Gastroesophageal Reflux in Infants

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Resident Education Series

Reviewed by Jyoti Ramakrishna, MD of the Professional Education Committee

Case

- 6 week old F presents to primary care clinic with vomiting
- Bottle feeding
- “Large amount” of nonbloody, nonbilious emesis following >50% of feeds
- Fussy following feeds, but consolable
- Weight gain excellent
- Baby is now fed Enfamil Gentlease (3rd formula) and parents are asking about medications

Objectives

- To briefly review the definitions, natural history, and mechanisms of GER and GERD
- To discuss the diagnosis of GERD in infants and the warning signs suggesting other more worrisome disorders
- To discuss the management options for physiologic GER and for GERD

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Definitions

GER	Passage of gastric contents into esophagus
GERD	Symptoms or complications that may occur when gastric contents reflux into esophagus or oropharynx
Regurgitation	Passage of refluxed gastric contents into oral pharynx
Vomiting	Expulsion of refluxed gastric contents from mouth

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Mechanisms of GER in the Infant

- Angle of His underdeveloped
- Inadequate gastric accommodation
- Supine position + gravity = GER

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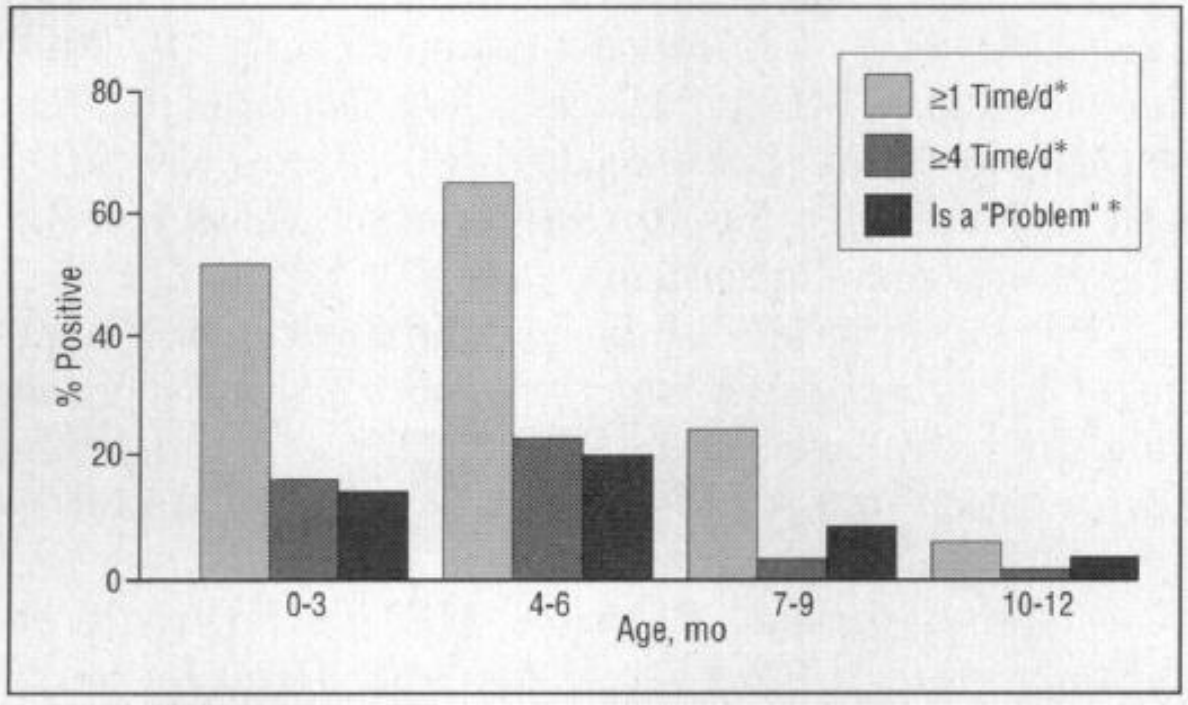
GER Prevalence

- Nelson et al. *Arch Pediatr Adolesc Med* 1997
  - Cross-sectional study of 19 pediatric practices in Chicago, IL
  - Survey parents of 948 pediatric patients (<13 months)
  - Excluded infants born prematurely, with chronic medical or developmental condition, or had been ill in the past two weeks



