Upper Airway Resistance Syndrome, Insomnia, and Functional Somatic Syndromes

Snoring is probably the main reason that patients with sleep-disordered breathing (SDB) have been referred. Otolaryngologists often see these patients. Internists and pulmonary specialists have recognized an association between SDB and obesity. Historically, the first sleep and breathing studies were performed on very obese patients (“pickwickians”) who had developed multiple cardiovascular complications. The majority of these patients were men. The presence of nonobese male SDB patients was emphasized thereafter, and the term obstructive sleep apnea syndrome (OSAS) was coined. The associated cardiovascular risks and repetitive episodes of nocturnal hypoxemia attracted widespread medical attention. Decreases in daytime performance and professional competence, mostly due to sleepiness, led these patients to accept unattractive treatments such as permanent tracheostomy and nasal continuous positive airway pressure. Not all treatments such as permanent tracheostomy and nasal continuous positive airway pressure transmitted to the CNS in the same way in OSA patients as in UARS patients and healthy individuals. In addition, OSA patients present significantly reduced vasodilation (monitored by laser Doppler perfusion) with electrical stimulation of peripheral nerve endings in the mucosa of the soft palate. Cortical response during wakefulness and non-rapid eye movement sleep has been measured with the rapid application of loads that are resistant to breath. Awake OSAS patients present with a normal auditory evoked response and respiratory-related evoked potential (with reduced amplitude of only one of the respiratory-related evoked potential waves [N550]). However, during non-rapid eye movement sleep, despite a perfectly normal auditory evoked response, inspiratory occlusions led to a blunted cortical response.

In agreement with the above findings, spectral analyses of the sleep EEG of healthy individuals, patients with UARS, and patients with OSAS have shown a similar dichotomy of results. Central leads on OSAS patients, compared to control subjects, present an important anomaly. They show a complete destructuring of sleep with a significant decrease in Δ power, which often is considered an index of sleep homeostasis. Impairment is seen in other EEG bands without significant increases in the other EEG bands. This increase in absolute power is seen in successive sleep cycles throughout the night. Δ power, which may be related to the...
“need (or pressure) to sleep,” does not seem to decline throughout the night as in healthy subjects. The pressure still exists at the end of the night in UARS subjects, despite a substantial amount of $\Delta$ power in the sleep cycles during the night, which is a major difference compared to OSAS patients. The significant increase in $\alpha$ power in UARS patients, which is not present in OSAS patients, suggests that the cortex is continuously challenged and is in an arousal status.

OSAS subjects do not respond well to occlusive respiratory stimuli during several successive breaths while asleep. This lack of adequate response leads to a decrease in tidal volume and the development of hypoxemia. The repetitive stimulation induced by successive occlusive breaths and the development of abnormal blood gas levels, which is a poor stimulus during sleep, eventually corrects the sleep-related problem. UARS subjects are able to correct their problem much more quickly, probably due to the appropriate processing of local sensory inputs but at the cost of continuous cortical arousal. In this issue of CHEST (see page 87), Gold et al use visual scoring to confirm the power spectrum analysis data reported on UARS. The usage of the cyclical alternating pattern scoring system can better confirm the increase in $\alpha$-$\Delta$ sleep (which is better labeled $\Delta$-$\alpha$ sleep).

A lot of confusion exists when the notion of arousal is discussed. Neurophysiologic studies on arousal should refer to the pioneering and fundamental work of Moruzzi. Sensory stimuli during wakefulness or sleep causes monosynaptic and polysynaptic reflexes at many levels of the CNS, including, for example, the spinal cord, medulla, pons, and upper brainstem. The response will differ depending on the recruitment triggered by the stimulation. The most efficient response involves the cortex. During sleep, the continuous good functioning of our vital organs shows that the CNS controls are maintained and that our subcortical structures integrate input. This information then is transmitted to structures that control the autonomic nervous system. A joint motor and autonomic adjustment is needed when polysynaptic reflexes are induced and an appropriate complex subcortical response is requested. Habituation to repetitive auditory stimulation has been demonstrated during sleep with absence of EEG arousal. A reinvestigation of the published data on auditory stimuli that did not cause arousals show that they caused autonomic activation and a change in heart rate. An autonomic nervous system response can be observed with or without motor response.

