

CONSEQUENCES OF UNTREATED OSA MORE THAN DAYTIME SOMNOLENCE

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Learning Objectives

- ▣ Define and Describe Apnea and Obstructive Sleep Apnea (OSA)
- ▣ Describe Physiologic Characteristics of OSA
- ▣ Review Commonly Understood Consequences
- ▣ Examine Less Commonly Understood Problems
- ▣ Review Impact of Treatment
- ▣ Case Review
- ▣ Provide Add'l Resources



What is Apnea OSA & Who Cares?

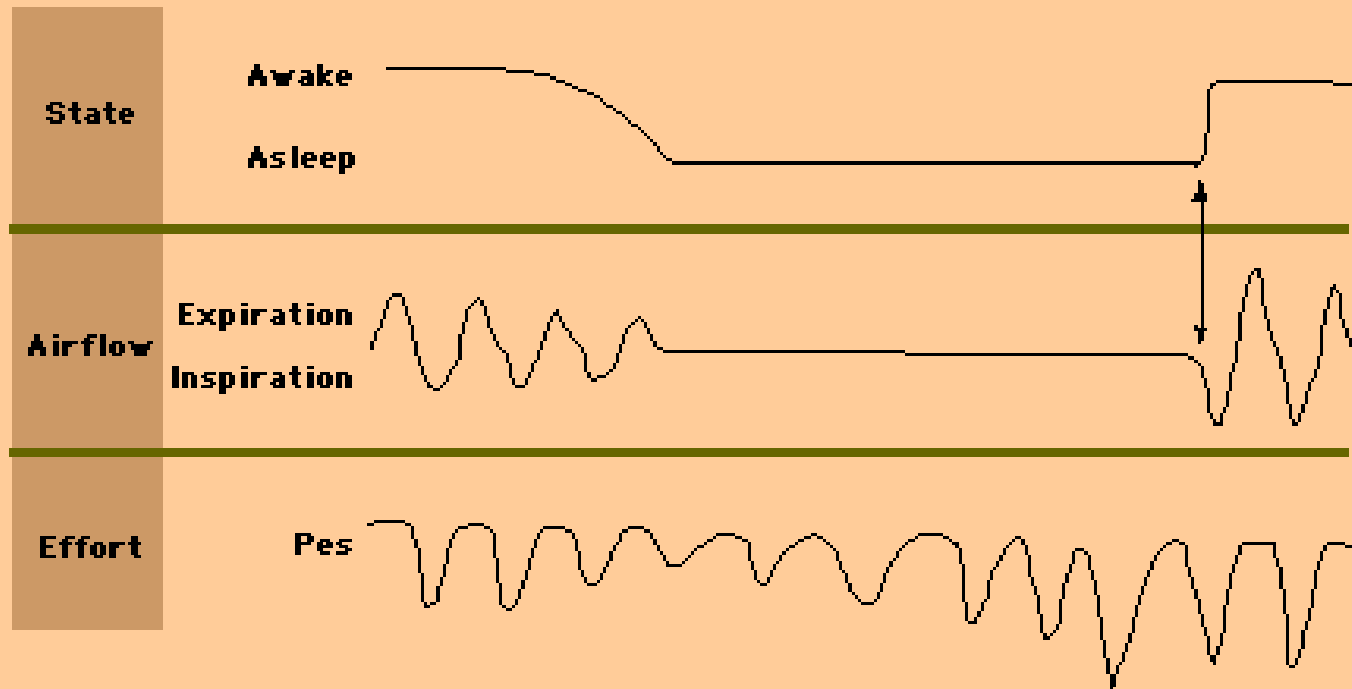
- ▣ Cessation of Breathing in excess of 10-15 seconds.
 - *Obstructive Sleep Apnea*: If due to airway closure
 - *Central Sleep Apnea*: If impaired signal from the brain (Pons & Medulla Oblongata)
- ▣ Who Cares???:
 - OSA appears to affect millions of Americans; many of whom are yet to be diagnosed.
 - May cause over \$4 Billion in Additional and possibly Avoidable Medical Costs.