Natural History

- Martin et al. *Pediatrics* 2002
  - Objective: To determine the natural history of infant "spilling" (regurgitation/vomiting) during the first two years of life
  - Prospective birth cohort was followed with daily symptom diaries during the first two years of life
    - Parents recorded whether their child vomited most feeds (50% or more) on a daily basis

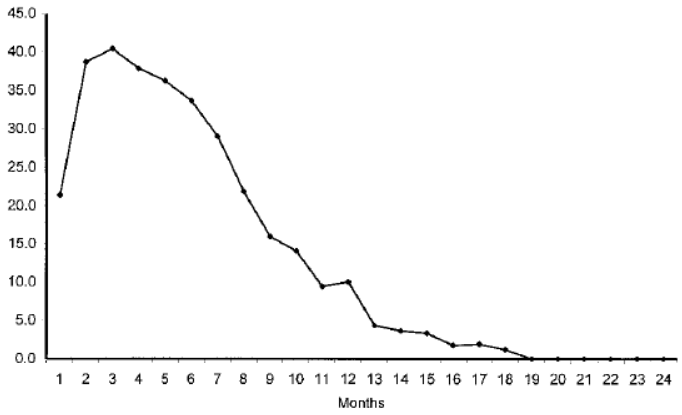


Fig 2. Proportion (%) of children who spilled.

When to worry?

• GER becomes GERD when reflux of gastric contents causes troublesome symptoms and/or complications

- Physiologic GER can become GERD when:
  - Insufficient clearance and/or buffering of material refluxed into esophagus
  - Delayed gastric emptying
  - Anatomic abnormality (hiatal hernia)
- Signs & symptoms suggesting GERD
  - FTT (with feeding difficulty)
  - Irritability
  - Dysphagia
  - Odynophagia
  - Arching

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Diagnosis of GERD

- Diagnosis is made clinically
  - Not easy!
- Symptoms and signs are nonspecific and unreliable
  - Individual symptoms in children generally are not highly predictive of findings of GERD by objective studies
- Major role of the history and physical is to exclude other more worrisome disorders that present with vomiting

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Warning Signals In Vomiting Infant Requiring Further Investigation

- Bilious or continuous vomiting
- GI bleeding
- Onset of vomiting after 6 months of life
- Failure to thrive
- Diarrhea, constipation
- Fever
- Lethargy
- Hepatosplenomegaly
- Macro/microcephaly
- Bulging fontanelle
- Seizures
- Abdominal tenderness, distention
- Documented or suspected genetic/metabolic syndrome

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Y Vandenplas and CD Rudolph et al, *J Pediatr Gastroenterol Nutr* 2009

Diagnosis of GERD

- Barium contrast radiography
  - Indication is detection of anatomic abnormalities
  - Neither sensitive nor specific for diagnosing GERD
    - Brief duration produces false-negatives
    - Frequent occurrence of non-pathological reflux during the examination produces false-positives

