

Pediatric GER

When and how to treat

Nadine Yazbeck, MD
Pediatric GI and Nutrition
American University of Beirut-Medical Center

October 26, 2008

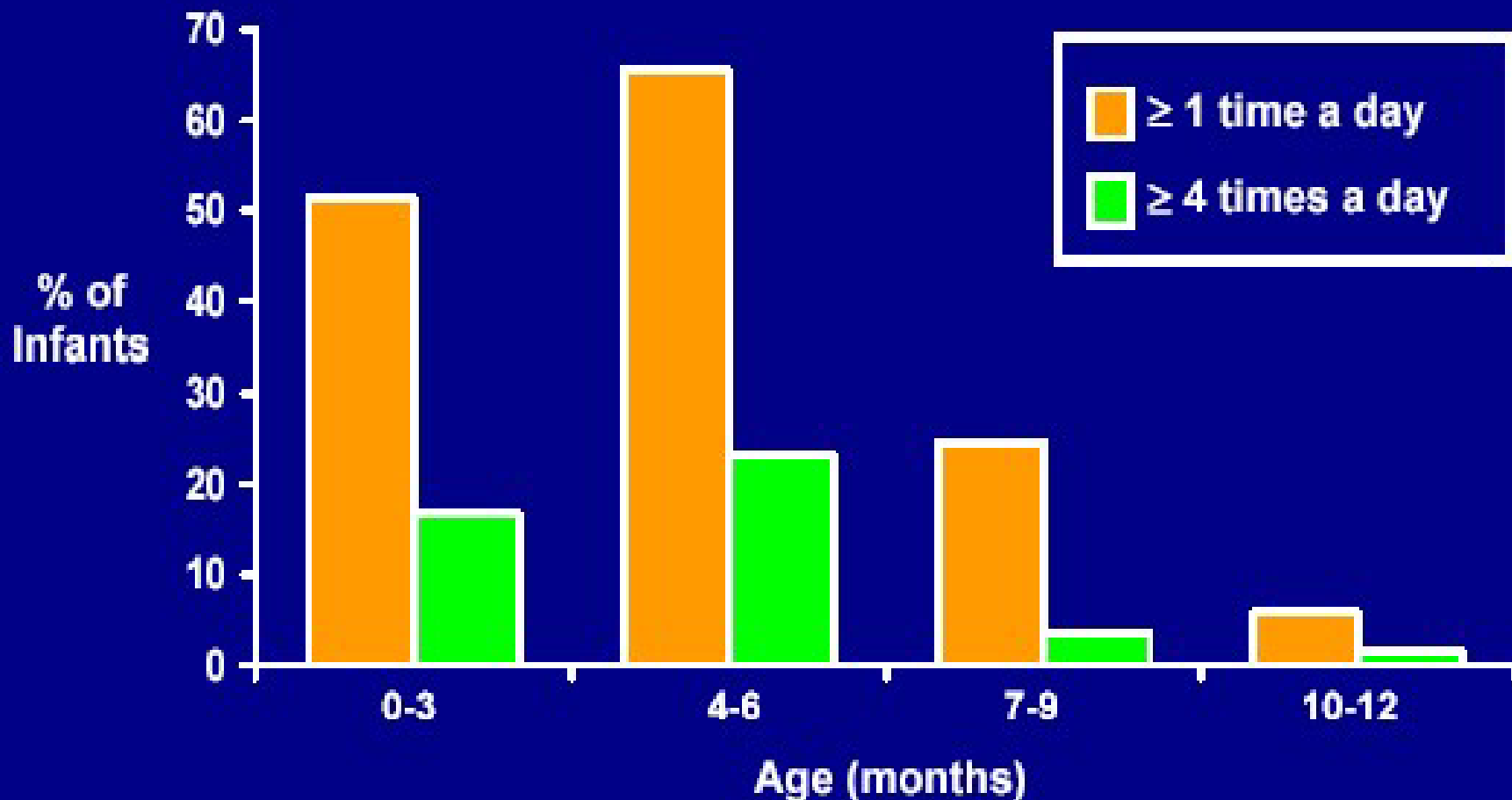
Definition

GER	Passage of gastric content into esophagus
Regurgitation	Effortless passage of refluxed gastric content into oral pharynx
Vomiting	Expulsion of refluxed gastric contents from mouth
GERD	Gastric contents reflux into the esophagus or oropharynx and produce symptoms

