# AMERICAN COLLEGE OF OSTEOPATHIC INTERNISTS Board Review in Sleep Medicine

Timothy J. Barreiro, DO, MPH, FCCP, FACOI, FACP Section Chair, 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)
- Review the potential treatment options for sleep related disorders.
- Identify key subtypes of sleep apnea (Cheyne-Stokes & obesity hypoventilation syndrome) and review their consequences.

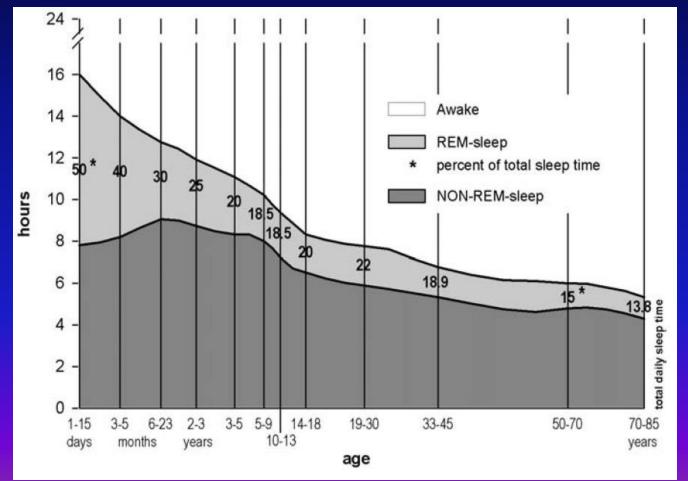
### Normal Adult Sleep Overview

- 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)

Sources: ATS Core Curriculum 2014: Part III. Adult Sleep Medicine. Ann Am Thorac Soc Vol 11, No 9, pp 1480

## **Physiologic Changes in Sleep**

 Body clock shifts earlier with age, however, REM sleep remains relatively constant.



Sources: Hobson. Sleep and Dreaming. In: Fundamental Neuroscience. 1999; Roffwarg et al. Science, 1996; 152:604

### Insomnia Overview of the Problem

- Lifetime prevalence 30 35% ("serious" in 15%)
- Much worse in elderly: Sex ratio: ♀ ≥ ♂
- Short-term insomnia: Days to a few weeks stress event.
- Persistent insomnia: Months to years.
   Types:
  - Medical (pain, thyroid, arthritis, GERD)
  - Psycho-physiological + substances
  - Primary insomnia

Winkelman JW. Insomnia Disorder. N Engl J Med 2015; 373:(15): 1437 - 44.

### Question

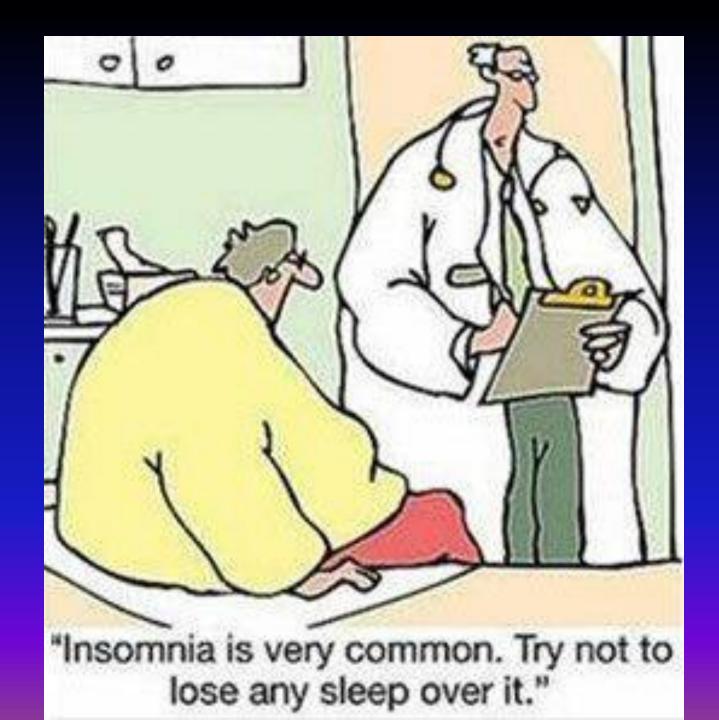
Which of the following statements about insomnia is false?

