The upper airway is a complex structure that serves as the conduit from the external environment to the intrathoracic airways and lungs. The anatomic regions of the upper airway (Figure 50-1) include the nasal cavity, nasopharynx, velopharynx behind the soft palate, oropharynx, hypopharynx, and larynx. This conduit has a variety of functions, including the filtering and conditioning of air, olfaction, mastication and deglutition, phonation, coughing, and protection of the lower airways and lungs from large particulate material.

This chapter focuses on the physiology and pathophysiology of the respiratory-related functions of the upper airway. The discussion of other upper airway functions is limited to their interaction with respiratory function.

ANATOMY AND PHYSIOLOGY OF THE UPPER AIRWAY

Nose
To enter the upper airway, air flows rapidly upward through the anterior nares or nasal vestibules, which are 1 cm–diameter channels in the anterior portion of the nose. Coarse hairs or vibrissae within the vestibules serve to filter larger particulate matter. The air then encounters the nasal septum, which divides the nasal passage into two fossae. The lateral walls of the fossae contain irregular projections known as the turbinates, which create turbulent flow and reduce flow rate. This prolongs contact of the inspired air with the nasal mucosa, which at this level is richly supplied with a system of subepithelial capillaries and venous sinusoids, along with submucosal glands and goblet cells. The rich vascularization of the mucosa provides for humidification and temperature conditioning of the inspired air. Production of a mucous layer by glandular structures provides for trapping of particulate matter. Nasal secretions produced by the highly vascular mucosa are rich in immunoglobulins, cytokines, and other cytolytic substances, and there is extensive mucosal production of nitric oxide by the nose and paranasal sinuses; all of these have potent antimicrobial activity. There is thus considerable filtering, temperature conditioning, and humidification of the air traversing the nasal fossae, which have an important protective function for the lower airways.

Although the nose accounts for over 50% of upper airway flow resistance in normal, awake persons, it is the preferred route of breathing during resting ventilation. As ventilatory drive increases, some dilatation of the nares and vasoconstriction of the nasal mucosa may help to reduce airflow resistance, but as demands increase, the mouth opens and the lower-resistance oropharyngeal route is recruited, although at the cost of reduced conditioning of the inspired air. Other functions of the nose include olfaction and a contribution to phonation, in that the nose acts as a resonating chamber for some components of speech.

Pharynx
This structure consists of the nasopharynx, oropharynx, and hypopharynx. Inspired air exits the nasal passages posteriorly through 2.5 × 1.5 cm openings known as the choanae and enters the nasopharynx. The nasopharynx extends from the choanae down to the lower margin of the soft palate. The segment of the nasopharynx immediately behind the soft palate has been termed the velopharynx. The mucosa of the posterior nasopharyngeal wall contains a collection of lymphoid tissue termed the single pharyngeal or adenoid tonsil. This structure can hypertrophy and produce nasal obstruction, which often contributes to obstructive sleep apnea (OSA) in children. As with the palatine tonsils between the anterior and posterior tonsillar pillars lower down, the adenoid tends to involute after puberty.

The muscular structures in the wall of the nasopharynx and soft palate play a major role in speech, swallowing, and breathing. These muscles act to partition airflow between the oral and nasal routes, particularly under conditions of increased ventilatory drive. The palatal muscles are also important in the maintenance of airway patency.
The oropharynx lies behind the oral cavity and extends from the soft palate superiorly to the tip of the epiglottis inferiorly. The lateral walls include the anterior (palatoglossal) and posterior (palatopharyngeal) tonsillar pillars, which merge superiorly into the soft palate and between which lie the fossae of the palatine tonsils. The posterior pharyngeal wall is largely composed of the pharyngeal constrictor muscles, whereas the posterior aspect or base of the tongue lies anteriorly. This structure serves as the main conduit for both solids and liquids from the mouth to the esophagus and for the flow of air through to the larynx. The coordination of these various neuromuscular functions is achieved through reflex control involving neural afferents in the pharyngeal mucosa; these project to pontomedullary centers, which integrate this information and regulate swallowing and respiratory functions.

Swallowing is characterized by initial elevation of the larynx, followed by active contraction of the oropharynx, leading to shortening and constriction of the pharynx to actively propel food toward the esophagus. The normal coordination of this action in humans is such that swallowing occurs almost exclusively during late expiration in seated humans and is accompanied by respiratory inhibition, that is, prolongation of expiratory time, and other processes, such as vocal cord closure and laryngeal elevation, that assist in protecting the laryngeal aperture.7–9

In contrast to the passage of food during swallowing, airflow through the oropharynx is passive, being driven by the negative intrathoracic pressure generated by the respiratory pump muscles. However, whereas the nasal and laryngeal segments of the upper airway are supported by bony and cartilaginous structures, the pharynx is a collapsible muscular tube. There is clear evidence that the stability and patency of this structure during breathing depend upon tonic and phasic activation of muscles surrounding the airway, which act to stiffen and dilate the pharynx during inspiration.10–13 These muscles include the genioglossus muscle, which positions and stabilizes the tongue, palatal muscles such as the tensor and levator palatini and the palatoglossus and palatopharyngeus muscles, and muscles that stabilize the hyoid bone, such as the geniohyoid and sternohyoid muscles. If the dilating musculature is not sufficiently activated, collapse of this segment will occur during inspiration, due to a suction effect of the negative intraluminal pressure associated with inspiratory airflow. Thus, in generating inspiratory impulses, the brainstem respiratory controller produces a sequential wave of respiratory muscle activation, with initial activation of pharyngeal dilators, which stiffen and dilate this conduit. Subsequently, laryngeal activation leads to opening of the glottic aperture, chest wall muscle activation that stiffens and expands the chest wall, and diaphragmatic activation.14–16

Pharyngeal caliber is also modulated by important reflex mechanisms that regulate within-breath levels of phasic muscle activation. Both tonic and phasic activity of pharyngeal dilators and the protective reflexes are reduced during sleep, which leads to increased airflow resistance during sleep in normal subjects and can contribute to collapse of the upper airway in patients with OSA.

The hypopharynx extends downward from the upper margin of the epiglottis to the lower border of the cricoid cartilage, serving as the conduit from the oropharynx to the laryngeal inlet and esophagus. The piriform recesses lie on each side of the hypopharynx. These recesses serve to direct food boluses down and away from the larynx in transit to the esophagus. During swallowing, as noted above, there is laryngeal constriction and a movement of the epiglottis in order to protect the laryngeal aperture.

