

Acid Mediated Disorders

Current Topics
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Topics for Discussion

IN

- Diagnosis
- Medical management
 - Prokinetics
- Surgical management
- Esophagitis
 - Eosinophilic
 - Barrett's
- Asthma
- *Helicobacter pylori*

OUT

- Infant physiologic GER
- Preterm neonatal GER
- Apnea
- ALTE
- Otitis media and sinusitis
- Cisapride and tegaserod
- Endoscopic therapy

Causative Factors

TABLE 1. *Pathophysiologic determinants of GERD*

Refluxate toxicity

- Gastric acid secretion
- Duodenogastric reflux

Intrinsic gastric volume and pressure

- Gastric compliance
- Gastric emptying (20)
- Gastric acid volume secretion

Extrinsic pressure on gastric contents

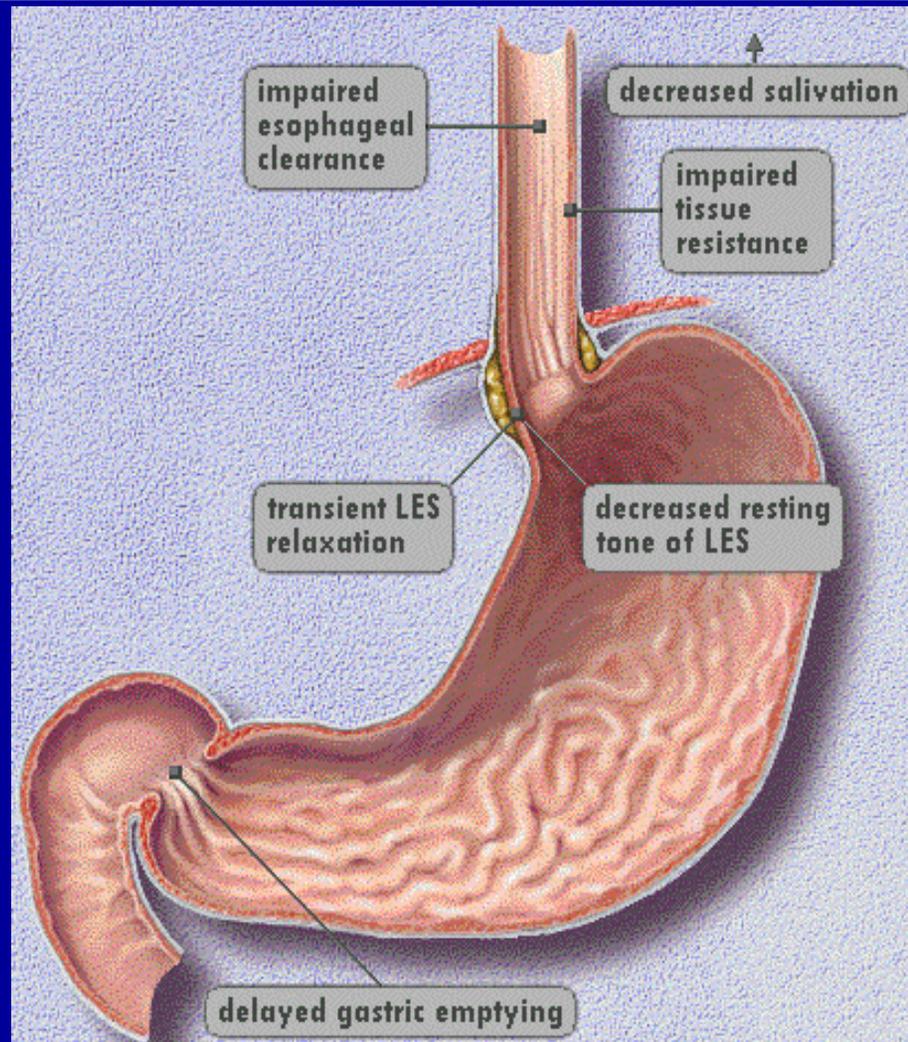
- Weight (obesity (22))
- Somatic motor tone (spasticity (34))
- Somatic and crural episodic contractions (cough, wheeze, ... (35,36))

Gastroesophageal barrier

- Lower esophageal sphincter tone
- Gastric fundic sensory thresholds
(for Transient Lower Esophageal Sphincter Relaxations)
- Crural diaphragm location (relative to sphincter location) and function

Esophageal defenses

- Salivary secretion
- Peristaltic motor function
- Esophageal cytoprotection



Genetics of GERD

- Familial clustering
 - GERD
 - Hiatal hernia
 - Barrett's esophagus and adenocarcinoma
- "Severe pediatric GERD" locus: *chromosome 13q14*
 - Conflicting studies linking locus to phenotype
 - Specific gene defect suspected but excluded
- Multifactorial pathogenesis
 - Implies genetic heterogeneity in pediatric GERD

GER Disease

SYMPTOMS

- Recurrent vomiting
- Poor weight gain
- Irritability
- Heartburn/epigastric pain
- Hematemesis
- Dysphagia
- Feeding refusal
- Globus sensation
- Chronic cough/wheeze
- Hoarseness