The lack of discrimination between CNS activation and autonomic responses (which are subcortical phenomena) and arousal (which is a cortical function) is an issue. Few studies have adequately addressed this physiologic dissociation. This is even more of a problem when devices have been reported to investigate autonomic arousal, which is a misnomer when studying autonomic activation. This also explains the important differences in sensitivity and specificity that are found in devices using autonomic indicators to find arousal. Corrections should be made by the analytic systems sold with these devices to try limiting the recognition of autonomic responses to those associated only with arousal.

UARS patients appear to present with a very different ability to respond to certain respiratory stimuli during sleep than OSA patients. The stimuli may lead to CNS activation, but very often it will lead to an EEG arousal. This difference in responses between UARS and OSA patients will lead to different clinical presentations. Gold et al document well that the clinical presentation may be unspecific in UARS patients, but the general practitioner should know the symptoms they outline. This syndrome is not associated with important upper airway histologic lesions and cardiovascular complications. In addition, not all women with UARS are chronic snorers. The method to be used to study these subjects during sleep has not been well-resolved, including Gold et al, who only studied airway collapsibility. And, we still do not know the natural history of UARS.

One may conceive, for example, that the sleep fragmentation induced by UARS may lead to less activity, weight increase, and complications associated with secondary obesity. But a recent randomized study on the treatment of insomnia associated with UARS also has indicated that waking up during the night may lead to anxiety that is related to sleep and to conditioned sleep onset and sleep maintenance insomnia. What wakes a person up is different from what keeps the person awake. UARS must be considered as a possible cause of somatic functional syndromes that may be as common in men as in women.

Christian Guilleminault, MD, BiolD
Rita Davé, MD
Stanford, CA

Drs. Guilleminault and Davé are affiliated with the Stanford University Sleep Disorders Clinic.
Correspondence to: Christian Guilleminault, MD, BiolD, Stanford Sleep Clinic, Suite 3301, 401 Quarry Rd, Stanford, CA 94305; e-mail: cguil@stanford.edu

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Respiratory Failure Early After Lung Transplantation

Now That We Know the Extent of the Problem, What Are the Solutions?

Over the last 20 years, lung transplantation has emerged as a valid treatment option for a wide range of advanced lung diseases. Surgical advances combined with newer immunosuppressant medications have improved outcomes; however, both the short-term and long-term survival after lung transplant continues to lag behind other solid-organ transplants. Survival for lung transplant recipients at 1 year, 3 years, and 5 years is approximately 76%, 58%, and 47%, respectively. Early respiratory failure and death after lung transplant can result from airway complications, hyperacute rejection, acute rejection, infection, or ischemia/reperfusion lung injury (IRLI). Graft failure secondary to bronchial dehiscence is now rare with improved surgical techniques. Hyperacute rejection, infrequently described in lung transplantation, results from preformed antibodies that target antigens in the allograft vascular endothelium and cause extensive thrombosis and complement activation. Acute rejection occurs in > 60% of lung recipients despite current immunosuppressive protocols, but usually responds to augmented immunosuppression and rarely leads to early graft loss. Infections complications, such as bacterial pneumonia or cytomegalovirus, have been described as a common etiology of respiratory failure and mortality in the early posttransplant period. IRLI or reimplantation response is characterized by the development of bilateral pulmonary infiltrates, declining lung compliance, and worsening of gas exchange in the immediate posttransplant period after exclusion of rejection, infection, and heart failure. Severe IRLI has been reported to occur in 15 to 30% of patients. Despite the increasing experience with lung transplantation, all of these problems contribute to the development of early respiratory failure and a 1-year mortality of approximately 25%.

In this issue of CHEST (see page 165), Chatila et al have attempted to determine the incidence and attributable mortality of acute respiratory failure from any cause after lung transplantation. They studied 80 consecutive patients who underwent single or bilateral lung transplantation between 1994 and 1999 at a single center. Postoperative respiratory failure was defined as the need for mechanical ventilation for > 48 h after transplant or the need for reintubation prior to hospital discharge. They found that 44 of 80 lung transplant recipients (55%) acquired acute respiratory failure. In-hospital mortality was significantly higher among patients who acquired acute respiratory failure compared to those who did not, 45% vs 3%. More than 50% of the episodes of acute respiratory failure were attributable to IRLI, and < 10% were attributed to infectious etiologies. Allograft rejection and airway complications contributed to 5% and 11% of the episodes of respiratory failure, respectively. Similar to prior studies, they found that the development of IRLI was associated with an increased incidence of acute respiratory failure and in-hospital mortality.

Based on the results of Chatila et al, it appears the main cause of early morbidity and mortality after lung transplant has shifted away from infections to