

Pediatric GI “Poop-pourri”: Gluten, Constipation and Reflux

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Connecticut Academy of Family Physicians Symposium

Aqua Turf Club

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Disclosures

- Speaker: Nutricia
- Consultant: Advanced Medical

Objectives

- Define the Gluten/Wheat related clinical disorders
- Briefly summarize causes of constipation in children, evaluation and treatment options
- Discuss reflux related terms and discuss management of reflux in infants and children

Celiac Disease and Gluten Related Disorders

**TRICK – NO WHEAT!
REAL OR FAD?**



Goals

- Review the definition, epidemiology and clinical presentation of celiac disease and other gluten/wheat related disorders
- Discuss the pathophysiology related to each disorder
- Review the diagnosis and treatment of celiac disease.

Wheat/Gluten - Related Disorders

Wheat Allergy
(<0.1%)

No gene associated
IgE mediated
Infants & Toddlers

Serum
Specific IgE

Celiac Disease
(1%)

HLA DQ2/DQ8
Autoimmune
Any Age

Celiac Disease
Autoantibodies

Duodenal
biopsy (Gold
Standard)

Non-Celiac Gluten
Sensitivity
(? %)

No gene associated
Immune-mediated?
Mostly Adults

No Diagnostic
marker/test

Wheat: The Satanic Substance

Gluten

- Exists in the endosperm of grains (wheat, rye, barley)
- Consists of gliadin and glutenin
- High levels of proline and glutamine make the protein resistant to digestion
- Gliadin, the main antigen of gluten, is cytotoxic.



Wheat Allergy

- T cell activation, cross linking of IgE by repeat sequences in gluten
- 27 different potential wheat allergens
 - Prolamine (Gliadins)
 - Glutelin (Glutenins)
 - Albumin and Globulin
 - Wheat pollen and grass allergies
 - Derivative allergies





Celiac Disease Defined

- An immune-mediated systemic disorder elicited by gluten and related prolamines in genetically susceptible individuals and characterized by the presence of a variable combination of gluten dependent clinical manifestations, CD-specific antibodies, HLA-DQ2 or DQ8 haplotypes, and enteropathy.

ESPGHAN Guidelines for the Diagnosis of Coeliac Disease in Children and Adolescents: An evidence based approach. Husby, S.; Koletzko, S.; Korponay-Szabó, I.R.; Mearin, M.L.; Phillips, A.; Shamir, R.; Troncone, R.; Giersiepen, K.; Branski, D.; Catassi, C.; Leigeman, M.; Mäki, M.; Ribes-Koninckx, C.; Ventura, A.; Zimmer, K.P.; The ESPGHAN Working Group on Coeliac Disease Diagnosis Review Article: PDF Only, JPGN, awaiting publication.

Celiac Disease Defined

- Silent CD – positive celiac specific antibodies, HLA, and small bowel biopsy without symptoms.
- Latent CD – compatible HLA, no enteropathy in a patient who has had gluten-dependent enteropathy at some other time of their life.
- Potential CD – positive celiac specific antibodies, compatible HLA but normal biopsies.

Prevalence

- Large multicenter study from 32 states
- 13145 patients enrolled
- Ages from 0 to over 60 years
- 1:133 (0.75%) general, not at risk patients
 - 1:105 in adults
 - 1:320 in children
- 1:22 (4.54%) in first degree relatives (10%) in some studies
- 1:39 in second degree relatives
- Prevalence as high in relatives with symptoms as relatives without symptoms.



Fasano A, Berti I, Gerarduzzi T, et. Al. Prevalence of Celiac Disease in At-Risk Groups in the United States. Arch Intern Med. 2003; 163: 286-292.

Prevalence

- In Finland, prevalence has nearly doubled to 2% of the population (doubling in last 20 years)
- Celiac disease is now described in India and the Middle East.



•Armstrong M, Robins G, Howdle P;
Current Opinion in Gastro 2009,
25:110-109



Catassi C, Fasano A. Current
Opinion in Gastroenterology
2008, 24: 687-691.

Increased Prevalence of Celiac Disease

- Not due to improved detection only
- Spread of western style diets
- Exclusion of breast feeding
- Timing of the introduction of wheat
- Gluten is increasingly used as an additive in processed foods and other products
- Over 100 years of cross and select breeding for higher yields, adaptation to climate change, disease resistance and bread making.

Presentation

- 1:3 to 1:7 adults with celiac disease are asymptomatic.



Intestinal manifestations

- Diarrhea
- Abdominal pain
- Weight loss
- Abdominal distention
- Gluteal wasting
- Failure to thrive
- Anorexia
- Vomiting
- Constipation



Extraintestinal Manifestations

- Anemia (28-50%)
- Folic acid deficiency (12%)
- B12 deficiency (5%)
- Short stature
- Arthritis (26%)
- Increased serum liver enzymes (40%)
- Skin rashes
- Aphthous Stomatitis
- Enamel defects - pitting, grooving (10-40%)
- Neurologic signs (peripheral neuropathy, headache, white matter lesions)
- Osteoporosis
- Fractures (2-2.5 fold increase risk)



Associated conditions

- Other autoimmune diseases –
 - Type 1 diabetes mellitus (3-12%),
 - Thyroid disease
 - Ulcerative colitis/Crohn's
 - Addison's disease
 - Autoimmune thrombocytopenia
 - Sarcoidosis,
 - Autoimmune liver disease (12-13%)
- Dermatitis herpetiformis
- Selective IgA deficiency (2-8%)
- Infertility, miscarriages, delayed puberty



Theories –

1. Untreated celiac leads to onset of other autoimmune diseases
2. Association is secondary to linkage of genes predisposing for both.

Fasano A. Current Opinion in Gastroenterology 2006, 22:674-679.

Associated conditions

- Down syndrome (5-12%)



- Turner (2-5%)

