Topic: Gastroesophageal Reflux Disease in Children: Diagnosis and Management

Learning objectives: At the completion of this module, learners will be able to:

1. Describe the natural history of gastroesophageal reflux (GER) in infants.
2. Distinguish GER from gastroesophageal reflux disease (GERD).
3. List the symptoms that may indicate GERD.
4. Discuss the limitations of available diagnostic tests for GERD.
5. Outline a step-wise management approach for GERD.
CASE:

You meet your new patient, AJ, a 2 month-old African-American male, and his parents today for a “well visit” and immunizations. The family moved to Pittsburgh from Cambridge, MA about a month ago. AJ’s father is a PhD from Harvard who is starting a teaching career at a local University and AJ’s mother is a lawyer who has accepted an offer at a local law office which specializes in medico-legal cases.

While you are talking with the parents, AJ spits up a moderate amount of formula which he took in the waiting room about 10 minutes ago. Mrs. J tells you that he has been a “spitty” baby since birth and things have not changed at all despite his change to soy formula about a month ago. In the last one week or so, AJ has been intermittently crying and refusing to feed. Occasionally, the parents have also noticed back arching after feedings. The parents are quite concerned about AJ’s symptoms. He is their only child. The parents tragically lost an infant boy about 2 years ago to “SIDS”.

Dr J interrupts your history to ask you how common “spitting” is in normal infants, as well as AJ’s chances of “outgrowing” his symptoms.

Question 1. Describe the prevalence and natural history of GER in healthy infants.
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Answer:

GER symptoms are present in approximately 50-70% of healthy infants. The symptoms usually peak by 4 months of age. Approximately 50% resolve by 6 months, 75% by 12 months and 95% by 18 months of age. Less than 5% of infants carry the symptoms into their childhood (1).

Then, Mrs. J. asks you if AJ has “GER” as his pediatrician in Massachusetts diagnosed.

Question 2. Distinguish GER from GERD, regurgitation, and vomiting.
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Answer:

**Gastroesophageal reflux (GER):**

Gastroesophageal reflux (GER) is the passage of gastric contents into esophagus. This can be a physiologic process seen in healthy infants, children and adults. These episodes are brief and do not cause any significant symptoms, complications or esophageal injury.

**Regurgitation:**

Effortless passage of refluxed gastric contents into the oral pharynx.

**Vomiting:**

Expulsion of refluxed gastric contents from the mouth.

**Gastroesophageal reflux disease (GERD):**

Gastroesophageal reflux disease (GERD) is associated with persistent symptoms and reflux-related complications which vary depending upon the age of the child. According to 2013 practice guidelines (2), symptoms or conditions can be esophageal or extraesophageal, both of which are associated with mucosal injury on upper endoscopy.

- Esophageal symptoms include vomiting, feeding refusal, irritability, failure to thrive, dysphagia, abdominal or substernal/retrosternal pain, and esophagitis.
- Established extraesophageal conditions include respiratory symptoms (cough, laryngitis, and wheezing in infancy) and dental erosions.
- Proposed extraesophageal manifestations include pharyngitis, sinusitis, and recurrent otitis media (2).

Symptoms of GERD present during childhood are moderately likely to persist during adolescence and adulthood. In a study of 207 patients who were diagnosed with GERD in childhood, about one third had persistent symptoms during early adulthood (approximately 15 years later) (3)

Question 3. What additional questions do you ask AJ's parents to determine if AJ has GER or GERD?
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Answer:

1. Ask about signs and symptoms of GERD.

Signs/Symptoms of GERD (by age group):

**Infants:**
- Persistent spitting or vomiting (after almost every feed)
- Feeding refusal
- Irritability and back arching
- Failure to thrive
- Respiratory symptoms: chronic cough, choking, recurrent stridor, recurrent pneumonia, wheezing
- Apparent Life Threatening Events (ALTE)