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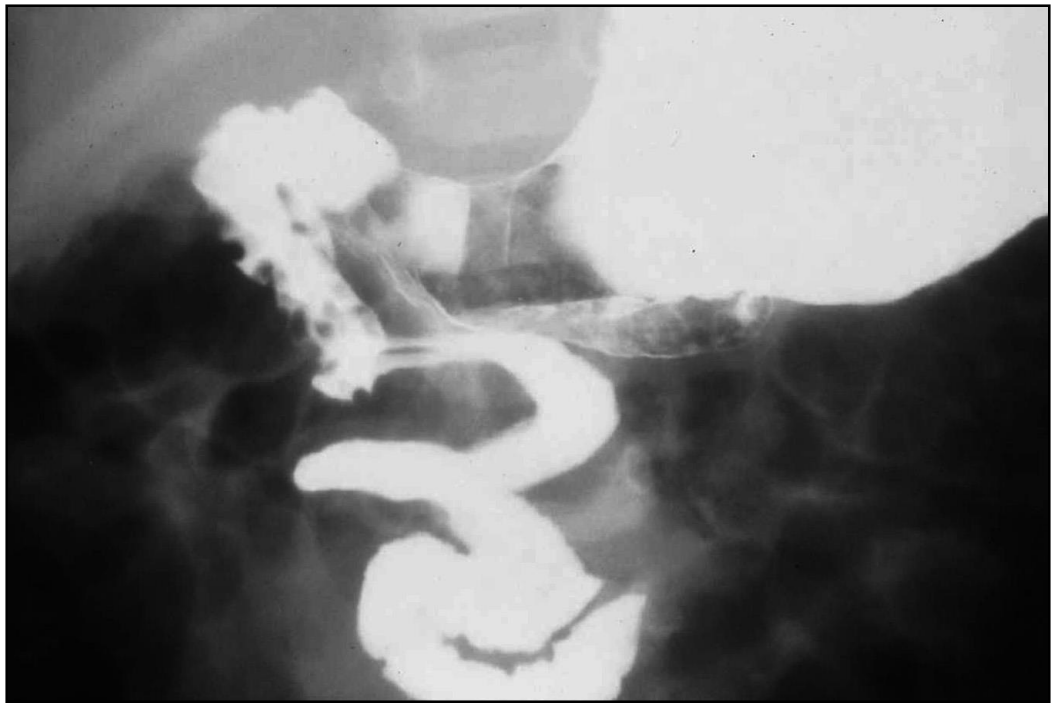
Pyloric stenosis



Malrotation

Diagnosis of GERD

- Esophageal pH monitoring
  - Gold standard
  - Measures the frequency and duration of acid reflux episodes (drop in esophageal pH < 4.0)
    - Measures reflux index (RI)
    - Other parameters: total number of episodes, number of episodes lasting > 5 minutes, patient position during episode, awake vs. asleep

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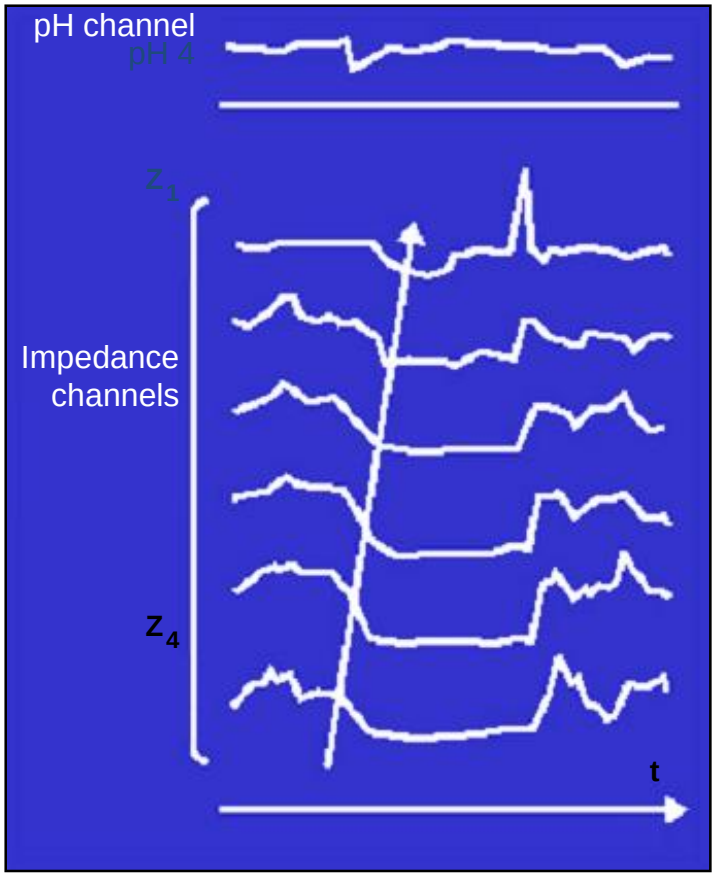
Multiple Intraluminal Electrical Impedance Measurement



Advantages

- Detects nonacidic GER episodes
- Detects brief (<15 s) acidic GER episodes
- Useful for studying respiratory symptoms and GER in infants

