Manifestation and Diagnosis of Pediatric Laryngopharyngeal Reflux

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Grand Rounds Presentation
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Pediatrics Reflux: Introduction

- Up to two-thirds of infants exhibit signs of reflux (Nelson 1997)
- A majority of those children will outgrow their reflux by their second year of age
- Laryngopharyngeal reflux (LPR) has gained increasing recognition as a common pediatric disorder over the past few years .

Classification

- Physiologic
  - **Infrequent reflux symptoms in the absence of abnormalities**
  - **Asymptomatic**
  - **Rarely during sleep**
  - **Often postprandial**
- Secondary
  - **neurologic disease or esophageal dysmotility**
- Pathologic
  - **Symptomatic**
  - **GERD or LPRD**

WHAT IS THE DIFFERENCE BETWEEN GERD & LPR?

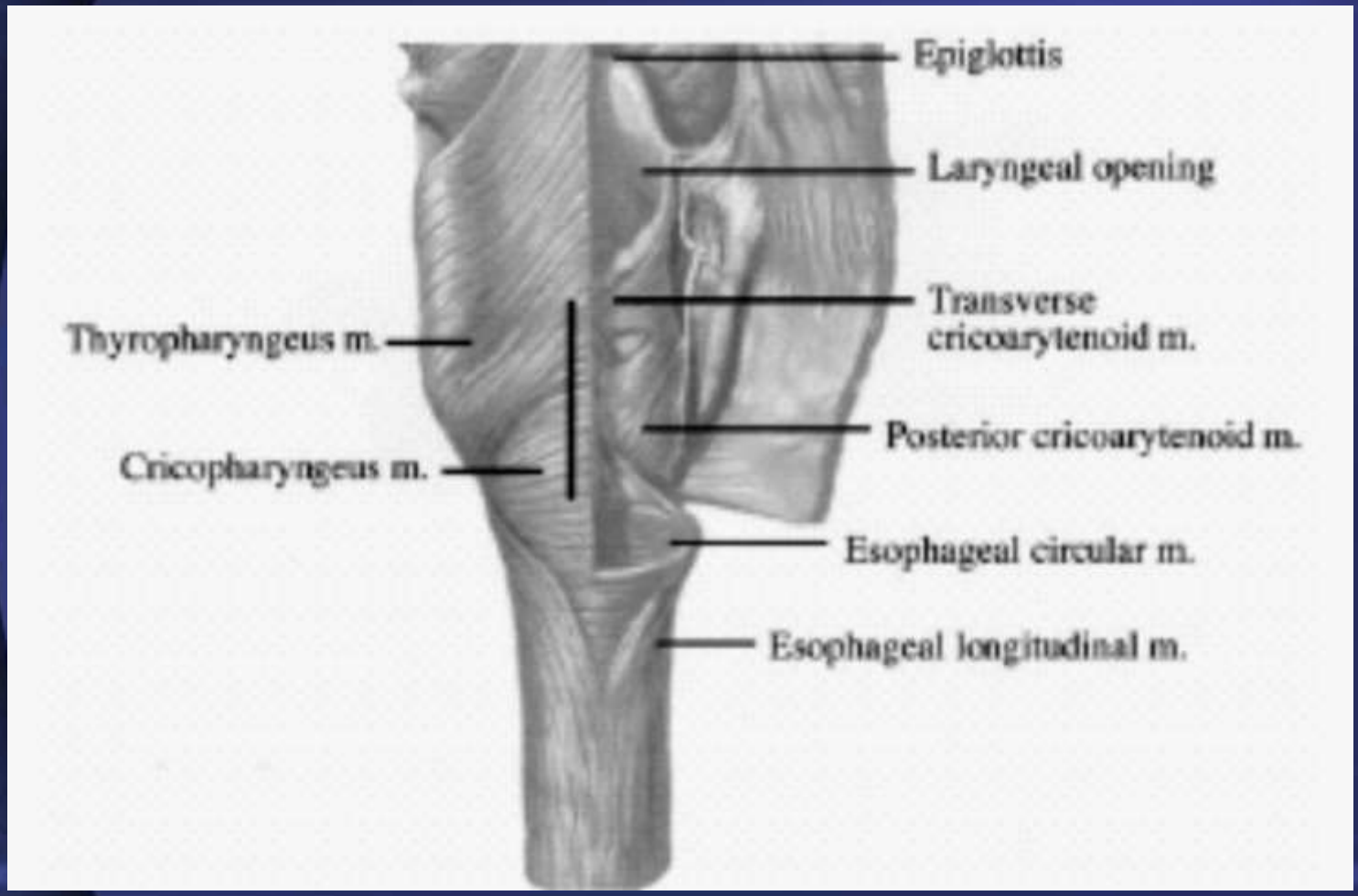
- Gastroesophageal reflux (GER)
  - Retrograde flow of gastric contents into the esophagus
- Laryngopharyngeal reflux (LPR)
  - Extraesophageal reflux (EER)
  - denotes the gastric contents that reaches beyond the upper esophageal sphincter (UES) into oropharynx and/or nasopharynx

LPR vs. GER

LPR	GER
Daytime, upright	Nighttime, supine
< 10 %	< 22 %
Normal esophageal motility	Esophageal dysmotility
Laryngeal/ Pharyngeal symptoms	Gastrointestinal symptoms, heartburn

