Sleep Apnea and Heart Diseases

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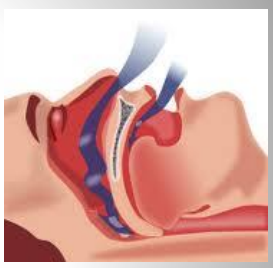
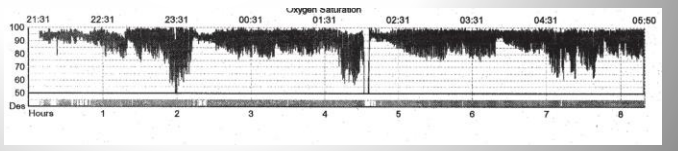
Obstructive sleep apnea (OSA)

- a very common medical condition
- 5% to 15% of the population
  - Up to 24% of middle aged population
  - 90% undiagnosed
- repetitive occlusions of the posterior pharynx
- oxyhemoglobin desaturation
- persistent inspiratory efforts
- arousal from sleep





Obstructive sleep apnea (OSA)

- Obese Middle-aged Male
- But also
  - women
  - thin individuals
- Most common symptoms
  - Loud snoring
  - Excessive daytime sleepiness
  - Witnessed apneas

The majority do not have airway abnormalities

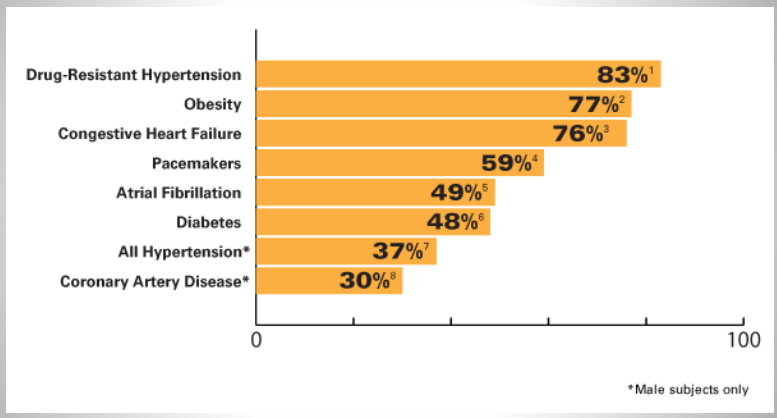
Anatomic Misfortune

Systemic Illness

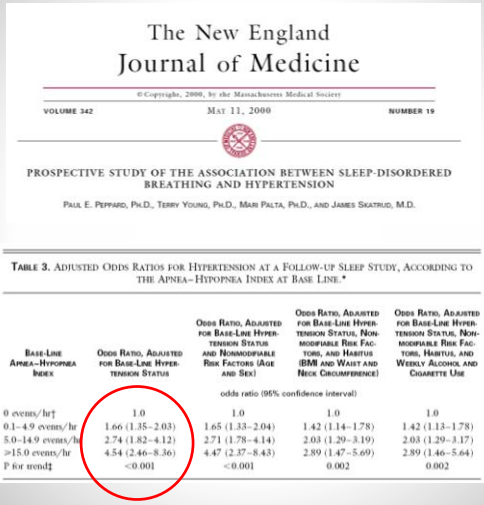
Cardiologist?

- **Acute effects of apnea**
  - Reduced myocardial oxygen delivery
  - Decreased cardiac output
  - Increased myocardial oxygen demand
  - Sympathetic nervous system activation
  - Increase in left ventricular afterload
  - Increased blood pressure (non-dipping)
  - Increased heart rate
  - Cardiac arrhythmias (up to 50% of OSA)
  - Nocturnal myocardial ischemia
  - Nocturnal pulmonary edema

Cardiologist?



Cardiologist?



The New England Journal of Medicine

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PROSPECTIVE STUDY OF THE ASSOCIATION BETWEEN SLEEP-DISORDERED BREATHING AND HYPERTENSION

PAUL E. PEPPARD, PH.D., TERRY YOUNG, PH.D., MARI PALTA, PH.D., AND JAMES SKATRUD, M.D.

