

Diagnosis and Treatment of Gastroesophageal Reflux in Infants and Children

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Gastroesophageal reflux is defined as the passage of stomach contents into the esophagus with or without accompanied regurgitation (spitting up) and vomiting. It is a normal physiologic process that occurs throughout the day in infants and less often in children and adolescents. Gastroesophageal reflux disease (GERD) is reflux that causes troublesome symptoms or leads to medical complications. The diagnoses of gastroesophageal reflux and GERD are based on the history and physical examination. Diagnostic tests, such as endoscopy, barium study, multiple intraluminal impedance, and pH monitoring, are reserved for when there are atypical symptoms, warning signs, doubts about the diagnosis, or suspected complications or treatment failure. In infants, most regurgitation resolves by 12 months of age and does not require treatment. Reflux in infants may be treated with body position changes while awake, lower-volume feedings, thickening agents (i.e., rice cereal), antiregurgitant formula, extensively hydrolyzed or amino acid formulas, and, in breastfed infants, eliminating cow's milk and eggs from the mother's diet. Lifestyle changes to treat reflux in children and adolescents include sleeping position changes; weight loss; and avoiding smoking, alcohol, and late evening meals. Histamine H₂ receptor antagonists and proton pump inhibitors are the principal medical therapies for GERD. They are effective in infants, based on low-quality evidence, and in children and adolescents, based on low- to moderate-quality evidence. Surgical treatment is available, but should be considered only when medical therapy is unsuccessful or is not tolerated. (*Am Fam Physician*. 2015;92(8):705-714. Copyright © 2015 American Academy of Family Physicians.)



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► **Patient information:** A handout on this topic, written by the authors of this article, is available at <http://www.aafp.org/afp/2015/1015/p705-s1.html>.

Gastroesophageal reflux in children is the passage of stomach contents into the esophagus. It is a normal physiologic process, occurring throughout the day in infants and less often in children and adolescents, typically after meals. It may be asymptomatic or cause mild, nontroubling symptoms such as regurgitation or occasional vomiting. Regurgitation (spitting up) is the passive movement of stomach contents into the pharynx or mouth. Vomiting is the forceful movement of stomach contents through the mouth by autonomic and voluntary muscle contractions, sometimes triggered by reflux.¹⁻³

Gastroesophageal reflux disease (GERD) is reflux that produces troublesome symptoms for the patient (i.e., recurrent expressions of pain or unhappiness beyond the norm for the patient's age) and may lead to complications, such as reflux esophagitis, strictures, respiratory complications, failure to thrive, and, rarely, Barrett esophagus and esophageal adenocarcinoma.¹⁻⁴ This article discusses the diagnosis and treatment of gastroesophageal reflux and GERD in infants

and children based on guidelines from the U.K.'s National Institute for Health and Care Excellence and from the North American and European Societies for Pediatric Gastroenterology, Hepatology, and Nutrition.^{2,3}

Background

The lower esophageal sphincter is the primary barrier to gastroesophageal reflux. Most reflux events are caused by transient lower esophageal sphincter relaxation triggered by postprandial gastric distention.⁵ Frequent large-volume feedings, short esophagus, and supine positioning predispose infants to regurgitation or vomiting induced by transient lower esophageal sphincter relaxation. This relaxation continues into childhood, but growth and upright positioning decrease its frequency.⁶ Reflux may be liquid, solid, gas, or a combination of these. It may also be acidic, weakly acidic, or nonacidic. The degree of reflux acidity has not been associated with symptom severity.⁷

The following conditions are associated with increased risk of GERD (listed from highest to lowest odds ratio): hiatal hernia

Table 1. Clinical Features that Distinguish Gastroesophageal Reflux from GERD in Infants and Children

<i>Body system</i>	<i>Gastroesophageal reflux features</i>	<i>GERD features</i>	<i>Signs and symptoms requiring further evaluation</i>
Vital signs and growth parameters	Normal weight gain	Poor weight gain or weight loss, failure to thrive	Fever Failure to thrive
Gastrointestinal	Little difficulty with feedings Symptoms are not bothersome to the infant or child	Feeding refusal or prolonged feedings Postprandial irritability in infants Dysphagia or odynophagia Recurrent vomiting Heartburn in children Chest pain, epigastric pain, nonlocalized abdominal pain Regurgitation and/or vomiting beyond 18 months of age	Bilious vomiting Persistent, forceful vomiting Onset of vomiting after six months of age Gastrointestinal bleeding Persistent diarrhea or constipation Abdominal tenderness or distension, hepatosplenomegaly
Respiratory	No significant symptoms	Chronic cough, wheezing, or hoarseness Asthma Recurrent laryngitis, pneumonia, sinusitis, or otitis media Apnea or cyanosis (i.e., apparent life-threatening event)	Apnea or cyanosis (i.e., apparent life-threatening event)
Nervous system	No neurobehavioral symptoms	Sandifer syndrome (neck tilting in infants)	Sandifer syndrome Lethargy Bulging fontanelle Micro- or macrocephaly Seizures Neurodevelopmental delay or other disorders

GERD = gastroesophageal reflux disease.