- William Syndrome



Pathophysiology

Increased Intestinal Permeability

Toxic gluten needs to gain access to the immune system of the lamina propria

Transcellular mechanism

Transcytosis of partially degraded toxic
33 – mer of gluten

Modulated by increase gamma-interferon

Paracellular mechanism

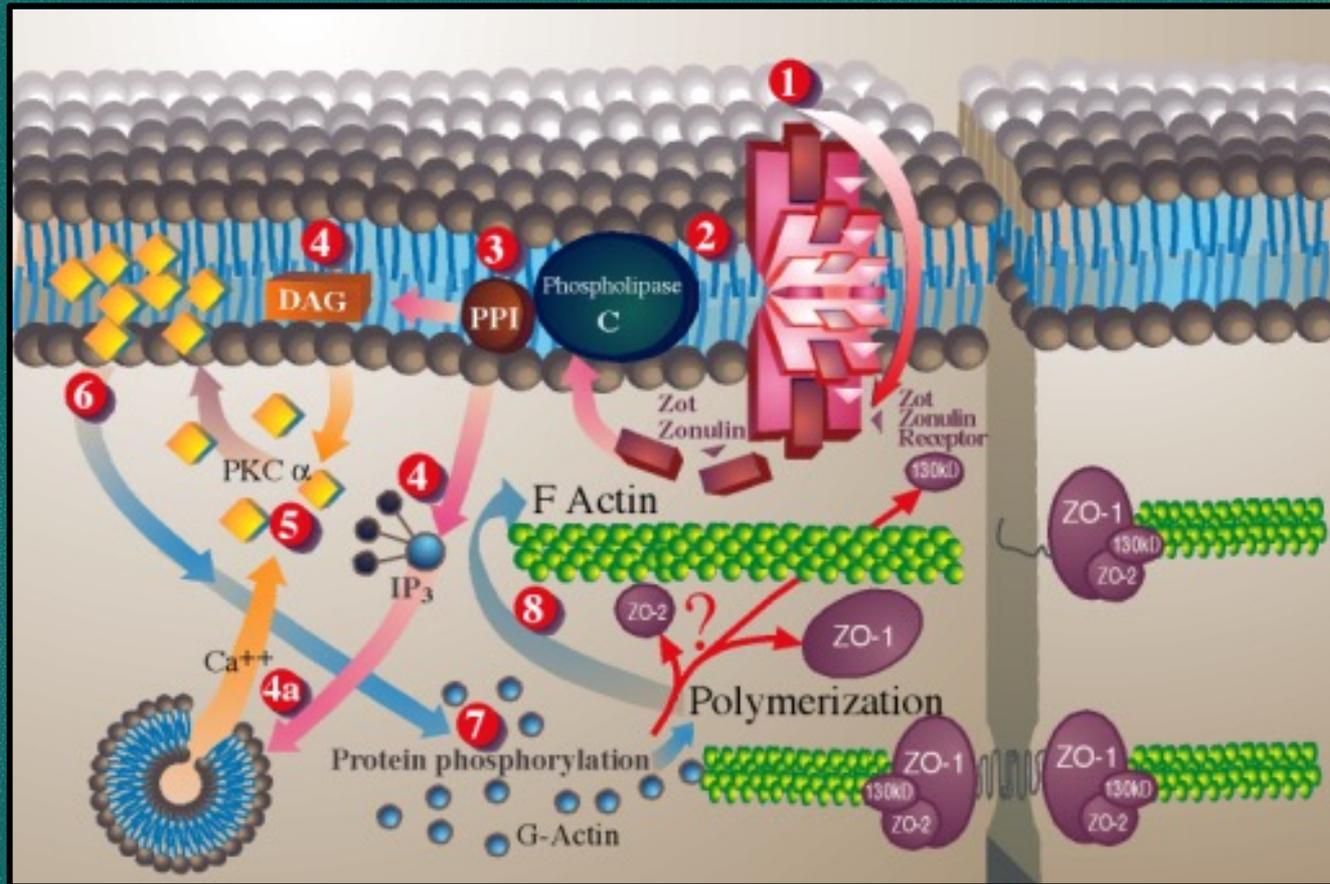
action of zonulin on tight junctions

Paracellular mechanism

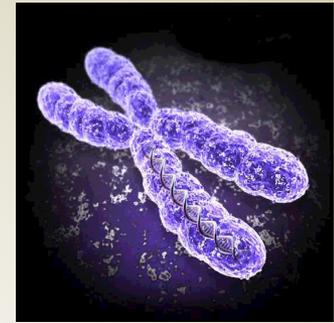
- **Gliadin binds to the chemokine receptor CXCR3 which then stimulates the release of ZONULIN from epithelial cells**
- **Zonulin is a precursor molecule to haptoglobin-2**
- **Zonulin regulates the movement of fluid, large molecules, and immune cells between body compartments**
- **In celiac disease, gluten prompts increased zonulin secretion**

Fasano, A. Surprises from Celiac Disease. Scientific American, Aug 2009, vol. 301, issue 2, p54-62.

Proposed Zonulin Mechanism of Action



Genetics



- Celiac is strongly associated with the HLA Class II region on chromosome 6
- 95-99% of patients with celiac disease carry the gene for DQ2 or DQ8
- 30-40% of the general population have one of these mutations
- Only 3-5% of people expressing DQ2/DQ8 develop celiac disease
- These mutations are necessary but not sufficient for disease.
- HLA DQ2 homozygous individuals have a 5X higher risk of disease development

Diagnosis

Who do you screen?



- Children and adolescents with otherwise unexplained intestinal and extraintestinal manifestations of celiac.
- Asymptomatic children and adolescents with increased risk for CD
 - Associated illnesses
 - 1st degree relative with CD

Diagnosis

- Serology for screening
 - IgA level
 - Anti-endomysial antibody (sensitivity 85-98%, specificity 98-100%)
 - Tissue transglutaminase IgA/IgG
 - TTG IgA $>10X$ the upper limit of normal has a 100% positive predictive value for disease
 - Antigliadin antibodies are no longer recommended for screening – poor sensitivity and specificity (BUT maybe more sensitive in children < 2)
 - Small bowel biopsy is REQUIRED (?) for diagnosis

Diagnosis

- Deamidated gliadin peptides IgA/IgG (DGP)
 - 82% sensitive but almost 99% specific
 - Permits identification of celiac disease in IgA deficient patients and children < 2 years old.



Diagnosis

- HLA DQ typing has a poor specificity for CD (about 54%)
- Is helpful in EXCLUDING the disease (HLA DQ2/DQ8 negative)
- ESPGHAN has recommended the use of HLA DQ typing in high risk groups as the first line screening test. If DQ2/DQ8 negative – no further workup is indicated.
- Also used to support the diagnosis of celiac in patients with strong clinical suspicion and high CD specific antibodies but no small bowel biopsy.

And if the screening tests are
positive. . .



REFER TO GI!!!

**PLEASE, PLEASE, PLEASE
DO NOT START A GLUTEN FREE DIET!!!**

Alternative diagnosis

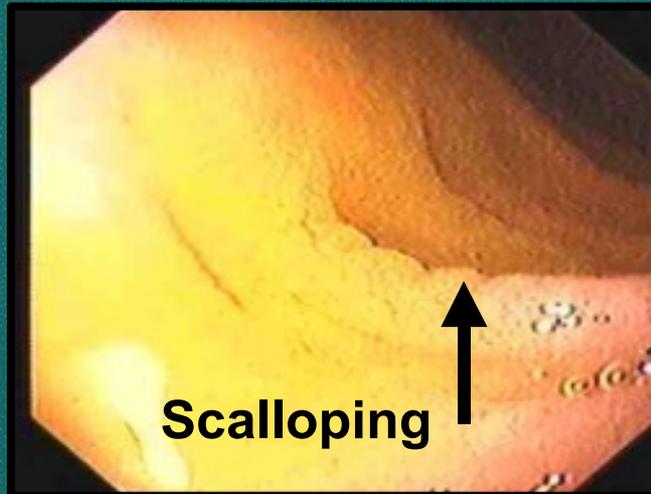
- **Cow's milk allergy**
- **Eosinophilic Esophagitis**
- **Bacterial overgrowth**
- **Giardia lamblia**
- **Primary immunodeficiency**
- **Inflammatory bowel disease**
- **Intestinal lymphoma**



Endoscopic Findings



Normal Appearing

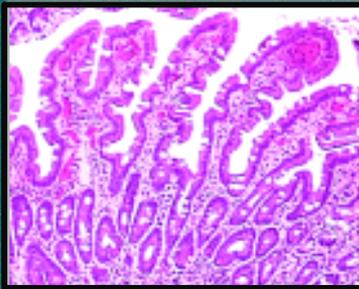


Scalloping

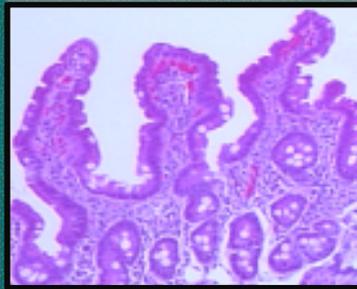


Nodularity

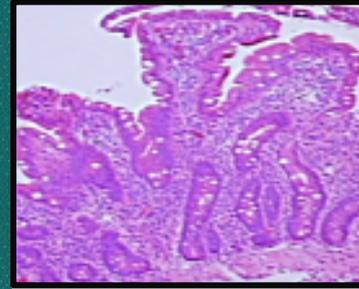
Histological Features



Normal 0



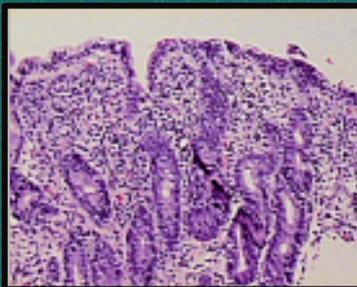
Infiltrative 1



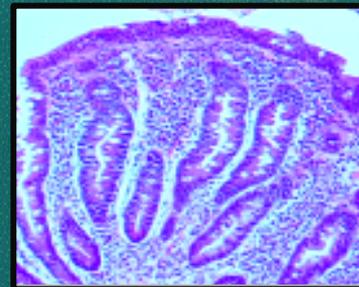
Hyperplastic 2



Partial atrophy 3a



Subtotal atrophy 3b



Total atrophy 3c

Treatment

- LIFE LONG gluten free diet is the only lasting treatment for celiac disease
- Approximately 70% of patients have symptomatic improvement within 2 weeks of starting the diet
- Unfortunately, compliance may be as low as 40%



National Restaurant Chains with Gluten Free Menus

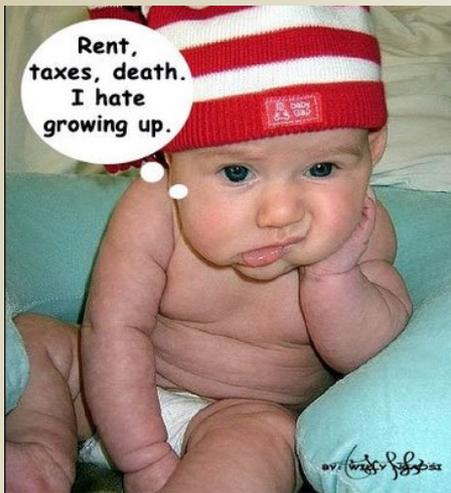
Outback Steakhouse
Flemmings Prime Steakhouse
Ninety Nine (Uncle Louie's favorite)
Olive Garden
PF Chang's
Boston Market
Chili's
On the Border
Ruby Tuesday's
UNO



Histological improvement

- 65% in 2 years, 85% within 5 years and 91% after 5 years on a gluten free diet





We Restrict Gluten to Prevent Complications of Untreated Celiac disease

- Short stature
- Dermatitis herpetiformis
- Dental enamel hypoplasia
- Recurrent stomatitis
- Fertility problems
- Osteoporosis
- Gluten ataxia and other neurological disturbances
- Refractory celiac disease and related disorders
- Intestinal lymphoma

Gluten sensitivity

- The development of adverse reactions when eating gluten containing products without associated small intestinal injury, less severe clinical picture, normal TTG autoantibodies, no associated autoimmune disease
- First described in 1978
- Occurs in approximately 10 % of the population?
- Is a distinct clinical entity
- Conserved intestinal barrier function



