Sleep Disordered Breathing: OSA, CSA, Pathophysiology and Diagnosis

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Sleep Disordered Breathing: Subsets

- Intermittent Snoring
- Obstructive Sleep Apnea (OSA)
  - Obstructive Sleep Hypopnea (OSHA)
  - Obstructive Sleep Apnea Syndrome (OSAS)
- Upper Airway Resistance Syndrome (UARS)
- Central Sleep Apnea (CSA)
- Mixed Apnea (OSA and CSA)
- Overlap Syndrome

Sleep Apnea

- **Obstructive sleep apnea (OSA):**
  Repetitive interruption of ventilation during sleep caused by collapse of the pharyngeal airway
- **Central sleep apnea (CSA):**
  Repetitive cessation of ventilation during sleep resulting from loss of ventilatory drive
- **Mixed apnea**

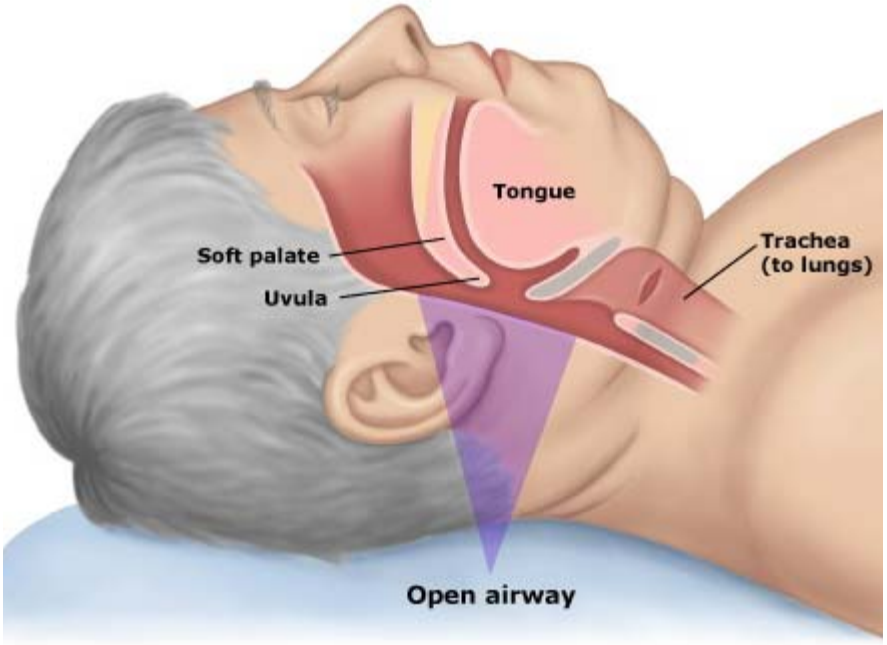
  Starts with CSA and ends with OSA

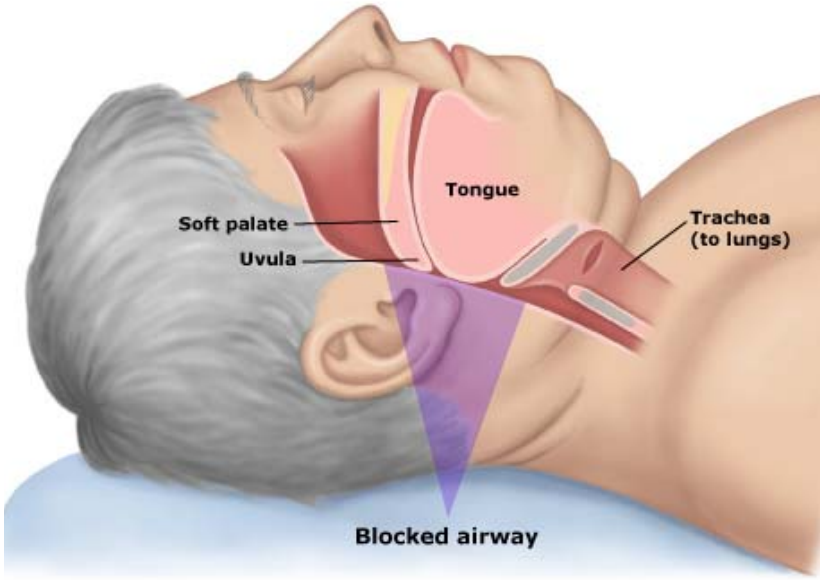
Central Sleep Apnea

- High altitude-induced periodic breathing
- Idiopathic CSA
- Narcotic-induced central apnea
- Obesity-hypoventilation Syndrome (OHS)
- Cheyne-Stokes breathing (CSB)

(Eckert DJ et al. Chest 2007; 131: 595-607)

Airways In Normal Subjects And Patients With OSA During Sleep

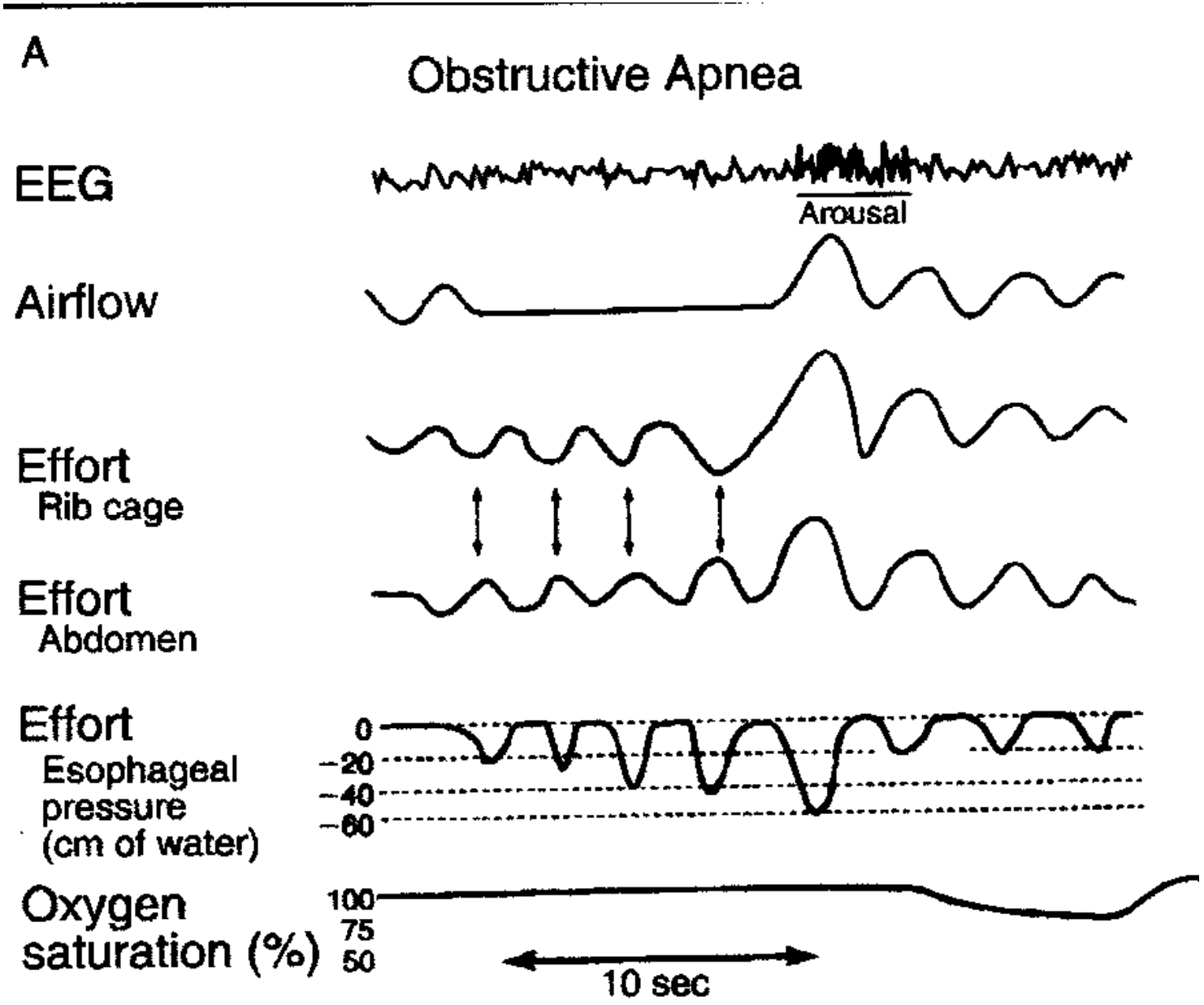




Obstructive Sleep Apnea (OSA)

- **OSA is cessation or near complete cessation (>90% reduction) of airflow for more than or equal to 10 seconds despite continuing ventilatory effort.**
- **5 or more such episodes per hour of sleep**
- **(Usually associated with a decrease of ≥ 4% in oxyhemoglobin saturation)**