Stavroulaki. Intern J of Ped Otol 2006

Upper Esophageal Sphincter



Sivarao Am J Med 2000

Pathophysiology

- Exact etiology unknown
- Direct acid and/or pepsin injury
- Neural-mediated laryngospasm, throat clearing, coughing

Mucosal injury in LPR

- Laryngeal epithelium more susceptible to damage from refluxate than esophageal epithelium
- Pepsin causes depletion of laryngeal protective proteins and carbonic anhydrase
- Pepsin adhered to laryngeal epithelium can be activated during an acidic reflux episode

Johnston N 2003, 2007

History and Physical

Infants

Regurgitation/vomiting, dysphagia, anorexia, growth failure, abnormal crying, sleeping disorders, irritability or torticollis (Sandifer's syndrom)

Apnea or life-threatening events

Upper-airway problems: recurrent croup, laryngomalakia, subglottic stenosis

Chronic respiratory disease

Children

Laryngotracheal complains: chronic cough, dyspnea, dysphonia

Pharyngeal complains: persistent sore throat, halitosis, globus sensation, referred otalgia, dental erosion

Rhinologic complains: nasal obstruction, rhinorrhea, headache

Chronic respiratory disease

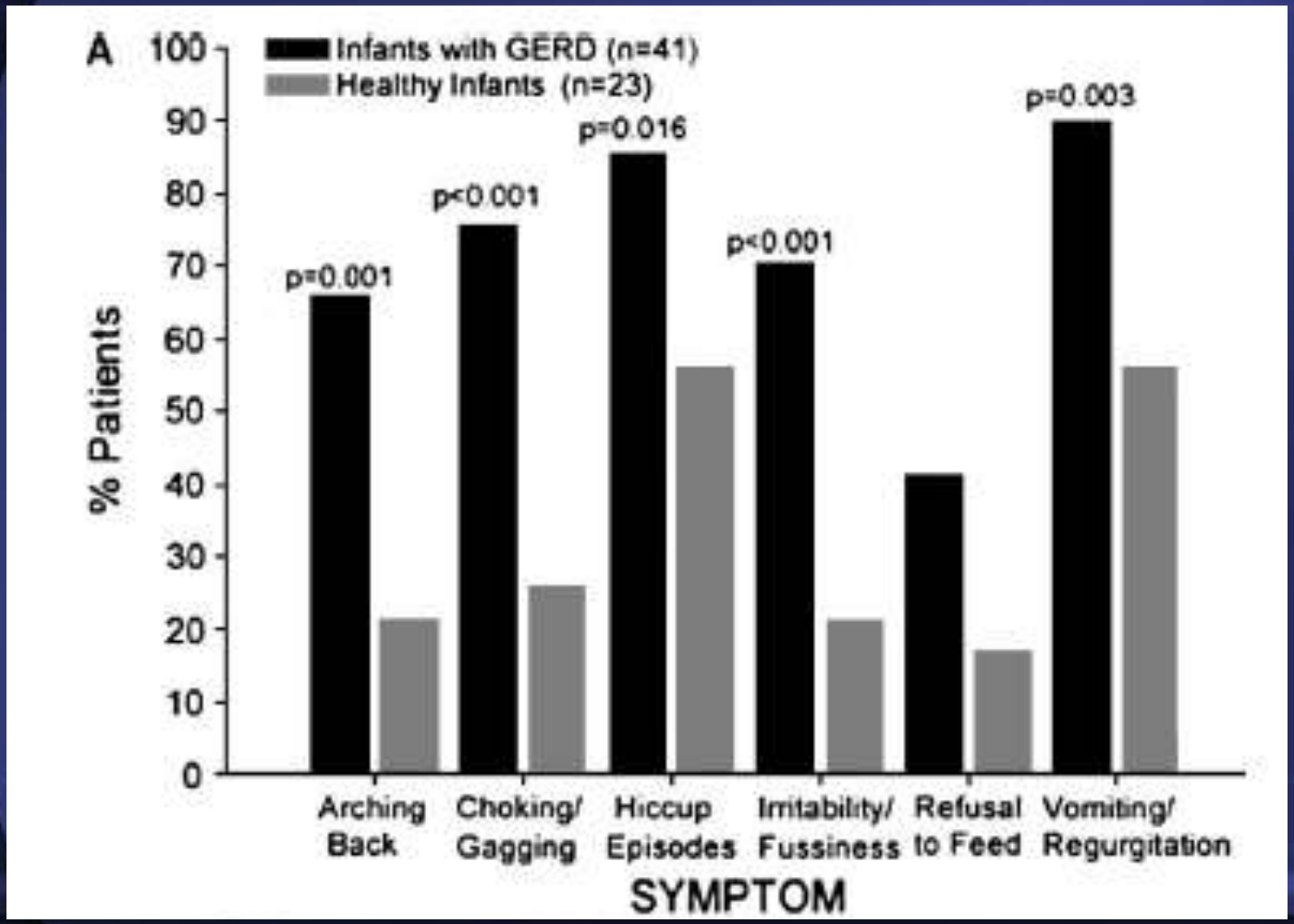
Gastrointestinal symptoms: regurgitation/vomiting, nausea, chest or abdominal pain, heartburn

