LETTERS TO THE EDITOR

Readers are encouraged to write letters to the editor concerning articles that have been published in CLINICAL GASTROENTEROLOGY AND HEPATOLOGY. Short, general comments are also considered, but use of the Letters to the Editor section for publication of original data in preliminary form is not encouraged. Letters should be typewritten and submitted electronically to http://www.editorialmanager.com/cgh.

Reflux Is Unlikely to Occur During Stable Sleep

Dear Editor:

Regrettably, the article by Gagliardi et al in the September 2009 issue of Clinical Gastroenterology and Hepatology inappropriately reinforces, both in its title and in its contents, the unproven assertion that reflux occurs during stable sleep. Also regrettably, the accompanying editorial by Harding endorses the concept that nocturnal reflux occurs predominantly during stable sleep, even though the important interaction of sleep with transient lower esophageal sphincter relaxations is recognized in this editorial.

There is now ample evidence that the onset of acidification in the distal esophageal body signals the onset of flow of acid gastric contents into the esophagus, usually to within a second or so. Therefore, this is the key time point for any analysis of whether reflux occurs during stable sleep or actually during arousal from sleep. Harding refers to “long reflux episodes (>5) minutes during sleep.” This commonly used but incorrect terminology is misleading, because the period of transient relaxation during which flow can occur usually only lasts about 10 seconds and rarely more than 30 seconds. Harding is really referring to a prolonged episode of esophageal acidification caused by a much briefer flow of acid content into the esophagus. This might seem to be a semantic quibble, but it is important to make this distinction from a mechanistic point of view.

The analysis criteria of Rechtschaffen and Kales were used unmodified by Gagliardi et al. Accordingly, sleep stage was scored as the stage most prevalent within epochs of 30 seconds, on the basis of the polysomnographic recording. This use of 30-second blocks of time is too crude an approach for examination of the cause-and-effect relationship between arousals and the onset of acid reflux.

Some years ago, colleagues and I used a second-by-second polysomnographic analysis approach, adapted from that of Rechtschaffen and Kales. Accordingly, sleep stage was scored as the stage most prevalent within epochs of 30 seconds, on the basis of the polysomnographic recording.

Figure 1. Gastroesophageal reflux after swallowing-induced peristalsis. Onset of reflux is indicated by the dashed line. Before reflux, the lower esophageal sphincter (LES) relaxed appropriately after 2 swallows, which occurred during an arousal from sleep. After the second peristaltic sequence, LES pressure returned to its initial resting value, but it then collapsed without any identifiable precipitating motor event. During this inappropriate LES relaxation, acid reflux occurred, accompanied by a common cavity phenomenon. Immediately after reflux, a feeble, nonperistaltic, simultaneous contraction occurred in the mid and distal esophagus, followed 1 minute later by a single primary peristaltic sequence triggered by 2 closely spaced swallows, which caused only a slight increase in esophageal pH. The subject then fell back asleep. No further swallows or esophageal motor activity occurred until 20 minutes later, when the subject had another arousal. During this 20-minute sleep interval the esophageal pH climbed very slowly but remained <4.0. (Reproduced with permission from the American Society for Clinical Investigation: Dent J, et al. Mechanism of gastroesophageal reflux in recumbent asymptomatic human subjects. J Clin Invest 1980;65:256–267.)
Rechtschaffen and Kales, in a study on overnight reflux in healthy volunteers. As well as polysomnographic recordings, esophageal pH, swallowing, esophageal body motility, and lower esophageal sphincter pressure were monitored. These measurements showed that in the sleep period, transient lower esophageal sphincter relaxations and acid reflux only occurred during wakefulness or arousals. The occurrence of transient lower esophageal sphincter relaxations, consistent with the concept that occurrence of transient relaxations requires the “permission” of higher centers.

These observations do not by any means exclude the possibility that esophageal acidification might lead to an arousal, presumably because of the development of heartburn during sleep, as a result of failure of adequate esophageal acid clearance before a return to sleep after an arousal-related reflux episode. We documented some very long episodes of low pH in the esophagus during sleep in healthy subjects (Figure 1). In such episodes, the brevity of an arousal during which the acid reflux occurred prevented occurrence of any further acid-cleaning esophageal body motor activity until the next arousal. During the period of sleep after the reflux-associated arousal, the low distal esophageal pH changed hardly at all until the next arousal, which usually cleared the acid caused by arousal-associated swallowing. Our data indicate that if such an event actually causes an arousal because it generates symptoms that intrude on sleep, it is because reflux occurred during the prior arousal.

Naturally, it must be conceded that such detailed data on sleep stage and onset of reflux as we gathered in healthy subjects are still not available for patients with reflux disease. Despite this, our study provides a mechanistic framework for building of a better understanding of night-time reflux in reflux disease patients than exists in the more recent literature.

Hopefully, future studies into reflux and sleep, an important and intriguing topic, will use second-by-second analyses. This approach is crucial to understanding the temporally closely related events of arousal and onset of reflux. As a result, the development and testing of therapy for reflux that occurs within the sleep period would hopefully be better targeted. Also on semantics, whatever else is done, it would be helpful to develop terminology but not to use the term sleep-related GER, as suggested by Harding. This term blurs an already well-demonstrated cause-and-effect relationship and is only a little better than “supine GER.”

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Conflicts of interest
The authors disclose no conflicts.


Reply. The comments of Professor Dent are greatly appreciated. Our current study did not measure transient lower esophageal sphincter relaxation, only esophageal pH. In all cases, acid reflux events preceded the arousal response, not the opposite as suggested by Dent. Thus, it would seem that reflux causes arousal, not arousal causing reflux.

The polysomnographic recordings in our study clearly show the relationship in a very objective manner. The arousals in response to an acid reflux event were not associated with symptoms of heartburn. The arousal response was inhibited by the hypnotic, prolonging swallow-induced clearance. Dent’s suggestion that an arousal causes reflux would lead to the opposite outcome.

The 1980 study of Dent cannot be extrapolated beyond historic importance. The studies evaluated reflux in relation to transient lower esophageal sphincter relaxation in normals. Our study documents the central asymptomatic arousal response to reflux, as recorded by polysomnography, under the influence of a hypnotic in proven reflux patients. The relationship of gastroesophageal reflux and sleep disorders is a challenging field of investigation.

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The authors disclose no conflicts.

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Prevalence, Diagnosis, and Profile of Autoimmune Pancreatitis Presenting With Features of Acute or Chronic Pancreatitis

Dear Editor:

The article by Sah et al in the January edition of Clinical Gastroenterology and Hepatology is an outstanding overview of a large series of patients with autoimmune pancreatitis (AIP). I find it interesting that most patients with AIP had elevated immunoglobulin G (IgG) 4 levels despite their clinical presentation. The IgG4 level is an important tool in working up suspected patients, but the authors do not mention what hap-