



CE/CME

## Pediatric GERD

*Clinician Reviews*. 2013 May;23(5):40-47**Author(s):** [Ellen D. Mandel, DMH, MPA, PA-C, CDE](#); [Claudia Ashforth, PA-S](#); [Kristine Daugherty](#)

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**Expires May 31, 2014**

As with US adults, infants and children appear to be at increased risk for gastroesophageal reflux disease (GERD). Lacking a cardinal symptom in children and often linked with conf symptoms, pediatric GERD challenges the primary care clinician to make an early diagnosis, preventing progressive damage and possible complications. Management begins with pharmacologic and surgical options are reserved for specific pediatric patients.

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*CE/CME No: CR-1305*

### PROGRAM OVERVIEW

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### EDUCATIONAL OBJECTIVES

- Differentiate between *gastroesophageal reflux* and *gastroesophageal reflux disease* (GER and GERD, respectively) in the pe symptomatology and risk factors.
- Explain typical and atypical presentations of GERD as factors in the differential diagnosis.
- Describe diagnostic testing options for GERD and their appropriate use in infants and children with suspected GERD.
- Discuss age-appropriate strategies to reduce the symptoms of GERD in children, including lifestyle changes and pharmacol

### FACULTY

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*The authors have no significant financial relationships to disclose.*

### ACCREDITATION STATEMENT

This program has been reviewed and is approved for a maximum of 1.0 hour of American Academy of Physician Assistants (A credit by the Physician Assistant Review Panel; and by the Nurse Practitioner Association New York State (The NPA) for 1.0 co valid for one year from the issue date of **May 2013**.



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*As with US adults, infants and children appear to be at increased risk for gastroesophageal reflux a cardinal symptom in children and often linked with confounding extra-esophageal symptoms, pe the primary care clinician to make an early diagnosis, preventing progressive damage and possib Management begins with conservative lifestyle changes; pharmacologic and surgical options are pediatric patients.*

Traditionally, gastroesophageal reflux disease (GERD) has been viewed as an adult disease, but it is now recognized as a disc children. A teenager with heartburn, a child with complaints of chest pain, and a coughing infant refusing to feed may all be e the literature reveals an increased incidence of GERD in both adults and children, making it one of the five most common gas conditions in the United States.<sup>1</sup>

US pediatric hospitalization rates associated with GERD significantly increased from 1995 to 2000, accounting for 4% of these review of ICD-9 codes in a large claims database, GERD was diagnosed in 12.3% of North American infants and in 1% of other In another recent study in which pediatric endoscopy data from 1999 to 2002 were analyzed, 9.5% of children age 1 year and had erosive esophagitis.<sup>4</sup>

It is unclear whether the increased frequency in diagnosis of GERD should be attributed to improved diagnostic strategies or disease prevalence.<sup>1</sup> In any event, a timely diagnosis of GERD is essential to allow for appropriate intervention and early symy reduce the risk for complications.

Overall, GERD is primarily a Western disease, affecting an estimated 10% to 15% of this geographic population. It is associatec dietary trends, and other causes.<sup>5</sup> Prevalence of GERD in the general population has been shown to vary across ethnic group Hispanic descent are more likely to be affected than whites, with symptoms of GERD least common among Asian-Americans.

Since pediatric GERD is seen in primary care settings in the same rising numbers as associated hospital admissions, clinician: care must be aware of its contributing factors, treatment modalities that are most effective in reducing symptoms, and strateg disease. Treatment choices vary according to patient age-groups: infants (younger than 1 year), children ages 1 to 11 years, an

## **DISTINGUISHING GERD FROM GER**

*Gastroesophageal reflux* (GER) is the term used to describe the passage of gastric contents, including stomach acid, fluids, ar esophagus, with or without regurgitation or vomiting.<sup>6</sup> GER is a normal, common physiologic process among infants, in whom stomach size, and predominance of the recumbent position allow reflux to occur during transient relaxation of the lower esop

Healthy infants and children may have asymptomatic episodes of GER; or episodes may be short, lasting less than three minu postprandially.<sup>6</sup> Only when GER involves blood loss, esophagitis, strictures, nutritional deficits, and/or apnea should GERD be