OSA: Diagnosed via Polysomnogram

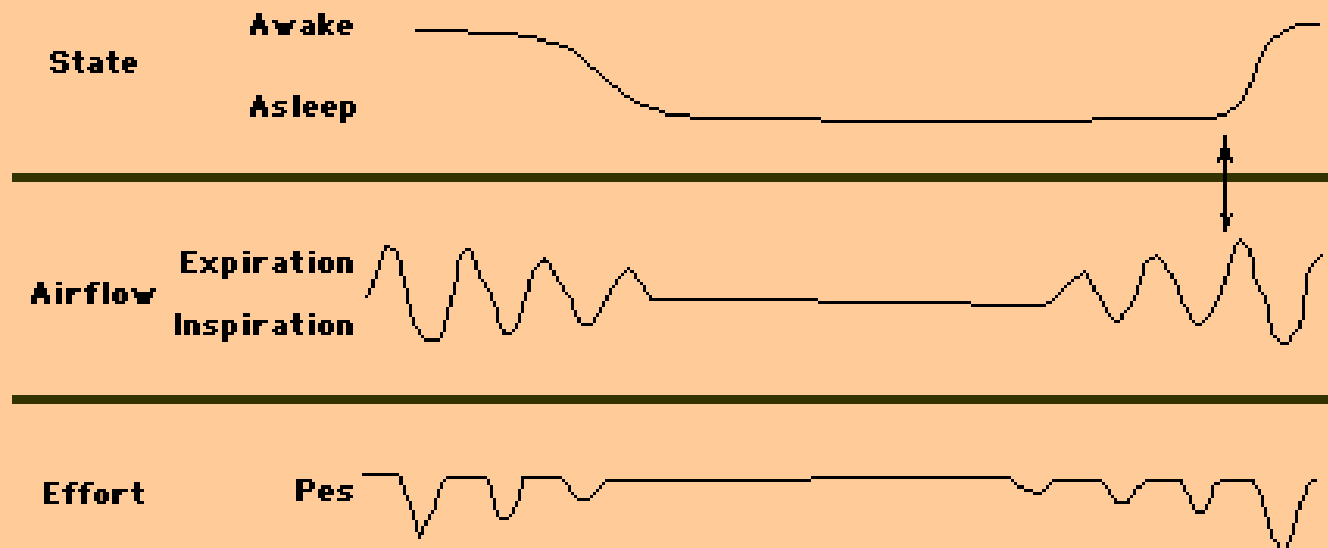
- ▣ AKA: Sleep Study
- ▣ Polysomnogram = gold standard
- ▣ All night recording of the patient's sleep
- ▣ Variables simultaneously measured
 - Eye movements
 - Airflow
 - Respiratory movements
 - Leg movements
 - EEG
 - Pulse oximetry
 - ECG