SIGNS/FINDINGS

- Esophagitis
- Stricture
- Laryngitis
- Recurrent pneumonia
- Sandifer posturing
- Anemia
- Dental erosions

Diagnostic Approach

- H & P
- Empiric acid suppression therapy
 - Time-limited trial is cost-effective
 - Long term therapy requires accurate diagnosis
- UGI: anatomic abnormalities
- EGD/Bx
 - Assess for esophagitis presence and severity
 - Exclude infx, Crohn's, EE
- pH monitoring
 - Temporal assn. between *acid* reflux and frequent sx
 - Adequacy of acid suppression therapy
 - Diurnal variation
 - Provocative feeds or regular diet?
 - What about *non-acid* reflux?

Evidence from ≥ 1 well designed case-control or cohort study



Non-acid reflux

- 1/3 of all GER events
- Predominantly in 1st hr after meal
- Impedance monitoring
 - Detects resistance to current flow
 - EM catheter with electrodes
 - Combination with pH probe
 - picks up both acid and non-acid GER
 - May be useful in cases of GERD not responsive to PPI or in extraesophageal reflux disease
 - Proposed therapies: Baclofen, EndoCinch (studies in adults)

Best Evidence

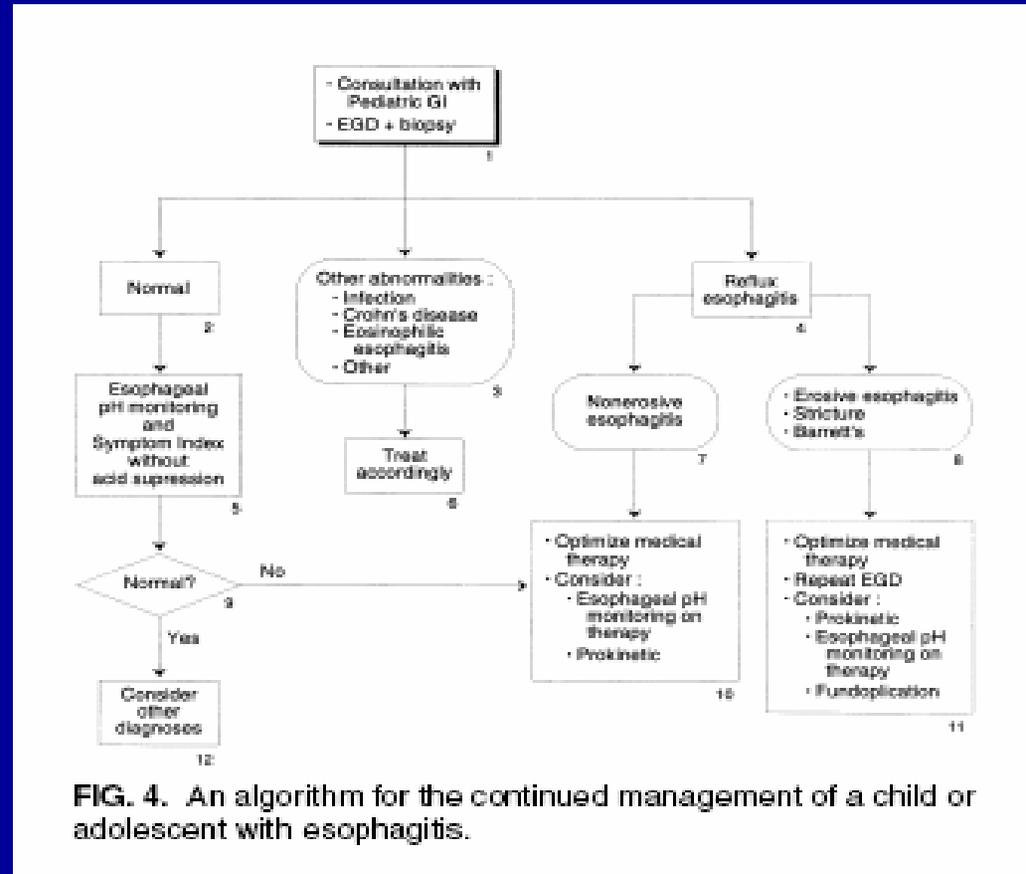
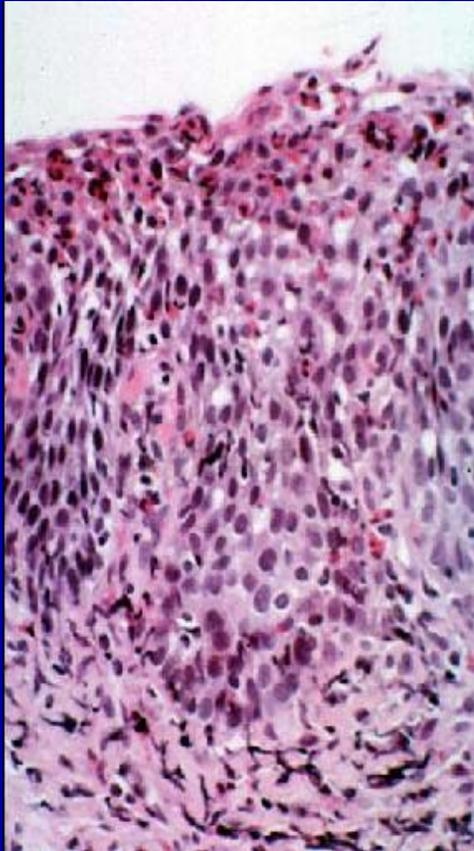
DIAGNOSIS