Conclusions

- Celiac disease, Wheat allergy, and wheat sensitivities are different entities
- Celiac disease is becoming much more prevalent
- First degree relatives should be screened
- Endoscopy is still recommended prior to starting a gluten free diet



Constipation

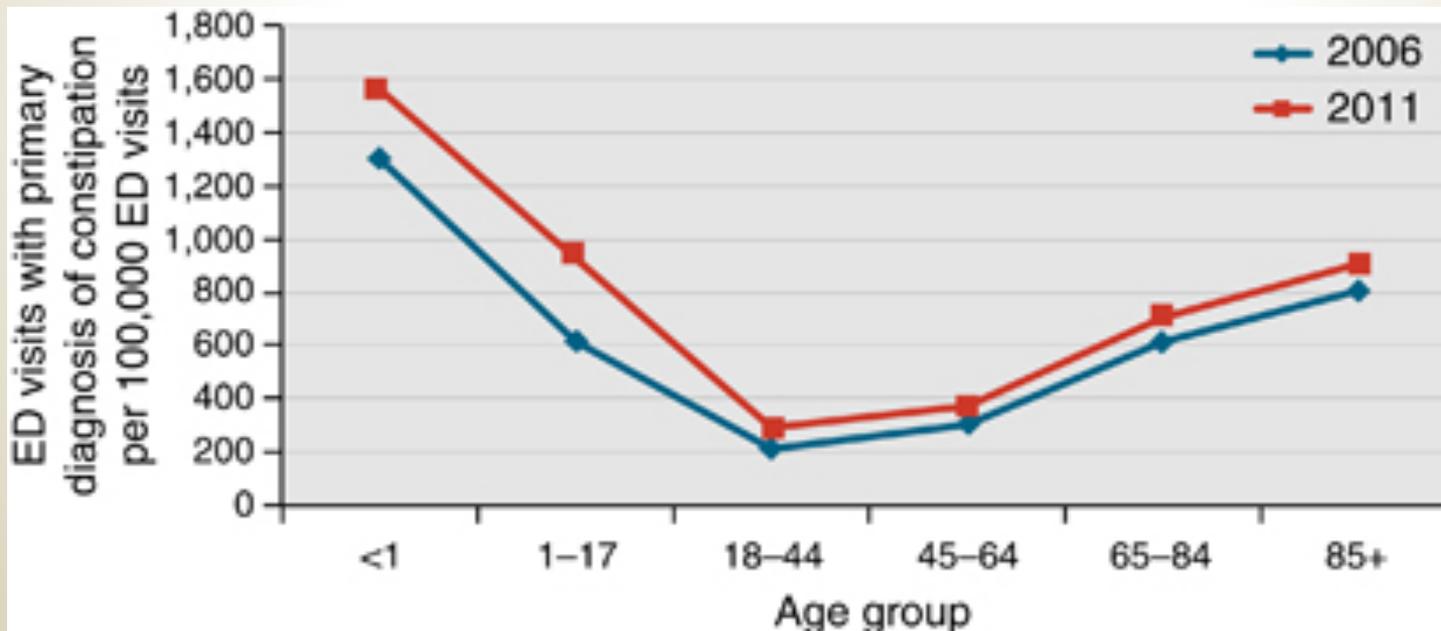
**IS THE PLUMBING NOT
WORKING?**

Constipation beyond infancy

- Common problem in children
- 3-10% visits to general pediatrics clinics
- 25% referrals to Peds GI
- Worldwide prevalence 0.7% to 29.6%
- Peak incidence time of toilet training

The Cost of Constipation

- Mean cost per patient rose by 56% (\$1,474 to \$2,306)
- Aggregate national cost increased by 121%



Background

- Constipation is often due to infrequent bowel movements which is associated with large painful defecation.
- Most common causes of constipation are functional fecal retention and fecal withholding
- Accompanying symptoms may include irritability, decreased appetite, and/or early satiety, which may disappear immediately following passage of a large stool.

Functional Constipation

Definition – Rome III

- 2 or more of the following in a child with a developmental age of at least 4 years with insufficient criteria for diagnosis of IBS
 - Two or fewer defecations in the toilet per week
 - At least one episode of fecal incontinence per week
 - History of retentive posturing or excessive volitional stool retention
 - History of painful or hard bowel movements
 - Presence of a large fecal mass in the rectum
 - History of large diameter stools which may obstruct the toilet

Bristol Stool Chart

Type 1		Separate hard lumps, like nuts (hard to pass)
Type 2		Sausage-shaped but lumpy
Type 3		Like a sausage but with cracks on its surface
Type 4		Like a sausage or snake, smooth and soft
Type 5		Soft blobs with clear-cut edges (passed easily)
Type 6		Fluffy pieces with ragged edges, a mushy stool
Type 7		Watery, no solid pieces. Entirely Liquid

Colon

- Reabsorbing water and electrolytes
- Serves as temporary storage
- Prominent mixing pattern

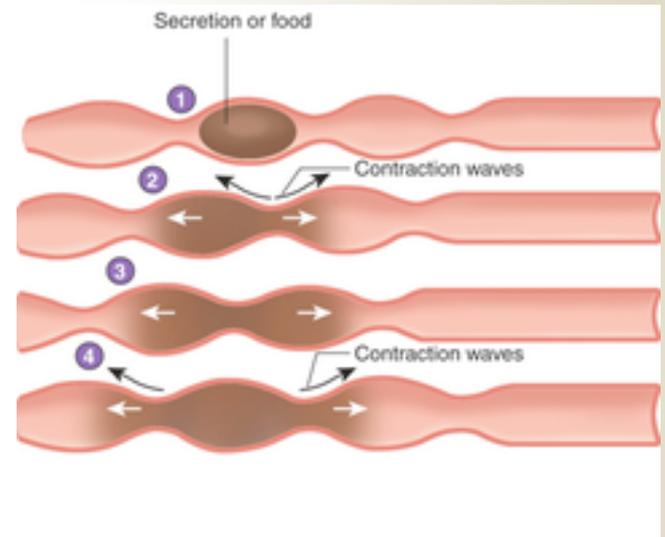


Colonic Motor Activity

- Segmental – single contractions or bursts
- Propagated
 - Low amplitude propagated contractions (LAPC)
 - High amplitude propagated contractions (HAPC)
 - Periodic rectal motor activity (PRMA)

Segmental Contractions

- Single contractions or bursts
- Account for most of colonic activity
- Waves 3-50 mmHg
- Slow down colonic transit allowing optimal absorption of contents and propulsion of fecal content over short distances



Propagated Contractions

- LAPC (<50 mmHg)
 - Seem to be associated with passage of flatus and involved in the transport of colonic fluid contents
- HAPC (>80 mmHg)
 - Usual mean amplitude of 150 mmHg migrating across at least 30 cm for >10 sec
 - Accounts for transport of colonic contents over large portions of colon
 - Occur about 4-10x/day mostly after meals, upon awakening and maybe accompanied by borborygmi

HAPC's decrease in number and segmental contractions increase during postnatal maturation of colonic manometry

Rectum

- Unique motility pattern = Periodic rectal Motor activity
- Discrete bursts of phasic and tonic pressure waves with frequency of >3 /minute
- Can migrate retrograde at night and serve as an intrinsic nocturnal brake

A thorough history and complete physical examination are adequate to accurately diagnose functional constipation