Obstructive Apnea



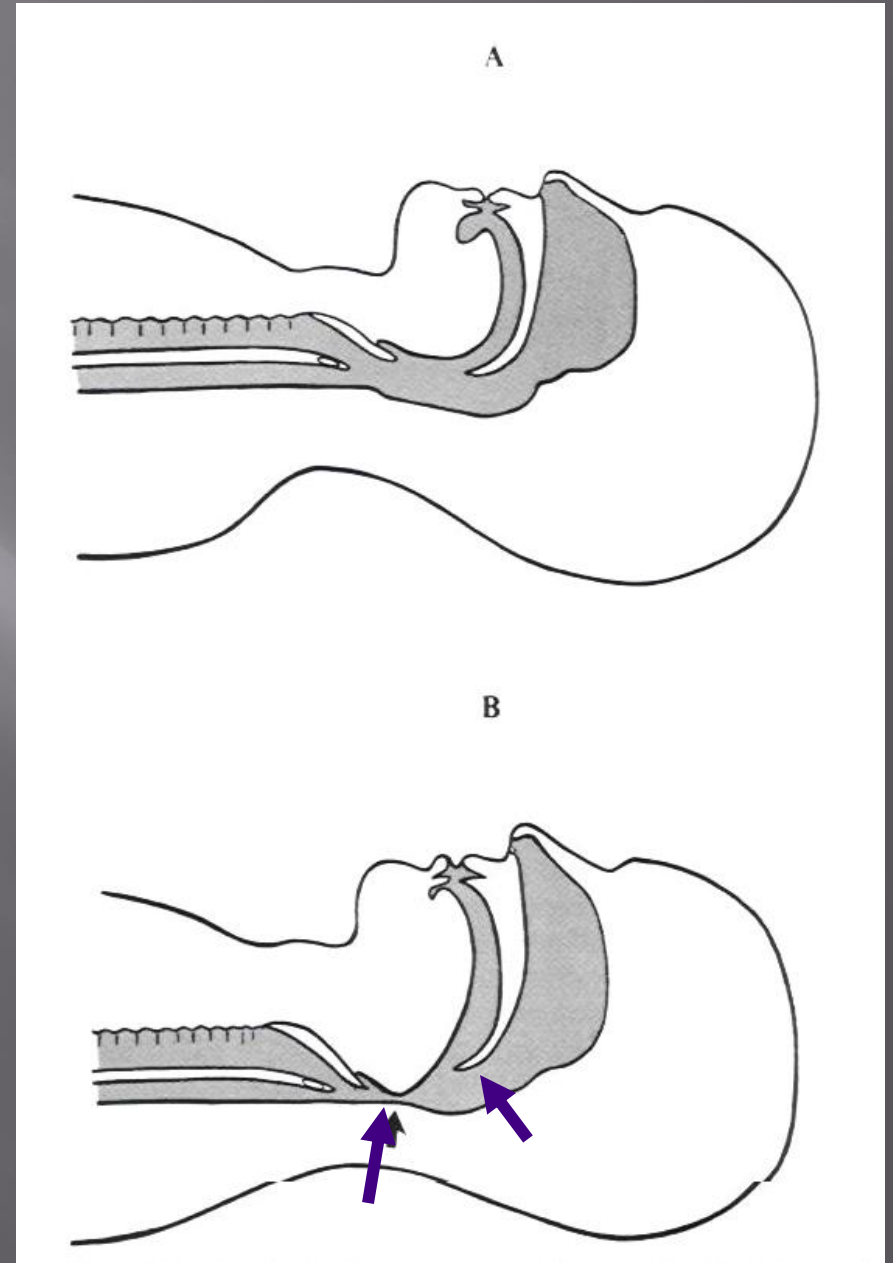
Obstructive sleep apnea Obstructive sleep apnea in which there is continuing respiratory effort, as shown by progressively increasing fluctuations in esophageal pressure (Pes) at the time of cessation of airflow. The arrow illustrates that arousal in obstructive apnea occurs simultaneously with the resumption of airflow.

Central Apnea



Central sleep apnea There is no respiratory effort, as shown by absence of changes in esophageal pressure (Pes), at the time of cessation of airflow. The arrow illustrates that arousal in central apnea typically occurs in the middle of the hyperpneic phase.

Mechanisms & Sites of Obstruction with OSA



OSA “Poster Child”



Commonly Understood Consequences

- ▣ Subjective: Sleepiness & Snoring
 - Higher Risk for Motor Vehicle & Industrial Accidents.
- ▣ Objective (Measurable)
 - Cessation of breathing followed by arousal
 - Hypoxemia
 - Tachycardia
 - EEG Changes
 - Increase in Stress Hormones