Limitations

- Normal values in pediatric age groups not yet defined
- Analysis of tracings time-consuming
- Portable device unavailable for outpatient studies

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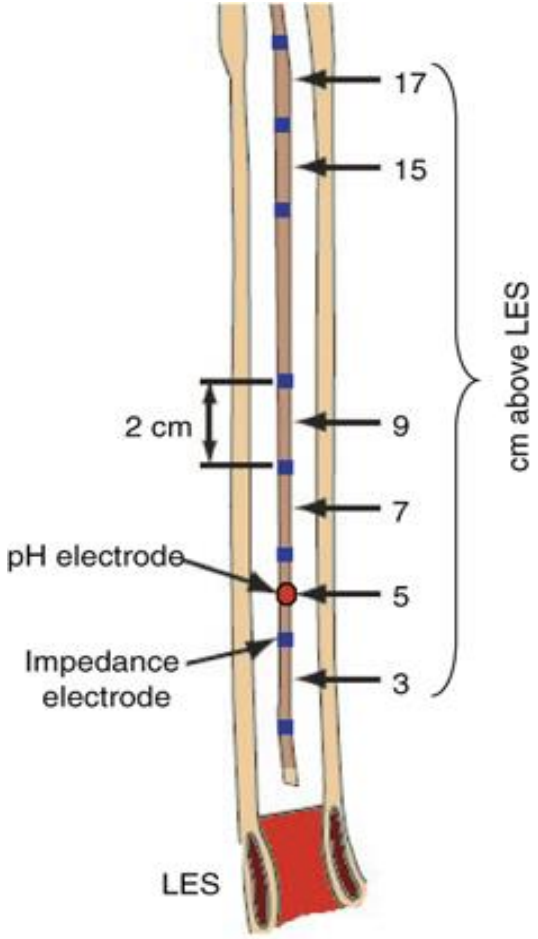
Impedance Measurement



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http://www.nature.com/ajg/journal/v104/n2/fig_tab/ajg200823f2.html

Esophagogastroduodenoscopy (EGD)

