Chapter 14
Sleep Apnea

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Introduction

Sleep disorders are very common in the primary care setting. Sleep deficiency/deprivation is a common health problem in the United States. Around 7–19% of adults in the USA reported not getting enough sleep, 40% report falling asleep unintentionally, and 50–70 million Americans have chronic sleep disorders [1]. Based on International Classification of Sleep Disorders (ICSD-3), insomnia is the most common sleep disorder in the general population followed by sleep-disordered breathing, including obstructive sleep apnea/hypopnea syndrome and central sleep apnea [2].

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E. Sydney et al. (eds.), *Handbook of Outpatient Medicine*,
https://doi.org/10.1007/978-3-319-68379-9_14

ICSD3 Classifies Sleep Disorders into Seven Major Categories [2]

1. Insomnia
2. Sleep-disordered breathing disorders
3. Central disorders of hypersomnolence
4. Circadian rhythm sleep-wake disorder
5. Parasomnias
6. Sleep-related movement disorder
7. Other sleep disorders

Sleep apnea is classified as obstructive sleep apnea/hypopnea syndrome (OSAHS) and central sleep apnea (CSA).

Prevalence

Obstructive sleep apnea prevalence varies widely, with 9–38% having OSA (AHI 5 events/h). It is also seen more in men and in the elderly. Moderate to severe forms of OSA with an apnea-hypopnea index (AHI of 15 events/h) in the general population ranged from 6 to 17% and as high as 49% with advanced age [3].

Sleep History

In addition to general medical, surgical, family, caffeine intake, medication history (specifically herbal remedies or over-the-counter medications), the focused sleep history should include a general question about excessive daytime sleepiness (EDS) or fatigue (including history of sleepiness while driving and accidents), difficulty falling asleep at night or maintaining sleep, sleep latency, snoring, nocturnal awakenings, witnessed apneas, sleeping position (lateral, supine, or prone), resuscitative snorts, restless legs, limb movements (noted by the partner), bedtime, wake time, daytime naps, sleep paralysis, and cataplexy.

Screening Questionnaires to Assess the Risk of OSA

Commonly used questionnaires to assess the risk of OSA are the Epworth sleepiness score with STOP-Bang questionnaire [4, 5].

STOP-Bang Questionnaire

S	Snoring
T	Tired or sleepy
O	Observed apneas
P	Pressure (Hypertension)
B	BMI >35
A	Age >50 years
N	Neck circumference >16 in. in men and 15 in. in women
G	Gender: Male

0–2, low risk of OSA; **3–4**, moderate risk of OSA; and **5–8**, high risk of OSA

Adapted from: Chung F, Subramanyam R, Liao P, Sasaki E, Shapiro C, Sun Y. High STOP-Bang score indicates a high probability of obstructive sleep apnoea. Br J Anaesth. 2012 May;108(5):768-75. doi: 10.1093/bja/aes022. Epub 2012 Mar 8. www:stopbang.ca

Epworth sleepiness score (ESS) is the most widely used in clinical practice to evaluate the severity of sleepiness. Developed by Murray Johns at Epworth Hospital in Melbourne, Australia, this validated an eight-item questionnaire about the person's chance of dozing in differing circumstances. Dozing probability is designated as none (0), slight (1), moderate (2), or high (3) for eight situations [6], which are **sitting and reading, watching TV, sitting inactive in a public place, being a passenger in a car for an hour, lying**

down in the afternoon, sitting and talking to someone, sitting quietly after lunch with no alcohol, and stopping for few minutes in traffic while driving.

Understanding ESS Score

0–10	Normal range in healthy adults
11–14	Mild sleepiness
15–17	Moderate sleepiness
18 or higher	Severe sleepiness

Focused Physical Exam

Attention should be paid to the pharyngeal examination. Increased BMI is a risk factor for OSA, especially when associated with short neck or increased neck circumference. Overall, narrowed pharyngeal space, in addition to enlarged tonsils and adenoids, increases the risk of OSA. Craniofacial abnormalities also increase the risk of obstructive sleep apnea/hypopnea syndrome (OSAHS), as do abnormalities associated with reduced pharyngeal space [7].