More Occult Consequences

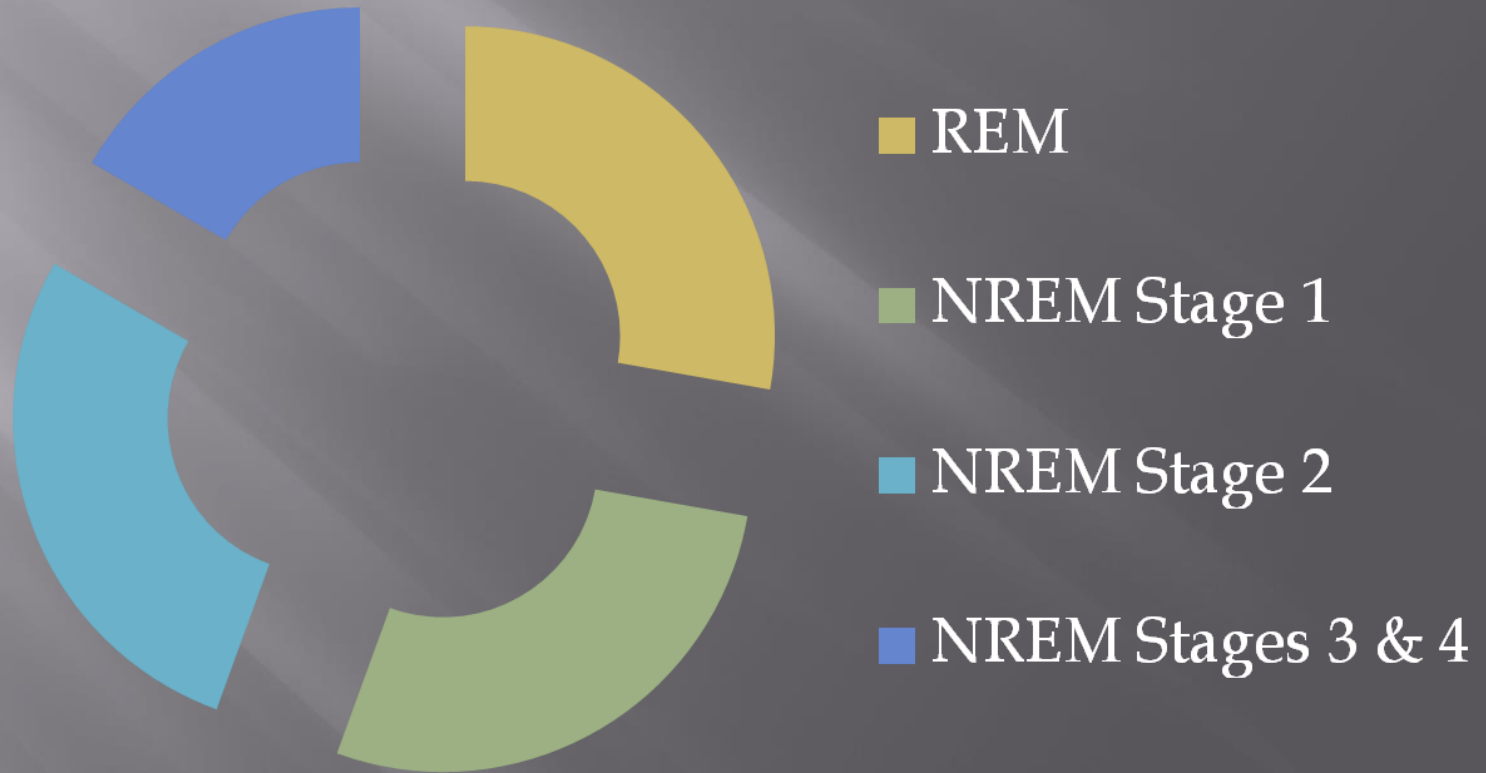
- ▣ Neuropsychological Sequelae
- ▣ Physical Trauma
- ▣ Metabolic Derangements
- ▣ Hypertension
- ▣ Heart and Vascular Disease

Normal Sleep Cycle & Mechanism for Daytime (Sleepiness)

- ▣ Sleep is divided into 2 general phases
 - Rapid eye movement (REM)
 - Non-rapid eye movement (NREM)
- ▣ REM
 - Absence of electromyographic activity
 - Alternates with NREM ~every 90 minutes
- ▣ NREM
 - Stage 1: Slow eye movements
 - Stage 2
 - Stages 3 and 4 (slow-wave sleep)
 - ▣ Also called delta sleep
 - ▣ Breathing is reduced during this stage