**Larynx**

The structure of the larynx, and in particular the cartilaginous skeleton and musculature, is illustrated in Figure 50-2, which also illustrates the action of the musculature on glottic patency.3,17–19 In addition to the thyroid, cricoid, and arytenoid cartilages, the epiglottic cartilage, which descends to protect the laryngeal aperture during swallowing, is also considered to be part of the laryngeal apparatus. The larynx plays an integral role in all upper airway functions, including respiration, phonation, cough, swallowing, and vomiting. As with the pharyngeal structures, these activities are initiated and coordinated by brainstem centers, with modulation by afferent neural inputs from the airway itself. In the case of the larynx, there is a rich sensory array of mucosal sensory receptors, which respond to changes in airflow, pressure, temperature, and laryngeal position. Impulses from these receptors are conveyed centrally through the superior laryngeal nerve to modulate laryngeal function and breathing pattern. Motor innervation of the laryngeal musculature is conveyed through the recurrent laryngeal nerves, with the exception of the cricothyroid muscle, which is supplied by the external branch of the superior laryngeal nerve. The recurrent laryngeal nerves arise from the vagus nerve within the thorax and travel superiorly along the mediastinal structures to the larynx. On the right, the recurrent laryngeal nerve arises at the level of the subclavian artery.
and on the left, the nerve arises at the level of the aortic arch. Disease processes, including intrathoracic disease, that disrupt the recurrent laryngeal nerve therefore lead to vocal cord paralysis and laryngeal dysfunction, which has implications for all of the other functions of the larynx.

Although protective closure of the larynx during swallowing is part of the integrated deglutition process, there is also a more basic laryngeal protective response called the “glottic closure reflex.” This is characterized by a short-latency activation of the adductor muscles to rapidly close the glottic aperture in response to stimulation of the laryngeal mucosa by tactile or chemical stimuli. This is therefore a critical response that protects against aspiration of foreign material into the upper airway. It is of note that, in contrast to the situation in many mammalian species, the human reflex is not crossed, so that damage to the superior laryngeal nerve on one side can result in failure of ipsilateral vocal fold closure, thereby increasing the risk of aspiration. 

Although the glottic closure reflex represents a crucial protective mechanism, the response may become exaggerated in some disease conditions, leading to laryngospasm or prolonged glottic closure following withdrawal of the inciting stimulus.

With respect to the respiratory function of the larynx, during inspiration the posterior cricoarytenoid muscle, the only vocal cord abductor muscle, is activated to widen the glottic aperture. There is simultaneous activation of the cricothyroid muscle, which acts to lengthen the vocal fold. The concurrent lengthening and abduction of the folds lead to an increase in glottic cross-sectional area, thus reducing resistance to inspiratory airflow. The posterior cricoarytenoid muscle relaxes during expiration, whereas the cricothyroid muscle may remain active, to maintain the length of the cords. Under some conditions, there is active contraction of the adductor muscles to narrow the aperture and produce expiratory “braking.” This strategy is adopted in an attempt to maintain end-expiratory lung volume. This occurs, for example, in neonates with respiratory distress syndrome and is manifested as expiratory grunting due to glottic closure. An extreme instance of prolonged glottic closure appears to occur in apnea of prematurity, in which experimental evidence has demonstrated that apneas are associated with active glottic closure.

In some patients, laryngeal function becomes disturbed such that there is intermittent inspiratory closure of the vocal cords. This condition has been variously termed vocal cord dysfunction syndrome, paradoxical vocal cord motion, and laryngismus stridulus. The clinical presentation may mimic both asthma and organic upper airway obstruction and may be acute and lead to endotracheal intubation. Spirometric flow–volume curves are very helpful in making the diagnosis (see below). A substantial proportion of affected individuals also have asthma; patients without asthma are often women who have been misdiagnosed as asthmatic. This syndrome typically occurs in the absence of any evident structural laryngeal disease, and the mechanisms responsible are unclear. However, psychogenic factors appear to play a role as the dysfunction is intermittent, may be worse in times of emotional stress, and, even if sustained during wakefulness, tends to disappear during sleep. Furthermore, psychiatric disorders are common among affected individuals. Treatment approaches include patient education, psychotherapy as needed, and referral to a speech pathologist.

The larynx also plays a major role in phonation. Although sound can be produced passively by creating airflow through the larynx, the generation of speech or song requires finely controlled activation of laryngeal muscles. These muscles act to shape and position the vocal cords to generate speech and modulate the spatial relationship between the cricoid and thyroid cartilages to vary the pitch of the sound produced. Further modulation of sound is produced superiorly in the pharynx and nasal cavity. Breathing during speech is characterized by rapid inspiration, followed by prolonged expiration, during which the subglottic pressure is maintained relatively constant as the fine motor actions of the laryngeal apparatus produce sound. Stuttering appears to represent an example of an altered interaction between laryngeal and respiratory function during speech, the mechanisms for which remain poorly understood.

CLINICAL PHYSIOLOGY OF UPPER AIRWAY OBSTRUCTION

CLINICAL DESCRIPTION

Obstruction of the upper airway can occur in various clinical contexts and disease states, although it is much less
common than obstructive disease of the lower airway, such as asthma or chronic obstructive pulmonary disease (COPD). Unfortunately, the clinical presentation of the two may be very similar (dyspnea and noisy breathing), so that the less common diagnosis of upper airway obstruction may be missed if a careful clinical evaluation and appropriate testing are not performed. A missed diagnosis, particularly in the context of acute or severe upper airway obstruction, may have devastating consequences for the patient as appropriate treatment may be delayed beyond the point of severe airway compromise and respiratory arrest.

A hallmark clinical feature of upper airway obstruction is dyspnea with stridor, a loud, constant-pitch inspiratory sound that indicates obstruction of the extrathoracic airway. Severe extrathoracic or variable intrathoracic large airway obstruction may also cause expiratory prolongation and a wheeze-like sound, making it difficult to distinguish from disease of the lower airways. Other symptoms associated with upper airway obstruction include cough, hoarseness, dysphagia, and orthopnea, depending upon the location and nature of the obstructing lesion. Although it is beyond the scope of this chapter to provide an exhaustive description of causes of upper airway obstruction, a list of common pathologies is provided in Table 50-1.