OSA/SDB (Obstructive Sleep Apnea/Sleep-Disordered Breathing)

Definition

OSA is defined by repetitive complete obstruction (apnea) or partial obstruction (hypopnea) of the collapsible part of the upper airway during sleep [8]. Apnea or hypopnea is cessation of breathing or decreased breathing for 10 s, associated with oxygen desaturation of at least 3% and followed by an arousal. Hypopnea is defined by the decrease in airflow by 30–50%, associated with at least 3% oxygen desaturation,

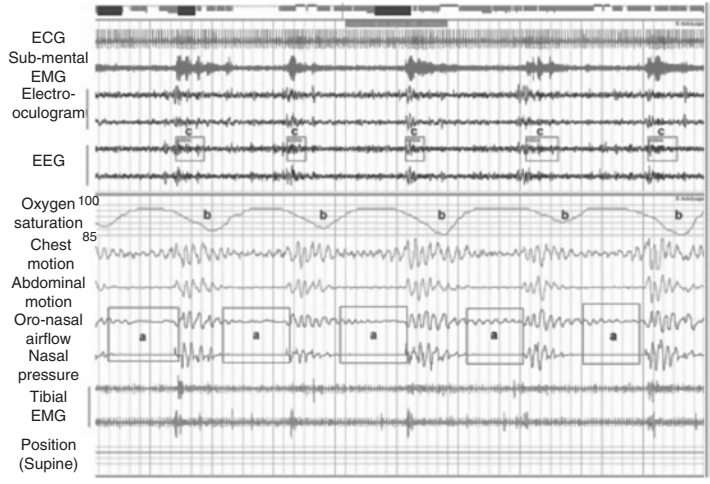

FIG. 14.1 Five-minute epoch of supine stage II sleep in a subject with severe OSA. Cessation (apnea) in breathing (**a**) result in arterial oxygen desaturation (**b**) and EEG arousal from sleep (**c**). Chest wall motion continues during the apneas indication that the events are due to upper airway obstruction [25]

followed by an arousal. AHI is the sum of apneas and hypopneas per hour of sleep. Respiratory disturbance index (RDI) is also used interchangeably with AHI (Fig. 14.1).

Primary snoring is defined by normal AHI with snoring. Ninety-four percent of patients with OSA have snoring. Classically, the three clinical features of OSA are loud snoring, witnessed apneas, and excessive daytime sleepiness. Sleep apnea is classified as mild (AHI 5–15 per hour of sleep), moderate (AHI 15–30 per hour of sleep), and severe (AHI >30 per hour of sleep).

Risk Factors

Risk factors include male sex, obesity, large neck circumference, narrowed pharynx or airway, certain craniofacial abnormalities, family history, postmenopausal women, smoking, chronic gastroesophageal reflux disease (GERD), and other

chronic medical conditions including CHF, ESRD, chronic lung disease (asthma, COPD, and IPF), stroke/TIA, acromegaly, hypothyroidism, PCOS, and pregnancy. Seventy-five percent of individuals with OSA have underlying obesity [9].

Pathophysiology

Obstructive sleep apnea is characterized by recurrent functional collapse of the pharyngeal airway, causing reduced or cessation of airflow with ongoing effort to breathe. This leads to intermittent hypoxia and disturbed sleep, leading to nonrestorative sleep. Upper airway collapse is worse in REM sleep. In obese individuals, it is hypothesized that large deposits of fat in the neck cause the upper airway to collapse in the supine position during sleep. Clinical features of OSA and SDB (sleep-disordered breathing) include loud snoring, nocturnal choking with resuscitative snorts, witnessed apneas, EDS, fatigue, poor concentration, morning headaches, nocturnal polyuria, and nocturnal angina. Most of the symptoms are related to disruption of normal sleep architecture. Patients have associated obesity, increased neck circumference, greater than 17 in. in men and greater than 15 in. in women, hypertension, metabolic syndrome, and anatomic abnormalities.

Diagnosis

Usually nocturnal polysomnography (PSG) in a center or out-of-center sleep testing (OCST), which is also called at home sleep testing (HST), helps diagnose OSA (see Fig. 14.2).

Differential Diagnosis of Excessive Daytime Sleepiness (EDS)

Other conditions that lead to EDS are depression, chronic sleep deprivation, restless legs syndrome (RLS), periodic limb movement disorder (PLMD), narcolepsy, shift work sleep disorder, and jet lag.