The pathologic process known as *GERD* involves persistent, troublesome symptoms resulting from continued mucosal expos damaging the lining of the esophagus and possibly leading to erosive esophagitis.<sup>6,10,11</sup> Endoscopic findings indicating GERD- damage include visible tears in the esophageal mucosa near the gastroesophageal junction<sup>6</sup> (see Figure 1). In one single-cen of patients with pediatric GERD who underwent endoscopy had erosive esophagitis.<sup>4</sup>

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## **SIGNS AND SYMPTOMS**

Symptoms of GERD vary among adults and children in different age-groups. According to the Montreal definition, which was developed and modified by an international panel of pediatric gastroenterologists,<sup>10,12</sup> GERD should be suspected in inf

to thrive and exhibit the symptoms listed in Table 1.<sup>10,12</sup> Clinicians should also consider GERD in older children and adolescents with heartburn, since it is the most common initial presenting symptom.<sup>10,13</sup> Of note, a 2010 database study of UK children with GERD incidence before age 1 year and the greatest incidence among 16- to 17-year-olds.<sup>5</sup>

GERD should also be considered in pediatric patients who complain of vague symptoms of “stomachache” or nausea, abdominal pain or chest pain, since children may have trouble describing the sensation of heartburn.<sup>6,10</sup> Children may also present with extra-esophageal complaints, such as dry cough, asthma-like symptoms, sore throat, hoarseness, sleep apnea, or dysphagia, all of which can be complications of GERD.<sup>10,11</sup> Researchers have suggested that GERD contributes to and/or exacerbates pulmonary fibrosis, asthma, and chronic cough.<sup>6,10</sup> Therefore, clinicians should consider GERD in children with these seemingly unrelated illnesses.

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## RISK FACTORS

Certain pediatric groups are at increased risk for severe GERD, with or without complications. Neurologic impairment can cause anatomic abnormalities such as hiatal hernia can impair lower esophageal sphincter function, allowing acid to rise into the esophagus. Lists illnesses and congenital conditions that are considered predisposing factors for severe, chronic GERD.

When seeing patients in these populations, clinicians should specifically focus on relevant GI symptoms during the history and physical exam. Clinicians should also consider long-term monitoring for complications or changes that might indicate new-onset GERD.

### Overweight and Obesity

Although data are limited on the relationship between pediatric GERD and obesity,<sup>14</sup> associated research findings seem to conflict with the established relationship in adult patients. While certain study groups found an association between obesity, elevated BMI, and increased waist circumference with an increase in symptoms of GERD (eg, regurgitation, heartburn),<sup>15,16</sup> others found no significant correlation between overweight and reflux esophagitis.<sup>14,17</sup> Notably, one analysis found a significant correlation between male gender and incidence of GERD.<sup>17</sup>

Although the evidence is not conclusive, clinicians are encouraged to counsel the older children among their patients on the importance of BMI reduction—encouraging them to achieve an overall healthier lifestyle and avoid diseases associated with excess weight.

## DIFFERENTIAL DIAGNOSIS

In infants with unusual symptoms, certain GI conditions such as obstructive disorders (eg, pyloric stenosis), motility disorders, must be ruled out with further diagnostic testing.<sup>6,7</sup> Red-flag symptoms that warrant further investigation include hematemesis, diarrhea, abdominal tenderness or distention, constipation, bilious vomiting, onset of vomiting after age 6 months, failure to thrive, microcephaly, fever, lethargy, and hepatosplenomegaly.<sup>6,7</sup> More common differentials are described below.