**physiologic testing for upper airway obstruction**

Forced expiratory and inspiratory spirometry with recording of the flow–volume curve is the most important physiologic tool for the diagnosis of upper airway obstruction. Examples of normal and pathologic flow–volume curves are shown in Figure 50-3. Normally, there is an initial rapid rise in expiratory flow to a peak value that is dependent on effort, lung elastic recoil, and flow in the large airways. As lung volume decreases, flow becomes effort-independent and determined by the balance between lung recoil and flow resistance in progressively smaller airways. During forced inspiration, flow is effort dependent throughout, with the peak value occurring at midinspiration. Peak expiratory flow rate is considerably larger than peak inspiratory flow rate because of the effects of lung elastic recoil. However, at 50% of vital capacity, forced inspiratory flow (FIF50) is somewhat greater than forced expiratory flow (FEF50), due in part to normal inspiratory dynamic compression of the airways. Thus, the normal FIF50/FEF50 ratio is slightly greater than 1.

Obstructing lesions of the upper airways may be either fixed or variable; that is, lesions produce narrowing that varies with pressures acting across the airways during inspiration and expiration (Figure 50-4). In the case of variable intrathoracic large airway obstruction (see Figure 50-3B), during expiration, pleural pressure is more positive than intratracheal pressure, leading to dynamic compression of the airway and thereby increased airway narrowing and reduced expiratory flow. However, during inspiration, there is a net distending pressure across the large airway, so that patency of the lumen tends to increase, yielding a relative preservation of inspiratory flow rate. The FIF50/FEF50 ratio will therefore be well above 1, typically in the range of 2 to 3.

In the case of variable extrathoracic upper airway obstruction (see Figure 50-3C), the pressure surrounding the airway is atmospheric, so that during inspiration, there is a net negative transmural pressure, which tends to worsen...
airway narrowing and reduce inspiratory flow. In contrast, during expiration, the positive pressure within the airway produces a transmural distending pressure and reduces the extent of narrowing, resulting in increased expiratory relative to inspiratory flow. Thus, the FIF₅₀/FEF₅₀ ratio will be less than 1.

The anatomy of many upper airway lesions, however, is such that the degree of obstruction is not materially influenced by the pressures acting across the airway, with resultant comparable reductions in both inspiratory and expiratory flow (see Figure 50-3D). In this case, the FIF₅₀/FEF₅₀ ratio may be close to 1.

From Figure 50-3, it can be seen that inspection of the flow–volume curve and recognition of the characteristic changes in pattern are crucial to the recognition of upper airway obstruction. It is important to emphasize that one cannot rely solely upon tabular data from simple spirometry to exclude the diagnosis of upper airway obstruction. Because flow in the medium and small airways contributes significantly to forced expiratory volume in 1 second (FEV₁), substantial large airway obstruction may be present before significant changes in FEV₁ occur. When concomitant airway disease, such as COPD, is present, the sensitivity of spirometry for the detection of upper airway obstructing lesions is even lower. Peak expiratory flow rate is much more sensitive for the presence of expiratory large airway obstruction, and a hallmark finding in tabular data is the detection of an increase with helium of more than 50% in either peak expiratory or inspiratory flow. Heliox administration is also a useful, albeit temporary, therapeutic adjunct in the clinical management of upper airway obstruction.

Mediastinal masses may cause intrathoracic large airway obstruction that varies with body position. Owing to gravitational factors, intrathoracic large airway obstruction resulting from anterior mediastinal masses may be more prominent when the patient is supine. Airway obstruction can worsen with the chest wall relaxation that occurs on the induction of anesthesia, so that preoperative and postoperative airway management in such patients requires careful attention. The positional variation of large airway obstruction can be evaluated by assessing changes in peak flow rates during seated versus supine spirometry.

In the context of acute, severe extrathoracic upper airway obstruction (eg, epiglottitis, foreign body aspiration, or acute laryngeal injury), inspiratory intrathoracic driving pressures may become extremely negative, and this, in turn, may lead to the development of "negative-pressure pulmonary edema." This is believed to be due to a combination of increased venous return leading to increased pulmonary blood volume and negative pericapillary interstitial tissue pressure caused by large negative intrapleural pressures, resulting in forces that favor fluid transudation into the interstitium. In some patients, left ventricular (LV) dysfunction is believed to also contribute because of increased LV wall transmural pressure, that is, afterload, resulting from the negative intrapleural pressure. Management of this condition primarily involves management of the upper airway obstruction.

**PATHOPHYSIOLOGY OF UPPER AIRWAY COLLAPSE DURING SLEEP: OBSTRUCTIVE SLEEP APNEA**

**Clinical Description**
OSA is characterized by repeated episodes of upper airway obstruction during sleep. This important condition is highly prevalent in the adult population, being estimated to affect 2 to 9% of women and 4 to 15% of men, depending on the precise definitions used and the population under study. OSA also occurs in the pediatric age group, although with considerably lower prevalence. OSA is associated with considerable morbidity, increased health care resource utilization, and, probably, increased mortality. Apneic episodes are characterized by upper airway closure and progressively increasing respiratory efforts driven by chemoreceptor and mechanoreceptor stimuli, which then provoke arousal from sleep and reopening of the
These events result in sleep fragmentation, repetitive hypoxemia, and swings in heart rate, blood pressure, and cardiac output, which are responsible for the clinical sequelae of OSA. The latter include excessive daytime sleepiness, impaired concentration, cognitive functions and memory, and mood disturbances. There is a rapidly growing body of data linking OSA to increased cardiovascular risk, including hypertension, cardiac ischemic events, arrhythmia, cerebrovascular accidents, congestive heart failure, and pulmonary hypertension. Severe OSA can also be associated with changes in ventilatory control and hypoventilation during wakefulness, typically in the context of underlying lung dysfunction. There is also growing evidence of a link between OSA and asthma. These issues are discussed further below and in a subsequent chapter.

OSA should be suspected clinically in patients with a history of heavy habitual snoring and excessive daytime sleepiness. Sleep testing is performed to establish the diagnosis. The current “gold standard” test is complete overnight polysomnography performed in a sleep laboratory. This test involves recording of the electroencephalogram, electrooculogram and submental electromyogram for sleep–wake staging, pulse oximetry, determination of airflow with an oronasal thermistor or through nasal pressure (currently the method of choice), determination of respiratory effort with inductance plethysmography, piezoelectric sensors or mercury strain gauges around the thorax and abdomen or with an esophageal balloon (typically reserved for research studies or special clinical cases), determination of body position with mercury switch or video recording, recording of sound (snoring) with a microphone, and detection of periodic limb movements with leg electromyographic electrodes. A typical polysomnographic tracing from a patient with severe OSA is shown in Figure 50-5.