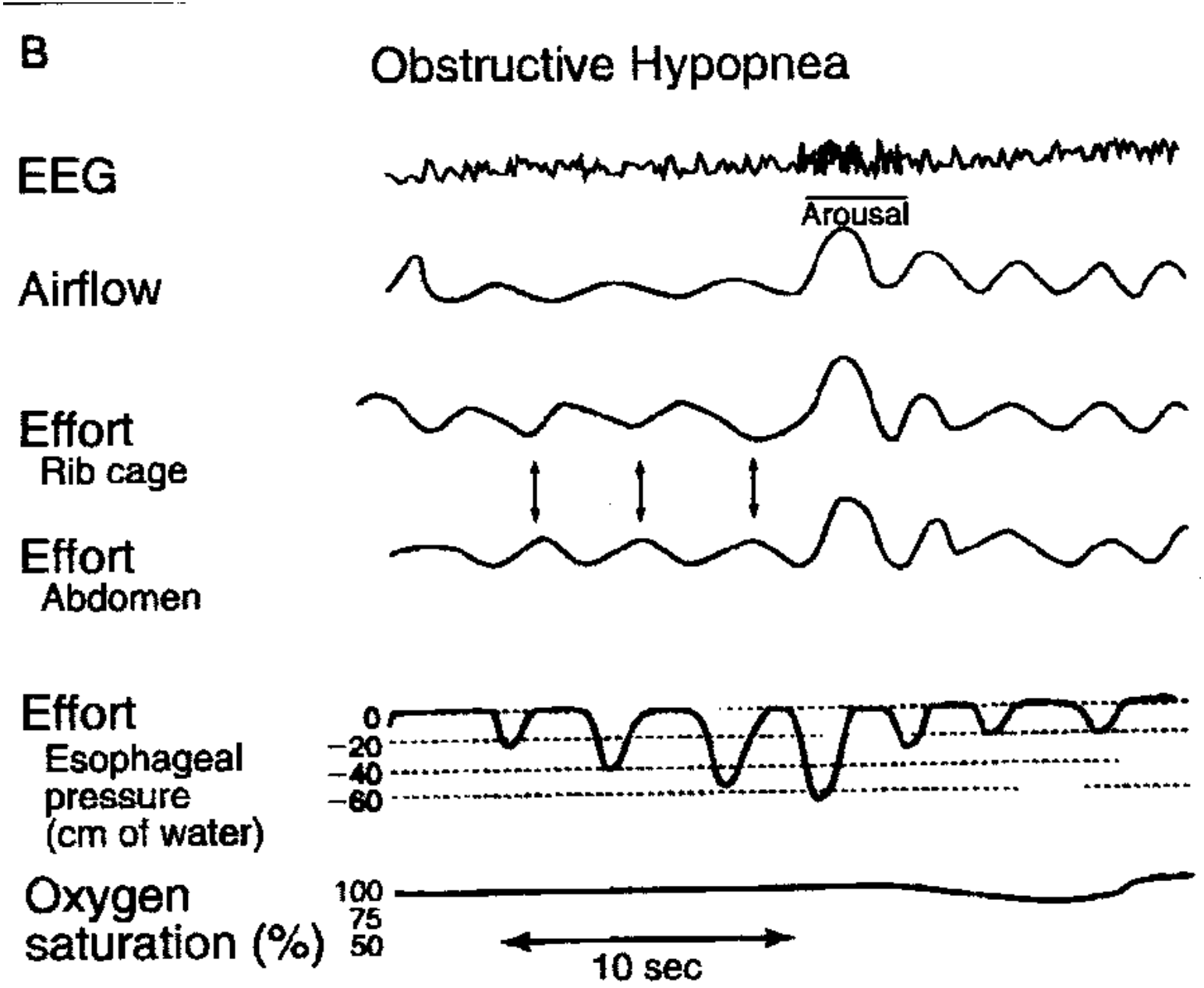
(American Academy of Sleep Medicine, 2005)


A
Obstructive Apnea
EEG
Arousal
Airflow
Effort
Rib cage
Effort
Abdomen
Effort
Esophageal
pressure
(cm of water)
0
−20
−40
−60
Oxygen
saturation (%)
100
75
50
10 sec

Obstructive Sleep Hypopnea

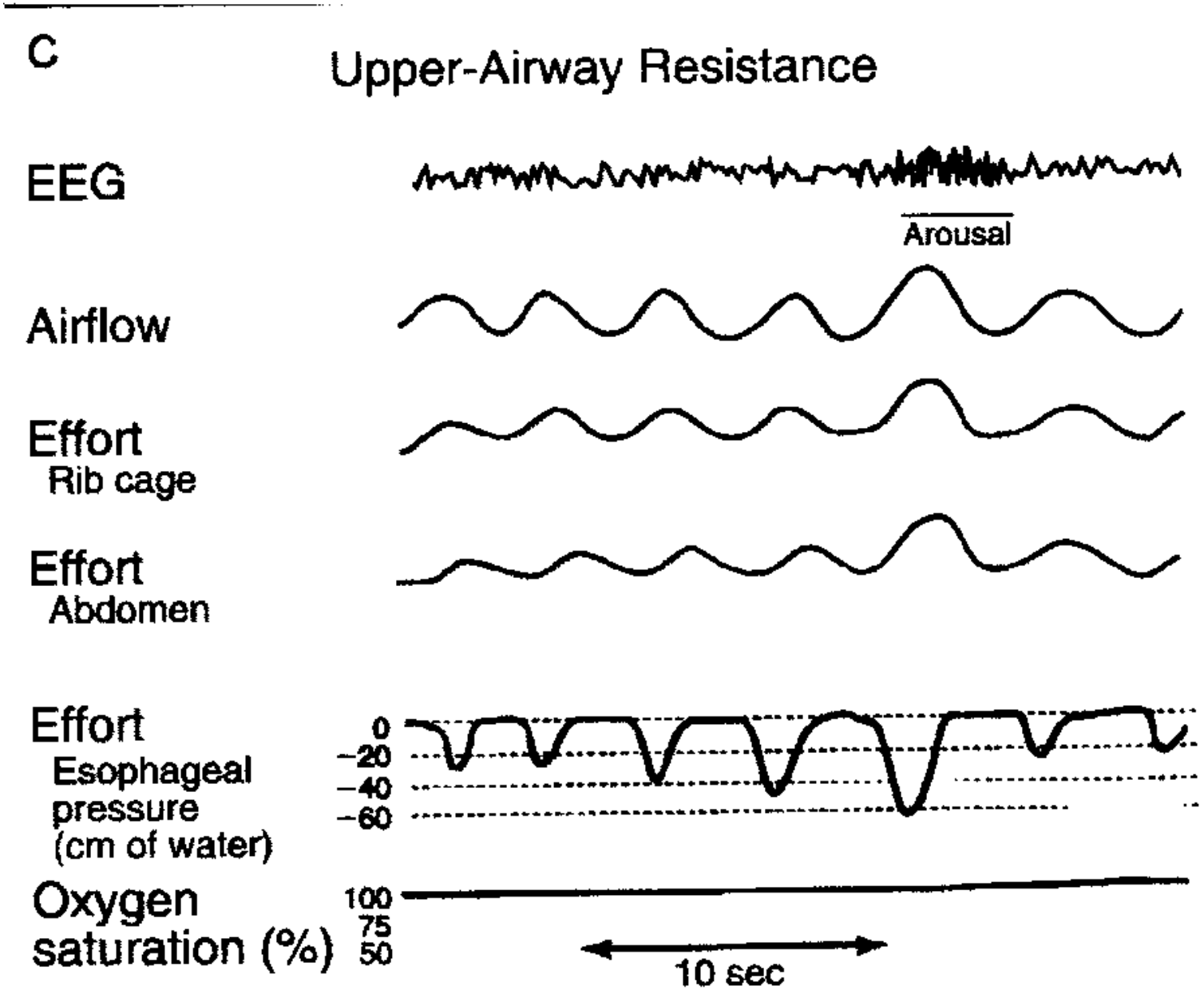
- A reduction in airflow > 50% compared with baseline
- Followed by an arousal from sleep
- Associated with a decrease in oxyhemoglobin saturation of ≥ 3%
- The event lasts 10 seconds or longer

(American Academy of Sleep Medicine, 2005)


B
Obstructive Hypopnea
EEG
Arousal
Airflow
Effort
Rib cage
Effort
Abdomen
Effort
Esophageal
pressure
(cm of water)
0
−20
−40
−60
Oxygen
saturation (%)
100
75
50
10 sec

Upper-airway Resistance

- **No significant decrease in airflow (snoring is usual).**
- **15 or more episodes of arousal per hour of sleep.**
- **No significant decrease in oxyhemoglobin saturation.**


C
Upper-Airway Resistance
EEG
Arousal
Airflow
Effort
Rib cage
Effort
Abdomen
Effort
Esophageal
pressure
(cm of water)
0
−20
−40
−60
Oxygen
saturation (%)
100
75
50
10 sec

Reporting of Obstructive Events

- **Apnea-Hypopnea Index (AHI)**

  Number of apneas and/ or hypopneas per hour of sleep confirmed by electro encephalogram (EEG)

- **Respiratory Disturbance Index (RDI)**

  Number of apneas, hypopneas and respiratory effort related arousals (RERAs) per hour of sleep, confirmed by EEG.

