While it is known that neural activation of pharyngeal muscle exhibits respiratory periodicity and is an integral part of the respiratory control system, the mechanical consequences of neuromuscular activity in upper airway muscles are not well understood. Clinical and physiologic studies of Remmers et al., Brouillete and Thach, and others are evidence to presume a relationship between pharyngeal muscle activation and upper airway obstruction during sleep. In these studies, reduction in upper airway muscle activity—genioglossus, geniohyoid, etc.—was associated with the onset of upper airway obstruction. Comments on the cause-effect relationship of this association acknowledged that basic mechanical properties of the airways and on the link(s) between upper airway muscle activity and airway patency were not well understood. Yet, the usual interpretation of these studies involves an implicit assumption of a direct relationship between muscle activity and airway patency. This interpretation has led to theories concerning a central pathogenesis for obstructive apneas and too often unsuccessful therapeutic attempts to treat these apneas by altering respiratory drive. We have evolved a different theory of the maintenance of pharyngeal patency and will argue for the relative unimportance of muscle activation in the initiation of obstructive apneas during sleep.

SKELETAL MUSCLE ACTION ON THE AIRWAY

The structural elements inherent in the processes that maintain pharyngeal patency include muscular, nonmuscular, and mucosal factors. These will be discussed in turn; however, a potentially important architectural feature of the pharyngeal airway is the mechanical linkage between the air-conducting airway and the surrounding, extraluminal structures. While the pharyngeal constrictors are attached directly onto the pharyngeal mucosa, the rest of the pharyngeal muscles act on the airway indirectly, through their attachments to the tongue or hyoid. The nature of the mechanical linkage between hyoid and tongue muscles and airway size or shape is unclear. It is clear, however, that this linkage is indirect and limited in extent, i.e., it is confined essentially to the hyo-epiglottic ligament, and to whatever effect is exerted through the potential space between the hyoid and mucosal surface of the airway wall.

What does muscle contraction do to the pharyngeal airway? Studies of the nasal valve and of the larynx support an assumption that muscles directly affect airway patency. Activation of “dilator” muscles decreases upper airway resistance, and inactivation of these muscles increases resistance to airflow. Muscle activation seems to achieve these effects through muscle shortening and airway enlargement. In contrast, studies of muscles in the pharyngeal region of the airway do not support this assumption. While some “dilator” muscles do lengthen, others shorten with respiratory activation—even when the end-mechanical result is a dilating force on the airway. This finding illustrates the difficulty in assigning a specific mechanical outcome to the activity in any one pharyngeal muscle.

Yet it can be shown in anesthetized animals that the upper airway volume increases during each inspiratory effort; this enlargement is due in large part to contraction of the upper airway skeletal muscles. Pharyngeal muscles, in particular, appear to enlarge the airway through anterior displacement of the hyoid bone. Since, in the absence of some rigidity, resting size is not a very useful attribute for flow, muscle activation has also been thought to influence airway elasticity by making the walls of the airway more rigid. There is, however, no good evidence that muscle activation...
reduces airway compliance. Clinical evidence used in support of this claim is the association between reduced muscle activity and upper airway obstruction during sleep. While there are indications that increased upper airway compliance is the pathogenic factor in obstructive sleep apnea, many processes other than the lack of upper airway muscle tone could increase upper airway compliance.

There is some direct evidence to suggest that muscle activity may not increase the rigidity of the airway walls. A partial pressure/volume curve of the upper airway can be produced in an anesthetized dog made apneic by hyperventilation. The pressure/volume curve produced while the muscles are silent has a slope similar to that obtained when muscle activation causes changes in pressure and volume, during conditions of increasing upper airway muscle activity. The closing pressure of the isolated upper airway is another index of upper airway rigidity and, in an anesthetized rabbit, generally is of the order of −10 cmH2O. In spontaneously breathing, anesthetized rabbits, Brouilette and Thach demonstrated that increased respiratory drive resulted in an increase in this closing pressure indicating that upper airway muscle activity made the airway harder to close. Their observation that death resulted in a fall in closing pressure indicated that some factor(s) during life helped maintain airway stability. They suggested that muscle activity was this factor.

We have found that administration of gallamine to halt skeletal muscle activity in the apneic, anesthetized rabbit will produce little change in the airway closing pressure; subsequent death, however, results in the airway being significantly easier to close (Olson and Strohl, unpublished observations). This latter observation suggests that muscle activity alone does not predominantly affect upper airway stability.

