AMERICAN COLLEGE OF OSTEOPATHIC INTERNIST
BOARD REVIEW - SLEEP MEDICINE

Timothy J. Barreiro, DO, MPH, FCCP, FACOI, FACP
Associate Professor of Medicine
NIH Health Minority & Harvard Macy Scholar
Ohio University Heritage College of Osteopathic Medicine
Northeast Ohio Medical University
Director Pulmonary Health & Research Center
tbarreir@neomed.edu

Disclosures

I have no disclosures, conflicts of interest related to this subject or talk

Learning Objectives

• Describe the normal & physiologic changes that occur during sleep.

• Define the risks, diagnosis and consequences of sleep apnea (OSA) along with potential treatment options.

• Identify key subtypes of sleep apnea (Cheyenne-Stokes and obesity hypoventilation syndrome) and know their consequences.
Normal Adult Sleep Overview

- Non REM (Stages I – 3)
  - Stage 1: light sleep
  - Stage 2: deep sleep
  - Stage 3: deeper sleep
- 75% of total sleep time (TST)
- Majority of sleep is in Stage 2
- REM (Rapid Eye Movement): Dream Sleep
  - 25% of total sleep
  - Cycles every 90 - 120 minutes
  - Majority occurs in early morning (3 - 7 am)


Physiologic Changes in Sleep

- Less deep sleep (stage 3) with age.
- More light sleep & increased awakenings.
- Body clock shifts earlier = earlier sleep time & awakening. However, REM sleep remains relatively constant.


Insomnia Overview of the Problem

- Lifetime prevalence 30 - 35% (“serious” in 15%)
- Much worse in elderly: Sex ratio: \( \geq 3 \)
- Short-term insomnia: Days to a few weeks - stress event.
- Persistent insomnia: Months to years.
- Types:
  - “Medical”
  - “Psychological” (co-morbid psychiatric diagnosis)
  - Persistent psycho-physiological +/- or substances
  - Primary insomnia

Question
Which of the following statements about insomnia is false?

A. Roughly 50% of those with insomnia have a psychiatric disorder.
B. Various illnesses are associated with insomnia (SOB, pain, IBS, limitations in mobility).
C. A meta analysis of 20 studies concluded that persistent insomnia is associated with doubling of the risk of incident major depression.
D. Insomnia is a rare condition.

Persistent Insomnia - Medical
• Due to medical problems (i.e. pain, PLMD)
  • 50% is due to active psychiatric illness:
    • depression, bipolar, schizophrenia,
    • 1/5th of depressed patients have hypersomnia (“atypical depression”, associated with bipolar spectrum illness),
    • 4/5th have depressed patients have insomnia

Persistent Insomnia
Psychophysiological
• Psychophysiological (“learned” or “behavioral”) insomnia:
  • patients have chronic muscle tension,
  • use bedroom for all their activities,
  • “can’t turn my mind off,”
  • variable bedtime,
  • start projects in late evening,
• Treatment:
  • Cognitive behavior therapy,
  • Sleep logs,
  • Correct erroneous ideas about sleep, relaxation,
  • Sleep study is rarely necessary,
  • Use of hypnotics to be short-term only.
Insomnia Treatment

- **Short-Term Insomnia**: forms a huge fraction of general practice (exam stress, marital breakup, illness in family, financial).
  - Rx: BZDs, Zopiclone, Zaleplon for 1-4 weeks. Talk about the stressor!! Do not Rx too long.

- **Persistent Insomnia**: Keep up your search for dx of depression, bipolar, anxiety.
  - Rx: sedating antidepressants or mood stabilizers long-term.

Sleep Case Question

A 23 year old woman is referred for excessive sleepiness after having fallen asleep while driving. She reports that her sleepiness has been present since high school, and she often struggles to remain awake. She occasionally feels weak in the knees when laughing. Once, she fell to the ground while laughing during a party and could not get up for 1-2 minutes. If she is sleepy while driving, she may imagine seeing an animal in the road. Once she was terrified to find herself unable to move for a minute after awakening.

Which of the follow test is most appropriate at this time?

