American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN™

CLINICAL REPORT

Gastroesophageal Reflux: Management Guidance for the Pediatrician

abstract

FREE

Recent comprehensive guidelines developed by the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition define the common entities of gastroesophageal reflux (GER) as the physiologic passage of gastric contents into the esophagus and gastroesophageal reflux disease (GERD) as reflux associated with troublesome symptoms or complications. The ability to distinguish between GER and GERD is increasingly important to implement best practices in the management of acid reflux in patients across all pediatric age groups, as children with GERD may benefit from further evaluation and treatment, whereas conservative recommendations are the only indicated therapy in those with uncomplicated physiologic reflux. This clinical report endorses the rigorously developed, well-referenced North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition guidelines and likewise emphasizes important concepts for the general pediatrician. A key issue is distinguishing between clinical manifestations of GER and GERD in term infants, children, and adolescents to identify patients who can be managed with conservative treatment by the pediatrician and to refer patients who require consultation with the gastroenterologist. Accordingly, the evidence basis presented by the guidelines for diagnostic approaches as well as treatments is discussed. Lifestyle changes are emphasized as first-line therapy in both GER and GERD, whereas medications are explicitly indicated only for patients with GERD. Surgical therapies are reserved for children with intractable symptoms or who are at risk for life-threatening complications of GERD. Recent black box warnings from the US Food and Drug Administration are discussed, and caution is underlined when using promoters of gastric emptying and motility. Finally, attention is paid to increasing evidence of inappropriate prescriptions for proton pump inhibitors in the pediatric population. *Pediatrics* 2013;131:e1684–e1695

Jenifer R. Lightdale, MD, MPH, David A. Gremse, MD, and SECTION ON GASTROENTEROLOGY, HEPATOLOGY, AND NUTRITION

KEY WORDS

gastroesophageal reflux, gastroesophageal reflux disease, pediatrics, guidelines, review, global consensus, reflux-related disease, vomiting, regurgitation, rumination, extraesophageal symptoms, Barrett esophagus, proton pump inhibitors, diagnostic imaging, impedance monitoring, gastrointestinal endoscopy, lifestyle changes

ABBREVIATIONS

GER—gastroesophageal reflux
GERD—gastroesophageal reflux disease
GI—gastrointestinal
H2RA—histamine-$_2$ receptor antagonist
MII—multiple intraluminal impedance
PPI—proton pump inhibitor

www.pediatrics.org/cgi/doi/10.1542/peds.2013-0421

doi:10.1542/peds.2013-0421

All clinical reports from the American Academy of Pediatrics automatically expire 5 years after publication unless reaffirmed, revised, or retired at or before that time.

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

INTRODUCTION

Gastroesophageal reflux (GER) occurs in more than two-thirds of otherwise healthy infants and is the topic of discussion with pediatricians at one-quarter of all routine 6-month infant visits.[1,2] In addition to seeking guidance from their pediatricians, parents often request evaluation by pediatric medical subspecialists.[3] It is, therefore, not surprising that strongly evidence-based guidelines incorporating

state-of-the-art approaches to the evaluation and management of pediatric GER have been welcomed by both general pediatricians and pediatric medical subspecialists and surgical specialists. GER, defined as the passage of gastric contents into the esophagus, is distinguished from gastroesophageal reflux disease (GERD), which includes troublesome symptoms or complications associated with GER.[4] Differentiating between GER and GERD lies at the crux of the guidelines jointly developed by the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition and the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition.[4] These definitions have further been recognized as representing a global consensus.[5] Therefore, it is important that all practitioners who treat children with reflux-related disorders are able to identify and distinguish those children with GERD, who may benefit from further evaluation and treatment, from those with simple GER, in whom conservative recommendations are more appropriate.

GER is considered a normal physiologic process that occurs several times a day in healthy infants, children, and adults. GER is generally associated with transient relaxations of the lower esophageal sphincter independent of swallowing, which permits gastric contents to enter the esophagus. Episodes of GER in healthy adults tend to occur after meals, last less than 3 minutes, and cause few or no symptoms.[6] Less is known about the normal physiology of GER in infants and children, but regurgitation or spitting up, as the most visible symptom, is reported to occur daily in 50% of all infants.[7,8]

In both infants and children, reflux can also be associated with vomiting, defined as a forceful expulsion of gastric contents via a coordinated autonomic and voluntary motor response. Regurgitation and vomiting can be further differentiated from rumination, in which recently ingested food is effortlessly regurgitated into the mouth, masticated, and reswallowed. Rumination syndrome has been identified as a relatively rare clinical entity that involves the voluntary contraction of abdominal muscles.[9] In contrast, both regurgitation and vomiting can be considered common and often nonpathologic manifestations of GER.

Symptoms or conditions associated with GERD are classified by the practice guidelines as being either esophageal or extraesophageal.[4] Both classifications can be used to define the disease, which can be further characterized by findings of mucosal injury on upper endoscopy. Esophageal conditions include vomiting, poor weight gain, dysphagia, abdominal or substernal/retrosternal pain, and esophagitis. Extraesophageal conditions have been subclassified according to both established and proposed associations; established extraesophageal manifestations of GERD can include respiratory symptoms, including cough and laryngitis, as well as wheezing in infancy.[10,11] Although older studies from the 1990s suggested that GERD may aggravate asthma, recent publications have suggested that the impact of GERD on asthma control is considerably less than previously thought.[10,12–18] Other extraesophageal manifestations include dental erosions, and proposed associations include pharyngitis, sinusitis, and recurrent otitis media. Patients can be described clinically by their symptoms or by the endoscopic description of their esophageal mucosa. GERD-associated esophageal injuries and complications found on endoscopy include reflux esophagitis, less commonly peptic stricture, and rarely Barrett esophagus and adenocarcinoma.

Although the reported prevalence of GERD in patients of all ages worldwide is increasing,[5] GERD is nevertheless far less common than GER. Population-based studies suggest reflux disorders are not as common in Eastern Asia, where the prevalence is 8.5%,[19] compared with Western Europe and North America, where the current prevalence of GERD is estimated to be 10% to 20%.[20] New epidemiologic and genetic evidence suggests some heritability of GERD and its complications, including erosive esophagitis, Barrett esophagus, and esophageal adenocarcinoma.[21–23] A few pediatric populations at high risk of GERD have also been identified, including children with neurologic impairment, certain genetic disorders, and esophageal atresia[24,25] (Table 1). The prevalence of severe, chronic GERD is much higher in pediatric patients with these "GERD-promoting" conditions. These patients may be more prone to experiencing complications of severe GERD than patients who are otherwise healthy.[26]

Population trends hypothesized to contribute to a general increase in the prevalence of GERD include global epidemics of both obesity and asthma. In some instances, GERD can be implicated as either the underlying etiology (ie, recurrent pneumonia in

TABLE 1 Pediatric Populations at High Risk for GERD and Its Complications

Neurologic impairment
Obese
History of esophageal atresia (repaired)
Hiatal hernia
Achalasia
Chronic respiratory disorders
Bronchopulmonary dysplasia
Idiopathic interstitial fibrosis
Cystic fibrosis
History of lung transplantation
Preterm infants

the premature infant exacerbated by GERD) or a direct repercussion (ie, obesity leading to GERD) of such conditions. In the great majority of cases, however, GERD and comorbidities are known to occur simultaneously in patients without a clear causal relationship.

