

Disorders of Respiratory Control

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INTRODUCTION

During the transition between wakefulness and sleep, input from the behavioral control system decreases, the hypoxic drive to breathe is reduced, and the ventilatory response to partial pressure of carbon dioxide in arterial blood (P_{aCO_2}) is diminished. These changes are most dramatic during rapid eye movement (REM) sleep. *Sleep-disordered breathing* refers to a diverse group of conditions in which these physiologic variations are heightened, resulting in abnormal respiratory function and fragmented sleep.

Of the sleep-related disorders, sleep apnea has received the most attention. *Apnea* is the complete cessation of airflow for 10 seconds or longer. *Hypopnea* is a significant decrease in airflow. Occasional episodes of apnea and hypopnea are expected during normal sleep, and their frequency increases with age. However, in patients with sleep apnea, the frequency and duration of the episodes are increased, leading to sleep fragmentation and to hypoxemia and hypercapnia. Upper airway obstruction (i.e., obstructive sleep apnea [OSA]) or decreased central respiratory drive (i.e., central sleep apnea) may be the cause of sleep apnea. Some patients have both disorders.

Some studies suggest that the prevalence of sleep-disordered breathing may be as high as 9% among women and 24% among men, but prevalence levels depend on the definition used. Sleep-disordered breathing is usually defined as a respiratory disturbance index or frequency of abnormal respiratory events that number at least five episodes per hour of sleep. Prevalence estimates are higher for the older adult population, with some studies finding a more than 80% prevalence among older patients. Children are also affected, although less frequently (about 2%).

For a deeper discussion on this topic, please see Chapter 100, "Obstructive Sleep Apnea," in Goldman-Cecil Medicine, 25th Edition.

OBSTRUCTIVE SLEEP APNEA

Definition and Epidemiology

OSA is the most common of the sleep apnea syndromes. It is thought to affect almost 6% of middle-aged and older men; it is less common among women. In these patients, the upper airway relaxation that occurs during sleep produces complete occlusion of the airway and, consequently, cessation of airflow. After various periods of airway occlusion, the patient arouses, reestablishes muscle tone, and opens the airway. This vicious cycle is repeated many times during the night, resulting in recurring episodes of hypoxemia. During airway occlusion, sympathetic tone is

increased, resulting in vasoconstriction and hypertension, which persists during the waking hours. OSA is the most common identifiable cause of systemic hypertension (level 1 evidence). With airway occlusion, intrathoracic pressure becomes more negative with inspiration. Episodes of hypoxemia can be associated with cardiac arrhythmias, cardiovascular events, and all-cause mortality (level 1). These events are thought to be linked mechanistically to the increased incidence of stroke and coronary artery disease in patients with OSA.

An important physiologic consequence of airway occlusion is arousal from sleep, resulting in fragmented sleep. Because apneas are more frequent during REM sleep, patients complain of lack of refreshing sleep. Patients with OSA have an increased incidence of motor vehicle crashes, presumably related to somnolence while driving. These patients have an increased incidence of diabetes mellitus and other manifestations of the metabolic syndrome. The cardiovascular complications of OSA appear to be at least partially reversible with treatment of OSA with continuous positive airway pressure (CPAP) (level 2-3 evidence).

Clinical Presentation

The diagnosis of OSA is suggested when patients complain of morning headaches, recurrent awakenings, and daytime somnolence that affects daytime activities, including driving. Complaints of snoring and gasping episodes may be elicited from sleeping partners. Difficulties in maintaining sleep as a result of frequent awakenings may lead to mood effects and decreased quality of life. Recent weight gain, use of sedatives and sleeping pills, or alcohol intake may heighten these symptoms.

The primary risk factors for OSA are obesity (variable) and abnormal upper airway anatomy caused by macroglossia, a long soft palate and uvula, enlarged tonsils, or micrognathia. Patients may have an increased neck diameter (>17 inches in men; >16 inches in women). A narrow oropharynx as a result of a small pharyngeal opening or redundant soft tissue is often observed. Patients may be hypertensive and, in extreme cases, may have right-sided heart failure, which results from prolonged episodes of hypoxemia and pulmonary vasoconstriction that lead to pulmonary hypertension.

Diagnosis and Differential Diagnosis

Chest radiographic images and pulmonary function testing are usually not helpful in the evaluation of patients with sleep apnea. In some cases, OSA is associated with the obesity-hypoventilation syndrome, which is characterized by significant obesity associated with chronic hypoventilation and hypercapnia (i.e., Pickwickian syndrome). In these cases, arterial blood gas