Katja Kovacic, MD, is a pediatric gastroenterologist at Children’s Hospital of Wisconsin and an assistant professor of Gastroenterology at the Medical College of Wisconsin.

In Western countries, 2-8 percent of children are diagnosed with gastroesophageal reflux disease (GERD), and proton-pump inhibitors prescribed for reflux account for the highest drug expenditure in the United States. Gastroesophageal reflux (GER) refers to the passage of gastric contents into the esophagus with or without regurgitation, and it is a physiologic process occurring several times per day during transient relaxations of the lower esophageal sphincter (LES). In healthy infants and children GER causes no significant symptoms. Regurgitation or spitting up occurs daily in about 50 percent of infants who are under 3 months of age, and regurgitation resolves spontaneously in nearly all healthy infants by 12-14 months of age.

Gastroesophageal reflux disease is present when reflux causes troublesome symptoms or complications. The vast majority of children with reflux symptoms do not have identifiable erosions on upper endoscopy examination and are classified as having nonerosive reflux disease.
Presentation and risk factors
Reflux can sometimes trigger vomiting. This is likely triggered by the stimulation of pharyngeal sensory afferent nerves by the refluxate. Symptoms that may be associated with GERD include:

- Recurrent regurgitation with/without vomiting
- Heartburn or chest pain
- Epigastric discomfort
- Infant irritability
- Dysphagia/odynophagia
- Cough
- Wheezing
- Hoarseness
- Stridor
- Poor weight gain

It is important to note that many of these symptoms may be clues to other disorders, including cow’s milk intolerance, peptic ulcer disease, eosinophilic esophagitis, rumination syndrome, pulmonary disease, tracheomalacia, esophageal atresia, tracheoesophageal fistula and even foreign body ingestion. You can infer a diagnosis of GERD when there is a clear association of symptoms with reflux events in the absence of alternative diagnoses.

Familial clustering of GERD and its complications – such as hiatal hernia, erosive esophagitis and Barrett’s esophagus – suggest a genetic predisposition. Other risk factors for GERD include alterations in protective mechanisms. These include decreased neural protective reflexes of the aerodigestive tract due to brain pathology, insufficient clearance and buffering of the refluxate, compromised epithelial healing and repair and delayed gastric emptying. Specific pediatric populations at risk of GERD include those with neurological impairment, obesity, esophageal atresia, repaired achalasia, certain genetic syndromes, chronic lung disease and premature birth. The presence of hiatal hernia compromises all of the antireflux barriers of the LES, allowing for more frequent transient LES relaxations.

Diagnostic testing
A patient’s history and physical examination are generally sufficient to diagnose GERD. However, atypical symptoms and extraesophageal complications – including chronic cough, chest pain and apparent life-threatening events – may require further investigation. The majority of apparent life-threatening events are not related to GERD. Small studies indicate that about 15 percent of life-threatening episodes can be associated with GERD.

Few tests can specifically diagnose reflux or predict response to therapy. Instead, diagnostic tests are mainly useful to document the presence of pathologic reflux, establish a causal relationship between reflux and symptoms, assess effectiveness of therapy and exclude other conditions.

Upper Endoscopy
Biopsy findings on upper endoscopy (eosinophilia, basal cell hyperplasia, elongated papillae, etc.) are insufficiently sensitive or specific for diagnosing GERD. Similarly, the absence of these histological findings does not effectively rule out GERD. Macroscopic findings of mucosal
erythema, pallor and abnormal vascular markings are also very nonspecific and represent a variation of normal mucosa. When found, the presence of visible mucosal breaks and erosions of distal esophagus is a fairly reliable indicator of reflux esophagitis. Further, upper endoscopy is an important tool to rule out other conditions such as eosinophilic esophagitis and peptic ulcer disease or complications of esophagitis such as peptic strictures or Barrett’s esophagus.

**Barium contrast study**
Upper gastrointestinal contrast study is neither sensitive nor specific for the diagnosis of GERD. The high frequency of physiologic reflux may cause false positive results while the brief duration of the test is insufficient to evaluate for GERD. Therefore, the test should be used to detect anatomical abnormalities such as hiatal hernia, achalasia, trachea-esophageal fistula, esophageal stricture, pyloric stenosis and intestinal malrotation.

