ABDSM BOARD REVIEW COURSE

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OVERVIEW

- Basic Sleep Medicine (7%)
- Polysomnography (5%)
- Medical and Sleep Disorder History (10%)
- OSA Treatment – Medical and Surgical (7%)
- Pediatrics (5%)

TOTAL = 34%
IN THE PATHOPHYSIOLOGY OF SLEEP APNEA, AIRWAY PATENCY AND STABILITY IS PROMOTED BY WHICH FACTOR?

A. Increased lung volume
B. Shorter mandible
C. Increased parapharyngeal fat deposition
D. Negative inspiratory pressure
E. Reduced pharyngeal muscle dilator activity
COMPARED TO THE UPPER AIRWAY PHYSIOLOGY IN NON-OSA CONTROLS, PATIENTS WITH OSA TEND TO HAVE ALL OF THE FOLLOWING EXCEPT:

A. More positive critical closing pressure (more collapsible airway)
B. Decreased genioglossus muscle activity during wakefulness
C. Smaller cross-sectional area on airway imaging studies
D. Abnormal negative pressure reflex
E. Evidence of neuromuscular dysfunction
OSA is associated with a decrease in which of the following cytokines:

A. Leptin  
B. Ghrelin  
C. Adiponectin  
D. CRP  
E. TNFa
WHICH OF THE FOLLOWING STATEMENTS IS TRUE ABOUT OSA AND HYPERTENSION?

A. Ambulatory blood pressure is increased in OSA patients primarily due to increased salt intake associated with elevated ghrelin levels.

B. Ambulatory blood pressure normally increases in the early morning before awakening and this increase is blunted in OSA.

C. Untreated OSA is associated with a similar risk of hypertension at all OSA severity levels.

D. Untreated severe OSA is associated with a 7-fold increased risk of hypertension.

E. The risk of hypertension in untreated OSA is due intermittent hypoxia, sympathetic overactivation, inflammation, and other complex factors.
RISK OF FATAL AND NON-FATAL CARDIOVASCULAR EVENTS IS SIGNIFICANTLY INCREASED IN PATIENT WITH:

A. Mild OSA
B. Severe OSA
C. Severe OSA on CPAP therapy
D. Both A & B
E. A, B, & C
BASIC SLEEP MEDICINE

- Overview/Epidemiology of OSA
- Pathophysiology of OSA
- Health consequences of OSA
PUBLIC HEALTH SIGNIFICANCE

- Sleep disorders are very common
- 50-70 million in US have chronic sleep problem affecting health and/or daytime function
- 20% of all serious motor vehicle crashes associated with driver sleepiness
- Identified need to:
  - Increase public awareness
  - Increase health care professional awareness, education, and training
  - Develop and expand diagnostic and therapeutic services
  - Emphasize long-term patient care models and chronic disease management strategies
  - Invest in interdisciplinary academic health centers that emphasize clinical care, training, and research
  - Create a national research network

Sleep disorders and sleep deprivation: an unmet public health problem. Institute of Medicine of the National Archives, 2006.
OSA PREVALENCE – WISCONSIN COHORT

• General population (1993 data\(^1\)):
  • AHIL>5: 24% of men, 9% of women
  • AHIL>5 and sleepy: 4% of men, 2% of women
• Increase in obesity → Increase in OSA prevalence\(^2,3\)
• 10% weight gain:\(^4\)
  • 6-fold increased risk of mod-sev OSA
  • 32% increase in the AHIL


**OSA – HEALTH CARE COSTS**

- Compared annual medical cost prior to Dx of OSA to matched non-OSA controls
  - 238 OSA cases: $2720
  - 476 controls: $1384
- Conclusions:
  - OSA patients had higher medical costs (~2x)
  - OSA severity correlated with cost
  - OSA: $3.4 billion extra cost/yr in US


OVERVIEW

- Upper airway that is too narrow and too collapsible
- Repetitive upper airway obstruction during sleep that impacts:
  - Sleep, daytime function, quality of life
  - Cardiovascular risk, health, longevity
IMPACT ON SLEEP, DAYTIME FUNCTION, AND QUALITY OF LIFE:

- Snoring
- Frequent awakenings at night
- Frequent urination at night
- Unrefreshing sleep
- Morning headaches*
- Memory loss
- Difficulty with attention/concentration
- Mood disorder/Irritability
- Daytime sleepiness (7x increased risk of MVA)**


IMPACT ON CARDIOVASCULAR RISK, HEALTH, LONGEVITY:

- Reflux disease
- Systemic hypertension
- Coronary artery disease
- Atrial fibrillation
- Heart attack
- Stroke
- Pulmonary hypertension
- Diabetes/metabolic syndrome
- Dementia
- Cancer risk
- Mortality

WHY DO WE TREAT SLEEP APNEA?

1. Improve symptoms/quality of life

2. Reduce the cardiovascular/health risks
HOW DO WE TREAT SLEEP APNEA?

• CPAP/BIPAP
• Oral appliance
• Surgery
  • Adjunct
  • Sole
• Weight loss
• Adjunctive measures:
  • Positional therapy
  • Smoking cessation
  • Treating allergies, reflux, etc
  • Orthodontics
• New approaches
  • Nasal EPAP (Provent)?
  • Hypoglossal nerve stimulation?
  • Oropharyngeal physical therapy?
  • Intraoral negative pressure?
  • Medications?
BASIC SLEEP MEDICINE

- Overview/Epidemiology of OSA
- Pathophysiology of OSA
- Health consequences of OSA
PATHOPHYSIOLOGY – COMPLEX AND MULTIFACTORIAL

- Anatomical
  - Craniofacial structure
  - Pharyngeal anatomy
  - Nose
  - Obesity
  - Airway edema
  - Surface tension
  - Lung volume
- Neuromuscular
  - Pharyngeal sensation
  - Central respiratory drive
  - Tonic activity of upper airway dilator muscles
  - Arousal threshold
  - Loop gain (peripheral and central chemoreceptor response)

TREATMENT OF OSA

- Anatomical
  - Craniofacial structure
  - Nose
  - Pharyngeal anatomy
  - Obesity
  - Airway edema
  - Surface tension
  - Lung volume

- Neuromuscular
  - Pharyngeal sensation
  - Central respiratory motor output
  - Tonic activity of upper airway dilator muscles
  - Arousal threshold
  - Loop gain (peripheral and central chemoreceptor response)

- Positive pressure
- Oral appliance
- Weight loss
- Surgery
- Medications?
- Oropharyngeal exercises?
- Electrical stimulation?

Phenotyping OSA patient/airway may have therapeutic implications
**PATHOPHYSIOLOGY – STARLING RESISTOR**

- \( P_{c\text{rit}} = P_{\text{in}} \) when airway collapse occurs
- Pressure gradient during airflow = \( P_{\text{us}} - P_{c\text{rit}} \) (independent of \( P_{\text{ds}} \))
- Effective therapy requires widening differential between \( P_{\text{us}} \) and \( P_{c\text{rit}} \)
  - Increase \( P_{\text{us}} \) (CPAP)
  - Decrease \( P_{c\text{rit}} \)
    - Weight loss
    - Oral appliance
    - Surgical modifications of upper airway
    - Augment active neuromuscular control of airway muscle tone


PATHOPHYSIOLOGY – BALANCE OF FORCES

**Airway collapse**
- Negative inspiratory pressure
- Extraluminal positive pressure
- Fat deposition
- Mandibular deficiency

**Airway patency**
- Pharyngeal dilator activity
- Lung volume

OSA PATIENTS HAVE:

- Narrower airway
- More collapsible airway
- Elevated genioglossus muscle activity during wakefulness
  - Compensation?
  - Denervation/renervation injury?


During sleep (Wake → NREM → REM): Progressive loss of compensation. Defective compensation in OSA patients:
- Central hypoxic injury?
- Peripheral neuropathy due to inflammation, vibratory trauma?