Stavroulaki. Intern J of Ped Otol 2006

Carr et al. 2000

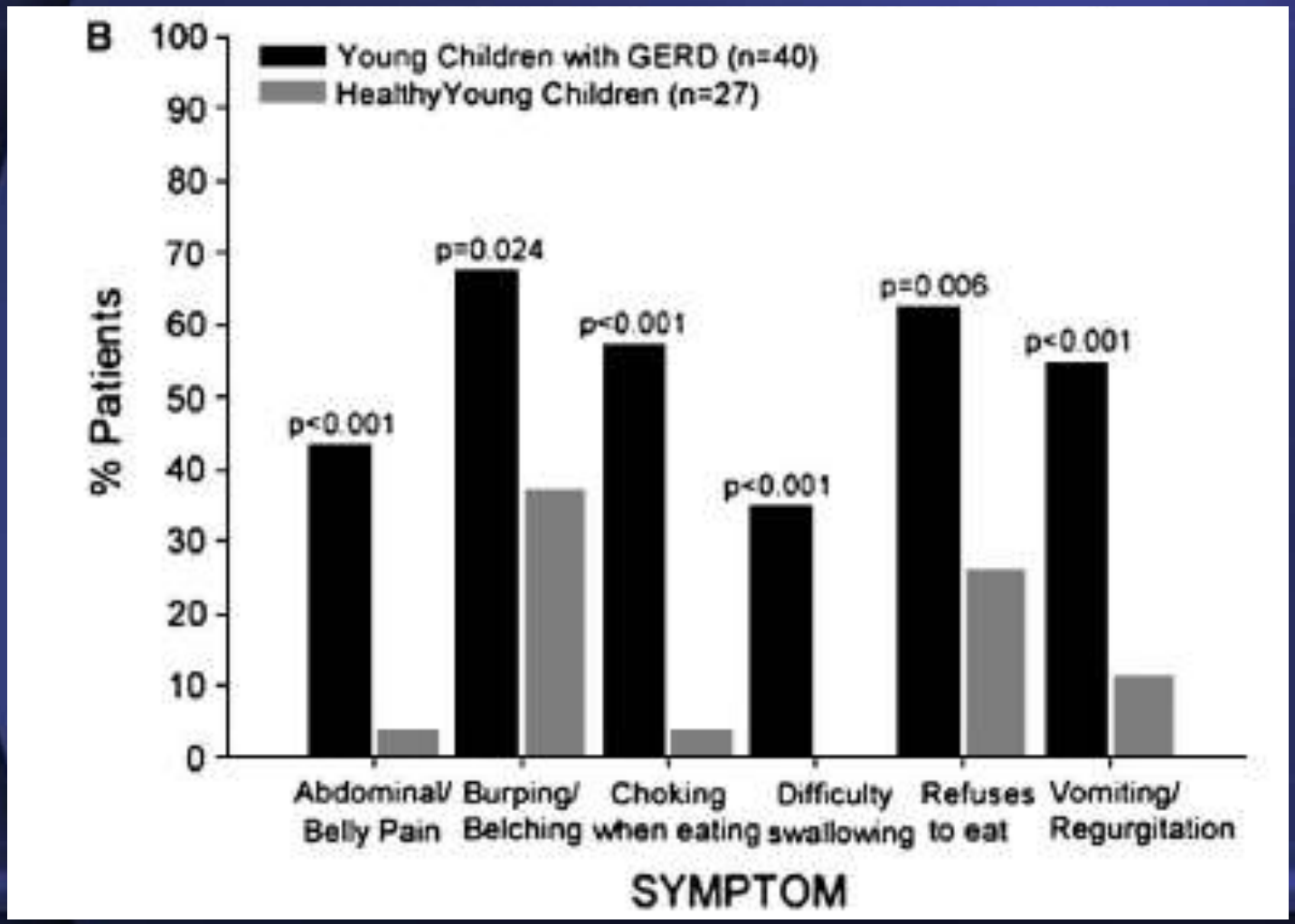
- Retrospective chart review
- 2 groups:
  - 214 children diagnosed with GERD
  - 81 without GERD
- Significant difference in symptoms between groups:
  - Stertor
  - Cyanotic spells
  - Frequent emesis
  - Choking/ gagging
  - Failure to thrive

Symptoms: Infants



Deal L et al. J Pedi Gastro and Nutrition 2005. EBM B

Symptoms: Young children



Deal L et al. J Pedi Gastro and Nutrition 2005. EBM B

Reflux-related Otolaryngologic disorders

- Chronic cough
- Rhinosinusitis
- Laryngitis
- Globus pharyngeus
- Dysphagia
- Airway obstruction
- Apnea
- Asthma
- Recurrent coup
- Laryngomalacia
- Stridor
- Subglottic stenosis
- Vocal cord nodule/ granuloma

Esophageal Biopsy Study

Problem	Positive Biopsy (%)	Negative Biopsy
Asthma	75	25
Recurrent croup	75	25
Cough	81	19
Apnea	75	25
Sinusitis	100	0
Stridor	63	27
Laryngomalacia	75	25
Subglottic stenosis	68	32
Post. Glottic edema	81	19