**Esophageal pH monitoring**
This test measures esophageal acid exposure quantitatively and compares it with normative data. Pediatric norms, especially for infants, are lacking. The frequent feedings of infants may buffer refluxate and also confound study results, hence existing parameters should be regarded as guidelines and individually interpreted. Both catheter and wireless techniques are available. A reflux episode is defined as an esophageal pH drop <4. Esophageal pH monitoring may be useful to assess the efficacy of anti-secretory therapy and to temporally correlate symptoms (e.g., cough, chest pain) with acid reflux episodes, however, the severity of pathologic acid reflux does not always correlate with symptom severity and reflux complications. The clinical utility of pH monitoring for the assessment of extra-esophageal complications of GERD, along with its sensitivity and specificity, are not well established.

**Esophageal pH-impedance monitoring**
Many patients have symptoms despite persistent use of acid suppression medications. Non-acid and weakly acidic reflux can also cause symptoms and are especially common in children and in the postprandial period. Esophageal pH-impedance monitoring not only detects acid by a pH sensor but also non-acid reflux episodes by impedance. This catheter-based technique is based on measuring the resistance to alternating current (i.e., impedance) of the contents of the esophagus. It is thus able to detect esophageal bolus transit. Compared with pH monitoring alone, this method allows for superior temporal association between symptoms and reflux along with detection of composition (gas versus liquid), height and direction of refluxate (reflux versus swallow). Given that it can detect non-acid reflux, the test can be used while on acid suppression to assess treatment efficacy.

**Treatment**
Adding thickening agents (such as rice cereal) to formulas or using commercial antiregurgitant formulas can decrease the frequency of overt regurgitation. However, the frequency of reflux episodes is not clearly decreased when measured by pH-impedance studies. The flat prone compared to flat supine infant position reduces acid reflux episodes, but with the risk of sudden infant death syndrome, prone position should not be recommended. pH impedance studies indicate that the amount of reflux is similar in the left-side down and prone positions while the semi-supine position attained in a car seat actually exacerbates reflux. There is no data on positioning for reflux beyond infancy but adolescents, like adults, may benefit from elevation of
the head of the bed and left lateral decubitus positioning. Beyond infancy, current evidence does not support or refute dietary changes to treat GERD, but experts still recommend avoidance of caffeine, chocolate, spicy foods and alcohol if they provoke symptoms. Weight loss should be recommended in obese individuals.

Histamine-2 receptor antagonists decrease acid secretion from gastric parietal cells and increase gastric pH within 30 minutes of administration. However, tachyphylaxis has been observed after only six weeks of therapy and should be considered with chronic use. In some infants, H2RAs can cause irritability, headache, somnolence and other side effects. This could be interpreted as persistent GERD and result in inappropriate dose increases.

Proton-pump inhibitors inhibit acid by blocking the H+-K+ ATPase (also known as the proton pump) on gastric parietal cells. They produce higher and faster rates of healing of erosive esophagitis than H2RAs. Compared with H2RAs, PPIs maintain gastric pH alkaline for longer periods and also inhibit gastric acid secretion post-prandially. This also reduces post-prandial gastric volume, which improves volume (non-acid) reflux. PPIs are thus considered superior to H2RAs. No placebo-controlled trial in infants with symptoms of reflux has shown any benefit of PPIs, and they are not approved for use in children under 1 year of age. Side effects of PPIs – such as headache, nausea, constipation and diarrhea – occur in 2-7 percent of children and may resolve with a lower dose. Increasing evidence links acid suppression with community-acquired pneumonia, gastroenteritis, fungal infections and necrotizing enterocolitis in preterm infants. This is thought to be due to alterations of gastric and intestinal flora. Drug interactions with PPI also deserve consideration. A patient should be referred to a gastroenterologist in treatment-refractory cases or when a patient is unable to wean off acid suppression.

Antireflux surgery (Nissen fundoplication) may be of benefit in select children who have failed extended medical therapy or who have serious complications of GERD, such as recurrent aspiration. There is a lack of studies in children without severe underlying conditions and little objective post-operative data to evaluate surgical outcomes. Children with neurological impairment predisposing to severe GERD are at high risk of operative failure and morbidity. Complications include disruption of the wrap and slippage into chest, dysphagia and difficulties with eructation and vomiting. Altered gastric capacity, accommodation and sensory response may result in gas-bloat syndrome, early satiety, retching and dumping syndrome. Before surgical referral, nonreflux conditions need to be carefully excluded and surgical complications discussed with family.

References

To refer a patient
Visit chw.org/refer or call (414) 266-2460 or toll-free (800) 266-0366.

To make an appointment
Call Central Scheduling at (414) 607-5280 or toll-free (877) 607-5280.

For more information
chw.org/gi