

What Every Sleep Doctor Needs to Know about Gastroenterology

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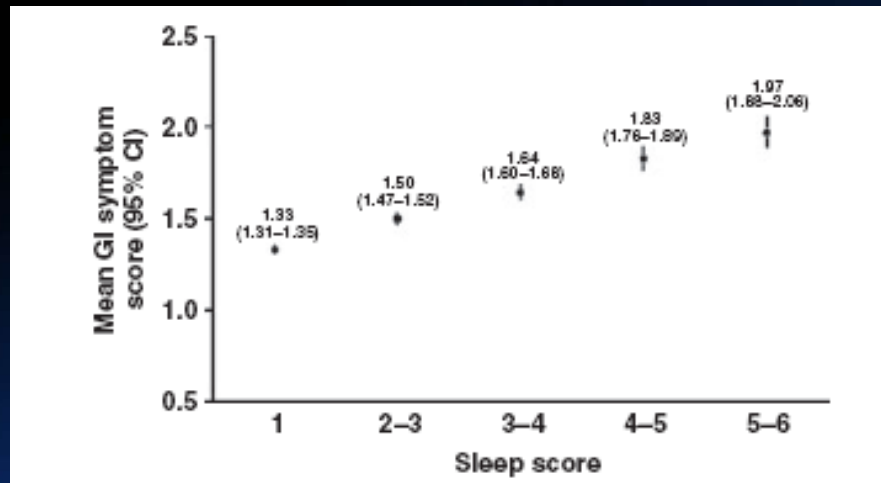
Outline

- Will focus on GERD and IBS—most common
- Pathogenesis of reflux
- Responses to reflux during sleep
- Prevalence of sleep disturbances in IBS



GI Symptom Score vs. Sleep Disturbance in a General Population

(Cremonini F. et.al. Neurogastroenterol. Motil. 2009; 21: 128-135)

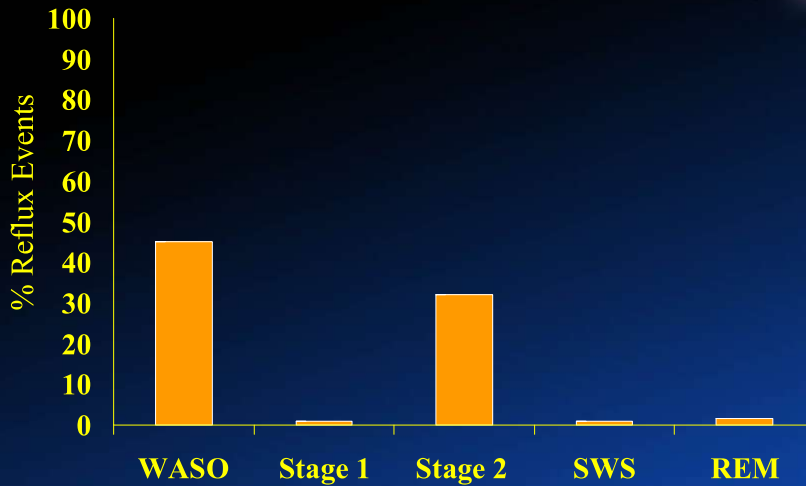


GERD and Sleep Epidemiology

(Jansson et.al. Clin. Gastro. Hep. 2009; 7; 960-965)

- Population based study using data from two large health surveys in Norway
 - 3153 subjects who reported severe reflux symptoms
 - 40212 subjects without reflux symptoms
- Multivariate analysis adjusted for age, sex, smoking, obesity, anxiety and depression
- Positive associations were observed for risk of GERD and:
 - Insomnia complaints (OR = 2.2 P<.0001)
 - Sleeplessness (OR=2.5 P<.0001)
 - Problems falling asleep (OR=2.2 P<.0001)