The raw data tracings from the sleep study are scored by a technologist to identify sleep–wake state for each consecutive 30-second period (epoch) of the night, according to standard criteria. The respiratory signals are scored to identify apneas (10 seconds of complete cessation of airflow) and hypopneas (event lasting >10 seconds, with reduced airflow associated with oxygen desaturation and/or brief arousal from sleep), and whether these are obstructive or central in nature (associated or not with ongoing respiratory effort during events). Summary data are generated in both tabular and graphic form to describe the physiology of sleep, breathing, and other events through the night (Figure 50-6). Although

![Figure 50-5](image-url)
Physiology of the Upper Airway and Upper Airway Obstruction in Disease

the polysomnogram therefore provides extensive physiologic information, which is useful in the clinical setting, this is a time- and cost-intensive testing procedure of limited availability. Owing to the prevalence of OSA and issues of limited access to full polysomnography, there is a growing reliance on simplified tests that record oximetry alone, or oximetry with airflow and respiratory effort channels, to establish the diagnosis.

**MECHANISMS OF UPPER AIRWAY COLLAPSE DURING SLEEP**

As described above, the pharyngeal airway can be considered as a collapsible tube, the patency of which is determined by a balance between forces tending to close the airway, such as intraluminal suction pressure during breathing, and forces acting to maintain airway patency, notably the activation of upper airway dilator muscles. The current broad conception of OSA pathophysiology is that upper airway anatomic dimensions are reduced in affected patients, leading to compensatory activation of upper airway dilators. Muscle activity is therefore adequate during wakefulness to maintain airway patency, but at sleep onset, when upper airway tonic and phasic activity are reduced and protective reflexes are inhibited, airway closure supervenes.\textsuperscript{12,13,42}

The evidence supporting these concepts, as well as other potential factors contributing to the pathophysiology of OSA, is considered in the following sections. A schematic of the mechanisms contributing to upper airway collapse during sleep is shown in Figure 50-7.

**Upper Airway Anatomy in OSA**

Upper airway collapse during sleep in OSA occurs predominantly in the retropalatal and retroglossal airway, that is, the velopharynx and oropharynx.

**Factors Affecting Upper Airway Calibre**

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<td>Traction on UA</td>
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<td>Lower</td>
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<td>Adaptation</td>
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<td>Normal Sleep-related Decrement</td>
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<th>Collapse</th>
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<td>Reduced EELV, Less Traction</td>
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<td>Increased</td>
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<td>More Positive</td>
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<td>Injury, Dysfunction</td>
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<td>Marked vs. Heightened</td>
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<td>Blunted (latency, amplitude)</td>
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<td>Neural, Muscular Dysfunction</td>
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<td>Altered Airway Calibre, Tissue Characteristics, Neuromuscular fxn</td>
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**FIGURE 50-6** Composite hypnogram from a patient with severe obstructive sleep apnea and hypopnea. Individual apneas and hypopneas are indicated by vertical bars on the “Respiratory” graph. The patient was awake from 1:45 am to 3:15 am, so that no respiratory disturbance occurred during that time. Note that in this patient the severity of respiratory disturbance is influenced by sleep stage and body position. Oxygen desaturation is more severe during rapid eye movement (REM) than during non-REM sleep, in part due to increased length of events related to increased arousal threshold during REM. During stage 2, non-REM sleep apneas predominate when the patient is supine (eg, 10 pm), whereas hypopneas predominate when the patient is on the side (eg, 1 am), due to gravitational effects on upper airway caliber. This results in positional effects on event-associated oxygen desaturation.

**FIGURE 50-7** Schematic of mechanisms contributing to upper airway collapse during sleep in obstructive sleep apnea.
There is abundant evidence that the airway dimensions are reduced in OSA patients in comparison with normal control subjects. Techniques that have been used to study airway size include cephalometry, fluoroscopy, acoustic reflection, videodendoscopy, computed tomography, and magnetic resonance imaging (MRI). The accumulated data indicate that both reductions in the dimensions of the bony craniofacial framework and increases in the size of soft tissue structures surrounding the airway may contribute to reduced airway dimensions. Alterations in craniofacial proportions that have been described include reduced length of the mandibular ramus, inferior positioning of the hyoid bone, and retroposition of the maxilla. In addition to circumferential narrowing, increased airway length may also be a factor. Increased distance between the hyoid bone and the mandibular plane found in cephalometric studies and increased airway length found in a recent MRI modeling analysis appear to be associated with an increased likelihood of upper airway collapse.

Increases in soft tissue dimensions that have been found in imaging studies include enlargement of the soft palate, tongue, parapharyngeal fat pads, and lateral pharyngeal walls. These increases contribute to anatomic narrowing and may also contribute to increased tissue pressure, which favors airway collapse. The increased tissue volume probably reflects changes that also affect mechanical characteristics of the tissues, leading to altered airway biomechanics (see below). Several mechanisms appear to contribute to these soft tissue changes. Upper airway edema has been found clinically, histologically, and by MRI scanning. This may result from upper airway trauma during obstructive events, hypoxemia, systemic inflammation, or a combination of factors. Mucosal edema improves with nasal continuous positive airway pressure (CPAP) treatment of OSA. Increased deposition of fat in the upper airway in obese patients contributes to narrowing, particularly in the region of the parapharyngeal fat pads, but elsewhere in the upper airway as well. Weight gain is also associated with increased amounts of fat-free tissue, some of which is muscle, such that obesity may contribute to increased upper airway muscle mass. The latter may also be due to loading with hypertrophy or muscle injury and edema, which is discussed further below. Genetic factors probably also play a role in determining soft-tissue volume, in a manner analogous to craniofacial structure.

Lung Volume Effects on Upper Airway Size Studies in both humans and animals have shown that upper airway caliber is influenced by changes in lung volume, such that decreased lung volume is associated with decreased upper airway dimensions and increased airflow resistance. This appears to be due to effects of tracheal tug on upper airway length and/or wall characteristics. OSA patients appear to have greater lung volume dependence of upper airway caliber than normal subjects. Assumption of the recumbent position is associated with reduced expiratory lung volume, and obese patients have particularly marked reductions in supine functional residual capacity. Furthermore, lung volume may also decrease during the course of obstructive apnea. These reductions in lung volume would therefore contribute to reduced upper airway caliber, further increasing the predisposition to collapse.