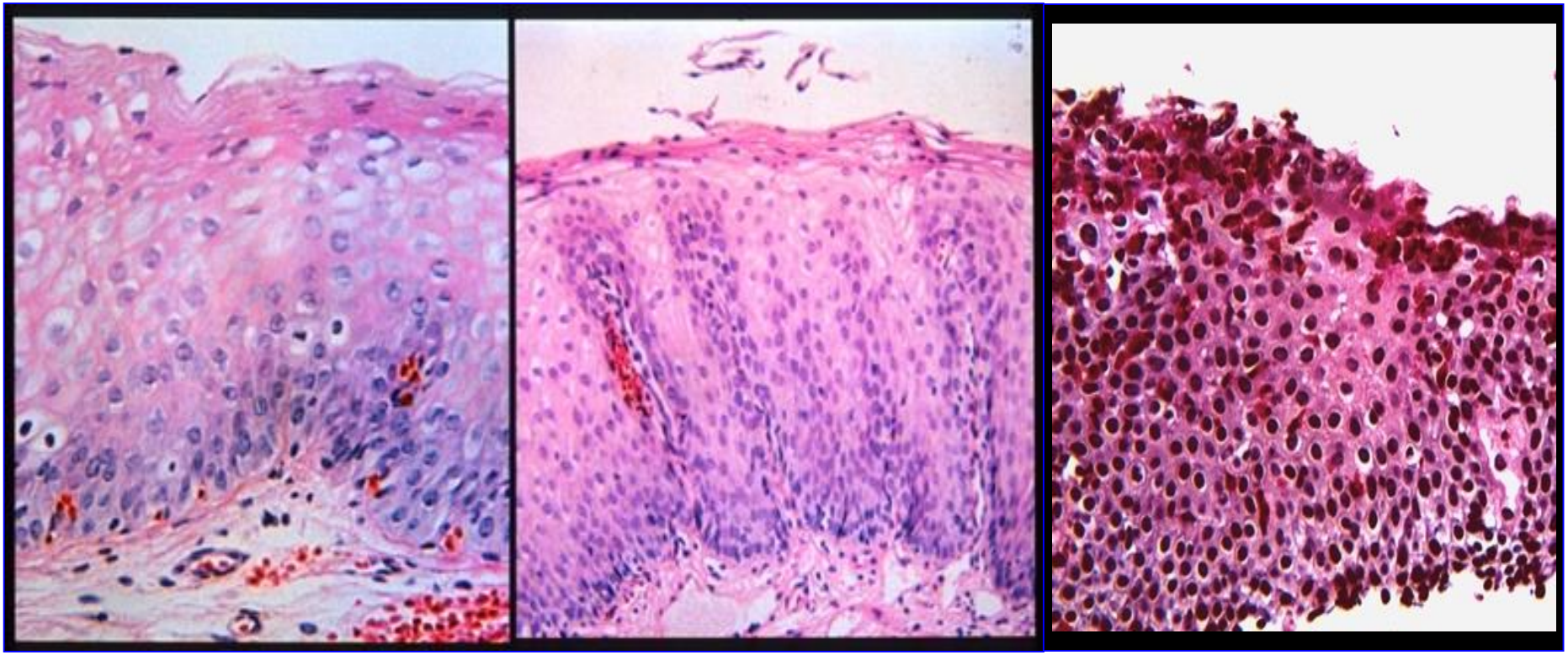
Advantages

- **Enables visualization and biopsy of esophageal epithelium**
- **Determines presence of esophagitis, other complications**
- **Discriminates between reflux and non-reflux esophagitis**

Limitations

- **Need for sedation or anesthesia**
- **Endoscopic grading systems not yet validated for pediatrics**
- **Poor correlation between endoscopic appearance and histopathology**
- **Generally not useful for extra-esophageal GERD**

Esophageal Histology



Normal esophagus

GER

Eosinophilic esophagitis

Scintigraphy

Advantages

- Detects acidic and non-acidic GER
- Evaluates gastric emptying
- May demonstrate aspiration

Limitations

- Lack of standardized techniques
- Absence of age-specific normative data
- Period of observation limited to early postprandial period

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Treatment: Reassurance

- The natural history of **physiologic** reflux in most infants is resolution as lower esophageal sphincter function matures
- Parental education, guidance, and support are always required
  - Usually sufficient to manage healthy, thriving infants with symptoms consistent with physiologic GER
- Often, the best approach is to sympathize with the family and present the natural history data

2009 Guidelines: Lifestyle Changes in Infants

- Avoid overfeeding
- Thicken formula (up to 1 tbsp per 1-2oz)
- Avoid “carseat” positioning
- Upright positioning after feeds (less effective than thickening feeds)
- Consider 2-4 week trial of hypoallergenic formula