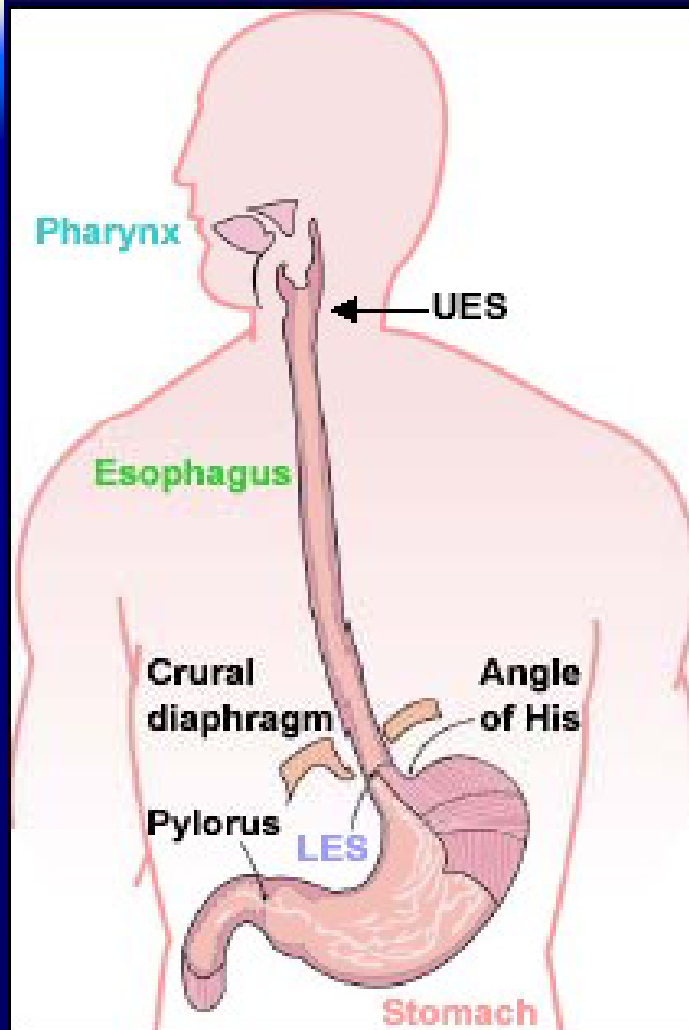
Why is GERD increasingly being diagnosed and treated?

- Increased recognition
- Increase in risk factors
- Increase in mimickers of GERD
- Prevalence of GERD truly increasing
- Overdiagnosis and treatment

Prevalence of Regurgitation in Infancy

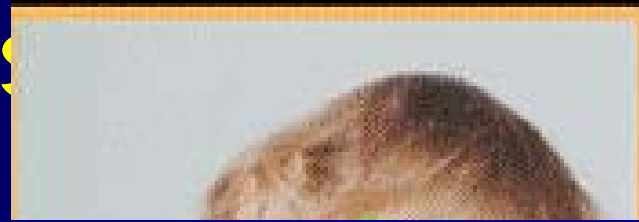


Pathogenic Factors in GERD



- **Mechanisms of GER:**
 - TLESR
 - Delayed gastric emptying
 - Impaired esophageal clearance
 - Impaired airway protection

Symptoms



- Recurrent vom., regurgitation
- Weight loss
- Irritability
- Dysphagia
- Sarcoidosis
- Hoarseness
- Apnea
- Wheezing



ALTE

(Acute Life Threatening Event)

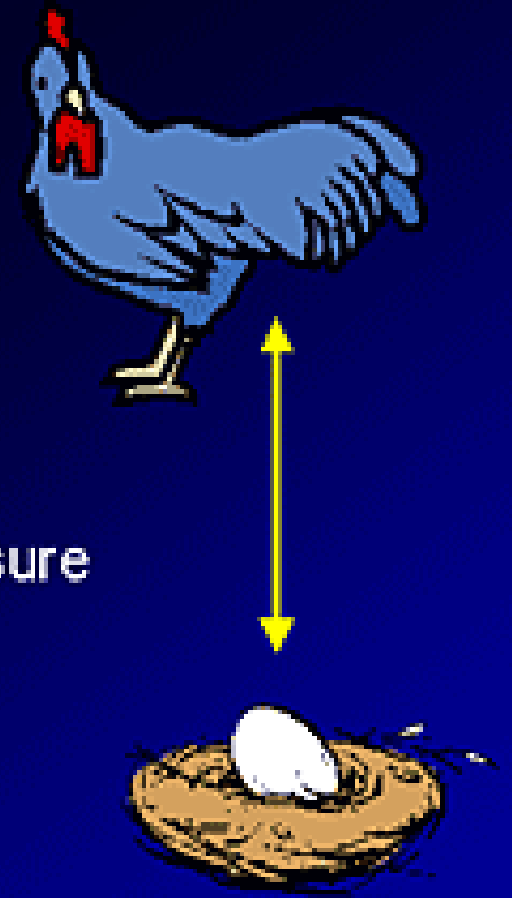
Defined as a frightening episode in infant that is characterized by apnea, change in color, change in muscle tone, choking or gagging and requiring intervention by caretaker

