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INTRODUCTION — Gastroesophageal reflux disease (GERD) is present when passage of gastric contents into the esophagus causes troublesome symptoms or complications [1]. The range of symptoms and complications of GERD in children varies with age.

This topic review focuses on the clinical manifestations and diagnosis of GERD in children and adolescents. Other topic reviews relevant to gastroesophageal reflux (GER) and GERD in the pediatric age group are:

- Management of gastroesophageal reflux disease in children and adolescents

- Gastroesophageal reflux in infants

- Gastroesophageal reflux in premature infants

These discussions are generally consistent with an official consensus statement and systematic review issued by the North American Society of Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN) and European Society of Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) [1], and the American Academy of Pediatrics (AAP) [2]. The full text of the NASPGHAN guidelines is available at the society website.

DEFINITIONS — "Gastroesophageal reflux" (GER) refers to the retrograde passage of gastric contents into the esophagus, with or without regurgitation and/or vomiting [3]. This is a normal physiologic process that occurs in healthy infants, children, and adults. Most episodes are brief and do not cause symptoms, esophageal injury, or other complications. In contrast, "gastroesophageal reflux disease" (GERD) is present when the reflux episodes are associated with complications or troublesome symptoms [1,2].

The term "regurgitate" describes reflux to the oropharynx, and "vomit" describes expulsion of the refluxate out of the mouth, but not necessarily repetitively or with force. The terms are often used interchangeably in clinical practice. In this review, we will use the term "regurgitate" to describe obvious GER into the mouth, whether or not the refluxate is expelled from the mouth. Recurrent regurgitation and vomiting are often caused by GER, but occasionally are caused by more serious problems, including underlying anatomic, metabolic, or neurologic abnormalities, which should be considered when indicated by the patient's clinical presentation. (See 'Recurrent vomiting or regurgitation' below.)

The term "rumination" describes a separate phenomenon in which food is voluntarily regurgitated into the mouth, masticated, then reswallowed. This disorder should be considered as a possible cause of GER, but it has a behavioral etiology and treatment. (See 'Recurrent vomiting or regurgitation' below and "Approach to the infant or child with nausea and vomiting", section on 'Rumination syndrome'.)

EPIDEMIOLOGY — Few large population-based studies have described the epidemiology of gastroesophageal reflux disease (GERD) in children. Most studies focus on the prevalence of GERD in specific groups. Comparison among studies is also limited by the use of different definitions of GERD and the variable extent to which other possible causes of symptoms that were attributed to GERD were investigated.

Prevalence — According to a large community-based study of children in the United States, the prevalence of various symptoms suggestive of gastroesophageal reflux (GER) was 1.8 to 8.2 percent [4]. Among

adolescents, 3 to 5 percent complained of heartburn or epigastric pain, and 1 to 2 percent used antacids or acid-suppressing medication. The prevalence of GERD in adults in the western world is approximately 10 to 20 percent [5]. Contrary to previously held beliefs, GERD does not appear to be limited to western countries. The prevalence of GERD in children appears to be rising worldwide, although it is unclear whether the rise reflects increasing case identification, or increases in obesity or other conditions that promote GERD [6].

Higher rates of GERD are seen among children with a history of prematurity, pulmonary diseases, developmental and neuromuscular disorders such as cerebral palsy and muscular dystrophy. Children with Down syndrome are also at increased risk for GERD and other esophageal motor abnormalities for reasons that are poorly understood [7,8]. These groups of children also appear to be at increased risk for developing respiratory complications related to GERD and represent a significant proportion of children referred for antireflux surgery. Complications of GERD, including Barrett esophagus and esophageal adenocarcinoma, are more common in individuals who had repair of esophageal atresia in the perinatal period as compared with individuals without this congenital defect [9,10]. GERD also appears to be relatively common in children with obesity or cystic fibrosis [1]. (See "Cystic fibrosis: Overview of gastrointestinal disease".)

Natural history — Regurgitation in infants is common and typically decreases or resolves during the first year of life (see "Gastroesophageal reflux in infants"). Although the problem usually resolves by the end of infancy, there is a weak association with GERD later in life. As an example, frequent regurgitation during infancy or a history of GERD in the mother (but not the father) predicts the risk of reflux-related symptoms during childhood. This was demonstrated in a prospective cohort study in which children who had more than 90 days of frequent regurgitation during the first two years of life were more likely to have heartburn around nine years of age [11].

Symptoms of GERD during childhood may persist into adolescence and adulthood ("tracking"). In a survey of 207 patients who were diagnosed with GERD through an endoscopic examination showing esophagitis in childhood (mean age five years), about one-third had symptoms of significant GERD during early adulthood (approximately 15 years later) [12]. At least 9 (up to 23) percent had weekly symptoms of GER. Among those responding to the survey, 30 percent were currently taking acid-suppressing medications, and 24 percent had undergone fundoplication. Other studies have shown similar results, but the lack of prospective trials limits the reliability of these observations [13].