Information from references 2 through 4, and 19.

(including congenital diaphragmatic hernia), neurodevelopmental disorders, cystic fibrosis, epilepsy, congenital esophageal disorders, asthma, and prematurity.⁸⁻¹² Obesity and parental history of reflux may also be risk factors for GERD in children.^{2,3,13-15}

Epidemiology

Regurgitation is common during infancy, occurring at least once daily in one-half of infants up to three months of age. The prevalence peaks at four months of age, with two-thirds of infants regurgitating at least once daily¹⁵ and approximately 40% regurgitating with most feedings.¹⁶ Regurgitation declines precipitously afterward, dropping to 14% by seven months of age and to less than 5% between 10 and 14 months of age.^{15,16} Further decline in the incidence of regurgitation occurs during the second year of life.¹⁷

Gastroesophageal reflux symptoms remain common in childhood and adolescence. Approximately 2% to 7% of parents of three- to nine-year-olds report their child experiencing heartburn, epigastric pain, or regurgitation within the previous week, whereas 5% to 8% of adolescents report similar symptoms.¹⁸

GERD is much less common with an incidence of 1.48 cases per 1,000 person-years in infants, declining until 12 years of age, and then peaking at 16 to 17 years of age (2.26 cases in girls and 1.75 cases in boys per 1,000 person-years in 16- to 17-year-olds). Overall, the childhood prevalence of GERD is estimated at 1.25% to 3.3%, compared with 5% among adults.^{1,8}

Clinical Evaluation

Gastroesophageal reflux by definition is the presence of nontroublesome reflux. The diagnosis of GERD is usually based on parent- or adolescent-reported symptoms that are attributable to gastroesophageal reflux and are troublesome to the patient. *Table 1* differentiates gastroesophageal reflux from GERD, and describes the warning signs and symptoms of both that require further evaluation.^{2-4,19} *Figure 1* outlines the evaluation and treatment of gastroesophageal reflux and GERD.^{2,19}

Infantile gastroesophageal reflux may present with frequent regurgitation or vomiting, postprandial irritability, prolonged feeding or feeding refusal, or back arching. Progressively worsening projectile vomiting in

Diagnosis and Treatment of Recurrent Regurgitation or Vomiting in Infants and Heartburn in Children

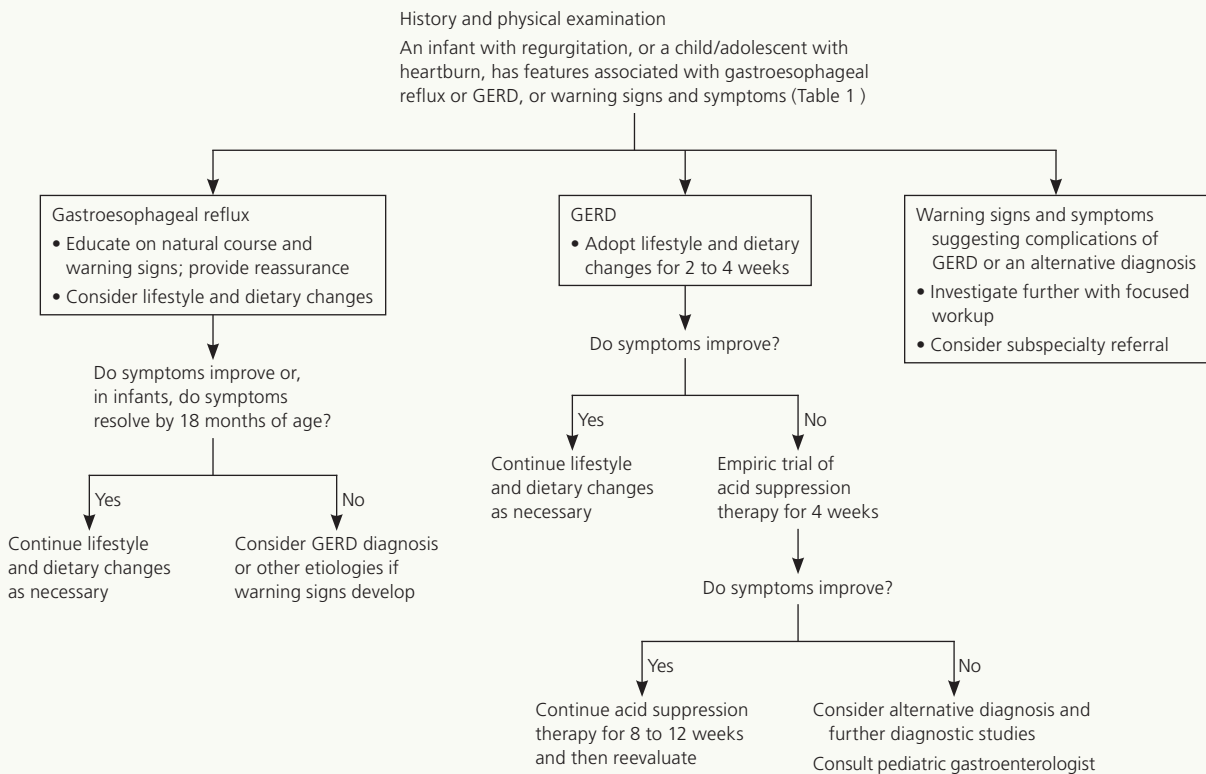


Figure 1. Approach to the infant with recurrent regurgitation or vomiting, or the child/adolescent with heartburn. (GERD = gastroesophageal reflux disease.)