- A. > 50% with insomnia have a psychiatric disorder.
- B. Various physical symptoms are associated with insomnia (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.

Winkelman JW. Insomnia Disorder. N Engl J Med 2015; 373:(15): 1437 – 44 Ford DE et al Epidemiologic study of sleep disturbance and psychiatric disorders: an opportunity for prevention? JAMA 1989; 262: 1479- 84.

### **Insomnia Treatment**

- Short-Term Insomnia: 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 treat too long.
- Persistent Insomnia: Keep up your search for diagnosis of depression, bipolar, anxiety.
  - Treatment: Cognitive behavioral therapy, sedating antidepressants or mood stabilizers long-term.



### **Sleep Case Question**

A 23 year old is referred for excessive sleepiness after having fallen asleep while driving. She often struggles to remain awake. She occasionally feels weak when laughing. Once, she fell to the ground while laughing during a party and could not get up for a few minutes. If she is sleepy she imagines seeing animals. Once she was terrified to find herself unable to move after awakening.

Which of the follow test is most appropriate?

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

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

Thorpy MJ. Delayed diagnosis of Narcolepsy Sleep Med 1004; 15: 502 -507. Scammell, TE.N Engl J Med 2015; 373:2654-2662.

# 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** 

Aldrich, MS. N Engl J Med 1990; 323:389-394. Scammell, TE.N Engl J Med 2015; 373:2654-2662.

### **Narcolepsy Tetrad**

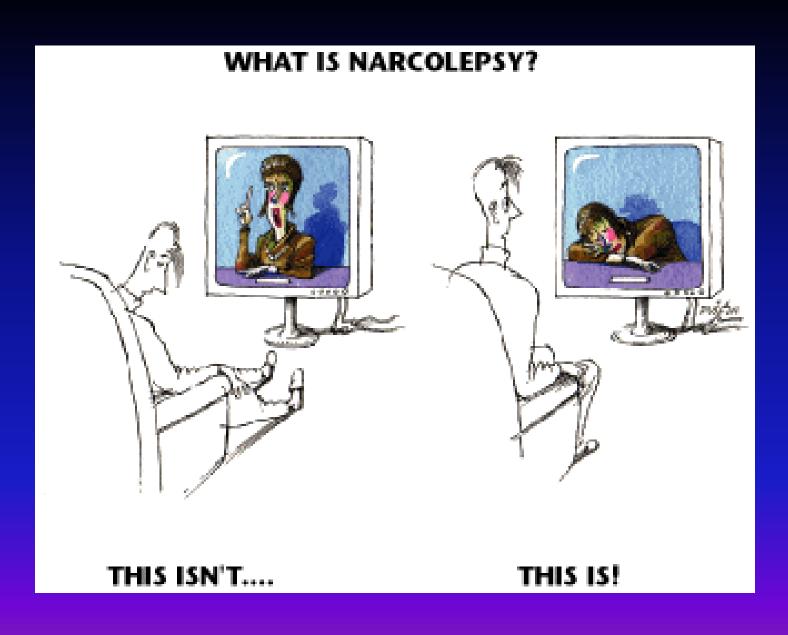
Narcolepsy Symptoms	Sensitivity	Specificity
Daytime Sleepiness	100%	Low
Cataplexy Hallucinations	60 – 70%	100%
Hypnagogic	30 – 60%	Common
Hypnopompic	30 – 60%	Low
Sleep paralysis	25 – 50%	Low

Atri 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 bodymass index (BMI).
- B. Complex auditory hallucinations are common.
- C. Rapid-eye-movement (REM) sleep can occur at any time of day.
- D. Symptoms usually begin in midlife.