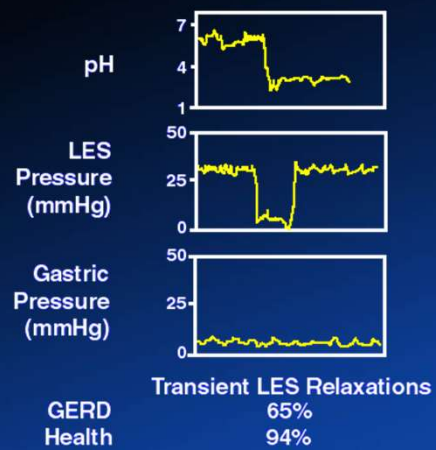
GER During Sleep



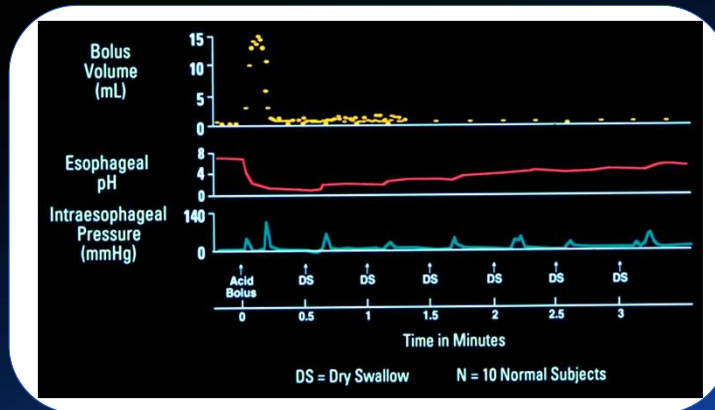
(Penzel et.al. Eur.Resp.J. 1999; 14: 1266-70)

Most Common Cause of GER Transient Lower Esophageal Sphincter Relaxation (TLESR)

Not due to decreased
LES pressure---
majority of reflux
events are due to
TLESR

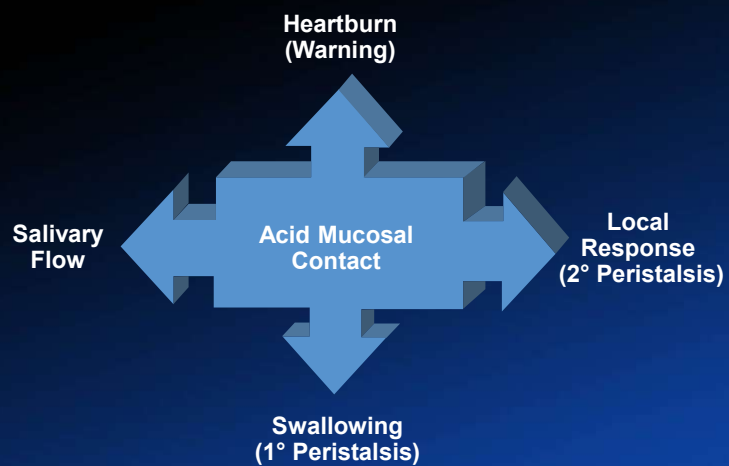


Mechanisms of Esophageal Acid Clearance Volume Clearance and Acid Neutralization



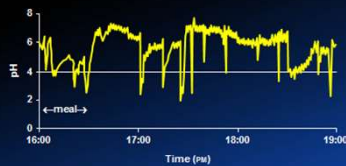
Adapted from Helm JF, et al. *N Engl J Med.* 1984;310:284

Defenses Against Acid Contact All of these are inhibited during sleep

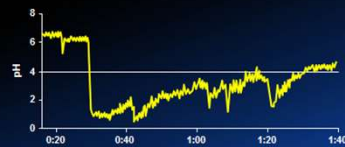


Pattern of Reflux During Daytime and Sleep

Normal Postprandial Reflux (in Normal Volunteer)

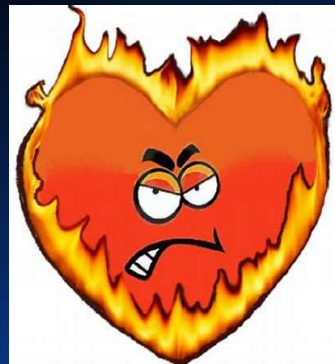


Sleep Reflux Supine Sleep Condition



Sleep Related GER

- The pattern of reflux is notably different during sleep ie fewer reflux events, but longer acid clearance times
- Sleep alters the waking response to acid mucosal contact (**sleep affects GER**)
- GER during sleep causes sleep fragmentation and sleep complaints (**GER affects sleep**)
- May have respiratory consequences (nighttime wheezing)





Clinical Consequences of Sleep Related GER



Sleep Quality and Sleep Related GER

(Dickman et.al. J.Clin. Sleep Med. 2007; 3; 505-513)

