Excluding unusual environments (such as outer space, reverse Trendelenburg position, classrooms, or baby strollers), sleep typically occurs with the patient in the supine position. This position often allows the stomach contents to remain in contact with the opening to the lower esophagus and provides the opportunity for gastroesophageal reflux to occur. Going to bed immediately after a meal or conditions with delayed emptying increase the amount and proximity of gastric contents to the lower gastroesophageal sphincter. Obesity also contributes to the likelihood of GER while in the supine position by increasing intra-abdominal pressures and decreasing the gastric volume. Because the majority of the factors are present in all sleeping individuals, the likelihood of GER is increased even in individuals without evident disease.

Two studies\(^1,2\) have demonstrated the amount and frequency of GER that occur in healthy subjects. Huxley and colleagues\(^2\) assessed the incidence of aspiration during sleep and under conditions of depressed consciousness. Their data demonstrated that 45% of sleeping patients and more than 70% of individuals with depressed consciousness had some degree of aspiration. Gleeson and

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colleagues\(^1\) sought to extend the work of Huxley and associates and determine the amount of aspirate that occurred in the sleeping individual. Similar to the findings of Huxley and colleagues, nearly 50% of the subjects were found to have detectable levels of radioactive tracer in the pulmonary parenchyma after one or both of the two study nights. Although GER was frequent, the aspirated volumes were small (0.01 mL to 0.2 mL) and were not likely to be clinically significant. Together, these data show that a significant portion of healthy individuals have GER regularly and suggest that factors decreasing the protective mechanisms will likely increase the frequency and volume of the aspirate.

The upper airway’s involvement in GER is not intuitively evident, as most factors studied affect the lower esophageal sphincter (LES). The upper airway, however, can be adversely affected by GER and may also have a pathophysiologic role in the development of GER.\(^3\) Abnormalities in the cough generation, defective acid clearance mechanisms, the role of the upper airway in the generation of arousals,\(^4\) age,\(^5\) and disorders of respiration\(^6\)–\(^9\) may all play a role in the development and pathophysiology of GER.

In obstructive sleep apnea (OSA), the upper airway narrows or closes intermittently during sleep, resulting in increased airflow resistance with a decrease in airflow or complete cessation of airflow.\(^9\) The source of the problem relates to the structure of the upper airway and functional interrelationships involving the pharyngeal muscles. The pharyngeal muscles may be separated into two functional groups: a pharyngeal dilator group and a pharyngeal constrictor group. At the beginning of each normal breath, there is tonic activation of the pharyngeal dilator mechanism that maintains the patency of the pharynx throughout inspiration. In OSA, the pharyngeal dilator mechanism is dysfunctional; structural abnormalities of the airway or physical obstructions to airflow cause intermittent obstruction of the airflow during sleep. The reduction in airflow or the increase in airway resistance (or both) can arouse the patient and fragment sleep. Fragmentation of sleep leads to sleep deprivation and a depression of sensorium that may decrease the ability to protect against aspiration. In addition, when airway obstruction or an increase in airway resistance occurs, the normal response increases muscle effort and leads to increasingly negative intrathoracic pressures.

Recurrent increases in the transdiaphragmatic pressure gradient associated with increased respiratory effort, as have been shown to occur in OSA, could contribute to GER by increasing the pressure gradient across the LES and facilitating a retrograde flow of gastric contents. Although the transdiaphragmatic pressure gradient during respiratory events should be proportional to the degree of obstruction and the respiratory drive, variation in respiratory events between patients\(^10\)–\(^11\) makes any correlation with severity difficult.\(^12\) In addition, the effect of a patient’s age\(^5\)–\(^13\) or sleep stage (or both) on respiratory effort has been proposed as a confounding influence. In a study of more than 100 patients, Krieger and coworkers\(^13\) assessed the influence of both age and sleep stage on respiratory effort during obstructive respiratory events. In their study, only patients with moderate to severe sleep apnea were included and effort was assessed using esophageal pressure monitoring. All the separate indices of respiratory effort demonstrated consistent trends across conditions. Their findings were consistent with the concept that the intensity of the respiratory effort is less during rapid-eye-movement (REM) sleep and declines with advancing age but does not correlate with the frequency of respiratory events.

Mechanisms of gastroesophageal reflux during sleep
Several mechanisms have been proposed to increase GER in patients with OSA, including low negative intrathoracic pressures, arousals, movements, low esophageal sphincter tone, and an increase in the pressure gradient from the stomach to the lower esophagus. The most common mechanism proposed to cause GER in patients with OSA, marked negative intrathoracic pressure, has been evaluated in several studies. Graf and associates\(^12\) attempted to determine if GER events were related to the severity of OSA. They used the apnea index (AI) as a marker of severity and separated patients into two groups (AI > 5 to < 15, and AI > 15). The results suggest that a direct link between GER and OSA is unlikely; however, the authors did not account for the poor correlation between AI and OSA severity. Heinemann and colleagues\(^14\) found that 68% to 76% of patients with OSA had significant GER. The majority of these studies indicate that no direct association exists between obstructive respiratory events and the occurrence of GER events.

Penzel and associates\(^7\) attempted to correlate waking and sleeping events in patients with OSA and found that the accumulated time with low esophageal pH readings was higher during the day than at night, but did note that 71% of the sleeping events were preceded by respiratory events. These data would suggest that OSA is unlikely to cause GER events through alterations of intrathoracic pressures during respiratory events; however, these data should not be interpreted as meaning that there is no relationship between the two diseases or that they are independent. The increased incidence of GER in OSA suggests that an association exists, but it may be more complex than originally thought and would need to account for differences in sleep stage, respiratory effort, effects of age, and extent of GER not related to OSA.