### **Multiple Sleep Latency Test**

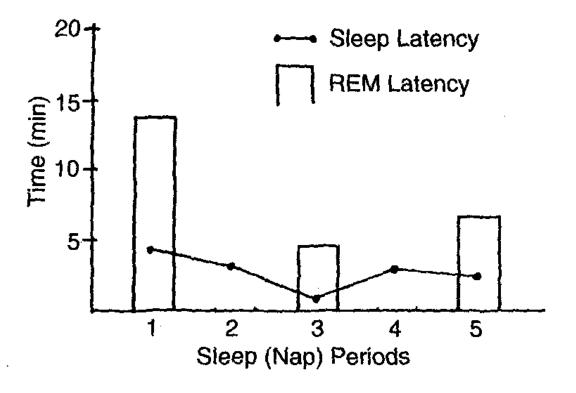


Figure 35. The results of L.I.'s Multiple Sleep Latency Test.

Sleep, Dreaming, & Sleep Disorders: An introduction" (2<sup>nd</sup> ed.) by William H. Moorcroft, New York, University Press of America Inc., 1993, ISBN 0-8191-9251-1. page 329.

### **Sleep Question**

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

- A. Patient report a normal QoL score.
- B. MSLT is optional.
- C. Cataplexy often is reduced with a low dose of an antidepressant.
- D. No genetic factors are present.

### **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) QHS (analog of GHB, GABA analog)



A 52-year-old is evaluated in follow-up after undergoing total knee arthroscopy weeks ago. Although the surgical procedure was uncomplicated, he requires reintubation in the recovery room following to persistent hypoxemia. He was extubated 24 hours later without difficulty. Chest radiograph was normal, and the remainder of the hospitalization was uneventful.

He is on three medications for high blood pressure. Examination reveals normal temperature and blood pressure of 128/84 mmHg; his heart rate is 78 bpm; respiratory rate is 14; BMI is 38. Oxygen saturation is 97% on room air. The examination is notable for a low-lying soft palate and thick neck. Lungs & cardiac examinations are normal. The surgical incision is healing, and the remainder of the examination is unremarkable.

Which are the following is most appropriate next step in management?

- A. Overnight pulse oximetry
- B. Polysomnography
- C. StopBANG questionnaire
- D. No additional testing

Practice guidelines for perioperative management of patients with obstructive sleep apnea: An updated report by the American Society of Anesthesiologist Task Force on Perioperative Management of patients with obstructive sleep apnea. Anesthesiology 2000; 14 (2): 268-286.

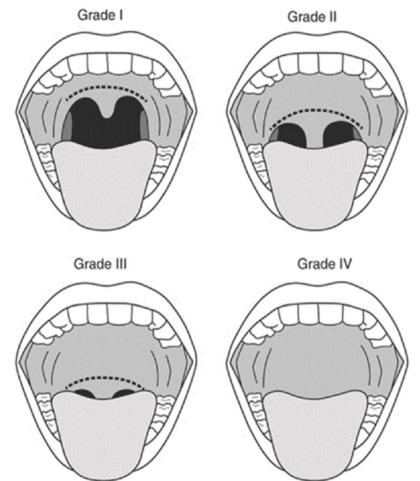
### Obstructive Sleep Apnea Risk Factors

- 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)

Strohl KP, et al; An official American Thoracic Society Clinical Practice Guideline: sleep apnea, sleepiness, and driving risk in noncommercial drivers. Am J Respir Crit Care Med. 2013;187:1259-66. [PMID: 23725615]

### Obstructive Sleep Apnea Risk Factors

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

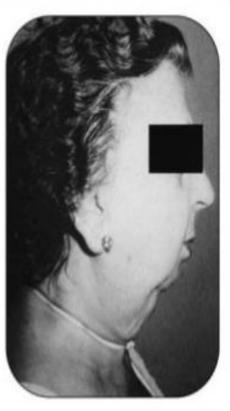


#### **Modified Mallampati Classification**

The mouth is evaluated with the patient in a sitting position with higher risk for OSA. Grade I = soft palate, uvula, tonsillar fauces, and pillars visible; grade II = soft palate, uvular, 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





Guilleminault C et al. Sleep Apnea Syndromes. New York: Alan R. Liss, 1978.