CLINICAL FEATURES OF GERD

Troublesome symptoms or complications of pediatric GERD are associated with a number of typical clinical presentations in infants and children, depending on patient age[5] (Table 2). Reflux may occur commonly in preterm newborn infants but is generally nonacidic and improves with maturation. A full discussion of reflux in neonates and preterm infants is beyond the scope of this report.

Guidelines have distinguished between manifestations of GERD in full-term infants (younger than 1 year) from those in children older than 1 year and adolescents. Common symptoms of GERD in infants include regurgitation or vomiting associated with irritability, anorexia or feeding refusal, poor weight gain, dysphagia, presumably painful swallowing, and arching of the back during feedings. Relying on a symptom-based diagnosis of GERD can be difficult in the first year of life, especially because symptoms of GERD in infants do not always resolve with acid-suppression therapy.[5,27] GERD in infants can also be associated with extraesophageal symptoms of coughing, choking, wheezing, or upper respiratory symptoms.[7] The incidence of GERD is reportedly lower in breastfed infants than in formula-fed infants.[27] In line with the natural history of regurgitation, GERD in infants is considered to have a peak incidence of approximately 50% at 4 months of age and then to decline to affect only 5% to 10% of infants at 12 months of age.[7,8]

TABLE 2 Common Presenting Symptoms of GERD in Pediatric Patients

Infant	Older Child/Adolescent
Feeding refusal	Abdominal pain/ heartburn
Recurrent vomiting	Recurrent vomiting
Poor weight gain	Dysphagia
Irritability	Asthma
Sleep disturbance	Recurrent pneumonia
Respiratory symptoms	Upper airway symptoms (chronic cough, hoarse voice)

Common symptoms of GERD in children 1 to 5 years of age include regurgitation, vomiting, abdominal pain, anorexia, and feeding refusal.[28] Generally, GERD causes troublesome symptoms without necessarily interfering with growth; however, children with clinically significant GERD or endoscopically diagnosed esophagitis may also develop an aversion to food, presumably because of a stimulus-response association of eating with pain. This aversion, combined with feeding difficulties associated with repeated episodes of regurgitation, as well as potential and substantial nutrient losses resulting from emesis, may lead to poor weight gain or even malnutrition.

Older children and adolescents are most likely to resemble adults in their clinical presentation with GERD and to complain of heartburn, epigastric pain, chest pain, nocturnal pain, dysphagia, and sour burps. When eliciting a history in school-aged children with suspected GERD, it may be important to directly ask patients themselves about their symptoms rather than relying strongly on parent report. In 1 study, adolescents were significantly more likely than their parents to report themselves to be experiencing symptoms of sour burps or nausea.[1] Extraesophageal symptoms in older children and adolescents can include nocturnal cough, wheezing, recurrent pneumonia, sore throat, hoarseness, chronic sinusitis, laryngitis, or dental erosions. In a pediatric patient with GERD and dental erosions, the progression of tooth structure loss may be indicative that existing therapy for GERD is not effective. Conversely, stability of dental erosions is 1 measure of adequacy of GERD management.

DIAGNOSTIC STUDIES

For most pediatric patients, a history and physical examination in the absence of warning signs are sufficient to reliably diagnose uncomplicated GER and initiate treatment strategies. Generally speaking, diagnostic testing is not necessary. The reliability of symptoms to make the clinical diagnosis of GERD is particularly high in adolescents, who often present with heartburn typical of adults.[29–31] Nevertheless, dedicating at least part of a clinical visit to obtaining a clinical history and performing a physical examination are also essential to exclude more worrisome diagnoses that can present with reflux or vomiting (Table 3).

To date, no single symptom or cluster of symptoms can reliably be used to diagnose esophagitis or other complications of GERD in children or to predict which patients are most likely

TABLE 3 Concerning Symptoms and Signs ("Warning Signs" in Figures) for Primary Etiologies Presenting With Vomiting

Bilious vomiting
GI tract bleeding
Hematemesis
Hematochezia
Consistently forceful vomiting
Fever
Lethargy
Hepatosplenomegaly
Bulging fontanelle
Macro/microcephaly
Seizures
Abdominal tenderness or distension
Documented or suspected genetic/metabolic syndrome
Associated chronic disease

to respond to therapy.[21] Nonetheless, a number of GERD symptom questionnaires have been validated and may be useful in the detection and surveillance of GERD in affected children of all ages. Kleinman et al developed a questionnaire for infants that was validated for documentation and monitoring of parent-reported GERD symptoms.[30] Another questionnaire by Størdal et al[32] for pediatric patients 7 to 16 years of age compared favorably with results of pH monitoring. As yet another example, the GERD Symptom Questionnaire developed by Deal et al[33] appears valid for differentiating children with GERD from healthy controls but has not been compared with objective standards, such as pH monitoring or endoscopic findings.

The strategy of using diagnostic testing to diagnose GERD may also be fraught with complexity, because there is no single test that can rule it in or out. Instead, diagnostic tests must be used in a thoughtful and serial manner to document the presence of reflux of gastric contents in the esophagus, to detect complications, to establish a causal relationship between reflux and symptoms, to evaluate the efficacy of therapies, and to exclude other conditions. The diagnostic methods most commonly used to evaluate pediatric patients with GERD symptoms are upper gastrointestinal (GI) tract contrast radiography, esophageal pH and/or impedance monitoring, and upper endoscopy with esophageal biopsy. Upper GI tract series are useful to delineate anatomy and to occasionally document a motility disorder, whereas esophageal pH monitoring and intraluminal esophageal impedance represent tools to quantify GER. Upper endoscopy with esophageal biopsy represents the primary method to investigate the esophageal mucosa to both exclude other conditions that can cause GERD-like symptoms and evaluate for esophageal injury attributable to GERD.[4]

Upper GI Tract Series

Upper GI tract contrast radiography generally involves obtaining a series of fluoroscopic images of swallowed barium until the ligament of Treitz is visualized. According to the new guidelines, the routine performance of upper GI tract radiographic imaging to diagnose GER or GERD is not justified,[4] because upper GI tract series are too brief in duration to adequately rule out the occurrence of pathologic reflux, and the high frequency of nonpathologic reflux during the examination can encourage false-positive diagnoses. Additionally, observation of the reflux of a barium column into the esophagus during GI tract contrast studies may not correlate with the severity of GERD or the degree of esophageal mucosal inflammation in patients with reflux esophagitis. It is recognized that upper GI tract series are useful in the evaluation of vomiting to screen for possible anatomic abnormalities of the upper GI tract.[4] For example, in infants with bilious vomiting, an upper GI tract series may be useful for evaluating for possible malrotation or duodenal web. Persistent, forceful vomiting in the first few months of life should be evaluated with pyloric ultrasonography to evaluate for possible pyloric stenosis. An upper GI tract series should be reserved if the results of the pyloric ultrasound are equivocal.