Obstructive Sleep Apnea Syndrome (OSAS)

- **Obstructive sleep apnea (OSA)**

  1. Mild: AHI ≥ 5 and < 15

  2. Moderate: AHI ≥ 15 and < 30

  3. Severe: AHI ≥ 30

- **Obstructive Sleep Apnea Syndrome (OSAS)**

  Apnea-hypopnea index (AHI) ≥ 5 with excessive day time sleepiness

Obesity-hypoventilation and Pickwickian syndrome

- **The obesity-hypoventilation syndrome (OHS) consists of obesity, sleep disordered breathing, hypoxia and chronic hypercapnia during wakefulness in the absence of other known causes of hypercapnia.**
- **OHS was described as "Pickwickian syndrome" in a case report in 1956 and this patient had resembled a character depicted by Dickens in his story, "The Posthumous Papers of the Pickwick Club", because both were obese with excessive hypersomnolence.**

Overlap syndrome

- **Overlap syndrome is defined as the occurrence of both chronic obstructive pulmonary disease (COPD) and sleep apnea- hypopnea syndrome (SAHS) in an individual. Both are common diseases affecting adult population mostly over 40 years of age.**

Prevalence rates of Sleep disordered breathing (Population based International Studies)

Year	Author & Place	Sample size (n)	PSG (n)	Age (years)	Estimated Prevalence (OSAS) %
1988	Gislason *et al* (Sweden)	4064	61	30-60	1.4
1993	Young *et al* (Wisconsin, USA)	3513	624	30-60	4 (M) 2 (F)
1994	Bearpark *et al* (Australia)	NA	294	40-65	3.1
1994	Olson *et al* (Australia)	1188	193	35-69	4.2
2001	Bixler *et al* (Pennsylvania, USA)	16603	1741	20-99	3.5
2001	Duran *et al* (Spain)	2794	400	30-70	3.2

Prevalence rates of Sleep disordered breathing (Indian Studies)

Year	Author & Place	Study Population (Questionnaire based)	PSG (n)	Age (years)	Estimated Prevalence OSAS (%)
2004	Udwadia et al (Mumbai)	Male Insurance Claimers (568)	254	35-65	7.5
2006	Vijayan et al (Delhi)	Community study (7975) M=4050, F=3925	411/47	18-103	2.4 (M) 1.0 (F)
2006	Sharma et al (New Delhi)	Community study (2150)	150	30-60	4.96 (M) 2.03 (F)
2007	Reddy et al (New Delhi)	Community study (2505)	356	30-60	4.0 (M) 1.5 (F)

Estimations based on number of PSG studies done with extrapolation to the screened population; PSG = Polsomnography,, n=No. of polysomnography studies, OSAS = Obstructive sleep apnoea syndrome

(Udwadia ZF et al AJRCCM 2002; 165: 1217-39. Vijayan VK et al Chest 2006; 130: 92S, Sharma SK et al Ind J Med Res 2010;131:165-170)

Pathophysiological Changes

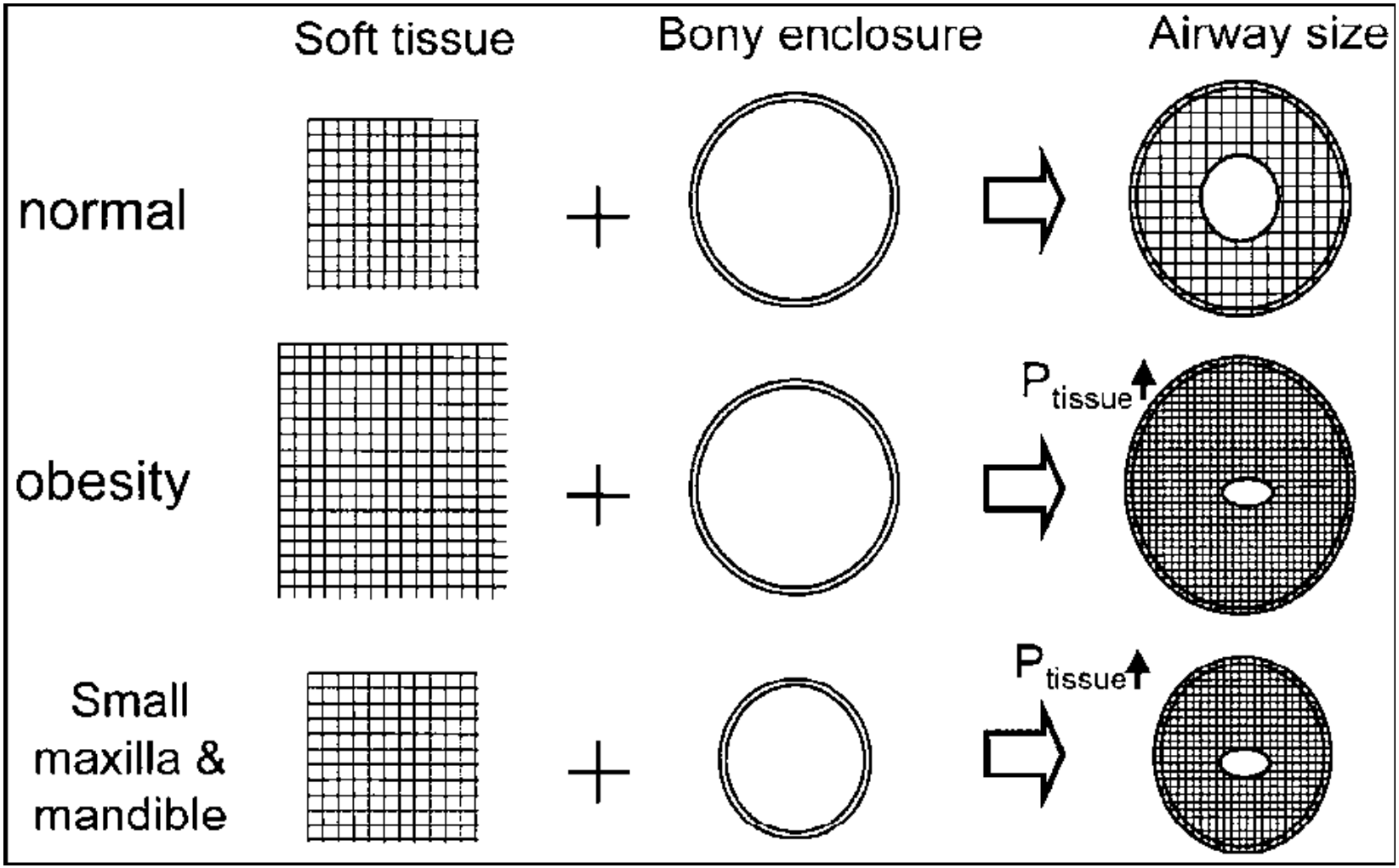
Risk Factors:
Non-modifiable Factors

- Age
- Male Gender
- Ethnicity (Being black, Hispanic)
- Anatomical abnormalities of craniofacial region and upper airway
- Neck circumference (Thick neck, circumference >17 inches in males, > 16 inches in females)
- Genetic predisposition (A family history of sleep apnea)

Risk Factors:
Modifiable Factors

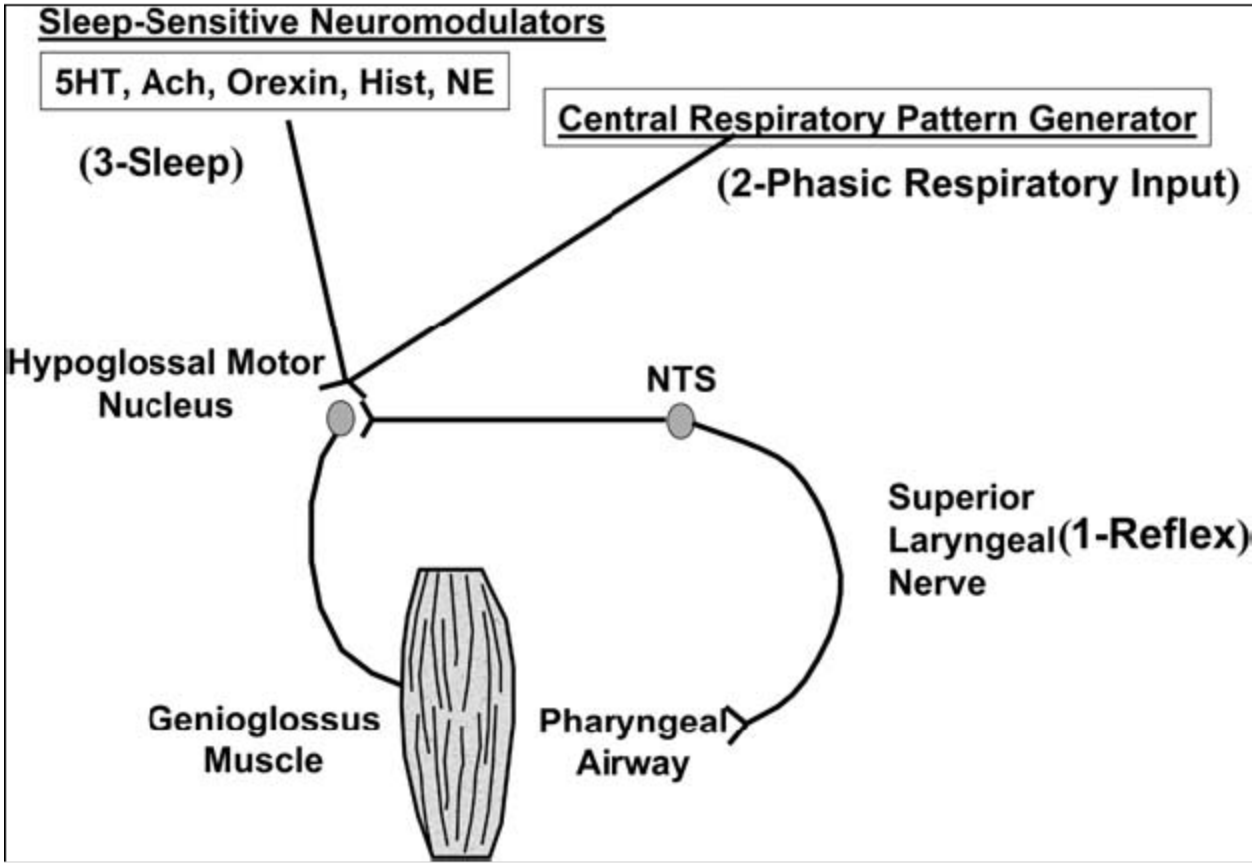
- Obesity
- Use of alcohol, sedatives or tranquilizers
- A narrowed airway (enlarged tonsils or adenoids)
- Smoking
- Chronic nasal congestion
- Hypertension
- Diabetes mellitus
- Menopause

Interaction Between Soft Tissue and the Upper Airway Bony Structure and Their Combined Effect on Airway Size



