or oropharynx. The sleep fragmentation caused by arousal is responsible for sleep deprivation and EDS.

Clinical Manifestation

OSA typically manifests with a combination of EDS and snoring in a patient who is overweight. Other symptoms include apneic pauses or "choking" witnessed by the bed partner, and less specific symptoms such as morning headaches, depression, impaired cognition, and sexual dysfunction. On examination, the body mass index (>10 kg/m^2) and neck circumference (>17 inches for men or 16 inches for women) predict OSA. If the patient is not obese, abnormalities of the craniofacial anatomy or upper airways (e.g., retromicrognathia, macroglossia, tonsillar hypertrophy) should be sought.

Diagnosis and Differential Diagnosis

Other causes of EDS should be considered, but in a typical case of OSA, the diagnosis is usually obvious and easily confirmed by overnight PSG. Apneas are defined as cessation (90% reduction) of airflow, whereas hypopneas are 30% to 90% reductions of airflow; both last 10 seconds or longer. These events are called *obstructive* if they occur with respiratory effort and *central* if they occur with no respiratory effort. The apnea-hypopnea index (AHI) is the total number of apneas plus hypopneas per hour, and an AHI score greater than 5 is considered abnormal. An AHI score of 5 to 10 is mild, 10 to 15 is moderate, and more than 15 is severe.

Respiratory effort–related arousals are episodes of decreased airflow with increased effort and crescendo snoring that result in arousals, and they define upper airways resistance syndrome. They represent a compensated degree of OSA. The PSG quantifies the severity in terms of event frequency (i.e., AHI), oxygen desaturation, sleep disturbances (i.e., arousals and fragmentation), and arrhythmias. With some limitations, diagnostic PSG can be performed at home with portable systems if OSA is the likely cause and there are no signs of underlying neurologic disease.

Treatment and Prognosis

Depending on severity, treatment modalities include weight loss, positional measures to prevent sleeping supine, oral appliances for mild disease, and positive airway pressure (PAP) modalities and surgery for moderate to severe disease. For patients with moderate to severe OSA, the initial treatment is PAP; its main limitation is patient compliance. Maximizing the patient's comfort with nasal pillows, humidification, and attention to mask fit is important. PAP requires a titration study to determine the type continuous positive airway pressure (CPAP) (e.g., auto-CPAP, bilevel PAP) and pressure settings appropriate for each patient. When PAP modalities do not work, stimulants and wake-promoting agents can be used as adjuncts to help EDS.

Central sleep apnea is often associated with other cardiopulmonary abnormalities such as heart failure. It is also treated with CPAP initially, but it often requires specialized pulmonary care.

It is important to treat OSA because it has many complications. They include hypertension, coronary artery disease, stroke, diabetes mellitus, depression, and cognitive impairment.

NARCOLEPSY

Definition and Epidemiology

Narcolepsy affects at least 2 in 1000 individuals. Narcolepsy includes a tetrad of excessive sleepiness, cataplexy, sleep paralysis, and hypnagogic hallucinations. The full tetrad occurs in approximately 1 of 5000 people.

Pathophysiology

Narcolepsy is a disorder of rapid eye movement (REM) sleep regulation caused by disordered hypocretin neurotransmission, likely resulting from an autoimmune loss of hypocretin neurons in the lateral hypothalamus. It has a major genetic component, as evidenced by strong human leukocyte antigen (HLA) associations such as HLA-DQB1*0602 in black and white populations and HLA-DR2 in Japanese populations. The daytime symptoms of narcolepsy are accompanied by the intrusion of REM sleep into wakefulness.

Clinical Presentation

The mean age of onset of narcolepsy is in the mid-20s, but two peaks occur around 15 and 35 years of age. EDS is severe and almost constant, and the urge to sleep can be sudden and irresistible (i.e., sleep attacks).

Of the three accessory symptoms, cataplexy is the most specific and helpful for diagnosis. Cataplexy without narcolepsy is exceptional. Narcolepsy without cataplexy is more difficult to identify, and overlaps occur with idiopathic hypersomnia. Cataplexy is characterized by brief (seconds to a few minutes) loss of muscle tone (i.e., intrusion of REM atonia) triggered by emotions, most commonly laughter but also elation, surprise, and fear. If severe, the patient may fall. With milder attacks, a head nod or slurred speech can occur.

Hypnagogic hallucinations that are vivid and dreamlike and that occur at sleep onset are more specific for narcolepsy than hypnopompic (i.e., sleep offset) hallucinations. Sleep paralysis is the often frightening experience of inability to move while aware, usually on awakening. In addition to the tetrad, patients frequently have episodes of automatic behaviors with no recall, which can resemble complex partial seizures. Nocturnal sleep is often fragmented by frequent arousals, vivid dreams, or leg movements.

Diagnosis and Differential Diagnosis

Other causes of EDS, especially the more common OSA, should be sought. A PSG should be obtained the night before the MSLT. The PSG can exclude OSA as a cause of EDS, and an MSLT with a sleep latency of less than 8 minutes and two sleep-onset episodes of REM confirms the diagnosis. Alternatively, a CSF hypocretin level less than 110 pg/mL can confirm the diagnosis. HLA typing is more useful to exclude narcolepsy than to diagnose it because it is sensitive but not specific.

Treatment and Prognosis

Stimulants (e.g., amphetamines, methylphenidate) are still used for the treatment of EDS, but newer wake-promoting agents are more widely used. They include modafinil (100 to 400 mg twice daily) and the longer-acting, once-daily armodafinil (150 to