Information from references 2 and 19.

the first months of life is concerning for pyloric stenosis and requires immediate imaging and surgical referral. Recurrent nonprojectile vomiting or regurgitation beyond 18 months of age is uncommon and suggests GERD or more concerning pathology.^{2,3,20} Poor weight gain, parent-reported abdominal pain, and coughing or choking during feeding may also suggest GERD and warrant further workup. Billious vomiting at any age, particularly in the first few months of life, is an emergency and suggests intestinal obstruction.²¹ Gastrointestinal bleeding also requires further workup.

Sandifer syndrome, a lateral head tilt with contralateral chin rotation, is a rare cause of infantile torticollis attributable to GERD.²² Subspecialist referral should be considered to differentiate it from more concerning movement disorders involving dystonia, seizures, and infantile spasms.² Apparent life-threatening events (i.e., witnessed, frightening events characterized by apnea, color change, marked change in muscle tone, choking, or gagging) are commonly attributed to GERD, lower respiratory tract infection, and seizures.²³ These events require investigation and hospitalization before diagnosing GERD as the cause.²⁴

Children older than eight years are considered reliable historians and self-report a higher incidence of GERD symptoms than parental reporting.¹⁸ Similar to adults, older children and adolescents may report heartburn, regurgitation, odynophagia, dysphagia, retrosternal or epigastric pain, anorexia, or poor weight gain.²⁵

GERD may also present with extraesophageal manifestations such as cough, wheezing, laryngitis, pneumonia, recurrent sinusitis, or otitis media.^{4,26}

The feeding history should be reviewed to identify overfeeding, eating habits, or food triggers contributing to reflux symptoms. A review of the patient's medical history can identify conditions predisposing children to GERD. Physical examination should include growth measurements to assess for failure to thrive, which requires further investigation before assigning GERD as the cause. Head and neurologic examinations should look for bulging fontanelle, macro- or microcephaly, and evidence of neurodevelopmental disorders. The lung fields should be auscultated for stridor and wheezing. An abdominal examination should be performed for tenderness, distension, hepatosplenomegaly, peritoneal signs, and palpable masses.²

Gastroesophageal Reflux in Children

Diagnostic testing is generally not necessary because it has not been found to be more reliable than the history and physical examination for diagnosing gastroesophageal reflux or GERD.²⁷ Tests should be reserved for situations with atypical symptoms, warning signs, or doubts about the diagnosis; suspected complications of GERD or other conditions; or failure of initial therapies. *Tables 2^{2,3,28-33} and 3³⁴⁻⁴³* highlight the common and less common differential diagnosis of GERD. When exploring alternate diagnoses, the patient's age (infant vs. child or adolescent) can narrow the differential.

Initial Treatment

Parents of healthy infants should be reassured that most regurgitation resolves spontaneously by the end of the first year of life. For children and adolescents, gastroesophageal reflux treatment should incorporate lifestyle changes and, in the absence of GERD, does not routinely require pharmacologic intervention.³

CONSERVATIVE MANAGEMENT

Most infants, children, and adolescents who have reflux improve with conservative measures. In infants, feeding changes may reduce symptoms. For formula-fed infants, reducing feeding volumes in overfed infants, or offering smaller and more frequent feeds, may decrease reflux episodes and should be tried first.^{2,3} Adding thickening agents (i.e., 1 tbsp rice cereal per oz of formula) decreases observed regurgitation and esophageal regurgitant height, but does not reduce the reflux index (percentage of time the esophageal pH is less than 4) and can lead to excess weight gain.^{2,44,45} Commercially available antiregurgitant formulas decrease observed regurgitation but not the number of reflux episodes.² Extensively hydrolyzed or amino acid formulas may reduce reflux episodes in infants allergic to cow's milk protein. For breastfeeding infants, removing immunogenic foods (e.g., cow's milk, eggs) from the mother's diet may improve symptoms.^{2,4,19}

Changing the infant's body position while awake can be effective. The flat prone and left-side down positions are associated with fewer reflux episodes but should be recommended only in awake, observed infants during the postprandial period.^{2,46} Sleeping infants should always be placed in the supine position, however, to decrease the risk of sudden infant death syndrome.³ Prone sleeping may be considered after one year of age when the risk of sudden infant death syndrome decreases dramatically.² Certain infant sleep positioners are approved by the U.S. Food