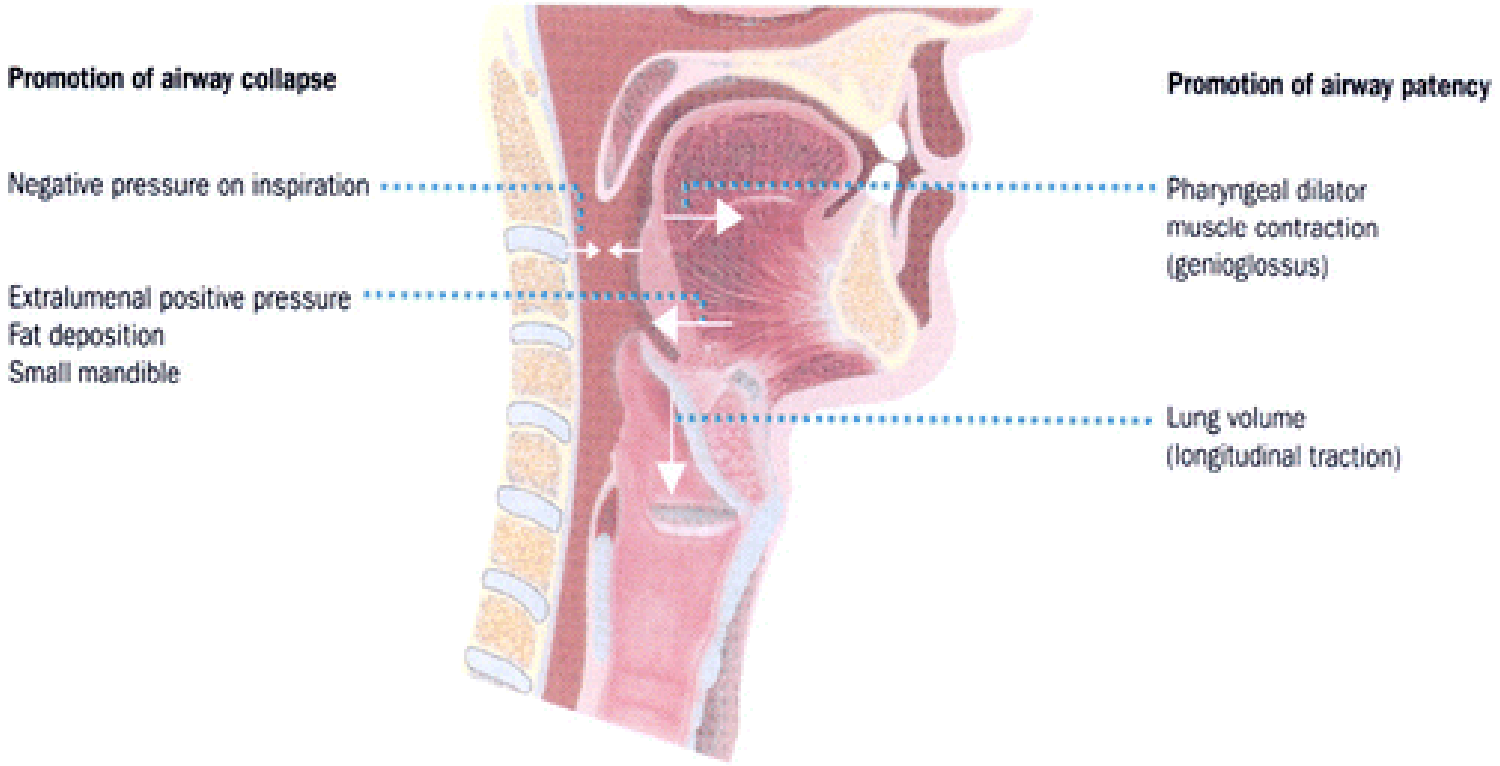
(Watanabe T et al. Am J Respir Crit care Med 2002; 165: 260-65)

Major Sources of Neural Input to the Genioglossus Muscle



(White DP. Am J Respir Crit Care Med 2005; 172: 1363-1370)

Sagittal Section of Normal Pharyngeal Airway: Major Variables Contributing to Airway Patency/Collapse



White DP. Am J Respir Crit Care Med 2005; 172: 1363-1370

OSA-induced Biological Changes

- **Intermittent hypoxia**
  - **Repeated episodes of hypoxia (10 s to 2 min) and normoxia (2-4 min) resembling ischemia/ reperfusion events**
  - **Hypoxic/ischemic phase: The cells adapt to low O_2 environment**
  - **Reoxygenation/reperfusion phase: Sudden increase of O_2 in the cells resulting in the production of ROS**
- **Intermittent hypercapnea**
- **Sleep fragmentation**

(Suzuki YJ et al. Free Radical Biology and Medicine 2006;40:1683-1692)

Pathophysiological Changes in OSA

- Intrathoracic pressure changes
- Sympathetic activation
- Oxidative Stress
- Systemic inflammation
- Metabolic dysregulation
- Endothelial dysfunction
- Hypercoagulation
- Neurohumoral changes

Intrathoracic Pressure Changes

- **Repetitive inspiratory efforts against a closed upper airway lead to increased negative intrathoracic pressure**
- **An increase in transmural gradients across the atria, ventricles and aorta**
- **This is similar to Muller maneuver (inspiration against closed glottis, lead to a pleural pressure of -30 cm water)**
- **These lead to autonomic and hemodynamic instability**

Sympathetic Nerve Activation

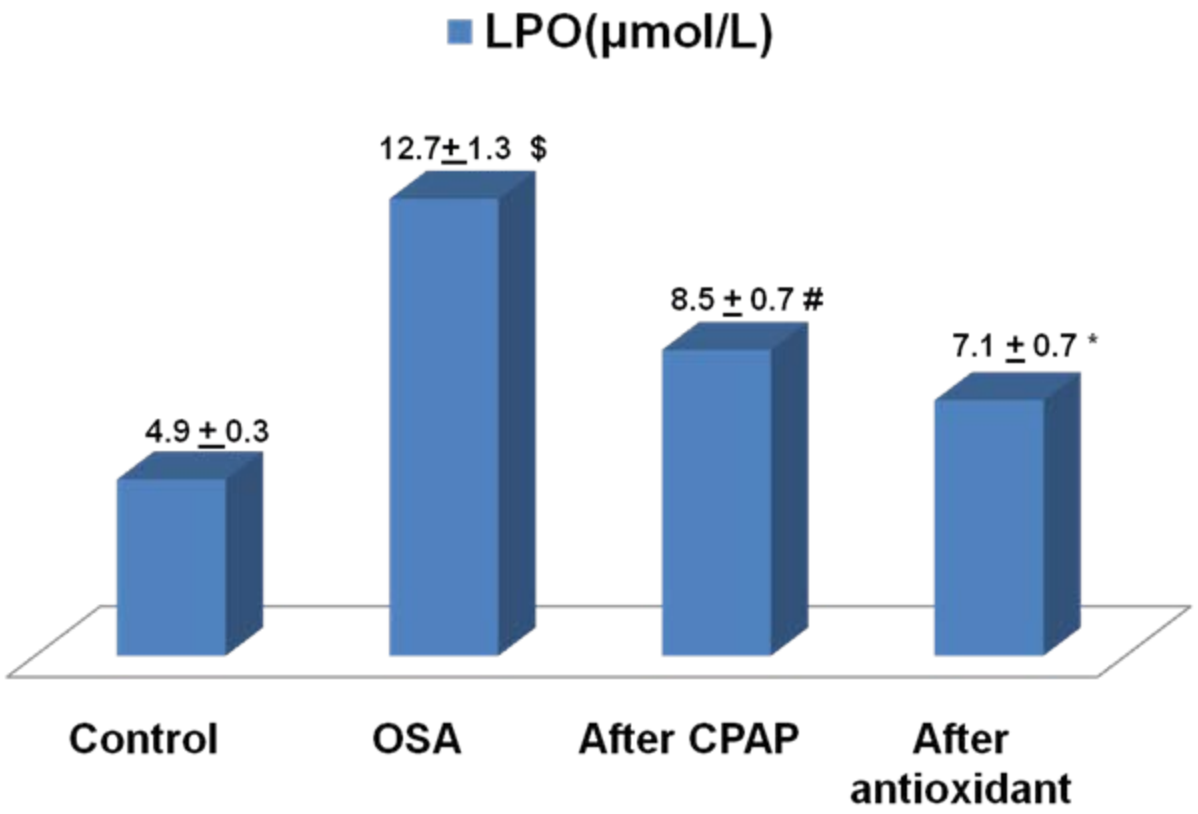
- Increase in sympathetic activity during sleep due to activation of peripheral chemo-receptors (hypoxia, hypercapnea, apnea)
- Results in peripheral vasoconstriction and increase in BP
- Increased concentrations of catecholamines in urine
- An increase in resting heart rate during wakefulness
- Thus chronic sympathetic nerve activation

OSA and Oxidative Stress

- **Abnormal lipid peroxidation: Thiobarbituric acid-reactive substance (TBARS) formation is higher in patients with OSA compared to healthy subjects**
- **CPAP treatment decreased the nocturnal levels of TBARS and peroxides in patients**
- **Inhibition of xanthine oxidase by allopurinol and use of supplemental Vitamin C improved endothelial function in OSA patients**
- **Increased 8-hydroxy-2'-deoxyguanosine excretion in patients with severe OSA suggesting oxidative DNA damage**
- **Increased oxidized low-density lipoprotein levels**
- **OSA is associated with increased oxidative stress**

(Gozal D and Gozal LK. Am J Respir Crit Care Med 2008; 177: 369-379)