Several questions related to the epidemiology and natural history of GERD in children remain unanswered. We have only a partial understanding of the relationship between GER and respiratory diseases, including asthma, chronic cough, and recurrent pneumonia. In addition, the relationship between childhood GERD and GERD-related complications in adulthood is unclear. Finally, the healthcare burden related to the diagnosis and treatment of childhood GERD and the impact of GERD on quality of life for children and their families have not been fully examined.

CLINICAL MANIFESTATIONS — The most common symptoms of gastroesophageal reflux (GER) and gastroesophageal reflux disease (GERD) vary according to age, although overlap may exist.

- Infants – GER is common in infants and usually is not pathological. Regurgitation is present in 50 to 70 percent of all infants, peaks at age four to six months, and typically resolves by one year. A small minority of infants with GER develop other symptoms suggestive of GERD, including irritability, feeding refusal, hematemesis, anemia, respiratory symptoms, and failure to thrive. The clinical manifestations and management of GER in this age group is discussed separately. (See "Gastroesophageal reflux in infants".)

- Preschool – Preschool age children with GERD may present with intermittent regurgitation. Less commonly, they may have respiratory complications including persistent wheezing. Decreased food intake, poor weight gain, or food aversion without any other complaints may be a symptom in young children. All of these symptoms are nonspecific and insufficient to make a definitive diagnosis of GERD.

A more specific symptom of GERD is Sandifer syndrome, an unusual posturing consisting of arching of the back, torsion of the neck, and lifting up of the chin [1]. Sandifer syndrome is found in typically-developing preschool-aged children, as well as those who are developmentally delayed, as in the original descriptions. (See "Acquired torticollis in children", section on 'Sandifer syndrome'.)

- School-aged children and adolescents – The pattern of symptoms and complications of GERD in older children and adolescents resembles that seen in adults. The cardinal symptoms are chronic heartburn and/or regurgitation [14]. Complications of GERD, including esophagitis, strictures, Barrett esophagus, and hoarseness due to reflux-induced laryngitis, also may be seen. Older children may complain of nausea, dysphagia (difficulty swallowing) and/or epigastric pain, but many pre-adolescents will not localize pain and report diffuse abdominal discomfort. (See "Barrett's esophagus: Epidemiology, clinical manifestations, and diagnosis" and "Approach to chronic cough in children".)

GERD-related chest pain is not well-described by young children. Young or nonverbal children may be observed pounding their chest. GERD is common in children with autism, and may be manifested only by unexplained or self-injurious behaviors. In older children, chest pain typically is described as squeezing or burning, located substernally sometimes radiating to the back, lasting from minutes to hours, and resolving either spontaneously or with antacids. It usually occurs after meals, awakens patients from sleep, and may be exacerbated by emotional stress.

Extraesophageal disorders that are associated with GERD also may be seen in older children and adolescents. In a large case-control study of children without neurologic defects, GERD was an independent risk factor for developing sinusitis (adjusted odds ratio [OR] 2.3), laryngitis (OR 2.6), asthma (OR 1.9), pneumonia (OR 2.3), and bronchiectasis (OR 2.3) (see 'Asthma' below and 'Recurrent pneumonia' below) [15]. GER is also hypothesized to contribute to otitis media with effusion, but causality has not been proven. (See "Otitis media with effusion (serous otitis media) in children: Clinical features and diagnosis", section on 'Pathogenesis'.)

AVAILABLE DIAGNOSTIC TECHNIQUES — The following sections summarize characteristics of the tests that are used to evaluate individuals with symptoms of gastroesophageal reflux (GER) or gastroesophageal reflux disease (GERD). The clinical approach to selecting among these tests depends on the patient's presenting characteristics. (See 'Suggested approach for common clinical scenarios' below.)

Empiric treatment — An empiric trial of acid suppression is often used as a diagnostic test, and is suggested for older children and adolescents with uncomplicated heartburn [1]. The trial typically consists of a two- to four-week course of acid-suppressing medication (eg, a proton pump inhibitor [PPI]). An empiric trial of a PPI may not be a valuable diagnostic test in infants and young children, in whom symptoms of GERD are less specific; however, response after a two-week trial of a PPI has been used as inclusion criteria for clinical trials in infants with GER [16]. Studies in adults suggest that empiric treatment is a cost-effective approach in selected patients, although the applicability of these results to children is uncertain [17]. (See 'Heartburn' below and "Medical management of gastroesophageal reflux disease in adults".)

Barium contrast radiography — Barium studies of the esophagus are neither sensitive nor specific for the diagnosis of GERD. When compared with esophageal pH studies, barium studies of the esophagus have a sensitivity ranging from 31 to 86 percent, specificity of 21 to 83 percent, and positive predictive value of 80 to 82 percent [18-23].

Although radiologic evaluation is not useful to confirm or exclude GERD [1,2,24], imaging is useful in a young infant with intractable reflux, to identify congenital abnormalities such as an antral web, pyloric stenosis, annular pancreas, duodenal web, or malrotation [25]. Imaging may also be useful in the evaluation of selected patients with atypical presenting features, such as dysphagia or odynophagia, in whom it may identify hiatal hernia, Schatzki's ring, achalasia, or strictures associated with acid or eosinophilic esophagitis. (See 'Dysphagia or odynophagia' below.)