TABLE 3. ADJUSTED ODDS RATIOS FOR HYPERTENSION AT A FOLLOW-UP SLEEP STUDY, ACCORDING TO THE APNEA–HYPOPNEA INDEX AT BASE LINE.*

BASE-LINE APNEA–HYPOPNEA INDEX	ODDS RATIO, ADJUSTED FOR BASE-LINE HYPERTENSION STATUS	ODDS RATIO, ADJUSTED FOR BASE-LINE HYPERTENSION STATUS AND NONMODIFIABLE RISK FACTORS (AGE AND SEX)	ODDS RATIO, ADJUSTED FOR BASE-LINE HYPERTENSION STATUS, NONMODIFIABLE RISK FACTORS, AND HABITUS (BMI AND WAIST AND NECK CIRCUMFERENCE)	ODDS RATIO, ADJUSTED FOR BASE-LINE HYPERTENSION STATUS, NONMODIFIABLE RISK FACTORS, HABITUS, AND WEEKLY ALCOHOL AND CIGARETTE USE
	odds ratio (95% confidence interval)			
0 events/hr†	1.0	1.0	1.0	1.0
0.1–4.9 events/hr	1.66 (1.35–2.03)	1.65 (1.33–2.04)	1.42 (1.14–1.78)	1.42 (1.13–1.78)
5.0–14.9 events/hr	2.74 (1.82–4.12)	2.71 (1.78–4.14)	2.03 (1.29–3.19)	2.03 (1.29–3.17)
≥15.0 events/hr	4.54 (2.46–8.36)	4.47 (2.37–8.43)	2.89 (1.47–5.69)	2.89 (1.46–5.64)
P for trend‡	<0.001	<0.001	0.002	0.002

Neurologist?

- Stroke
  - Severe OSA in men is associated with a significantly increased risk of fatal and nonfatal cardiovascular events (OR 2.87 and 3.17)
  - Any degree of OSA doubles the risk of stroke
- Cognitive Impairment and depression
  - Class A evidence for association with OSA *(young 2002)*
- *OSA is a neurologic disease*

OSA: A Neurologic Disease

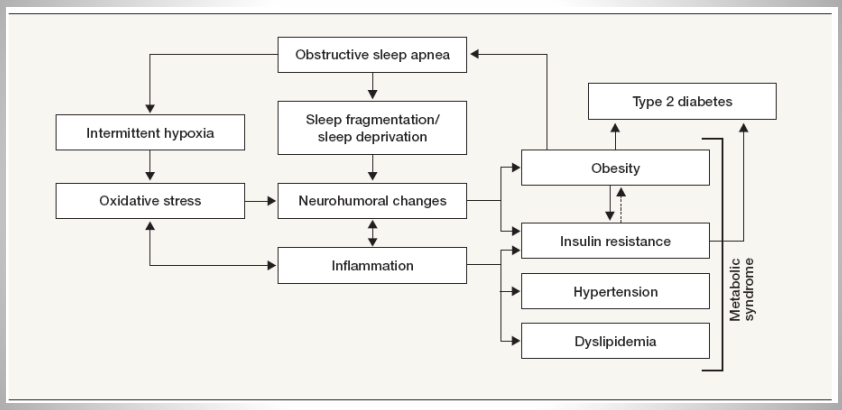
- Excessive Daytime Sleepiness
  - A hallmark of OSA
  - mechanisms of EDS in OSA remain unexplained
- Measures of EDS are not associated AHI, hypoxaemia or slow-wave sleep



OSA: A Neurologic Disease

- A local motor neuropathy that involves the pharyngeal region
  - Reduced palatal muscle tone
  - Focal degeneration of myleinated fibres in palate
- Sleep-specific dampening of cortical processing of inspiratory effort related information
- Arousal thresholds are blunted in OSA patients
- Reduced cortical arousability, increasing the duration of apneas and predisposing to additional events
- Related to epilepsy in the elderly and refractory