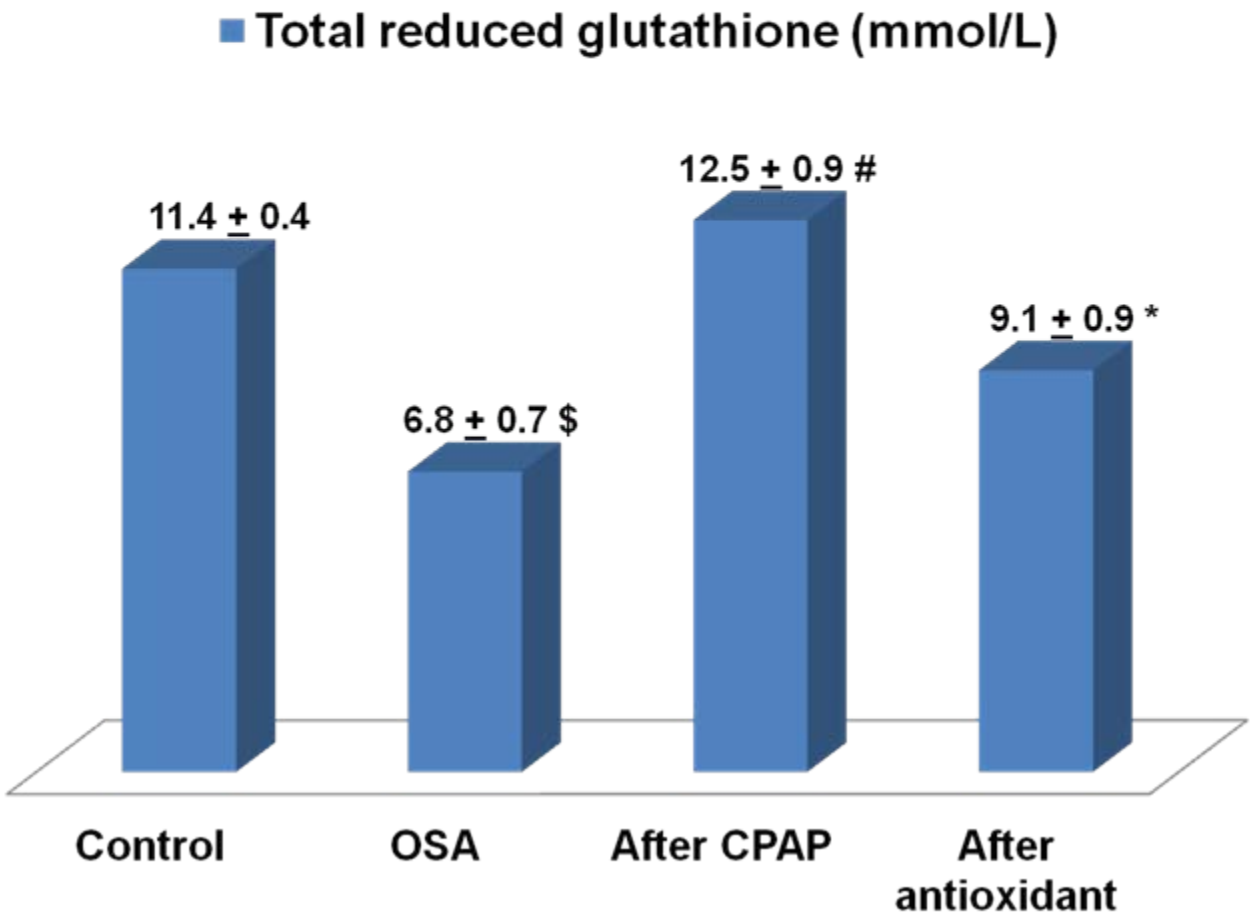
Oxidative Stress in OSA: Lipid Peroxidation (LPO)-TBARS



$ <0.001, compared to control, # <0.05 compared to baseline OSA, *<0.01 compared to baseline OSA

(Singh TP, Patial K, Vijayan VK, Ravi K. Indian J Chest Dis Allied Sci 2009; 51: 217-24)

Oxidative Stress in OSA:Total Reduced Glutathione



$ <0.001, compared to control, # <0.01 compared to baseline OSA, * <0.05 compared to baseline OSA

(Singh TP, Patial K, Vijayan VK, Ravi K. Indian J Chest Dis Allied Sci 2009; 51:217-24)

OSA and Systemic Inflammation

- CD4 and CD8 T cells of patients with OSA undergo phenotypic and functional changes, with a shift towards type 2 cytokine dominance and increased IL-4 expression
- IL-10 negatively and TNF-α positively correlated with severity of OSA
- Increased circulating levels of CRP in OSA
- Increase in NF-kB, an important factor for activation of inflammatory pathways
- Increased expression of adhesion molecules and increased adhesion of monocytes to human endothelial cells

(Gozal D and Gozal LK. Am J Respir Crit Care Med 2008; 177: 369-379)

OSA and NO-dependent Endothelial Function

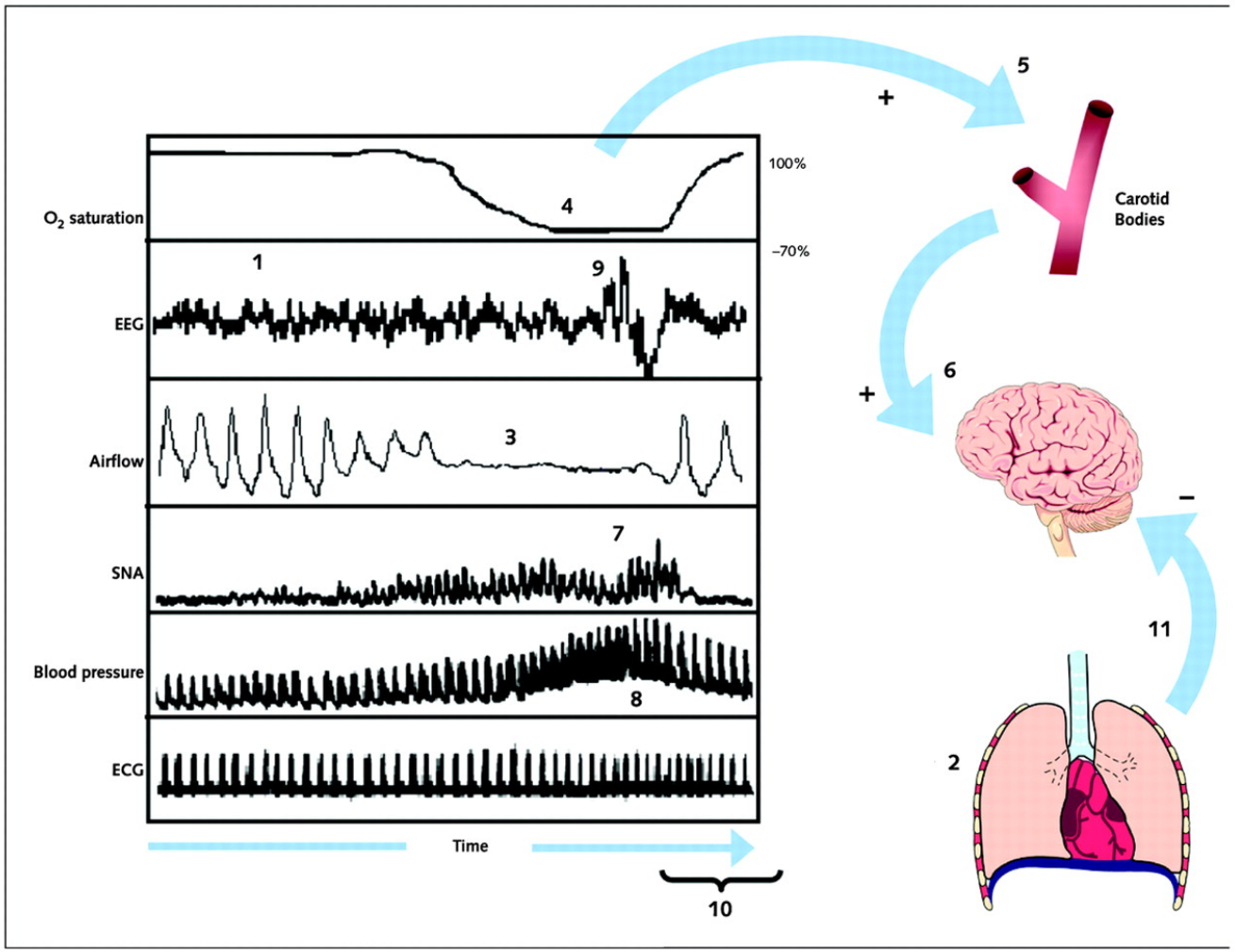
- Reduced NO in OSA in exhaled alveolar NO fraction
- Endothelial dysfunction as evidenced by altered NO-dependent vasodilatation in OSA
- Reduced NO- release from the endothelium
    - Oxidative stress
    - Interaction between NO and free radicals lead to formation of peroxynitrite promoting a variety of biological cascades leading to atherosclerosis

(Gozal D and Gozal LK. Am J Respir Crit Care Med 2008; 177: 369-379)