A. Order a sleep study
B. Multiple sleep latency test
C. Cognitive behavioral therapy
D. Discuss sleep hygiene

Differential Diagnosis of Chronic Daytime Sleepiness

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Distinguishing Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insufficient Sleep</td>
<td>Sleep decreases with more sleep on weekends and holidays.</td>
</tr>
<tr>
<td>Sleep Apnea</td>
<td>Snoring, witness sleep, obesity, Upper airway changes, Large tongue, Small jaw.</td>
</tr>
<tr>
<td>Periodic limb movement</td>
<td>Sleep disrupted by kicking movements, often occurs with the RLS, Iron deficiency, uremia, and neuropathy.</td>
</tr>
<tr>
<td>Shift work disorder</td>
<td>Sleepiness when working at night, insufficient sleep during the day.</td>
</tr>
<tr>
<td>Depression</td>
<td>Increase time in bed but little function sleepiness on testing.</td>
</tr>
</tbody>
</table>

Narcolepsy

- Daytime Sleepiness
- Disrupted nighttime sleep
- Fragments of REM sleep
  - Cataplexy - sudden, brief episodes of muscular weakness/tone
  - Hypnagogic hallucinations - vivid, dream-like hallucinations at the beginning or end of sleep
  - Hypnopompic Hallucinations - (during awakens)
- Sleep paralysis - inability to move upon awakening


Narcolepsy Tetrad

<table>
<thead>
<tr>
<th>Narcolepsy Symptoms</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daytime Sleepiness</td>
<td>100%</td>
<td>Low</td>
</tr>
<tr>
<td>Cataplexy</td>
<td>60 – 70%</td>
<td>100%</td>
</tr>
<tr>
<td>Hallucinations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypnagogic</td>
<td>30 – 60%</td>
<td>Common</td>
</tr>
<tr>
<td>Hypnopompic</td>
<td>30 – 60%</td>
<td>Low</td>
</tr>
<tr>
<td>Sleep paralysis</td>
<td>25 – 50%</td>
<td>Low</td>
</tr>
</tbody>
</table>

Al-A et al. Sleep Medicine for the Neurologist. Hospital Med 13(5) 2009

Sleep Case Question

Which one of the following statements about the clinical manifestations of narcolepsy is true?

A. Affected persons tend to have a low body-mass index (BMI).
B. Complex auditory hallucinations are common.
C. Rapid-eye-movement (REM) sleep can occur at any time of day in affected persons.
D. Symptoms usually begin in midlife.
**Loss of Orexin in Human Narcolepsy Type I**

- Normal
- Narcolepsy

**Multiple Sleep Latency Test**

- PSG the night before
- 5 opportunities to nap, every 2 hours
  - 20 minutes to fall asleep
  - If fall asleep, allow 15 minutes of sleep
- Data obtained:
  - Number of naps in which sleep is obtained
  - Mean sleep latency
    - If no sleep, 20 minutes for that nap
  - Number of SOREMs [Sleep Onset Rapid Eye Movement]
Sleep Question

Which one of the following statements about the pathogenesis, diagnosis, and treatment of narcolepsy is true?

A. An affected parent has a normal QoL score.
B. Overnight polysomnography is optional.
C. Cataplexy often is reduced with a low dose of an antidepressant.
D. Genetic factors do not appear to play an important role.

Treatment of Narcolepsy

- Wake-promoting agents
  - Modafinil / Armodafinil (Provigil / Nuvigil)
    - Likely increase dopamine signaling
  - Amphetamines
    - e.g Methylphenidate
- REM-suppressing drugs
  - Increases norepinephrine and serotonin
    - Venlafaxine (Effexor, Effexor XR, Lanvexin)
    - Fluoxetine (Prozac)
    - Tricyclic
    - Sodium oxybate (Xyrem) at bedtime (analog of GHB, GABA analog)
Obstructive Sleep Apnea

Risk Factors

- Age (≥ with age = 50% at 65 years old)
- Gender (♂ 2-3x ≥ ♀)
- Post menopausal state (3x risk)
- Family History of Sleep apnea
- Overweight & Obesity (neck size, >BMI)
- Upper airway anatomic changes
  - (micrognathia, retrognathia, TMJ, macroglossia)
- Medical Conditions
  - Atrial Fibrillation
  - Heart Failure (Diastolic & Systolic)
  - Down’s syndrome, Thyroid, Polycystic Ovarian