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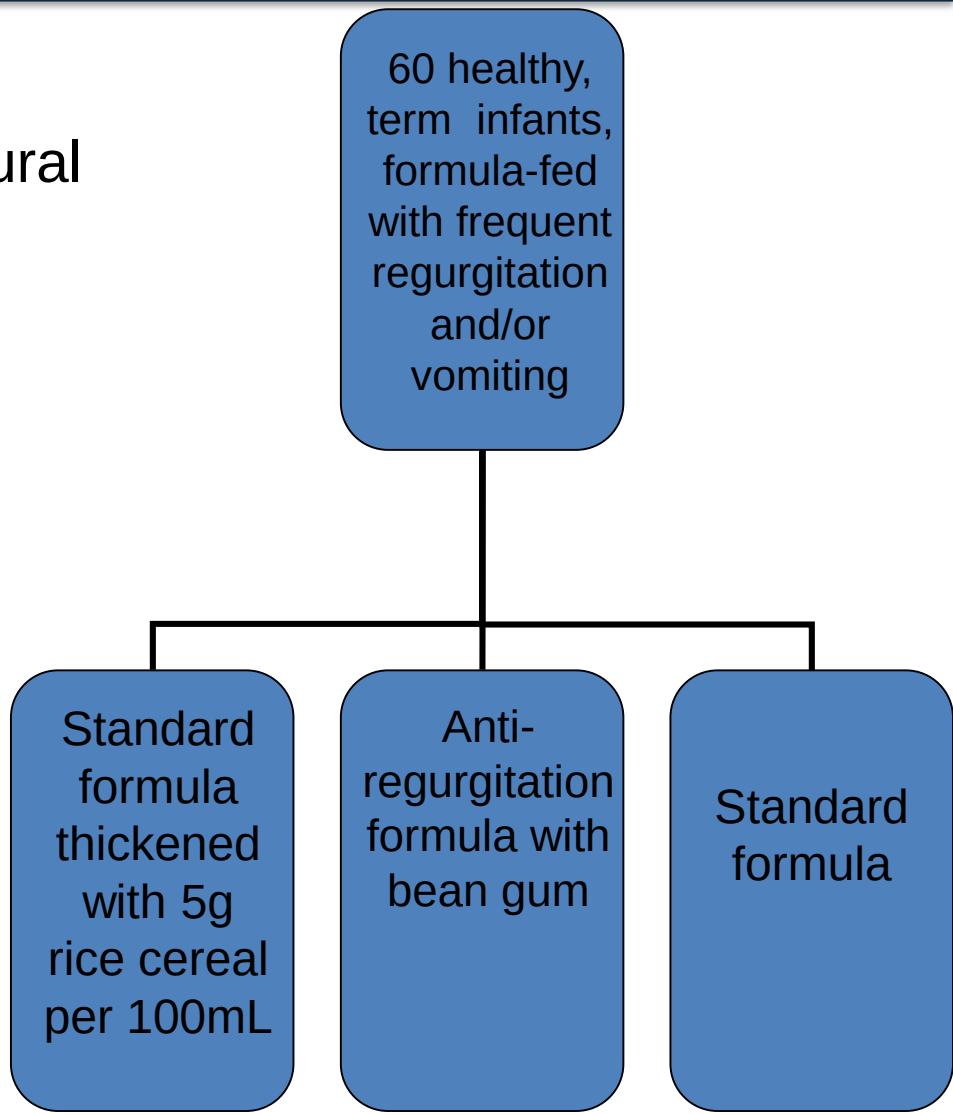
Treatment: Lifestyle Changes

- Hegar et al. *JPGN* 2008
  - Statistically significant natural decrease in regurgitation frequency in all 3 groups



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Treatment: Lifestyle Changes

- The bottom-line:
  - The use of AR formula and formula with added thickener may result in the reduction of regurgitation—but how much of this is related to natural history?
  - Reduced volume feedings may be useful—but necessary to monitor caloric intake/weight gain

Treatment: Pharmacologic Therapies

- Histamine-2 receptor antagonists
  - Decrease acid secretion by inhibiting histamine-2 receptors on parietal cells
  - Ranitidine has been shown, in infants, to reduce the time that gastric pH is <4
  - Pharmacokinetic studies in children show that gastric pH begins to increase within 30 minutes of administration and **lasts for 6 hours (TID or QID dosing)**
  - Drawbacks
    - Tachyphylaxis
    - Side effects in infants: irritability, head-banging, headaches

Treatment: Pharmacologic Therapies

- Proton Pump Inhibitors
  - Inhibit acid secretion by blocking Na-K-ATPase (the parietal cell proton pump)
  - Adult studies show that PPI's produce higher and faster healing rates for esophagitis than H2RA's
    - Maintain gastric pH at or above 4 for longer periods of time
    - Inhibit meal-induced acid secretion
    - Facilitate gastric emptying
    - Effect does not diminish with chronic use
  - No PPI has been approved for use in children younger than 1 year of age!
    - Few pharmacokinetic data for PPIs in infants

Is There Evidence to Support Increase in the Use of PPIs in Infants?