Yellon R. Am J Med 108: 131S, 2000. EBM B

Chronic Rhinosinusitis

- Reflux-induced chronic inflammation of nasal cavity
- Lack of prospective double-blind RCT
- Concurrent role of allergy
- Phipps CD 2000 (EBM B) :
  - Higher incidence of GER in sinusitis patients
  - Symptoms improved after GER treatment
- Bothwell MR 1999 (EBM C) :
  - 89% (25/28) of sinusitis patients who met criteria for FESS show improvement w/o surgery with GERD treatment

Otitis Media

- Nasopharyngeal inflammation causing Eustachian tube dysfunction
- Crapko 2007
  - Prospective non-randomized
  - Middle ear effusion collected after myringotomy for OME children
  - Pepsin detected in ~ 60% samples
  - pH: 6-7.6 (pepsin inactive)

Chronic cough

- Holinger and Sanders 1991
  - Retrospective
  - 72 children with chronic cough > 1 month and normal chest x-ray
  - Associated with:
    - Asthma (32%), sinusitis (23%), GERD (15%)

Asthma

- Esophageal instillation of acid has been shown to induce bronchospasm and reduce peak flow
- Debley 2006:
  - Prospective cross-sectional study
  - 2397 adolescents
  - GERD 8x more common in asthma patients
  - Higher morbidity (ER/ clinic visits, missed school) from asthma if + GERD

Apnea

- Possible mechanisms: Laryngospasm, aspiration, glottic closure reflex
- Herbst 1979
  - Retrospective
  - 14 infants with apneic events and pH probe proven GERD
  - Apnea resolved after GERD treatment

Reflux-induced stridor

- "Pseudo-laryngomalacia"
- Intermittent, not affected by changes in position
- Mechanisms:
  - Acid induced laryngospasm
  - Rapid breathing with esophageal irritation
- Bouchard S 1999:
  - Retrospective
  - 58% of 105 children with stridor and GERD by pH probe
  - 83% of those improve with anti-reflux meds
- Flexible laryngoscopy to evaluate for laryngomalacia

Laryngomalacia

- Most common cause of stridor in infants
- Prolapse of supraglottic tissues into glottis
- Negative pressure created by prolapse causes upward H^+ flow
- 50-80% laryngomalacia patients with GERD
- Flexible laryngoscopy
- Direct laryngoscopy and bronchoscopy in prolonged symptomatic patients because of risk of synchronous lesion is 15-30 %
- May peform esophagoscopy and biopsy if airway is robust. Otherwise, perform pH probe

Subglottic stenosis

- Acid causes ulceration, basilar hyperplasia, edema of the subglottic mucosa
- Yellon R 1997:
  - Retrospective
  - 80% of 26 children who underwent laryngotracheal reconstruction had at least 1 positive test for GER
  - Barium swallow/ pH monitoring / esophageal biopsy / scintiscan

Diagnostic test for GER/ LPR

- Laryngoscopy
- Bronchoscopy
- Esophagoscopy with biopsy
- Barium Esophagram
- Scintiscan
- 24-hr pH monitoring
- Esophageal intraluminal impedance

Barium Esophagram

- Used mainly if suspect anatomical abnormalities: Achalacia, web, stricture
- Sensitivity: 20-60%
- Specificity: 64-90%
- Positive predictive value: 80-82%
- Limitation: High false negative rate due to short sampling period

Nuclear Scintigraphy

- Oral ingestion of technetium-labeled food
- Also detects aspiration, non-acidic reflux, and gastric emptying
- Sensitivity: 15- 59%
- Specificity: 83- 100%
- Limitations:
  - Only measure initial postprandial period
  - Lack of standardized techniques
  - Lack of normative data

Direct Laryngoscopy and Bronchoscopy

- Limited data in Pediatric population
- Carr MM 2001
- Prospective non-RCT
- Indications for DLB: Trach surveillance, persistent stridor, dysphonia, etc.
- 77 children, 50 (65%) GERD +ve based on:
  - pH monitoring
  - Barium esophagram
  - Scintiscan
  - Esophageal biopsy

Carr et al. (Cont'd)

- Example of Laryngeal findings:
  - **Post-glottic edema**
  - **Arytenoid edema**
  - **TVF edema**
  - **Lingual tonsil enlargement**
- Cricotracheal findings:
  - **Edema**
  - **Cobblestoning**
  - **Subglottic stenosis**
  - **Blunting of carina**
  - **Increased secretions**
- Mild symptom (score = 1), severe (score = 2)
- GERD + group has significantly higher laryngeal and/or cricotracheal scores
- Score $\geq$ 7
  - **Sensitivity: 76%**
  - **Specificity: 86%**

Laryngeal Pseudosulcus

Carr MM 2005

Branski et al. 2002

- Prospective randomized blinded trial
- Adult study
- 120 stroboscopic exam of larynx
- Primary complaint of dysphonia x 6 months
- Analyzed by 5 otolaryngologists
- 5-point scale rating
  - Erythema and edema of anterior commissure, vocal folds, arytenoids
  - GER symptoms

Results of Branski et al.

TABLE I.
Summary of Individual Rater Data for Each Measured Descriptive Variable.