Mechanical Properties of the Upper Airway The cross-sectional area of the pharynx is determined by the interaction between the mechanical characteristics of this structure, that is, compliance of the wall, and the transmural pressure. The passive mechanical properties of the upper airway in OSA have received considerable attention. Schwartz and colleagues have modeled the upper airway as a Starling resistor and produced an extensive literature assessing the collapsibility of the pharyngeal airway under passive conditions. This typically involves the application of a range of positive and negative airway pressures, with extrapolation from steady-state pressure-flow relationships to determine the pressure associated with airway closure, or critical pressure, \( P_{\text{crit}} \). During sleep, \( P_{\text{crit}} \) values are about \(-13 \text{ cm H}_2\text{O}\) in normal subjects, about \(-6 \text{ cm H}_2\text{O}\) in snorers, and about \(-2 \text{ cm H}_2\text{O}\) in patients with predominantly obstructive hypopnea; in apneic patients, the upper airway closing pressure is positive, often in the range +10 to +15 cm H₂O. Isono and colleagues have studied the static properties of the human pharynx under conditions of general anesthesia and muscle paralysis. These authors found that for OSA versus control subjects, the average and maximal velopharyngeal cross-sectional areas were smaller, closing pressures were higher, and area-pressure compliance curves were shifted down and to the right, indicative of increased collapsibility. Other authors have also shown reduced distensibility of the upper airway in OSA. Collectively, these data point to the presence of a smaller, more collapsible, and less distensible, that is, less compliant, airway in OSA.

During active breathing, the transmural pressure across the pharynx is another major determinant of cross-sectional area. The transmural pressure is determined by the balance between the intraluminal pressure, which is negative during inspiration, and the extraluminal or tissue pressure. The latter is determined by the volume and mechanical characteristics of tissues surrounding the airways and by the level of activation of surrounding constrictor and dilator muscles. Muscle activation will be considered in the following section. No direct measurements have been made of interstitial tissue pressure in humans, although measurements in anesthetized pigs showed positive extraluminal pressures that correlated with airway obstructive events. The occurrence of airway collapse under passive conditions without negative intraluminal pressure suggests that positive tissue pressures probably also exist in humans.

Surface tension contributes to pharyngeal collapsibility. This may be particularly important at the point where generation of an opening pressure is required to separate mucosal surfaces that have come into contact during complete airway collapse. However, surface forces will also influence the distensibility of the rounded pharyngeal structure throughout the respiratory cycle. Upper airway surface lining fluid from OSA subjects shows increased surface tension in comparison with that of fluid.

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from control subjects.\textsuperscript{58} Topical application of artificial surfactant renders the upper airway less collapsible and can produce reductions in the severity of obstructive events during sleep in OSA patients.\textsuperscript{57}

**Neural Control of Pharyngeal Motor Activity** As discussed earlier in this chapter, the tonic and phasic activation of dilatory musculature surrounding the pharyngeal airway is critical to the prevention of airway collapse as negative intraluminal pressure during inspiration causes a decrease in transmural pressure. Results from several groups have indicated that the activity of upper airway dilators is greater in OSA patients than in normal subjects, and this is believed to represent a compensatory mechanism for the inherent anatomic compromise of the airway in such patients.\textsuperscript{59,60}

There are several major inputs influencing the activation of pharyngeal dilator muscles by the brainstem respiratory controller.\textsuperscript{13,61–63} As noted above, the normal integrated pattern of central respiratory output is such that there is preactivation of upper airway musculature before activation of the lower pump muscles occurs.\textsuperscript{14,15} Perturbations in this pattern, with delayed activation of upper airway dilators in relation to chest wall and diaphragm activation, have been reported in some patients with OSA, and this is believed to contribute to upper airway instability.\textsuperscript{15} Central output to upper airway motor neurons is also influenced by chemoreceptor stimulation, so that fluctuations in carbon dioxide level may destabilize output to the dilator muscles.

Most important for sleep apnea, however, is the influence of sleep-related decrements in pharyngeal motor output. Whereas the upper airway may be narrowed during wakefulness in OSA, obstruction occurs only during sleep, emphasizing the importance of state-dependent influences on upper airway control. Sleep onset in normal subjects is initially associated with reduced tonic and phasic activity of the genioglossus, geniohyoid, and palatal muscles. However, phasic muscle activity tends to recover as sleep is established, whereas muscles with a predominantly tonic pattern of activation tend to show further losses of activity as sleep deepens.\textsuperscript{13,42} It is therefore believed that reduced tonic activation is an important factor contributing to upper airway collapse. However, both phasic and tonic muscle activity may be potently inhibited during rapid eye movement (REM) sleep,\textsuperscript{64} accounting in part for the increased severity of OSA during REM versus non-REM sleep. A key observation in OSA patients is that the fall in upper airway dilator electromyographic activity associated with sleep onset appears to be substantially greater than in controls.\textsuperscript{65} Thus, upper airway dilator activity is greater during wakefulness, representing a compensation for upper airway size and mechanics, but appears to be lost at sleep onset.

The activity of upper airway dilators is also modulated by reflex inputs. The available evidence indicates that the most important local stimulus for activation of these muscles is intrapharyngeal negative pressure.\textsuperscript{13,66} Reflex activation by pulses of negative pressure applied to the upper airway has been described for the genioglossus, levator palatini, and palatoglossus muscles. This negative pressure reflex is impaired for the levator palatini and palatoglossus muscles in OSA versus control subjects. Furthermore, even in normal individuals, there is a decrease in the activity of this reflex at sleep onset. Thus, an important modulating influence on upper airway caliber is attenuated during sleep, and this is believed to predispose to upper airway collapse.

The afferent inputs to the negative pressure reflex arise from the mucosa of the oropharynx and larynx.\textsuperscript{66–68} The importance of mucosal afferents to upper airway motor control has been demonstrated in studies involving topical application of anesthetic to interfere with mucosal sensory receptor activity. Topical upper airway anesthesia leads to reduced dilator muscle activity and increased pharyngeal airflow resistance during wakefulness and sleep and can induce apnea and hypopnea in normal subjects, increase the frequency of obstructive events in snorers, and lead to delayed end-aneptic arousal and increased apnea duration in OSA subjects.\textsuperscript{67–69} Recently, we showed the presence of an impairment in mucosal mechanosensory function in the oropharynx of snorers and OSA patients, which partially improved in OSA patients following CPAP treatment.\textsuperscript{67} The severity of oropharyngeal sensory impairment correlates with the latency of the palatoglossus and genioglossus muscle reflex responses to pulses of negative pressure delivered to the upper airway, as described by Mortimore and Douglas.\textsuperscript{70} Therefore, the afferent neural impairment appears to contribute to impaired dilator reflex responsiveness, which probably has important implications for upper airway function. Additional studies using endoscopic sensory testing have also demonstrated impaired laryngeal sensation in OSA patients versus controls.\textsuperscript{68} Within the OSA group, there appeared to be two subgroups, one with normal sensation and another with abnormal sensation, the severity of which correlated with the apnea–hypopnea index. Thus, in some patients, an impairment of mucosal sensory function appears to contribute to OSA pathophysiology.