BEST PRACTICES IN GASTROENTEROLOGY: RECOMMENDATIONS FROM THE CHOOSING WISELY CAMPAIGN

<i>Recommendation</i>	<i>Sponsoring organization</i>
Avoid using acid blockers and motility agents such as metoclopramide for physiologic gastroesophageal reflux that is effortless, painless, and not affecting growth. Do not use medication in the so-called "happy spitter."	American Academy of Pediatrics
Don't treat gastroesophageal reflux in infants routinely with acid suppression therapy.	Society of Hospital Medicine (Pediatric)
Long-term acid suppression therapy for gastroesophageal reflux disease should be titrated to the lowest effective dose.	American Gastroenterological Association

Source: For more information on the Choosing Wisely Campaign, see <http://www.choosingwisely.org>. For supporting citations and to search Choosing Wisely recommendations relevant to primary care, see <http://www.aafp.org/afpl/recommendations/search.htm>.

and Drug Administration for gastroesophageal reflux treatment, but they have been implicated in several infant deaths and their use should have physician oversight.⁴⁷

Conservative treatments in older children and adolescents are largely extrapolated from adult studies. Interventions include dietary modification (e.g., avoiding triggers, such as alcohol), weight loss in children who are obese, smoking cessation, chewing sugarless gum after meals, and avoiding late evening meals. Sleeping with the head of the bed elevated or in the left lateral decubitus position may reduce reflux episodes.^{2,3,48,49}

PHARMACOLOGIC TREATMENT

For infants, children, and adolescents with GERD that does not improve with conservative treatment, an empiric four-week trial can be considered using acid suppression therapy with histamine H₂ receptor antagonists or proton pump inhibitors (PPIs).^{3,4,50,51} Shorter treatment duration or as-needed use is not recommended, and combination therapy has not proven effective.⁵² Common adverse effects include headache, nausea, diarrhea, abdominal pain, constipation, and dizziness.⁵²⁻⁵⁵ The induced acid suppression of H₂ antagonists and PPIs may increase the risk of community-acquired pneumonia and gastroenteritis in children, and candidemia and necrotizing enterocolitis in preterm infants.^{50,53,54}

H₂ antagonists decrease acid secretion by inhibiting H₂ receptors on gastric parietal cells. They improve clinical symptoms, decrease the reflux index, and improve histologic findings in infants, children, and adolescents; however, most studies have been of poor quality.^{2,52,56,57} The effectiveness of H₂ antagonists may be limited by tachyphylaxis (diminution of response) or tolerance with chronic use.^{2,55,58}

PPIs block sodium-potassium adenosinetriphosphatase (Na⁺,K⁺-ATPase) enzyme activity, which is the final step in parietal cell acid secretion. Low-quality

Table 2. Common Differential Diagnosis for Reflux in Infants and Children

<i>Diagnosis</i>	<i>Estimated frequency</i>	<i>Distinguishing features</i>	<i>Diagnostic testing</i>	<i>Comments</i>
Acute gastroenteritis ²⁸	0.5 to 1.9 illnesses per person annually in developed countries 2.5 illnesses per year in 2- to 3-year-olds; 5 illnesses per year in those attending day care	Nausea, vomiting, diarrhea Sudden onset, often short duration of symptoms Clinical dehydration (weight loss, prolonged capillary refill time, skin turgor)	Clinical diagnosis Microbiologic studies generally are not necessary	May occur in epidemics
Cow's milk allergy ²⁹	2% to 3% of infants in developed countries	Most develop symptoms before 1 month of age, often within 1 week of starting cow's milk protein-based formula 50% to 60% have atopic symptoms 20% to 30% have respiratory symptoms	Diagnosis requires controlled elimination and challenge testing Often presumptively diagnosed after trial of extensively hydrolyzed or amino acid formula	Most common food allergy in early childhood 45% to 50% remission rate at 1 year, 60% to 75% at 2 years, 85% to 90% at 3 years
Hiatal hernia ³⁰	10% to 80%	Reflux-associated symptoms	Barium study	May cause gastroesophageal reflux disease Higher prevalence seen in more severe cases of reflux esophagitis, including Barrett esophagus
Infantile colic ^{31,32}	5% to 19% of infants 0 to 4 months of age	Unexplained crying, often high pitched and inconsolable May have a bowel movement or pass gas near the end of the episode May curl up legs, clench fists, and tense abdominal muscles during crying	Clinical diagnosis: crying at least 3 hours per day on at least 3 days per week for at least 3 weeks	Infants are generally healthy, well fed, thriving, and younger than 6 months
Infectious etiologies outside the gastrointestinal tract ²	Disease specific	Fever, late onset of reflux symptoms after 2 months of age, poor weight gain, and other symptoms that localize the infection	Disease specific	Etiologies may include sepsis, meningitis, urinary tract infection, pneumonia, otitis media, and hepatitis
Rumination syndrome ³³	5% in boys and girls	Recently ingested food is effortlessly regurgitated into the mouth, masticated, and reswallowed	Clinical diagnosis 24-hour multiple intraluminal impedance with pH monitoring	More common in adolescents; often treated as an eating disorder

Information from references 2, 3, and 28 through 33.

evidence suggests that PPIs improve symptoms of GERD in infants; however, there is weak, conflicting evidence on whether they improve the reflux index, and no evidence of endoscopic improvement.^{50,52,53,57,59,60} Some experts suggest a short trial of PPI therapy in infants with GERD refractory to conservative measures.^{2,53} In older children and adolescents, PPIs effectively treat GERD symptoms, heal erosive disease, and are more effective than H₂ antagonists; additionally, their effectiveness does not diminish over time.^{2,50,52}