GER and ALTE

- Recurring regurgitation in 60-70% of infants with ALTE
- Abnormal esophageal pH studies in 40-80%
- Relationship between GER and obstructive or mixed apnea is most convincing when infant was: *awake, supine and fed within past hour*

Understanding the Relationship Between Asthma and GERD

- Does GERD cause asthma symptoms?
 - Indirect cause (reflex theory)
 - Direct cause (reflux theory)
- Does asthma cause GERD?
 - Asthma leads to decrease in pressure of lower esophageal sphincter
 - Coughing increases intra-abdominal pressure
 - Increased risk of GERD
 - Certain anti-asthmatic medications may increase risk of reflux (ie, theophylline, caffeine-containing compounds)



Findings in GERD

- Esophagitis
- Esophageal stricture
- Barrett's esophagus
- Laryngitis
- Recurrent pneumonia
- Anemia

Warning Signals Suggestive of a Non-GER Diagnosis

Recurrent vomiting

History and physical exam

Are there warning signals?

- Bilious or forceful vomiting
- Hematemesis or hematochezia
- Vomiting or diarrhea
- Abdominal tenderness or distention
- Onset of vomiting after 6 months of life
- Fever, lethargy, hepatosplenomegaly
- Macrocephaly, microcephaly, seizures

GER Guideline Committee

NASPGHAN

Testing for GERD

- Is there a single test for GERD?
- What question does each test answer
- How reproducible or reliable is the test
- Does it guide our management and when is it useful

Diagnostic Approaches

- Empirical medical treatment
- Upper GI radiography
- Esophageal pH monitoring
- Esophagogastroduodenoscopy
- Scintigraphy

Upper GI series



Advantages:

- Useful for detecting anatomical abnormalities

Limitations:

- Can not differentiate between physiologic and non physiologic GER episodes

Esophageal pH Monitoring



Advantages:

- Detects episodes of reflux
- Determines association acid GER-symptom
- Assesses adequacy of trt

Limitations:

- Can not detect non acidic reflux
- Can not detect GER complications associated with NI ranges

Upper Endoscopy (EGD)



Advantages:

- Visualization and biopsy
- Determines presence of esophagitis

Limitations:

- Need for sedation or anesthesia
- Not useful for extra esophageal GERD

Scintigraphy



Advantages:

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

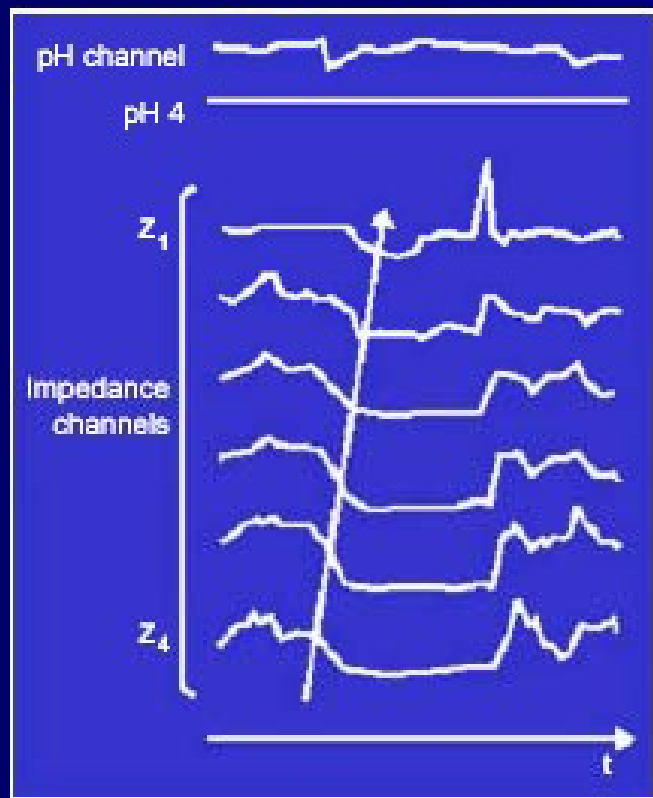
Limitations:

- Absence of age sp data
- Lack of standardized tech
- Observation early post prandial

New Diagnostic Tools

- Multiple Intraluminal Electrical Impedance
- 48 hours Wireless Ph Monitoring Capsule