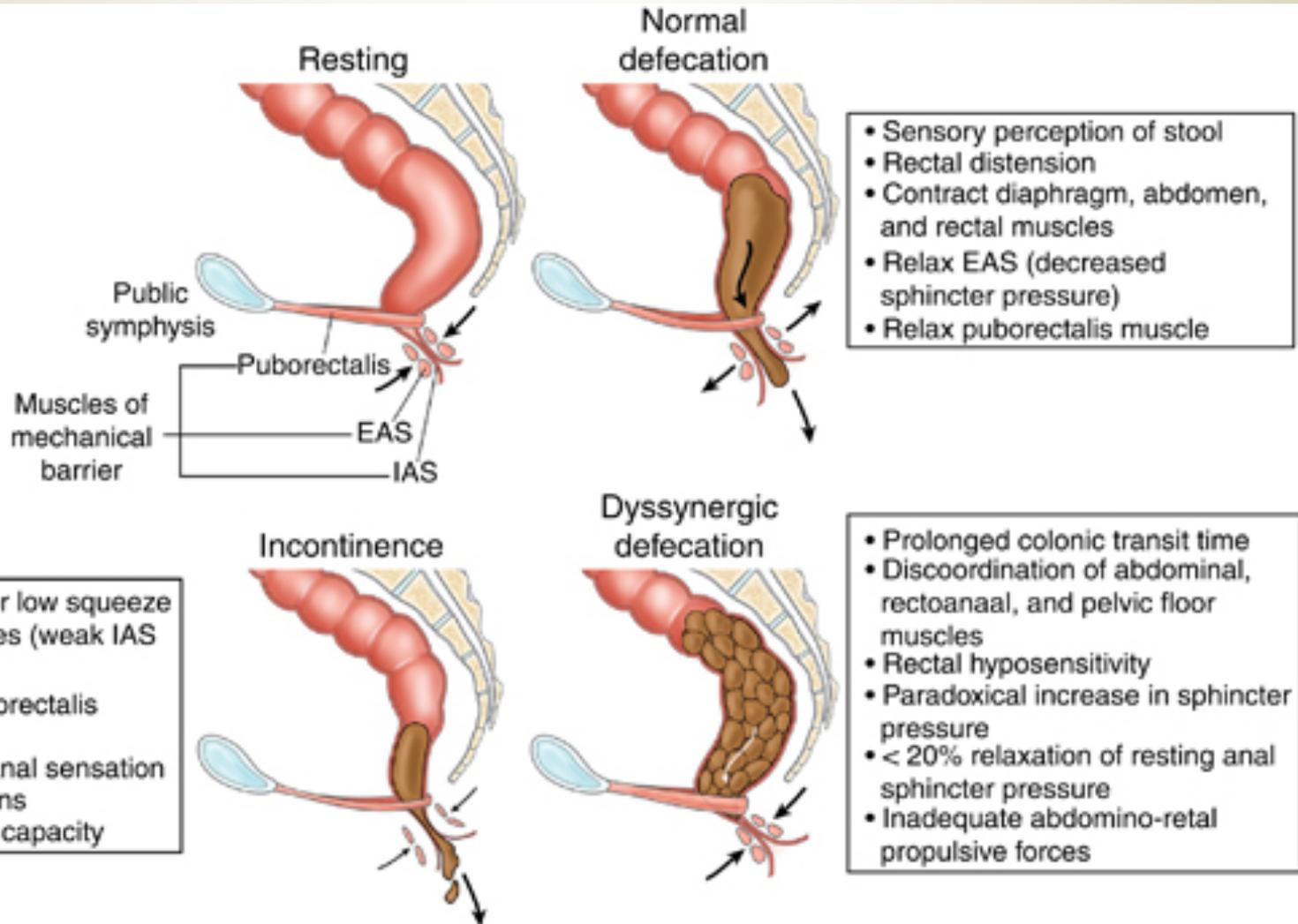


Stooling Patterns

– Varies with age

- An infant averages 2-4 stools a day. However, healthy breastfeeding babies may only stool 1-2x a week due to almost complete absorption of breast milk with little residue for stool formation
- Toddlers average 1 stool a day
- Preschoolers and older average 3-5 stools a week
- Adult frequency occurs at about 4 years of age

Normal vs. Altered Defecation



Schey, R. et al., *The American Journal of Gastroenterology* **107**, 1624-1633 (November 2012)

Etiology

- Most commonly caused by painful stools → voluntary withholding of feces → prolonged fecal stasis with resorption of fluids, increased size/ consistency of stools → Rectal dilation → Larger amounts of stool needed to activate rectal stretch receptors → Urge to defecate disappears, stool withholding becomes automatic

I have tried several options –
what is next?

CLINICAL GUIDELINE

CME

Evaluation and Treatment of Functional Constipation in
Infants and Children: Evidence-Based Recommendations
From ESPGHAN and NASPGHAN

*M.M. Tabbers, C. DiLorenzo, M.Y. Berger, C. Faure, M.W. Langendam, S. Nurko,
A. Staiano, Y. Vandenplas, and M.A. Benninga*

JPGN 2014

How much medication to give?

- Complete bowel evacuation is the first step
 - High dose polyethylene glycol (PEG) has been proven safe and effective when given at doses of 1-1.5 g/kg per day for 3-6 days
- Maintenance therapy
 - Enough medication should be used to reach a goal of regular, soft, and painless bowel movements and avoid re-accumulation of stool in the rectum

How long do I treat?

- Constipation is not self limiting
- Most children with not outgrow symptoms without treatment
- Maintenance Tx for at least 2 months
- Constipation sx's should be resolved for at least 1 month before stopping meds
- Treatment should be decreased gradually
- Medication should only be stopped once toilet training is established

Evaluation

- Abdominal X-Ray
- Radiopaque Markers (Sitz Markers)
- Barium enema
- Rectal biopsy
- MRI Lumbo-sacral spine
- Ano-rectal manometry
- Colonic Manometry

Labs

- Thyroid function tests
- Serum calcium level
- Serum lead level
 - Lead toxicity
- Sweat test if clinically indicated
 - Evaluates for cystic fibrosis
- TTG IgA, serum IgA (also include gliadin antibody if 2 years of age or less)

Treatment

- Medications
- High Fiber Diet
- Fiber supplements
- Frequent toileting in children with behavioral withholding
- Behavior modifications
- Rectal Irrigations
- Surgery - Cecostomy

Medication Options

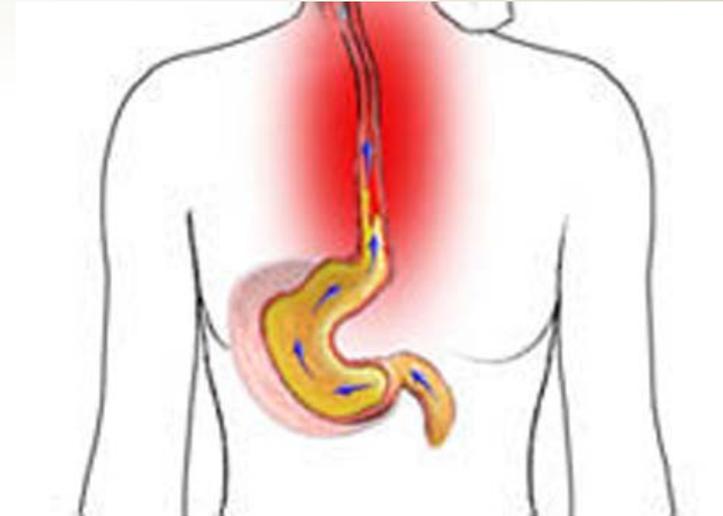
- Stool softeners
 - Mineral oil (lubricant): not recommended in children < 1 years old or with other aspiration risk
 - Docusate sodium
- Osmotic laxatives
 - Lactulose
 - Sorbitol
 - Polyethylene glycol 3350 (MiraLAX®)
 - Magnesium hydroxide
- ± Stimulant laxative for rescue therapy for short periods (< 30 days)
 - Senna
 - Bisacodyl

Newer Medications

- Lubiprostone – Activate CIC-2 Chloride channels
- Linaclotide – guanylate cyclase agonist

3 Rules

- Patient should take medications every day at the same time
- Sit on the toilet after breakfast, lunch and dinner and if experiencing belly cramps
- Adjust regimen if no stool in 48 hours, accidents, too hard or too loose stools
- Once doing well, continue for 6 months and then slowly wean



Gastroesophageal Reflux

TREAT OR NOT TO TREAT?

Goals

- Become aware of a guideline based approach for identifying which patients will benefit from treatment for gastroesophageal reflux disease (GERD)
- Discuss “red flag” signs and symptoms that should lead to further evaluation of GER/D in infants and children

Current Reports on GER/GERD in Infants

- Increased in past decade
- Describe inconsolable newborns who improved dramatically on proton pump inhibitors (PPIs)
 - Discussed “colic” as poorly understood
- Have contributed to 750% rise in use of PPIs in infants
 - 1999-2004
- Evokes questions of previous misdiagnosis vs. current overuse

WSJ Provocative Health Reporting:

- *“Even the terminology is confusing...most babies have reflux [and] it usually doesn’t hurt...”*
- *“GER becomes more-serious GERD if the infant won’t eat and stops gaining weight, vomits blood and is extremely irritable...”*

THE WALL STREET JOURNAL
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HEALTH JOURNAL | JULY 22, 2008
Baby Crying? Doctors Say It May Be Acid-Reflux Disease
By MELINDA BECK

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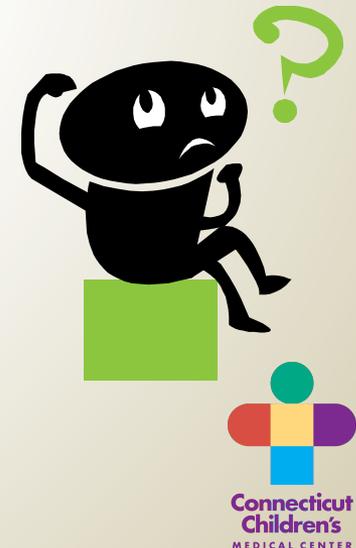
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Olivia Manganello was 1 month old when she started screaming, usually right after she nursed. Her family tried switching to formula, then different formulas, but nothing helped. Finally a pediatric gastroenterologist diagnosed gastroesophageal reflux disease (GERD) and put Olivia on Pepcid. "In two days, she was a completely different baby," says her mother, Trina Chiara of Avon, Conn.

Reading on Reflux
• Pediatric/Adolescent Gastroesophageal Reflux Assoc

Years ago, babies like Olivia were dismissed as having colic. Sometimes Valium was prescribed for their moms. Now, infants are

WHILE THE DEBATE ABOUT HEALTHCARE CONTINUES, WE'RE TAKING ACTION NOW.
LEARN MORE





GOOD NEWS!