- EGD/bx useful to exclude other disorders
- Perform esoph. bx even if mucosa appears grossly nl
- EGD useful in child over 2 y/o with recurrent vomiting

TREATMENT

- Elevation of HOB and left side positioning helpful
 - Children over 1 year old
- H2-blockers relieve sx and heal mucosa, but PPIs are superior to them for both
- Initial tx of esophagitis = lifestyle changes + PPI
- Histologic esophagitis: follow degree of sx relief
- Erosive esophagitis: follow endoscopically

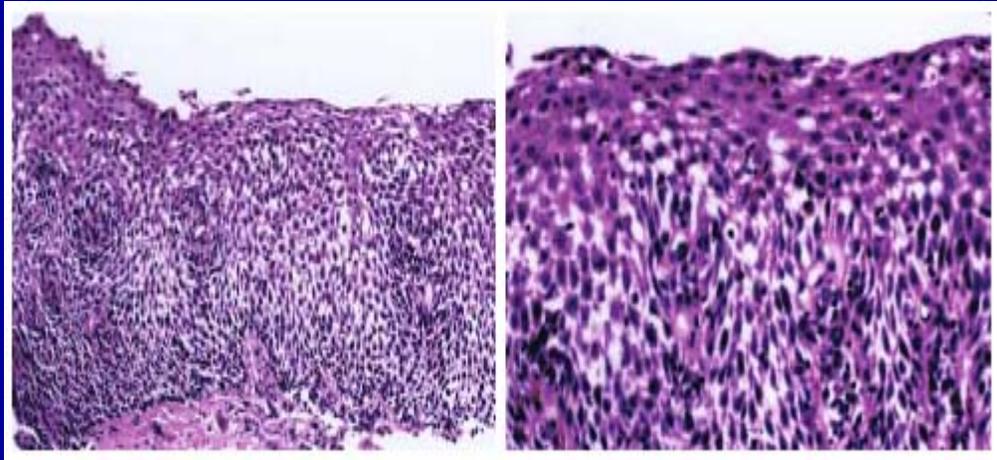
Esophagitis



Eosinophilic Esophagitis

Dx requires EGD/bx

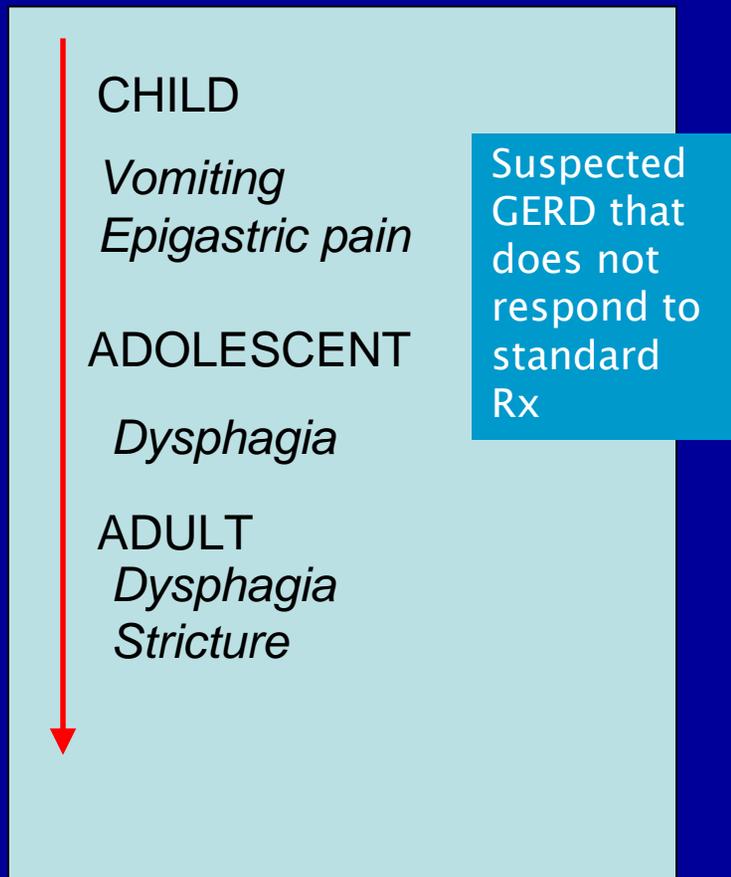
- Typical allergy tests not effective for dx
- Infiltrates can be in mid or distal esophagus
- Inflammation extends into submucosa
- Often normal pH probe study