**Preschool children:**
- Intermittent vomiting
- Abdominal pain
- Anorexia or refusal to eat

**Older children and adolescents:**
- Chronic heartburn and regurgitation
- Epigastric pain
- Chest pain
- Nocturnal pain
- Dysphagia
- Sour burps
- Nocturnal cough
- Wheezing
- Recurrent pneumonia
- Hoarseness
- Asthma
- Sore throat
- Chronic sinusitis
- Laryngitis
- Dental erosions

2. Ask about warning signs and symptoms which may indicate non-GERD causes for vomiting.

Warning signs/symptoms associated with vomiting:
• Bilious vomiting
• Constantly forceful vomiting
• Constipation
• Fever
• Lethargy
• Bulging fontanelle
• GI bleeding: hematemesis, hematochezia

• Abdominal distension, tenderness, hepatosplenomegaly
• Failure to thrive
• Genetic disorder (trisomy 21)
• Micro or macrocephally
• Seizures
• Associated chronic disease
Case continued:

You complete your history and physical exam. You find that AJ was born full term from an uncomplicated pregnancy and delivered by a repeat C-section. Except for gradually worsening episodes of spitting (non-projectile, non-bilious, non-bloody) after almost every feed, his medical history is unremarkable. He has had no respiratory problems. Occasional feeding refusal and back arching after feeds have recently developed. His formula intake has been adequate and he has been voiding and stooling sufficiently.

On physical examination, you find that AJ is a delightful infant growing along the 50th percentile for all his parameters (based on review of his previous records). His vital signs are stable and his examination, including careful abdominal palpation, is completely normal.

Question 4. What is your diagnosis for AJ? Does he have GER or GERD?
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Answer:

The history of spitting, feeding refusal and back arching after feeds and a normal physical exam are consistent with GERD.

Mrs. J asks you if any testing needs to be done.

Question 5. What is the role of diagnostic testing in GERD in children?
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Answer:

Specific testing is usually not required in children with typical features of GERD based upon history and physical examination. There is no single test which can rule GERD in or out. Diagnostic evaluation is recommended when the diagnosis is unclear, in children with warning symptoms and when the symptoms are refractory to treatment. In general, children with GERD having no warning symptoms and signs usually do not require any specific testing (4).

Question 6. What is the role of empirical treatment as a diagnostic test in children?
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Answer:

Empirical medical therapy is widely used in treating children with GERD. The efficacy of empirical trial of medical therapy as a diagnostic test, however, is not well established in children. Studies in adults have suggested that this may be a cost effective approach, but applicability to children is uncertain.

Question 7. What diagnostic procedures for GERD are available for children? What are the limitations of each procedure?
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Answer:

**Esophageal pH monitoring:**

This test permits the assessment of the frequency and duration of esophageal acid exposure and its relationship to symptoms. The reflux index (the percentage of total time that the esophageal pH is <4) is calculated after 24 hours of monitoring (5). In infants, a reflux index above 7% is considered abnormal. An abnormal reflux correlates strongly with the presence of esophagitis on endoscopy. In children with severe or atypical asthma, esophageal pH monitoring has been used to assess whether there is a temporal correlation between asthma symptoms and reflux.

However, as proposed in the guidelines issued by the North American Society for Pediatric Gastroenterology and Nutrition (2) esophageal pH monitoring is losing value as the primary modality to diagnose or manage GERD in the pediatric population and is not routinely indicated in the diagnosis of GERD. It is most helpful to assess the adequacy of acid suppression in children who remain symptomatic despite medical therapy.
Multichannel Intraluminal Impedance (MII)

MII allows detection of the direction of the moving bolus by measuring the change in the electrical impedance between the measuring electrodes. This can help distinguish a swallow from the regurgitated bolus and provides a better picture of the events than pH monitoring. A pH sensor is included as an additional channel on a single catheter. Combined pH/MII testing is becoming the test of choice to assess temporal relationships between GERD symptoms and reflux as well as associated apnea, cough and behavioral symptoms.