Endoscopy and histology — Endoscopic evaluation of the upper gastrointestinal tract is indicated for selected patients in whom esophagitis or gastritis is suspected. These include children or adolescents with heartburn, hematemesis, or epigastric abdominal pain that fails to respond to or relapses quickly after empiric treatment [1,24]. In addition, endoscopy may be valuable in the evaluation of patients with recurrent regurgitation, dysphagia, odynophagia, or a history of food impaction, or in children with frequent GER that persisted from infancy until after two years of age.

At endoscopy, the examiner inspects the visual appearance of the esophageal mucosa and anatomy, and takes a series of biopsies for histologic examination. The findings help to determine the presence and severity of esophagitis and complications, such as strictures or Barrett esophagus, and to exclude other disorders such as eosinophilic, peptic, or infectious esophagitis. The diagnostic yield of endoscopy in children with symptoms suggesting GERD is not well established. In one large series of children undergoing endoscopy due to GERD symptoms, 35 percent were found to have erosive esophagitis [26]. In another large series of children undergoing endoscopy for GER, only 13 percent had histologic evidence of esophagitis, whereas more than 50 percent of those undergoing endoscopy for dysphagia had gross and histologic abnormalities [27].

Endoscopy can be performed safely in infants, toddlers, and older children. Procedure-related complications of diagnostic endoscopy and biopsy are rare [28]. Complications requiring medical attention, including under- or over-sedation, occur in about 5 percent of cases [29,30]. The most common complication is transient sore throat or hoarseness, which occurs in about 35 percent of patients [30].

The endoscopy should include biopsies of the esophageal mucosa to evaluate for esophagitis, even if the esophagus appears normal on visual inspection [1,2,31]. Histologic abnormalities consistent with GERD include increased numbers of intraepithelial eosinophils, thickening of the basal cell layer, and elongation of the epithelial papillae [16,32,33]. In young children with esophagitis, the findings of basal zone hyperplasia are uncommon, and other histologic features, such as the presence of neutrophils and eosinophils, and dilated vascular channels in papillae of the lamina propria are more typically seen [16]. Patients with reflux-associated esophagitis should be treated with acid suppression, as discussed in a separate topic review. (See "Management of gastroesophageal reflux disease in children and adolescents".)

The histologic features described above are only moderately specific for GERD. In patients with markedly increased numbers of eosinophils in esophageal biopsies, the possibility of eosinophilic esophagitis (EoE) should be considered. EoE is a chronic immune-mediated disorder characterized by markedly increased intraepithelial eosinophils in greater numbers than noted in GERD. Symptoms of EoE and the number of intraepithelial eosinophils may not respond to acid suppression. EoE is increasingly recognized in children and adults, and the symptoms and histological findings overlap with those of GERD, such that in some cases it can be difficult clearly distinguish between the disorders [34,35]. The number and distribution of eosinophils can help distinguish GERD from EoE. In children with GERD, the eosinophilic inflammation tends to be mild (<15 eosinophils per high power field) and limited to the distal esophagus, whereas in children with EoE the inflammation tends to be severe (>15 eosinophils per high power field) and located in the mid or proximal esophagus. In addition, many patients with EoE have a history of atopy or peripheral eosinophilia, and are more likely to fail to respond to antireflux treatment. Diagnostic and treatment approaches to patients with suspected EoE are discussed in a separate topic review. (See "Clinical manifestations and diagnosis of eosinophilic esophagitis".)

Esophageal pH monitoring or impedance monitoring — Esophageal pH and multichannel intraluminal impedance (MII) monitoring permits the assessment of the frequency and duration of esophageal acid exposure and its relationship to symptoms. However, the results may not correlate consistently with symptom severity, although there is a correlation with the presence of esophagitis on endoscopy [1,33,36]. Therefore, pH monitoring can raise or lower suspicion of GERD, but is not a definitive diagnostic test, and is not useful in many clinical situations, especially in infants.

To perform pH monitoring, a microelectrode attached to a small catheter is passed through the nose and positioned in the distal esophagus. The position can be verified radiologically. In special situations, multiple sensors can be used to determine if acid reflux extends into the proximal esophagus. There are also devices that clip to the esophageal mucosa and remain in place for 24 hours, to allow recording of intraesophageal pH without the transnasal catheter. This technology can be used for older children and is particularly beneficial for children with autism in whom transnasal pH monitoring is often difficult to perform.

The "reflux index" is defined as the percentage of total time that the esophageal pH is less than 4; this provides an estimate of the cumulative esophageal acid exposure, which is considered to be the most valid measure of reflux. However, there is only a weak correlation between the reflux index and clinical symptoms, presence of esophageal disease, or response to therapy, and results of esophageal pH monitoring should be interpreted in the context of other clinical information. The reflux index usually is interpreted as follows [1]:

- Infants – Reflux index above 7 percent is considered abnormal, and between 3 and 7 percent is indeterminate.

- Older children and adults – Upper limit of normal for the reflux index between 4 and 7 percent.