Obstructive Sleep Apnea

Risk Factors

- Airway anatomic changes:
  - Micrognathia,
  - Retrognathia,
  - TMJ,
  - Macroglossia,
  - Neck circumference;
    - ♂ > 17 inches
    - ♀ > 16 inches

Modified Mallampati Classification
The mouth is evaluated in the sitting position with higher risk for OSA. Grade I = soft palate, uvula, tonsillar fauces, and pharynx visible; grade II = soft palate, uvula, and tonsillar fauces visible; grade III = only soft palate and base of uvula visible; grade IV = only hard palate visible.

Obstructive Sleep Apnea

Physical Examination

[Image of structural abnormalities]
Sleep Apnea
Consequences

- **Cardiovascular**
  - Increase risk for HTN, MI, Strokes & Sudden Death
  - Possibly worsens Diabetes (insulin resistance)
  - Risks; Dependent of desaturations not AHI

- **Psychological**
  - Higher rates of depression
  - Worsen quality of life (QoL)
  - Sexual Dysfunction

- **Neurological**
  - Cognitive deficiencies are higher

OSA Increases Co Morbid Health Risk

There is a strong association between sleep apnea, as measured by the apnea-hypopnea index, and the risk of traffic accidents.

<table>
<thead>
<tr>
<th>AHI Category</th>
<th>Case Patients (N=102)</th>
<th>Control Patients (N=102)</th>
<th>Unadjusted OR (95% CI)</th>
<th>Adjusted OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-20</td>
<td>29 (28.4)</td>
<td>7 (6.9)</td>
<td>8.2 (4.4-15.6)</td>
<td>11.1 (4.9-28.2)</td>
</tr>
<tr>
<td>20-30</td>
<td>21 (20.6)</td>
<td>6 (5.9)</td>
<td>6.3 (2.4-16.2)</td>
<td>7.2 (2.4-21.8)</td>
</tr>
<tr>
<td>&gt;30</td>
<td>15 (14.7)</td>
<td>5 (4.9)</td>
<td>5.4 (2.1-16.5)</td>
<td>8.1 (2.4-26.3)</td>
</tr>
</tbody>
</table>


OSA syndrome significantly increases the risk of stroke or death (HR ratio, 2.24) from any cause, and the increase is independent of other risk factors.
OSA Prevalence Co Morbid Health Risk

<table>
<thead>
<tr>
<th>Condition</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug Resistant Hypertension</td>
<td>80%</td>
</tr>
<tr>
<td>Severe Obesity</td>
<td>77%</td>
</tr>
<tr>
<td>Congestive Heart Failure</td>
<td>73%</td>
</tr>
<tr>
<td>Type 2 Diabetes</td>
<td>72%</td>
</tr>
<tr>
<td>Atrial Fibrillation, Depression, CVA</td>
<td>50%</td>
</tr>
<tr>
<td>All Hypertension</td>
<td>35%</td>
</tr>
<tr>
<td>Coronary Artery Disease</td>
<td>30%</td>
</tr>
<tr>
<td>Angina</td>
<td>30%</td>
</tr>
</tbody>
</table>

Prevalence of Sleep Apnea in co-morbid patients

Drug Resistant Hypertension
Jaget A et al. J Hypertension 2004
Severe Obesity
Katz T J. Obst Obes Surg. 2004
Congestive Heart Failure
Sakuma S et al. Pulmonary Med 2010
Type 2 Diabetes
Ehnhom et al. Endocrine Practice 2007
Atrial Fibrillation, Depression, CVA
Gama S & Holcomb 2004
All Hypertension
Spornen C et al. Ther Clin Pract 2002
Coronary Artery Disease
Scholz et al. Cardiology
Angina
Sanner et al. Clin Cardiology 2003

Sleep Question

A 59-year-old was evaluated for 4 month history of worsening lower extremity edema and dyspnea. Medical history significant for dyslipidemia, hypertension and diabetes. His current medications are simvastatin, lisinopril, aspirin and insulin.