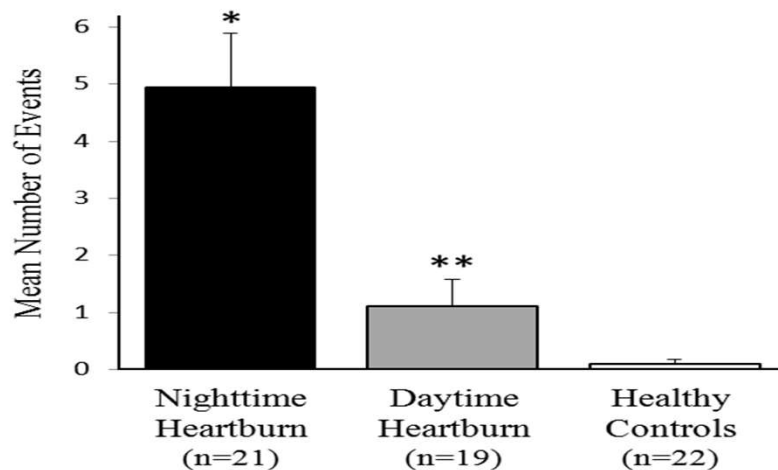
- Studied 48 GERD patients (63% EE)
 - All had 24hr pH monitoring and a variety of sleep and GERD questionnaires
 - 15 had sleep lab monitoring with pH study
- Results
 - Insomnia symptoms were correlated with GERD symptoms ($r=.33$ $P<.05$)
 - Overall sleep quality was negatively correlated with longer recumbent reflux events ($r= -.37$ $P<.01$)
 - Increase in sleep related acid contact time was associated with overall lower reported quality of sleep ($r=.43$ $P<.002$)

Sleep Quality and Sleep Related GER

(Orr et.al. *Diseases of the Esophagus* (2013) **, **--**
DOI: 10.1111/dote.12131)

- Studied 3 groups with PSG and pH monitoring
 - 24 GERD patients with nighttime HB at least twice/wk
 - 23 GERD patients with daytime HB only
 - 25 normal controls with no HB complaint
- Study measures
 - 24hr. pH monitoring with sleep lab monitoring
 - Questionnaires on sleep quality (PSQI and post sleep questionnaire)

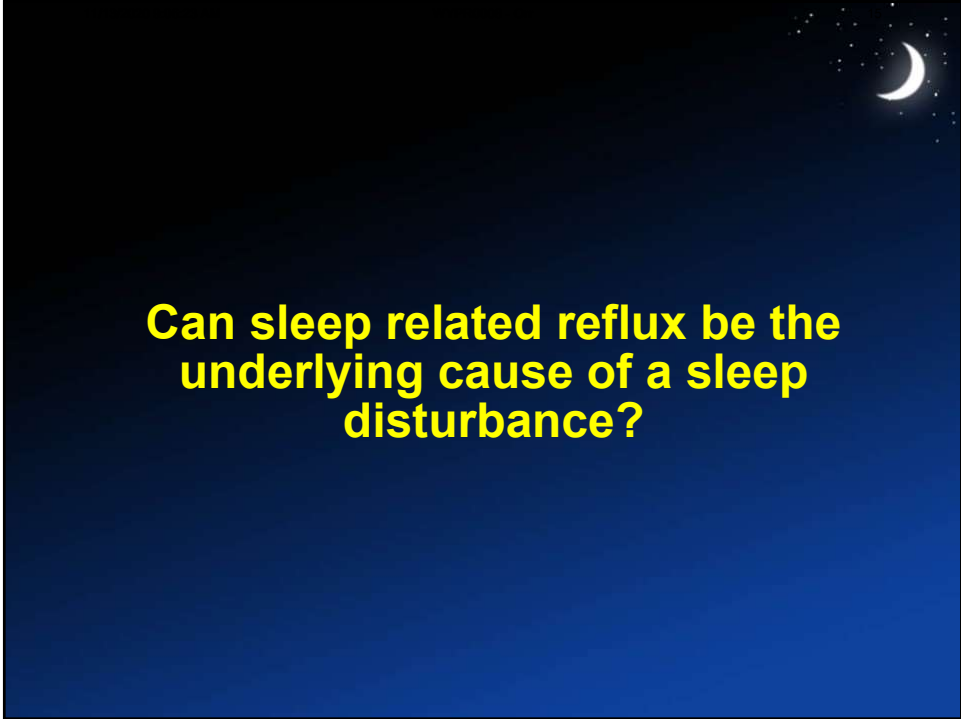
Figure 1. Number of Reflux Events After Sleep Onset by Group



Error bars represent +1 SE of the mean

* $p < .01$ vs. Daytime Heartburn and Normal Controls

** $p < .05$ vs. Normal Controls



Can sleep related reflux be the underlying cause of a sleep disturbance?