Esophageal pH Monitoring

Continuous intraluminal esophageal pH monitoring can be used to quantify the frequency and duration of esophageal acid exposure during a study period. The conventional definition of acid exposure in the esophagus is a pH <4.0, the pH most associated with a complaint of heartburn in adults. Esophageal pH metrics generally include an absolute number of reflux episodes detected during monitoring, the duration of reflux episodes detected, and the reflux index, which is calculated as the percentage of a study period during which esophageal pH is <4.0. Although esophageal pH monitoring may be useful for associating a temporal relationship between a symptom and acid reflux and to evaluate the efficacy of pharmacologic therapy on acid suppression, mounting evidence suggests poor reproducibility of pH testing, as well as a clear continuum between pH findings in physiologic GER and pathologic GERD. In turn, esophageal pH monitoring is losing value as a primary modality for diagnosing or managing pediatric GERD.[34]

Multichannel Intraluminal Impedance Monitoring

Multiple intraluminal impedance (MII) is an emerging technology for detecting the movement of both acidic and nonacidic fluids, solids, and air in the esophagus, thereby providing a more detailed picture of esophageal events than pH monitoring.[34] MII can be used to measure volume, speed, and physical length of both anterograde and retrograde esophageal boluses. Combined pH/MII testing is evolving into the test of choice to detect temporal relationships between specific symptoms and the reflux of both acid and nonacid gastric contents. In particular, MII has been used in recent years to investigate how GER and GERD correlate with apnea, cough, and behavioral symptoms.[35] According to the new guidelines, MII and pH electrodes can and should be combined on a single catheter.[4]

Gastroesophageal Scintigraphy

Gastroesophageal scintigraphy scans for reflux of ^{99m}Tc-labeled solids or liquids into the esophagus or lungs after administration of the test

material into the stomach. This nuclear scan evaluates postprandial reflux and can also quantitate gastric emptying; however, the lack of standardized techniques and age-specific normal values limits the usefulness of this test. Therefore, gastroesophageal scintigraphy is not recommended in the routine evaluation of pediatric patients with GER.[4]

Endoscopy and Esophageal Biopsy

It is certainly preferable to pursue conservative measures for treating GERD in children before considering the use of more invasive testing. In particular, any diagnostic benefits of pursuing upper endoscopy in pediatric patients suspected of having GERD must also be weighed against minimal, but not entirely negligible, procedural and sedation risks.[36] Nevertheless, the performance of upper endoscopy allows direct visualization of the esophageal mucosa to determine the presence and severity of injury from the reflux of gastric contents into the esophagus.[26] Esophageal biopsies allow evaluation of the microscopic anatomy.[24] Upper endoscopy with esophageal biopsy may be useful to evaluate inflammation in the esophageal mucosa attributable to GERD and to exclude other associated conditions with symptoms that can mimic GERD, such as eosinophilic esophagitis. Recent data confirm that approximately 25% of infants younger than 1 year will have histologic evidence of esophageal inflammation.[37] This test is indicated in patients with GERD who fail to respond to pharmacologic therapy or as part of the initial management if symptoms of poor weight gain, unexplained anemia or fecal occult blood, recurrent pneumonia, or hematemesis exist.

Upper endoscopy may also be helpful in the assessment of other causes of abdominal pain and vomiting in pediatric patients, such as esophageal or antral webs, Crohn esophagitis, peptic ulcer, *Helicobacter pylori* infection, and infectious esophagitis. Erosive esophagitis is reported less often in infants and children with GERD than in adults with GERD; however, a normal endoscopic appearance of the esophageal mucosa in pediatric patients does not exclude histologic evidence of reflux esophagitis.[5,8] Esophageal biopsy is beneficial in evaluating for conditions that may mimic symptoms of GERD, such as eosinophilic esophagitis, infectious esophagitis (*Candida* esophagitis or herpetic esophagitis), Crohn disease, or Barrett esophagus.[24] Because endoscopic findings correlate poorly with histologic testing in infants and children, performing esophageal biopsies during endoscopy is recommended for the evaluation of GERD in children.[4]

MANAGEMENT

The new guidelines describe several treatment options for treating children with GER and GERD. In particular, lifestyle changes are emphasized, because they can effectively minimize symptoms of both in infants and children. For patients who require medication, options include buffering agents, acid secretion suppressants, and promoters of gastric emptying and motility. Finally, surgical approaches are reserved for children who have intractable symptoms unresponsive to medical therapy or who are at risk for life-threatening complications of GERD.

LIFESTYLE CHANGES

Lifestyle Modifications for Infants

Lifestyle changes to treat GERD in infants may involve a combination of feeding changes and positioning therapy. Modifying maternal diet if infants are breastfed, changing formulas, and reducing the feeding volume while increasing the frequency of feedings may be effective strategies to address GERD in many patients. In particular, the guidelines emphasize that milk protein allergy can cause a clinical presentation that mimics GERD in infants. Therefore, a 2- to 4-week trial of a maternal exclusion diet that restricts at least milk and egg is recommended in breastfeeding infants with GERD symptoms, whereas an extensively hydrolyzed protein or amino acid–based formula may be appropriate in formula-fed infants.[4,30] It is important to note that this recommendation applies to the subset of infants with complications of GER, and not "happy spitters."

In 1 study of formula-fed infants, GERD symptoms resolved in 24% of infants after a 2-week trial of changing to a protein hydrolysate formula thickened with 1 tablespoon rice cereal per ounce, avoiding overfeeding, avoiding seated and supine positions, and avoiding environmental tobacco smoke.[3] Feeding changes can also be recommended in breastfed infants, because it is well known that small amounts of cow milk protein ingested by the mother may be expressed in human milk. Indeed, several studies have found that breastfed infants may benefit from a maternal diet that restricts cow milk and eggs.[38,39]

The feeding management strategy that involves the use of thickened feedings, either by adding up to 1 tablespoon of dry rice cereal per 1 oz of formula[30] or changing to commercially thickened (added rice) formulas for full-term infants who are not cow milk protein intolerant, is recognized as a reasonable management strategy for otherwise healthy infants with both GER and GERD.[4] On the other hand, all pediatric clinicians should be aware of a possible association between thickened feedings and necrotizing enterocolitis in preterm infants.[40] The Food and Drug Administration issued a warning regarding a

common commercially available thickening agent in 2011, suggesting that "parents, caregivers and health care providers not…feed 'SimplyThick' to infants born before 37 weeks gestation who are currently receiving hospital care or have been discharged from the hospital in the past 30 days."

Thickened feedings appear to decrease observed regurgitation rather than the actual number of reflux episodes. Little is known about the effect of thickening formula on the natural history of infantile reflux or the potential allergenicity of commercial thickening agents. Excessive energy intake may occur with long-term use of feedings thickened with rice cereal or corn. To this point, it is important to realize that thickening a 20-kcal/oz infant formula with 1 tablespoon of rice cereal per ounce increases the energy density to 34 kcal/oz. Commercially available antiregurgitant formulae contain processed rice, corn, or potato starch; guar gum; or locust bean gum and may present an option that does not involve excess energy intake by infants when consumed in normal volumes. To date, there has been little investigation into any relationship between use of added rice cereal or antiregurgitant formulae and childhood obesity.