His blood pressure is 144/86 mmHg, BMI is 42, neck circumference 18.5 inches. The exam is normal except venous stasis dermatitis and edema in the lower extremities. Data reveals a hemoglobin of 16.8 g/dL. Arterial blood gases pH 7.36, PCO2 of 52 mmHg, a PO2 of 53 mmHg. Echocardiogram shows a normal ejection fraction with dilated right ventricle with pulmonary systolic pressures of 78 mmHg. Chest radiograph is normal.

Which are the following is most likely diagnosis?

A. Cheyne-Stokes breathing
B. Chronic obstructive pulmonary disease
C. Interstitial lung disease
D. Obesity hypoventilation syndrome

Obesity Hypoventilation Syndrome

- Diagnosis:
  - BMI> 30 kg/m²
  - More common (25%) with BMI > 40 kg/m²
  - Elevated awake PaCO2 (> 45 mmHg)
  - Unable to attribute to other etiologies of hypoventilation (Drugs, CNS, Neuromuscular disease)
- Mechanism is unclear
- OSA is common (90%)
- Pulmonary HTN = OHVS >>> OSA
Sleep Case Question

30-year-old is evaluated for daytime fatigue for 9 months duration. He denies falling asleep while driving but falls asleep at other times during the day. He reports no leg symptoms. He has no significant medical history and takes no regular medications.

On exam: the vital signs are normal, BMI is calculated at 33. Neck circumference is 43 cm (17 inches). Pharynx is normal. The lungs, cardiovascular, & neurologic examinations are unremarkable.

In addition to counseling regarding sleep hygiene & weight loss, which is the following is the most appropriate management in this patient?

A. Advise alcohol abstinence
B. Initiate therapy with zolpidem (Ambien)
C. Order iron studies
D. Referred for polysomnography

Obstructive Sleep Apnea Testing/Diagnosis

- Many patients won’t have symptoms
  - > 50% don’t have sleepiness
  - Key: the absence of daytime sympotms does not rule out the disease
- Sleep partners history
  - Snoring & Witness Apnea (PPV 64%)

Obstructive Sleep Apnea Testing/Diagnosis

- Dissatisfied with sleep then...
- Screening Tests
  - Epworth Sleepiness Scale
  - Berlin Questionnaire (PCP)
  - STOP-BANG (Pre-Op)

Abirshami A.
A systematic review of screening questionnaires.

Sleep Apnea Syndrome Diagnostic Testing

- Polysomnography / Overnight Sleep Study
  - Considered the gold standard
  - > 5 events /hour with symptoms
  - > 15 events / hour with or without symptoms

- Home testing
  - Becoming more common (economics)
  - Indicated for high clinical suspicion without associate comorbidities (HF, Hypoventilation, COPD, Stroke)
  - Not for patients with insomnia, RLS, Narcolepsy

Types of Sleep Apnea

- Obstructive apnea: Complete cessation of airflow despite efforts to breathe

- Desaturation

- Snoring
Sleep Case Question

A 60-year-old is evaluated for 3 month history of loud snoring and “gasping” during sleep. He frequently falls asleep in a chair while reading. His medical history is unremarkable. Examination reveals normal vitals except for a blood pressure of 135/90 mmHg. BMI is 36, neck circumference is 45.7 cm (18 inches), he has a low-lying soft palate.

Polysomnography discloses severe obstructive sleep apnea with an apnea index of 44 per hour.

Which of the following is the most appropriate next step in treatment?

A. Continuous positive airway pressure  
B. Nocturnal oxygen therapy  
C. Oral dental appliance  
D. Upper airway surgery

Sleep Apnea

Treatment Options

- Avoidance of alcohol, sedatives & narcotics
- Position Therapy
  - Works only in combination
- Weight loss (next slide)
- Continuous Positive Airway Pressure (CPAP)
- Oral Appliance
  - CPAP more effective
  - Best for (obstructive) mild disease
- Surgery (UPPP, Maxillary Advancement)


Treatment for Sleep Apnea

Weight loss

- BMI Improves
  - 55.3 to 37.7 kg/m²
- AHI Improved
  - 54.7 to 15.8
- Residual disease
  - AHI < 10 (44%)
  - AHI < 5 (25%)

1% change weight = 3% change in AHI

Case Question

A 45 year old obese male present with snoring, witness apnea and daytime sleepiness. History includes HTN, depression and atrial fibrillation. Sleep study demonstrates severe OSA (AHI = 40). You initiate CPAP therapy.