≥ 20 eos/HPF confirms dx

Linear furrowing, white specks, fragile mucosa, trachealized rings (*but mucosa can be grossly normal*)

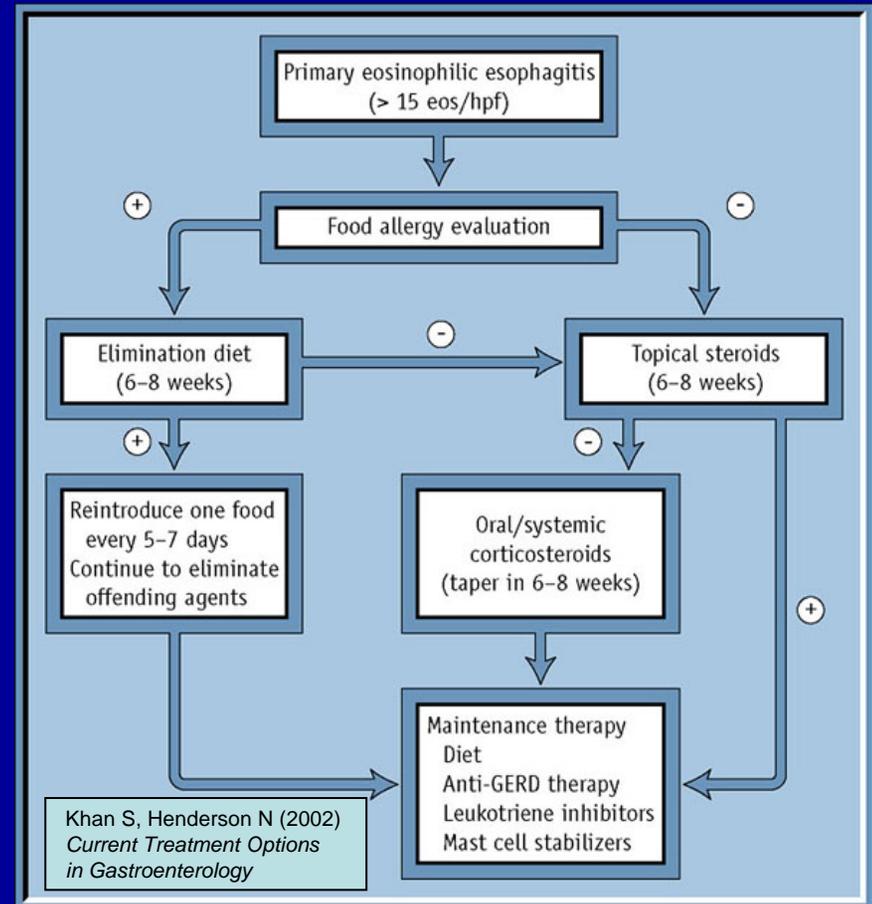
Eosinophilic Esophagitis



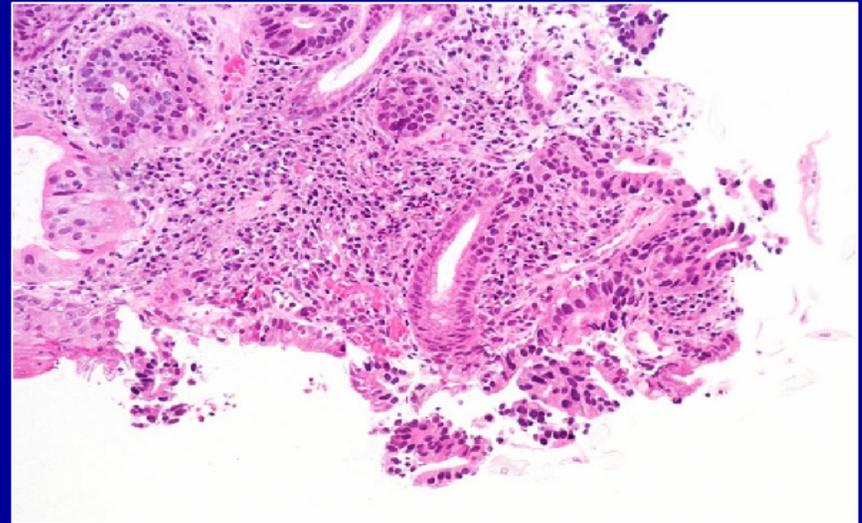
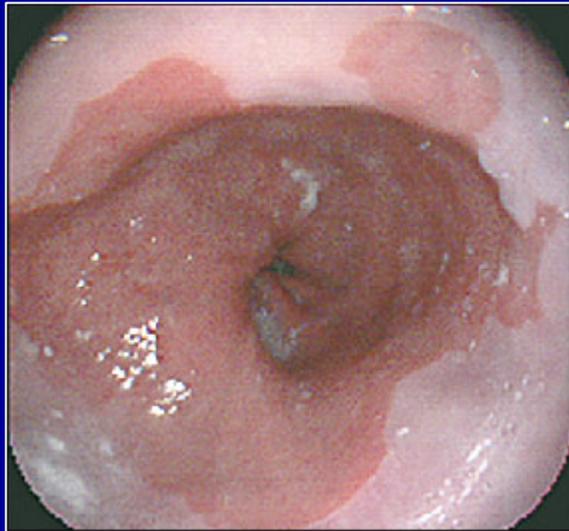
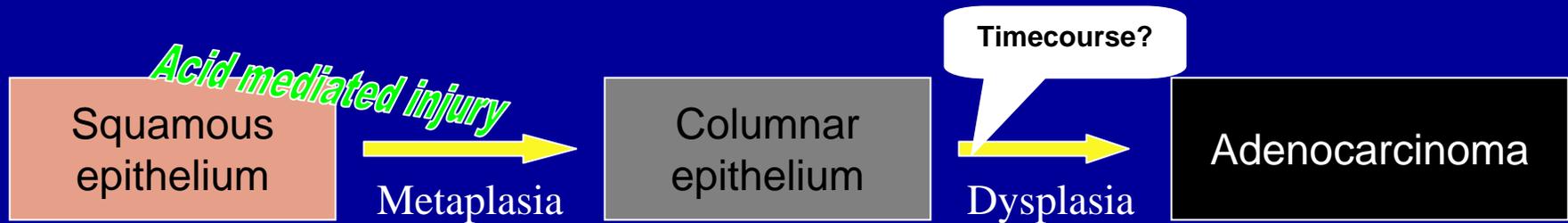
- Increasing incidence
 - Function of dx technology and increased index of suspicion
- Etiology unclear
 - Allergic disorder
 - Non-IgE mediated
 - Food allergy involved
 - Aeroallergens may play role
 - Immune dysregulation
 - Severe GERD?

