Mechanisms of Obstructive Sleep Apnea

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Obstructive sleep apnea (OSA) is characterized by intermittent inspiratory closure of the pharyngeal airway during sleep resulting in episodic hypoxemia and sleep disruption. Primary presenting symptoms are heavy snoring and excessive daytime sleepiness. Investigations conducted in the late 1970s and 1980s have enhanced our understanding of the etiology of OSA, but to date no single pathophysiologic mechanism has been identified. Thus, it is possible that the cause of OSA is multifactorial in any one individual or differs in different patients. At the conclusion, schema illustrating the importance of etiologic components and their interaction will be shown.

The following are categories of individual factors known to contribute to upper airway obstruction during sleep: (1) anatomic narrowing of the upper airway; (2) increased compliance or collapsibility of upper airway tissues; (3) reflexes affecting upper airway caliber; and (4) pharyngeal inspiratory muscle function. In this review, a critique of significant research developments addressing the pathophysiology of OSA will be presented.

Upper Airway Anatomy and Function

Upper Airway Structure

The upper airway participates in speech, swallowing, and breathing. The structures of this region are capable of performing each of these functions through a composite of both rigid and flexible structures. A complicated neuromuscular and sensory system guides the functioning of these structures. During sleep, the upper airway primarily serves as a ventilatory conduit. Surrounding the upper airway beneath the mucosa are multiple muscles, innervated by cranial and high-cervical nerves. These muscles are attached to various bony surfaces surrounding the pharynx. Muscles are divided into groups of those with dilator and constrictor actions. During wakefulness, the tonic activity of the dilating muscles is high, helping to preserve the patency of the upper airway. During sleep, measurements of electromyograms (EMG) demonstrate hypotonia of upper airway inspiratory muscles, leading to narrowing of the upper airway. Constrictor muscles assist in glottic closure, cough, and expiratory narrowing of the upper airway. These constrictor muscles have essentially no function in normal ventilation during sleep.

Normal Upper Airway Ventilatory Function in Sleep

Although most work has evaluated the upper airway as a unit, we now know that different segments of the upper airway have different characteristics during sleep. Interestingly, total nasal resistance does not change on transition from wakefulness to sleep. However, resistance within the right and left sides of the nose may fluctuate spontaneously in a fashion independent of gravity. Because the two nasal cavities are arranged in parallel, a large increase in resistance, or even total obstruction, on one side of the nose will not affect total nasal resistance to a major degree if the contralateral side continues to have a low resistance. Therefore, in unilateral nasal congestion, the impediment to airflow may be minimal and not lead to arousal. Surely, significant bilateral nasal congestion may increase resistance enough to disrupt sleep.

In healthy nonsnoring subjects, the supralaryngeal airway, distal to the nose, was found to narrow during nonrapid eye movement (NREM) sleep (Fig 1). This increase is higher in snorers without sleep apnea than in nonsnorers. The increase in resistance observed occurs primarily in the transpalatal or retropalatal airway, but it may also occur in the retroglossal or hypopharyngeal airway. Interestingly, although upper airway muscle tonic activity diminishes dramatically in rapid eye movement (REM) sleep, upper airway resistance does not increase beyond the levels found in NREM sleep. Possibly, this finding is due to a decrease in chest wall "pump" muscle activity that...

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creates the subatmospheric collapsing pressure generated within the upper airway (see below).

**Upper Airway Size and Function during Sleep in OSA**

The physiologic characteristics of the upper airway collapse that occurs in OSA are similar to, but are more extensive than, the physiologic findings seen in healthy nonapneic subjects. Measurements of differential pressures across the palate and the hypopharynx with transnasal catheters reveal that approximately half of OSA patients obstruct reproducibly at the level of the palate and half obstruct reproducibly below this level in the hypopharynx (Fig 2). These studies indicate that the site of obstruction is rather specific and that upper airway collapse does not necessarily involve the whole pharynx.

Of course, there are drawbacks to direct measurement of upper airway patency with catheters, such as use of a local anesthetic, presence of foreign body in the airway producing its own mechanical consequences and possibly inducing irritant reflexes. However, results derived from studies using intra-airway catheters are similar to findings where upper airway resistance was measured without such instrumentation. Using fast-scanning computed tomography (CT), Stein et al also found that upper airway obstruction in OSA patients was limited to specific upper airway segments, especially early in the apnea. However, these investigators noted that the obstruction extended to involve more of the pharynx late in the apnea in four of eight patients. Our pressure measurements do not confirm this observation.