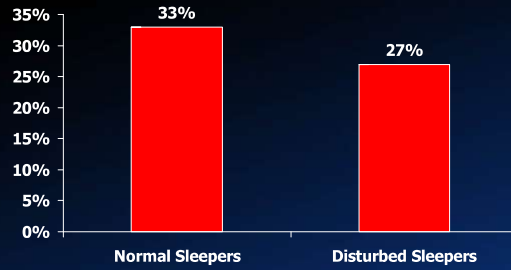


GER in Unexplained Sleep Disorders

(Orr et. al. Clin. Gastro. Hep 2008; 6; 1099-1104)

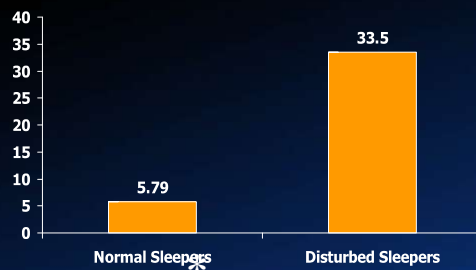
- 104 participants randomized **without symptoms of daytime or nighttime heartburn**
- Patients complained of sleep disturbance at least 3x/wk
- Each patient was studied for two nights in the sleep lab with distal esophageal pH monitoring
- 81 participants across 4 sites with complete data

Participants With Reflux On At Least One Night



NS

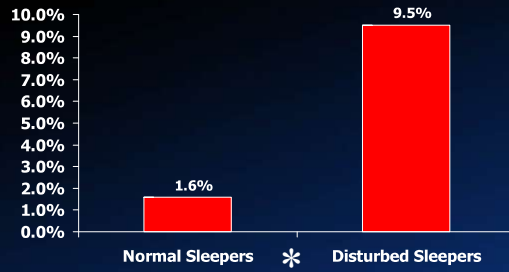
Average Duration of Reflux Events (minutes)



* $P < .01$ vs. Disturbed Sleepers

† One outlier excluded from this analysis

Acid Contact Time (among those with reflux only)



* $p < .01$

Is nighttime heartburn a distinct clinical entity?

Is Nighttime Reflux a Distinct Clinical Entity?

(Orr, W. Aliment. Pharmacol. Ther. 2010: 31: 47-56)

- Yes! But why???
- Sleep related GER shows distinct prolongation of acid clearance
- Patients with nighttime heartburn have a greater risk of developing esophagitis
- Patients with nighttime heartburn have a greater incidence of extra-esophageal symptoms (chest pain, cough etc.)
- Quality of life is significantly worse compared to those without nighttime heartburn
- Symptoms can be resolved with aggressive PPI Rx

Sleep alters visceral sensation in GERD

The Relationship Between Intensity Rating Score and Sleep Deprivation During an Acid Perfusion Test



* $p < 0.05$

Schey R *et al.*, *Gastroenterology* 2007; 133:1787-1795

Sleep Disturbance in Irritable Bowel Syndrome (Tu *et al.* *Neurogastro. Motil* 2017; 29; 1-11)

- Reviewed 21 studies (1169 IBS and 578 controls)
- Most measures were PSQI and daily diaries (2 weeks-8 weeks)
- Most studies employed both subjective (questionnaires or diaries) or objective (PSG) measures
- 71% reported some sleep complaint
- Frequently cited results of subjective measures (1145 subjects)
 - poor sleep quality
 - prolonged sleep latency
 - daytime dysfunction