Treatment of EE

- Most effective
 - Elimination diet
 - Elemental formula
 - LT inhibitors (montelukast)
- Less effective
 - Acid suppression
 - May improve sx but no effect on histology
 - Corticosteroids
 - sx and histologic relapses
- Not effective
 - Cromolyn sodium
 - Surgical GERD therapy



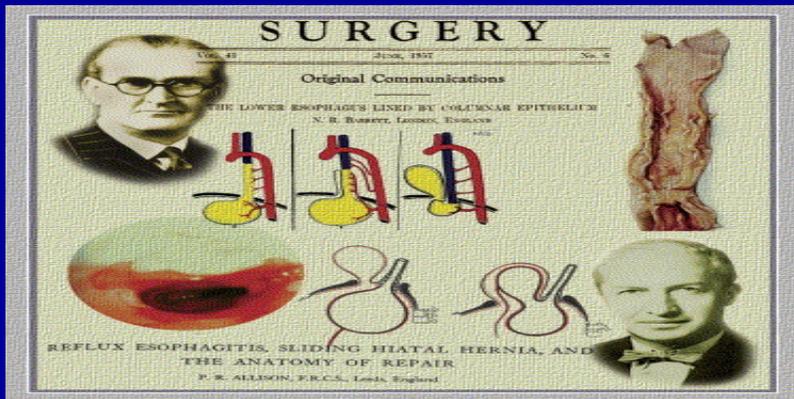
Barrett's Esophagus



Major risk factors = DURATION + SEVERITY of GERD

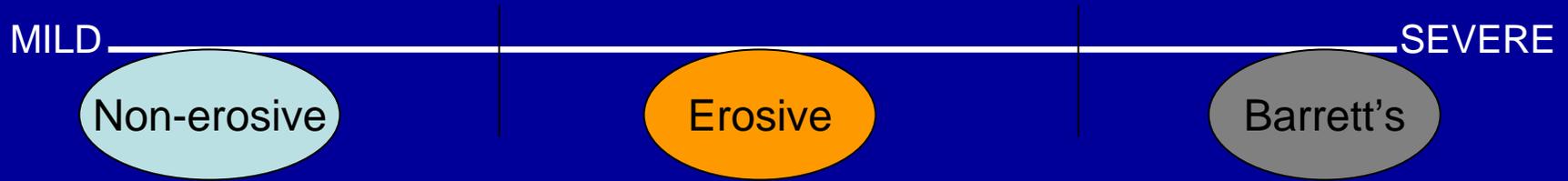
Barrett's

- Prevalence
 - Adults w/GERD: 15%
 - Children: 0.02-0.38%
 - 400 neurol. nl pts age 18m-25 y with GERD
 - Erosive esophagitis: 34%
 - Barrett's: 0
- Management
 - Surveillance EGD q 1-5 y
 - Aggressive acid blockade
 - Fundoplication
 - Endoscopic mucosal resection + photodynamic therapy
 - COX-2 inhibitors?



Are there any published pediatric guidelines?