If the upper airway obstruction is primarily present in a limited segment of the upper airway, it is possible that the airway is structurally narrowed at this specific site. Of course, tonsillar hypertrophy or other tissue enlargement as well as subatmospheric structures whose size is out of proportion to adjacent structures may both contribute to isolated narrowing, which could result in obstruction at the site of tissue abnormality during sleep. Stauffer et al recently found that the uvulae resected at the time of pharyngeal surgery in patients with OSA were longer and contained more muscle and more fat than the uvulae of cadaver controls. However, there was neither evidence as to the extent of airway narrowing produced by these anatomic abnormalities nor documentation of a relationship between the site of obstruction during sleep and anatomic abnormalities.

**Assessment of Upper Airway Size in OSA**

Because determination of the site of obstruction during wakefulness would be easier and more convenient than measurements made during sleep, investigators have used a variety of methods to examine the anatomy of upper airway segments during wakefulness. Fast CT scanning has been used by Shepard et al to quantify the cross-sectional area of different upper airway segments during specific phases of respiration. Figure 3 shows that the postpalatal airway is the narrowest portion of the supralaryngeal airway in both inspiration and expiration in awake supine healthy subjects. These findings are consistent with data obtained from sleeping normal subjects discussed above. Using standard CT scans, which do not allow
for coordination of imaging time with the timing of ventilation, both Haponik et al. and Suratt et al. found the oropharynx of OSA patients was smaller than the upper airway of control subjects. It is interesting that the data presented in these two studies demonstrate considerable overlap between upper airway segmental size of OSA patients and control subjects. Therefore, these studies indicate that the upper airway of OSA patients may or may not be anatomically narrow.

The volume of different pharyngeal segments has been studied with magnetic resonance imaging (MRI), a technique that allows for measurements of actual volume, not just cross-sectional area. Ryan et al. found the upper airway volume to be smaller in patients with OSA than in controls, but Rodenstein et al. found upper airway shape, but not volume per se, to be different between patients with OSA and control subjects. As with CT scan studies, these MRI studies demonstrate that upper airway anatomic narrowing may or may not be present in OSA patients.

Cephalometry, a classic orthodontic technique using a lateral roentgenogram performed in the erect body position to assess bony head and neck anatomy, has demonstrated that micrognathia or retrognathia is present in some OSA patients. Reports using this technique to define hyoid bone position and soft-tissue boundaries and thereby pharyngeal size are difficult to interpret because the size of the pharynx and position of the hyoid bone in the erect body position may not be representative of the anatomy of a patient in the supine position. In addition, minimal normative data exist for these latter two variables. Therefore, use of cephalometry as a diagnostic test, other than for assessing bony maxillary and mandibular abnormalities, is not yet fully defined.

Studies using acoustic reflection, a technique measuring pharyngeal cross-sectional area by analysis of a reflected sound wave administered through an oral mouthpiece, have found the oropharynx and hypopharynx to be narrow in both heavy snorers without OSA and OSA patients. However, this technique has some limitations. First, it is usually performed with the subject erect; but more importantly, it does not evaluate any of the airway above the level of or posterior to the soft palate. Interestingly, with this technique, there was no difference in the size of the pharynx at functional residual capacity in nonapneic snorers and apneic patients when groups were well-matched for gender and body size.

Lateral cervical fluoroscopy has been used in OSA patients during sleep, but no quantitative assessment has been performed in these studies. Because of a short neck length in some OSA patients, it is difficult to visualize the hypopharynx with fluoroscopy because of interference with the pharyngeal image by the shoulder.

**Meaning of Awake Upper Airway Size in OSA**

The relevance of these analyses of upper airway size performed during wakefulness to the size of the pharynx during sleep or to the site of obstruction in OSA is uncertain. Some studies suggest that there is little similarity between the upper airway characteristics awake and asleep. For instance, it has been shown that no relationship exists between the severity of the OSA, as determined by the number of apneas and hypopneas per hour of sleep, and the size of the upper airway awake. In contrast, it has been shown that a relationship does exist between upper airway size awake and asleep. In general, because of inconsistent results, these studies evaluating upper airway size in OSA imply that factors other than size alone may contribute to OSA. The inconsistency of such studies might also suggest that the OSA population is heterogenous, such that anatomic upper airway narrowing is surely present in some OSA patients while it may not be meaningful in other OSA patients.