Lifestyle changes that may also benefit infants with GERD include keeping them in the completely upright position or even placing them prone. Indeed, a number of recent studies that used impedance and pH monitoring have confirmed older studies that used pH monitoring to demonstrate significantly less GER in infants in the flat prone position compared with the flat supine position.[41,42] However, the guidelines are unequivocal that the risk of sudden infant death syndrome in sleeping infants outweighs the benefits of prone positioning in the management of GERD and, therefore, that prone positioning should be considered acceptable only if the infant is observed and awake.[4] Prone positioning is suggested to be beneficial in children older than 1 year with either GER or GERD, because the risk of sudden infant death syndrome is greatly decreased in older age groups.

Perceived and actual benefits of seated or semisupine positioning are also explored in the new guidelines. Semisupine positioning, particularly in an infant carrier or car seat, may exacerbate GER and should be avoided when possible, especially after feeding.[43] More recent data obtained with esophageal impedance–pH monitoring have confirmed that postprandial reflux occurs similarly when infants are in car seats as when they are supine but also suggests that being in a car seat for 2 hours after a feeding reduces reflux-related respiratory events.[44]

Lifestyle Modifications for Children and Adolescents

Lifestyle changes that may benefit GERD in older children and adolescents are more akin to recommendations made for adult patients, including the importance of weight loss in overweight patients, cessation of smoking, and avoiding alcohol use. Recommendations for conservatively managing GERD in older children and adolescents, likewise, may involve dietary modification and positioning changes, although the effectiveness of the latter as a treatment of GERD in older children has not been as well studied as in infants. In terms of dietary changes, older children and adolescents are advised to avoid caffeine, chocolate, alcohol, and spicy foods as potential symptom triggers. The guidelines also point out that 3 independent studies have demonstrated decreased reflux episodes with postprandial chewing of sugarless gum.[45–47]

PHARMACOTHERAPEUTIC AGENTS FOR PEDIATRIC GERD

Several medications may be used to treat GERD in infants and children. The 2 major classes of pharmacologic agents for treatment of GERD are acid suppressants and prokinetic agents (Table 4). Growing evidence that demonstrates the former to be more effective than the latter has led to an increased use of acid suppressants to manage suspected GERD in pediatric patients[4,39]; however, there is also significant concern for the overprescription of acid suppressants, particularly proton pump inhibitors (PPIs), and it is important to understand the new guidelines for medication indications.

Acid Suppressants

The main classes of acid suppressants are antacids, histamine-$_2$ receptor antagonists (H2RAs), and PPIs. The principles of using these medications 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 patients with GERD are listed in Table 4.

Antacids

Antacids are a class of medications that can be used to directly buffer gastric acid in the esophagus or stomach to reduce heartburn and ideally allow mucosal healing of esophagitis. There is limited historical evidence that on-demand use of antacids can lead to symptom relief in infants and children.[48] Instead, although antacids are generally seen as a relatively benign approach to treating pediatric

TABLE 4 Pediatric Doses of Medications Prescribed for GERD

Medications	Doses	Formulations	Ages Indicated by the Food and Drug Administration
Cimetidine	30–40 mg/kg/d, divided in 4 doses	Syrup	≥16 y
Ranitidine	5–10 mg/kg/d, divided in 2 to 3 doses	Peppermint-flavored syrup; Effervescent tablet	1 mo–16 y
Famotidine	1 mg/kg/d, divided in 2 doses	Cherry-banana-mint–flavored oral suspension	1–16 y
Nizatidine	10 mg/kg/d, divided in 2 doses	Bubble gum–flavored solution	≥12 y
Omeprazole	0.7–3.3 mg/kg/d	Sprinkle contents of capsule onto soft foods	2–16 y
Lansoprazole	0.7–3 mg/kg/d	Sprinkle contents of capsule onto soft foods or select juices Administer capsule contents in juice through nasogastric tube Strawberry-flavored disintegrating tablet Orally disintegrating tablet via oral syringe or nasogastric tube (≥8 French)	1–17 y
Esomeprazole	0.7–3.3 mg/kg/d	Sprinkle contents of capsule onto soft foods Administer capsule contents in juice through nasogastric tube	1–17 y
Rabeprazole	20 mg daily	Oral tablet	12–17 y
Dexlansoprazole	30–60 mg daily	Oral tablet	No pediatric indication
Pantoprazole	40 mg daily (adult dose)	Oral tablet	No pediatric indication

GERD, it is important to recognize that they are not entirely without risk. Indeed, several studies link aluminum-containing preparations with aluminum toxicity and its complications in children.[49–51] Similarly, milk-alkali syndrome, a triad of hypercalcemia, alkalosis, and renal failure, has been described in children receiving calcium-containing preparations and adds to a note of caution. According to the new guidelines, chronic antacid therapy is generally not recommended in pediatrics for the treatment of GERD.[4] In addition, the safety and efficacy of surface protective agents, such as alginates or sucralfate, an aluminum-containing preparation, have not been adequately studied in the pediatric population. As such, no surface agent is currently recommended as independent treatment of severe symptoms of GERD or erosive esophagitis in children.[4]

H2RAs

H2RAs represent a major class of medications that has completely revolutionized the treatment of GERD in children. H2RAs decrease the secretion of acid by inhibiting the histamine-$_2$ receptor on the gastric parietal cell. Expert opinion suggests little clinical difference between the various formulations of H2RAs. Randomized placebo-controlled pediatric clinical trials have shown that cimetidine and nizatidine are superior to placebo for the treatment of erosive esophagitis in children.[52,53] Pharmacokinetic studies in school-aged children suggest that gastric pH begins to increase within 30 minutes of administration of an H2RA and reaches peak plasma concentrations 2.5 hours after dosing. The acid-inhibiting effects of H2RAs last for approximately 6 hours, so H2RAs are quite effective if administered 2 or 3 times a day.

However, H2RAs inherently have some limitations. In particular, a fairly rapid tachyphylaxis can develop within 6 weeks of initiation of treatment, limiting its potential for long-term use. In addition, H2RAs have been shown to be less effective than PPIs in symptom relief and healing rates of erosive esophagitis. Although most of these downsides have been demonstrated most clearly in adults, they are also believed to affect children. It is also important to recognize that cimetidine has specifically been linked to an increased risk of liver disease and gynecomastia, and that these associations may be generalizable to other H2RAs.

PPIs

Most recently, PPIs have emerged as the most potent class of acid suppressants by repeatedly demonstrating superior efficacy compared with H2RAs. PPIs decrease acid secretion by inhibition of H^+, K^+-ATPase in the gastric parietal cell canaliculus. PPIs are uniquely able to inhibit meal-induced acid secretion and have a capacity to maintain gastric pH >4 for a longer period of time than H2RAs. These properties contribute to higher and faster healing rates for erosive esophagitis with PPI therapy compared with H2RA therapy. Finally, unlike H2RAs, the acid suppression ability of PPIs has not been observed to diminish with chronic use.