### 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

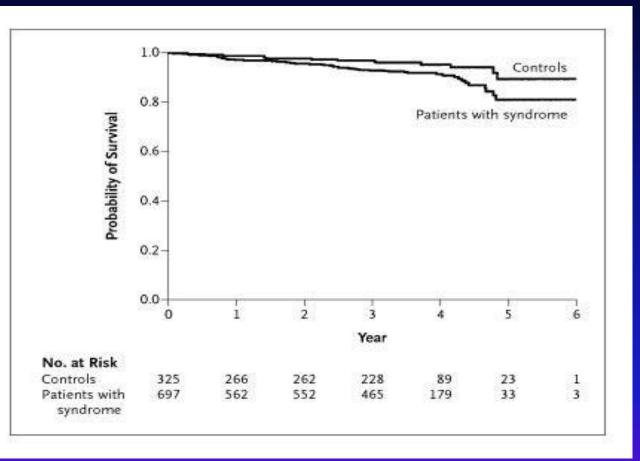
Cognitive deficiencies are higher

### **OSA Increase Co Morbid Health Risk**

N =1022

Study mean AHI = 35 Control AHI = 2

Results: Stroke or Death from any cause (hazard ratio, 2.24; 95 percent confidence interval, 1.30 to 3.86; P=0.004).



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.

H. Klar Yaggi, M.D., M.P.H., John Concato, M.D., M.P.H., et al. N Engl J Med 2005; 353:2034-2041

### Excessive Sleepiness and Driving Collisions, Cost and Fatalities Meta-Analysis of 6 studies:

#### Risk of MVC is > in drivers with OSA than those without OSA Consequences of OSA Philip P, 2010 810K collisions \$ 15.9 billion in cost Mukherjee S, 2012 1,44 fatalities Teran-Santos, 1999 George CF, 2007 Estimated cost-saving with CPAP Vennelle M, 2010 Prevent > 500k collisions Powell NB, 2010 Reduced cost by \$11 billion Save nearly 1,000 lives 0.5 2 5 10 **Odds Ratio**

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

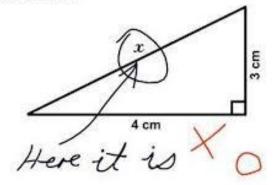
Strohl K, Brown D, Collop N., et al. American Thoracic Society Clinical Practice Guideline: Sleep Apnea, Sleepiness, and Driving Risk. An Update. Am J Respir Crit Care Med 2013; 187 (11): 1259–1266

### **OSA Prevalence Co Morbid Health Risk**

Drug Resistant Hypertension Logan AG et al. J Hypertension 2010		80%
<b>Severe Obesity</b> Keefe TJ. Obese Surg. 2004	77%	
<b>Congestive Heart Failure</b> Ferreira S et al. Pulmonary Med 2010	73%	
<b>Type 2 Diabetes</b> Elnhorn et al. Endocrine Practice 2007	72%	
Atrial Fibrillation, Depression, CVA50%Gami A. Circulation 2004		
All Hypertension35%Sjostrom C et al. Thorax 2002		
Coronary Artery Disease 30% Schafer et al. Cardiology		
Angina 30% Sanner et al. Clin Cardiology 2001		

H. Klar Yaggi, M.D., M.P.H., John Concato, M.D., M.P.H., et al. N Engl J Med 2005; 353:2034-2041

3. Find x.



There are 300 students in Year 10. Mary and Mark want to find out Year 10's favourite colour.

Mary asks 30 people.

Mark asks 150 people.

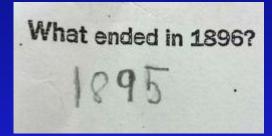
Mark says 'My conclusions are more likely to be reliable than Mary's'.

Why does Mark think he is right?