Effect of nasal continuous positive airway pressure on gastroesophageal reflux
Positive airway pressure, most commonly in the form of nasal continuous positive airway pressure (CPAP), is used to treat OSA in the majority of patients.\(^9\) Continuous positive airway pressure functions primarily by splinting the upper airway and reducing the obstruction to
airflow. In turn, the effective application of CPAP reduces or normalizes the negative intrathoracic pressures that are generated when trying to breathe against a closed glottis. Thus, there is a reduction in the pressure gradient across the LES that favors GER. Kerr and colleagues demonstrated the reduction in GER by CPAP during two consecutive days of esophageal pH monitoring in six patients with symptomatic GER and OSA. When the patients were treated with CPAP, the percent of time with an esophageal pH less than 4 dropped from 6.3±2.1 to 0.1±0.1 along with a decrease in frequency of GER. These effects were attributed to the reduction in arousals, movement, and a normalization of intrathoracic pressures. A subsequent study with healthy volunteers assessed the effect of CPAP on esophageal pressures and peristalsis. Continuous positive airway pressure effectively increased the esophageal pressures by 4.4 cm H2O and LES pressure by 13.2 cm H2O. These data and those of others suggest that the antireflux effect of CPAP is non-specific and might be due to increases in intraesophageal pressure, as opposed to intrathoracic pressures, or possibly due to reflex increases in LES tone. More recently, Founier and colleagues studied these mechanisms and found that there was no discernible increase in LES tone and that esophageal pressures were elevated, but this effect was probably due to external compression as opposed to increased intraluminal pressures.

**Treatment**

Although the association between GER and OSA has been questioned by some, the high incidence (53% to 76%) of GER in patients with OSA would suggest that some form of association between the two disorders exists and may affect treatment. The lack of an association between severity of OSA and GER would suggest that therapy should not be tailored to the severity of OSA, but rather to the severity and persistence of GER symptoms (Figure 1). These factors should be addressed early in the course of treatment. Once GER is identified, therapeutic interventions should not be delayed as the adverse effects on sleep may complicate the sleep study.

In contrast, patients with previously diagnosed and treated OSA must be evaluated to determine if previous or current intervention or both are effectively managing the patient’s OSA. In the setting in which therapy is found to be less than optimal, the clinician should consider alternative interventions to improve treatment efficacy. If the patient is not currently using positive airway pressure, then it should be strongly considered as it has been shown to decrease GER in OSA. In some patients, CPAP or bi-level positive airway pressure may be an ineffective therapy; however, lack of effectiveness is most commonly due to the patient’s nonadherence to the regimen. Surgical interventions many times do not provide effective control of OSA, and frequently, these patients have never been reevaluated after their surgery. Patients who have not had follow-up polysomnography to verify effectiveness, those with continued symptoms, or those whose symptoms have returned should be sent for an evaluation. Recurrence of OSA symptoms after surgery is known to occur in 40% to 50% of the patients who have an initial improvement. The recurrence usually occurs 3 to 5 years afterward.
after the surgery. Other modes of therapy should be similarly evaluated. In addition, if the patient has gained weight or has had difficult-to-control cardiovascular disease develop, then, polysomnography should also be repeated.

Because of the relatively high incidence of GER in OSA, the tendency would be to perform polysomnography on all patients with GER. The routine application of this practice should be discouraged unless appropriate clinical indications exist. The majority of patients with GER are not likely to have OSA. For this reason, GER does not serve as a good screening indicator of OSA. Nonetheless, OSA is a common disease and can complicate the therapy of GER. Therefore, patients with GER should be screened for symptoms that might suggest the presence of OSA, and finding such symptoms should lead to the consideration of polysomnography. The most common and suggestive historical elements are listed in Figure 2.

Medical therapy for GER in patients with OSA should be initiated by addressing several lifestyle changes in an attempt to reduce inciting factors (Figure 3). Many of these interventions have not been tested in clinical trials, but many patients find these changes reduce symptoms. In comparison to histamine 
H2-receptor blockers, the degree of improvement achieved by elevating the head of the bed is similar. The next increment in therapy should be the addition of one or more medications from different classes. The major categories of medications that are effective include: histamine H2-antagonists, proton pump inhibitors, antacids, and pro-kinetic agents. Finally, several surgical alternatives have demonstrated effectiveness at controlling symptoms and reducing secondary disease.

The follow-up of the patient with GER and OSA is complicated by the efficacy of the intervention and patient adherence to the treatment regimen. For the medical interventions, the same principles should be followed as outlined elsewhere. The symptoms for both disorders should be followed closely, and the treatment regimen should be altered to minimize these complaints. If less typical manifestations of the disease are present (such as cough, respiratory symptoms, recurrent respiratory illness), then these manifestations should also be aggressively treated and followed. Patients who are using CPAP or bi-level positive airway pressure should be monitored closely for adherence. Most positive airway pressure devices have some form of monitoring device to assess adherence. In recent years, these devices have added more sophisticated mechanisms for monitoring patients using computer technology, including the ability to monitor day-to-day use and adjust pressure settings. For patients with complicated illnesses, the enhanced monitoring capabilities of these devices are generally preferred.

One aspect of the therapeutic alternatives involves the treatment of OSA. Most of the interventions used to treat OSA have little or no known impact on GER. In a few studies, however, CPAP has been shown to decrease reflux time and volume. These findings might suggest that a secondary effect of CPAP could be the reduction of GER and an improvement in symptoms. Whether an individual could be effectively treated with CPAP alone without the continuation of other modes of therapy has not been studied. On the basis of our current knowledge, however, we would expect that patients with mild disease who responded completely without the use of medications or who could be withdrawn from medications without the recurrence of symptoms might be adequately treated in this manner. Patients with moderate to severe disease could be expected to require continuous therapy once their symptoms become stable.

References


