient alternatives are available, long-term antacid therapy is generally not recommended as the primary therapy for GERD in pediatric patients.

Surface Agent Therapy in Pediatric GERD

Sucralfate acts through a cytoprotective mechanism by adhering to peptic lesions of gastrointestinal epithelium. One randomized controlled pediatric trial reported similar treatment outcome with sucralfate compared to cimetidine. However, sucralfate is an aluminum-containing compound; at least in theory, therefore, a potential exists for aluminum toxicity in infants. Insufficient data is available to determine the safety of its use in children.

EVALUATION AND INITIAL MANAGEMENT OF CASE PATIENT

The case patient is diagnosed with mild GERD based on his history and symptoms. A barium swallow test is performed, which shows reflux below the level of the clavicles. The parents are instructed to thicken feedings with rice cereal and to keep the infant upright for 30 minutes after feedings.

Two days later the parents bring the infant to the children’s hospital emergency department following an apparent life-threatening event (ALTE). They report that 10 minutes after feeding, the infant stopped breathing and became slightly cyanotic. He started breathing again and turned pink after they administered rescue breaths. The vital signs in the emergency department are stable and no abnormalities are identified on the physical examination.

- What is the most appropriate next step in the management of this patient?
- What medication would be an appropriate treatment for this patient?

INFANTS WITH UNCOMPROMISED GER

Healthy-appearing infants who are growing normally with painless, effortless regurgitation are often referred to as “happy spitters.” These infants often respond to lifestyle changes such as thickened formula, small frequent feedings, frequent burping while feeding, and upright positioning after feeding. However, symptoms of cow’s milk protein allergy may mimic those of GERD. Therefore, in some formula-fed infants with symptoms of GERD, a 1- to 2-week trial of casein hydrolysate formula may be reasonable, especially in infants with associated diarrhea, which can be another symptom of milk protein intolerance. The prognosis of infants with uncomplicated GER is excellent; symptoms resolve by age 12 months in the majority of these infants. There is no evidence that pharmacologic therapy affects the natural history of uncomplicated GER in infants.

INFANTS WITH RECURRENT VOMITING AND FAILURE TO THRIVE

In contrast to the “happy spitter,” infants with GERD and failure to thrive require more aggressive diagnostic evaluation and management. The adequacy of caloric intake should be assessed in these infants. If caloric intake is adequate, a complete blood count and chemistry profile should be obtained, including serum alanine
aminotransferase levels, plasma ammonia level, and urinalysis, including urine ketone levels and reducing substances. In addition, the results of the newborn screening for hypothyroidism and galactosemia should be reviewed. An upper GI series with barium or water-soluble contrast is recommended to evaluate for anatomic causes of vomiting. If these studies are nondiagnostic, a trial of hypoallergenic formula and thickened feeding is recommended in combination with acid suppression therapy.

Mothers of breast-fed infants are advised to eliminate dairy products from their diet if milk protein intolerance is suspected.

Endoscopy with biopsy may be useful to rule out other causes of vomiting. If growth does not improve, nasogastric (NG) feeding may be indicated. In infants with intolerance to NG feeding due to delayed gastric emptying or suspected aspiration, transpyloric feeding tubes can be used.

**INFANTS WITH RECURRENT VOMITING AND IRRITABILITY**

Vomiting, irritability, and disturbed sleep can occur in infants with GERD. One study using simultaneous esophageal pH and video monitoring correlated grimming and episodes of acid reflux. A trial of acid suppression therapy can be prescribed with or without a change to a hypoallergenic formula. If symptoms do not improve, esophageal pH monitoring can be useful to determine whether irritability or sleep disturbance is temporally correlated with acid reflux. If the symptoms are related to GERD, an increase in acid suppression therapy (ie, switching from an H2RA to a PPI, or increasing the dose of a PPI) is indicated. Alternatively, endoscopy with biopsy can be performed to evaluate for the presence of esophagitis, which could account for the symptoms. If the diagnostic studies are normal and there is no response to therapy, it is unlikely that GERD is the cause of the symptoms.

Recurrent vomiting and irritability may also be seen in patients with eosinophilic esophagitis. In infants, eosinophilic esophagitis is commonly associated with milk protein allergy and may not respond well to acid suppressant therapy. In older children, oral corticosteroids are used for management of eosinophilic esophagitis.