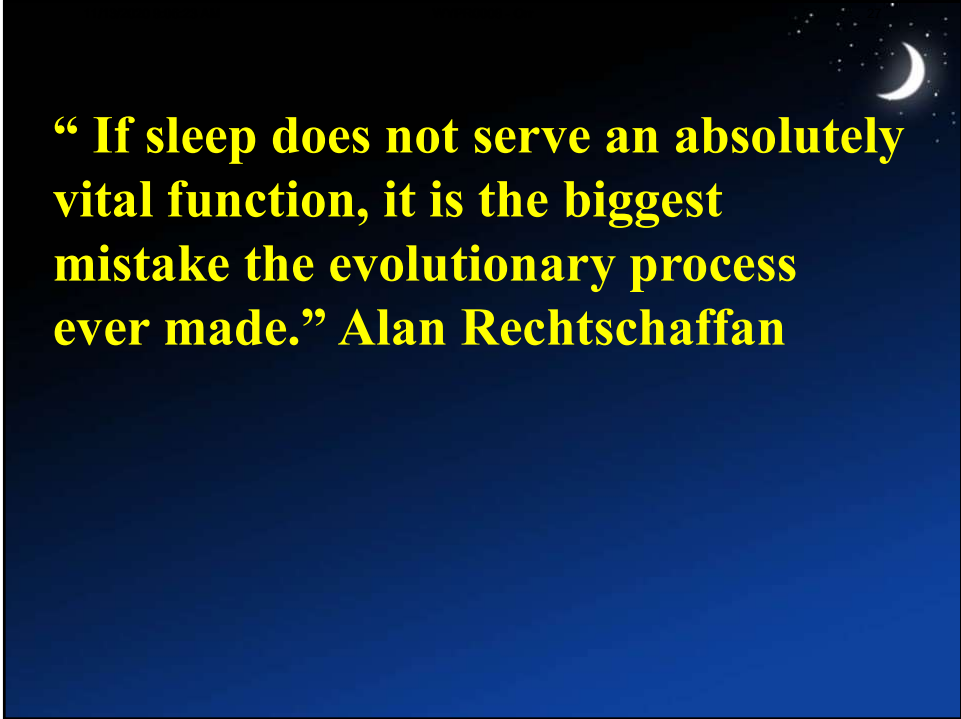
Sleep Disturbance Predicts Next Day Symptoms in IBS

(Buchanan et. al. J. Clin. Sleep Med. 2014; 10; 1003-1009)

- Sleep disturbance is commonly noted in patient with IBS
- Studied 24 women with IBS
- Used subjective (daily logs of sleep quality) and objective (actigraphy) measures of sleep.
- Daily log of IBS symptoms
- Studied over one full menstrual cycle
- Subjective reports of sleep disturbance significantly predicted next day symptoms of abdominal pain, anxiety and fatigue
- Daytime symptoms did not predict subsequent sleep
- This may relate to altered visceral sensitivity secondary to sleep disturbance

Conclusions

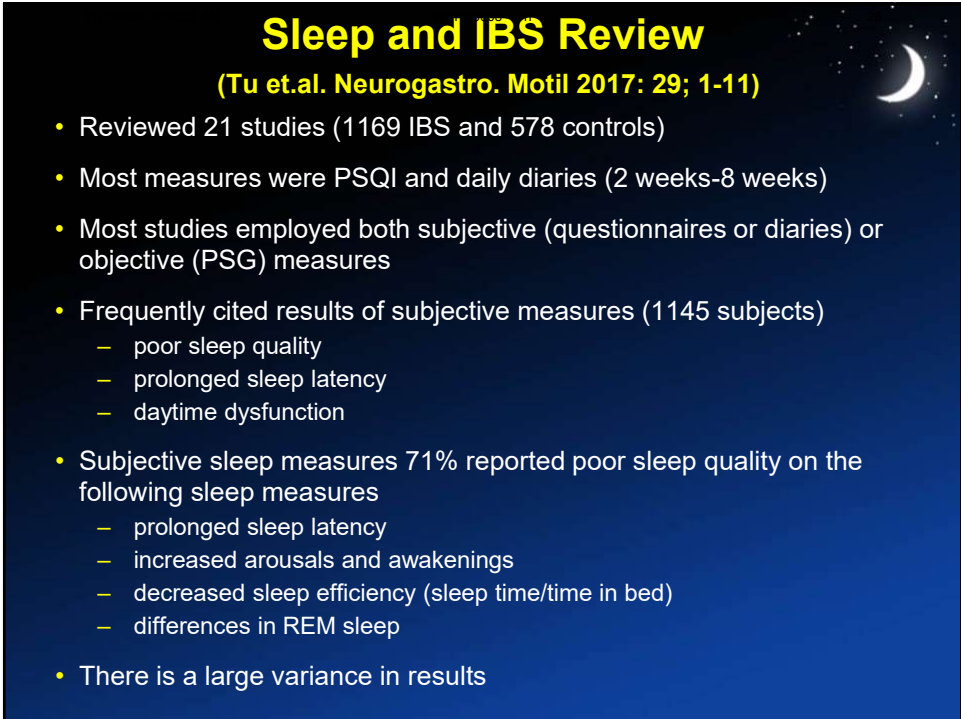
- Nighttime heartburn and associated sleep disorders are common among patients with GERD
- Physiological changes associated with sleep produce significant alterations in responses to acid mucosal contact
- Clinical consequences of sleep related GER argue that this is a distinct clinical entity requiring a more aggressive approach to treatment
- Sleep disorders are commonly noted in IBS patients and this may play an important role in the development of symptoms
- Clinicians should inquire about the presence of nighttime heartburn as well as it's frequency and severity as an indication of more severe and complicated GERD