	Rater 1		Rater 2		Rater 3		Rater 4		Rater 5	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Edema										
Anterior	0.2	0.6	1.2	0.9	0.7	0.7	0.7	0.7	0.4	0.9
Membranous folds	1.0	0.9	1.4	1.0	1.4	0.6	1.5	1.0	0.8	1.0
Arytenoids	1.1	1.0	0.2	0.5	1.9	0.7	1.9	0.9	0.7	1.0
Erythema										
Anterior	0.2	0.6	1.3	1.0	1.1	0.6	0.9	0.7	0.3	0.9
Membranous folds	0.6	0.8	1.3	1.0	1.4	0.7	1.0	0.8	0.4	0.9
Arytenoids	1.1	1.0	0.2	0.6	1.9	0.7	1.8	0.9	0.8	1.0
Pachydermia	1.3	1.0	0.5	0.6	1.6	0.7	1.1	0.8	0.6	0.9
Severity of GER	1.2	1.0	0.5	0.6	1.6	0.7	1.7	0.8	0.7	1.0
Likelihood GER component	1.4	1.2	0.5	0.6	1.7	0.7	1.6	0.8	0.6	1.0

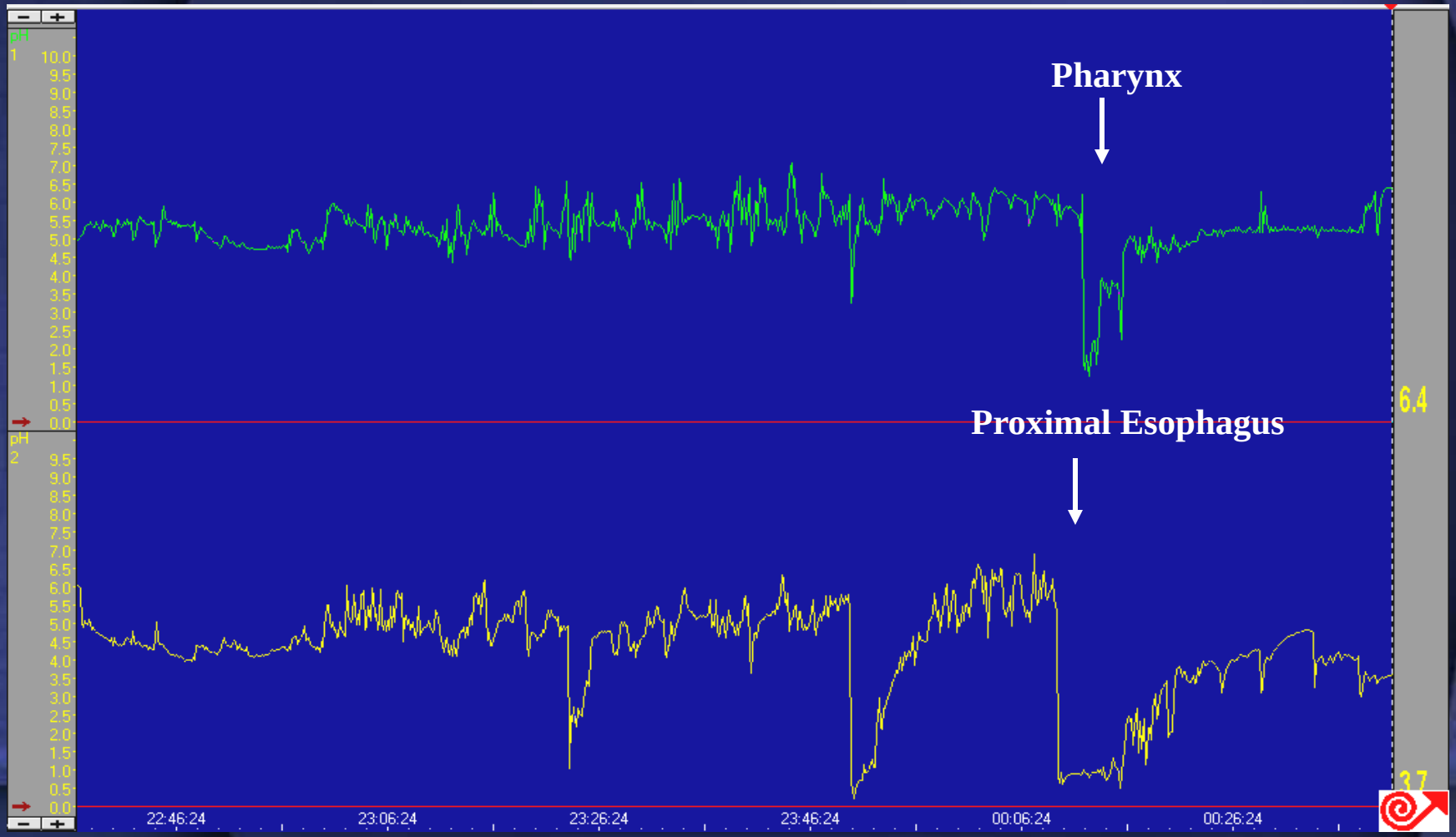
Esophagoscopy with biopsy

- Mucosal changes:
  - Erythema, edema, ulceration, erosion
- Structural abnormalities:
  - strictures, webs
- Histologic esophagitis:
  - Basal cell hyperplasia, increased papillary height, epithelial inflammation
- High positive predictive value
- Low negative predictive value

24-hour pH monitoring

- Measure frequency and duration of acid reflux
- Double pharyngoesophageal probe
  - Proximal: 2 cm above UES
  - Distal: 3 cm above LES
- Reflux episode:
  - pH < 4 for 15-30 s
  - Pharyngeal event must be preceded by esophageal event
  - Acid exposure time