The timing of dosing most PPIs is important for maximum efficacy. Both pediatricians and pediatric medical subspecialists must be diligent at educating their patients to administer PPIs, ideally, approximately 30 minutes before meals.[7] All clinicians should also recognize that the metabolism of PPIs is known to differ in children compared with adults, with a trend toward a shorter half-life, necessitating a higher per-kilogram dose to achieve a peak serum concentration

and area under the curve similar to those in adults.[45] A fairly wide range of effective doses is evident in children. For example, an open-label study of omeprazole in children revealed an effective dosage range of 0.7 to 3.3 mg/kg daily, on the basis of improvement in clinical symptoms and the results of esophageal pH monitoring.[47] Lansoprazole, 0.7 to 3.0 mg/kg daily, improved GERD symptoms and healed all cases of erosive esophagitis in the treatment of 1- to 12-year-old children with GERD.[48] Other trials of PPI therapy support the efficacy of treatment of severe esophagitis and esophagitis refractory to H2RAs in children.[4,45]

As in adults, PPIs are considered safe and generally well tolerated with relatively few adverse effects. In terms of their long-term use, published studies have reported PPI use for up to 11 years in small numbers of children.[16] The Food and Drug Administration has approved a number of PPIs for use in pediatric patients in recent years, including omeprazole, lansoprazole, and esomeprazole for people 1 year and older and rabeprazole for people 12 years and older. Nonetheless, the new guidelines strike a note of caution when discussing the dramatic increase in past years in the number of PPI prescriptions written for pediatric patients, particularly infants, who may be at increased risk of lower respiratory tract infections.[54–56]

Overuse or misuse of PPIs in infants with reflux is a matter for great concern. Placebo-controlled trials in infants have not demonstrated superiority of PPIs over placebo for reduction in irritability.[57] Headaches, diarrhea, constipation, and nausea have been described as occurring in up to 14% of older children and adults prescribed PPIs.[25,58] Although considered a benign histologic change, enterochromaffin cell hyperplasia has

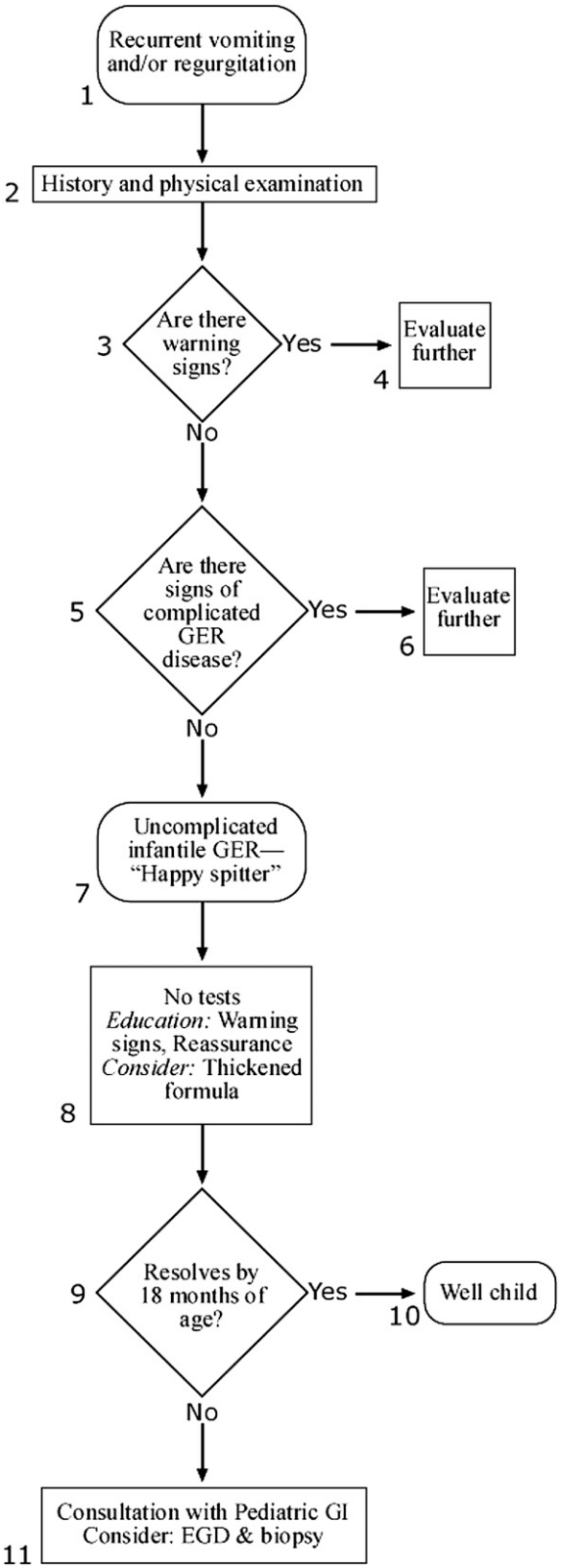

FIGURE 1
Approach to the infant with recurrent regurgitation and vomiting.

recently been demonstrated in up to 50% of children receiving PPIs for more than 2.5 years.[25] Finally, a growing body of evidence suggests that acid suppression, in general, with either H2RAs or PPIs, may be a risk factor for pediatric community-acquired pneumonia, gastroenteritis, candidemia, and necrotizing enterocolitis in preterm infants.[59,60]

Prokinetic Agents

Desired pharmacologic effects of prokinetic agents include improving contractility of the body of the esophagus, increasing lower esophageal sphincter pressure, and increasing the rate of gastric emptying. To date, efforts to design a prokinetic agent with benefits that outweigh adverse effects has proven difficult. Even metoclopramide, the most common prokinetic agent still available, recently received a black box warning regarding its adverse effects. Indeed, adverse effects have been reported in 11% to 34% of patients treated with metoclopramide, including drowsiness, restlessness, and extrapyramidal reactions. Although a meta-analysis of 7 randomized controlled trials of metoclopramide in patients younger than 2 years with GERD confirmed a decrease in GERD symptoms, it was clearly at the cost of such significant adverse effects.[61] Other drugs in this category include bethanechol, cisapride (no longer available commercially in the United States), baclofen, and erythromycin. Each works as a prokinetic by using a different mechanism. Nevertheless, after careful review, guidelines unequivocally state that there is insufficient evidence to support the routine use of any prokinetic agent for the treatment of GERD in infants or older children.[4]

Surgery for Pediatric GERD

Several surgical procedures can be used to decrease GER disorders in children. Fundoplication, whereby the gastric fundus is wrapped around the distal esophagus, is most common and can be performed to prevent reflux by increasing baseline pressure of the lower esophageal sphincter, decreasing the number of transient lower esophageal sphincter relaxations, and increasing the length of the esophagus that is intra-abdominal to accentuate the angle of His and reduce a hiatal hernia, if indicated.[17,56,57] Total esophagogastric dissociation is another operative procedure that is rarely used after failed fundoplication. Both procedures are associated with significant morbidity and do not reduce the risk of direct aspiration of oral contents. Careful patient selection is one of the keys to successful outcome.[17] Children who have failed pharmacologic treatment may be candidates for surgical therapy, as are children at severe risk of aspiration of their gastric contents. In most patients, if acid suppression with PPIs is ineffective, the accuracy of the diagnosis of GERD should be reassessed, because fundoplication may not produce optimum clinical results. Clinical conditions, such as cyclic vomiting, rumination, gastroparesis, and eosinophilic esophagitis, should