Although the mechanisms underlying impaired upper airway sensation remain unclear, histologic studies have demonstrated neural changes consistent with injury and repair that could represent the basis for mucosal sensorineural dysfunction.\textsuperscript{49,68} An accumulating body of data points to the presence of significant cellular inflammation in upper airway tissue.\textsuperscript{49,68} As noted above, this may be related to tissue injury resulting from vibration-associated trauma, hypoxemia, or other factors, including the state of systemic inflammation, which has been associated with both OSA and obesity. Inflammatory mechanisms or mechanical trauma may account for the neural injury observed in the upper airway mucosa, although further investigation is required to establish the precise mechanisms involved.

**Pharyngeal Muscle Function in OSA** There is accumulating evidence that OSA is associated with changes in the structure and function of the upper airway dilator muscles. Some of these changes appear to be adaptive in nature, whereas others are more consistent with injury and may lead to impaired contractile function, thus contributing to upper airway dysfunction. As noted above, upper airway dilator
activity is increased in OSA patients during wakefulness. Whereas sleep-related decrements in upper airway muscle activity contribute to upper airway collapse, the termination of obstructive events is associated with massive activation of upper airway dilators, which, it should be noted, occurs under hypoxic conditions. Thus, the evidence suggests that, overall, upper airway muscle activity is substantially increased in OSA. This raises the possibility that these muscles could undergo secondary changes as a direct consequence of their increased activity level. Skeletal muscle is well recognized to alter its phenotype in order to adapt to the prevailing demands placed upon it, thereby maximizing muscle efficiency. Properties such as muscle fiber size, contractile protein isoform profile, and metabolic enzyme content can be readily modified, with resultant changes in muscle performance. However, when excessive contractile demands are placed upon muscle, it is well documented that the structural integrity of the muscle cell can be physically disrupted by the forces produced during muscle contraction. This activity-induced injury is particularly prominent when the forces opposing muscle contraction result in muscle lengthening during activation, or so-called eccentric contraction.

Eccentric contractions of upper airway dilator muscles have been demonstrated during airway occlusion and progressive hypercapnia in anesthetized cats. Because similar events occur in human OSA, it has been hypothesized that eccentric contractions also occur in pharyngeal dilators in this condition, although at least two possible mechanisms: (1) muscles that are mechanically linked could contract against one another, as has been demonstrated for the sternohyoid and geniohyoid muscles during airway occlusion in anesthetized animals, and (2) large negative intraluminal pressures associated with pharyngeal obstruction, which could act to forcibly lengthen the opposing dilator muscles.

Petrof and colleagues, using the English bulldog, which suffers from OSA, found that the sternohyoid muscle, an important upper airway dilator muscle, showed evidence of fiber-type shift but also changes consistent with activity-induced muscle injury, consisting of abnormal fiber morphology (central nucleation, fissured and moth-eaten appearance), inflammatory cell infiltrates, and increased amounts of connective tissue. Muscle injury was also found in the geniohyoid muscle, another pharyngeal dilator. A subsequent MRI study using the bulldog model showed changes consistent with muscle edema or fibrosis in four of five pharyngeal muscles examined. These changes were not seen in limb muscles or in control animals. Thus, there is compelling evidence for muscle injury in this animal model of OSA.

Studies on human OSA tissues have also shown evidence of both adaptation and injury. Several smaller studies have shown histologic changes consistent with injury. However, studies by Series and colleagues on the musculus uvulae muscle did not show pathologic evidence of injury but demonstrated an increase in the proportion of fast-twitch (type IIa) fibers and the activity of enzymes of anaerobic metabolism in OSA patients. The force-generating capacity of the muscle was the same in OSA patients and control subjects when normalized for muscle cross-sectional area, but in a subsequent study, changes in the musculus uvulae muscle correlated with upper airway collapsibility. Patients with the most easily collapsible upper airway also showed the greatest increases in force production, type Ila fiber prevalence, anaerobic metabolism, and susceptibility to muscle fatigue. Carrera and Barbé studied genioglossus muscles from OSA patients and from controls; they also reported a shift to type II fiber type and specifically demonstrated increased fatigability of the genioglossus muscle in OSA. Thus, even in the absence of morphologic injury, adaptive changes induced by the contraction history of the upper airway muscles may also have adverse functional consequences.

In the discussion on pharyngeal motor control in the preceding section, it was noted that there is evidence for an upper airway afferent neuropathy in OSA, based on both sensory testing data and pathologic findings. There is evidence to suggest that there may, in fact, be a more diffuse upper airway neuropathy in OSA that also affects efferent nerves and may lead to muscle denervation. Woodson and colleagues reported demyelination in upper airway tissue specimens. Histologic evidence of motor denervation, such as fiber type grouping and grouped atrophy, has also been found in several recent studies. In a recent study of human upper airway surgical specimens from OSA and control subjects, we demonstrated increased nerve tissue proliferation within the muscle compartment, revealed by specific antibody to neural tissue (PGP 9.5), and also found groups of myocytes expressing neural cell adhesion molecule, a sensitive marker of muscle denervation. These findings suggest that denervation-related changes may contribute to upper airway muscle function in OSA.

