Gastroesophageal reflux is one of the most prevalent gastrointestinal problems that occurs in children. The term refers to the presence of gastric contents proximal to the stomach. It is not uncommon for many infants to have recurrent problems of spitting up and vomiting during the first year of life. This problem can range from the occasional “burp and spit-up” to life-threatening malnutrition from severe regurgitation with failure to thrive. When dangerous consequences exist secondary to gastroesophageal reflux, it is termed gastroesophageal reflux disease (GERD).

Gastroesophageal reflux is a physiologic occurrence that takes place more often during infancy and decreases with advancing age. Evaluation of most of these infants usually reveals no definable anatomic, metabolic, infectious, or neurologic cause of reflux.

Physiology

GERD results from an increased frequency or duration of reflux episodes, from increased noxiousness of the refluxate or from the refluxate reaching locations beyond the esophagus, such as the airway, which can produce untoward effects. The upper gastrointestinal (GI) tract distal to the mid-esophagus is composed of smooth muscle layers. It is the
peristaltic wave of contraction using these involuntary muscle layers which propels ingested food forward through the esophagus into the stomach. At the distal end of the esophagus lies the tonically contracted smooth muscle known as the lower esophageal sphincter (LES). This sphincter relaxes in accordance to allow the bolus of food from the esophagus to pass into the stomach. It is also the main barrier to the retrograde movement of gastric contents. It was previously thought that abnormalities in the resting tone of the LES with persistent LES hypotonia was responsible for gastroesophageal reflux during infancy. Current theory supports the possibility that the LES undergoes episodes of transient relaxations out of coordination with the normal esophageal peristaltic mechanism. These transient LES relaxations allow gastric contents to reflux into the esophagus. This hypothesis is based on current evidence showing this mechanism to be the primary mode of reflux in older children and adults with gastroesophageal reflux.

**Clinical presentation**

Gastroesophageal reflux occurs to some extent in all individuals throughout the day. It is considered physiologic if the person experiences no consequences of this reflux. Complications usually do not occur if the frequency and duration of reflux are within the normal range. For example, infants with regurgitation as the only manifestation of gastroesophageal reflux are considered to have physiologic reflux and are referred to as “happy spitters.” Although many older children and adults can report symptoms such as heartburn, infants often present with different manifestations of reflux. The majority of manifestations of GERD in infants are suprapedia, with regurgitation being the most frequently observed symptom of gastroesophageal reflux in infants. Infantile reflux becomes symptomatic during the first few months of life, peaks by 4 to 5 months, and usually resolves by 12 to 24 months of age. More than 90% of infants with reflux will stop vomiting by 18 months of age. Because most of these infants with symptoms of gastroesophageal reflux are thriving and healthy, they require little more than a careful history and examination with appropriate parental reassurance.

It is important to distinguish benign gastroesophageal reflux from pathologic GERD, which can manifest as malnutrition, respiratory disorders, esophagitis and its complications. As mentioned earlier, regurgitation is the most common manifestation of infant reflux. Although most often immediate postprandial, it can be delayed for up to 2 hours after feedings. Important differential diagnoses to be considered in evaluating a child with regurgitation include anatomic anomalies and milk protein allergy. Weight loss is one of the most common findings associated with regurgitant reflux. It may be secondary to both emesis with caloric loss and anorexia (presumably due to esophagitis). Crying and irritability resulting from esophagitis may be the nonverbal infant’s equivalent of the adult’s complaints of heartburn and chest pain. Also, behavior consisting of yawning, hiccups, arching, stretching, stridor, and mouthing has also been shown to be associated with onset of esophageal acidification. Distinguishing these symptoms of gastroesophageal reflux from infantile colic can be particularly challenging for the pediatrician. Inadequate caloric intake may be secondary to odynophagia, parental hesitancy to feed the infant because of increased regurgitation.