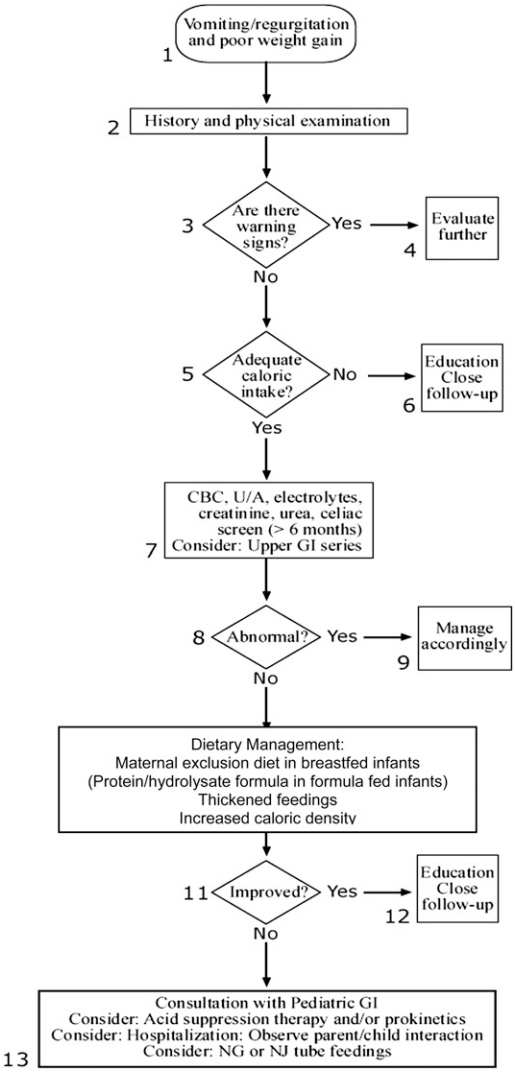

FIGURE 2
Approach to the infant with recurrent regurgitation and weight loss.

be carefully ruled out before surgery, because they are likely to still cause symptoms after surgery. If antireflux surgery is pursued, the new guidelines also stress the importance of providing families with adequate counseling and education before the procedure so that they have a "realistic understanding of the potential complications…including symptom recurrence."[4]

SUMMARY

The updated guidelines published in 2009 are particularly rich with descriptions of typical presentations of GERD across all pediatric age groups.[4] With an emphasis on evidence-based, best practice, they present a number of algorithms that can be of great use to both general pediatricians and pediatric medical subspecialists. The guidelines discuss the evaluation and management of recurrent regurgitation and vomiting in both infants and older children and the importance of distinguishing GERD from numerous other disorders. The figures shown demonstrate the recommended approaches for commonly encountered presentations of GERD in pediatric patients and are summarized here.

In the infant with uncomplicated recurrent regurgitation, it may be important to recognize physiologic GER that is effortless, painless, and not affecting growth (Fig 1). In this situation, pediatricians should focus on minimal testing and conservative management. Overuse of medications in the so-called "happy spitter" should be avoided by all pediatric physicians. Instead, pediatricians are well served to diagnose GER and provide significant parental education, anticipatory guidance, and reassurance. In turn, they will provide high-value, high-quality care without risk to their patients or unnecessary direct and indirect costs.

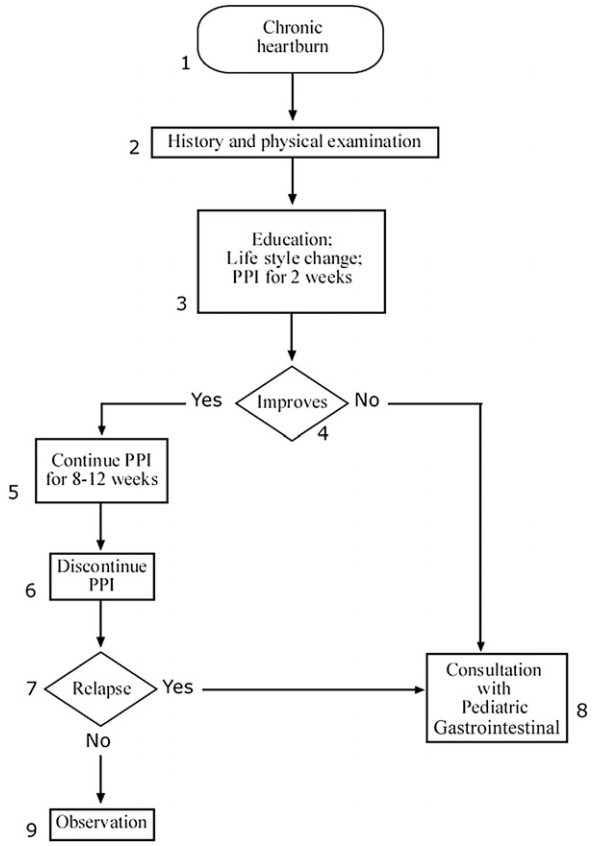

FIGURE 3
Approach to the older child or adolescent with heartburn.

Pediatricians must also be able to recognize infants with recurrent regurgitation and troublesome symptoms of GERD (Fig 2). The new guidelines emphasize weight loss as a crucial warning sign that should alter clinical management. Older children with heartburn may benefit from empirical treatment with PPIs (Fig 3). In general, there is a paucity of studies in pediatrics that demonstrate the effectiveness of this approach. Instead, it is essential to carefully follow all patients empirically treated for GERD to ensure that they are improving, because there are many clinical conditions that may mimic its symptoms. It cannot be overemphasized that pediatric best practice involves both identifying children at risk for complications of GERD and reassuring parents of patients with physiologic GER who are not at risk for complications to avoid unnecessary diagnostic procedures or pharmacologic therapy.[62–64]

LEAD AUTHORS
Jenifer R. Lightdale, MD, MPH
David A. Gremse, MD

SECTION ON GASTROENTEROLOGY, HEPATOLOGY, AND NUTRITION EXECUTIVE COMMITTEE, 2011–2012
Leo A. Heitlinger, MD, Chairperson
Michael Cabana, MD
Mark A. Gilger, MD
Roberto Gugig, MD
Jenifer R. Lightdale, MD, MPH
Ivor D. Hill, MB, ChB, MD

FORMER EXECUTIVE COMMITTEE MEMBERS
Robert D. Baker, MD, PhD
David A. Gremse, MD
Melvin B. Heyman, MD