### Eosinophilic Esophagitis

*Eosinophilic esophagitis* is an inflammatory condition of the esophagus, an apparent manifestation of food allergy (eg, milk protein) infiltrating mucosal eosinophils.<sup>6,18</sup> First identified in children (though also occurring in adults), eosinophilic esophagitis is becoming a more common cause of dysphagia than GERD.<sup>6</sup>

This recently discovered disease is often mistaken for GERD. While symptoms including heartburn and dysphagia occur in eosinophilic esophagitis can only be diagnosed via multiple endoscopic mucosal biopsies. Corticosteroid therapy has been found to be an effective treatment for this condition than acid suppression therapy.<sup>19</sup>

Current research is focused on a possible link between eosinophilic esophagitis and autoimmune disease, as many affected

asthma, allergic rhinitis, and/or eczema.<sup>19</sup> The increasing prevalence of childhood allergies should prompt clinicians to place on the short list of differentials when evaluating a child for GERD-type symptoms. Referral for evaluation by an allergist may a

### **Asthma**

GER may actually trigger asthma in some patients, even without symptoms of GERD.<sup>6</sup> While there is support for a possible link between asthma in infants and children, a definitive relationship cannot be confirmed without more reliable studies.<sup>20</sup> However, the possibility of GERD in a child who presents with symptoms indicative of asthma, such as wheezing, shortness of breath, cough

### **Other Extra-Esophageal Diseases**

Concern exists over apparent associations between GERD and other extra-esophageal illnesses. In addition to asthma, the MCG group<sup>10,12</sup> found a connection between GERD and other respiratory conditions, including chronic cough and chronic laryngitis. Researchers usually represent multifactorial disease processes, and GER can be an exacerbating factor rather than an independent condition.<sup>5,10</sup>

Further manifestations of extra-esophageal GERD include pneumonia, bronchiectasis, any apparent life-threatening event, laryngitis, and dental erosion. Again, causality has not been clearly established, and the shortage of high-quality studies with adequate sample sizes makes it impossible to confirm clear relationships.<sup>21</sup> It is therefore prudent for clinicians to evaluate any child with these non-GI conditions.

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## **EVALUATION AND DIAGNOSIS**

In 2009, the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition and the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition (NASPGHAN and ESPGHAN)<sup>6</sup> released international guidelines for the management of GERD, including evaluation, diagnosis, and treatment. Making a diagnosis of GERD in an infant or a toddler can be challenging, since specific pathognomonic symptoms are not known. Older children and adolescents are better able to articulate their presenting symptoms (as of adults); thus, a detailed history and physical exam are ordinarily adequate to diagnose GERD and introduce treatment in these children.

The diagnostic tool that is considered the gold standard for pediatric patients, including infants, is *24-hour esophageal pH monitoring*, which directly measures the quantity of acid present in the esophagus by way of an internal probe that is passed through the mouth. Esophageal pH monitoring quantifies the amount of acid to which the esophagus is exposed over this time period, compared with normal pediatric values.<sup>6,13</sup>

However, a newer combined *multichannel intraluminal impedance and pH monitoring* (MII/pH) tool offers advantages over esophageal pH monitoring as it detects nonacidic or weakly acidic reflux events, in addition to more obvious episodes of acidic reflux.<sup>6,13,22</sup>

Clinical benefits of the MII/pH are:

- Better efficiency than pH monitoring alone in the evaluation of respiratory symptoms and GERD
- Ability to correlate timing of reflux episodes with symptoms, including chronic cough, apnea, and other respiratory symptoms
- Improved accuracy in monitoring postprandial reflux episodes, which are typically less acidic.<sup>13,23</sup>

Additionally, MII/pH provides a graphic readout from which the duration, height, and frequency of the reflux episodes can be determined. A chief disadvantage to its use is the absence of standardized pediatric values.<sup>13</sup>

*Endoscopic biopsy* should not be used to establish whether esophagitis is due to reflux. Endoscopically visible breaks in the mucosa are the most reliable indicators of reflux esophagitis. However, because other signs, such as mucosal erythema, pallor, and leukoplakia, have normal variations, they cannot be considered evidence of reflux esophagitis.<sup>6</sup> Endoscopic biopsy is mainly recommended for suspected Barrett's esophagus (which is rare in children) or for eosinophilic esophagitis, as it can confirm infiltrating mucosal eosinophils.