- Orenstein et al. *J Pediatr* 2009
  - Multicenter, randomized, double-blind, placebo-controlled evaluating lansoprazole versus placebo
  - 162 infants (1-12 months) with symptomatic GERD who remained symptomatic (crying, fussing, or irritability) following 1 week of conservative management
  - Similar efficacy for lansoprazole and placebo
  - Adverse events more common in lansoprazole group

PPI Safety Concerns

Pediatrics

- Acute gastroenteritis (OR 3.58)
- Community acquired pneumonia (OR 6.39)
- *Clostridium difficile* infection

Adults

- Pneumonia
- *Clostridium difficile* infection
- Bacterial gastroenteritis
- Hip fracture in elderly

Canani RB, *Pediatrics* 2006;117:e817-e820 Laheij RJ, *JAMA* 2004; 292:1955-1960 Garcia Rodriqguez, *Clin Gastro Hepatol* 2007;5:1418-23
Dial S, *JAMA* 2005;294:2989-2995 Yang YX, *JAMA* 2006;296:2947-2953 Turco R, *Aliment Pharmacol Ther* 2010;31:754-759

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Available Prokinetic Agents Are Unproven or Ineffective

- Cisapride: Withdrawn
- Bethanechol: 1 randomized controlled trial (RCT)
- Erythromycin: no RCT
- Domperidone: available in Canada, no RCT
- Metoclopramide
  - Esophageal pH improvement in 1 of 6 RCT
  - Clinical improvement in 1 of 4 RCT
  - High incidence of adverse events (Black Box Warning)

No evidence based justification for routine use of these agents

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Treatment: Surgical Therapy

- Most of literature on surgical therapy in children with GERD consists of retrospective case series
- Anti-reflux surgery may be of benefit in children with confirmed GERD who have failed optimal medical therapy or who have **life-threatening complications of GERD**
- It is important to provide families with appropriate education and a realistic understanding of potential complications

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Treatment: Surgical Therapy

- Complications following antireflux surgery may be due to:
  - Alterations in fundic capacity
  - Altered gastric accommodation
  - Altered sensory responses
- Complications may include:
  - Gas-bloat syndrome
  - Early satiety
  - Dumping syndrome
  - Post-operative retching

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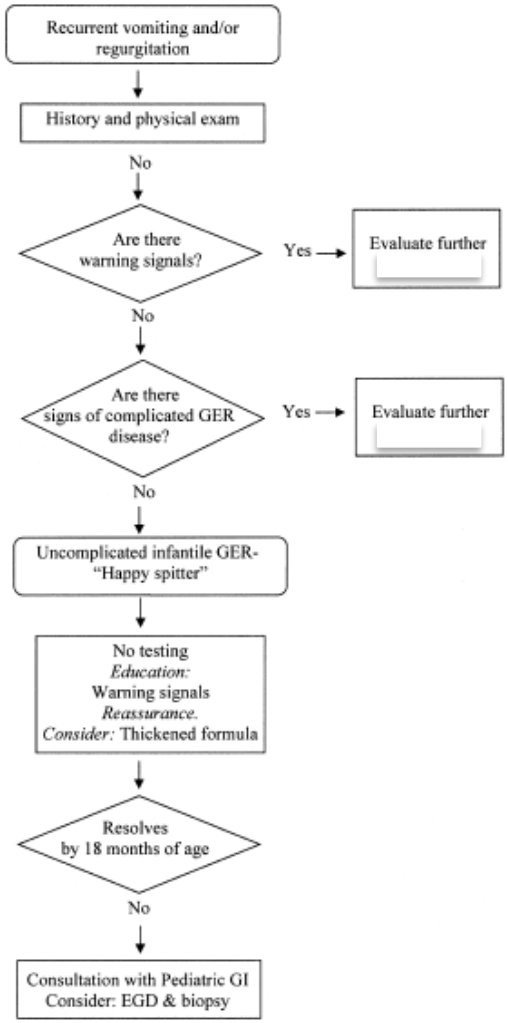
Summary Algorithm: Vomiting Infant -- Uncomplicated

- History and physical exam
  - Assess for warning signs/symptoms
- Parental education
  - Explain natural history
  - Feeding modification
  - ? 2 wk trial of hypoallergenic formula
- Medical therapy usually not necessary
- Further evaluation if symptoms don't resolve by 18-24 months



IG. 1. Approach to the infant with recurrent regurgitation and omiting.

Y Vandenplas and CD Rudolph et al, *J Pediatr Gastroenterol Nutr* 2009

Conclusions

- GER is common in infants
- GERD is relatively uncommon and is likely over diagnosed and over treated
- Pharmacologic and surgical therapies have potential risks which should be considered

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