Endoscopy and biopsy:

The sensitivity, specificity and predictive values of endoscopy and biopsy for the diagnosis of GERD have not been well established. The presence of esophagitis, however, strongly correlates with acid exposure. On the other hand, normal esophageal mucosa does not rule out reflux. It may help distinguish GERD from eosinophilic (allergic) esophagitis, pill esophagitis and Crohn’s disease.

Endoscopic evaluation is indicated in patients when esophagitis or gastritis is suspected, in patients who fail to respond or relapse quickly after empiric treatment, or for poor weight gain, anemia, fecal occult blood, recurrent pneumonia or hematomesis.

Scintiscan (Milk Scan):

This method uses consumption of technetium-labeled feeding. Scintiscan is used to detect pulmonary aspiration of stomach contents. This study can also assess the rate of gastric emptying. It is, however, a poor test for diagnosis of GERD.

Esophageal manometry:

This test has a minimal role in the diagnosis of GERD. It may be helpful in evaluating peristaltic function before antireflux surgery to exclude motor disorders.

Upper GI series:

The Upper GI series is neither sensitive nor specific for the diagnosis of GERD. The test is indicated to exclude an obstructive pathology such as pyloric stenosis, malrotation, hiatal hernia and annular pancreas.

Mrs. J asks you, “So, Doctor, what do you think we should do?”

Question 8. What is your management plan for AJ?
Question 8. What is your management plan for AJ?

Answer:

First-line treatment options

*Milk thickening agents:*

When thickening agents, such as rice cereal, are added to formula, the frequency of vomiting decreases (6). Thickening of the formula also increases its caloric density, which is beneficial in underweight infants. The caloric density of 1 oz of formula thickened with 1 tablespoonful of rice cereal is approximately 34 Kcal.

Remember to advise the parents to enlarge the hole of the nipple to allow for normal flow rate from the bottle (approximately 1 drop per second when the bottle is inverted.)

The Food and Drug Administration issued a warning against using ready-made thickening agents (i.e., “SimplyThick”) in preterm infants born < 37 weeks of gestation while in the hospital or within 30 days of hospital discharge.

*Formula change:*

Milk protein allergy can have a similar presentation as GERD. Several studies have shown that, in a subset of infants, elimination of cow’s milk from the diet decreased vomiting within 24 hours (7). Soy-based formula in treating reflux symptoms is not very helpful. If thickening of the formula does not help, gastroenterologists recommend a trial of hypoallergenic formula.

Hypoallergenic formulas include:

- Alimentum
- Nutramigen
- Pregestamil

*Positioning therapy:*

The traditional therapy of placing a child in an infant seat to reduce GER has not been proven effective by pH probe studies. However, in multiple studies esophageal pH monitoring has demonstrated that reflux is decreased when infants are placed in the prone position (8). It is uncertain if the prone position at a 30 degree angle is associated with less reflux than the prone flat position. Other studies have demonstrated that the prone position is superior to the semi-supine position such as sitting in an infant seat (9). In older children, GERD is decreased in the left lateral decubitus (left side down), and elevating the head of the bed 6 inches (10). Due to the increased risk of SIDS
related to prone positioning, the AAP recommends non-prone positioning during sleep (11).
Lifestyle Modifications for Children and Adolescents

Recommendations for older children and adolescents are similar to those for adults, including weight loss if overweight or obese (obesity can lead to GERD), smoking cessation and avoidance of alcohol consumption. In addition, patients are counseled to avoid caffeine, chocolate, and spicy foods.

Case continued:

AJ’s parents are quite impressed and satisfied (and so is your preceptor) with your answers to their questions. You decide with the parents to try first-line treatment for AJ’s symptoms: thickened feedings and a trial of hypoallergenic formula (Nutramigen). The parents rightfully decide not to put AJ in the prone sleeping position. You recommend a follow up visit in 2 weeks.