BASIC SLEEP MEDICINE

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PATHOPHYSIOLOGY: HEALTH CONSEQUENCES

- Health consequences
  - Cardiovascular
  - Neurocognitive
- Mechanisms
  - Sleep deprivation
  - Chronic intermittent hypoxia
  - Sympathetic overactivation
  - Chronic inflammation

CARDIOVASCULAR SEQUELAE

- Mechanisms
- Data
  - Hypertension
  - Cardiovascular Mortality
  - Metabolic syndrome/Diabetes


**CARDIOVASCULAR SEQUELAE**

- Multiple clinical effects of OSA
- Genetic predisposition/variability
- Multiple disease mechanisms linking OSA to CV disease

**Summary:**
- Prevalence of OSA increased in HTN, CHF, Afib, ESRD, CVA, CAD/MI.
- OSA contributes to progression of each disease
- Intermittent hypoxia is primary mechanism
- Treatment of OSA (mostly CPAP) has beneficial effect on CV disease

HYPERTENSION RISK

- Mechanisms
  - Sympathetic activation
  - Intermittent hypoxia
  - ‘Non-dipper’ theory


HYPERTENSION RISK

1. Wisconsin Sleep Cohort
   • Mod-Sev OSA $\rightarrow$ 2.89 odds ratio for having HTN at 4y F/U

2. Sleep Heart Health Study
   • Severe OSA $\rightarrow$ 1.5x increased risk of developing HTN (not statistically significant after controlling for BMI but mostly mild OSA and short F/U)

3. Zaragoza Sleep Cohort
   • Untreated OSA $\rightarrow$ 1.78-2.89x adjusted risk of incident HTN at 15y F/U


O’Connor GT et al. Prospective study of sleep-disordered breathing and hypertension: the Sleep Heart Health Study. Am J Respir Crit Care Med. 2009;179(1159-64.

1. Sleep Heart Health Study
   - Severe OSA → sig increased risk of CV events
   - Risk lowered with CPAP
2. Wisconsin Sleep Cohort
   - Severe OSA:
     • 3x increased risk of all-cause mortality
     • 5x increased risk of CV mortality
   - Mild-mod OSA: 1.5x increased risk (not stat sig)


METABOLIC SYNDROME

- **Definition:** combination of metabolic disturbances that together increase the risk of diabetes and CV disease
- **Hypothesis:** chronic inflammatory processes implicated in pathogenesis of cardiovascular disease in OSA
- **Pathophysiology:** chronic intermittent hypoxia and reperfusion injury
  - Sympathetic activation
  - Inflammation
  - Oxidative stress
- **Contributes to** endothelial injury, thrombogenesis, atherosclerosis
- **May provide** marker of OSA severity and treatment response

METABOLIC SYNDROME

• Sleep deprivation affects glucose metabolism
• Short sleep duration → obesity
• OSA is independent risk factor for the metabolic syndrome and DM
• OSA severity associated with degree of insulin resistance
• Complex multifactorial pathophysiology
• Causality, exact mechanisms, treatment effect still unclear*


METABOLIC SYNDROME - MECHANISMS

• HPA Axis (Hypothalamic-Pituitary-Adrenal Axis)
  • Important role in regulating sleep/wake, energy balance, fat distribution, and pathogenesis of obesity
  • Sleep deprivation and OSA both associated with increased cortisol

• Inflammation
  • HIF-1
    • Major regulator of oxygen homeostasis (carotid body)
    • Primarily protective but mediates cardiovascular responses to hypoxia
  • NF-κB
    • Primary proinflammatory transcription factor
    • Activated by intermittent hypoxia
  • Cytokines
    • CRP, TNF-α, IL-6, IL-8, ICAM-1
    • Insulin resistance, plaque formation, thrombosis

METABOLIC SYNDROME - ADIPOKINES

1. Leptin
   - ↑ in OSA with associated leptin resistance
   - Correlated with BMI, insulin, and TNFa

2. Ghrelin
   - ↑ in OSA
   - Regulates appetite

3. Adiponectin
   - ↓ in OSA
   - Antiinflammatory and insulin sensitivity

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