Multiple Intraluminal Electrical Impedance



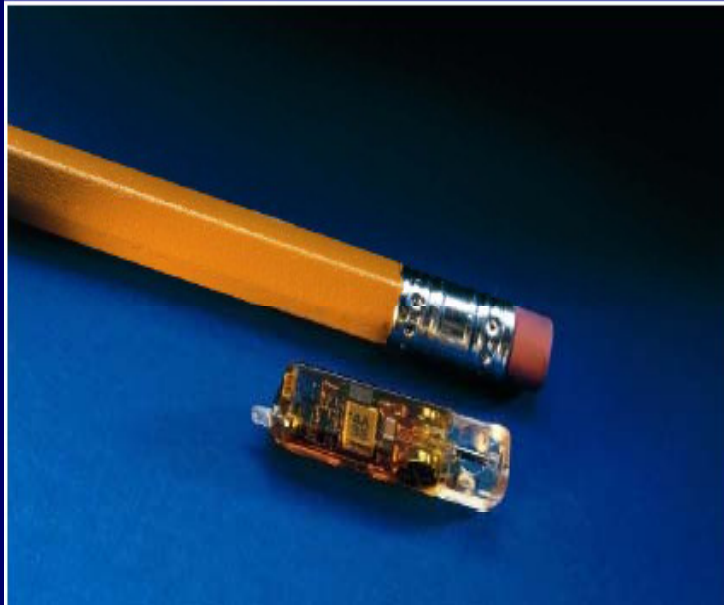
Advantages:

- Detects nonacid GER
- Useful for studying resp sympt and GER

Limitations:

- Normal values in ped not yet defined
- Analysis of tracings time-consuming

Wireless Capsule pH monitoring



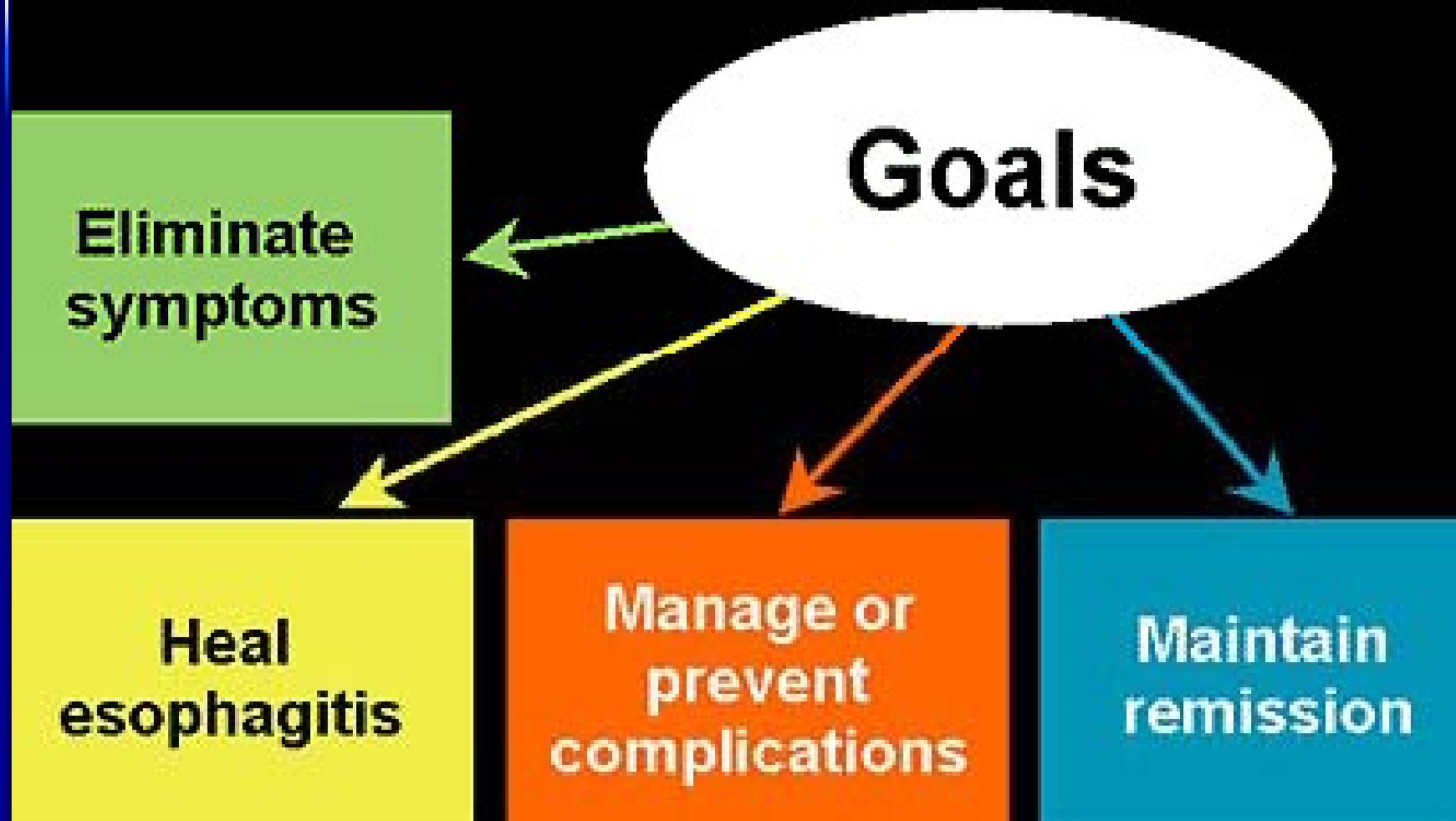
Advantages:

- 48 hrs recording
- More "patient friendly"

Limitations:

- Endoscopic placement
- Variability between day 1 and 2
- Cost

Goals of Treatment



Treatment Options

- Lifestyle Changes
- Pharmacotherapy
- Surgical Therapy

Conservative Therapy for GER in infants

- Normalize feeding volume and freq
- Thickened formulas
- Hypoallergenic formula trial for 1-2 w
- Prone positioning while the infant is awake, particularly in the postprandial period

Conservative Therapy for GER in Children

- Avoid large fatty meals
- Have dinner 1-1/2 to 2 hrs before bedtime
- Lose weight if obese
- Avoid caffeine, chocolate, spicy food and passive smoking
- Elevate head of bed

Pharmacotherapy

- Prokinetic Therapy
- Acid suppressant Therapy:
 - Histamine-2 Receptor Antagonists
 - Proton Pump Inhibitors

Prokinetic Agents

- Enhance esophageal peristalsis and accelerate gastric emptying
- Appear to increase LES pressure but do not reduce the frequency of episodes of acid reflux

Prokinetic Agents

- Cisapride: withdrawn
- Erythromycin: No RCT
- Domperidone: not available in US, no RCT
- Metoclopramide:
 - Esophageal pH improvement in 1 of 6 RCT
 - Clinical improvement in 1 of 4 RCT
 - High incidence of adverse events

Anti secretory Agents

- H-2 RAs:

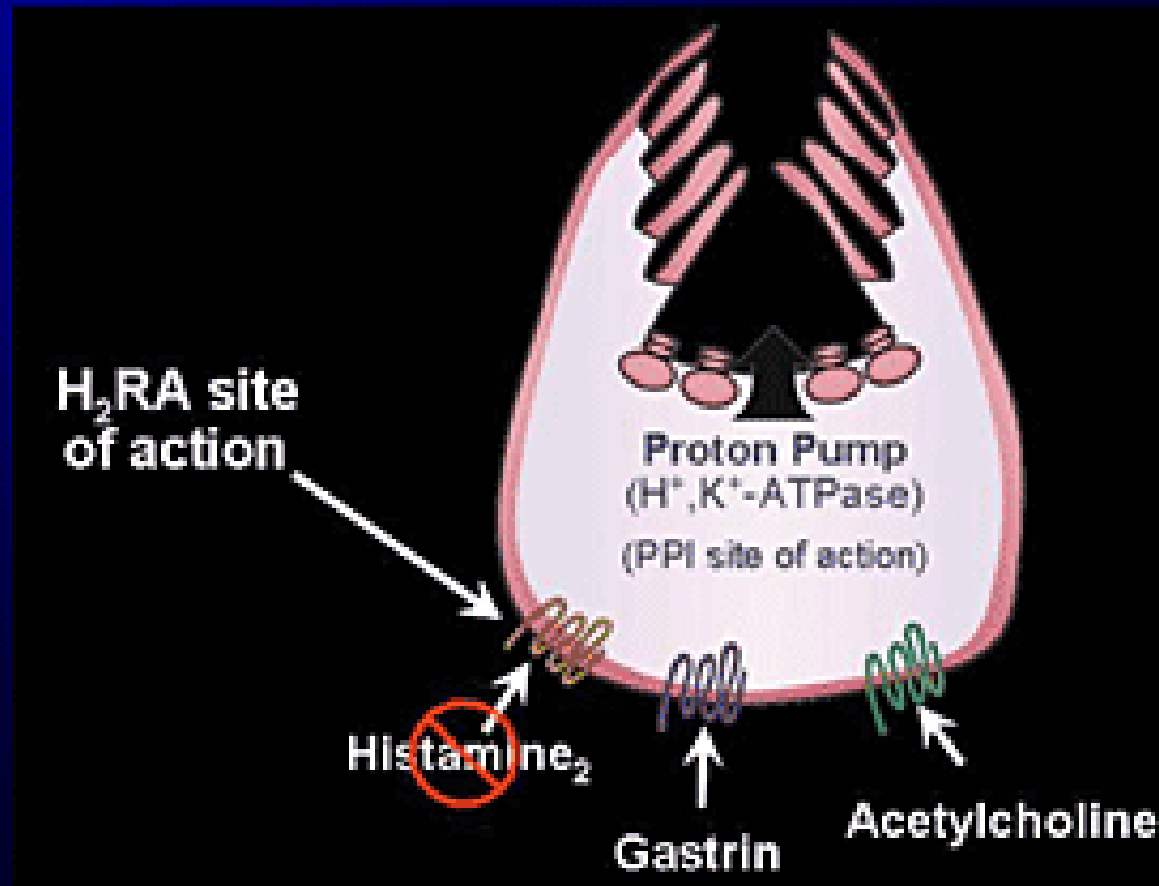
- Cimetidine, Famotidine, Nizatidine and Ranitidine