Two weeks later, AJ and his parents return to your office. AJ’s symptoms have worsened significantly. He now vomits what appears to be more than 50% of his intake every time he feeds. The vomiting is still non-projectile, non-bilious, and non-bloody. His parents have observed that AJ’s crying and back arching have significantly increased with feedings. His weight gain has dropped off to approximately 15 grams/day since his last visit. AJ’s examination otherwise remains unchanged.

Question 9. How do you revise your management plan to address AJ’s worsening symptoms?
Question 9. How do you revise your management plan to address AJ’s worsening symptoms?

Answer:

As first-line treatment has not been successful, pharmacologic therapy is the next option.

Goals of pharmacologic treatment are:

- Eliminate symptoms
- Heal esophagitis
- Manage or prevent complications
- Maintain remission

Flow Chart, Medications and Doses:

Review from the following link -

**Table 4 Pediatric Doses of Medications Prescribed for GERD – scroll to page 7 (e1690)**

**Flow Chart for Approach to Infant with GER – scroll to page 8 (e1691)**


**Acid suppressants:**

The antisecretory agents, histamine type 2 receptors antagonists (H2RAs) and proton pump inhibitors (PPIs) are superior in their efficacy and convenience to antacids and surface agents.

- **Histamine type 2 receptors antagonists (H2RAs)**

  These drugs inhibit histamine-2 receptors on the parietal cells of stomach mucosa. Multiple controlled trials have evaluated the efficacy of H2RAs in adults and far fewer studies are performed in children. Studies have shown that their benefit is greatest for patients with mild esophagitis and all the H2RAs are equally superior to placebo for relief of symptoms and healing of esophageal
mucosa (12). Tolerance eventually develops limiting their use in long term management of GERD.

Available H2Ras:

✔ Ranitidine (Zantac)
✔ Cimetidine (Tagamet)
✔ Nizatidine (Axid)
✔ Famotidine (Pepcid)

Ranitidine is most commonly used. Its recommended dose in GERD and erosive esophagitis in children in >1 month-16 years is 4-10 mg/kg/day divided twice daily.

- **Proton pump inhibitors (PPIs)**

These agents block acid secretion by irreversibly binding to and inhibiting the hydrogen-potassium ATPase pump on the luminal surface of parietal cell membrane. To be activated, PPIs require acid in the parietal cell canaliculus; they are most effective when the parietal cell is stimulated by a meal following a fast. PPIs are therefore administrated one-half hour before breakfast so that peak concentration coincides with the meal time.
Available PPIs:

- Omeprazole (Prilosec)
- Esomeprazole (Nexium)
- Lansoprazole (Prevacid)

PPIs is indicated when GERD is refractory to the therapy with H2Ras. Comparative studies have shown a clear advantage of PPIs over H2Ras. PPIs are reported to produce a greater reduction in acid secretion and have a longer duration of action than H2Ras. Sufficient data regarding long term safety and efficacy is not available in children.

Antacids:

Antacids neutralize gastric pH. **The long term use of antacids is not recommended in the treatment of pediatric GERD.** Significant aluminium absorption from aluminum-containing antacids can cause osteopenia and neurotoxicity.

Surface agents:

These agents work by creating a barrier impeding peptic injury to the mucosa. Two agents are available: sucralfate and sodium alginate. Sucralfate is aluminium sucrose sulfate and is not commonly used in children due to concerns related to aluminium toxicity. Use of sodium alginate, derived from seaweed, has not been shown to produce beneficial results. Surface agents are not recommended for the independent treatment of severe pediatric GERD.

Prokinetics:

Although these agents appear to increase lower esophageal sphincter pressure, they do not reduce the frequency of transient relaxation of the sphincter. The rationale for the use of the prokinetic agents is based on their ability to enhance esophageal peristalsis and accelerate gastric emptying.
According to the most recent guidelines, routine use of prokinetic agents (i.e., metoclopramide [Reglan], erythromycin, bethanechol, cisapride) in the treatment of pediatric GERD is NOT supported by evidence (2).