Which of the following outcomes would be most likely to improve with CPAP therapy?

A. Hypertension
B. Daytime sleepiness
C. Mood (depression)
D. Atrial Fibrillation

AASM Practice Parameters & Clinical Guidelines

- CPAP indications (standard)
  - Treatment for mild disease with symptoms
    - Improved BP control
    - Improves QoL
  - Treatment for moderate to severe disease
    - Improves subjective sleepiness


Obstructive Sleep Apnea Treatments

- Surgery (UPPP, Maxillary Advancement)

  - Laser assisted uvuloplasty not recommended
    - Only for snoring (apnea and symptoms worsened)
  - Best surgical options
    - Bariatric surgery
    - Maxillo-mandibular Advancement (MMA)
    - Adenotonsillectomy for pediatric population

- Data supporting other upper airway procedures inconsistent or incomplete.

Sleep Disorder
Treatment Summary

- PAP/nCPAP
- Mainstay of treatment across the spectrum
- Best data for moderate to severe disease
- Improvements in CV, Afib are inconsistent
- Overall compliance @ 6 months is approx. 60%
- Average use is 4 nights for 4 hours
- Compliance is lower if < 30 events per hour
- Almost 100% effective if used

Eur Respiratory Journal 2000; 16(5) 921 - 7

CPAP vs Mandibular Advancement Devices and Blood Pressure

- Change in SBP = 2.5 mm Hg
- Change in DBP = 2.0 mm Hg

OSA: The Bottom Line

• OSA is common, yet underdiagnosed

• Know the risk factors
  • > 50% don’t have symptoms “I sleep fine”

• Overnight Polysomnography remains the standard

• Portable (home) testing = no comorbidities.

• Most patient with continued sleepiness on CPAP are noncompliant, gained weight or are sleep deprived.

Central Sleep Apnea Syndromes

• Central apnea: Complete cessation of respiratory effort and airflow

• Characteristic
  • Crescendo decrescendo pattern (Cycles 60 – 90 sec)
  • Inversely proportion to LVEF

Cheyne Stokes Pattern
Central Sleep Apnea

- CSA = common in (33%) heart failure
  - Rule of 3 (1/3 OSA, 1/3 CSA, 1/3 neither)
  - Associated with increase morbidity & mortality in Heart Failure


Sleep Case Question

A 55-year-old with history of systolic heart failure (LVEF 35%) presents with symptoms of frequent awakening and daytime sleepiness. His wife states he breathes “rapid and slowly” all the time. Current medications are carvedilol, furosemide, digoxin and potassium. Exam reveals no distress, Mallampati score of 3 with clear lung and slight bilateral leg edema.

Which of the following would be the best treatment for this patient?

A. CPAP  
B. Oxygen  
C. Adaptive sevo-ventilation (ASV) Bilevel  
D. ACE inhibitor  
E. Auto-CPAP
Clinical Case Question

Which of the following is *not associated* with positive airway therapy (CPAP/Bilevel) in heart failure patients with central sleep apnea (CSA)?

A. Improved nocturnal oxygenation  
B. Increased the ejection fraction  
C. Lowered norepinephrine levels  
D. Increased the distance walked in six minutes  
E. Survival


Case Report Answer

- Initial management in Cheyne-Stoke Respiration
- Maximize medical therapy!
- CANPAP trial
- Study suggests that OSA has adverse effects on survival in patients with HF,
- Partially reversible with treatment by CPAP
- However, no mortality benefit!
- Although CPAP attenuated central sleep apnea, improved nocturnal oxygenation, increased the ejection fraction, lowered norepinephrine levels, and increased the distance walked in six minutes, it did not affect survival.


Summary

- Sleep apnea is common & increases with age.
- Risk factors for OSA: Obesity, Family history, Retrognathia, Treatment resistant hypertension, CHF, Atrial fibrillation, Stroke, & DM 2.
- PSG is the gold standard test; MSLT is for narcolepsy.
- Home testing is for high clinical suspicion and no significant comorbid conditions.
- Weight loss (> mild and moderate) & CPAP (all)