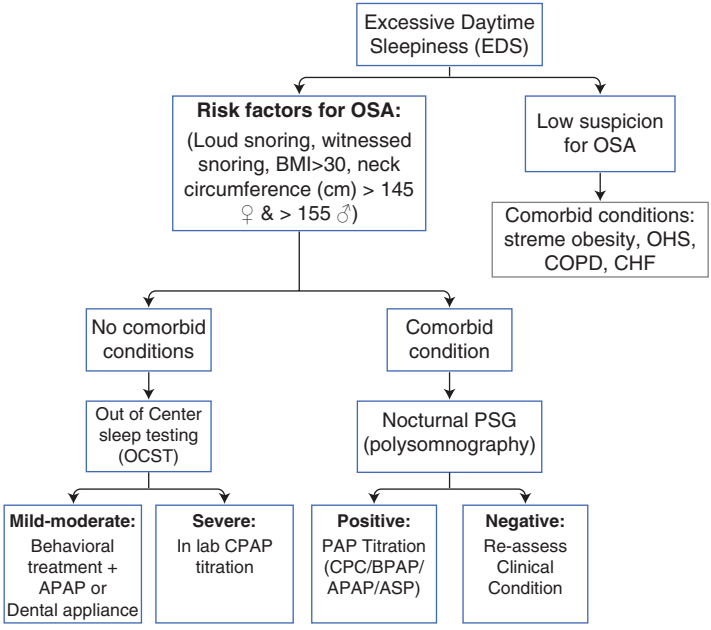

FIG. 14.2 Evaluation of excessive daytime sleepiness

Complications and Consequences of Untreated Sleep Apnea

There is increasingly more data to suggest that untreated sleep apnea is associated with metabolic syndrome, poor cardiovascular outcomes, HTN, and congestive heart failure [10, 11]. Recent data, however, states that there is significant decrease in morbidity, rather than mortality [4]; EDS is also associated with increased risk for injuries and motor vehicle accidents. Patients may have poor concentration and memory lapses leading to poor quality of life.

Treatment: OSAHS/SDB (usual therapy):

- Behavioral treatment: Weight loss and sleep hygiene
- Positive airway pressure (PAP), CPAP, BPAP, and ASV [12]
- Surgery (effective for mild OSA): Uvuloplasty when if indicated is effective for primary snoring with or without mild OSA [13]
- UPPP (uvulopharyngopalatoplasty) and MMA (maxillomandibular advancement)
- Laser-assisted uvuloplasty (LAUP) and radiofrequency ablation
- Hypoglossal nerve stimulation (moderate to severe OSA) [14]
- Hyoid surgery: Hyothyroidopexy and hyoid myotomy with suspension
- Dental appliances (oral appliance therapy)

The most effective treatment and first-line therapy is continuous positive airway pressure (CPAP) [12]. With new masks, complications and adverse effects are low; however, there is a high incidence of intolerance to the mask or pressure in patients with claustrophobia and anxiety disorders. Common complaints include oropharyngeal dryness, mask leak and fit, redness and excoriation of the facial skin, stomach bloating, and ear fullness. CPAP titration is recommended in all patients with comorbid conditions, like COPD, CHF, and OHS. Eight percent of patients have combined OSA with CSA.

Other treatments include medical and behavioral therapy with weight loss, bariatric surgery, and positional treatment. Supplemental oxygen, nasal decongestants, protriptyline, and SSRIs, however, have limited utility. These are more effective measures for mild to moderate OSA and as adjunctive treatment for all patients with OSA.

Modafinil is recommended to treat residual excessive daytime sleepiness in OSA patients, who have sleepiness despite effective PAP treatment [15].

Positional sleep apnea: There is 50% reduction in AHI during non-supine sleep in relation to supine sleep. These patients benefit from positional therapy.

Surgical treatment: The most commonly used nonsurgical device/oral appliance therapy for treatment of mild to moderate OSA is the dental appliance. Outcomes following pharyngeal surgeries were less consistent, and adverse effects were more commonly reported. Hypoglossal cranial nerve stimulation via an implantable neuro-stimulation system has been shown to be effective in moderate OSA to severe OSA according to a recent study [16].

STAR trial showed that upper airway stimulation is an effective therapy for moderate to severe OSA in patients who fail PAP therapy or unwilling to use PAP [14].

Drowsy driver syndrome and commercial drivers and pilots: Untreated or undiagnosed OSA can lead to drowsy driving syndrome and lead to fatal accidents. The National Highway Traffic Safety estimates drowsy driving leads to at least 6000 fatal crashes every year [17]. In addition to OSA, chronic sleep deprivation with underlying OSA can worsen EDS. Shift work sleep disorder (circadian rhythm type) and medications that can cause sleepiness can exacerbate EDS.