As discussed above, the edema and inflammatory cell infiltration of the upper airway mucosa described by several groups suggest that inflammatory mechanisms may contribute to upper airway dysfunction in OSA, leading, for example, to neuropathic changes. In the study just cited from the author's laboratory, we demonstrated increased inflammatory cell infiltration in OSA upper airway muscle. Furthermore, preliminary data from our laboratory have revealed increased expression of tumor necrosis factor-α and interleukin-1α in muscle tissue from patients with severe OSA versus those with mild OSA. It is now well established that cytokines can lead directly to muscle dysfunction. Thus, inflammatory changes in the upper airway may alter muscle function directly by this means or conceivably by contributing to neuropathy, which, in turn, may lead to muscle denervation. It is likely that muscle adaptation and injury are ongoing in a dynamic process in OSA, that different muscle groups within the upper airway may be affected differently, and that the extent of change and physiologic consequences for muscle function may vary between OSA patients. Further work will be required to further elucidate the contribution of upper airway muscle denervation and injury to the pathophysiology of this disorder, as well as to determine whether muscle changes may represent a potential therapeutic target in OSA.
OSA and Ventilatory Control  

There is a growing understanding of the effects of chemoreceptor sensitivity and ventilatory control instability on the pathogenesis of periodic breathing and central apnea. Differences in the control of breathing between wakefulness and sleep (e.g., the higher ventilatory setpoint and ventilatory chemosensitivity during wakefulness) lead to respiratory instability during the transition from wakefulness to sleep, accounting for apneas and hypopneas, which may be seen at sleep onset in normal subjects. Furthermore, recent work has shown that ventilatory responses are heightened at the instant of arousal from sleep in comparison to stable wakefulness. Thus, instability of the sleep–wake state per se may destabilize breathing. The state changes associated with apneas and hypopneas, that is, microarousal at the termination of events, followed by the rapid return to sleep, therefore represent a situation of inherently unstable respiratory control. Numerous investigators have postulated that altered chemoreceptor sensitivity or instability of other respiratory control mechanisms may therefore contribute to the pathogenesis of OSA. An early observation in support of this hypothesis was the occurrence of periodic breathing during sleep immediately following tracheostomy for OSA.

A large body of data has been generated concerning changes in classic chemoreceptor responses in OSA, although there have been rather inconsistent findings. Some authors have reported heightened hypoxic sensitivity, which was postulated to contribute to respiratory instability, whereas others have reported blunted hypoxic sensitivity. Hypercapnic ventilatory responsiveness has been reported to be normal or decreased in OSA and, if reduced, may improve following treatment with nasal CPAP.

Recently, Younes and colleagues used proportional assist ventilation (PAV) to evaluate ventilatory control stability in OSA patients. With the upper airway stabilized during sleep by nasal CPAP, increasing levels of PAV (controller gain) were applied up to the point at which periodic breathing was elicited. It was found that patients with severe OSA were much more susceptible to the development of periodic breathing than patients with mild-to-moderate OSA, indicating increased endogenous loop gain in the severe group. The mechanisms underlying this ventilatory instability, and its precise role in the pathogenesis of OSA, remain to be established.

Although the role of changes in chemoreceptor sensitivity in the pathogenesis of OSA remains unclear, there is strong evidence that severe OSA may produce secondary changes in ventilatory control, namely hypoventilation during wakefulness. This occurs in a subset of OSA patients who appear to be the group at risk for decompensation and respiratory failure in the context of intercurrent medical illness, or in some cases simply because of inexorable progression of the changes associated with sleep-disordered breathing. Most patients with OSA and daytime hypoxemia and/or hypercapnia have some underlying lung dysfunction, such as COPD or obesity-related or neuromuscular restrictive impairment. OSA patients with hypercapnia have been described as demonstrating impaired ventilatory recovery after apnea. This may represent a blunting or failure of load compensation mechanisms in such patients and may contribute to a “resetting” of the chemoreceptors, leading to awake hypoventilation. Daytime blood gases typically improve dramatically or normalize following effective treatment of OSA, supporting the concept that the nocturnal respiratory disturbance leads to the development of awake hypoventilation.

OSA and Asthma  

There is growing evidence of a link between OSA and asthma. In a recent study at McGill, 26 consecutive refractory asthmatic subjects were evaluated in comparison with 21 age-matched and gender-matched control subjects with moderate asthma. The prevalence of OSA in both groups was dramatically increased over population normal values, with a tendency for OSA to be more prevalent among subjects with severe asthma (16/26, 62%) than among those with moderate asthma (10/21, 48%) and for OSA to be somewhat more severe among the refractory asthma group. These findings, together with evidence from other case series, suggest that OSA may contribute to worsened asthma control. For example, Chan and colleagues studied nine patients with severe asthma and snoring or OSA who suffered frequent nocturnal asthma attacks despite maximum bronchodilator therapy. CPAP treatment of upper airway obstruction during sleep improved asthma control, as reflected in asthma symptoms, bronchodilator use, and peak flow rates.

There are several mechanisms by which OSA and asthma could interact. There is evidence that stimulation of upper airway mechanoreceptors during snoring and apneas can lead to reflex bronchoconstriction. Alternatively, gastroesophageal reflux occurs frequently in OSA patients and is a well-recognized exacerbating factor in asthma. Treatment of asthma with corticosteroids may contribute to OSA by increasing obesity and/or pharyngeal myopathy. Finally, as noted above, there are considerable data documenting upper airway inflammation in OSA and growing evidence that this plays a role in OSA pathophysiology. The links between rhinosinus inflammation and lower airway inflammation in asthma are well documented (termed the “united airway hypothesis”). It may therefore be that pharyngeal involvement represents part of a continuum of airway inflammatory involvement. There may thus be a reciprocal interaction between these disease processes, such that worsening of OSA may contribute to worsened asthma control and vice versa. This concept is supported by the clinical data cited above concerning the effects of OSA treatment on asthma control. Research efforts are ongoing to further evaluate the mechanisms of the OSA–asthma interaction and to more systematically assess the effects of OSA treatment on asthma control.

Physiologic Aspects of Diagnostic Testing for OSA  

In recent years, recording of nasal pressure has emerged as a sensitive indicator of upper airway narrowing. Introduction of a standard nasal oxygen cannula into the nares, with connection of the tubing end to a differential pressure transducer referenced to atmosphere, provides for
Sleep Disordered Breathing

A semiquantitative assessment of nasal airflow. Of greater interest is the fact that the shape of the inspiratory pressure curve during tidal respiratory cycles shows flattening indicative of flow limitation as upper airway narrowing occurs, in the same way that forced maximal curves reveal extrathoracic upper airway obstruction, as discussed earlier in this chapter. This technique provides for the detection of subtle episodes of upper airway narrowing.

Respiratory effort was traditionally measured by using an esophageal catheter to estimate pleural pressure. This invasive approach has largely been replaced by techniques involving the use of sensors on the rib cage and abdomen to detect respiratory effort and movement. The most sensitive of these is respiratory inductance plethysmography, which provides data on changes in thoracoabdominal motion resulting from partial or complete upper airway obstruction. Partial or complete rib cage paradoxical motion is often seen during apneas and hypopneas and can provide confirmatory evidence of increasing respiratory effort in the context of upper airway obstruction.