**CHILDREN 2 YEARS OR OLDER WITH RECURRENT VOMITING**

Recurrent non-bilious, non-bloody vomiting, occurring between once daily and once weekly, can be a presenting symptom of GERD in children older than 2 years. An upper GI series with barium contrast is recommended to rule out anatomic causes of vomiting. A trial of acid suppression therapy is often effective in reducing the frequency of vomiting. Some experts recommend starting with a trial of prokinetic therapy if the vomiting is not accompanied by pain. Upper endoscopy with biopsy may be indicated if the symptoms persist. If symptoms resolve, medication is stopped after 8 to 12 weeks. If symptoms recur, upper endoscopy is performed if it has not already been done. Maintenance therapy is an option in these patients as long as the symptoms are controlled with acid suppression or prokinetic agents.

**CHILDREN WITH HEARTBURN OR CHEST PAIN**

Heartburn or upper abdominal pain may be caused by GERD with or without esophagitis. Older children and adolescents may report symptoms similar to those noted by young adults, but younger children may not localize the pain. The pain may awaken the child from sleep and is increased upon awakening. Regurgitation of sour burps may also occur. Management approaches similar to those used in adults can be employed in these cases. Lifestyle changes and a 2- to 4-week trial of H2RA or PPI therapy is recommended. If there is no improvement, endoscopy with biopsy may be considered. If the symptoms resolve, acid suppression therapy is continued for 8 to 12 weeks. If symptoms recur after therapy is stopped, endoscopy is indicated if it was not already performed. Long-term therapy is sometimes required in patients who improve with treatment, even in the absence of esophagitis.

**CHILDREN WITH DYSPHAGIA OR RESISTANCE TO FEEDING**

Esophagitis may cause dysphagia or feeding resistance in infants or older children. The sensation of food sticking in the throat or chest while swallowing suggests an esophageal disorder. An upper GI series with barium contrast can be helpful in these patients to rule out anatomic abnormalities such as vascular rings or strictures and motility disorders such as achalasia. Upper endoscopy with biopsy may also be indicated, as radiographic signs of esophagitis are usually not seen in pediatric GERD. If esophagitis is diagnosed, initial treatment with PPIs results in more rapid improvement compared to H2RAs. If the child was previously given a trial of acid suppression therapy, a higher dose of PPI may be necessary before relief of symptoms occurs.

**INFANTS WITH APPARENT LIFE-THREATENING EVENTS**

An ALTE in infants is an episode frightening to the observer that includes apnea, change in color (cyanosis or pallor), change in muscle tone (limpness or stiffness), or choking and gagging, that requires intervention by
the caretaker. Recurrent vomiting occurs in 60% to 70% of infants with ALTEs43 and 40% to 80% may have abnormal results of esophageal pH monitoring.44 Esophageal acid infusion reproduced apnea or oxygen desaturation in selected patients.45 Possible mechanisms for this association include laryngospasm triggered by acid stimulation of laryngeal, pharyngeal, or esophageal chemoreceptors. Despite the observation that acid reflux is temporally associated with apnea in selected patients, in larger studies of unselected infants with a history of ALTE, no convincing relationship between GERD and apnea or bradycardia has been found. The subset of infants with “awake apnea,” which occurs while the infant is in the supine position within 1 hour of feeding, is more likely to respond to treatment of GERD.

At present, there are no predictive signs, symptoms, or tests to determine which infants with a history of ALTE are at risk for future life-threatening episodes or sudden death. In patients with a history of ALTE in which the role of GERD is uncertain, esophageal pH monitoring may be indicated to assess whether there is a temporal association between acid reflux and ALTE.

The effectiveness of medical therapy for GERD-associated ALTE has not been well studied. A trial of acid suppression therapy may be prescribed. Surgical therapy is also utilized in selected patients, but there are no studies comparing the efficacy of medical versus surgical management of GERD-associated ALTE.

**CHILDREN WITH ASTHMA**

Symptoms of GERD are common in children with asthma. The incidence of abnormal results of esophageal pH monitoring ranges from 25% to 75% in children with asthma. Esophageal acid exposure may contribute to airway hyperresponsiveness and variable airflow obstruction.