**Figure. Clinical presentations of gastroesophageal reflux.**

- Gastrointestinal system
  - Emesis
  - Regurgitation
  - Failure to thrive
  - Belching
  - Choking
  - Gagging
  - Malnourishment
  - Ruminating
  - Esophagitis
  - Chest pain
  - Irritability
  - Peptic stricture
  - Barrett’s esophagus
  - Excessive crying
  - Anemia
  - Bradycardia
  - Feeding refusal
  - Apparent life-threatening event
  - Dysphagia
  - Sandifer’s syndrome (gastroesophageal reflux with torticollis)

- Respiratory system
  - Reactive airway disease
  - Apnea
  - Hiccups
  - Cough
  - Aspiration pneumonia
  - Bronchopulmonary dysplasia
  - Bronchitis
  - Stridor
  - Hoarseness
  - Subglottic stenosis
  - Laryngospasm
  - Sudden infant death syndrome
tation, and increased losses secondary to persistent emesis. It is important to note that children with reflux-induced failure to thrive first fall from the weight curve and then may demonstrate a delay in linear growth.8

Some important complications of reflux and prolonged acid exposure are strictures and Barrett’s esophagus. Barrett’s esophagus is columnar metaplasia of the distal esophagus. Because of the limited chronicity of reflux in infants, these presentations of prolonged acid exposure are not as common in infants but are nonetheless important to note. Strictures can present with symptoms of dysphagia in relation to ingestion of solids and expulsion of undigested food. The prevalence of Barrett’s esophagus is rare in the pediatric population and is often asymptomatic. The presence of Barrett’s esophagus, however, increases the risk of adenocarcinoma of the esophagus later in life.9 Children with neurologic impairments who are unable to express symptoms such as heartburn are at particular risk for long-term consequences of GERD. Anemia and hypoalbuminemia in this population should alert the pediatrician to evaluating the esophagus as a possible site of a pathologic process.

Association of gastroesophageal reflux with respiratory symptoms

The cause-and-effect relationship between respiratory symptoms and gastroesophageal reflux can often be quite puzzling. Many reports have associated reflux in children with upper and lower respiratory tract disorders.3 Upper respiratory symptoms can result from aspiration of esophageal contents into the airway, causing edema and inflammation, which, in turn, can produce symptoms of stridor and laryngospasm. It is also important to evaluate swallowing function in some patients as aspiration of oral contents may be the etiology of pneumonia. A barium swallow under fluoroscopy may show laryngeal pooling of saliva as the source of upper respiratory tract irritation. Obstructive apnea can result from laryngospasm; thus, it is important that infants who present with symptoms such as an apparent life-threatening event be evaluated for reflux. Lower respiratory tract symptoms such as asthma, bronchitis, or pneumonia have been frequently correlated with gastroesophageal reflux. These symptoms are more common in older children and may also result from similar mechanisms of aspiration as mentioned earlier.

It has become clear that other mechanisms may also play an important role in respiratory symptoms related to reflux.7 It has been shown that instillation of acid into the esophagus of asthmatic patients increases airway resistance.4 This reflex bronchospasm mediated via vagal pathways has been shown to respond to treatment of the reflux. Interestingly enough, this relationship between respiratory symptoms and reflux has more than one facet. Many of the modes of pharmacotherapy for a reactive airway, including β-adrenergic agonists and xanthes, can lower the LES tone, thereby increasing the propensity for reflux. Also, the increased abdominal pressure from coughing and wheezing and the increased negative intrathoracic pressure from hicups and stridor can exacerbate reflux.9 Of further note, nocturnal symptoms, including cough in an asthmatic patient, are especially suggestive of underlying reflux.

Diagnostic evaluation

Diagnostic evaluation begins with a detailed history and physical examination. This approach is helpful in distinguishing nonreflux disorders from gastroesophageal reflux and in assessing which patients can be managed simply with conservative treatment.1 Each of the diagnostic tests available can assess reflux from different perspectives.3 Because numerous methods of evaluating reflux exist, some guidelines in test selection may prove helpful. For patients whose symptoms are suggestive of esophagitis, esophagastroduodenoscopy with an esophageal biopsy would be a reasonable route. A pH probe is useful in evaluating patients with respiratory manifestations of reflux. Barium fluoroscopy can be helpful in suspected obstructive or anatomic anomalies. It also provides insight into swallowing function. Endoscopy is beneficial in assessing children to exclude peptic ulcer disease and other causes of gastritis/esophagitis such as Helicobacter pylori infection.1