Natural History



Kerzner B, PAS Symposium 2005

Paradigm 2005

GERD is a lifelong disorder,
but its severity is not necessarily progressive

Proportion of adults who had childhood GERD symptoms

	Adult refluxers (n = 225)	Adult nonrefluxers (n = 154)	P value
Spit up as infant	23 (8.8%)	6 (3.8%)	0.02
Abdominal pain (epigastric pain)	48 (21.3%)	17 (11.0%)	0.009
Heartburn/chest pain	67 (29.7%)	14 (9.0%)	0.000001
Dysphagia	52 (23.1%)	20 (12.9%)	0.01
Underweight	47 (20.1%)	18 (11.6%)	0.02
Asthma	50 (22.2%)	9 (5.8%)	0.00002

$P < 0.05$ was considered statistically significant.
Adapted from Waring et al., 2002 (20).

Medical Therapy

PPI

- Similar healing of erosive and nonerosive esophagitis in children and adults
- Key is using enough drug and using it right¹
 - Children 1-10 y/o need higher per kg dosing
 - Increased metabolism of PPI thru cyt 2A19, 3A4
 - Omeprazole: 0.7-3.3 mg/kg/d (15-80 mg/d)
 - Lansoprazole: 1-1.5 mg/kg/d
 - Administer q AM just before 1st meal of day
 - Dose BID (or PM H2-blocker) in severe cases
 - Switch between PPIs if necessary
 - Safety
 - Omeprazole has been studied up to 2 years duration in children (11 y in adults)
 - Lansoprazole only up to 6 months duration
 - Benign fundic gland polyps unrelated to duration of therapy or dosing²

1. Hassall E (2005) *J. Pediatr.* and PAS Symposium 2005.

2. Brown P. (2000) *Curr Opin Pediatr.*

Medical Therapy

Prokinetics

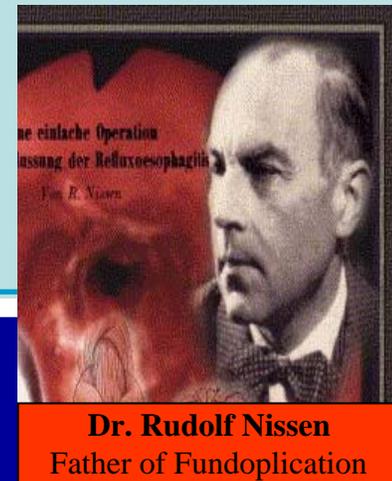
Metoclopramide

- Not efficacious
 - 12 studies in children since 1985
 - 7/9 controlled studies: NO significant improvement in GER sx
 - Increasing dose above 0.1 mg/kg/d: no improved response
- Adverse effects
 - Extrapyramidal sx can occur even at lower doses
 - incidence of EPS higher in children
 - Tardive dyskinesia can be prolonged

Erythromycin

- Improves feeding tolerance in infants
 - 8/9 placebo-controlled studies
 - Dosing: 1.5-12.5 mg/kg q 6 h
 - Limited evidence in older children with GERD or gastroparesis
 - *Need better outcome measures*
- Risks
 - Pyloric stenosis
 - In preterms or neonates
 - QT prolongation
 - IV form in infants
 - Bacterial resistance

Antireflux Surgery



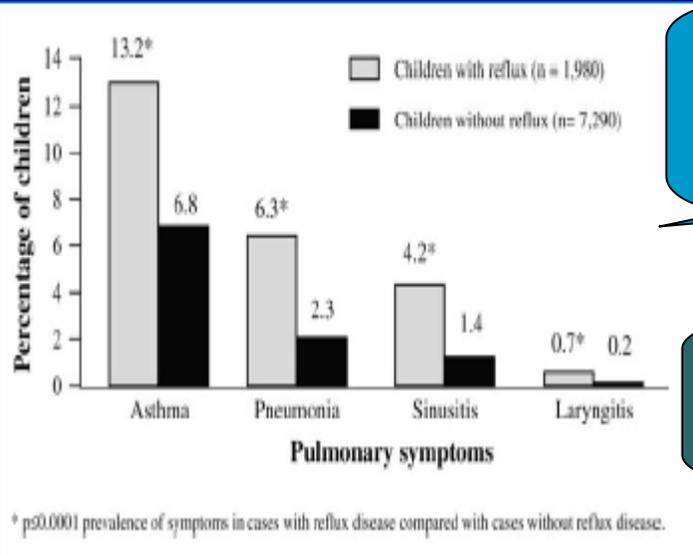
- Historical mainstay of Rx of severe GERD
 - Remains widely used
 - Increasing rate of use in 12-24 month age group
 - 14% of pediatric pts w/suspected GERD had fundoplication w/o diagnostic evaluation
- Not curative or even long-term solution
 - High rates of failure
 - Recurrence of GERD sx
 - Morbidity
 - Gas bloat syndrome
 - Esophageal dysmotility and pseudo-obstruction
 - Occasional mortality