STAFF
Debra L. Burrowes, MHA

REFERENCES

1. Nelson SP, Chen EH, Syniar GM, Christoffel KK; Pediatric Practice Research Group. Prevalence of symptoms of gastroesophageal reflux during childhood: a pediatric practice-based survey. *Arch Pediatr Adolesc Med*. 2000;154(2):150–154
2. Campanozzi A, Boccia G, Pensabene L, et al. Prevalence and natural history of gastroesophageal reflux: pediatric prospective survey. *Pediatrics*. 2009;123(3):779–783
3. Shalaby TM, Orenstein SR. Efficacy of telephone teaching of conservative therapy for infants with symptomatic gastroesophageal reflux referred by pediatricians to pediatric gastroenterologists. *J Pediatr*. 2003;142(1):57–61
4. Vandenplas Y, Rudolph CD, Di Lorenzo C, et al; North American Society for Pediatric Gastroenterology Hepatology and Nutrition; European Society for Pediatric Gastroenterology Hepatology and Nutrition. Pediatric gastroesophageal reflux clinical practice guidelines: joint recommendations of the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition (NASPGHAN) and the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN). *J Pediatr Gastroenterol Nutr*. 2009;49(4):498–547
5. Sherman PM, Hassall E, Fagundes-Neto U, et al. A global, evidence-based consensus on the definition of gastroesophageal reflux disease in the pediatric population. *Am J Gastroenterol*. 2009;104(5):1278–1295, quiz 1296
6. Shay S, Tutuian R, Sifrim D, et al. Twenty-four hour ambulatory simultaneous impedance and pH monitoring: a multicenter report of normal values from 60 healthy volunteers. *Am J Gastroenterol*. 2004;99(6):1037–1043
7. Rudolph CD, Mazur LJ, Liptak GS, et al; North American Society for Pediatric Gastroenterology and Nutrition. Guidelines for evaluation and treatment of gastroesophageal reflux in infants and children: recommendations of the North American Society for Pediatric Gastroenterology and Nutrition. *J Pediatr Gastroenterol Nutr*. 2001;32(suppl 2):S1–S31
8. Martin AJ, Pratt N, Kennedy JD, et al. Natural history and familial relationships of infant spilling to 9 years of age. *Pediatrics*. 2002;109(6):1061–1067
9. Fernandez S, Aspirot A, Kerzner B, Friedlander J, Di Lorenzo C. Do some adolescents with rumination syndrome have "supragastric vomiting"? *J Pediatr Gastroenterol Nutr*. 2010;50(1):103–105
10. Sheikh S, Goldsmith LJ, Howell L, Hamlyn J, Eid N. Lung function in infants with wheezing and gastroesophageal reflux. *Pediatr Pulmonol*. 1999;27(4):236–241
11. Sheikh S, Stephen T, Howell L, Eid N. Gastroesophageal reflux in infants with wheezing. *Pediatr Pulmonol*. 1999;28(3):181–186
12. Mastronarde JG, Anthonisen NR, Castro M, et al; American Lung Association Asthma Clinical Research Centers. Efficacy of esomeprazole for treatment of poorly controlled asthma. *N Engl J Med*. 2009;360(15):1487–1499
13. Kiljander TO, Junghard O, Beckman O, Lind T. Effect of esomeprazole 40 mg once or twice daily on asthma: a randomized, placebo-controlled study. *Am J Respir Crit Care Med*. 2010;181(10):1042–1048
14. Littner MR, Leung FW, Ballard ED, II, Huang B, Samra NK Lansoprazole Asthma Study Group. Effects of 24 weeks of lansoprazole therapy on asthma symptoms, exacerbations, quality of life, and pulmonary function in adult asthmatic patients with acid reflux symptoms. *Chest*. 2005;128(3):1128–1135
15. Sopo SM, Radzik D, Calvani M. Does treatment with proton pump inhibitors for gastroesophageal reflux disease (GERD) improve asthma symptoms in children with asthma and GERD? A systematic review. *J Investig Allergol Clin Immunol*. 2009;19(1):1–5
16. Chan WW, Chiou E, Obstein KL, Tignor AS, Whitlock TL. The efficacy of proton pump inhibitors for the treatment of asthma in adults: a meta-analysis. *Arch Intern Med*. 2011;171(7):620–629
17. DiMango E, Holbrook JT, Simpson E, et al; American Lung Association Asthma Clinical Research Centers. Effects of asymptomatic proximal and distal gastroesophageal reflux on asthma severity. *Am J Respir Crit Care Med*. 2009;180(9):809–816
18. Gibson PG, Henry RL, Coughlan JL. Gastro-oesophageal reflux treatment for asthma in adults and children. *Cochrane Database Syst Rev*. 2003;(2):CD001496
19. Jung HK. Epidemiology of gastroesophageal reflux disease in Asia: a systematic review. *J Neurogastroenterol Motil*. 2011;17(1):14–27
20. Dent J, El-Serag HB, Wallander MA, Johansson S. Epidemiology of gastro-oesophageal reflux disease: a systematic review. *Gut*. 2005;54(5):710–717
21. Cameron AJ, Lagergren J, Henriksson C, Nyren O, Locke GR, III, Pedersen NL. Gastroesophageal reflux disease in monozygotic and dizygotic twins. *Gastroenterology*. 2002;122(1):55–59
22. Chak A, Faulx A, Eng C, et al. Gastroesophageal reflux symptoms in patients with adenocarcinoma of the esophagus or cardia. *Cancer*. 2006;107(9):2160–2166
23. Mohammed I, Cherkas LF, Riley SA, Spector TD, Trudgill NJ. Genetic influences in gastro-oesophageal reflux disease: a twin study. *Gut*. 2003;52(8):1085–1089
24. Hassall E. Endoscopy in children with GERD: "the way we were" and the way we should be. *Am J Gastroenterol*. 2002;97(7):1583–1586
25. Hassall E, Kerr W, El-Serag HB. Characteristics of children receiving proton pump inhibitors continuously for up to 11 years duration. *J Pediatr*. 2007;150:262–267, 267.e1
26. Hassall E. Decisions in diagnosing and managing chronic gastroesophageal reflux disease in children. *J Pediatr*. 2005;146(suppl 3):S3–S12
27. Orenstein SR, McGowan JD. Efficacy of conservative therapy as taught in the primary care setting for symptoms suggesting infant gastroesophageal reflux. *J Pediatr*. 2008;152(3):310–314
28. Gupta SK, Hassall E, Chiu YL, Amer F, Heyman MB. Presenting symptoms of nonerosive and erosive esophagitis in pediatric patients. *Dig Dis Sci*. 2006;51(5):858–863
29. Salvatore S, Hauser B, Vandemaele K, Novario R, Vandenplas Y. Gastroesophageal reflux disease in infants: how much is predictable with questionnaires, pH-metry, endoscopy and histology? *J Pediatr Gastroenterol Nutr*. 2005;40(2):210–215
30. Kleinman L, Revicki DA, Flood E. Validation issues in questionnaires for diagnosis and monitoring of gastroesophageal reflux disease in children. *Curr Gastroenterol Rep*. 2006;8(3):230–236
31. Gold BD, Gunasekaran T, Tolia V, et al. Safety and symptom improvement with esomeprazole in adolescents with gastroesophageal reflux disease. *J Pediatr Gastroenterol Nutr*. 2007;45(5):520–529
32. Størdal K, Johannesdottir GB, Bentsen BS, Sandvik L. Gastroesophageal reflux disease in children: association between symptoms and pH monitoring. *Scand J Gastroenterol*. 2005;40(6):636–640
33. Deal L, Gold BD, Gremse DA, et al. Age-specific questionnaires distinguish GERD symptom frequency and severity in infants and young children: development and initial validation. *J Pediatr Gastroenterol Nutr*. 2005;41(2):178–185
34. Rosen R, Lord C, Nurko S. The sensitivity of multichannel intraluminal impedance and

the pH probe in the evaluation of gastroesophageal reflux in children. *Clin Gastroenterol Hepatol*. 2006;4(2):167–172