- There is a pediatric global definition of GER vs. GERD
- There are Pediatric Gastroesophageal Reflux Clinical Practice Guidelines
 - Endorsed by the North American and European Societies for Pediatric Gastroenterology, Hepatology, and Nutrition
 - Basis of a 2013 Clinical Report from the American Academy of Pediatrics (AAP)
- Intended to be used in daily practice of all practitioners when evaluating and managing children with reflux disease

Global consensus especially useful because physiologic GER is now recognized to be relatively common in babies and kids...

<i>(Mean upper limit of normal)</i>	Infants (N=509)	Children (N=48)	Adults (N=432)
# daily reflux episodes	73	25	45
# reflux episodes lasting \geq 5 min	9.7	6.8	3.2
Reflux index (% of time pH < 4)* *over approx 24 hours	11.7%	5.4%	6%

Rudolph CD, Mazur LJ, Liptak GS, et al. Guidelines for evaluation and treatment of gastroesophageal reflux in infants and children: recommendations of the North American Society for Pediatric Gastroenterology and Nutrition. *J Pediatr Gastroenterol Nutr.* 2001;32(supplement 2):S1–S31

Clinical Cases

- A. 5 month old who effortlessly spits-up 6–10x/day, but seems comfortable and is growing well
- B. 4 month old who is losing weight is reported to vomit 2–3x/day, and seems increasingly fussy with feeds
- C. 15 year old who presents complaining of heartburn

So What is GER??? And What is GERD???

- Understanding the difference
 - May help to avoid overclassifying patients with GERD vs. physiologic GER
 - May avoid overtesting
 - May avoid overtreatment
 - May help identify when to refer patients to specialists

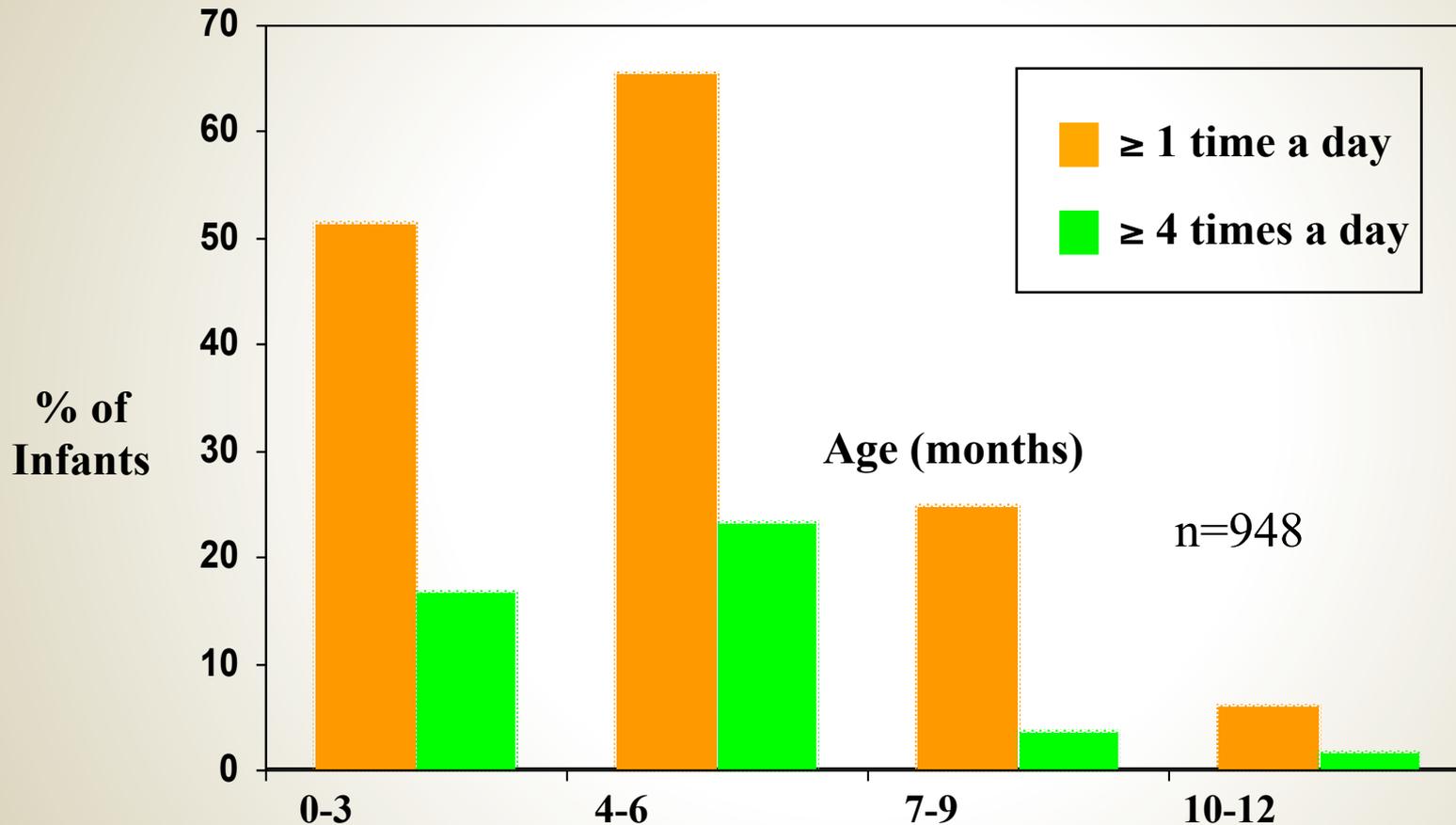
GER

- Gastroesophageal Reflux
 - The passage of gastric contents into the esophagus
 - Occurs with/without regurgitation and vomiting
- GER is a normal physiologic process
 - Several times/day in healthy infants, children, and adults

Most Episodes of GER

- Last < 3 minutes
- Occur in the postprandial period
- Cause few or no symptoms
- GER can cause vomiting
 - A coordinated autonomic and voluntary motor response with forceful expulsion of gastric contents
- Regurgitation (“spitting up”) is the most visible symptom of GER
 - Occurs daily in 50% of infants < 3 months of age
 - Resolves spontaneously in most by 12–14 months

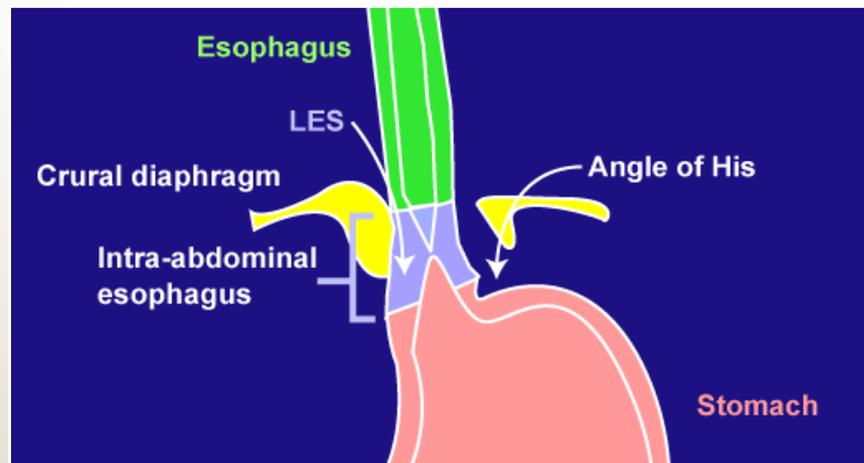
Prevalence of Regurgitation in Infancy



Adapted from Nelson SP, Chen EH, Syniar GM, et al. Prevalence of symptoms of gastroesophageal reflux during infancy. A pediatric practice-based survey. Pediatric Practice Research Group. *Arch Pediatr Adolesc Med.* 1997;151(6):569-572

Physiology of GER

- GER occurs during transient relaxations of the lower esophageal sphincter (LES)
 - Relaxation of the LES that is unaccompanied by swallowing permits gastric contents into the esophagus
- LES is not a “true” sphincter
 - Comprised of crural support, an intra-abdominal segment, and the “angle of His”



WHEN DOES GER “become” GERD

- Aberrance in normal physiology
 - Insufficient clearance and buffering of refluxate
 - Decreased rate of gastric emptying
 - Abnormalities in efficacy of epithelial repair
 - Decreased neural protective reflexes
- **Global Consensus: GERD is defined to be present when reflux of gastric contents causes either *troublesome* symptoms or complications**

Troublesome symptoms or complications of reflux

- Recurrent vomiting and poor weight gain in infant
- Recurrent vomiting and irritability in infant
- Recurrent vomiting in older child
- Heartburn in child/adolescent
- Esophagitis
- Dysphagia or feeding refusal
- Apnea or ALTE
- Asthma
- Recurrent pneumonia
- Upper airway symptoms
- Unusual arching or seizure-like movements (Sandifer syndrome)

Complications of Reflux

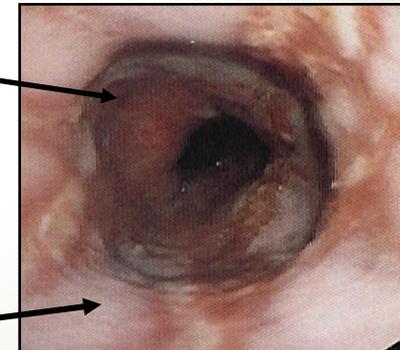
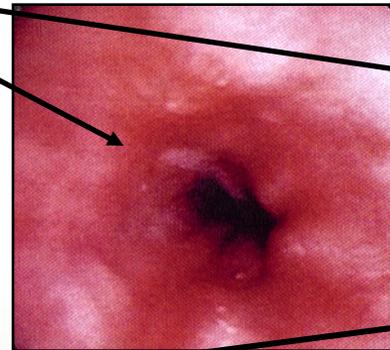
Is there a danger to not recognizing and treating it?