*Nuclear scintigraphy* uses imaging to time the passage of a radioisotope-labeled meal through the upper GI tract. It can provide information on gastric emptying, which may be delayed in children with GERD. It may also be useful in diagnosing aspiration in patients with respiratory symptoms.<sup>6</sup> Because standardized techniques and age-specific norms are lacking, however, nuclear scintigraphy is not recommended for patients with other potentially reflux-related symptoms. The sensitivity of this test is low, and negative results may not exclude reflux and aspiration.<sup>6</sup>

*Barium contrast radiography (upper GI series)* is not recommended due to its poor sensitivity and specificity. This test is useful for identifying anatomical anomalies, however.<sup>6</sup>

For infants and toddlers with symptoms suggestive of GERD, the NASPGHAN/ESPGHAN authors<sup>6</sup> find no evidence to support pharmacologic treatment to confirm the diagnosis. For older, verbal children and adolescents who present with heartburn and regurgitation, a 4-week trial (as long as 4 weeks) of acid suppressants may be used to identify acid reflux as the cause of these symptoms.

Based on the guidelines by Vandenplas et al,<sup>6</sup> a clinician's initial approach to evaluation for GERD and its diagnosis should be based on history and physical exam and the least invasive diagnostic process possible. The child's specific symptoms and suspected involved organ systems will dictate the use of progressively invasive diagnostic strategies.

## **MANAGEMENT OF GERD**

### **Conservative Treatment**

Nonpharmacologic, age-appropriate approaches focus on diet and lifestyle changes. An effective treatment option for infants is to thicken the formula, resulting in decreased visible reflux and regurgitation.<sup>6,8</sup> Recommended amounts of thickened formula are four to eight daily feedings, depending on the age of the patient; infants close to 1 year require only four feedings.<sup>8</sup> For breastfed infants, breast milk can be thickened with rice cereal and given at comparable volumes.<sup>8</sup>

Recommendations from the NASPGHAN/ESPGHAN clinical practice guidelines<sup>6</sup> include a two- to four-week trial of an extensively hydrolyzed formula for formula-fed infants who vomit frequently. These formulas are considered hypoallergenic and contain shorter protein chains for easier digestion.<sup>8</sup>

Lifestyle changes recommended for adults with GERD can also be tailored for use in pediatric patients (see Table 3<sup>8,11</sup>). They include avoidance of overfeeding by giving smaller portions at greater frequency (as described above), avoidance of foods known to cause GERD (e.g., chocolate, caffeine, citrus, fatty foods, and tomato products), avoidance of cigarette smoke, restriction of eating and drinking close to bedtime, elevation of the head of the bed or crib (use of a pillow is not recommended for children younger than 1 year), and a left-sided sleeping position for adolescents.<sup>6,11</sup>

Holding infants upright for 30 minutes after feeding with ample burping may reduce reflux.<sup>11</sup> In infants, the prone position provides the greatest benefit for reducing acid reflux, according to findings from one study based on pH monitoring.<sup>13</sup> Nonetheless, the association between prone positioning and sudden infant death syndrome (SIDS) has led to recommendations of supine positioning when infants sleep unobserved.<sup>6</sup> Perhaps supervised "tummy time" several times per day (eg, after feeding) can help reduce symptoms in infants.

Finally, breastfeeding mothers are advised to avoid consuming cow's milk, eggs, and soy products, as their presence in breast milk may promote reflux in an infant with unrecognized food allergy.<sup>6,8</sup>

### **Pharmacologic Treatment**

Since esophagitis develops as a result of continuous acid exposure from the refluxate, the primary pharmacologic therapy for GERD is aimed at acid reduction in the upper GI tract. Current pharmacologic options include histamine<sub>2</sub>-receptor antagonists (H<sub>2</sub>RAs) and proton pump inhibitors (PPIs).<sup>6</sup> H<sub>2</sub>RAs have been shown to alleviate symptoms and promote mucosal healing. To their disadvantage, long-term use can lead to drug tolerance.