Barium swallow

Upper GI barium fluoroscopy is an important diagnostic tool in evaluating a child for reflux. Although not a sensitive test in diagnosing GERD, it is useful in eliminating other pathologic processes that can cause regurgitation in an infant, including gastrointestinal obstruction, malrotation, intermittent volvulus, and numerous other possible congenital causes for emesis. A contrast study of the upper GI tract also can be useful in ruling out the presence of a large hiatal hernia. Barium esophagraphy has variable sensitivity secondary to brief monitoring time and poor specificity owing to the presence of physiologic reflux in healthy individuals.1 Also, a barium swallow is not helpful in terms of evaluating gastric emptying.

Monitoring with pH probe

Esophageal pH monitoring has often been called the “gold standard” for evaluating reflux. This test is helpful when evaluating a child with nonregurgitant reflux who presents with symptoms of esophagitis. It can quantify the frequency and duration of reflux episodes. Despite its utility in detecting reflux, however, it is not helpful in determining whether reflux is causing symptoms or disease.7 Pediatric patients can tolerate this test fairly well as it allows for the ability to monitor a child in a nearly physiologic setting with a normal dietary intake for 24 hours. Although the pH probe has the ability to detect acid reflux, its sensitivity is greatly diminished in the postprandial period, as ingested food or formula buffers the gastric acidity. Even though reflux of these contents may occur, the buffering effect makes the pH probe unable to detect it. To enhance the sensitivity of this test, some have suggested the use of apple juice (pH 3.5) with some feedings during pH probe monitoring.9 Finally, pH probe moni-
toring has also been used extensively to evaluate response to therapy.

**Scintigraphy**

Scintigraphic evaluation for GERD uses a gamma counter for continuous imaging after a single technetium 99m radiolabeled meal. Also known as a “milk scan,” this test has an advantage over the pH probe of detecting reflux after a physiologically neutral pH meal. The rate of gastric emptying can also be evaluated by a milk scan, which can provide useful information for children with diagnosed reflux and those undergoing evaluation for fundoplication to determine whether they will need a procedure to facilitate gastric emptying. The gastroesophageal scintiscan can also detect pulmonary aspiration of gastric contents which may help to correlate reflux with pulmonary symptomatology. Disadvantages of this scan include its insensitivity for late postprandial reflux, the requirement for children to be immobile for lengthy periods during the scan, the brief period of evaluation, and inability to rule out anatomic anomalies that may help to correlate reflux with anatomic anomalies.

Management

When considering management of reflux in young children, it is important to take into account that in contrast to older children and adults, most infants with symptomatic reflux will outgrow these symptoms within a year. When beginning therapy for gastroesophageal reflux, one should always consider conservative therapy first, including lifestyle modifications. One can then proceed to pharmacotherapy, including a prokinetic agent and even acid-reducing therapy if symptoms of esophagitis are present. Finally, surgical management should be reserved for patients with serious sequelae unresponsive to the previously mentioned modalities.

Lifestyle changes for infants begin with postural manipulations to decrease the incidence of reflux. Avoidance of seated and supine positions, especially postprandially, and encouragement of prone positioning reduces the number of reflux episodes; however, placement in the prone position has been associated with an increased incidence of sudden infant death syndrome (SIDS). Most SIDS that occur in the prone position can be attributed to suffocation from puffy bedding. Therefore, if this type of bedding is eliminated and parents are thoroughly educated regarding risks and benefits, the prone position can be used. The American Academy of Pediatrics recommendation that most infants sleep in a supine position exempts those with GERD. Also in contradiction to previous recommendations, there has been shown to be no additional benefits of elevation of the head of the bed of infants.

Dietary modifications for infants with GERD include the thickening of milk formula with rice cereal and decreasing the volume at each feeding. This thickened formula should result in increased caloric content of feedings instead of the usual 20 calories per ounce. This therapy has been shown to decrease the number and volume of emesis episodes. The main side effects from these thickened feedings include promoting constipation and increasing the velocity of weight gain. Small and frequent feedings are also recommended in that they may decrease gastric volumes and, therefore, the quantity of reflux may decrease. Clear liquids, such as water and juice, should be eliminated from the diet.