Mark is a man Because

The first cells were probably ...?

one



Diabetes. Brian has Type I diabetes X

# **Sleep Question**<sup>30%</sup>

A 59-year-old was evaluated for a 4 month history of worsening lower extremity edema and dyspnea. Medical history is positive 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. Exam is normal except venous stasis dermatitis and bilateral edema. Tests reveal a hemoglobin of 16.8 g/dL. Arterial blood gases pH 7.36, PCO<sub>2</sub> of 52 mmHg, a PO<sub>2</sub> of 53 mmHg. Echocardiogram shows a normal ejection fraction with dilated right ventricle with elevated pulmonary systolic pressures. Chest radiograph and FEV<sub>1</sub> are normal.

#### Which of the following is the 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/m<sup>2</sup>
- (25%) with BMI > 40 kg/m<sup>2</sup>
- (50%) with BMI > 50 kg/m<sup>2</sup>
- 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

### Obstructive Sleep Apnea Testing/Diagnosis



Sleep partners history
Snoring & Witness Apnea (PPV 64%)

### **Sleep Case Question**

30-year-old is evaluated for daytime fatigue for 9 months. 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 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 <u>does not</u> rule out the disease
  - Sleep partners history
    - Snoring & Witness Apnea (PPV 64%)

Epstein LJ et al; Adult Obstructive Sleep Apnea Task Force of the American Academy of Sleep Medicine. Clinical guideline for the evaluation, management and long-term care of obstructive sleep apnea in adults. J Clin Sleep Med. 2009;5:263-76. [PMID: 19960649]

### Obstructive Sleep Apnea Testing/Diagnosis

http://epworthsleepinessscale.com

- Dissatisfied with sleep then...
- Screening Tests
   (All have Low Quality of Evidence)
  - Epworth Sleepiness Scale
  - Berlin Questionnaire (PCP)
  - STOP-BANG (Pre-Op)

#### Abrishami A,

A systematic review of screening questionnaires.

Can J Anaesth. 2010;57:423-38. & Anesthesiology 2008; 108: 812

Qaseem A. Clinical Guidelines of OSA. Ann Intern Med 2014; 161: 210 -220.

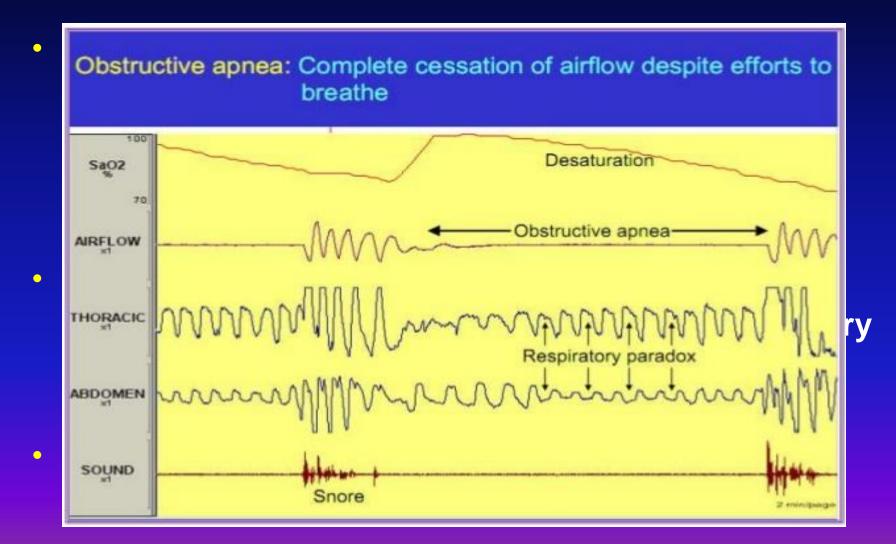
S	Does the patient <b>snore</b> loudly (louder than talking or loud enough to be heard through closed doors)?	Y/N
T	Does the patient often feel <b>tired</b> , fatigued, or sleepy during the day?	Y/N
0	Has anyone <mark>observed</mark> the patient stop breathing during their sleep?	Y/N
P B	Does the patient have, or is the patient being treated for, high blood pressure?	Y/N
B	Does the patient have a BMI of more than 35?	Y/N
а	Age. Is the patient older than 50?	Y/N
n	Is the patient's neck circumference greater than 40cm?	Y/N
g	Gender. Is the patient male?	Y/N
Sco	ring: Y≥3 = high risk of OSA	
500	Y < 3 = low risk of OSA	

Screening tool for OSA: STOP-Bang

### 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 <u>without</u> associate comorbidities (HF, Hypoventilation, COPD, Stroke)
  - Not for patients with insomnia, RLS, Narcolepsy

### Types of Sleep Apnea Obstructive apnea



### **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. Examination reveals a blood pressure of 135/90 mmHg. BMI is 38, 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. (normal <5 per hour) Which of the following is the most appropriate treatment?