The diagnosis of GERD may be considered in asthmatic children who respond poorly to asthma therapy. Esophageal pH monitoring may be helpful in determining whether a temporal correlation exists between a symptom such as cough or wheezing and acid reflux. A study of asthmatic children with abnormal results of pH monitoring demonstrated improvement in peak flow measurements after ranitidine therapy without changes in asthma therapy.46 Response to acid suppressant therapy is not immediate, and studies in adults suggest that at least 3 months of therapy may be required before improvement in respiratory symptoms occurs.

Several studies demonstrate improvement in asthma after antireflux surgery in children with GERD confirmed by esophageal pH monitoring.24 Indications for antireflux surgery in children with both GERD and asthma include recurrent pneumonia, failed bronchodilator therapy, dependence on medical therapy, and severe esophagitis. A history of GERD symptoms prior to surgery, preoperative response to medical therapy for GERD, and recurrent aspiration with GERD were predictive of improvement of asthma after antireflux surgery.

**CHILDREN WITH RECURRENT PNEUMONIA AND GERD**

GERD-related aspiration pneumonia can occur even in the absence of esophagitis. The child with recurrent pneumonia should be evaluated for anatomic abnormalities, aspiration during swallowing, ingestion of a foreign body, cystic fibrosis, and immunodeficiency, in addition to GERD. Patients with associated neuromuscular disease or esophageal or laryngeal abnormalities are at higher risk for GERD-related aspiration.

Helpful diagnostic tests in children with recurrent pneumonia and GERD include an upper GI series to evaluate for anatomic abnormalities such as tracheoesophageal fistula and a videofluoroscopic swallowing study or a fiber-endoscopic swallowing evaluation to assess for direct aspiration while swallowing. Esophageal pH monitoring may also be indicated, but normal results do not exclude GERD as a cause of aspiration pneumonia. Flexible bronchoscopy with pulmonary lavage for lipid-laden macrophages can detect evidence of aspiration, but lipid-laden macrophages may be present even in normal individuals. Nuclear scintigraphy is a specific test for aspiration, but is not sensitive, so a negative test result does not rule out GERD-associated aspiration.

The management of children with GERD-associated aspiration pneumonia usually involves medical or surgical therapy. Surgery may be necessary in patients with impaired lung function to prevent further pulmonary damage. If pulmonary function is only minimally impaired, a trial of medical therapy with acid suppression with careful follow-up can be considered. The preservation of pulmonary function should be one of the main objectives in the management of these patients.

**CHILDREN WITH NEUROLOGIC IMPAIRMENT**

One third of children with severe psychomotor delay have clinically significant GERD. In many, GERD is exacerbated by the presence of large hiatal hernias. Many of these children present with such severe symptoms that they are unable to keep down sufficient nutrients and they lose weight. Erosion of the dental enamel is a very common finding in these patients. They also may have other complications, such as aspiration pneumonia, blood loss from erosive esophagitis, and stricture formation. Esophagitis may respond to antisecretory therapy, but many of these patients will require surgical treatment.
The use of PPIs has dramatically increased the number of patients with neurologic impairment that respond to medical treatment. The group that does not respond to medical therapy will require some form of fundoplication. Unfortunately, these patients may have a high rate of perioperative complications.

It is not uncommon after fundoplication for the child to persist with problems consistent with GERD symptoms. It is possible that delayed gastric emptying may play a role in the failure of fundoplication in these patients. A gastric emptying study prior to fundoplication may be an effective means of determining which patients would benefit from a procedure that would facilitate gastric emptying and could be performed at the same time the fundoplication is performed (eg, antroplasty, which can be performed laparoscopically).

**CASE RESOLUTION**

The case patient is admitted for observation to the pediatric intensive care unit. A modified barium swallow is negative for aspiration. Esophageal pH monitoring demonstrates 79 episodes of acid reflux during the 24-hour study. Eight episodes of coughing and choking occur during the study, 6 of which are temporally associated with acid reflux. No apnea or bradycardia occurs during the study. Esophagostroduodenoscopy is grossly normal; however, the biopsy of the esophagus shows histologic evidence of esophagitis. The infant is started on omeprazole (1 mg/kg daily) and is discharged with the diagnosis of GERD with esophagitis.

On a follow-up visit 4 weeks after discharge, the parents report that the infant has had fewer episodes of regurgitation, has been less irritable, and there have been no more ALTEs. The infant is feeding well and is growing, and he is now at the 25th percentile in weight and length for age.

**REFERENCES**