OSA Causes Fragmentation of Sleep Stages

Stages of Sleep



Results of Sleep Stage Fragmentation

- ▣ Disruption of homeostasis
 - Duration of Sleep
 - Duration & number of each sleep cycle
- ▣ Changes in circadian rhythm
 - Sleep – wake cycles
- ▣ Insufficient cerebral recovery
- ▣ Multi-organ system fatigue

Neurobehavioral Effects

- ▣ Daytime Sleepiness
- ▣ Sizable effect on the ability to sustain attention over time
 - Less on reaction time
 - More impact on the quality of the performance
- ▣ Moderate to severe OSA negatively impacts memory and executive performance
- ▣ Social impairment
 - Overall Quality of Life (QOL)
 - Diminished social functioning
- ▣ High prevalence of minor psychiatric morbidity. Mild to Moderate Depression

Neurobehavioral Effects

- ▣ Sleepiness/tendency to fall asleep
 - *Multiple Sleep Latency Test (MSLT)*: requires subjects to try to fall asleep during daytime nap opportunities lasting 20 min or less. The latency from lights out to sleep onset is the principal outcome measure.
 - ▣ Severe OSA = < 5 min., some 2 SD below normal mean values of 12.
 - *Epworth Sleepiness Scale*: is commonly used subjective test of sleepiness

Epworth Sleepiness Scale

Situation Chance of Dozing: Ratings → 0 = No Chance of Dozing
3 = Very High Chance

- ▣ Sitting and reading
- ▣ Watching TV
- ▣ Sitting, inactive in a public place (e.g. a theatre or a meeting)
- ▣ As a passenger in a car for an hour without a break
- ▣ Lying down to rest in the afternoon when circumstances permit
- ▣ Sitting and talking to someone
- ▣ Sitting quietly after a lunch without alcohol
- ▣ In a car, while stopped for a few minutes in the traffic

Total Score:

- ▣ 0-10 Normal range
- ▣ 10-12 Borderline
- ▣ 12-24 Abnormal

Effects on Trauma & Accidents

- ▣ Mainly secondary to Neurologic Effects
- ▣ Sleepiness, difficulty concentrating , etc. cause motor vehicle and industrial accidents.
- ▣ Very high incidence and “cost” with truck drivers
- ▣ Strong index of suspicion if accident has a atypical features:
 - Fell asleep during the day
 - Witnessed difficulty staying awake or concentrating
 - Patient is normally an outstanding worker/ driver
 - Other risk factors present

Metabolic Effects: Insulin Resistance

- ▣ Mechanism of Insulin Resistance Believed to be Associated with:
 - Altered adrenergic function
 - Direct effects of hypoxemia on the pancreas & glucose regulation
 - Release of pro-inflammatory cytokines that affect metabolism

Physiologic Results of Insulin Resistance

- ▣ Hyperglycemia resulting from both:
 - An impaired insulin level responsiveness to glucose,

and

- Decreased insulin effectiveness in:
 - ▣ Stimulating glucose uptake by skeletal muscle
 - ▣ Restraining hepatic glucose production

The Evidence: OSA and Impaired Glucose Metabolism

Meslier et al 2003

- ▣ 595 male patients referred for polysomnography underwent a 2 hour oral glucose tolerance test.
- ▣ 494 pts had OSAS (AHI > 10)
- ▣ Outcomes: *Blood glucose increased with severity of sleep apnea*
- ▣ Insulin sensitivity decreased with increasing severity of sleep apnea

More Evidence: Impaired Glucose Metabolism

- ▣ Punjabi et al 2003 [Review]
 - Habitual snoring is associated with abnormal fasting glucose and insulin values independent of age and BMI
 - Prospective data from two separate studies indicate that *habitual snoring is associated with more than a 2-fold risk of developing DM type II* over a ten year period
 - Several studies have suggested that a reduced oxygen saturation and AHI are predictive of glucose intolerance and insulin resistance

Hypertension: Mechanism

- ▣ Individual episodes of sleep apnea cause acute surges in HR and BP at apnea termination driven by;
 - Hypoxia
 - Stress Hormones
- ▣ Epidemiologic evidence and physiologic studies in humans and animals support the idea that chronic exposure to repeated apneas may lead to a sustained HTN via increased SYMPATHETIC TONE