Prokinetic agents have been proposed for GERD treatment, but their use is limited because of adverse effects or lack of consistent evidence.^{2,50,61,62} Antacids buffer

stomach contents but are associated with milk alkali syndrome and are not recommended in children younger than 12 years.² Antacids are a reasonable option in adolescents for dyspepsia or heartburn, but do not decrease the frequency of reflux.³ Surface protective agents, such as sucralfate (Carafate), have some effectiveness for esophagitis, but have inadequate evidence for childhood GERD and are not recommended as sole treatment.² *Table 4* describes pharmacologic treatments for GERD.^{4,50-52}

Diagnostic Testing

If symptoms do not improve with acid suppression therapy, diagnostic testing is warranted to evaluate treatment

Table 3. Less Common Differential Diagnosis for Reflux in Infants and Children

Diagnosis	Estimated frequency	Distinguishing clinical features	Diagnostic testing	Comments
Achalasia ^{34,35}	Incidence = 0.18 cases per 100,000 person-years (average age at diagnosis = 10.9 years)	Gradual dysphagia for solids, then liquids Eating behaviors to overcome contracted lower esophageal sphincter (moving side to side, stretching, eating slowly, walking after eating) Difficulty belching	Barium study (classic bird's beak sign) Manometry	Treatment: pneumatic dilation, onabotulinumtoxinA (Botox) injection, or laparoscopic myotomy of the lower esophageal sphincter
Crohn disease ³⁶	Incidence = 9.5 to 11.4 per 100,000 person-years	Abdominal pain, diarrhea, weight loss; dysphagia or odynophagia if esophagus is involved Extraintestinal manifestations include arthritis, skin disease (erythema nodosum, pyoderma granulorum), eye disease (eposcleritis, uveitis), liver disease	Endoscopy with biopsy	Male:female ratio = 1.5:1 in prepubescent children Incidence in childhood increases with age
Cyclic vomiting syndrome ^{37,38}	Prevalence estimated at 0.3% in school-aged children	Diagnostic criteria: 5 or more attacks in any interval, or 3 or more attacks over 6 months Episodic attacks of intense nausea/vomiting lasting hours to days, occurring at least 1 week apart Vomiting 4 or more times per hour for at least 1 hour during attacks	Clinical diagnosis	Preventive measures: avoid excitation, fatigue, fasting, and food triggers; regulate menses Pharmacologic prevention options include tricyclic antidepressants or propranolol For acute attacks: consider antiemetics, triptans (off-label) in adolescents
Eosinophilic esophagitis ^{39,40}	Incidence = 0.7 to 10 per 100,000 person-years	Atopy in up to 60% of children	Endoscopy with biopsy	Consider in children with symptoms that do not improve with acid suppression therapy
Intestinal atresia ⁴¹	Duodenal atresia: 0.9 per 10,000 live births Jejunioileal atresia: 0.7 per 10,000 live births	Abdominal distension, bilious vomiting in first days of life Failure to pass meconium Delayed or protracted symptoms when there is a partial obstruction	Barium study (classic double bubble sign) Often observed on prenatal ultrasonography with polyhydramnios	Duodenal atresia is associated with Down syndrome Jejunioileal atresia is typically due to vascular compromise
Intestinal malrotation ⁴²	1 in 500 live births	Abdominal pain and bilious vomiting Older infants and children may have chronic colicky abdominal pain, solid food intolerance, failure to thrive, recurrent nonbilious vomiting, gastrointestinal bleeding	Barium study	Male:female ratio = 2:1 40% present within first week of life; 50% by 1 month of age; 75% by 12 months of age
Pyloric stenosis ⁴³	2 to 5 per 1,000 live births in developed countries	Nonbloody, nonbilious projectile vomiting Often presents at 2 to 4 weeks of age Olive-sized abdominal mass	Upper abdominal ultrasonography	Male:female ratio = 4:1 Requires urgent surgical pylorotomy

Information from references 34 through 43.

failure, identify complications of GERD, establish a relationship between atypical symptoms and reflux, and exclude other diagnoses. The advantages and limitations of various tests are summarized in *eTable A*.

Upper endoscopy with biopsy is considered when reflux does not respond to initial treatments. It is the

principal method of evaluating the esophageal mucosa for complications of GERD and excluding other possible causes, such as eosinophilic esophagitis, esophageal webs, and infectious esophagitis.^{1,2,27}

Esophageal pH monitoring is the most widely used test to quantify the frequency of reflux over 24 hours using