To summarize, data available assessing upper airway size in OSA, three possible conclusions can be offered: (1) anatomic narrowing actually contributes to OSA in some but not all patients; (2) our techniques are too crude to define existing anatomic abnormalities present in all OSA patients; and/or (3) pharyngeal size per se may not be a primary etiologic factor in OSA. Of course, studies examining the static upper airway size do not address the effect of dynamic factors that may contribute to OSA, such as pharyngeal compliance, reflexes, and inspiratory muscle activity.

**Upper Airway Compliance and Collapsibility**

Discussion of upper airway compliance or collapsi-
bility can be separated into five categories: (1) the intrinsic compliance or collapsibility of pharyngeal tissues; (2) “effective” compliance; (3) pharyngeal muscle tone; (4) the effect of edema or vascular congestion of the airway mucosa on airway collapsibility and size; and (5) mucosal stickiness.

**Intrinsic Pharyngeal Compliance**

We know little about the intrinsic passive compliance of the pharyngeal tissues because of the difficulty in determining isolated pharyngeal volume and intraluminal pressure measurements during a totally relaxed state. One study approached this subject by evaluating collapsibility of pharyngeal tissues of recently deceased infants, a model where the effect of muscle activity was eliminated.\(^5\) It was found that the oropharynx was often closed when the infant lay in a supine position. If the oropharynx was not closed, it took very little suction pressure applied to the airway to close it. In contrast, a higher suction pressure was required to close the nasopharynx (mean of 9 cm \(H_2O\)). Substantially more pressure was needed to close the hypopharynx (mean of 30 cm \(H_2O\)). The results of this study suggest that the tissues surrounding the oropharyngeal airway are inherently quite collapsible. Unfortunately, there are no analogous studies in adults.

**“Effective” Compliance**

The acoustic reflection technique was used by Hoffstein et al\(^{21}\) and Bradley et al\(^{22}\) to evaluate dynamic upper airway collapsibility or what these investigators term “effective” compliance. “Effective” compliance was defined as the expiration to residual volume. These investigators found that patients with OSA displayed a greater decrease in their pharyngeal cross-sectional area than did controls, demonstrating excessive upper airway collapsibility in OSA. Suratt et al\(^{26}\) eliminated the effect of active inspiration by applying a vacuum to the upper airway with the subjects relaxed at functional residual capacity. These investigators demonstrated that OSA patients had a more collapsible upper airway than control subjects. The extent of narrowing present under these experimental conditions during wakefulness correlated with the degree of arterial oxygen desaturation and the number of apneas that occurred during sleep. Assessing dynamic upper airway collapse during sleep, Issa and Sullivan\(^{27}\) determined the pressure at which the upper airway closed in asleep OSA patients during active breathing. Consistent with the clinical observation that obstructive apneas are predominantly distributed in stages 1 and 2 and REM sleep, it was found that upper airways collapsed at a lower suction pressure in stages 1 and 2 and REM sleep than in stages 3 and 4. Also, the upper airway was observed to be more readily collapsed in the supine than in the lateral body position.

**Tonic Muscle Activity**

The effect of upper airway muscle activity, which would surely be expected to influence upper airway collapsibility, was not assessed in these human studies of upper airway compliance. However, the effect of this muscle activity on the level of negative intraluminal pressure required to close the upper airway has been studied in animals. In lightly anesthetized rabbits, Brouillette and Thach\(^ {24}\) showed that far less suction pressure was required to collapse the upper airway after hypoglossal nerve section than before nerve section, and that less suction pressure was required to collapse the upper airway immediately following death than was required during anesthesia. Their observations indicate that the mechanical activity of the upper airway muscles is instrumental in preventing upper airway collapse. However, a somewhat different conclusion was reached by Olson and Strohl.\(^ {25}\) In anesthetized rabbits, these investigators found that upper airway collapsing pressure did not change significantly with skeletal muscle paralysis but did decrease with death. This study indicates that factors within the upper airway tissue other than active muscle tension per se influenced upper airway patency. Such factors might be vascular volume, and during life, vascular tone and vascular pressures.