Lifestyle modifications in older children include changes in positioning and dietary restrictions. Optimal positioning includes maintaining an upright position while awake and sleeping prone. Elevating the head of the bed may provide benefit in this age group as opposed to infants. Dietary measures include avoidance of large meals, acidic foods and beverages, and foods that lower LES tone, including carbonated beverages, coffee, and alcohol. Also, fasting several hours before bedtime might decrease the number of reflux episodes. Chewing gum is another product that should be discouraged as aerophagia may be increased with chewing. Weight reduction in obese individuals and avoidance of tight clothing should also be encouraged. A final recommendation includes avoiding exposure to tobacco smoke in all ages of children.

**Pharmacotherapy**

Prokinetic pharmacotherapy has traditionally been the first choice of medication because these agents address the most prominent clinical presentation, regurgitation. Acid suppression is added when esophagitis is clinically suspected or demonstrated. Cisapride had been one of the first choices for prokinetic agents in managing reflux until its recent removal from the market. Metoclopramide hydrochloride has been found to increase LES tone and gastric emptying via dopaminergic effects. It has a relatively narrow therapeutic window for dosing. The most common side effects are drowsiness and irritability. Although extrapyramidal side effects with dystonic reactions can occur, they are less com-
mon in the pediatric population than in adults. Bethanechol chloride, a muscarinic agonist, has been shown to increase LES tone but is seldom used in practice secondary to its relative ineffectiveness in reducing reflux and its undesirable side effects of cramping and diarrhea. Domperidone is similar in action to metoclopramide, but recent studies have found it to have only marginal benefits.

For patients in whom the diagnosis of esophagitis is made, the addition of acid suppression therapy can provide relief. Histamine H2-blockers have been used successfully in pediatric patients. Limited data, however, are available regarding appropriate dosing in the pediatric age group. It has been suggested that popular dosing regimens are probably subtherapeutic. Cimetidine and ranitidine hydrochloride are the most widely used of these agents. Proton pump inhibitors provide much greater reduction in acid secretion compared with histamine H2-blockers and are often used in children who require more complete acid suppression, such as those with severe chronic respiratory disease or neurologic impairment.  As with adults, the safety of long-term therapy with omeprazole is unknown at this time. Sucralfate has also been shown to be a useful agent in children with symptoms of primarily esophagitis.

**Surgical therapy**

The Nissen fundoplication, which involves a 360-degree wrap of the fundus around the distal esophagus to increase LES pressure, has been the most common procedure for GERD, with efficacy rates ranging from 60% to greater than 90%. Sometimes a pyloroplasty is combined with this procedure for patients with delayed gastric emptying in addition to GERD. The recent trend toward a more conservative approach derives from the fact that the developmental resolution of GERD in infants usually occurs in the second year of life. Failure of medical management is an accepted indication for surgery and has been especially helpful in the case of children with neurologic impairment, repaired esophageal atresia, and chronic lung disease.

**Comment**

GERD is a well-recognized entity in infants and children. It is important for the physician to become skilled in distinguishing physiologic from pathologic reflux. Many infants have regurgitation as the primary presentation of reflux. Although more common in older children, symptoms of esophagitis should not be ignored in infants. Also, one should always consider reflux as a contributory factor in a patient who has chronic respiratory symptoms. The diagnosis of gastroesophageal reflux is initially based on clinical suspicion and can be well supported by many tests that may be indicated on the basis of the primary symptomatology. The pH probe is probably the easiest to administer and most widely used measure for documenting reflux in young patients. The management of gastroesophageal reflux begins with first determining the need for specific treatment based on age, nutritional status, and response to previous interventions. Most infants will outgrow pathologic reflux within a year of diagnosis, and this likelihood should be taken into serious consideration when contemplating therapy, especially surgical correction. Increased knowledge and experience with prokinetic and acid-suppressive agents hold the promise of great benefit for our young patients.

**References**