Table 4. Medications for Gastroesophageal Reflux Disease in Infants and Children

<i>Medication</i>	<i>Dosage*</i>	<i>Formulation</i>	<i>Comments</i>	<i>Cost†</i>
Histamine H₂ receptor antagonists				
Cimetidine	Neonates: 5 to 10 mg per kg per day, divided every 8 to 12 hours Infants: 10 to 20 mg per kg per day, divided every 6 to 12 hours ≤ 12 years: 20 to 40 mg per kg per day, divided every 6 hours > 12 years: 400 mg every 6 hours or 800 mg every 12 hours	Oral solution	Affects cytochrome P450, vitamin D metabolism, endocrine function Improves symptom scores, reflux index, and histologic and endoscopic findings in infants and children	\$40 for one 270-mL bottle (300 mg per 5 mL)
Famotidine (Pepcid)	0 to 3 months: 0.5 mg per kg per day 3 to 12 months: 0.5 mg per kg twice daily 1 to 16 years: 0.5 mg per kg twice daily	Oral suspension	Lacks evidence showing effectiveness in infants and children Approved for up to 8 weeks of use in infants and up to 6 weeks of use in adolescents	\$75 (\$180) for one 50-mL bottle (40 mg per 5 mL)
Nizatidine (Axid)	6 months to 11 years: 5 to 10 mg per kg per day, divided every 12 hours ≥ 12 years: 150 mg twice daily	Oral solution	Improves symptom scores in infants; improves reflux index and histologic and endoscopic findings in infants and children	\$40 (\$55) for one 60-mL bottle (15 mg per mL)
Ranitidine	Infant to 16 years: 5 to 10 mg per kg per day, divided every 12 hours; maximum dosage of 300 mg per day > 16 years: 150 mg twice per day	Syrup	Most commonly used H ₂ receptor antagonist No evidence for symptomatic improvement in infants, but has shown symptomatic benefit in children Improves reflux index and histologic and endoscopic findings in infants and children	\$30 for one 60-mL bottle (15 mg per mL)
Proton pump inhibitors				
Esomeprazole (Nexium)	1 to 11 years: 10 mg per day ≥ 12 years: 20 mg per day (alternative dosage for infants, children, and adolescents: 0.7 to 3.3 mg per kg per day)	Sprinkle contents of capsule onto food	Approved for up to 8 weeks of treatment Improves reflux index in infants; no evidence of improvement in symptom scores Improves symptom scores and histologic and endoscopic findings in children	\$200 (\$260) for 30 capsules (20 mg)
Lansoprazole (Prevacid)	3 to 12 months: 7.5 mg twice daily or 15 mg per day 1 to 11 years: ≤ 30 kg: 15 mg per day > 30 kg: 30 mg per day ≥ 12 years: 30 mg per day	Sprinkle contents of capsule onto food or into juice; disintegrating tablet	Improves symptom scores, reflux index, and histologic and endoscopic findings in children No evidence of effectiveness in infants Approved for 12 weeks of use in children and 8 weeks of use in adolescents Well tolerated in children	\$40 (\$350) for 30 capsules (15 mg) \$130 (\$350) for 30 tablets (15 mg)
Omeprazole (Prilosec)	Infants: 0.7 mg per kg per day > 1 year and adolescents: 5 to < 10 kg: 5 mg per day 10 to < 20 kg: 10 mg per day ≥ 20 kg: 20 mg per day	Sprinkle contents of capsule onto food	Improves symptom scores and reflux index in infants and children Risk of respiratory infections in critically ill children	\$20 (\$210) for 30 capsules (10 mg)
Rabeprazole (Aciphex)	1 to 11 years: < 15 kg: 5 mg per day ≥ 15 kg: 10 mg per day ≥ 12 years: 20 mg per day	Tablet	Lacks evidence of effectiveness in infants and children Approved for up to 12 weeks of use in children 1 to 11 years of age Approved for up to 8 weeks of use in children 12 years and older, and in adolescents	\$40 (\$440) for 30 tablets (20 mg)

continues

Table 4. Medications for Gastroesophageal Reflux Disease in Infants and Children (continued)

Medication	Dosage*	Formulation	Comments	Cost†
Prokinetics				
Bethanechol	Children: 0.1 to 0.2 mg per kg per day, divided every 6 to 8 hours; 1 hour before meals	Tablet	Lacks evidence showing effectiveness in infants and children May induce respiratory bronchospasm	\$20 for 30 tablets (5 mg)
Erythromycin (E.E.S.)	1.5 to 12.5 mg per kg every 6 to 8 hours	Oral suspension	Lacks evidence showing effectiveness in infants and children No specific dosing recommendations for GERD Associated with hypertrophic pyloric stenosis in infants younger than 6 weeks	NA (\$325) for one 100-mL bottle (200 mg per mL)
Metoclopramide	0.1 to 0.2 mg per kg three to four times per day	Oral solution	Not recommended for routine treatment of GERD 34% of treated patients have adverse effects (drowsiness, restlessness, rare extrapyramidal symptoms); use is generally not recommended	\$4 for one 60-mL bottle (5 mg per 5 mL)
Buffering agents				
Antacids (magnesium or aluminum hydroxide)	Not recommended < 12 years; dosing varies depending on antacid	Tablet	FDA approved for infants (magnesium hydroxide only), children, and adolescents May produce milk alkali syndrome; caution in renal disease	—
Surface protective agents				
Sucralfate (Carafate)	Dosing not well established; in children, 40 to 80 mg per kg per day divided every 6 hours has been used	Tablet; oral suspension	Constipation, dizziness, light-headedness	\$15 (\$80) for 30 tablets (1 g) NA (\$45) for one 120-mL bottle (1 g per 10 mL)

FDA = U.S. Food and Drug Administration; GERD = gastroesophageal reflux disease; NA = not available.