“ If sleep does not serve an absolutely vital function, it is the biggest mistake the evolutionary process ever made.” Alan Rechtschaffen

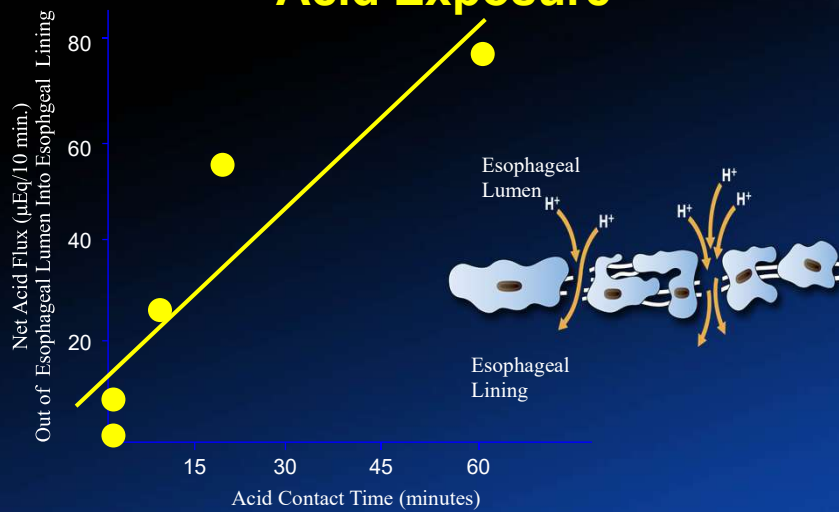
Sleep and IBS Review

(Tu et.al. Neurogastro. Motil 2017: 29; 1-11)

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- Reviewed 21 studies (1169 IBS and 578 controls)
 - Most measures were PSQI and daily diaries (2 weeks-8 weeks)
 - Most studies employed both subjective (questionnaires or diaries) or objective (PSG) measures
 - Frequently cited results of subjective measures (1145 subjects)
 - poor sleep quality
 - prolonged sleep latency
 - daytime dysfunction
 - Subjective sleep measures 71% reported poor sleep quality on the following sleep measures
 - prolonged sleep latency
 - increased arousals and awakenings
 - decreased sleep efficiency (sleep time/time in bed)
 - differences in REM sleep
 - There is a large variance in results

Why is acid mucosal contact important?

H⁺ Ion Movement and Duration of Acid Exposure



L. Johnson and J.W. Harmon, *Experimental Esophagitis in a Rabbit Model: Clinical Relevance*, 8 J. Clin. Gastroenterol. 25 (Supp. 1) (1986)

GERD Symptoms

- GERD symptoms are common—estimated as high as 20% (symptoms once a week)
- GERD symptom manifestation assumes a threshold level of symptom load –interaction of esophageal acid sensitivity and parameters of the refluxate (volume, pH etc.)
- Up to 20% of erosive esophagitis patients are asymptomatic
- The true prevalence is thus unknown



Sleep Related GER and Acid Clearance: The Physiology

- GER does occur during sleep
- Reflux events are less frequent during sleep
- Acid clearance is typically prolonged during sleep
- Sleep markedly alters the physiological response to acid mucosal contact.

Prevalence of Nocturnal GERD Symptoms

Among Patients With Weekly Heartburn—AGA Survey¹



- 57% report waking up during sleep
- 40% report impact on ability to work the next day

Among Patients With GERD Symptoms—Farup et al²



- 54% wake up from sleep

¹American Gastroenterological Association. Gallup Survey. May 2000.
²Farup C et al. *Arch Intern Med.* 2001;161:45-52.

Pathophysiology of GER—Most Commonly Associated with a Transient Relaxation of the Lower Esophageal Sphincter

Altering Transient Lower Esophageal Sphincter Relaxations