The Evidence: Hypertension

▣ Wisconsin Sleep Cohort Study

- Increased risk for development of HTN in pts with OSA over a 4 to 8 year follow up period
- Outcome: *Severity of OSA increased risk for development of HTN independent of baseline HTN status, age, gender, BMI, alcohol and cigarette use*

▣ Sleep Heart Health Study

- Large cross-sectional study (6132 participants)
- Outcomes:
 - ▣ *Elevated risk for HTN found in subjects with SDB*
 - ▣ Association between SDB and HTN was seen regardless of age, gender, ethnicity, BMI

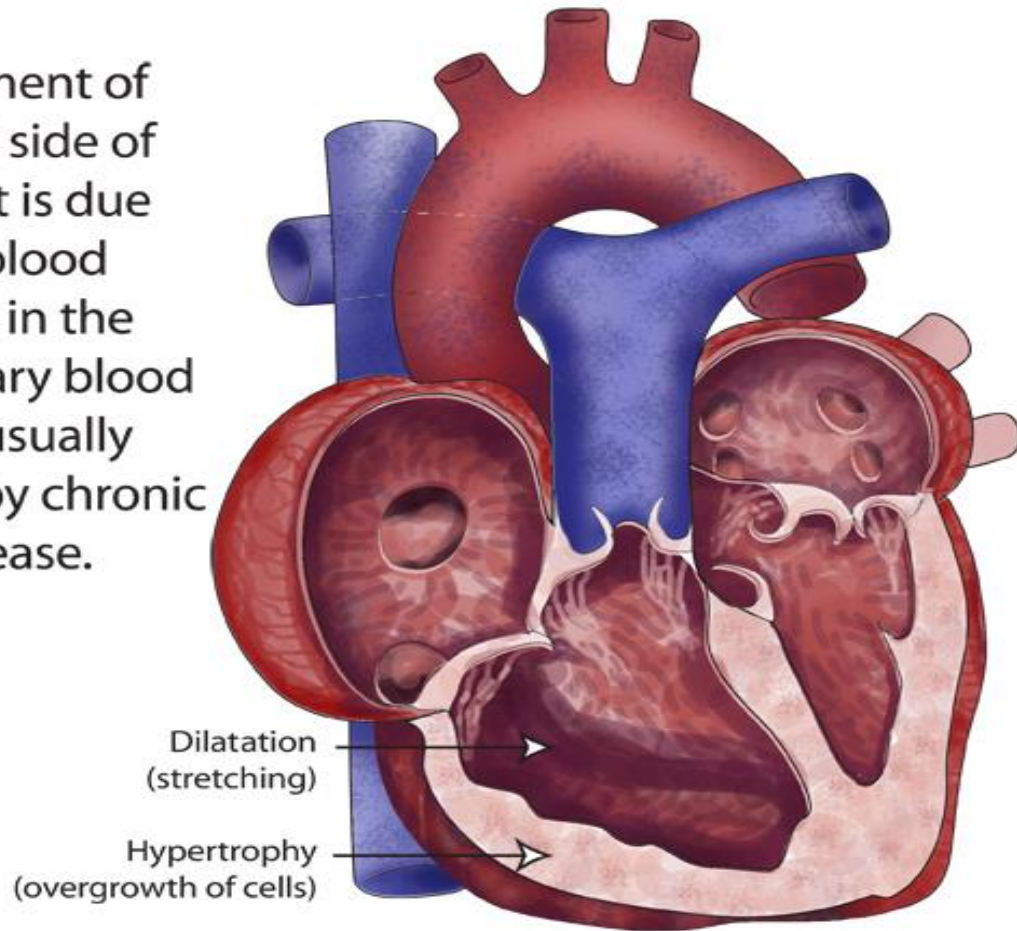
OSA and Cardiovascular Disease

- ▣ Abnormalities associated with OSA may contribute to the initiation and progression of cardiac and vascular pathology
 - Sympathetic activation
 - ▣ Vasoconstriction
 - ▣ Tachycardia
 - Endothelial dysfunction
 - ▣ Increased levels of endothelin may lead to sustained vasoconstriction
 - Vascular oxidative stress
 - ▣ Production of free radicals and vascular wall ischemia-reperfusion injury
 - Increased coagulation