Multichannel intraluminal impedance monitoring (MII) is a newer technique that permits measurement of all reflux episodes, including those that are acidic, weakly acidic and alkaline. MII is available at many centers, and usually is used in combination with pH monitoring so that episodes of acid reflux may be distinguished from non-acid reflux. In a trial comparing the two techniques, combined MII-pH monitoring detected reflux events that caused symptoms twice as often as pH monitoring alone [37]. Although pediatric standards for MII have not been established, the technique can be helpful to determine whether there is a correlation between reflux episodes and certain symptoms [38]. MII is discussed in a separate topic review. (See "Esophageal multichannel intraluminal impedance testing".)

Uses — Esophageal pH monitoring or MII can be useful in the following clinical situations [1,24,39]:

- Atypical symptoms of reflux – In patients with the following symptoms, esophageal pH or MII/pH monitoring is sometimes useful to determine whether there is a temporal correlation between symptoms and episodes of reflux.

    • Laryngeal symptoms – Nocturnal stridor or cough raise the possibility of an association with GERD. A dual-channel esophageal pH monitor, with electrodes in both distal and proximal esophagus, is particularly valuable for evaluating patients with these symptoms. However, no consensus exists on the pH criteria that should be used for defining pathologic reflux in this setting [40,41].

    • Atypical asthma – Wheezing that is positional (eg, recumbent) in nature, or asthma that is severe, non-seasonal, and refractory to standard treatment, raise the possibility of an association with GERD. In patients with such symptoms, esophageal pH or MII/pH monitoring can assess whether there is a temporal correlation between symptoms and GER [42]. However, empiric trials of acid suppression also may be used in this situation. (See 'Asthma' below.)

    • Recurrent pneumonia – In patients with recurrent pneumonia, it is difficult to establish whether esophageal reflux contributes to the problem. Although patients with aspiration tend to reflux more frequently into the proximal esophagus as compared with healthy patients, esophageal pH monitoring has low sensitivity and specificity in detecting whether aspiration pneumonia is related to reflux in the individual patient [39]. Nonetheless, esophageal pH or MII/pH monitoring may help establish the diagnosis in selected patients with suspected aspiration, when combined with other investigations, including videofluoroscopic swallowing evaluation, bronchoscopy, and/or endoscopy. (See 'Recurrent pneumonia' below.)

- Nonverbal children with suspected GERD – In nonverbal children (eg, those with autism), behavioral changes or self-injurious behavior may be the only symptoms of GERD. In this case, an empiric trial of acid-suppressing medication or, in some patients, esophageal pH or MII/pH monitoring, can be used to assess whether there is a temporal correlation between reflux events and the behavioral symptoms. Upper endoscopy may also be beneficial in diagnosing esophagitis.

- Distinguishing between GERD and EoE – Both EoE and GERD are associated with increased eosinophils in the esophagus, and in some children distinguishing between the disorders may be difficult. In this situation, a trial of sustained acid suppression is performed to exclude GERD as a cause of the esophageal eosinophilia. To compound the problem of distinguishing the two conditions, there is an entity known as PPI-responsive EoE, which may or may not be distinct from EoE. Alternatively (or in addition), documentation of a normal esophageal pH or MII/pH monitoring helps to support a diagnosis of EoE. (See "Clinical manifestations and diagnosis of eosinophilic esophagitis".)

- Gastroesophageal reflux symptoms not responsive to medical or surgical therapy – Esophageal pH studies can determine the adequacy of acid suppression in children who remain symptomatic despite being treated with a PPI, or after surgical treatment for GERD. If the pH study shows adequate acid suppression, alternative explanations for the symptoms should be sought (eg, EoE or alkaline reflux). If uncontrolled acid reflux is documented, acid suppressive treatment should be optimized.(See "Management of gastroesophageal reflux disease in children and adolescents", section on 'Pharmacotherapy'.)

- Infants with apnea – If infants have repeated episodes of apnea, esophageal pH or MII/pH monitoring may be useful to determine if these are triggered by GERD. However, the association can be made only if positive events are identified simultaneously by polysomnography or oxycardiorespirography. These tests are not useful for the routine evaluation of infants who have experienced an apparent life-threatening event (ALTE), except in selected patients with recurrent ALTE. (See "Gastroesophageal reflux in infants" and "Acute events in infancy including brief resolved unexplained event (BRUE)", section on 'Gastroesophageal reflux or swallowing dysfunction'.)

Limitations — Esophageal pH or MII/pH monitoring does not detect anatomical abnormalities or esophagitis. Thus, it is **not** generally useful in the following clinical situations [14,39]:

- Evaluation of patients presenting with typical symptoms of GER, heartburn, or epigastric pain – Empiric trials of acid suppression and endoscopy will provide more definitive information about the clinical diagnosis and severity for these patients. (See 'Heartburn' below.)

- Patients with esophagitis diagnosed by endoscopy – Abnormal reflux index correlates strongly with the presence of esophagitis on endoscopy (approximately 95 percent of children with esophagitis will have an abnormal reflux index) [33,36], but does not contribute to the diagnosis of the esophagitis. Therefore, esophageal pH or MII/pH monitoring is not a helpful investigation in patients with established esophagitis, except to investigate reasons for inadequate response to therapy.