Normal mid- and distal esophagus



**Erosive esophagitis:
grade 2 and grade 4**

Z-line

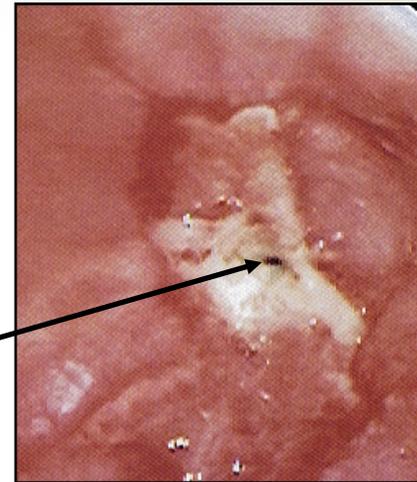
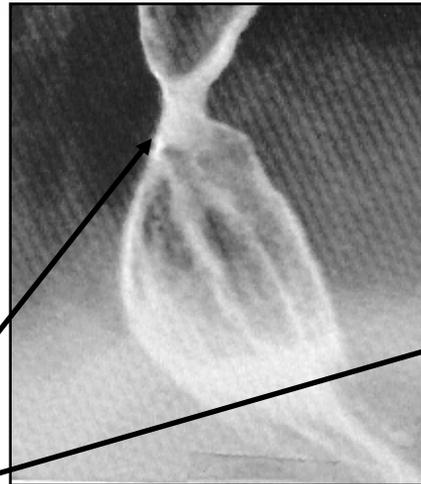


Erosions

Complications of Reflux

**Esophageal stricture secondary to GERD:
radiography and endoscopy**

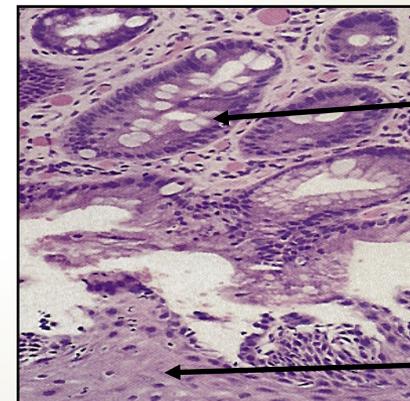
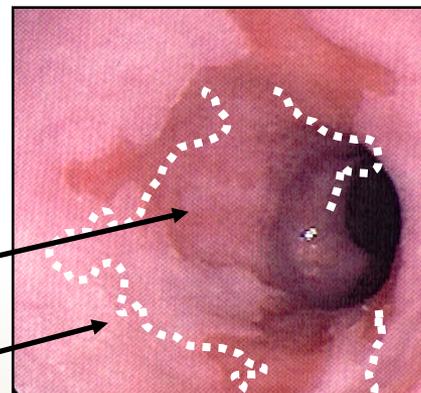
Stricture



**Barrett's esophagus:
endoscopy and histology**

Barrett's

Normal



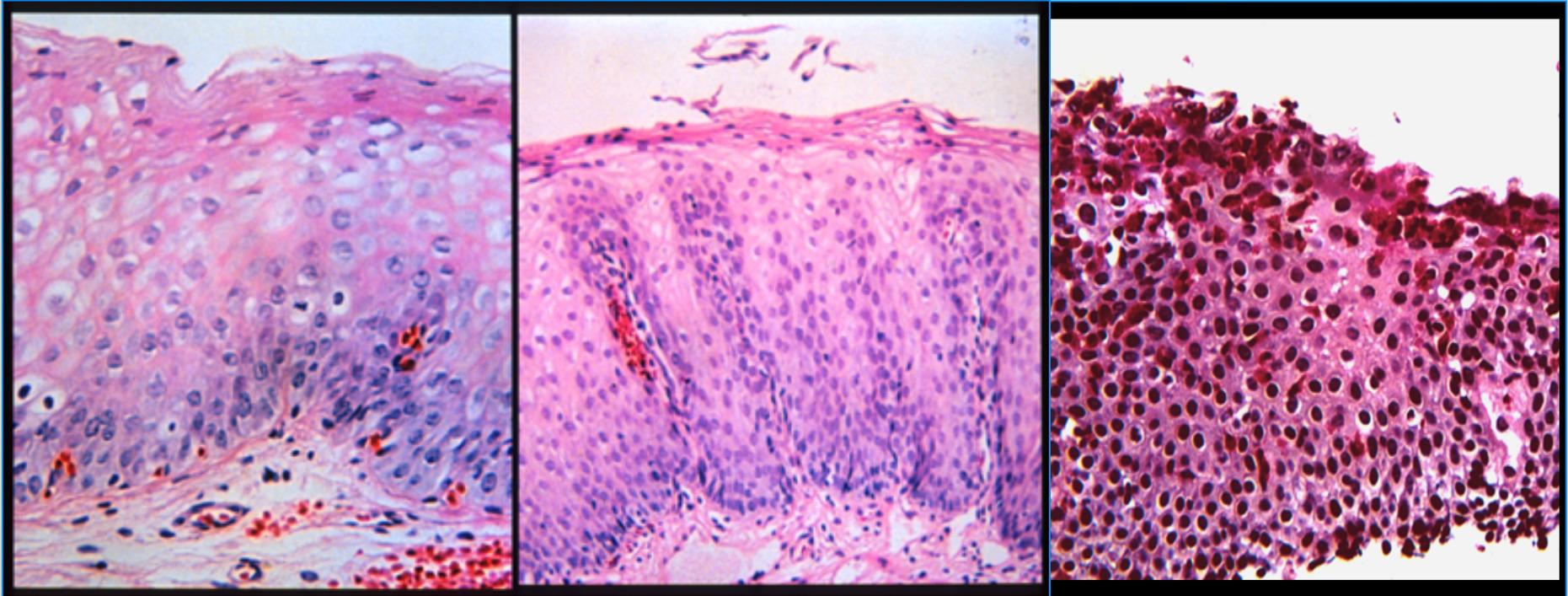
Barrett's

Normal

Endoscopic Biopsies

- Useful to evaluate for a variety conditions, but are not required for diagnosis of GERD
- Possible findings on biopsy:
 - Gastroesophageal reflux
 - Food allergy or intolerance
 - Primary eosinophilic esophagitis
 - Drug induced
 - Infection
 - *Candida*
 - Herpes simplex
 - Cytomegalovirus

Pathologic esophagitis



Normal esophagus

Peptic esophagitis

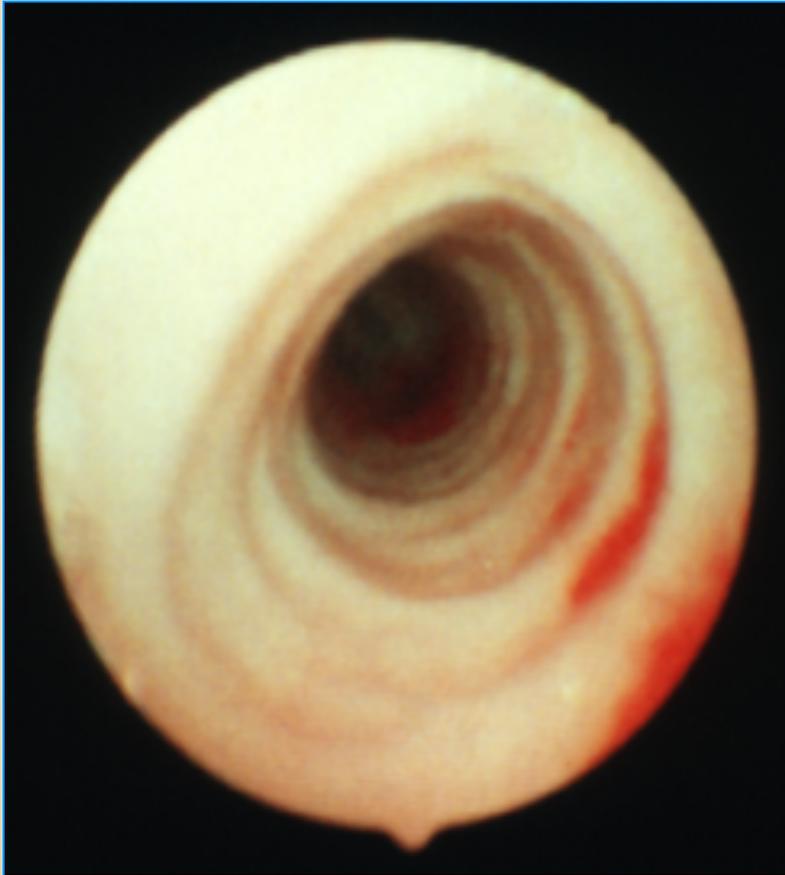
Eosinophilic esophagitis

EH, epithelial height; PL, papillary layer; BL, basal layer

Normal: PL ~ 40% of epithelial height; BL ~ 15%

GERD: PL ~ 90% of epithelial height; BL ~ 30%

Eosinophilic Esophagitis



Genetics of Reflux

- Cluster studies suggest inheritability of GER/GERD and their complications
 - Hiatal hernia
 - Erosive esophagitis
 - Barrett's esophagus
 - Esophageal adenocarcinoma
- Swedish Twin Registry
 - Increased concordance in monozygotic vs. dizygotic