OSA and Cardiovascular Disease (Cont)

- ▣ Cor Pulmonale: Right heart enlargement, secondary to pulmonary vasoconstriction from hypoventilation.
- ▣ Mechanism:
 - Hypoventilation
 - ↓
 - Pulmonary vasoconstriction
 - ↓
 - Inc. R. Heart pre-load
 - ↓
 - R. Heart Hypertrophy
 - ↓
 - R. Heart Failure.

Enlargement of the right side of the heart is due to high blood pressure in the pulmonary blood vessels, usually caused by chronic lung disease.



The Evidence: Heart and Vascular Disease

- ▣ Marin et al: Published results of 10 year observational study of:
 - 377 primary snorers
 - 403 pt with untreated mild to moderate OSA
 - 235 pts with severe OSA who refused treatment
 - 372 pts with OSA treated with CPAP
 - 264 healthy pts

- ▣ Outcome: *Patients with untreated severe OSA, were 3 times more likely to have myocardial infarct or stroke than the healthy control individuals*

- ▣ Milleron et al: Prospectively monitored 54 patients with both CAD ($\geq 70\%$ coronary artery stenosis) and OSA (AHI ≥ 15),
 - ▣ 25 of whom were treated with CPAP or upper airway surgery and 29 who declined treatment for OSA, for 86 months.
 - ▣ Outcome: Cardiovascular death, acute coronary syndrome, hospitalization for heart failure, or need for coronary revascularization was present in

- 24% of the treated patients

--versus--

- 58% of those who declined OSA treatment.

OSA Treatment: Some Pathophysiology is Reversible

- ▣ Mainly via Positive Pressure: BiPAP or CPAP
 - Determined via pressure titration
- ▣ Other Treatments:
 - Address risk factor:
 - ▣ Weight Loss
 - ▣ Avoid Alcohol
 - ▣ Smoking Cessation
 - Dental Appliance
 - Surgery: Uvulopalatopharyngoplasty (UPPP)

Treatment & Prognosis: Neurobehavioral

- ▣ Improvements in both subjective and objective tests of sleepiness are seen with CPAP therapy for OSA.
 - Improvements were moderate to large.
 - Subjective scores improve to a larger degree than objective scores.
- ▣ Evaluation of attention-based cognitive outcomes, there is a much more modest improvement of functioning with CPAP
- ▣ QOL: the large impairments in sleepiness and energy related QOL scores show substantial improvement with CPAP – those with the most severe OSA reap the most benefit

The Evidence: Treatment & Prognosis: Metabolic Disorders

Effect of CPAP

▣ Babu et al 2005

- 25 pts with DM type II, obesity (mean BMI 42.7), and OSA (mean AHI 56) were evaluated *before and after* a 90 day trial of CPAP
- Outcomes: There were *significant reductions in glucose values*
- Concluded that OSA is pathophysiologically related to impaired glucose homeostasis and that CPAP is an important therapy for pts with DM type II and OSA

▣ Harsch et al 2003

- ▣ Forty patients with AHI>20 were evaluated for insulin sensitivity before, 2 d after and 3 mos after treatment with CPAP.
- ▣ Outcomes: Insulin sensitivity significantly increased *after two days* and remained stable after three months of treatment.
- ▣ Patients with BMI < 30 had a much greater improvement in insulin sensitivity.

Treatment & Prognosis: Hypertension

- ▣ Treatment of OSA does appear to lower blood pressure although the literature is inconsistent
- ▣ A randomized, double-blind, placebo-controlled study of 46 moderate-severe OSA Patients:
 - Compared the effects on blood pressure of:
 - ▣ 1.) 2 weeks of CPAP,
 - ▣ 2.) sham-CPAP ,
 - ▣ 3.) supplemental nocturnal oxygen
 - *CPAP therapy resulted in a significant reduction in daytime mean arterial and diastolic blood pressure and nighttime systolic, mean, and diastolic blood pressure*
 - Nocturnal supplemental oxygen therapy improved oxyhemoglobin saturation, but did not affect blood pressure.