Procoagulant Activity

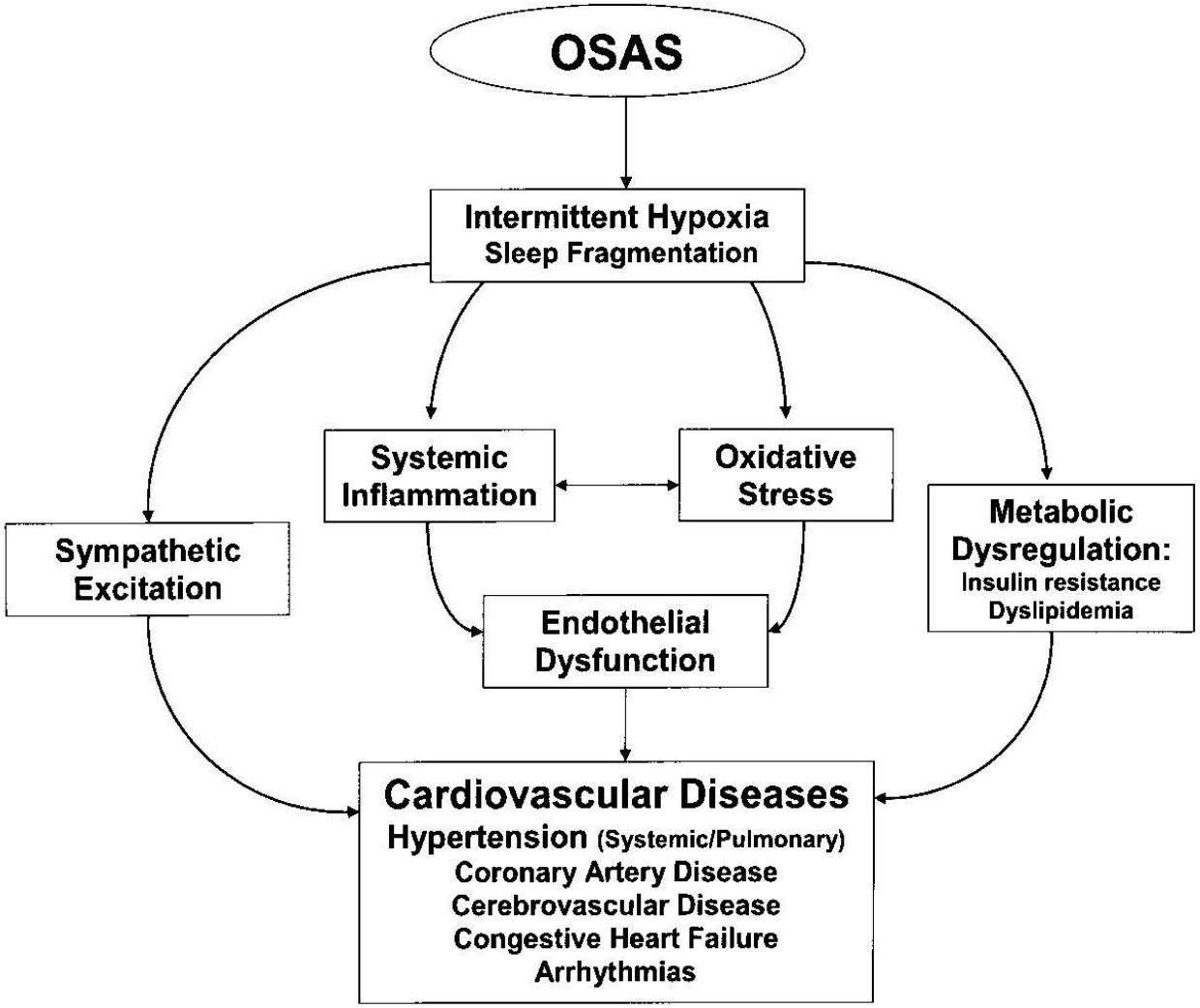
- Elevated levels of plasma fibrinogen
- Exaggerated platelet activity
- Reduced fibrinolytic activity
- Exaggerated platelet activity is reduced with CPAP treatment
- Hypercoagulable state in OSA

Pathophysiologic events in obstructive sleep apnea



Caples, S. M. et. al. Ann Intern Med 2005;142:187-197

OSAS and Cardiovascular Disease



(McNicholas WT. Am J Respir Crit Care Med 2009; 180: 692-700)

Diagnosis of OSA

Cardinal Features

- Loud snoring
- Excessive daytime sleepiness

Complications

- Hypoxemia
- Hypercapnia
- Cor pulmonale

Clinical Features: Daytime Symptoms

- Excess daytime sleepiness
- Cognitive and memory impairment
- Executive dysfunction (lack of concentration)
- Erectile dysfunction (impotence or decreased libido)
- Dry mouth
- Gastroesophageal reflux
- Morning headache

Clinical Features: Sleep Symptoms

- Loud snoring/snorting
- Non-restorative sleep
- Awakening with choking
- Observed episodes of breathing cessation during sleep (witnessed apneas by bed partner)
- Abrupt awakenings accompanied by shortness of breath
- Awakening with a dry mouth or sore throat

Clinical Features: Sleep Symptoms

- Difficult staying asleep (insomnia)
- Nocturnal polyuria
- Restless sleep
- Vivid dreams
- Gastroesophageal reflux
- Hypersalivation
- Diaphoresis

Clinical Features of OSA

- Obesity (particularly central, BMI >30 kg/m2)
- Large neck circumference (>40 cm)
- Narrow mandible, narrow maxilla
- Retrognathia
- Dental malocclusion, overbite
- Reduced nasal patency
- High and narrow hard palate
- Elongated and long-lying uvula
- Enlarged tonsils and adenoides
- Macroglossia

Diagnosis:
Assessment Of Sleepiness

- **Epworth sleepiness scale (ESS)**
- **Stanford sleepiness scale (SSS)**

Epworth Sleepiness Scale

In contrast to just feeling tired, how likely are you to doze off or fall asleep in the following situations? (This refers to your usual life in recent times. Even if you have not done some of these things recently, try to work out how they would have affected you.) Use the following scale to choose the most appropriate number for each situation:

0 = Would never doze
1 = Slight chance of dozing
2 = Moderate chance of dozing
3 = High chance of dozing

Situation	*Chance of Dozing*
Sitting and reading	_____
Watching TV	_____
Sitting inactive a public place (e.g., in a theater or at 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 lunch without alcohol	_____
In a car, while stopping for a few minutes in traffic	_____

Diagnosis

- Polysomnography

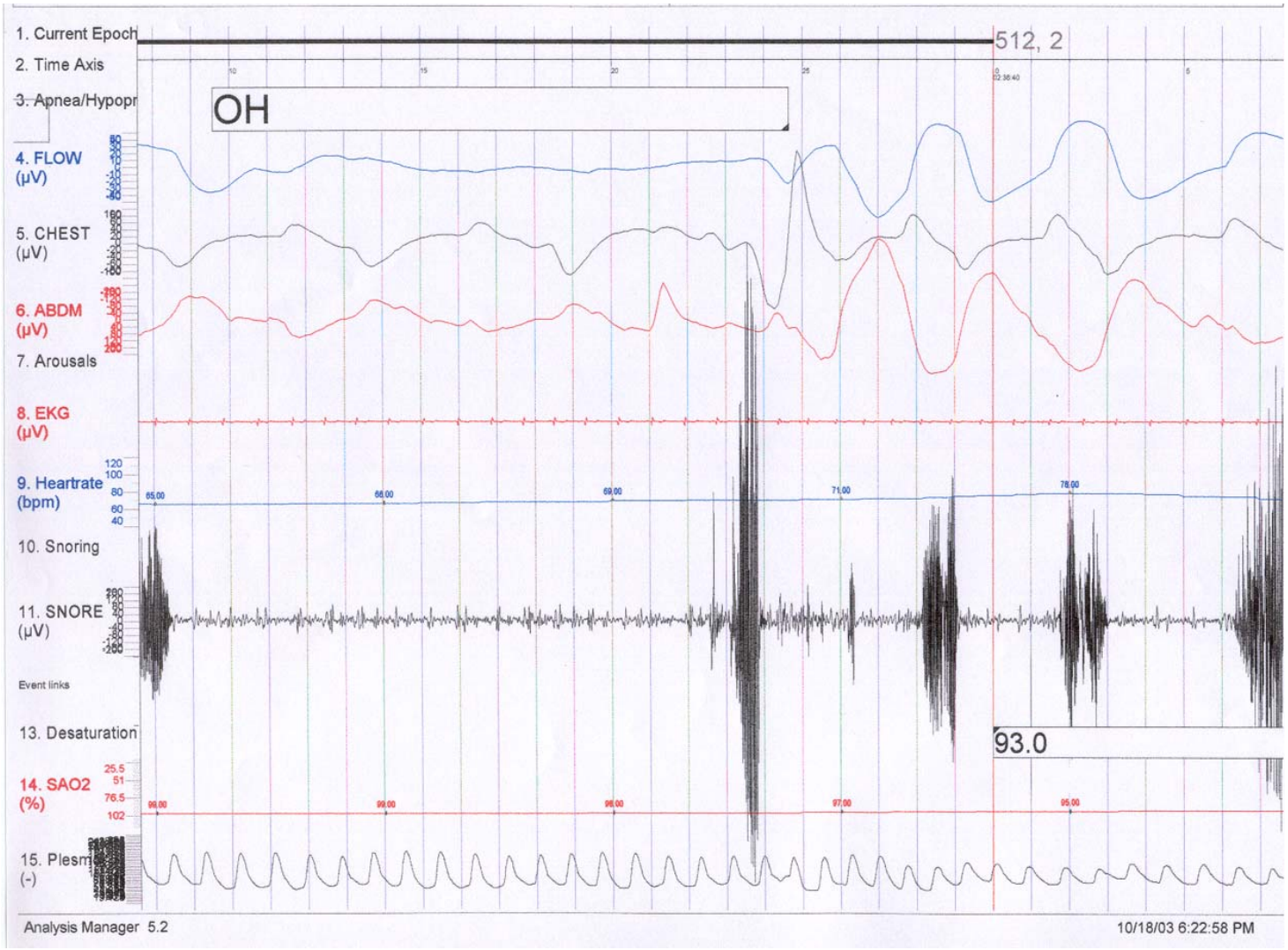
Alternatives to overnight PSG

- Partial channel PSGs
- Home monitoring devices: Actigraphy
- Radiology: CT, MRI, Cephalometry
- Functional imaging: Endoscopy, Acoustic reflections
- Automatic pressure titrating CPAP

Polysomnography

- **“Gold standard”**
- **Simultaneous monitoring of**
  Nasal and/or oral airflow
  Thoracoabdominal movement
  Electroencephalogram (EEG)
  Electro-oculogram (EOG)
  Electromyogram (EMG)
  Oxygen saturation