Vandenplas Y, Rudolph CD, Di Lorenzo C, et al. Pediatric gastroesophageal reflux clinical practice guidelines: joint recommendations of the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition (NASPHAN) and the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN). *J Pediatr Gastroesophageal Nutr.* 2009;49(4):548–557

High Risk Populations

- Several pediatric patient populations appear to be at higher risk of GERD
 - Neurologically impaired
 - Obese infants, children, and adolescents
 - Certain genetic syndromes
 - Esophageal atresia
 - Chronic lung diseases
 - History of prematurity

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History/Physical Examination

- Severity of reflux or esophagitis found on diagnostic testing does not directly correlate with symptom severity
- Major roles of History/Physical Exam when evaluating GERD
 - To exclude other worrisome disorders that present with vomiting
 - To recognize complications of GERD
- In infants and toddlers, there is no symptom or group of symptoms that can reliably diagnose GERD or predict treatment response
- In older children and adolescents, history and physical examination *are* generally sufficient to reliably diagnose GERD and initiate management

Symptoms and Signs of GER/GERD

Symptoms

- Recurrent regurgitation with/without vomiting
- Weight loss or poor weight gain
- Irritability in infants
- Heartburn or chest pain
- Hematemesis
- Dysphagia, Odynophagia, Feeding refusal
- Apnea spells
- Wheezing
- Stridor
- Cough
- Hoarseness
- Dystonic neck posturing (Sandifer syndrome)

Signs

- Esophagitis
- Esophageal stricture
- Barrett Esophagus
- Laryngeal/pharyngeal inflammation
- Recurrent pneumonia
- Anemia
- Dental erosion

Indications for Further Evaluation in Infants With Vomiting

- Bilious vomiting
- GI bleeding
 - Hematemesis
 - Hematochezia
- Consistently forceful vomiting
- Onset of vomiting after 6 months of life
- Severe failure to thrive
- Diarrhea
- Constipation
- Fever
- Lethargy
- Hepatosplenomegaly
- Bulging fontanelle
- Macro/microcephaly
- Seizures
- Abdominal tenderness or distension
- Documented or suspected genetic/metabolic syndrome
- Associated chronic disease

Differential Diagnosis of Vomiting in Infants and Children – GI

Gastrointestinal obstruction

- Pyloric stenosis
- Malrotation with intermittent volvulus
- Intestinal duplication
- Hirschsprung disease
- Antral/duodenal web
- Foreign body
- Incarcerated hernia

Other GI disorders

- Achalasia
- Gastroparesis
- Gastroenteritis
- Peptic ulcer
- Eosinophilic esophagitis/
gastroenteritis
- Food allergy
- Inflammatory bowel disease
- Pancreatitis
- Appendicitis

Important to Obtain a Feeding and Vomiting History

Feeding and dietary history

- Amount/frequency (overfeeding)
- Preparation of formula
- Recent changes in feeding type or technique
- Position during feeding
- Burping
- Behavior during feeding: choking, gagging, cough, arching, discomfort, refusal

Pattern of vomiting

- Frequency/amount
- Pain
- Forceful or not
- Blood or bile
- Associated fever, lethargy, diarrhea

Testing for Reflux Disorders

- No one test can be used to diagnose reflux, and instead must be matched to a clinical question
- Reflux tests are useful
 - To document the presence of GER(D)
 - To detect complications
 - To establish a causal relationship between GER and symptoms
 - To evaluate therapy
 - To exclude other conditions

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Diagnostic Approach

- Depends on symptoms and signs
- History and physical examination
- Upper gastrointestinal (GI) series
- Esophageal pH monitoring
- Esophagogastroduodenoscopy and biopsy
- Empirical medical therapy

Upper GI Radiography



Pyloric stenosis

Advantage

- Useful for detecting anatomic abnormalities

Limitations

- Cannot discriminate between physiologic and non-physiologic GER episodes



Malrotation

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 pH with impedance Monitoring

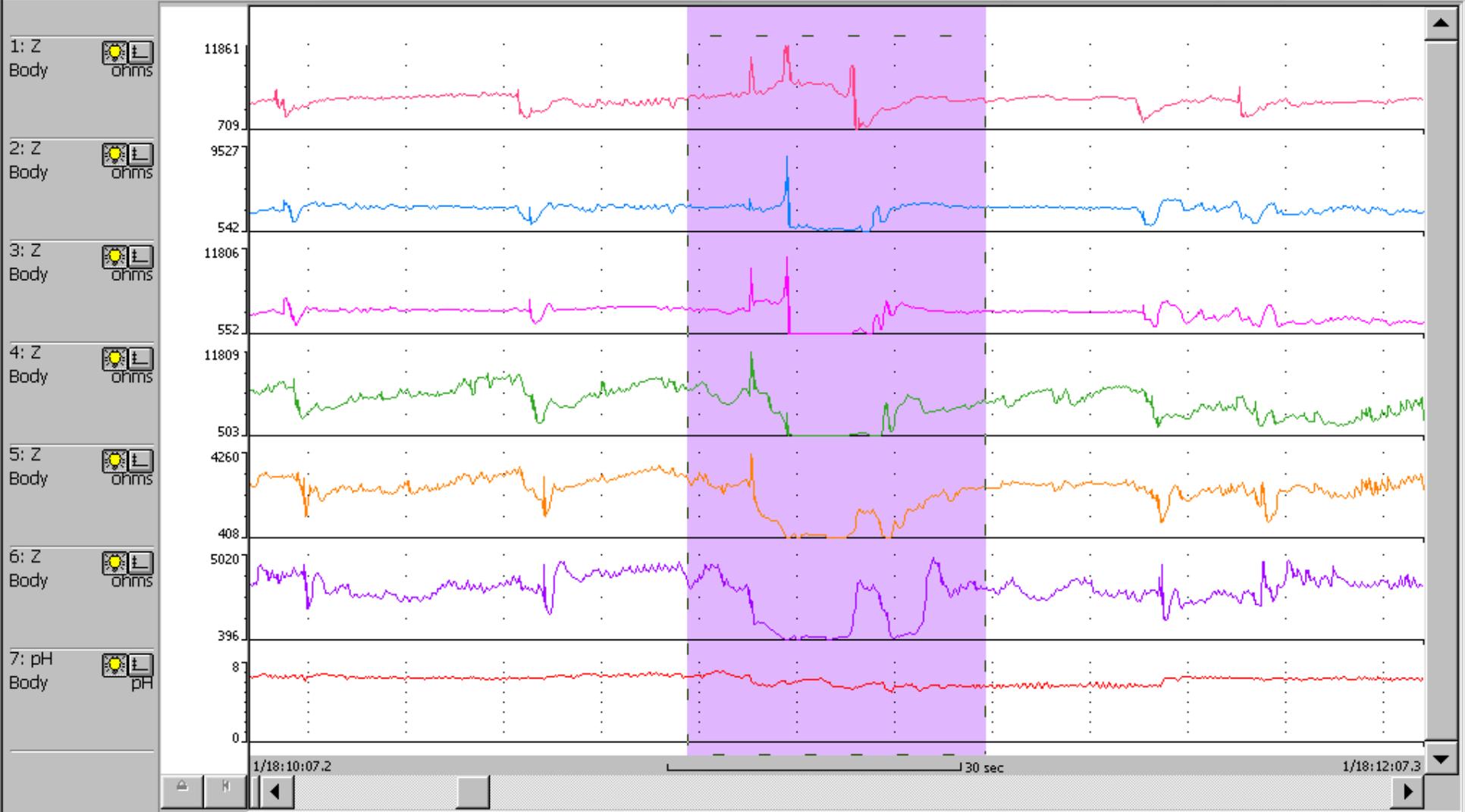


Advantages

- Detects episodes of reflux
- Determines temporal association between acid GER and symptoms

Limitations

- Cannot detect nonacidic reflux
- Cannot detect GER complications associated with “normal” range of GER
- Not useful in detecting association between GER and apnea unless combined with other techniques