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

Gottlieb DJ, et al. "CPAP versus oxygen in obstructive sleep apnea" N Engl J Med 2014; 370: 2276-2285. Chirinos JA, et al. "CPAP, weight loss, or both for obstructive sleep apnea" N Engl J Med 2014; 370 2265-2275.

## Sleep Apnea Treatment Options

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

Morgenthaler TI, et al; Standards of Practice Committee. Practice parameters for the medical therapy of obstructive sleep apnea. Sleep. 2006;29:1031-5



A 45 year old obese male presents 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 <u>alone</u>?

- A. Hypertension
- **B.** Sleepiness
- **C.** Mood (depression)
- **D.** Lower crp levels

Basner RC. "Cardiovascular morbidity and obstructive sleep apnea" N Engl J Med 2014; 370: 2339-2341.

#### 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

Qaseem A, Holty JE, Owens DK, Dallas P, Starkey M, Shekelle P. Management of obstructive sleep apnea in adults: a clinical practice guideline from the American College of Physicians. Ann Intern Med. 2014; 161:210-220.1

#### Obstructive Sleep Apnea Treatments

- Surgery (UPPP, Maxillary Advancement)
  - Best surgical options
    - Biartric surgery
    - Maxillo-mandibular Advancement (MMA)
    - Adenotonsillectomy for pediatric population
- Data supporting other upper airway procedures inconsistent or incomplete.

Surgical management of obstructive sleep apnea. Proc (Bayl Univ Med Cent). 2000 Oct; 13(4): 338–342.

## Sleep Disorder Treatment Summary

#### PAP/nCPAP

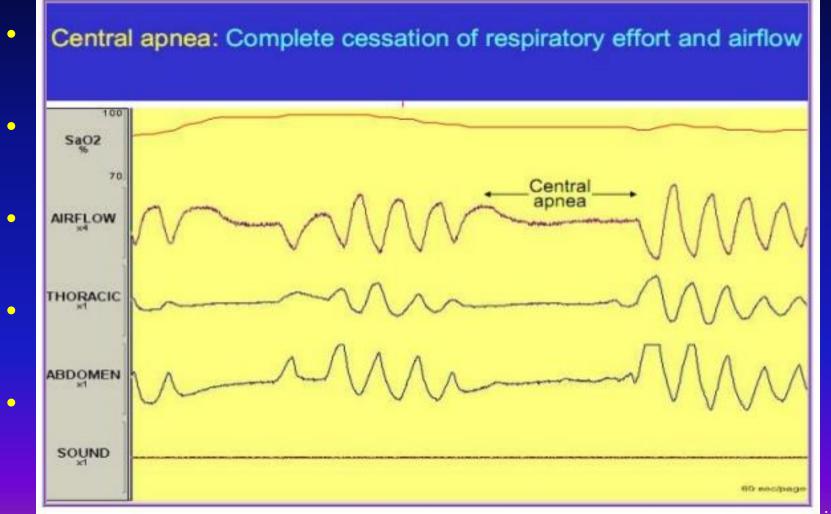
- Mainstay of treatment across the spectrum
- Best data for moderate to severe disease
- Improvements in CV, Afib are inconsistent
- Overall compliance @ 6 months is only 60%
- Compliance is lower if < 30 events per hour</li>
- Almost 100% effective if used

Strohl K, Brown D, Collop N., et al. An Official American Thoracic Society Clinical Practice Guideline: Sleep Apnea, Sleepiness, and Driving Risk in Noncommercial Drivers. An Update Am J Respir Crit Care Med 2013; 187 (11): 1259–1266

# **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**



Aurora RN et al. The treatment of Central Sleep Apnea in Adults:

Practice Parameters with an Evidence-Based Literature Review and Meta-Analyses. SLEEP 2012; 35(1):17-40.