Obstructive Sleep Apnea



Split-night Studies

- First half of the study night is used for diagnosis
- Second half to monitor response using CPAP
- Split-night studies are considered accurate and cost effective

Cardiorspiratory monitoring

- **Measurement of**

  Air flow

  Respiratory effort

  Oxygen saturation

  Heart rate

  But not EEG

- **Advantages**

  Price

  Portability

  Convenience to do the tests in homes

Overnight Oximetry

- **A screening test to identify patients who are at risk of having significant OSAH**
- **Should never be considered as a substitute for in-lab PSG or cardiorespiratory monitoring**
- **Limitations**

  i. Inability to detect apneas/hypopneas not associated with O2 desaturation

  ii. Nocturnal O2 desaturation may be related to sleep hypoventilation without UA obstruction (COPD, severe kyphoscoliosis, muscular dystrophy)

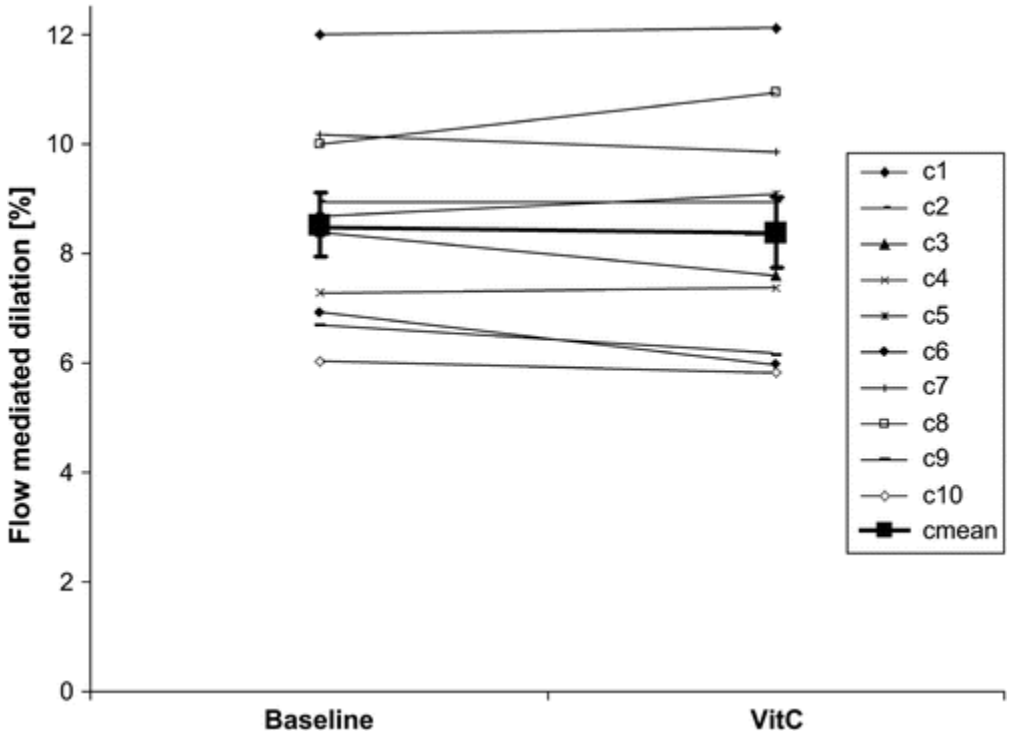

Thank you

Antioxidant Therapy in OSA

- Upper airway dilator muscle dysfunction is observed in patients with OSA and animal models of the disease
- Superoxide scavengers have been shown to increase upper airway muscle force in animal experiments (1)
- Exposure to intermittent hypoxia in patients with OSA shown to increase AHI , while antioxidants mitigated the increase (2)
- Antioxidant treatment may be beneficial as an adjunct therapy in OSA

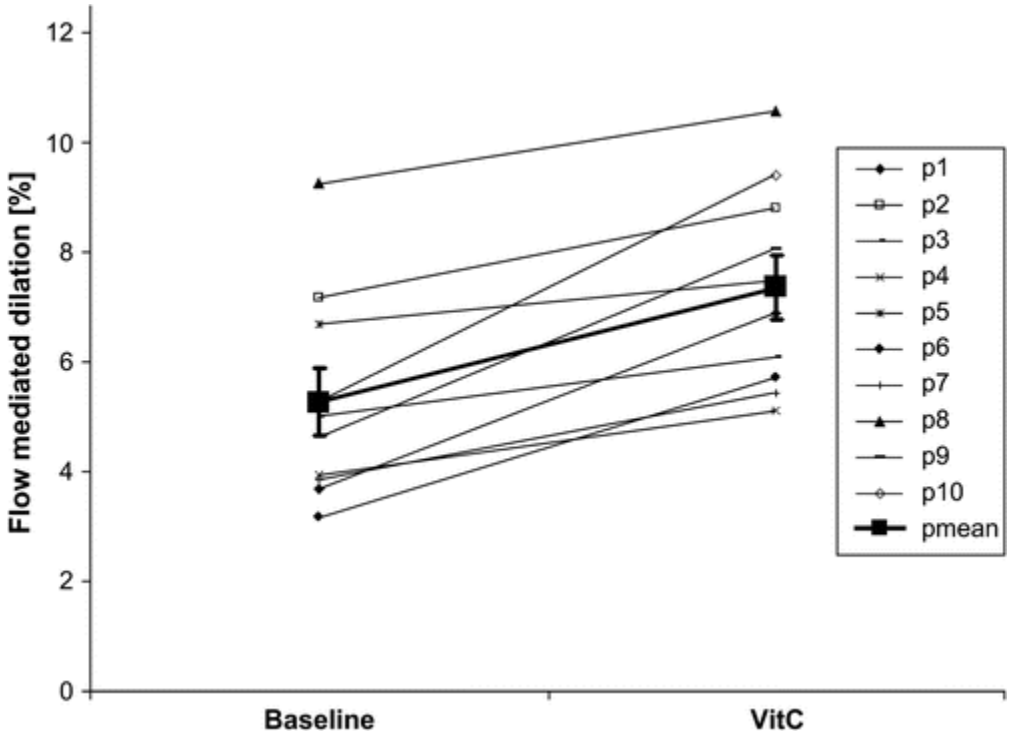
1. Skelly JR et al. Am J Respir cell Mol Biol 2010; 42: 725-31,
2. Am J Respir Crit Care Med 2009; 179: A6347

Flow-mediated dilation of the brachial artery at baseline and after intravenous administration of 0.5 g vitamin C in the control group



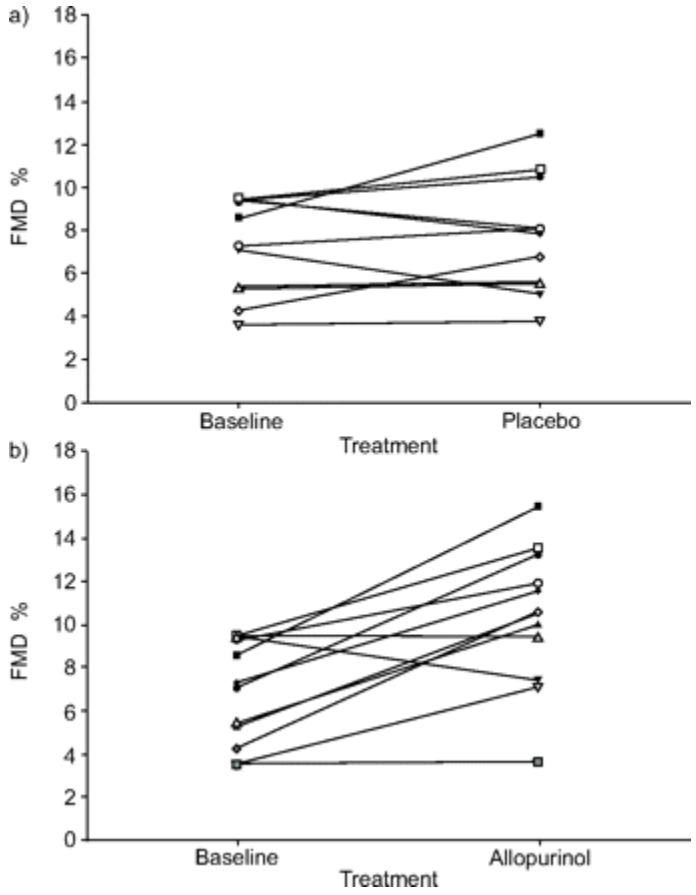
Grebe M et al Am J Respir Crit Care Med 2006; 173: 897-901

Flow-mediated dilation of the brachial artery at baseline and after intravenous administration of 0.5 g vitamin C in the OSA



Grebe M et al Am J Respir Crit Care Med 2006; 173: 897-901

Allopurinol improves endothelial function in sleep apnoea: a randomised controlled study



Elsolh AA et al. Eur Respir J 2006; 27: 997-1002

Childhood Obesity in India

- **North India**

  5.59% in the higher socio-economic strata

  0.42% in the lower socio-economic strata
- **South India**

  4.94% in 2003

  6.57% in 2005
- **USA: 16% in aged 6 to 19 years (1999-2002); Adults: 30.4%**
- **China: 7 to 9 years: 17% in females; 25% in males (2000)**

(Raj M and Krishna Kumar R. Indian J Med Res 2010; 132: 598-607)

Treatment

- Weight reduction
- Lifestyle modification
- Continuous positive airway pressure (CPAP)
- Medical therapy
- Surgical treatment
- Oral appliances- To keep upper airway open