Physiology of Treatment Approaches to OSA

There are several treatments aimed at compensating for the anatomic predisposition to upper airway collapse. Mandibular advancement splints, for example, act to advance the lower jaw in relation to other craniofacial structures, thereby increasing the anteroposterior oropharyngeal dimension. This approach does not compensate for other factors contributing to upper airway collapse during sleep, and there are limitations to its anatomic effects. Oral appliances are therefore effective in mild-to-moderate OSA but typically do not alleviate moderate-to-severe OSA. Surgical interventions are also aimed at compensating for reduced upper airway dimensions. In childhood OSA, hypertrophy of the adenoid and, to a lesser extent, the palatine tonsils is often a major factor contributing to airway compromise, so that adenoidectomy–tonsillectomy is a mainstay of treatment for OSA in the child. Maxillomandibular advancement surgery may be beneficial in the context of craniofacial insufficiency, for example, the marked micrognathia associated with Pierre–Robin syndrome. This approach may also be useful for nonobese adults with similar but more subtle craniofacial disproportion. Surgical intervention in general, however, has a much more limited role in adult OSA. Tracheostomy is highly effective as it bypasses the site of airway obstruction. However, there are adverse social as well as medical aspects of chronic tracheostomy, which severely limit the applicability of this intervention. A variety of approaches directed at reducing or stiffening soft palate tissue have been applied to adult OSA. These include conventional uvulopalatopharyngoplasty, laser-assisted uvuloplasty, radiofrequency-controlled...
thermoablation (somnoplasty), and other procedures. Overall, the results of these interventions have been highly disappointing in the context of moderate-to-severe OSA. This is undoubtedly due to the limited anatomic effects of these interventions, combined with the role of factors other than anatomic predisposition to upper airway collapse during sleep.

The treatment of choice for OSA is nasal CPAP. CPAP functions as a pneumatic splint for the upper airway. A sealed mask is applied over the nose, and a continuous positive pressure is applied to the mask from a blower unit to distend the airway. The pressure required to maintain airway patency is determined by anatomic, mechanical, neuromuscular, and state-dependent factors, such that a greater pressure may be required for the supine position than for the lateral decubitus position and during REM than during non-REM sleep. Traditionally, CPAP titration has been performed in the sleep laboratory, with manual adjustment to determine the minimum pressure required to maintain airway patency in all sleep stages and body positions. This pressure is then prescribed for home treatment. More recently, automated CPAP devices have become available, which continuously monitor the amplitude and contour of airflow with a pneumotachograph in the CPAP unit. A microprocessor then evaluates the adequacy of these signals and adjusts the pressure to respond to inspiratory flow limitation and/or reduced airflow. The concept is that this is a more physiologic approach that should match the treatment delivered to the dynamic changes in upper airway caliber determined by the factors described above. An algorithm for the diagnosis and management of OSA is shown in Figure 50-8.

UPPER AIRWAY IN CENTRAL SLEEP APNEA

Central sleep apnea is encountered in a variety of clinical conditions. It may be present as part of primary or secondary hypoventilation syndromes (hypercapnic central apnea) due to central nervous system (CNS) lesions or neuromuscular disease involving the respiratory muscles. Alternatively, nonhypercapnic forms of central apnea include idiopathic central sleep apnea and Cheyne–Stokes respiration (CSR) during sleep, which may occur in the setting of congestive heart failure, renal failure, or CNS lesions.

Although the upper airway is not believed to play a primary role in most of these conditions, there is evidence that upper airway instability and collapse are associated with central apnea and may contribute to its pathophysiology. Badr and colleagues have shown, using video-endoscopy, that upper airway collapse occurs in the context of hyperventilation-induced central apnea during sleep, even in normal subjects. Thus, the loss of respiratory drive due to induced hypocapnia leads to airway closure, confirming the importance of respiratory drive to upper airway muscles in maintaining airway patency. Conversely, there is evidence that upper airway collapse may induce central apneas. The clinical correlate of this is that patients with snoring and some obstructive apneas or hypopneas during REM sleep may demonstrate central events during non-REM sleep. Furthermore, some patients with predominant central apnea respond to nasal CPAP treatment, suggesting that upper airway closure contributes to these events. These findings may in part be explained by evidence indicating that stimulation of upper airway mechanoreceptors may result in reflex inhibition of inspiratory drive. Thus, stimulation of laryngeal receptors in experimental animals has been reported to induce apnea. Furthermore, we found that inhibition of upper airway mucosal receptors with the use of topical anesthesia resulted in increased respiratory effort during obstructive apneas in OSA patients. This points to the loss of an inhibitory influence on respiratory drive, with attenuation of airway sensory receptor function.

There has been considerable recent interest in CSR during sleep in the setting of chronic congestive heart failure. Sleep-disordered breathing is common among stable heart failure patients, occurring in up to 40%, with CSR representing the most common form. CSR is believed to both result from and lead to worsening of heart failure through complex mechanisms and has been shown to be associated with reduced survival for a given level of cardiac dysfunction. Treatment with nasal CPAP in this group leads to improvements in CSR, ventricular function, and quality of life. A multicenter trial (CAN-PAP) is currently under way to determine the effects of CPAP on mortality in heart failure patients with CSR. The mechanisms by which CPAP leads to improvement in CSR remain unclear. However, recent work at McGill, involving the forced oscillation technique to assess upper airway patency, has demonstrated that upper airway closure is frequent even during pure central events in heart failure patients with CSR. Furthermore, overlap between OSA and CSR has been described in this population. Thus, upper airway instability may also contribute to the pathogenesis of CSR.

SUMMARY AND CONCLUSIONS

This chapter has examined the normal structure and function of the upper airway, with an emphasis on the physiologic aspects of the integration of breathing with the variety of other upper airway functions. The most serious clinical disturbance of upper airway function is anatomic or functional obstruction with airflow compromise. We have considered the physiologic basis for both the clinical presentation and approach to diagnostic testing for the various forms of upper airway obstruction. Finally, we have considered sleep-disordered breathing and in particular OSA, a very common but, for many individuals, no less serious form of variable extrathoracic upper airway obstruction occurring during sleep. The research that has been directed at understanding the mechanisms underlying OSA has led to major advances in our knowledge of upper airway structure and function. Although considerable progress has been made, ongoing work aimed at further elucidating the mechanisms of OSA will undoubtedly broaden our understanding of upper airway function in general.
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