Treatment & Prognosis: Hypertension & Cardiovascular

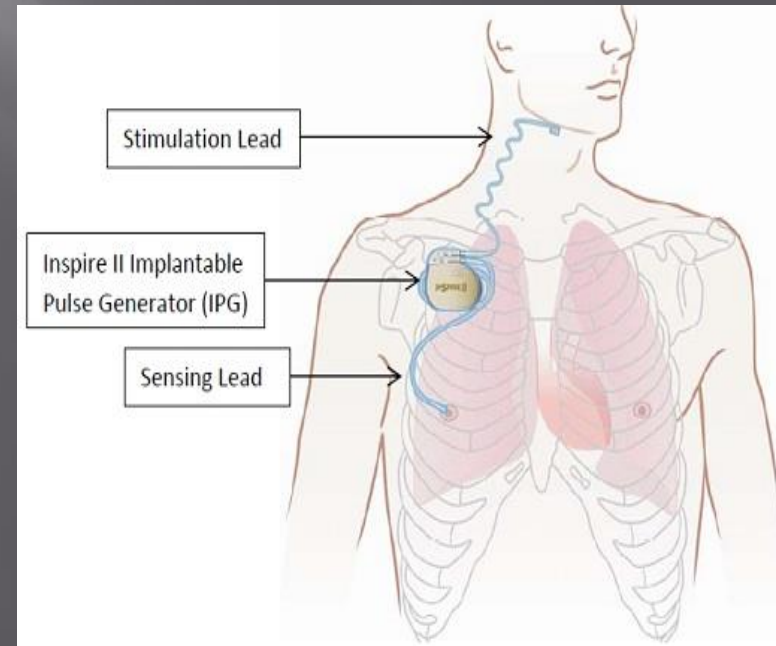
- ▣ Sajkov, D & McEvoy RD, Obstructive Sleep Apnea & Pulmonary Hypertension, Prog Cardiovasc Dis. 51 (5): 363-70, 2009
 - Cor Pulmonale from Certain Chronic Lung Disorders (COPD CF), is generally Irreversible.
 - However, Cor Pulmonale from OSA appears to have a reversible component.
 - ▣ Addresses Hypoventilation
 - ▣ Reverses Pulmonary Vasoconstriction
 - ▣ Decreasing R. Heart Preload

Case : The OSA “Poster Child”

- ▣ Case: 63 YO morbidly obese male presents with CC of orthopnea, frequent urination, excessive thirst, chronic fatigue and daytime sleepiness. Wife indicates that while sleeping, the patient snores very loudly with brief periods where “he seems to stop breathing.”
- ▣ Exam:
 - BBS: Equal, clear but decreased at bases
 - Vital Signs: Mild hypertension. Otherwise WNL
 - Notable Labs: Blood Glucose = 256, HgB 18.2.
 - CXR: Clear lungs with moderate cardiomegaly
- ▣ Plan of Care: Sleep study and referral to , Diabetes Clinic and Nutritional Services

A New OSA Treatment: Upper Airway Stimulation (UAS):

- An implantable nerve stimulator used to treat moderate to severe obstructive sleep apnea (OSA).
- Patient must have failed other conventional therapy (CPAP/BiPAP)



Other Considerations for the Future

- ▣ Should wider OSA screening be done for patients with evidence of cardiovascular disease?
- ▣ What are the long term effects of OSA treatment in terms of cardiovascular morbidity and mortality?
- ▣ Which interventions for OSA yield the highest benefit for the patient at the lowest cost?

Take Home Points--Conclusions

- ▣ OSA is implicated in neuropsychological changes that affect QOL
- ▣ OSA has been identified as an independent risk factor for HTN and insulin resistance
- ▣ OSA is indirectly implicated in cardiac and vascular disease
- ▣ Treatment (CPAP, BiPAP, Surgery) can help modify or reverse some of these secondary conditions.
- ▣ More Work still to be Done!!!

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