- PPIs:

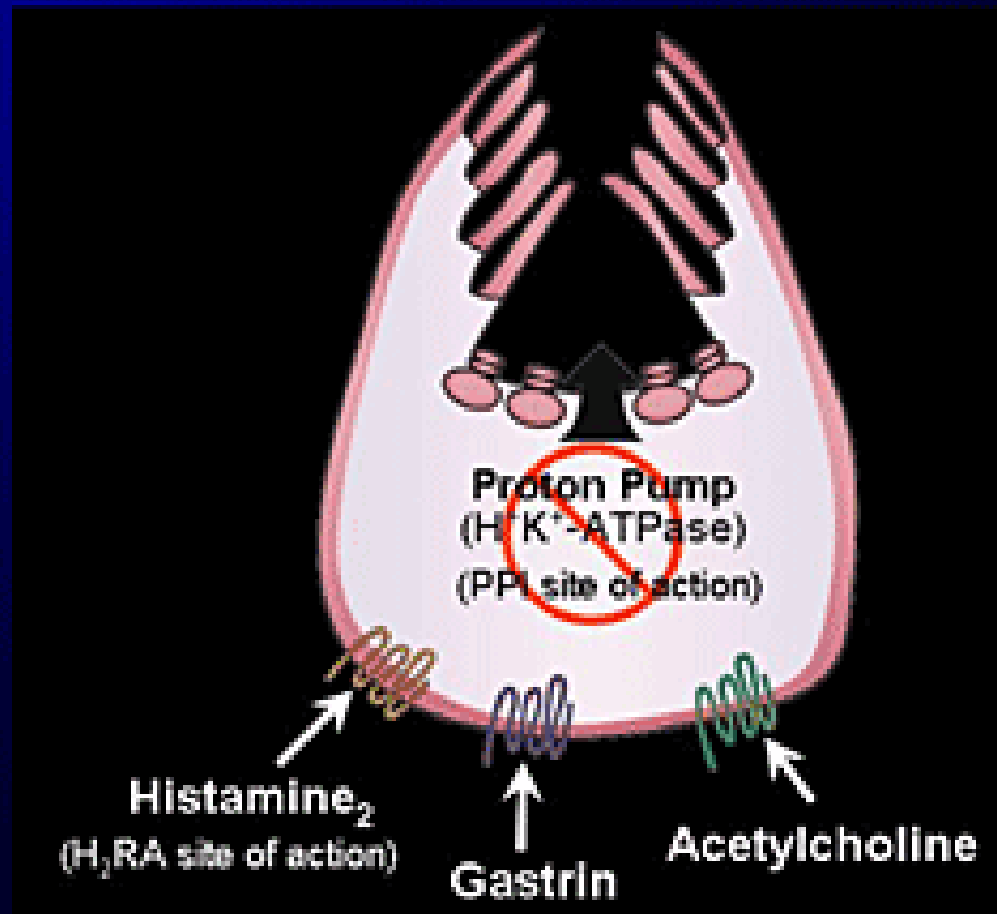
- Omeprazole and Lansoprazole

- Esomeprazole

H₂RA Mechanism of Action



PPI Mechanism of Action



- The first approved PPI for use in humans was Omeprazole in 1988
- Five members in this class of drugs are FDA approved for use in humans: *Omeprazole*, *Lansoprazole*, *Pantoprazole*, *Rabeprazole* and *Esomeprazole*
- Omeprazole and Lansoprazole were the first to be approved for use in children. Esomeprasol was approved in February 2008

Pharmacology

- Dosage range from 0.7 to 3.5 mg/kg/d
- Higher metabolic activity with decreased age
- Adm. Once or twice daily
- Bioavailability affected by time of adm since the parietal cell stimulation enhances effect