Warning signs of drowsy driving include yawning or blinking frequently, difficulty remembering the past few miles driven, missing an exit, driving away from the lane, and hitting the rumble strap on the side of the road. Drivers must be educated about not driving until CPAP is effectively instituted (nightly CPAP at least 4 h in 1 week). Sometimes testing by the maintenance of wakefulness test is required to document that sleepiness resolved with treatment. The National Transportation Safety Board has specific guidelines for diagnosis and treatment of OSA in commercial drivers.

Central disorders of hypersomnolence: This includes central sleep apnea (CSA), Cheyne-Stokes breathing, and narcolepsy. CSA is common in patients with neurological conditions or with CHF. CSA is characterized by lack of drive to breathe during sleep, resulting in decreased ventilation and compromised gas exchange. In contrast to OSA, in which ongoing respiratory efforts are present, CSA is characterized by lack of respiratory effort during cessation of airflow. However, considerable overlap exists in the pathophysiology and pathogenesis of OSA and CSA [18].

Symptoms of CSA include frequent nighttime awakenings, EDS, and increased risk of adverse cardiovascular complications. Unstable ventilator drive during sleep is a principal underlying feature.

Common types of CSA include:

- Idiopathic CSA
- Narcotic-induced central apnea
- Obesity hypoventilation syndrome (OHS)

Prevalence of CSA: The prevalence of CSA varies considerably but is less common than OSA. A prospective prevalence study of patients with heart failure and LVF <45% reported 37% of patients had CSA [19].

Pathophysiology: Again, there is a great overlap between CSA and OSA, and typically CSA is considered the primary diagnosis when 50 of the apneas are scored as central in origin (more than 10-s cessations of breathing in the absence of respiratory effort (Fig. 14.3).

CSA syndromes can be classified into two groups (as per wakefulness CO2 levels): hypercapnic and non-hypercapnic. Hypercapnic CSA can be classified broadly into abnormal central pattern generator output (will not breathe) or impairment of respiratory motor output caudal to respiratory generator (cannot breathe).

Treatment of CSA

- Twenty percent of CSA resolve spontaneously and by treatment of underlying condition, CHF, and renal failure
- Weight loss
- Avoid sleep deprivation
- Avoid alcohol and sleep promoting agents like benzodiazepines
- CPAP is used as first-line therapy
- Adaptive servo ventilation (ASV) like CPAP provides additional ventilator support based on breath by breath analysis

(continued)

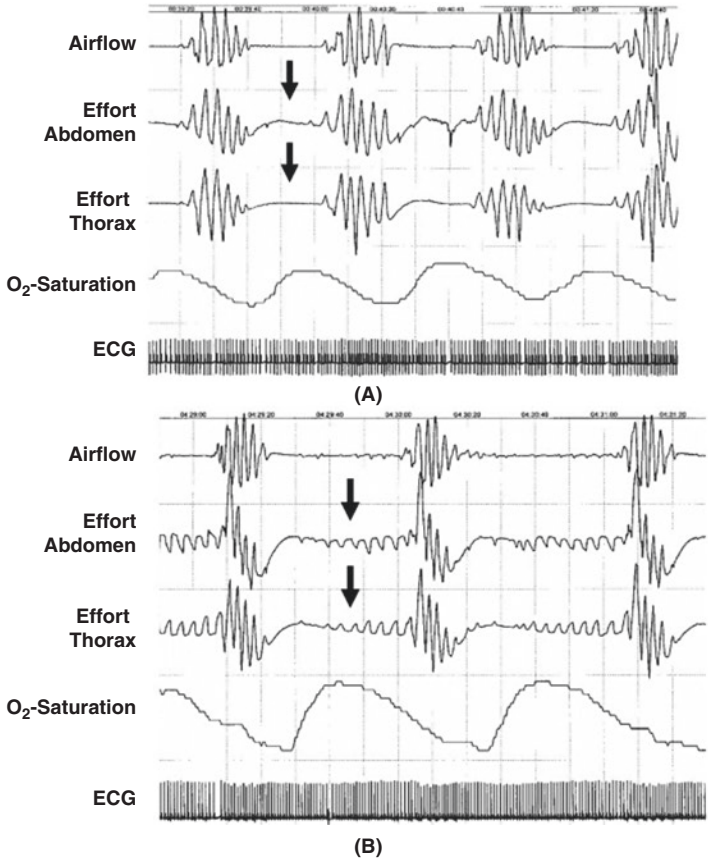

FIG. 14.3 Polysomnography (3 min) with central sleep apnea (**a**) and obstructive sleep apnea (**b**). Note the absence of chest efforts and abdominal movements in the absence of oronasal airflow in central sleep apnea but not in obstructive sleep apnea (*arrows*). Also, note the pronounced decrease in O2 saturation following each apnea episode [26]