**Vascular Volume**

Hutt et al\(^ {28}\) reported the effects of changing pharyngeal blood volume by administering intravenous nitroprusside to anesthetized, sympathectomized cats. Using MRI, these investigators demonstrated that mucosal blood volume increased and upper airway caliber diminished significantly following nitroprusside injection.\(^ {29}\) They found that the palatal airway became more edematous than any other upper airway segments. The palatal airway was found to be the most collapsible upper airway segment in their study. In addition, Parisi et al\(^ {30}\) identified a 7 percent increase in pharyngeal volume of normal awake humans after local application of the vasoconstrictor phenylephidine. These data suggest that blood volume changes may affect upper airway size and collapsibility. It is possible that the highly subatmospheric pressures that are present during or just prior to obstructive apneas might lead to increased vascular volume locally within the upper airway. However, it is difficult to conceive that changes in blood volume or edema could occur rapidly enough to explain the instantaneous changes in upper airway resistance seen in OSA patients during sleep, such as when the apnea is reversed instantaneously within an inspiratory effort.

**Mucosal Stickiness**

The concept of mucosal stickiness is based on the fact that there is hysteresis in the pressure-volume
relationship between opening and closing of the isolated upper airway of anesthetized rabbits. In these animals, it took more pressure to reopen the upper airway than it took to close it. Therefore, it was hypothesized that upper airway secretions could potentiate and contribute to the persistence of upper airway closure. In this study, production of increased quantities of pharyngeal mucus with methacholine administration actually made the upper airway more difficult to close, but also more difficult to reopen. Saline solution instillation into the upper airway did not produce this effect. Therefore, some property of mucus per se induced a change in the collapsibility of the upper airway, but not a change that completely potentiated collapse. To my knowledge, the role of mucus in OSA in humans has not been investigated.

How all these factors that alter upper airway collapsibility interact and which of them, acting singularly or in combination, may be abnormal in OSA has yet to be determined.

**Reflexes and Upper Airway Caliber**

Reflexes whose afferent limbs are located throughout the respiratory system may alter upper airway caliber through action on respiratory muscle function. These reflexes include those reflexes that originate in the suprabronchial airway, those that originate in the larynx or lungs, and cardiovascular reflexes.

**Upper Airway Pressure and Flow Reflexes**

These reflexes may affect respiration and upper airway caliber. Mathew and Farber have identified reflexes whose afferent branches are located within the nasal and pharyngeal mucosa. Studies in humans demonstrate that nasal occlusion, increased nasal flow, and increased nasal pressure also enhance upper airway inspiratory muscle activity, dilating the upper airway. The importance of these reflexes is supported by the observation that local anesthesia to the upper airway has been shown to result in obstructive apneas during sleep in healthy individuals and increase the apnea frequency in OSA patients. In OSA, because of tissue edema, these reflexes may be blunted and therefore may not adequately compensate for factors contributing to upper airway collapse.

These reflexes also could affect upper airway caliber by their action on chest wall inspiratory muscles. The results of this study may stimulate respiratory pump muscle activity. If active in adults, this reflex would decrease chest wall muscle contraction and thereby reduce the upper airway collapsing pressure generated by the contraction when airflow was reduced in the upper airway.

**Reflexes Originating in the Lower Respiratory System**

Reflexes with afferent receptors in the lower respiratory tract also may alter upper airway caliber. Lung demonstrated that an increase in lung volume decreased nasal resistance via a vagal reflex. Fouke and Strohl showed that changes in lung volume did not affect pharyngeal size in anesthetized animals. However, in human NREM sleep, Begle et al observed that total pulmonary resistance decreased with passive lung inflation. Since a decrease in resistance within the intrathoracic airways would be anticipated with an increase in lung volume, the investigators cannot be certain this maneuver also resulted in dilation of the upper airway. Different from the response to changes in static lung volume, alteration of dynamic inspiratory volumes may have the opposite effect.

There also may be a direct mechanical effect produced by changes in thoracic volume on upper airway volume. Van de Graaff found that downward motion of the thorax produced widening of the upper airway when all reflex pathways were severed. The reflexes described and direct mechanical effects may have a significant influence on upper airway caliber during sleep. However, the extent of their impact in the pathophysiologic condition of OSA has not yet been defined.

**Cardiovascular Reflexes**

Reflexes originating in the cardiovascular system may impact upper airway caliber. Salamone et al found that a change in systemic blood pressure affected hypoglossal nerve activity more than it affected recurrent laryngeal or phrenic nerve activity. Other work indicates cardiovascular reflexes alter upper airway patency and influence OSA. Cardiovascular reflexes affecting the upper airway have not been thoroughly evaluated. It is possible they may play a role in the pathogenesis of OSA.