35. Rosen R, Nurko S. The importance of multichannel intraluminal impedance in the evaluation of children with persistent respiratory symptoms. *Am J Gastroenterol*. 2004;99(12):2452–2458
36. Thakkar K, El-Serag HB, Mattek N, Gilger MA. Complications of pediatric EGD: a 4-year experience in PEDS-CORI. *Gastrointest Endosc*. 2007;65(2):213–221
37. Volonaki E, Sebire NJ, Borrelli O, et al. Gastrointestinal endoscopy and mucosal biopsy in the first year of life: indications and outcome. *J Pediatr Gastroenterol Nutr*. 2012;55(1):62–65
38. Isolauri E, Tahvanainen A, Peltola T, Arvola T. Breast-feeding of allergic infants. *J Pediatr*. 1999;134(1):27–32
39. Vance GH, Lewis SA, Grimshaw KE, et al. Exposure of the fetus and infant to hens' egg ovalbumin via the placenta and breast milk in relation to maternal intake of dietary egg. *Clin Exp Allergy*. 2005;35(10):1318–1326
40. Clarke P, Robinson MJ. Thickening milk feeds may cause necrotising enterocolitis. *Arch Dis Child Fetal Neonatal Ed*. 2004;89(3):F280
41. Bhat RY, Rafferty GF, Hannam S, Greenough A. Acid gastroesophageal reflux in convalescent preterm infants: effect of posture and relationship to apnea. *Pediatr Res*. 2007;62(5):620–623
42. Corvaglia L, Rotatori R, Ferlini M, Aceti A, Ancora G, Faldella G. The effect of body positioning on gastroesophageal reflux in premature infants: evaluation by combined impedance and pH monitoring. *J Pediatr*. 2007;151:591–596, 596.e1
43. Orenstein SR, Whitington PF, Orenstein DM. The infant seat as treatment for gastroesophageal reflux. *N Engl J Med*. 1983;309(13):760–763
44. Jung WJ, Yang HJ, Min TK, et al. The efficacy of the upright position on gastroesophageal reflux and reflux-related respiratory symptoms in infants with chronic respiratory symptoms. *Allergy Asthma Immunol Res*. 2012;4(1):17–23
45. Avidan B, Sonnenberg A, Schnell TG, Sontag SJ. Walking and chewing reduce postprandial acid reflux. *Aliment Pharmacol Ther*. 2001;15(2):151–155
46. Moazzez R, Bartlett D, Anggiansah A. The effect of chewing sugar-free gum on gastro-esophageal reflux. *J Dent Res*. 2005;84(11):1062–1065
47. Smoak BR, Koufman JA. Effects of gum chewing on pharyngeal and esophageal pH. *Ann Otol Rhinol Laryngol*. 2001;110(12):1117–1119
48. Cucchiara S, Staiano A, Romaniello G, Capobianco S, Auricchio S. Antacids and cimetidine treatment for gastro-oesophageal reflux and peptic oesophagitis. *Arch Dis Child*. 1984;59(9):842–847
49. Sedman A. Aluminum toxicity in childhood. *Pediatr Nephrol*. 1992;6(4):383–393
50. Tsou VM, Young RM, Hart MH, Vanderhoof JA. Elevated plasma aluminum levels in normal infants receiving antacids containing aluminum. *Pediatrics*. 1991;87(2):148–151
51. American Academy of Pediatrics, Committee on Nutrition. Aluminum toxicity in infants and children. *Pediatrics*. 1996;97(3):413–416
52. Gremse DA. GERD in the pediatric patient: management considerations. *MedGenMed*. 2004;6(2):13
53. Simeone D, Caria MC, Miele E, Staiano A. Treatment of childhood peptic esophagitis: a double-blind placebo-controlled trial of nizatidine. *J Pediatr Gastroenterol Nutr*. 1997;25(1):51–55
54. Barron JJ, Tan H, Spalding J, Bakst AW, Singer J. Proton pump inhibitor utilization patterns in infants. *J Pediatr Gastroenterol Nutr*. 2007;45(4):421–427
55. Orenstein SR, Hassall E. Infants and proton pump inhibitors: tribulations, no trials. *J Pediatr Gastroenterol Nutr*. 2007;45(4):395–398
56. Orenstein SR, Hassall E, Furmaga-Jablonska W, Atkinson S, Raanan M. Multicenter, double-blind, randomized, placebo-controlled trial assessing the efficacy and safety of proton pump inhibitor lansoprazole in infants with symptoms of gastroesophageal reflux disease. *J Pediatr*. 2009;154:514–520.e4
57. Moore DJ, Tao BS, Lines DR, Hirte C, Heddle ML, Davidson GP. Double-blind placebo-controlled trial of omeprazole in irritable infants with gastroesophageal reflux. *J Pediatr*. 2003;143(2):219–223
58. Tolia V, Fitzgerald J, Hassall E, Huang B, Pilmer B, Kane R III. Safety of lansoprazole in the treatment of gastroesophageal reflux disease in children. *J Pediatr Gastroenterol Nutr*. 2002;35(suppl 4):S300–S307
59. Canani RB, Cirillo P, Roggero P, et al; Working Group on Intestinal Infections of the Italian Society of Pediatric Gastroenterology, Hepatology and Nutrition (SIGENP). Therapy with gastric acidity inhibitors increases the risk of acute gastroenteritis and community-acquired pneumonia in children. *Pediatrics*. 2006;117(5). Available at: www.pediatrics.org/cgi/content/full/117/5/e817
60. Saiman L, Ludington E, Dawson JD, et al; National Epidemiology of Mycoses Study Group. Risk factors for Candida species colonization of neonatal intensive care unit patients. *Pediatr Infect Dis J*. 2001;20(12):1119–1124
61. Craig WR, Hanlon-Dearman A, Sinclair C, Taback S, Moffatt M. Metoclopramide, thickened feedings, and positioning for gastro-oesophageal reflux in children under two years. *Cochrane Database Syst Rev*. 2004;(4):CD003502
62. Marchant JM, Masters IB, Taylor SM, Cox NC, Seymour GJ, Chang AB. Evaluation and outcome of young children with chronic cough. *Chest*. 2006;129(5):1132–1141
63. Størdal K, Johannesdottir GB, Bentsen BS, et al. Acid suppression does not change respiratory symptoms in children with asthma and gastro-oesophageal reflux disease. *Arch Dis Child*. 2005;90(9):956–960
64. Chang AB, Connor FL, Petsky HL, et al. An objective study of acid reflux and cough in children using an ambulatory pHmetry-cough logger. *Arch Dis Child*. 2011;96(5):468–472

Gastroesophageal Reflux: Management Guidance for the Pediatrician

Jenifer R. Lightdale, David A. Gremse and SECTION ON GASTROENTEROLOGY, HEPATOLOGY, AND NUTRITION

Pediatrics 2013;131;e1684; originally published online April 29, 2013;
DOI: 10.1542/peds.2013-0421