(continued)

- Supplemental oxygen: may not be superior to PAP but better tolerated
- Addition of dead space ventilation with CPAP
- Inhalation of carbon dioxide
- Acetazolamide or theophylline
- Overdrive atrial pacing

Obesity hypoventilation syndrome: Is increasing in prevalence in the developed countries, ranging from 10 to 20%, 50% of patients with BMI greater than 50 are likely to have OHS.

OHS is defined as BMI >30, PaCo2 >45 mmHg, and FEV1/FVC ratio greater than 60% on pulmonary function testing. The triad of obesity, hypersomnolence, and awake hypercapnia in the absence of alternative neuromuscular, mechanical, or metabolic explanation for hypoventilation are the cornerstone for diagnosis. Eighty to ninety percent of patients with OHS have OSA with upper airway obstruction [20].

Narcotic-induced sleep-disordered breathing: Narcotics have been increasingly used for treatment of chronic pain, and a clear link between narcotic use and sleep-disordered breathing has been established. Several studies have shown the efficacy of noninvasive ventilation, particularly ASV (adaptive servo ventilation) in improving outcome measures of central apnea index [21].

Narcolepsy: Narcolepsy is a central cause of hypersomnia and a neurological disorder that affects sleep and wakefulness. In addition to excessive daytime sleepiness, it also causes "sleep attacks," cataplexy (muscle paralysis), and sleep-onset REM sleep (SOREM). It is underdiagnosed and therefore undertreated. Although the definite cause is unknown, it may be due to deficiency of hypocretin [22].

Circadian rhythm sleep-wake disorder: This group includes delayed sleep phase syndrome, advanced sleep phase disorder, jet lag, and shift work sleep disorder [23].

Parasomnias: These are mainly disorders of stage 3 or deep sleep and occur during the early period of sleep. Sleep walking, night terrors, and nocturnal seizures occur during this period.

Sleep-related movement disorders: Includes restless legs syndrome (RLS) and periodic limb movement disorder (PLMD) which is a condition with an irresistible urge to move the legs. In the general population, prevalence varies anywhere from 1 to 5% and is twice more common in women than in men. This is a disorder of sensorimotor integration and may have genetically determined dysregulation of iron transport across the blood-brain barrier. It is common in persons with iron deficiency and worse in pregnant women and persons with Parkinson's disorder and end-stage kidney disease [24]. Although associated with periodic leg movement disorder, a nocturnal polysomnography is not indicated for the diagnosis. History and measurement of serum ferritin levels are considered sufficient.

Dopamine agonists are considered the first line of therapy, and these include pramipexole, ropinirole, and Regitine. Alpha-2 delta drugs such as gabapentin are being considered as first-line therapy. Opioids may be used as alternative therapy. Intravenous iron may be considered in refractory RLS.

Clinical Pearls

- Obstructive Sleep apnea can be suspected by history and physical examination, but diagnosis and severity can only be assessed by a polysomnography or sleep study.
- Obstructive sleep apnea with no comorbid conditions can be treated with APAP (automated positive airway pressure devices).
- OSA with CHF, COPD, CHF, requires Positive airway pressure titration with Polysomnography.
- Special attention is to be given to Commercial drivers and pilots with OSA and especially when associated with shift work sleep disorder (Circadian Rhythm Sleep Disorder).

- Individuals with BMI >50 have underlying Obesity Hypoventilation syndrome and individuals with underlying heart failure can have Central Sleep Apneas, when Positive airway pressure therapy may need frequent follow up and consider repeat titration.
- Hypoglossal Nerve stimulation and dental appliances are effective in moderate to severe of Obstructive Sleep apnea, however it has not been tested in individuals with BMI >32.

Don't Miss This!

- Obstructive sleep apnea, although the commonest cause, is only one of the many causes of excessive daytime sleepiness (EDS). Do not miss other coexisting conditions like restless legs syndrome (frequent in pregnant individuals, individuals with end-stage kidney disease, patients on diuretics), narcolepsy, and the most common of all chronic sleep deprivation.
- For circadian rhythm sleep disorders, the best shift that causes least sleep disturbance is the 4PM–12MN shift.

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