PPIs are superior to H<sub>2</sub>RAs in symptom relief and esophageal healing without causing tolerance; however, although certain a for treatment of children age 1 year or older with GERD (including esomeprazole, lansoprazole, and omeprazole), use of PPIs year is controversial.<sup>6,13</sup> (See “New Solution for Pediatric GERD?”<sup>24,25</sup>)

According to results from existing studies of PPI use in infants with GERD ages 34 weeks to 1 year, PPIs are no more effective at symptom reduction than placebo.<sup>2,26</sup> Further, data to demonstrate efficacy of long-term PPI use in infants and toddlers are scant.<sup>6,27</sup> Safety results from various trials are inconsistent, ranging from no reported adverse effects to rare but severe adverse events, including necrotizing enterocolitis in infants, and lower respiratory tract infections, community-acquired pneumonia, gastric polyps, and acute gastroenteritis in children.<sup>2,26</sup>

The most common adverse effects of esomeprazole use in infants and children are nausea, vomiting, diarrhea, pyrexia, and headache.<sup>4,6</sup> Because of these potential risks, none of the PPIs is approved for use in infants younger than 1 year. However, a long as 4 weeks (along with lifestyle changes) for symptom reduction in older children is recommended by the NASPGHAN/ESPGHAN guidelines.<sup>2,6,13</sup>

Also based on the NASPGHAN/ESPGHAN guidelines,<sup>6</sup> empiric PPI therapy is not recommended in pediatric patients present asthma. One research team has reported that asthma symptoms may be validly treated with a PPI in patients who do not resp treatment *and* who have a high reflux index.<sup>28</sup> However, an absence of studies to support this finding makes a firm recomme

According to the NASPGHAN/ESPGHAN guidelines,<sup>6</sup> there is insufficient evidence to justify the use of prokinetic agents (eg, erythromycin, bethanechol, domperidone) for pediatric GERD, as their potential risks outweigh their potential benefits. Neither sucralfate recommended for long-term therapy, because PPIs and H<sub>2</sub>RAs are considered more effective.<sup>6</sup>

### **Surgical Treatment**

As with adults, surgery should be a last resort for treatment. Antireflux surgery is deemed appropriate only in children who ca medical therapy due to life-threatening complications, who cannot comply with the treatment schedule, or in whom medicati ineffective.<sup>6</sup>

The gold standard for the surgical treatment of GERD is laparoscopic *Nissen fundoplication*, a procedure in which the shape modified to provide strength and functional support to the lower esophageal sphincter.<sup>29</sup> Although children with heartburn, a symptoms, or steroid-dependent asthma have been found to benefit clinically from long-term medical therapy or antireflux su benefits of surgical versus medical treatment in these children is unknown.<sup>6</sup>

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### **PROGNOSIS AND FOLLOW-UP**

The large majority of infants respond well to conservative nonpharmacologic treatment and outgrow their reflux symptoms by maturation of muscle control and lower esophageal sphincter function.<sup>7</sup> Further testing and intervention is generally not requ and parents should be reassured by this information.<sup>6,7</sup> If regurgitation does not resolve by age 12 to 18 months, or if red-flag referral to a pediatric gastroenterologist is recommended.<sup>6</sup>

For older children and adolescents with GERD, lifestyle changes should be implemented first, followed by short-term pharma recommended by appropriate guidelines.

Children with other illnesses or complications, such as neurologic impairment,<sup>6</sup> premature birth, or a strong family history of se poorer prognosis and may require more aggressive diagnostic evaluation and management.<sup>7</sup> Complications such as esopha esophagus, which poses an increased risk for adenocarcinoma, require referral to a specialist for further evaluation.<sup>10</sup>

## CONCLUSION

GERD is no longer a condition found only in adults. Since primary care practitioners are increasingly likely to see GERD in the important for these clinicians to become familiar with the contributing factors, definitive signs and symptoms, diagnosis, and t Children at high risk for GERD should be followed closely and introduced to appropriate lifestyle modifications to avoid the tr GERD and its complications, whenever possible. In the differential diagnosis, respiratory illnesses and other extra-esophagea eosinophilic esophagitis in allergic patients, should be considered.

Practitioners should consult the 2009 NASPGHAN/ESPGHAN clinical practice guidelines for further details regarding the eva preferred treatment, management of pediatric GERD, and indications for specialist referral. Research is ongoing in many area of PPI use in pediatrics. More research is needed to clarify the theorized link between GERD and asthma.

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