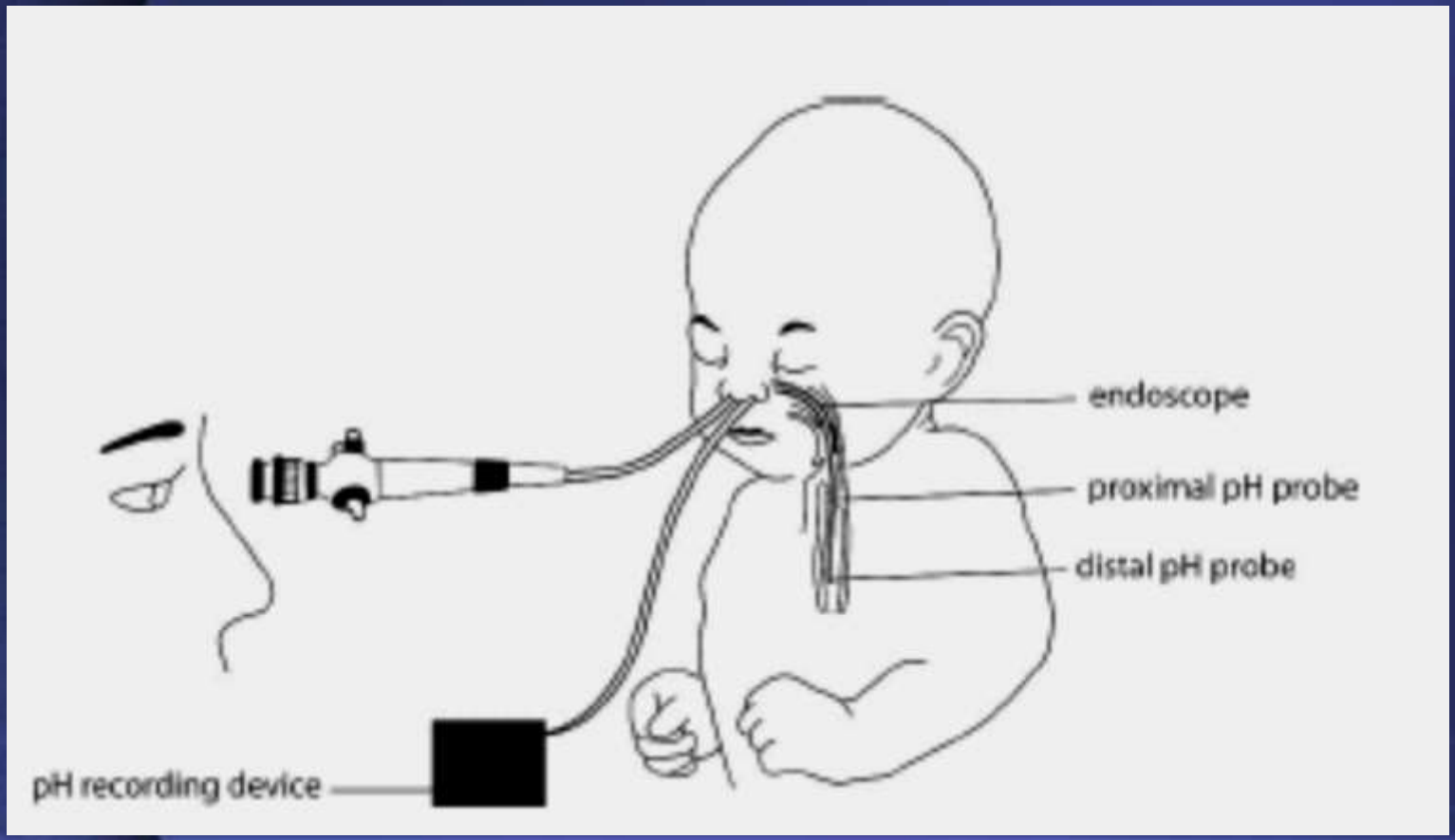
24-hour pH monitoring



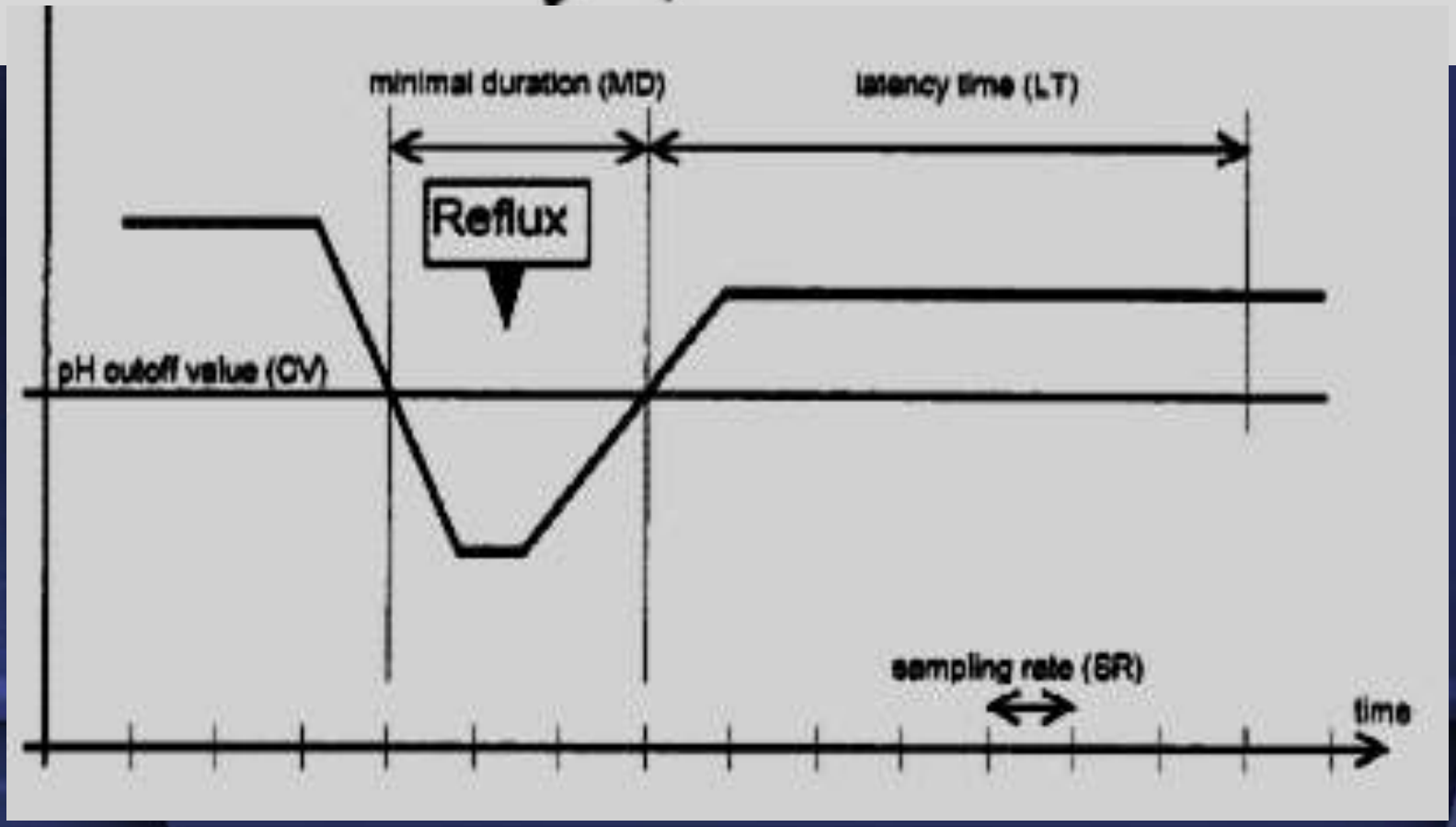
Little JP 1997

- Prospective study of 222 children
- Age: 1 day – 15 years
- 76 % with abnormal reflux finding at either probe
- 46 % with reflux event at pharyngeal probe but NOT esophageal probe
- Patients with laryngeal abnormalities, and emesis had significantly more pharyngeal acid reflux than patients with non-respiratory symptoms.

Ulualp 2007


endoscope
proximal pH probe
distal pH probe
pH recording device


19 seconds
30 seconds
pH channel
pH 4


minimal duration (MD)
latency time (LT)
Reflux
pH cutoff value (CV)
sampling rate (SR)
time

Wenzl 2002

Limitations of pH monitoring

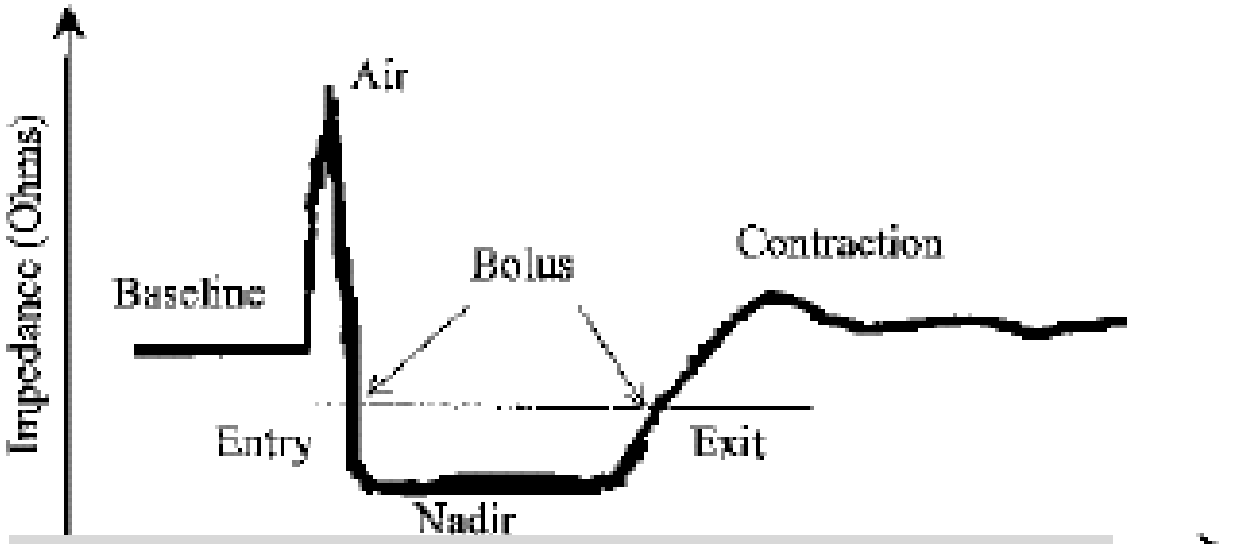
- Patient's factor
  - Inconvenience / discomfort
  - Time consuming
  - Insurance coverage / cost
- May miss intermittent episodes of LPR
- Does not detect non-acidic episodes
- Variability in defining a significant reflux event

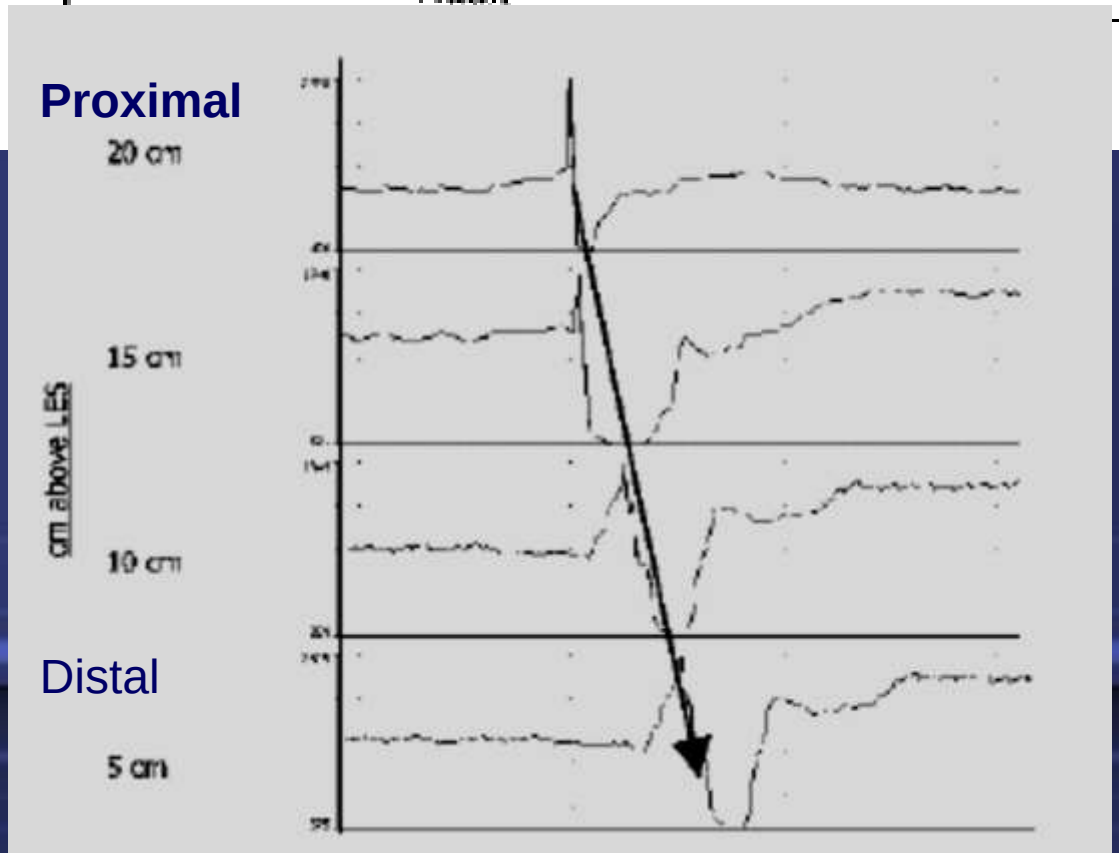
Joniau et al. 2007

- Adult study
- Meta-analysis of 11 prospective studies
- 192 normal controls
- 512 reflux laryngitis diagnosed by reflux symptoms index/ score
- Double probe 24-hour pH monitoring
- No statistical significance in pharyngeal reflux events between normal and reflux laryngitis groups
- Only 38% reflux laryngitis patients show pharyngeal reflux event in pH monitoring

Multi-channel Intraluminal Impedance (MII)

- Measure impedance produced by flow of food bolus (high ionic content and conductivity) in esophagus
- Able to detect passage of solid, liquid, or gaseous bolus
- Intraluminal impedance rapidly decreases as bolus passes through measuring segment
- Can combine with pH probe to detect acidic and non-acidic episodes





Tutuian 2003

pH probe vs. Impedance

- Rosen R 2006
- Prospective non-randomized
- 25 untreated children, 25 treated with PPI
- Sensitivity in untreated group: No difference (~ 80 % vs. 76%)
- In treated group: sensitivity of impedance group significantly higher (80% vs. 47%)

Empiric treatment of LPR

- Widely used but not validated in Pediatric population
- **Lifestyle modification:**
  - Thickening of feeds
  - Prone positioning
  - Weight loss for older children/ adolescent
- **Prokinetic agent:**
- **Acid suppressive therapy:**
  - H2 blocker vs. Proton pump inhibitor (limited data)

Conclusions

- LPR is common among pediatric population and is implicated in many otolaryngologic disorders
- At present, there is no ideal diagnostic tool for pediatric LPR
- Well-designed controlled studies are needed to provide more information for diagnosis and management of pediatric LPR


Thank you!