Optimal Timing of PPI dose

- Single PPI dose

Administer one half-hour before breakfast

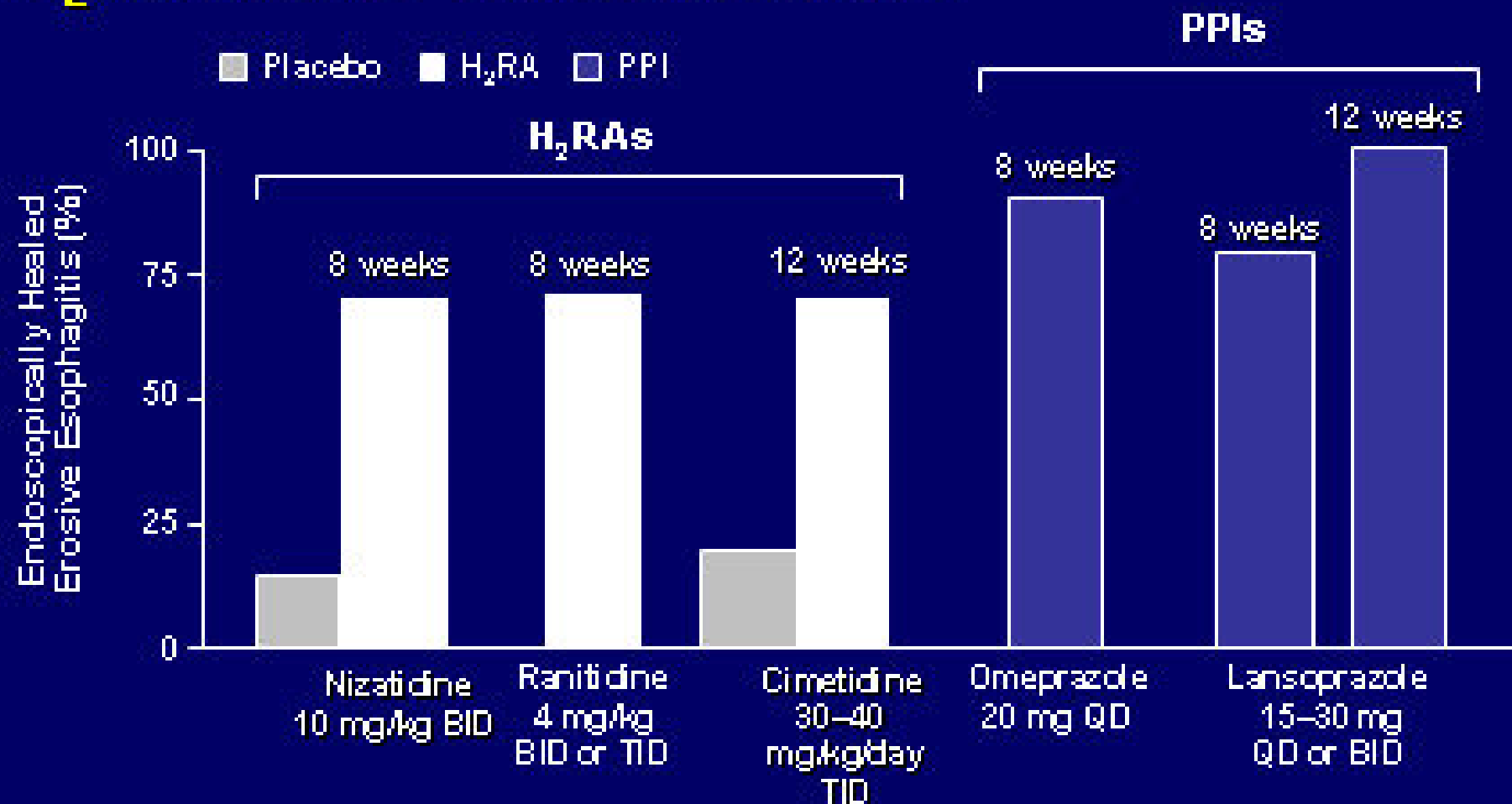
- If second PPI dose

Administer one half-hour before evening meal

Results of PPI Studies in Children

- Heal severe erosive esophagitis in all patients including those refractory to other medications
- Resolution and or improvement of the majority of GERD related symptoms
- Children require higher doses on per Kg basis than adults because of greater metabolic capacity

Erosive Esophagitis Healing Rates of H₂RAs and PPIs in Children



Cucchiara S, et al. *J Pediatr Gastroenterol Nutr.* 1989;8:150-156.
 Karjane M, Kane R. *Arch Pediatr Adolesc Med.* 1995;149:267-271.
 Simeone D, et al. *J Pediatr Gastroenterol Nutr.* 1997;25:51-55.
 Tolia V, et al. *J Pediatr Gastroenterol Nutr.* 2002;35:S308-S313.