- Patients in whom alkaline reflux is suspected – In some patients, alkaline (rather than acid) reflux is suspected due to pyloric insufficiency or other abnormalities. In this case, standard esophageal pH monitoring is not helpful, but MII (or combined MII and pH monitoring) may be beneficial in detecting neutral and alkaline reflux. (See "Esophageal multichannel intraluminal impedance testing".)

- Infants with frequent regurgitation – In infants, esophageal pH or MII/pH monitoring is generally not useful to distinguish between infants with uncomplicated reflux and those with esophagitis or other pathological manifestations of GERD. Infants with failure to thrive or other symptoms suggesting pathological GERD require evaluation, but esophageal pH or MII/pH monitoring is rarely helpful in establishing the diagnosis [1,39]. However, in selected infants with discrete episodes of irritability or other symptoms thought to be related to GER, these tests may be used to establish whether there is a

temporal relationship between occult reflux episodes and their specific symptoms. (See "Gastroesophageal reflux in infants".)

Bronchoalveolar lavage — Bronchoscopy with bronchoalveolar lavage is occasionally used to assess for evidence of recurrent small-volume aspiration. If aspirates contain a high percentage of lipid-laden macrophages, aspiration is thought to be more likely. However, this technique has low sensitivity and specificity. Even with careful measurement protocols, there is considerable overlap in findings between patients with aspiration and normal controls, so the technique is not generally useful [1,43]. (See "Aspiration due to swallowing dysfunction in infants and children", section on 'Potential biomarkers of aspiration'.)

Nuclear scintigraphy — Tests employing nuclear scintigraphy are designed to detect aspiration and/or delayed gastric emptying. However, due to low sensitivity and specificity they have a limited role in the evaluation of GERD in children. Small amounts of technetium-99m are either mixed with milk and given to the patient to drink (gastroesophageal scintigraphy, also known as a "milk scan") or directly instilled into the mouth (salivagram). Gamma camera images of the chest are taken at intervals to detect the distribution of the isotope in the stomach, esophagus, and lungs. (See "Aspiration due to swallowing dysfunction in infants and children", section on 'Gastroesophageal scintigraphy and salivagram'.)

Gastrointestinal scintigraphy (milk scan) can detect aspiration of refluxed material into the lungs, unlike esophageal pH monitoring or MII. However, its sensitivity and specificity are poor when compared with other clinical or radiographic measures of aspiration. As a result, this test has a limited role in the diagnosis and management of GERD in children [1,2]. The same technique can be used to detect abnormalities in gastric emptying, which may be valuable when gastroparesis is suspected as a cause of the reflux, or when surgical intervention for GERD is contemplated. (See "Approach to the infant or child with nausea and vomiting", section on 'Gastroparesis' and "Gastroparesis: Etiology, clinical manifestations, and diagnosis", section on 'Scintigraphic gastric emptying'.)

In selected patients who experience recurrent aspiration, a salivagram may be helpful in determining whether the aspiration is caused by swallowing problems (antegrade aspiration) as opposed to GERD (retrograde aspiration) [44]. However, salivagrams appear to have low specificity due to frequent false-positive results, especially in infants and young children, and must be correlated with clinical evidence for aspiration.(See "Aspiration due to swallowing dysfunction in infants and children", section on 'Gastroesophageal scintigraphy and salivagram'.)

Esophageal manometry — Esophageal manometry is of minimal use in the diagnosis of typical GERD [1]. Its main purpose is to diagnose a primary motor disorder such as achalasia in patients with suggestive findings on barium contrast radiography. In addition, some providers use esophageal manometry to evaluate peristaltic function before antireflux surgery. If significant esophageal dysmotility is detected, antireflux surgery should be approached with caution, because it might exacerbate difficulties with swallowing food and/or saliva. (See "Surgical management of gastroesophageal reflux in adults".)

DIAGNOSTIC APPROACH

History — The differential diagnosis of gastroesophageal reflux disease (GERD) in children is broad, particularly when the principal complaint is regurgitation, vomiting, or abdominal pain (table 1). The diagnostic possibilities can be narrowed based upon the age of the child and the pattern of symptoms, using a thorough medical history (table 2) (see "Approach to the infant or child with nausea and vomiting"). The history should include the following elements:

- Presence of heartburn or abdominal pain, regurgitation or vomiting, water brash, and whether there is associated nausea

- Onset of symptoms and relation to meals

- Dysphagia (difficulty swallowing) or odynophagia (pain while swallowing)

- Underlying disorders including neurologic dysfunction or congenital anomalies

- Asthma, pneumonia, or chronic cough

- Medication history

In addition to the above, the history should seek information about occult or recognized constipation. This is because functional constipation is frequently associated with dyspeptic symptoms including gastroesophageal reflux (GER), heartburn, and nausea [45,46]. In many cases, the constipation is unrecognized and the dyspeptic symptoms are the presenting complaint [45]. This probably occurs because the constipation delays gastric emptying via an intraintestinal reflex, termed the "cologastric brake" [46]. A rectal examination should be performed to determine if the rectal vault is packed with hard stool. Effective treatment of the underlying constipation may relieve the dyspeptic symptoms and avoid invasive procedures or long-term pharmacotherapy for presumed GERD. (See "Constipation in infants and children: Evaluation".)