*—For H_2 receptor antagonists and proton pump inhibitors, the listed dosages are based on FDA recommendations for gastroesophageal reflux, GERD, or heartburn.

†—Estimated retail cost based on information obtained at <http://www.goodrx.com> (accessed June 11, 2015). Generic price listed first; brand price listed in parentheses.

Information from references 4, and 50 through 52.

the reflux index.²⁷ Increasingly, pH monitoring is combined with multiple intraluminal impedance to evaluate GERD. Multiple intraluminal impedance plus pH monitoring is considered superior to pH monitoring alone because it can differentiate acidic, weakly acidic, or non-acidic reflux; identify solid, liquid, or gas reflux; and better determine the temporal correlation between reflux and atypical symptoms. The high cost, high interobserver variability, and the lack of well-designed studies supporting its diagnostic accuracy limit its use.^{2,27,63}

A barium study (upper gastrointestinal series) is useful for evaluating for anatomic causes of symptoms, particularly dysphagia and odynophagia, and bilious vomiting. It should not routinely be used to diagnose GERD or assess its severity.³ The brevity of the study produces a high false-negative rate, whereas the high prevalence of nonpathologic gastroesophageal reflux in the general population leads to a high false-positive rate.⁶⁴

Questionnaires may be used to quantify and track symptoms (eTable B), and to assess treatment response, but they lack specificity in diagnosing gastroesophageal reflux or GERD.^{1,27,65} Daily symptom diaries have not been validated in children.²

Surgical Treatment

Surgical options are available and should be considered in children with complications from severe GERD if medical therapy is unsuccessful or is not tolerated. Surgical options include complete or partial Nissen fundoplication. Newer endoscopic approaches performed in adults have been studied in children. Surgical treatments have significant risk of reflux recurrence and should be considered carefully.⁶⁶

Data Sources: A PubMed search was conducted using the key terms reflux, gastroesophageal reflux, and gastroesophageal reflux disease, limited in children age 0 to 18, and combined in separate searches with

SORT: KEY RECOMMENDATIONS FOR PRACTICE

<i>Clinical recommendation</i>	<i>Evidence rating</i>	<i>References</i>
The diagnosis of gastroesophageal reflux and GERD should be based primarily on history and physical examination findings because other diagnostic tests have not shown superior accuracy.	C	2-4, 27
Conservative treatments are the first-line strategies for most infants, older children, and adolescents with reflux and GERD.	C	2-4
A trial of extensively hydrolyzed or amino acid formula in formula-fed infants, or maternal dietary modification in breastfed infants, is warranted when reflux is presumed to be caused by an allergy to cow's milk protein.	C	2, 4, 19
Histamine H ₂ receptor antagonists are an option for acid suppression therapy in infants and children with GERD.	B	2, 3, 52, 56, 57
Proton pump inhibitors are reasonable treatment options for GERD in older children and adolescents, but their use in infants is questionable because of a lack of proven effectiveness.	B	2, 3, 50, 52, 53, 57

GERD = gastroesophageal reflux disease.

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to <http://www.aafp.org/afpsort>.

epidemiology, etiology, pathophysiology, diagnosis, management, and treatment for reflux-related topics, including clinical reviews, randomized controlled trials, systematic reviews, and meta-analyses. Also searched were the Cochrane Database of Systematic Reviews, the National Guideline Clearinghouse database, and Essential Evidence Plus. In addition, a search was conducted using individual diagnoses within the differential diagnosis of reflux as key terms, limited in children age 0 to 18, and combined in separate searches with etiology, diagnosis, management, and treatment. Relevant publications from the reference sections of cited articles were also reviewed. Search dates: January through July 2014, and February and July 2015.

The opinions or assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the Department of Defense, the U.S. Army Medical Corps, or the U.S. Army at large.

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Table A. Advantages and Limitations of Diagnostic Tests for Gastroesophageal Reflux