# **Cheyne Stokes Pattern**

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

Hiperpres	Mpopnea	Арная	Hperpres		
_///	\/\		Ŵ	$\mathbb{M}$	

# **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 breaths "rapid and slowly" all the time. Current medications are carvedilol, furosemide, digoxin and potassium. Exam reveals normal vitals with clear lung and slight bilateral leg edema. He is found to have central sleep apnea.

Which of the following would be the best treatment for this patient ? A. CPAP B. Oxygen C. Adaptive sevo-ventilation (ASV) D. ACE inhibitor E. Auto-CPAP

Aurora RN et al. The treatment of Central Sleep Apnea in Adults: Practice Parameters with an Evidence-Based Literature Review and Meta-Analyses. SLEEP 2012; 35(1):17-40.



#### American Academy of Sleep Medicine

#### Safety Notice August 2015

The American Academy of Sleep Medicine (AASM) Board of Directors is reviewing "The Treatment of Central Sleep Apnea Syndromes in Adults: Practice Parameters with an Evidence-Based Literature Review and Meta-Analyses," which was published in 2012 and includes the following recommendation:

4.2.3a Adaptive Servo-Ventilation (ASV) targeted to normalize the apnea-hypopnea index (AHI) is indicated for the treatment of CSAS related to CHF. (STANDARD)

In response to a Field Safety Notice issued by ResMed in May 2015, the <u>AASM advised</u> <u>physicians</u> to stop prescribing ASV to treat central sleep apnea in patients with symptomatic heart failure and left ventricular ejection fraction (LVEF) <45%. Physicians are encouraged to read the full statements from the AASM and ResMed for important patient care recommendations, including ResMed's clarification that ASV therapy is contraindicated for patients with symptomatic, chronic heart failure with reduced LVEF and moderate to severe predominant central sleep apnea.

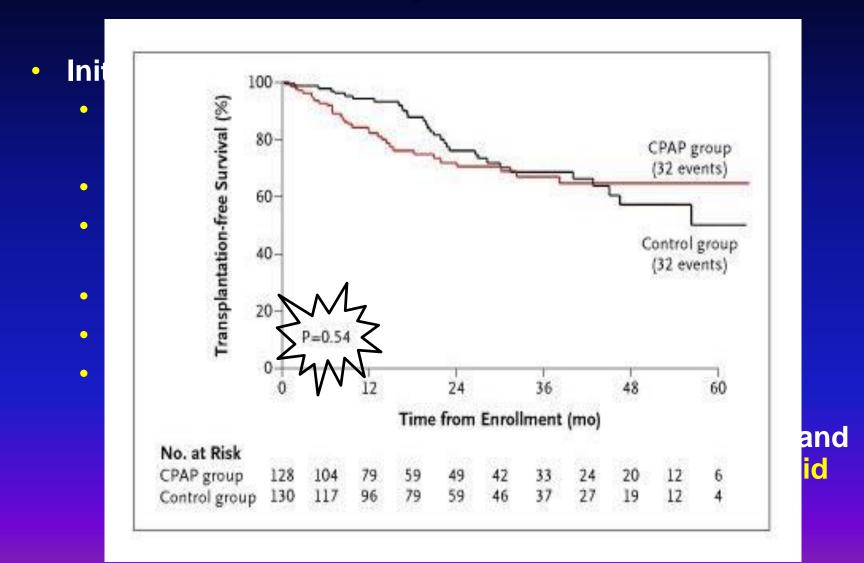
# **Clinical Case Question**

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

Aurora RN et al. The treatment of Central Sleep Apnea in Adults: Practice Parameters with an Evidence-Based Literature Review and Meta-Analyses. SLEEP 2012; 35(1):17-40.

## **Case Report Answer**



Bradley, T et al. N Engl J Med. 2005; Volume 353;19:2025-2033.

## 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)