**Inspiratory Muscle Function**

There have been several concepts proposed addressing the role of upper airway muscle function, or dysfunction, in the pathophysiologic condition of OSA: (1) the balance of forces or respiratory muscle imbalance theory; (2) the critical pressure concept; and (3) the effects of periodic breathing on upper airway mechanics during sleep. Although components of these concepts surely overlap, they will be discussed separately.

**Balance of Forces Theory**

The balance of forces theory proposes that upper airway size is affected by a balance of forces. Dilating forces are generated by pharyngeal muscle activity, and collapsing forces are generated by chest wall muscles. This relationship between muscle forces is influenced by other factors such as initial airway size,
The concept that inspiratory muscle imbalance may occur is based on the findings that upper airway and lower respiratory muscles respond quantitatively differently to the same ventilatory stimulus. Studies in anesthetized animals, naturally sleeping animals, and in humans show that at low levels of ventilatory stimulation, there is predominant activity of the chest wall inspiratory muscles relative to the activity of the upper airway muscles. However, once the stimulus increases beyond a certain threshold, this relationship reverses, and there is a predominance of the upper airway muscle inspiratory activity relative to that of the chest wall. Relative activity of the upper airway and chest wall inspiratory muscle activities affect upper airway caliber. Series et al demonstrated that when normal subjects rebreathed hyperoxic air, the progressive hypercapnia was associated with a progressive decrease in upper airway resistance. In a high-drive state, there is preferential activation of upper airway inspiratory muscles and during a low-drive state there is preferential suppression of this activity. Alternating between high-drive and low-drive states results in wide fluctuations in upper airway caliber, such as seen in OSA. This pattern is shown schematically by Longobardo et al in their modeling experiments of periodic breathing (Fig 4).

**Critical Pressure Concept**

It is hypothesized that the pharynx has the same properties as a Starling resistor. In this model maximal flow through the upper airway is determined by the pressure within (or possibly around) the collapsible upper segment airway. Two factors, upstream resistance and subatmospheric airway driving pressure generated by chest wall muscle contraction, set the transmural pressure within the collapsible segment. In OSA patients, the collapsing pressure needed to close the upper airway is much lower than that needed to close the upper airway on nonapneic subjects. In OSA patients the driving pressure or upstream (nasal) resistance is either too large or the pharynx is too collapsible, and upper airway inspiratory closure occurs. In snoring nonapneic subjects but also in normal subjects, inspiratory flow becomes limited in that further increases in driving pressure do not produce an increase in flow. In this situation as the driving pressure increases, the collapsible portion of the Starling resistor must progressively narrow since flow does not increase. This concept that the upper airway behaves like a Starling resistor is consistent with the findings that the upper airway tends to collapse within a limited upper airway segment in OSA patients.

**Periodic Breathing**

There is evidence that periodic breathing produces a mechanical effect on the upper airway during sleep. In normal subjects we found periodic breathing pro-

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**Figure 4.** Modeling of chest wall and upper respiratory muscle activities in obstructive sleep apnea. When the upper respiratory muscle activity decreases relative to the activity of the chest wall muscles, the upper airway collapses. When the upper respiratory muscle activity increases relative to that of the chest wall muscles, the upper airway opens (reprinted with permission from Respir Physiol 1982; 50:311-33).

**Figure 5.** Fluctuation in peak inspiratory chin and chest wall muscle electrical activities is associated with changes in upper airway resistance. Periodic breathing was produced in healthy subjects in nonrapid eye movement sleep with mild hypoxia. During periodic breathing when the chin/chest wall electromyographic (EMG) relative activity decreased below a certain point, in this example below 0.7, the upper airway resistance increased hyperbolically (triangles). If in a particular periodic breathing cycle, the chin/chest wall ratio did not decrease below this threshold level, resistance did not increase (dots) (reprinted with permission from Am Rev Respir Dis 1987; 135:899-906).
duced by mild hypoxia resulted in an imbalance in the chest wall and upper airway inspiratory muscle EMG activity.\textsuperscript{50} When upper airway inspiratory muscle tonic and phasic inspiratory activity decreased more than chest wall muscle activity in the hypopneic portion of the periodic breathing cycle, upper airway resistance increased hyperbolically (Fig 5). In contrast, as the upper airway activity increased relative to that of the chest wall muscles, for instance in the hyperpneic portion of the periodic breathing cycle, resistance decreased. Oral et al\textsuperscript{60} showed a similar phenomenon in healthy humans with a combined stimulus of hypoxia and added inspiratory resistive loads. In this study, hypoxia with or without the load was required to induce the periodic breathing and high upper airway resistance or obstructive apneas. Martin et al\textsuperscript{64} demonstrated that this phenomenon existed in OSA in that upper airway resistance gradually increased breath to breath as the apnea approached in the hypopneic portion of the periodic breathing cycle.