Suggested approach for common clinical scenarios — The previous discussion underscores the variable presentation of GERD in infants and children and the need to modify the diagnostic approach based upon the patient's age, type of symptoms, and their severity. The following sections will provide general recommendations for diagnosis in infants and children with commonly seen clinical presentations. These recommendations are consistent with the guideline issued by the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition (NASPGHAN) [1].

Recurrent vomiting or regurgitation — Otherwise healthy children with recurrent vomiting or regurgitation after reaching the age of 18 months usually require evaluation. The differential diagnosis of regurgitation and vomiting is broad, and depends on the age group and associated symptoms (table 1). For otherwise healthy children and adolescents with recurrent regurgitation or vomiting and no other symptoms, a thorough history and physical examination is often sufficient to exclude diagnoses other than GER. For adolescents, the clinician should specifically ask about cannabis use. (See "Cannabis use and disorder: Epidemiology, comorbidity, health consequences, and medico-legal status", section on 'Hyperemesis syndrome'.)

Warning signs that suggest a diagnosis other than GERD include fever, weight loss or faltering growth, abdominal tenderness or distension, bilious vomiting, marked hematemesis, hepatosplenomegaly, headache or new neurologic symptoms, or other systemic symptoms. Patients with any of these features warrant additional steps in the evaluation. (See "Approach to the infant or child with nausea and vomiting".)

The differential diagnosis of GERD includes several disorders that should be explored by the history:

- Gastroparesis – Gastroparesis is the condition of impaired gastric emptying. This may cause postprandial vomiting, which usually occurs several hours after eating. Viral-induced gastroparesis may begin acutely after an episode of gastroenteritis and persist for several weeks or months thereafter, and occasionally as long as 18 months. (See "Approach to the infant or child with nausea and vomiting", section on 'Gastroparesis'.)

- Rumination or psychogenic vomiting – Rumination syndrome is a psychogenic disorder in which the individual voluntarily regurgitates and re-swallows food, apparently as a self-comforting or habitual measure. The repeated episodes usually occur immediately after a meal. Rumination is more common among individuals with developmental disabilities but also occurs among typically developing children, adolescents, and adults. The disorder may be initially triggered by an episode of gastroenteritis, GERD, or by body weight concerns, as a form of bulimia [47]. Distinguishing rumination from GERD may be difficult, and requires a high index of suspicion. (See "Approach to the infant or child with nausea and vomiting", section on 'Rumination syndrome' and "Approach to the infant or child with nausea and vomiting", section on 'Bulimia or psychogenic vomiting' and "Eating disorders: Overview of epidemiology, clinical features, and diagnosis".)

- Pregnancy – For postmenarchal girls with vomiting, the clinician should explore the possibility of pregnancy, with testing if indicated.

Additional evaluation is appropriate if the history does not suggest the above disorders, and if the GER symptoms are frequent, cyclical or persistent, and cause distress. In this case, the evaluation usually should include an upper gastrointestinal series to look for anatomic abnormalities. An upper endoscopy with biopsy may be helpful in determining if the child has esophagitis (either peptic or eosinophilic esophagitis). In older children or adolescents with heartburn or other symptoms suggestive of GERD, a two- to four-week trial of acid suppression may be used as a diagnostic test for peptic disease as an alternative to endoscopy [1].

Heartburn — Children or adolescents with heartburn can be treated empirically with lifestyle changes and an empiric trial of acid suppressing medication (eg, PPI) for two to four weeks. A clear and complete response to acid suppression supports the diagnosis of GERD. Persistent or recurrent symptoms should prompt a referral for an upper endoscopy with biopsy, especially if any dysphagia is present. (See "Management of gastroesophageal reflux disease in children and adolescents".)

Dysphagia or odynophagia — Patients with dysphagia (difficulty swallowing) or odynophagia (pain with swallowing) usually should undergo specific evaluation.

Patients with dysphagia typically complain of difficulty initiating a swallow, or the sensation of solids or liquids getting stuck in the esophagus [14]. Dysphagia for solids is most commonly caused by esophageal inflammation related to GERD, eosinophilic esophagitis, or esophageal stricture [48]. These patients should be evaluated by upper endoscopy with biopsies, to examine the esophageal mucosa. Dysphagia for liquids as well as solids raises the possibility of a motility disorder such as achalasia. The first step in the evaluation for achalasia is a radiograph of the chest, looking for a lack of air in the stomach and an intraesophageal air-fluid level. A barium esophagram is beneficial to look for esophageal distension and the classic 'bird beak' appearance as well as the possibility of a stricture. (See "Clinical manifestations and diagnosis of eosinophilic esophagitis" and "Achalasia: Pathogenesis, clinical manifestations, and diagnosis".)