Safety Profiles of H2RAs

H2RA	Adverse Events/Precautions
Cimetidine	Rash, bradycardia, dizziness, nausea, vomiting, hypotension, gynecomastia (up to 4%), reduces hepatic metabolism of theophylline and other medications, neutropenia, thrombocytopenia, agranulocytosis
Famotidine	Headache (4.7%), dizziness (1.3%), constipation (1.2%), diarrhea (1.7%), nausea
Nizatidine	Headache (16.6%), dizziness, constipation, diarrhea (7.2%), nausea (5.4%), anemia, urticaria
Ranitidine	Headache, dizziness, fatigue, irritability, rash, constipation, diarrhea, thrombocytopenia, elevated transaminases

Safety Profiles of PPIs

PPI	Adverse Events
Esomeprazole	Headache (~5%), diarrhea, nausea, abdominal pain, respiratory infection, flatulence, gastritis
Lansoprazole	Headache (3%), constipation (5%), diarrhea, abdominal pain, nausea, elevated transaminase, proteinuria, angina, hypotension
Omeprazole	Headache (2.4%), diarrhea (1.9%), abdominal pain, nausea, rash (1.1%), constipation, vitamin B12 deficiency
Pantoprazole	Headache (6-9%), diarrhea (4-6%), abdominal pain (1-4%), nausea
Rabeprazole	Headache (2.4%), diarrhea, abdominal pain, nausea

Rudolph et al, *J Pediatr Gastroenterol Nutr* 2001;32:S1 and Scott et al,

Approaches to Acid-Reducing Therapy

Step Down



- Begin treatment with PPI
- Maintain improvement with PPI
- Switch to H2RA

Step Up



- Begin treatment with H2RA
- Inadequate response → PPI
- Inadequate response → ↑ PPI dose

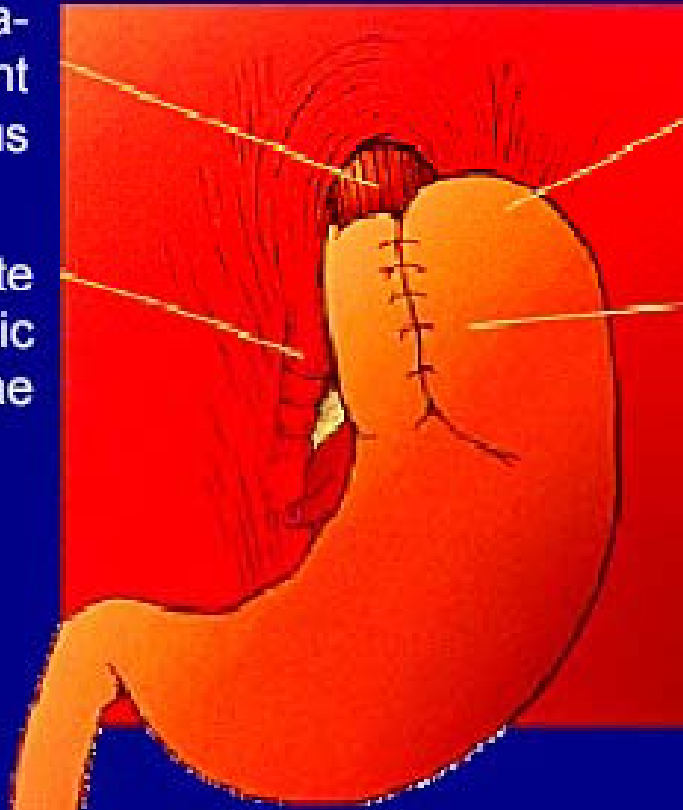
What if all this doesn't work?

- Biopsy proven esophagitis continues in spite of intensive therapy for 6-24 months
- There is symptom relief on meds but relief is not maintained after weaning
- Intolerance to the medications

Antireflux Surgery

Restore intra-abdominal segment of esophagus

Approximate diaphragmatic crurae



Reduce hiatal hernia when present

Wrap fundus around LES to reinforce antireflux barrier

Outcomes of Anti-Reflux Surgery in Children

Success rate (complete relief of symptoms)	57 – 92%
Mortality related to operation	0 – 5%
Overall complication rate	2 – 45%
Dumping syndrome	NA
Gas bloat syndrome	2 – 8%
Small-bowel obstruction	1 – 11%
Wrap failure	1 – 13%
Reoperation rate	3 – 19%

Conclusion

- GER and GERD are frequent conditions in infants, children and adolescent
- PPIs are the drug of choice in severe reflux
- *Good history and clinical judgment are essential for optimal evaluation and management*