**Inspiratory Timing**

Another interesting variable that affects upper airway caliber is the timing of inspiratory activity of the upper airway and chest wall inspiratory muscles. During resting ventilation in animals and man, it has been demonstrated that inspiratory activity of the upper airway motor neurons and other muscles begins before the activity of the phrenic nerve, diaphragm, and thorax.\textsuperscript{62,63} Recently, we found that the relative timing of inspiratory electrical activity of the upper and lower respiratory muscles in sleep apnea patients was closely correlated with breath-to-breath as well as within-breath changes in upper airway resistance\textsuperscript{64} in these patients.\textsuperscript{64} The mechanism of these timing differences is uncertain but might be related to pontomedullary ventilatory activity. In this regard, it is known that different ventilatory motorneuron pools may have different thresholds of activation for a given level of "ventilatory drive" activity.\textsuperscript{65,66} These results are consistent with the modeling experiments of Longobardo et al.\textsuperscript{58}

**CO\textsubscript{2} Threshold**

Another factor that affects the level of ventilatory drive activity during sleep is the CO\textsubscript{2} threshold for breathing. During wakefulness, very severe levels of hypocapnia and alkalosis are required to induce central apnea. During sleep, however, the degree of hypocapnia and alkalosis needed to induce the apnea is much less than during wakefulness.\textsuperscript{67}

The next step in our pathophysiologic model is to combine the concept of inspiratory muscle imbalance with that of isolated regional upper airway collapse. We could speculate that if, for example, the obstruction occurs at the palatal level, then there is exaggerated palatal muscle hypotonia during the low-drive phase of the periodic breathing cycle. In contrast, if the obstruction is more distal in the airway, in the hypopharynx we would predict there would be diminished tonic activity of muscles surrounding this region of the upper airway.

**Summary**

This article has reviewed the anatomic, compliance, reflex, and respiratory muscle variables that affect upper airway caliber and abnormalities which may precipitate upper airway collapse during sleep. One or more of these variables may be important in the mechanism of OSA in any given patient.

First, anyone with anatomic narrowing of the upper airway is susceptible to OSA. However, we do know if anatomic narrowing of the upper airway is necessary for the development of OSA. Surely, heavy snoring produces pharyngeal trauma and possibly edema or inflammation, which in turn may narrow the upper airway. Submucosal adipose tissue or cervical adipose tissue may compress the airway when the tonic electrical activity of the pharyngeal muscles decreases with sleep onset.

Data reviewed support the idea that the upper airway of OSA patients may be more collapsible than

![Figure 6: Effect of upper airway/chest wall inspiratory muscle relative activity on upper airway caliber and ventilation during sleep. An increased upper airway/chest wall inspiratory activity ratio produces pharyngeal dilatory activity, low upper airway resistance, and higher tidal volume breaths. A low upper airway/chest wall inspiratory activity ratio results in pharyngeal narrowing, high upper airway resistance, and low tidal volumes or obstructive apneas. Fluctuation of the upper airway/chest wall inspiratory muscle relative activity results in periodic breathing and its mechanical consequences.](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21639/ on 04/02/2017)
the upper airway of nonapneic subjects. Intrinsic tissue abnormalities have not been demonstrated that might be responsible for this collapsibility. Changes in collapsibility found are consistent with, and may be due to, changes in tonic and phasic contraction of upper airway muscles. Abnormalities in reflexes affecting upper airway size surely might exist in OSA. Edema or inflammation of pharyngeal tissues might not only narrow the upper airway but might also impair normal function of the receptors responsible for initiating protective reflexes.

We propose the fluctuation between a low- and a high-drive state contributes to upper airway collapse in OSA. With this fluctuation the balance of forces and critical pressure concepts discussed above come into play (Fig 6). By stimulating upper airway inspiratory muscles, CO₂ eliminates the hypopneic, low-drive, high-resistance periods and thereby reduces the number of apneas. In addition, preferential stimulation of upper airway muscle activity dilates the upper airway per se.

If the relative value of each of these factors can be determined diagnostically, perhaps therapy can be made more specific. By being more specific, therapy should be more successful than the present practice of prescribing a particular therapy, regardless of the specific mechanism responsible for the OSA in a given patient.

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