Antireflux Surgery

- High-risk GERD pts most likely to have problems
 - Neurologic impairment ("static encephalopathy")
 - Double complication rate, 3X morbidity, 4X re-operation rate
 - Within mean 3.5 y, 71% recurrence of sx, 25% operative failure
 - Esophageal surgery (repaired esoph. atresia)
 - Chronic lung dz (BPD, CF, asthma)
- Beware the flawed study (Fonkalsrud EW et al. *Pediatrics* 1998)
 - Reported "good" to "excellent" results in 85% of NI and 94% of NN children
 - No hypothesis, objective endpoints or outcome measures
 - Subjective outcomes not defined and "poor" not offered
- Best candidates for fundoplication
 - Neurologically normal
 - Well-established GERD by endoscopy
 - Prior response to PPI therapy

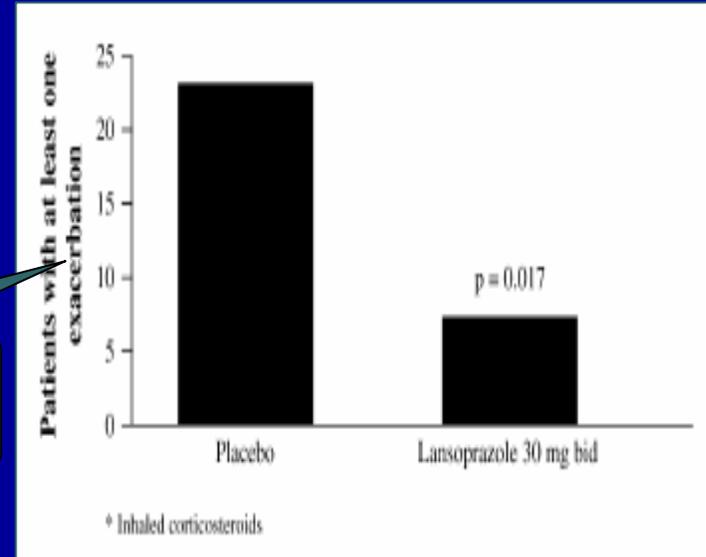


GER and Asthma



GER is associated with asthma and other airway problems

Acid suppression helps control asthma flares



- Asthma promotes GER by altering intrathoracic and intra-abdominal pressures
- GER promotes asthma
 - Reflux theory: refluxate directly stimulates airway bronchospasm and inflammation
 - Reflex theory: refluxate stimulates vagal reflex and bronchospasm thru shared innervation

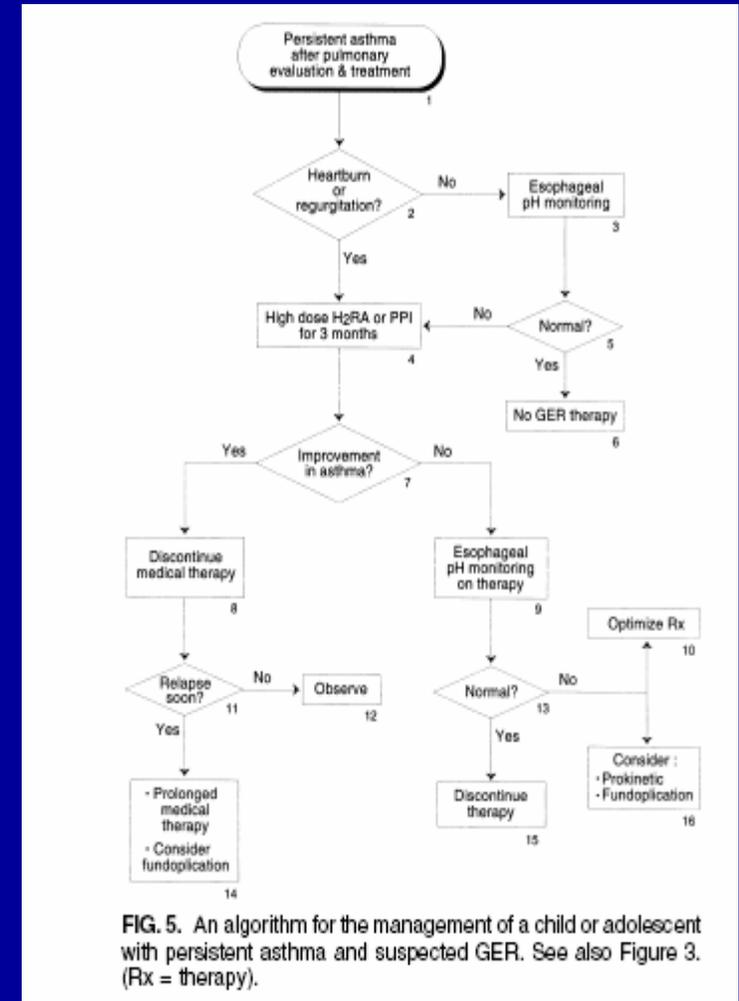
Asthma and GER

Who to work up for GER

- Frequent exacerbations
 - Despite good compliance
- Nocturnal sx > once/wk
- GER sx precede resp. sx
- Lack of response to corticosteroids
 - > 2 bursts/yr prednisone
- Asthma beginning after 3 y/o
- Recurrent pneumonia