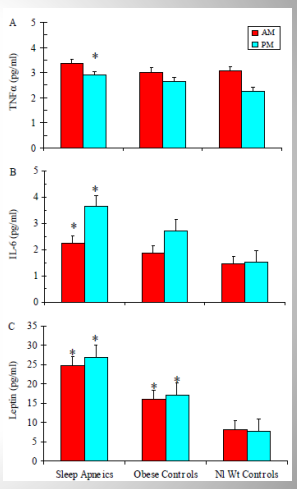
Sleep Apnea and Atherosclerosis



Tasali E, Ip MSM. 2008

Sleep Apnea and Atherosclerosis

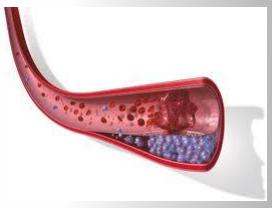
- Elevated TNF-α
- Elevated IL-6
- Elevated leptin
- Higher mean fasting glucose
- High mean plasma insulin
- Elevated CRP



Vgontzas et al. 2005

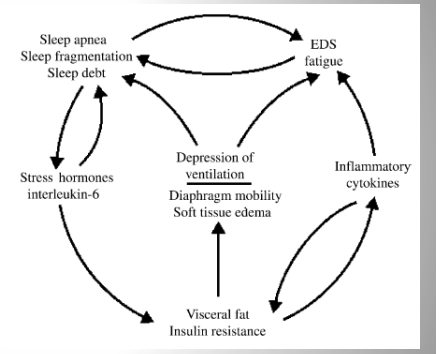
Sleep Apnea and Atherosclerosis

- Vascular endothelial dysfunction
- Increased platelet aggregability
- Increased endothelin
- Reduced nitric acid and prostacyclin availability
- Higher adhesion molecule expression
- Hyperfibrinogenemia
- Not clear if these are independent or due to association with metabolic syndrome



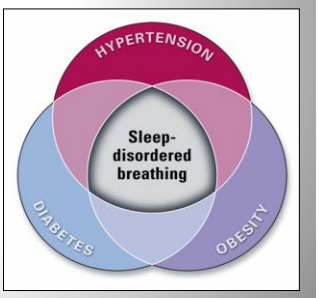
Sleep Apnea and Insulin resistance

- Sleep apnea is associated with insulin resistance independently of obesity
- Severity of OSA correlates to measures of insulin resistance *(Brooks et al 1994)*
- OSA and insulin resistance correlate even in non-obese subjects *(ip et al 2002)*



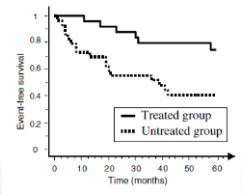
OSA: a manifestation of the metabolic syndrome

- About 60% of OSA patients have the syndrome
- Strong association with obesity
- Strong association with hypertension and diabetes
- More common in women with PCOS
- OSA and the metabolic syndrome have similar age distributions *(young et al 1993)*



Continuous Positive Airway Pressure (CPAP) therapy

- Most successful therapy for OSA
- Reduces leptin
- Reduces hypercortisolemia
- Reduces sympathetic activation
- Inconsistent effect on insulin resistance indices
- Very significant reduction of risk of MI and Stroke



Milleron et al 2004

Medical Treatment for Obstructive Sleep Apnea?

- Etanercept *(Vgontzas et al 2004)*
  - TNF-α antagonist
  - Pilot study
  - Marked decrease in sleepiness
  - Significant decreased in AHI
- Donepezil *(Sukys-Claudino et al 2012)*
  - Small RCT
  - Elderly
  - Significant effect on AHI, desaturation and sleepiness
- Exercise *(Peppard et al. 2004)*
  - Independent of weight loss

The Message

- Know
  - Sleep Apnea is very common but often undiagnosed
  - Carries > two-fold risk of MI and Stroke
- Test
  - Sleep Apnea is easily diagnosed
  - Polysomnography is not a difficult test

- Treat
  - **The main goal of treating sleep apnea is reduction of cardiovascular complications**
- Read
  - **Sleep Apnea and Cardiovascular Disease *Circulation 2008***

Thank you