A common cause of odynophagia (pain with swallowing) in adolescents is pill esophagitis. This is caused by direct mucosal injury by certain drugs including tetracyclines (doxycycline and minocycline) that are commonly used for treatment of acne, or by anti-inflammatory agents including aspirin. Pill esophagitis is likely in patients who have sudden onset of odynophagia any time during the course of treatment with one of these drugs, especially if the pill is swallowed with little or no liquid and/or taken just before bedtime [1]. If the symptoms are mild, then it is reasonable to treat these patients empirically with sucralfate or a proton pump inhibitor (PPI) in addition to stopping the offending medication. If the symptoms are severe or progressive, it is important to perform an upper endoscopy prior to initiating treatment, to exclude infectious causes of esophagitis that cause odynophagia, including candida, cytomegalovirus, and herpes. (See "Medication-induced esophagitis".)

Uncommon causes of dysphagia that may present in children or adolescents include motility disorders (eg, myotonia) and systemic sclerosis (scleroderma) (table 3). (See "Approach to the evaluation of dysphagia in adults", section on 'Symptom-based differential diagnosis'.)

Asthma — GER may be a trigger for asthma in some patients. Abnormal reflux, as measured by symptoms or by esophageal pH monitoring, occurs in 25 to 75 percent of children with persistent asthma, and the association increases with severity of either condition, but whether this association is causal remains unclear [49,50]. Many studies have shown clinical improvement in asthma when patients are treated for GER [49,51]. However, predicting which patients are likely to respond to treatment remains problematic [1,52].

For patients with asthma and symptoms that strongly suggest GERD (including heartburn in older children and adolescents, or chronic regurgitation or vomiting in infants and younger children), we suggest a three-

month trial of acid suppression. (See "Management of gastroesophageal reflux disease in children and adolescents".)

GER may trigger asthma in some patients even in the absence of symptoms of GERD. Therefore, many experts recommend esophageal pH or MII/pH monitoring or an empiric three-month trial of vigorous acid suppression for patients with either of the following characteristics, particularly if they lack seasonal or allergic symptoms [1,49]:

- Nocturnal asthma more than once a week

- Continuous requirement for oral corticosteroids, high-dose inhaled corticosteroids, more than two courses of oral corticosteroids per year, or persistent asthma that does not allow the patient to be weaned from medical management

Similar approaches are used for adult patients with asthma and possible GERD. (See "Gastroesophageal reflux and asthma".)

Recurrent pneumonia — GERD can be associated with recurrent pneumonia, especially in patients with underlying neurologic dysfunction, or with anatomical abnormalities that predispose to aspiration, such as cleft lip/palate, choanal atresia, or micrognathia. Such patients should be evaluated for swallowing dysfunction using videofluoroscopy and/or fiberoptic endoscopic evaluation of swallowing. Esophageal pH monitoring has low sensitivity and specificity in detecting whether aspiration pneumonia is related to reflux in an individual patient, but may help establish the diagnosis in selected patients with suspected aspiration when combined with other investigations. (See "Aspiration due to swallowing dysfunction in infants and children".)

Other than direct evaluation of swallowing for patients with suspected swallowing dysfunction, no techniques are available to determine definitively whether GERD is causing chronic aspiration in an individual patient. Measurement of lipid-laden macrophages (obtained by bronchoalveolar lavage) and nuclear scintigraphy have been used for this purpose, but neither technique can reliably determine whether a patient has chronic aspiration [1]. (See 'Bronchoalveolar lavage' above and 'Nuclear scintigraphy' above.)

Patients with recurrent pneumonia should also be evaluated to exclude underlying causes other than GERD, including foreign body aspiration, cystic fibrosis (CF), or immunodeficiency. A history of choking is highly suggestive of foreign body aspiration, even if the choking occurred days or weeks prior to the onset of respiratory symptoms. An H-type tracheoesophageal fistula should also be considered in a child with recurrent pneumonia, especially if the same segment of the lung is always involved. (See "Airway foreign bodies in children" and "Congenital anomalies of the intrathoracic airways and tracheoesophageal fistula", section on 'Tracheoesophageal fistula and esophageal atresia'.)

Chronic cough — Most authorities suggest that GERD is not a common cause of isolated chronic cough in children, except in those with neurologic abnormalities predisposing to aspiration, as described above. Children with chronic cough should be evaluated for a variety of underlying causes, including asthma. A chronic "wet" cough typically has an underlying cause other than GERD, including foreign body aspiration or protracted bacterial bronchitis. (See "Approach to chronic cough in children" and "Causes of chronic cough in children", section on 'Overview of causes in children'.)

Other conditions — Stridor, hoarseness, sinusitis, otitis media have been associated with GERD, mostly in case reports and case series in children. Neither the association with GER nor response to antisecretory therapy have been established by controlled studies [1]. Therefore, other potential etiologies should be investigated in patients with these symptoms or signs. (See "Otitis media with effusion (serous otitis media) in children: Clinical features and diagnosis", section on 'Pathogenesis' and "Common causes of hoarseness in children", section on 'Gastroesophageal reflux/laryngopharyngeal reflux'.)

Similarly, in the majority of infants with apnea or apparent life-threatening events (ALTEs), GER is not the cause. In the few cases in which GER is strongly suspected with recurrent apnea, combined MII/pH esophageal monitoring and polysomnographic recording with symptom diary may help establish cause and effect. (See 'Esophageal pH monitoring or impedance monitoring' above and "Acute events in infancy including brief resolved unexplained event (BRUE)", section on 'Gastroesophageal reflux or swallowing dysfunction'.)