Other Histories in the Infant/Child With Suspected GERD

Past medical history

- Prematurity
- Growth and development
- Past surgery and hospitalizations
- Newborn screen results
- Recurrent illnesses (croup, pneumonia, asthma)
- Symptoms of hoarseness, fussiness, hiccups
- Apnea
- Previous weight and height gain

Medications

- Current vs. Recent
- Prescription
- Non-prescription

Family psycho-social history

- Sources of stress
- Maternal or paternal drug use
- Post partum depression

Family medical history

- Significant illnesses
- Family history of GI disorders
- Family history of atopy

Growth chart

- Height
- Weight
- Head circumference

Conservative Therapy for GER

For Infants

- Normalize feeding volume and frequency
- Consider thickened formula
- Consider non-prone positioning during sleep
- Consider trial of hypoallergenic formula

For Older Children

- Avoid large meals
- Do not lie down immediately after eating
- Lose weight, if obese
- Avoid caffeine, chocolate, and spicy foods that provoke symptoms
- Eliminate exposure to tobacco smoke

Treating physiologic GER in infants

- Once the diagnosis of GER is established
 - Parental education, reassurance, and anticipatory guidance are recommended
 - Dietary changes and thickening of formula can be considered
- In general no other intervention is necessary
- If symptoms worsen or do not resolve by 12 to 18 months of age or “warning signs” develop, referral to a pediatric gastroenterologist is recommended

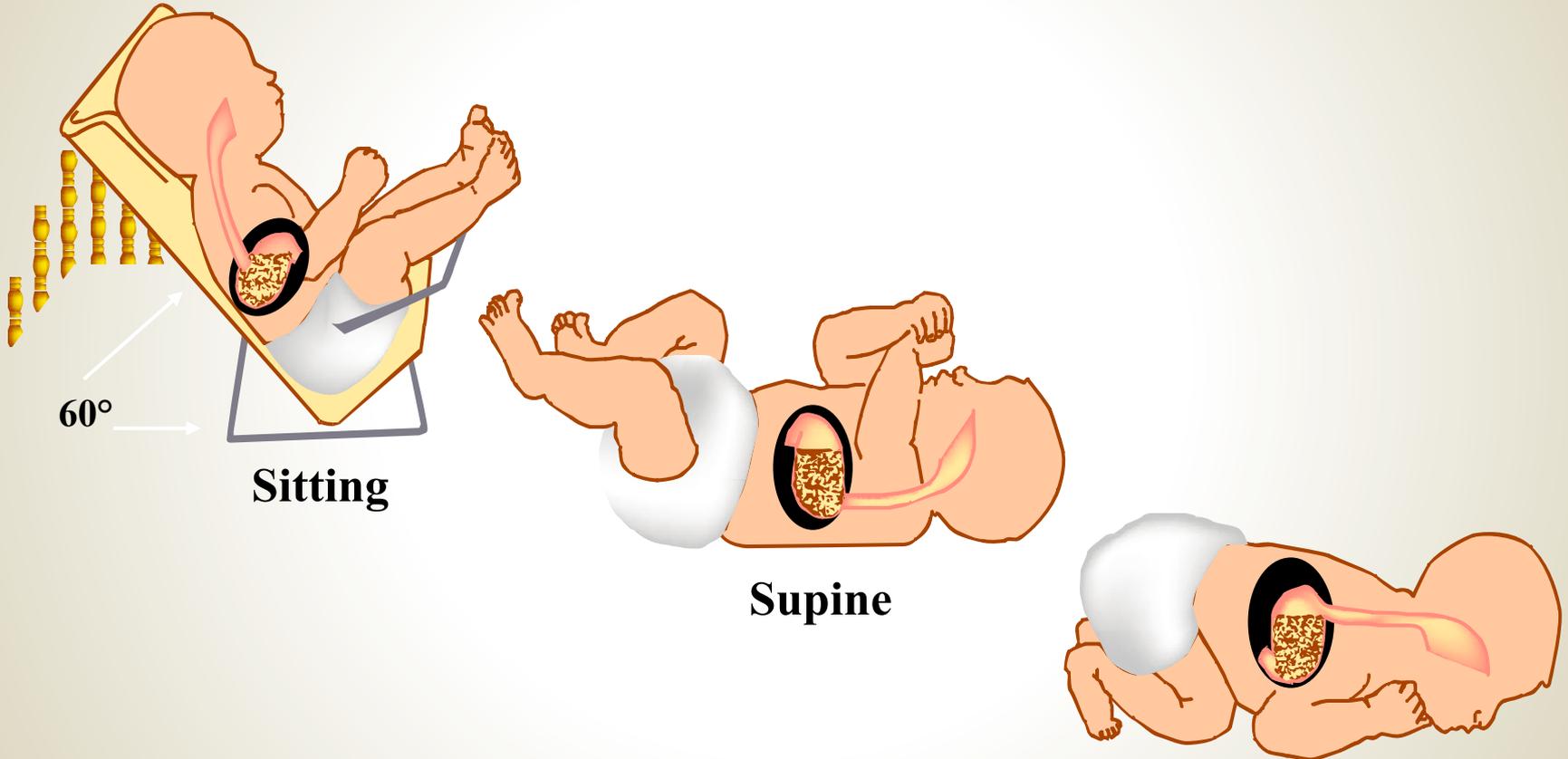
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Treatment of GER in infants

- Evidence supports
 - 2–4 week trial of an extensive protein hydrolysate in formula fed infants with vomiting
 - Thickening of formula which may decrease visible reflux (regurgitation)
 - Supine position for sleeping
- If no improvement, referral to a pediatric gastroenterologist may be appropriate

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Positioning and GER



Adapted from Ramenofsky ML, Leape LL. Continuous upper esophageal pH monitoring in infants and children with gastroesophageal reflux, pneumonia, and apneic spells. *J Pediatr Surg.* 1981;16(3):374-378

Prone

Positioning Therapy for GERD

For Infants

- Non-prone positioning during sleep is recommended
 - Supine positioning confers lowest risk for SIDS and is preferred
- Prone positioning may be considered in cases where risk of death from GER complications outweighs potential increased risk of SIDS
- If prone positioning is recommended, discuss rationale with parents
- Avoid soft bedding, pillows, loose sheets near infant

For Older Children

- Left side positioning during sleep may be beneficial
- Elevate head of bed
- Avoid lying down immediately after eating

American Academy of Pediatrics, Task Force on Infant Sleep Position and Sudden Infant Death Syndrome. Changing concepts of sudden infant death syndrome: implications for infant sleeping environment and sleep position. *Pediatrics*. 2000;105(3 Pt 1):650–656; Rudolph CD, Mazur LJ, Liptak GS, et al. Guidelines for evaluation and treatment of gastroesophageal reflux in infants and children: recommendations of the North American Society for Pediatric Gastroenterology and Nutrition. *J Pediatr Gastroenterol Nutr*. 2001;32(supplement 2):S1–S31

Treatment of GERD in Older Children

- A left sided sleeping position with elevation of the head of the bed may decrease symptoms and GER
- In adults, obesity and late night eating are associated with increased reflux
 - To date, no evidence to support specific dietary restrictions to decrease symptoms of GER in pediatric populations
- Appropriate to trial acid suppression

Goals of Pharmacotherapy

- Control symptoms
- Promote healing
- Prevent complications
- Improve health-related quality of life
- Avoid adverse effects of treatment

Medical Treatment of GERD

- Both Histamine-2 receptor antagonists (H2RAs) and PPIs
 - Produce relief of symptoms and mucosal healing of GERD
 - Are superior to buffering agents, alginates, and sucralfate
- PPIs are superior to H2RAs in relieving symptoms and healing esophagitis.
- Potential side effects of each currently available prokinetic agent outweigh the potential benefits
 - No evidence for routine use of metoclopramide, erythromycin, bethanechol, or domperidone for GERD

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PPIs in Adults With GERD

- Most potent inhibitors of acid secretion
- Both pharma *and* numerous randomized controlled trials
 - Superior to H2RAs in relieving reflux symptoms and healing esophagitis
 - Effective in patients unresponsive to high-dose H2RA
 - Superior to H2RAs in maintaining remission of esophagitis
- Demonstrated safety in patients treated for 1.4 to 11.2 years (N=230 patients)

PPIs in Infants and Children With GERD

- Pharmacologic studies with omeprazole and lansoprazole
- No randomized placebo-controlled trials have demonstrated improvement of GERD in children

Optimal Timing of PPI Dose

Single PPI dose:

**Administer half-hour
before breakfast**

If second PPI dose:

**Administer half-hour
before evening meal**

Available Prokinetic Agents Are Unproven or Ineffective

- **Cisapride:** withdrawn
- **Bethanechol:** only 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 (~30% prevalence) of adverse events

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Treatment of GERD in Older Children

- Lifestyle changes with a 4-week PPI trial are recommended.
- If symptoms resolve, continue PPI for 3 months
- If symptoms persist or recur after treatment, child should be referred to a pediatric gastroenterologist

Conclusions

- It is important to clarify whether a pediatric patient has physiologic GER or pathologic GERD
- There are guidelines for appropriate testing and treating of children with reflux disease...
 - Also useful for deciding when to refer to subspecialists

Thank you!

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