<i>Test</i>	<i>Advantages</i>	<i>Limitations and disadvantages</i>
Acid suppression therapy as a diagnostic method ^{A1}	Four-week trial can be considered in older children and adolescents (extrapolated from adult studies)	Improvement after trial of therapy does not necessarily confirm GERD
Barium study ^{A1-A4}	<p>Can identify reflux regardless of pH</p> <p>Can reveal anatomic causes of GERD (esophageal webs and strictures, tracheoesophageal fistula, esophageal and intestinal atresia, achalasia, pyloric stenosis, malrotation)</p> <p>Useful in assessing projectile or bilious vomiting, vomiting undigested food, or failure to thrive</p> <p>Can identify aspiration related to reflux</p> <p>Can evaluate mechanisms of swallowing; may be able to identify a motility disorder</p> <p>Useful in evaluating accompanying dysphagia or odynophagia</p> <p>Less invasive diagnostic study</p> <p>Routinely available</p>	<p>Poor sensitivity and specificity for GERD</p> <p>Findings do not correlate well with severity of symptoms or histologic findings</p> <p>Radiation exposure; children should not be exposed to prolonged fluoroscopy</p>
Endoscopy with biopsy ^{A1,A5,A6}	<p>Direct visualization and histologic evaluation</p> <p>Can identify complications of GERD (e.g., reflux esophagitis, Barrett esophagus, esophageal adenocarcinoma)</p> <p>Can assess response to acid suppression therapy</p> <p>Useful in evaluating accompanying dysphagia or odynophagia</p>	<p>Cannot determine whether nonacidic reflux is occurring</p> <p>Endoscopic and histologic esophageal findings in GERD are nonspecific and correlate poorly with symptom severity</p> <p>Procedural and sedation risks</p>
Esophageal manometry ^{A1}	<p>Can measure mechanisms of swallowing</p> <p>Can identify transient lower esophageal sphincter reflux</p> <p>Useful in diagnosing motility disorders and achalasia</p>	<p>Cannot reliably confirm GERD</p> <p>Cannot predict response to medical or surgical therapies</p>
Esophageal pH monitoring ^{A1,A2,A5-A7}	<p>Quantifies acidic reflux using the reflux index (percentage of time that esophageal pH < 4.0; > 7% is abnormal, 3% to 7% is equivocal, < 3% is normal)</p> <p>Can evaluate relationship between atypical symptoms and reflux</p> <p>Can assess response to acid suppression therapy</p>	<p>Severity of acidic reflux does not correlate well with severity of symptoms, complications, or histology</p> <p>Reflux index cannot account for symptomatic nonacidic, weakly acidic, or gas reflux</p> <p>Multiple intraluminal impedance combined with pH monitoring is considered superior to pH monitoring alone</p> <p>Sensitivity of 41% to 81% for GERD diagnosis</p> <p>Often a 24-hour test; may require overnight hospitalization</p>
Multiple intraluminal impedance with pH monitoring ^{A6,A7}	<p>Determines frequency, duration, velocity, volume, and height of acidic, weakly acidic, and nonacidic reflux</p> <p>Distinguishes solid, liquid, and gas reflux</p> <p>Can evaluate relationship between atypical symptoms and reflux</p> <p>Can assess response to acid suppression therapy</p> <p>Provides more information than pH monitoring alone</p> <p>Ambulatory devices are available</p>	<p>High cost</p> <p>Unclear if it improves diagnostic accuracy or therapeutic decision making over pH monitoring alone</p> <p>Inter- and intraobserver variability; lacks standardized methods of interpretation</p> <p>Often a 24-hour study; may require overnight hospitalization</p> <p>Requires patient/parent reliability in documenting symptoms accurately</p>

continues

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eTable A. Advantages and Limitations of Diagnostic Tests for Gastroesophageal Reflux (continued)

Test	Advantages	Limitations and disadvantages
Nuclear scintigraphy ^{A1,A2}	<ul style="list-style-type: none"> Can identify reflux regardless of pH Can identify aspiration related to reflux Can identify delayed gastric emptying 	<ul style="list-style-type: none"> Poor sensitivity (15% to 59%) vs. pH monitoring alone in diagnosing GERD Lacks standardized method of interpretation Cannot identify late postprandial reflux or reflux independent of eating
Questionnaires ^{A2,A5,A6,A8}	<ul style="list-style-type: none"> Can quantify and track symptoms of GERD Best validated questionnaire is the Infant Gastroesophageal Reflux Questionnaire-Revised; has high sensitivity but low specificity (eTable B) 	<ul style="list-style-type: none"> Cannot reliably confirm GERD Cannot reliably predict complications of GERD or predict treatment response
Ultrasonography ^{A1}	<ul style="list-style-type: none"> Diagnostic method of choice in evaluating for pyloric stenosis Can identify hiatal hernia and the position of the lower esophageal sphincter Can detect fluid movements (i.e., reflux) over a short period of time at the gastroesophageal junction 	Not recommended for routine evaluation of GERD

GERD = gastroesophageal reflux disease.

Information from:

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eTable B. Selected Items from the Infant Gastroesophageal Reflux Questionnaire

How often does the baby usually spit up?
How much does the baby usually spit up?
Does the spitting up seem to be uncomfortable for the baby?
Does the baby refuse feedings even when hungry?
Does the baby have trouble gaining enough weight?
Does the baby cry a lot during or after feedings?
Do you think the baby cries or fusses more than normal?
How many hours does the baby cry or fuss each day?
Do you think the baby hiccups more than most babies?
Does the baby have spells of arching back?
Has the baby ever stopped breathing while awake or struggled to breathe, or turned blue or purple?

NOTE: These items were found to be the most discriminative for the original Infant Gastroesophageal Reflux Questionnaire.

Information from Kleinman L, Rothman M, Strauss R, et al. The infant gastroesophageal reflux questionnaire revised: development and validation as an evaluative instrument. Clin Gastroenterol Hepatol. 2006;4:593.