INFORMATION FOR PATIENTS — UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topics (see "Patient education: Acid reflux (gastroesophageal reflux disease) in children and adolescents (The Basics)")

- Beyond the Basics topics (see "Patient education: Acid reflux (gastroesophageal reflux disease) in children and adolescents (Beyond the Basics)" and "Patient education: Acid reflux (gastroesophageal reflux) in infants (Beyond the Basics)")

SUMMARY AND RECOMMENDATIONS

- Gastroesophageal reflux (GER) is common in infants, as manifested by regurgitation, and is generally not pathological. The regurgitation usually resolves by 18 months of age. Gastroesophageal reflux disease (GERD) refers to GER that is associated with pathological complications. (See 'Epidemiology' above and 'Definitions' above.)

- The differential diagnosis of gastroesophageal reflux disease (GERD) in children is broad, particularly when the principal complaint is regurgitation, vomiting, or abdominal pain (table 1). The diagnostic possibilities can be narrowed based upon the age of the child and the pattern of symptoms, using a thorough medical history (table 2). (See 'History' above.)

- Symptoms that are **not** typical for GERD include fever, weight loss or faltering growth, abdominal tenderness or distension, bilious vomiting, marked hematemesis, hepatosplenomegaly, headache or new neurologic symptoms, or other systemic symptoms. Patients with these symptoms should be carefully evaluated for other disorders. (See 'Recurrent vomiting or regurgitation' above and "Approach to the infant or child with nausea and vomiting".)

- Symptoms that suggest the possibility of GERD include (see 'Clinical manifestations' above):

  - Recurrent regurgitation that continues after two years of age

  - Refusal of food, especially solids

  - Frequent complaints of heartburn

  - Dysphagia (difficulty swallowing)

  - Severe or progressive asthma that is not responsive to standard therapy for asthma

  - Recurrent pneumonia, particularly in children with neurologic dysfunction

- Chronic hoarseness or stridor

When children present with these symptoms, further workup is appropriate. (See 'Suggested approach for common clinical scenarios' above.)

- The evaluation should include assessment for the possibility of occult or associated constipation, since constipation causes secondary reflux or dyspeptic symptoms in many children. (See 'History' above and "Constipation in infants and children: Evaluation".)

- For patients presenting with mild or moderate symptoms of heartburn, initial empiric treatment with acid suppressing drugs is reasonable. Persistent or recurrent symptoms should prompt referral for an upper endoscopy with biopsy, especially if any dysphagia is present. (See 'Empiric treatment' above.)

- Endoscopic evaluation of the upper gastrointestinal tract is indicated for patients with heartburn or epigastric abdominal pain that fails to respond to or relapses quickly after empiric treatment, or those with dysphagia or odynophagia. In addition, endoscopy may be valuable in the evaluation of patients who continue to have recurrent regurgitation after two years of age. (See 'Suggested approach for common clinical scenarios' above and 'Endoscopy and histology' above.)

- Endoscopic evaluation is necessary to establish the diagnosis of esophagitis. Most esophagitis is related to GERD, but eosinophilic esophagitis is increasingly recognized. Treatment of esophagitis is discussed separately. (See 'Endoscopy and histology' above and "Clinical manifestations and diagnosis of eosinophilic esophagitis" and "Management of gastroesophageal reflux disease in children and adolescents".)

- Evaluation with esophageal pH monitoring or multichannel intraluminal impedance monitoring (MII), bronchoalveolar lavage, nuclear scintigraphy, or esophageal manometry is only useful in specific clinical situations, and does not generally contribute to the diagnosis of a child with typical heartburn. Barium contrast radiography is neither sensitive nor specific for the diagnosis of GERD, but may be used in selected patients to exclude anatomic abnormalities. (See 'Available diagnostic techniques' above and 'History' above.)

- In some patients, GER may be a trigger for asthma. Therefore, in patients with severe or refractory asthma, or those with frequent nocturnal asthma, an empiric trial of effective acid suppression is appropriate. (See 'Asthma' above and "Gastroesophageal reflux and asthma".)

- Children with dysphagia should have a barium esophagram to evaluate for motility disorders, inflammatory strictures and anatomic causes of the symptoms; upper endoscopy may also be helpful in diagnosing esophagitis. In children with odynophagia (painful swallowing), diagnostic endoscopy should be performed rather than empiric treatment with acid suppression due to the possibility of infectious esophagitis. An esophageal motility study is helpful in diagnosing primary motility disorders such as achalasia. (See 'Dysphagia or odynophagia' above.)

- In most children with stridor, hoarseness, sinusitis, otitis media, and apnea, GER is not the cause. Therefore, other potential etiologies should be considered in patients with these symptoms or signs. In the few cases of suspected GER associated with recurrent apnea, esophageal monitoring using combined multichannel intraluminal impedance and pH (MII/pH) and polysomnographic recording may help establish cause and effect. (See 'Other conditions' above.)

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