Question 10: What are the complications of GERD?
Question 10: What are the complications of GERD?

Answer:

The respiratory complications include asthma, apnea, ALTE, chronic cough and recurrent pneumonia. The relationship between asthma and GERD is controversial as both are common pediatric disorders which can co-exist. Some studies have shown that GERD can be a contributing factor, particularly to some refractory cases of asthma. A study correlating asthma with GERD showed a 13.2% prevalence with reflux versus 6.8 % prevalence in children without reflux and the difference was statistically significant (14). Neurologically impaired children are at higher risk for developing reflux and aspiration.

The other complications of GERD include hoarseness, laryngitis, sinusitis, dental erosions and recurrent otitis media.

Chronic esophageal acid exposure can lead to reflux esophagitis, stricture, Barrett esophagus and adenocarcinoma. Barrett esophagus and adenocarcinoma rarely develop in the pediatric population.

Case continued:

Based on your knowledge of pharmacologic treatment, you prescribe a trial of acid suppression with ranitidine (a H2RA) and plan a follow-up visit in 2 weeks. In planning for AJ’s return visit, you consider other available management options.

Question 11: In the event that AJ’s symptoms do not improve on pharmacologic therapy, what other treatment options exist?
**Question 11:** In the event that AJ’s symptoms do not improve on pharmacologic therapy, what other treatment options exist?

**Answer:**

If AJ does not improve on pharmacologic therapy, it is advisable to consult with a pediatric gastroenterologist.

One additional treatment modality for GERD is **surgery**.

**Surgery:**

Surgery is considered in children with GERD who have persistent symptoms despite medications and who cannot be weaned from medical therapy. The Nissen fundoplication is the procedure of choice. The procedure has been performed laproscopically with good results.

**Case, continued:**

You see AJ and his parents 2 weeks after the medical therapy was initiated. Mrs. J tells you that AJ’s symptoms have resolved significantly. AJ is spitting only occasionally and his crying and back arching with feeds have resolved almost completely. AJ’s weight gain has been 30 grams/day since his last visit. AJ’s parents are extremely pleased and they are looking forward to his 4 month visit with you!
Take Home Points:

1. GER symptoms are present in approximately 50-70% of healthy infants. The symptoms usually peak by 4 months of age. Approximately 50% resolve by 6 months, 75% by 12 months and 95% by 18 months of age.

2. Gastroesophageal reflux (GER) is the passage of gastric contents into esophagus and can be a physiologic process seen in healthy infants, children and adults. These episodes are brief and do not cause any significant symptoms, complications or esophageal injury. Gastroesophageal reflux disease (GERD) is associated with persistent symptoms and reflux-related complications which vary depending upon the age of the child. Symptoms or conditions can be esophageal or extraesophageal, both of which are associated with mucosal injury on upper endoscopy.

3. Symptoms that may indicate GERD vary based on the age group. In infants, symptoms include persistent spitting/emesis, feeding refusal, irritability, back arching, FTT, respiratory symptoms, and/or ALTE. In preschool children, symptoms include vomiting, abdominal pain, and refusal to eat. In older children and adolescents, symptoms include heartburn, epigastric pain, chest pain, dysphagia, sour burps, wheeze, nocturnal cough or pain, among others.

4. Diagnostic procedures for GERD have their limitations. Esophageal pH monitoring is losing value as the primary modality to diagnose or manage GERD in the pediatric population and is not routinely indicated in the diagnosis of GERD. Normal esophageal mucosa on endoscopy does not rule out reflux. Milk scan is a poor test for GERD. UGI is neither sensitive nor specific for GERD.

5. First-line treatments for infants with GERD include milk thickening, formula change, and/or positioning changes. First-line treatments for older children and adolescents include lifestyle changes (smoking cessation, weight loss, avoidance of alcohol, caffeine, spicy foods, chocolate). If first-line treatment is unsuccessful, pharmacologic therapy is the next option (H2RAs, PPIs, etc).
References:


