

## Asthma, GERD and Laryngeal Pharyngeal Reflux (LPR)

Richard F. Lockey, M.D.  
Division of Allergy and Immunology  
Department of Internal Medicine  
University of South Florida  
College of Medicine  
and  
James A. Haley Veterans' Medical Center  
Tampa, Florida, USA

## Outline

1. Definition and Description
2. Symptoms
3. Prevalence and Impact
4. Pathogenesis
5. Complications
6. Diagnosis
7. GERD and Upper Airway Disorders
8. GERD and Asthma
9. Management

## Outline

1. Definition and Description
2. Symptoms
3. Prevalence and Impact
4. Pathogenesis
5. Complications
6. Diagnosis
7. GERD and Upper Airway Disorders
8. GERD and Asthma
9. Management

## Definitions

- GER: backflow of stomach contents into the esophagus, usually acidic
- GERD: abnormal GER
  - DeMeester score with pH probe
  - Dobhan criteria for proximal GERD
  - May result in inflammation of esophagus
- LPR: laryngopharyngeal reflux

## Heartburn

- Heartburn is the most common manifestation of GERD
- The word 'heartburn' is often misinterpreted by patients<sup>1</sup>
- Description of heartburn as "a burning feeling rising from the stomach or lower chest up towards the neck" can help patients to recognize this symptom<sup>1</sup>
- When heartburn is the main or only symptom experienced by a patient, it is strongly suggestive of the presence of GERD<sup>2</sup>

<sup>1</sup>Carlsson et al. Scand J Gastroenterol 1998  
<sup>2</sup>Klauser et al. Lancet 1990

## Definition

- **Laryngopharyngeal Reflux:** a form of gastroesophageal reflux disease that produces prominent symptoms and signs in the pharynx and larynx characterized by acute, chronic, and intermittent laryngitis and pharyngitis.

<http://www.medilexicon.com/medicaldictionary.php>  
December 1, 2010

## Outline

1. Definition and Description
2. Symptoms
3. Prevalence and Impact
4. Pathogenesis
5. Complications
6. Diagnosis
7. GERD and Upper Airway Disorders
8. GERD and Asthma
9. Management

## Atypical symptoms of GERD

- Throat clearing
- Hoarseness
- Globus
- Chronic cough
- Laryngospasm
- Sore throat
- Chest pain
- Wheezing

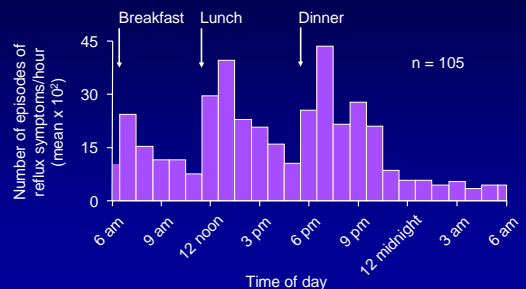
<sup>1</sup>Mujica et al. Postgrad Med 1999  
<sup>2</sup>DeVault et al. Am J Gastroenterol 1999

## Symptom patterns in GERD

- Reflux-related symptoms occur predominantly after meals
- Reflux-related symptoms are often triggered by
  - unusually large meals
  - fatty, spicy, or acidic foods
  - bending, stooping, or lying down
  - lifting, straining, or other strenuous activities
- The frequency of reflux-related symptoms varies widely

Johnsson et al. Gullet 1992

## Distribution of GERD symptoms over 24 hours

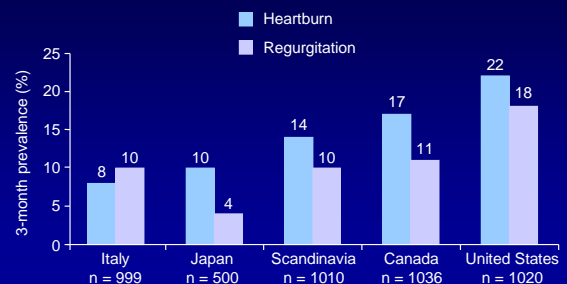


Johnsson et al. Gullet 1992

## Outline

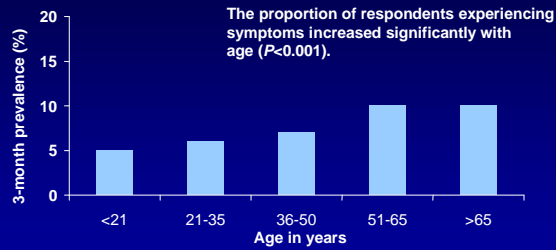
1. Definition and Description
2. Symptoms
3. Prevalence and Impact
4. Pathogenesis
5. Complications
6. Diagnosis
7. GERD and Upper Airway Disorders
8. GERD and Asthma
9. Management

## Prevalence of GERD worldwide



Stanghellini. Scand J Gastroenterol 1999

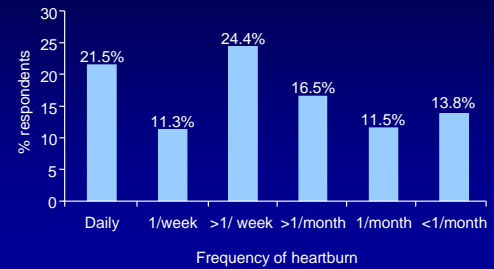
## Age-adjusted prevalence of GERD symptoms: the DIGEST study



N=5581

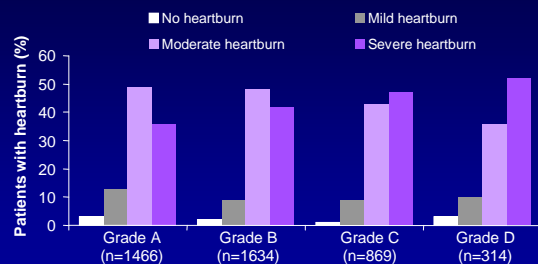
Includes all respondents from US, Canada, European countries, and Japan.  
Stanghellini. Scand J Gastroenterol 1999

## Frequency of heartburn



Oliveria et al. Arch Intern Med 1999

## Severity of GERD symptoms does not correlate with severity of disease



N=4283

Levine et al. Am J Gastroenterol 1999

## Outline

1. Definition and Description
2. Symptoms
3. Prevalence and Impact
4. Pathogenesis
5. Complications
6. Diagnosis
7. GERD and Upper Airway Disorders
8. GERD and Asthma
9. Management

## Pathogenesis of GERD – overview

- GERD results from exposure of the esophageal mucosa to refluxed gastric contents
- In most patients with GERD, exposure of the esophagus to refluxate is greater than normal
- In a minority of patients, exposure is within normal limits; in these patients, GERD may be due to decreased mucosal resistance to refluxate

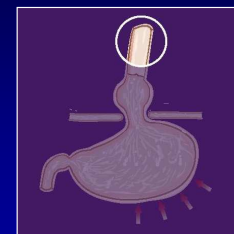
<sup>1</sup>DeVault et al. Am J Gastroenterol 1999

<sup>2</sup>Dent et al. Gut 1998

<sup>3</sup>Shi et al. Gut 1995

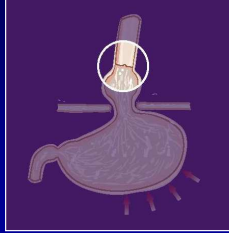
## Defective esophageal clearance

- Ineffective peristalsis
- Reduced salivary secretion
- Reduced secretion from esophageal submucosal glands



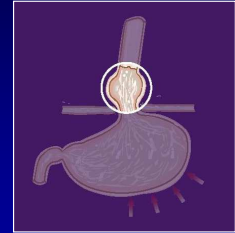
## LES 'dysfunction'

- Inappropriate and prolonged transient relaxations
- Reduction in basal LES pressure/tone



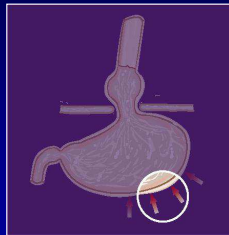
## Hiatal hernia

- May trap a reservoir of gastric contents above the diaphragm, increasing reflux
- May compromise LES function



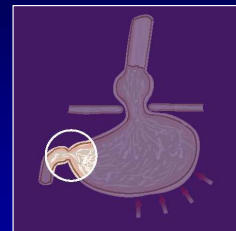
## Increased intra-abdominal pressure

- Pregnancy
- Obesity
- Bending
- Straining
- Coughing
- Tight clothes

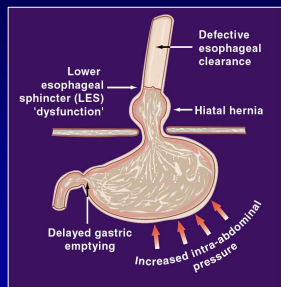


## Delayed gastric emptying

- May result in an increase in the volume of gastric contents available for reflux into the esophagus
- Exact role in GERD remains to be clarified



## Causes of increased exposure of the esophagus to gastric refluxate



## Medications that may aggravate GERD symptoms by damaging the esophageal mucosa

- Tetracycline
- Quinidine
- Potassium chloride tablets
- Iron salts
- Aspirin and other NSAIDs
- Bisphosphonates

## Medications that may aggravate GERD symptoms by impairing LES function

- $\beta$ -adrenergic agonists
- Theophylline
- Anticholinergics
- Tricyclic antidepressants
- Progesterone
- $\alpha$ -adrenergic antagonists
- Diazepam
- Calcium channel blockers

## Outline

1. Definition and Description
2. Symptoms
3. Prevalence and Impact
4. Pathogenesis
5. **Complications**
6. Diagnosis
7. GERD and Upper Airway Disorders
8. GERD and Asthma
9. Management

## Complications of GERD

- Esophageal
  - Barrett's esophagus
  - adenocarcinoma
  - stricture
  - ulceration
  - bleeding
- Extra-esophageal
  - asthma
  - reflux laryngitis
  - vocal cord ulcers
  - subglottic stenosis
  - tracheal stenosis

## Outline

1. Definition and Description
2. Symptoms
3. Prevalence and Impact
4. Pathogenesis
5. Complications
6. **Diagnosis**
7. GERD and Upper Airway Disorders
8. GERD and Asthma
9. Management

## Diagnostic methods in GERD

- History
- Rhinoscopy
- Endoscopy
- Empiric therapy
- pH monitoring
- Radiology

## History

- History-taking is the primary diagnostic tool for GERD
- Typical GERD can usually be diagnosed on the basis of history alone

## Outline

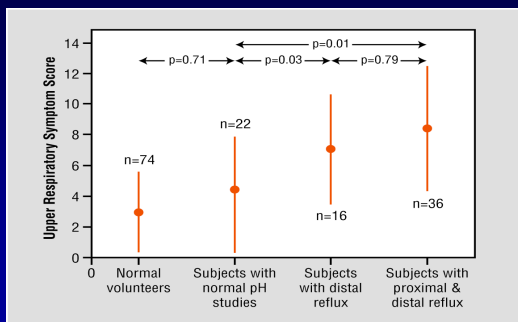
1. Definition and Description
2. Symptoms
3. Prevalence and Impact
4. Pathogenesis
5. Complications
6. Diagnosis
7. GERD and Upper Airway Disorders
8. GERD and Asthma
9. Management

## GERD and Chronic Rhinosinusitis

- Upper respiratory symptoms frequent among subjects with symptomatic GERD Dx'd by esophageal study
- GERD associated with chronic rhinosinusitis in children and adults

Theodoropoulos DS et al. *Am J Respir Crit Care Med* 2001;164:72-6  
 Barbero G.J. *Otolaryngol Clin North Am* 1996;29:27-38  
 Phipps CD et al. *Arch Otolaryngol Head Neck Surg* 2000;126:831-6  
 Ulualp SO et al. *Am J Rhinol* 199;13:197-202  
 DiBaise et al. *Ann Int Med* 1998;129:1078-83

## GERD and Upper Airway Disorders

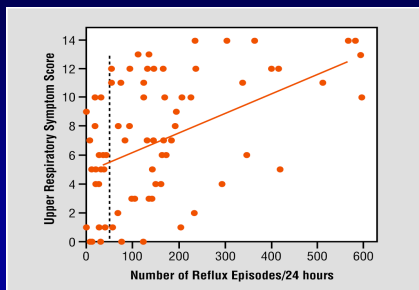


Theodoropoulos DS, Ledford DK, Lockey RF et al. *Am J Respir Crit Care Med* 2001;164:72-76

## GERD and Upper Airway Disorders Pathophysiology

- Direct irritation by acid
- Neurogenic reflex (increased vagal tone)
- Neurogenic inflammation
- Visceral sensitivity

## GERD and Upper Airway Disorders Pathophysiology



Theodoropoulos DS, Ledford DK, Lockey RF et al. *Am J Respir Crit Care Med* 2001;164:72-76

## GERD and Upper Airway Disorders Pathophysiology

### Odds Ratio of GERD

URS Score > 4	1.5
URS Score = 8	3.8
URS Score = 11	6.8

Theodoropoulos DS, Ledford DK, Lockey RF et al. *Am J Respir Crit Care Med* 2001;164:72-76

## GERD and Upper Airway Disorders Pathophysiology

### Upper Airway Symptoms Related to GER or GERD

- Throat clearing
- Voice change
- Hoarseness
- Cough
- Post nasal drip
- Nasal congestion

Theodoropoulos DS, Ledford DK, Lockey RF et al. *Am J Respir Crit Care Med* 2001;164:72-76

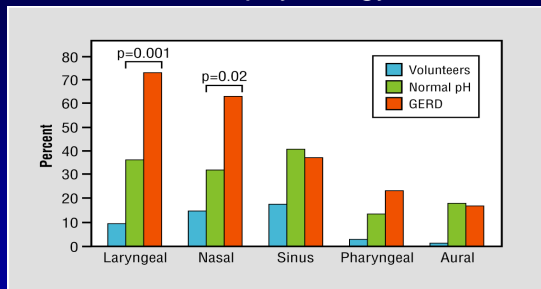
## GERD and Upper Airway Disorders Pathophysiology

### Upper Airway Symptoms Possibly Related to GER or GERD

- Rhinorrhea
- Sneezing
- Sinusitis
- Sinus Headache
- Ear ache/fullness
- Otitis media with effusion
- Serous otitis media
- Upper airway itching

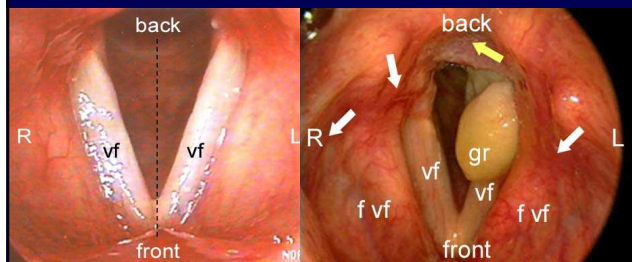
Theodoropoulos DS, Ledford DK, Lockey RF et al. *Am J Respir Crit Care Med* 2001;164:72-76

## GERD and Upper Airway Disorders Pathophysiology



Theodoropoulos DS, Ledford DK, Lockey RF et al. *Am J Respir Crit Care Med* 2001;164:72-76

## GERD and Upper Airway Disorders



From www.voiceproblem.org

## Outline

1. Definition and Description
2. Symptoms
3. Prevalence and Impact
4. Pathogenesis
5. Complications
6. Diagnosis
7. GERD and Upper Airway Disorders
8. GERD and Asthma
9. Management

## GERD and Asthma

- William Osler noted "... attacks may be due to direct irritation of the bronchial mucosa or ... indirectly, too, by reflex influences from the stomach...".
- Up to 80% of patients with asthma have GERD.

Smith LJ, Winslow C. Asthma and Surgery. In *Asthma & Rhinitis 2*. Bussee W and Holgate S (eds). Blackwell Science 2000, pp 1834-5.

## Risk factors for exacerbation of difficult-to-treat asthma

136 subjects

- 39 had 3 severe exacerbations/yr
- 29 had 1 severe exacerbation/yr

Brinke, et al. *Eur Respir J* 2005; 26: 812.

## Conclusions

- 1) Odds ratio (OR) associated with 3 exacerbations
  - a) severe sinus disease, OR 3.7
  - b) GERD, OR 4.9
  - c) URIs, OR 6.9
  - d) Psychological dysfunction, OR 10.8
  - e) Obstructive sleep apnea, OR 3.4
- 2) All patients with frequent exacerbations had 1/5 while 52% had 3/5

Brinke, et al. *Eur Respir J* 2005; 26: 812.

## Effects of 24 weeks of lansoprazole on asthma in patients with GERD symptoms

Multicenter, DB, randomized, placebo-controlled trial of 206 subjects with moderate-to-severe asthma with reflux symptoms given lansoprazole, 30 mg bid vs. placebo.

Littner MR, et al. *Chest* 2005; 128: 1128.

## Conclusion

Did not improve symptoms by:

- a) Assessment by:
  - 1) participant
  - 2) investigator
- b) Pulmonary function studies
- c) Decrease in albuterol use

But did:

- a) **Decrease asthma exacerbation**
- b) **Improve quality of life.**

Littner MR, et al. *Chest* 2005; 128: 1128

## Cochrane Data Base Review of GERD Treatment for Asthma in Adults and Children (2006)

- 12 randomized controlled trials of Rx for GERD in adults and children
- 2 independent reviewers
- Interventions included proton pump inhibitors (6), H<sub>2</sub> receptor antagonists (5), surgery and conservative management (1)
- Temporal relationship in 4 trials found between asthma and GERD
- Anti-reflux Rx did not consistently improve lung function, asthma symptoms, nocturnal asthma and medication use
- **Conclusion: No overall improvement but subgroups may gain benefit**

## GERD and Asthma

- Kiljander TO et al. *Am J Respir Crit Care Med* 2006;173:1091-7
  - 24 week DBPC trial in subjects with asthma and nocturnal asthma symptoms, GERD or both
  - PPI twice daily
  - No benefit in peak flow, exacerbations or asthma symptoms
  - Subjects with both nocturnal symptoms and GERD had increase in peak flow but not improvement in FEV<sub>1</sub>, rescue inhaler use, symptoms scores or nocturnal awakening



### **Am Respir Crit Care Med 2009; 180:809-16**

- 304 subjects with inadequately controlled asthma
  - 53% had GERD by 24 hr pH probe
  - 38% had proximal GERD (subset of 242)
- GERD was **NOT** associated with SABAs, ICS dose, BHR, PFT (proximal or distal GERD did not affect results)
- GERD was associated with oral CS, AQOL
  - Proximal lowest QOL

### **GERD and Asthma**

- American Lung Association Asthma Clinical Research Centers NEJM 2009;360:1487-99.
  - 6 month DBPC trial of 412 with persistent asthma with therapy but without definite symptoms of GERD (GERD symptoms  $\geq 2$  per week not allowed)
    - Treatment esomeprazole 40 mg bid
  - Primary Outcome: episodes of poor asthma control
  - Secondary Outcome: BHR, spirometry, symptom scores, QOL, nocturnal awakenings

### **GERD and Asthma**

- American Lung Association Asthma Clinical Research Centers NEJM 2009;360:1487-99.
- No difference in the 2 groups
  - 2.5 episodes of poor control/yr with esomeprazole, 2.3 episodes with placebo
  - No difference in secondary outcomes
- 40% of subjects with asthma and no GERD symptoms had abnormal 24 hr pH probe

### **Meta Analysis PPI Therapy for Adults with Asthma**

- Chan WW et al. Arch Int Med 2011;171: 620-629
  - 1950 through Jan 2010
  - Primary outcome AM Peak Flow
    - Secondary outcomes PM Peak Flow, FEV1, symptoms and QOL
  - 11 trials with 2524 patients
  - AM Peak Flow increased by 8.68 L/min [95% CI 0.85-32.95]
    - No improvement in any secondary outcome

### **Meta Analysis: PPI Therapy for Adults with Asthma**

- Chan WW et al. Arch Int Med 2011;171: 620-629
  - Conclusion: PPI therapy in adults with asthma results in a small, statistically significant increase in AM Peak Flow that is not of clinical significance. There is insufficient evidence to recommend empirical use of PPIs for routine treatment of asthma in adults.

### **Study of Acid Reflux Therapy for Children with Asthma (SARCA)**

- Presented at ATS meeting in May 2011
- Children with symptomatic asthma on ICS and no symptoms of GERD, 6-16 years of age, DBPCRT
  - Primary outcome: Exacerbations
  - Subset with pH probe data
- No difference in asthma outcomes with PPI and subjects with abnormal pH probe did not benefit, though numbers relatively small

## Outline

1. Definition and Description
2. Symptoms
3. Prevalence and Impact
4. Pathogenesis
5. Complications
6. Diagnosis
7. GERD and Upper Airway Disorders
8. GERD and Asthma
9. Management

## GERD and Asthma and Upper Airway Disorders

### Treatment

- Empiric acid suppression
  - Proton pump inhibitors
  - H2 blockers
- Lifestyle changes
  - Diet
  - Weight loss
  - Cigarette smoking
  - ETOH
  - Elevation head of bed
- Modification of Rx's which aggravate GER
- Increase dose of PPIs after 6-8 weeks
- Confirmatory testing or GI consultation

Thank you!