**Elastic Elements of the Airway Wall**

The need for active muscle contraction in order to resist collapse of the upper airway appears to have been assumed, rather than demonstrated. Part of the basis for this assumption has been the lack of other proposed explanations for the resistance to collapse. The intrinsic elastic properties of the airway depend partly upon the contractile state of the muscle and partly upon its associated structures (connective tissue, blood vessels, etc). A substantial fraction of the stiffness of contracting muscle, and most of the stiffness of relaxed muscle, is due to connective tissue; changes in the amount of connective tissue in a muscle can dramatically change its compliance. Further, the impact of activation on the stiffness of a muscle depends upon how it contracts and whether other muscles also contract. Contraction at low tension has relatively little effect on muscle stiffness, possibly because relatively few actin-myosin cross-bridges are formed. Although the tension of contracted upper airways is not known, it is reasonable to suspect that it might be low, since the force they are normally called upon to oppose is small. The passive elastic properties of the airway muscles may, therefore, account for a substantial part of the collapse resistance of the airway in the living and, presumably, accounts for all of the collapse resistance seen in newly dead animals. Finally, the indirect coupling of the muscles to the airway suggests that even rather large changes in the stiffness of muscles might have little effect upon the compliance of the airway at the site of potential collapse.

Independent of muscle effects, flexion and extension of the neck influences the mechanics of the upper airway. In the studies in which radiographic images were performed, it was not the mass of the tongue per se that narrowed the airway in flexion, rather it was the tissue between the airway and the hyoid. The nature and mechanical features of this space are unknown. In addition, another element that would resist passive airway closure, and is independent of skeletal muscle activation or posture, is the vascular supply to and surrounding the airway. Muscle stiffness can vary with perfusion pressure. The diastolic (ie, relaxed) stiffness of papillary muscle is related to the perfusion pressure in its vascular bed. The mucosal vascular bed of the airway is perfused at 20 to 30 cmH2O; presumably, this level of pressure, even partially transmitted to the airway wall, could also resist distortion in a way that would contribute to collapse resistance. Changes in blood pressure and/or the vascularity of the airway wall could affect airway stability and influence airway patency. Finally, any basic measurement of structural stability will depend upon an ability to determine specific compliance, including reliable estimates of transluminal pressure, at the site(s) of airway collapse.

**Clinical Studies**

Thus, the features of the airway wall that influence luminal patency and airway stability include both slowly varying (vascular pressure, tissue elasticity) and rapidly varying (muscular) effects. While current studies have not addressed their relative importance in the pathogenesis of obstructive apneas during sleep, there is evidence that some properties related to compliance might be important. Brown et al obtained acoustic measurements, during wakefulness, of the change in pharyngeal size during inspiratory and expiratory efforts against an external obstruction. They determined that patients who snored and had apneas had a greater change in pharyngeal area for a given change in airway pressure than age/weight-matched patients who snored but were without sleep apneas. This difference was apparent even though the measurements were made in the upright posture and during wakefulness. Suratt et al demonstrated that patients with multiple episodes of obstructive sleep apnea would collapse their upper airway in response to
breathing against a sub-atmospheric pressure while those without apnea could resist closure. These studies were performed during wakefulness but while the subjects were in the supine position.

Studies by Sullivan and co-workers (as summarized in reference 21) are perhaps more relevant to understanding the mechanics of the upper airway during sleep. Their studies have shown that the upstream pressure upon inspiration is a major determinant of airway patency. Subjects who had never snores required sub-atmospheric pressures in the nasal mask to induce upper airway collapse during sleep; patients with obstructive apneas required positive pressure, as referenced to atmosphere, to prevent airflow closure. Patients who had snores but had few apneas were intermediate between the two groups.

All of the studies cited above support the general notion that differences in upper airway compliance could be associated with sleep apnea. Patients studied were in generally good neurologic health, ie, other than symptoms of sleepiness, there were no signs of neuromuscular weakness or upper airway muscle pathology. Hence, it may be reasonable to suggest that neural control was relatively intact. If so, then upper airway muscle chemical and non-chemical reflex control, while not tested, would not be expected to explain the mechanical differences between healthy subjects and patients with partial or complete upper airway obstruction. Consequently, it is possible that mechanical properties rather than neuromuscular control problems account for the differences in upper airway function between healthy subjects and patients with sleep apnea.

AN HYPOTHESIS

We propose the following schema for considering the relative influence of muscular and non-muscular factors in the initiation of obstructive apneas during sleep. While resting size of the upper airway may indeed be small in patients with multiple obstructive apneas during sleep,26 size alone might only predispose the airway to collapse. Some lack of rigidity is required for airway occlusion. There is evidence that the action of the upper airway muscles causes change in airway size, not compliance of the airway wall. The likelihood of airway collapse is increased if muscle activity is reduced, because the reduction in muscle activity results in a smaller airway not because airway compliance is increased. If the airway compliance is low, airway collapse will not occur even in the absence of muscle activity. The ability of the airway to resist collapse is dependent upon the mechanical arrangement of the jaw and hyoid apparatus, which allow for a specific pharyngeal size, and on the properties of the airway wall. We suggest that episodes of upper airway collapse during sleep are due to an underlying abnormality in upper airway compliance. Furthermore, clinical expression of this mechanical abnormality can be graded. Obstruction during sleep is rendered cyclic by a compensatory, homeostatic response by the central regulator, resulting in changes in muscle activation that affect upper airway size.

REFERENCES