References


Pathophysiology and Treatment of Central Sleep Apnea

Apneas occurring during sleep are divided into those in which inspiratory efforts are absent (central sleep apnea, CSA) and those in which inspiratory efforts are present, and airflow is absent because the upper airway is occluded (obstructive sleep apnea, OSA). Obstructive sleep apnea is much more common in adult patients, but a few have predominantly central apneas. Patients with CSA tend to be older than the average patient with sleep apnea, often have associated neurologic disease, and are less likely to display the typical clinical picture of sleep apnea. The article by Issa and Sullivan in this issue (see page 165) reports the significant therapeutic observation that nasal CPAP is effective in the treatment of CSA, and uses this observation to propose a new theory of the pathogenesis of CSA.

From an immediately practical point of view, the present article has three points to make: (1) as a diagnostic consideration, the distribution of CSA and OSA in an individual can depend on posture; in all eight patients of Issa and Sullivan, CSA was confined to the supine posture. (2) CSA can be effectively treated with nasal CPAP, and this treatment is effective long-term. (3) Higher nasal pressures are required to treat CSA than to treat OSA, so that CSA can occur in patients in whom OSA has been abolished. Others have reported studies in which nasal CPAP was relatively ineffective for CSA, but this may have occurred because they did not use high enough pressures. These results underscore the fact that the effective use of nasal CPAP requires meticulous evaluation of each patient and individualized therapy.

Nasal CPAP may not be a complete answer to the therapeutic problems of CSA, because difficulty in managing the apparatus at home may be a major problem for neurologically impaired patients. Tracheostomy, however, is not likely to be any better in this regard, and will usually be much worse; low flow oxygen may be the best approach in the very infirm CSA patient.

It has been generally believed for some time that OSA and CSA are alternative manifestations of a single underlying pathology. Obstructive apneas are thought to occur when there is inadequate motor drive to upper airway muscles in the presence of effective diaphragmatic contraction, and central apnea is easily conceptualized as a closely related but more severe phenomenon, with inadequate drive to both the upper airways muscles and the diaphragm. However, the exact etiology of CSA and its relationship to OSA have been elusive. Issa and Sullivan now suggest that central apnea is secondary to passive upper airway closure, which causes stimulation of mucosal sensory receptors and reflex apnea.

The argument presented by Issa and Sullivan to support their suggestion is that: (1) central apneas occurred when the patients were supine, and passive airway closure is more likely in supine subjects; (2) in two patients, airway anesthesia abolished apneas; and (3) in one patient, airway occlusion produced by nasal obstruction was followed by brief expiratory pauses. Some aspects of this argument require careful consid-
eration. It is, of course, true that snoring and OSA are worse in subjects sleeping supine than in those sleeping prone or in the lateral posture. However, there is no evidence that passive airway closure actually occurs commonly in sleeping subjects in the supine posture. Issa and Sullivan have previously reported that airway closure is easier to induce in supine than in lateral posture, but still in all cases some negative pressure was required to close the airway. Equally, there is no reason to believe that passive airway closure does not occur in these patients, but demonstration of the fact would lend support to Issa and Sullivan’s hypothesis. The physiology of upper airway sensory receptors is complex and poorly understood, and although there is evidence of receptors that could mediate the reflex, the authors propose there is also evidence inconsistent with the hypothesis. For instance, there are in humans upper airway flow receptors whose stimulation depresses inspiratory efforts and whose inactivation by airways closure would presumably increase the likelihood of breathing. In OSA, there is a progressive increase in breathing efforts in the presence of a closed airway, so some explanation is needed of the absence of the mucosal apnea reflex in this situation. Even more puzzling is the fact that when Issa and Sullivan’s CSA patients have OSA they also exhibit progressive increases of inspiratory effort. Why would they respond differently to airway occlusion when they were supine than when in the lateral posture? The response to airway anesthesia is persuasive evidence in the authors’ favor, and it is to be hoped that more patients will be studied in this way. Clarification of this point is especially important since it is reported that in animals upper airway anesthesia causes airway obstruction.

The demonstration that both CSA and OSA respond to nasal CPAP seems strong evidence that the same pathophysiologic processes cause both disorders. How these processes lead to one or another dominant form of apnea is unclear. Issa and Sullivan’s hypothesis raises two possibilities: airway mucosal sensation could be abnormal and cause the disorder, or normal mucosal inputs could be mishandled by malfunctioning central neural pathways. The frequency of clinically apparent neurologic disease in CSA patients suggests the latter, but this is speculation. Exploration of these possibilities should significantly advance understanding of the role of upper airway sensation in normal and abnormal respiratory function.

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Transvenous Endomyocardial Biopsy

Clinical Indications, Potential Complications, and Future Applications

A large number of diagnostic tests are available to evaluate the different categories of cardiovascular disease. These tests can provide a multitude of insights regarding the quality and magnitude of cardiovascular dysfunction, and some of these tests provide insights regarding the etiology and pathogenesis of specific cardiovascular disease. However, much of cardiology emphasizes functional physiologic diagnosis and categorization with little emphasis placed upon the specific underlying pathogenetic mechanisms. Comparatively little work has been done regarding the biochemical and/or cellular physiologic mechanisms responsible for the decrease in cardiac performance, when compared to the huge amount of data collected describing cardiac performance and ways to measure it.

Organ biopsy with microscopic inspection of the tissue damage represents one of the diagnostic mainstays when evaluating diseases confined primarily to certain organs, eg, liver, bone marrow, and skin. Prior to development of the Konno biopsy in 1962, no method of obtaining endomyocardial tissue for histologic evaluation was available, except for high complication rate methods employing a transthoracic needle biopsy or a surgical open thoracotomy. With development and modification of the transvenous catheter, multiple small samples of endomyocardial tissue could be obtained with a high degree of certainty and with a minimal complication rate. This biopsy forceps allows evaluation of myocardial histopathology during life without undergoing a major surgical procedure. Thus, heart biopsies could be obtained employing catheterization rather than surgical procedures and risks.

In 1986, the major controversy surrounding the technique of transvenous endomyocardial biopsy (TEB) concerns the clinical indications for its use. TEB has been employed to provide diagnostic information in the evaluation of patients with cardiomyopathy. The most widely accepted cardiomyopathy classification scheme is division of cardiomyopathy patients into