Recommended approach

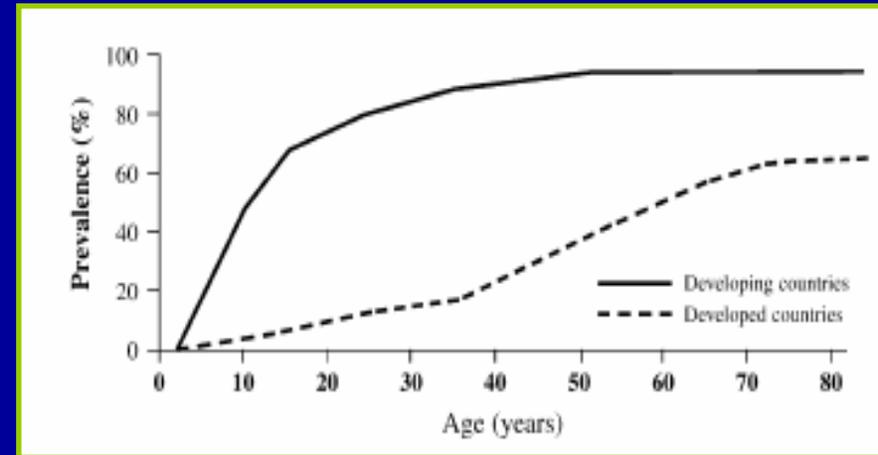
3-month therapeutic trial of PPI in higher than std doses (even BID)



The Dreaded *Helicobacter*



- Infects $\geq 50\%$ humans
 - Most are asymptomatic
 - Almost always acquired in childhood
 - Risk factors
 - Infected family member
 - Crowded living conditions
 - Lower socioeconomic status
 - Daycare
 - Immigrant/intl. adoptee
 - Transmission
 - Fecal-oral
 - Oral-oral
 - Within families



Why care about H. pylori infection?

- Duodenal ulcer disease
- Atrophic *corpus* gastritis: precursor to gastric adenocarcinoma or MALT lymphoma
- Iron deficiency anemia
- Growth retardation (possible association)

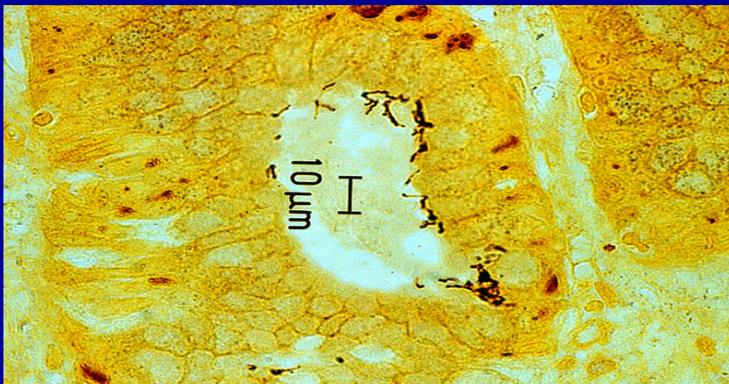
Diagnosis



TABLE 2. Tests for *Helicobacter pylori* and *Helicobacter*-related disorders

Invasive tests requiring endoscopy	
Biopsies and histology	← Gold Std
Rapid urease testing	
Bacterial culture	
Polymerase chain reaction of bacterial DNA	
Non-invasive tests	
Serum and whole blood antibody	
Saliva antibody	
Urine antibody	
Stool antigen	
Urea breath testing	

- Indications for testing
 - DU or GU
 - Endoscopically dx'd
 - Radiographically definitive
 - MALT lymphoma
 - Follow-up of documented *H. pylori* disease
- Not recommended
 - Asymptomatic children
 - Recurrent abdominal pain without documented PUD
 - Family hx of gastric cancer or recurrent PUD



Treatment



- Indications
 - DU/GU with Hp on bx
 - Prior hx DU/GU with active Hp
 - Atrophic gastritis w/intestinal metaplasia + Hp
 - Judgement call:
 - Hp+ gastritis w/o PUD
- Not recommended
 - Asymptomatic child + family member w/Hp, PUD, or gastric cancer
 - Hp+ child with nonulcer dyspepsia or functional abdominal pain

**Table. North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition
Position Statement: Recommended Regimens
for *Helicobacter pylori* Treatment**

First-line regimens, each agent administered twice-daily for 10 to 14 days

- Proton pump inhibitor (1-2 mg/kg/day) plus amoxicillin (50 mg/kg/day) plus clarithromycin (15 mg/kg/day)
 - Proton pump inhibitor (1-2 mg/kg/day) plus amoxicillin (50 mg/kg/day) plus metronidazole (20 mg/kg/day)
 - Proton pump inhibitor (1-2 mg/kg/day) plus metronidazole (20 mg/kg/day) plus clarithromycin (15 mg/kg/day)
-

Functional GI Problems in the Adolescent