severe during REM (rapid eye movement) sleep, when neuromuscular output to the skeletal muscles is particularly low, and in the supine position due to gravitational forces.

Individuals with a small pharyngeal lumen require relatively high levels of neuromuscular innervation to maintain patency during wakefulness and thus are predisposed to excessive airway collapsibility during sleep. The airway lumen may be narrowed with enlargement of soft tissue structures (tongue, palate, and uvula) due to fat deposition, increased lymphoid tissue, or genetic variation. Craniofacial factors such as mandibular retroposition or micrognathia, reflecting genetic variation or developmental influences, also can reduce lumen dimensions. In addition, lung volumes influence the caudal traction on the pharynx and consequently the stiffness of the pharyngeal wall. Accordingly, low lung volume in the recumbent position, which is particularly pronounced in the obese, contributes to collapse. A high degree of nasal resistance (e.g., due to nasal septal deviation or polyps) can contribute to airway collapse by increasing the negative intraluminal suction pressure. High-level nasal resistance also may trigger mouth opening during sleep, which breaks the seal between the tongue and the teeth and allows the tongue to fall posteriorly and occlude the airway.

Pharyngeal muscle activation is integrally linked to ventilatory drive. Thus, factors related to ventilatory control, particularly ventilatory sensitivity, arousal threshold, and neuromuscular responses to CO_2, contribute to the pathogenesis of OSAHS. A buildup in CO_2 during sleep activates both the diaphragm and the pharyngeal muscles, which stiffen the upper airway and can counteract inspiratory suction pressures and maintain airway patency to an extent that depends on the anatomic predisposition to collapse. However, pharyngeal collapse can occur when the ventilatory control system is overly sensitive to CO_2, with resultant wide fluctuations in ventilation and ventilatory drive and in upper airway instability. Moreover, increasing levels of CO_2 during sleep result in central nervous system arousal, causing the individual to move from a deeper to a lighter level of sleep or to awaken. A low arousal threshold (i.e., awaken to a low level of CO_2 or ventilatory drive) can preempt the CO_2-mediated process of pharyngeal muscle compensation and prevent airway stabilization. A high arousal threshold, conversely, may prevent appropriate termination of apneas, prolonging apnea duration and oxyhemoglobin desaturation severity. Finally, any impairment in the ability of the muscles to compensate during sleep can contribute to collapse of the pharynx. The relative contributions of risk factors vary among individuals. Approaches to the measurement of these factors in clinical settings, with consequent enhancement of "personalized" therapeutic interventions, are being actively investigated.

Risk Factors and Prevalence The major risk factors for OSAHS are obesity and male sex. Additional risk factors include mandibular retrognathia and micrognathia, a positive family history of OSAHS, genetic syndromes that reduce upper airway patency (e.g., Down syndrome, Treacher-Collins syndrome), adenotonsillar hypertrophy (especially in children), menopause (in women), and various endocrine syndromes (e.g., acromegaly, hypothyroidism).

Approximately 40–60% of cases of OSAHS are attributable to excess weight. Obesity predisposes to OSAHS through the narrowing effects of upper airway fat on the pharyngeal lumen. Obesity also reduces chest wall compliance and decreases lung volumes, resulting in a loss of caudal traction on upper airway structures. Obese individuals are at a fourfold or greater risk for OSAHS than their normal-weight counterparts. A 10% weight gain is associated with a >30% increase in AHI. Even modest weight loss or weight gain can influence the risk and severity of OSAHS. However, the absence of obesity does not exclude this diagnosis.

The prevalence of OSAHS is two- to fourfold higher among men than among women. Factors that predispose men to OSAHS include android patterns of obesity (resulting in upper-airway fat deposition) and relatively great pharyngeal length, which exacerbates collapsibility. Premenopausal women are relatively protected from OSAHS by the influence of sex hormones on ventilatory drive. The decline in sex differences in older age is associated with an increased OSAHS prevalence in women after menopause.

Variations in craniofacial morphology that reduce the size of the posterior airway space increase OSAHS risk. The contribution of hard-tissue structural features to OSAHS is most evident in nonobese patients. Identification of features such as retrognathia can influence therapeutic decision-making.

OSAHS has a strong genetic basis, as evidenced by its significant familial aggregation and heritability. For a first-degree relative of a patient with OSAHS, the odds ratio of having OSAHS is approximately twofold higher than that for someone without an affected relative.

OSAHS prevalence varies with age, from 2–15% among middle-aged adults to >20% among elderly individuals. There is a peak due to lymphoid hypertrophy among children between the ages of 3 and 8 years; with airway growth and lymphoid tissue regression during later childhood, prevalence declines. Then, as obesity prevalence increases in middle life and women enter menopause, OSAHS again increases.

The prevalence of OSAHS may be especially high among patients with diabetes or hypertension. Individuals of Asian ancestry appear to be at increased risk of OSAHS at relatively low levels of body mass index, possibly because of the influence of craniofacial risk factors that narrow the nasopharynx. In the United States, African Americans, especially children and young adults, are at higher risk for OSAHS than their Caucasian counterparts. In a majority of adults with OSAHS, the disorder is undiagnosed.

Course of the Disorder The precise onset of OSAHS is usually hard to identify. A person may snore for many years, often beginning in childhood, before OSAHS is identified. Weight gain may precipitate an increase in symptoms, which in turn may lead the patient to pursue an evaluation. OSAHS may become less severe with weight loss, particularly after bariatric surgery. Marked increases and decreases in the AHI are uncommon unless accompanied by weight change.

APPROACH TO THE PATIENT: Obstructive Sleep Apnea/Hypopnea Syndrome (OSAHS)

An evaluation for OSAHS should be considered in patients with symptoms of OSAHS and one or more risk factors. Screening also should be considered in patients who report symptoms consistent with OSAHS and who are at high risk for OSAHS-related morbidities, such as hypertension, diabetes mellitus, and cardiac and cerebrovascular diseases.

SYMPTOMS AND HISTORY

When possible, a sleep history should be obtained in the presence of a bed partner. Snoring is the most common complaint; however, its absence does not exclude the diagnosis, as pharyngeal collapse may occur without tissue vibration. Gasping or snorting during sleep may also be reported, reflecting termination of individual apneas with abrupt airway opening. Dyspnea is unusual, and its absence generally distinguishes OSAHS from paroxysmal nocturnal dyspnea, nocturnal asthma, and acid reflux with laryngospasm. Patients also may describe frequent awakening or sleep disruption, which is more common among women and older adults. The most common daytime symptom is sleepiness. This symptom can be difficult to elicit and may be hard to distinguish from exercise-related fatigue, deconditioning, and malaise. In contrast to true sleepiness, the latter symptoms generally improve with rest. Other symptoms include a dry mouth, nocturnal heartburn, diaphoresis of the chest and neck, nocturia, morning headaches, trouble concentrating, irritability, and mood disturbances. Several questionnaires that evaluate snoring frequency, self-reported apneas, and daytime sleepiness can facilitate OSAHS screening. The predictive ability of a questionnaire can be enhanced by a consideration of whether the patient is male or has risk factors such as obesity or hypertension.