Weight Reduction

- **Weight loss should be recommended to overweight patients with OSA**
- **Loss of body weight as little as 10% is associated with clinically significant improvement in apnea-hypopnea index**
- **Long term effects of methods of weight loss (bariatric surgery and carbohydrate-restricted diets) are not assessed in longitudinal studies**

CPAP Titration

- **Titration is usually done by a trial and-error process, adjusting the applied pressure until those respiratory and sleep parameters considered to be clinically important are reduced to the degree judged to be acceptable.**

Autotitrating CPAP (A-CPAP)

- Fixed-pressure CPAP therapy is effective in most patients with OSAH
- However, the application of a single pressure value over time has potential drawbacks because the collapsibility of the upper airway varies not only during a single night but also long term
- A-CPAP devices modifies the applied pressure in real time, according to that required to maintain upper airway patency
- In theory, at any given time, these devices apply the lowest effective pressure

Features associated with Metabolic Syndrome

- Pro inflammatory state
- Pro Thrombotic state
- Hyperleptinemia
- Hypoadiponectinemia
- Hyperuricemia
- Endothelial dysfunction
- Microalbuminuria

Core Components of Metabolic Syndrome

- **Abdominal obesity**
- **Insulin resistance or glucose intolerance**
- **Hypertension**
- **Low serum high-density lipoprotein**
- **Elevated serum triglyceride**

(Metabolic syndrome: three of these five criteria)

(Tasali E and Ip MSM. Proc Am Thorac soc 2008; 5: 207-217)

Effect of CPAP versus Sham CPAP on Anthropometric Variables

Table 4. Effect of CPAP versus Sham CPAP on Anthropometric Variables.*

Variable	Treatment Effect		Difference (95% CI)	P Value†
	CPAP (N=86)	Sham CPAP (N=86)		
ESS score	−5.3±4.4	−0.6±2.0	−4.7 (−5.6 to −3.8)	<0.001
Weight (kg)	−0.37±2.45	0.33±2.20	−0.70 (−1.40 to −0.03)	0.03
BMI	−0.10±0.86	0.18±0.74	−0.29 (−0.51 to −0.06)	<0.001
Waist-to-hip ratio	−0.001±0.027	0.130±1.207	−0.131 (−0.389 to 0.127)	0.49
Percent of predicted neck circumference (%)	−0.72±2.47	0.02±3.16	−0.74 (−1.52 to 0.05)	0.07
Subcutaneous fat (cm^2)	−0.55±2.56	0.34±2.67	−0.89 (−1.67 to −0.12)	<0.001
Visceral fat (cm^2)	−1.05±2.63	0.01±2.18	−1.06 (−1.80 to −0.32)	0.01
Ratio of visceral fat to subcutaneous fat	−2.36±12.20	−0.48±8.27	−1.88 (−5.13 to 1.37)	0.49
CIMT (mm)	0.000±0.102	0.014±0.075	−0.014 (−0.040 to 0.001)	0.07

* Plus–minus values are means ±SD. Treatment effect was calculated by subtracting the value after the 3-month intervention period from the value before the period. Difference was calculated by subtracting the sham CPAP effect from the CPAP effect. CIMT denotes carotid intima–media thickness, and ESS Epworth Sleepiness Scale.

† P values were calculated with the use of the Wilcoxon signed-rank test.

Sharma SK et al. N Engl J Med 2011;365:2277-2286

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Effects of CPAP versus Sham CPAP on Components of the Metabolic Syndrome.

Table 3. Effects of CPAP versus Sham CPAP on Components of the Metabolic Syndrome.*

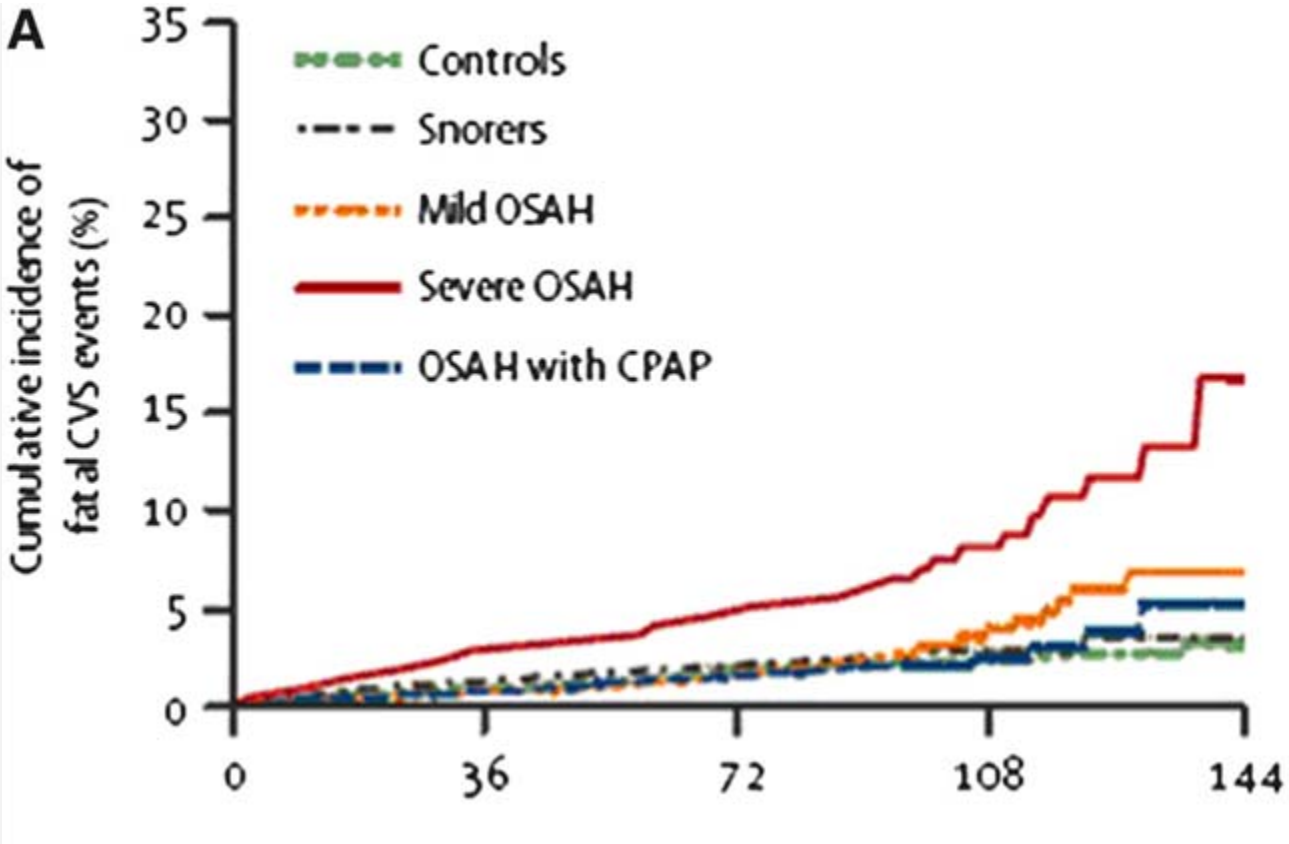
Variable	Treatment Effect		Difference or Odds Ratio (95% CI)	P Value†
	CPAP (N=86)	Sham CPAP (N=86)		
Abdominal circumference — cm	−0.53±2.42	0.20±3.49	−0.73 (−2.15 to 0.68)	0.32
Systolic blood pressure — mm Hg	−3.07±8.02	0.79±7.22	−3.86 (−6.37 to −1.35)	0.001
Diastolic blood pressure — mm Hg	−2.81±6.07	−0.33±5.25	−2.49 (−4.13 to −0.85)	<0.001
Fasting blood glucose — mg/dl	−1.78±11.37	−0.43±9.40	−1.35 (−4.43 to 1.74)	0.10
Fasting insulin — mU/liter	1.75±11.48	3.33±14.54	−1.59 (−5.60 to 2.42)	0.35
Insulin resistance	0.42±3.10	0.81±3.67	−0.39 (−1.40 to 0.62)	0.23
Glycated hemoglobin — %	−0.03±0.42	0.19±0.49	−0.21 (−0.36 to −0.07)	0.003
Triglycerides — mg/dl	−18.86±71.43	−0.21±80.75	−18.65 (−41.57 to 4.27)	0.02
Cholesterol — mg/dl				
Total	−9.36±31.46	3.90±21.95	−13.26 (−21.25 to −5.28)	0.005
HDL	−0.05±12.85	−0.08±12.28	0.04 (−3.82 to 3.89)	0.75
LDL	−5.72±26.56	3.83±20.44	−9.55 (−16.65 to −2.46)	0.008
Non-HDL	−9.32±32.94	3.98±22.74	−13.30 (−21.79 to −4.82)	0.009
HDL:total cholesterol	0.01±0.07	−0.01±0.07	0.02 (−0.01 to 0.04)	0.01
LDL:total cholesterol	0.00±0.08	0.01±0.07	−0.01 (−0.03 to 0.01)	0.58
Reversal of the metabolic syndrome — no. (%)	11 (13)	1 (1)	12 (9 to 99)	0.003

* Plus–minus values are means ±SD. Treatment effect was calculated by subtracting the value after the 3-month intervention period from the value before the period, except for reversal of the metabolic syndrome, for which percentages of patients with reversal of the syndrome are shown. Difference was calculated for all variables except the metabolic syndrome, by subtracting the sham CPAP effect from the CPAP effect; the value for reversal of the metabolic syndrome is the odds ratio. To convert values for glucose to millimoles per liter, multiply by 0.055. To convert values for triglycerides to millimoles per liter, multiply by 0.01129. To convert values for cholesterol to millimoles per liter, multiply by 0.02586.

† P values were calculated with the use of the Wilcoxon signed-rank test, except for reversal of the metabolic syndrome, for which Fisher's exact test was used.

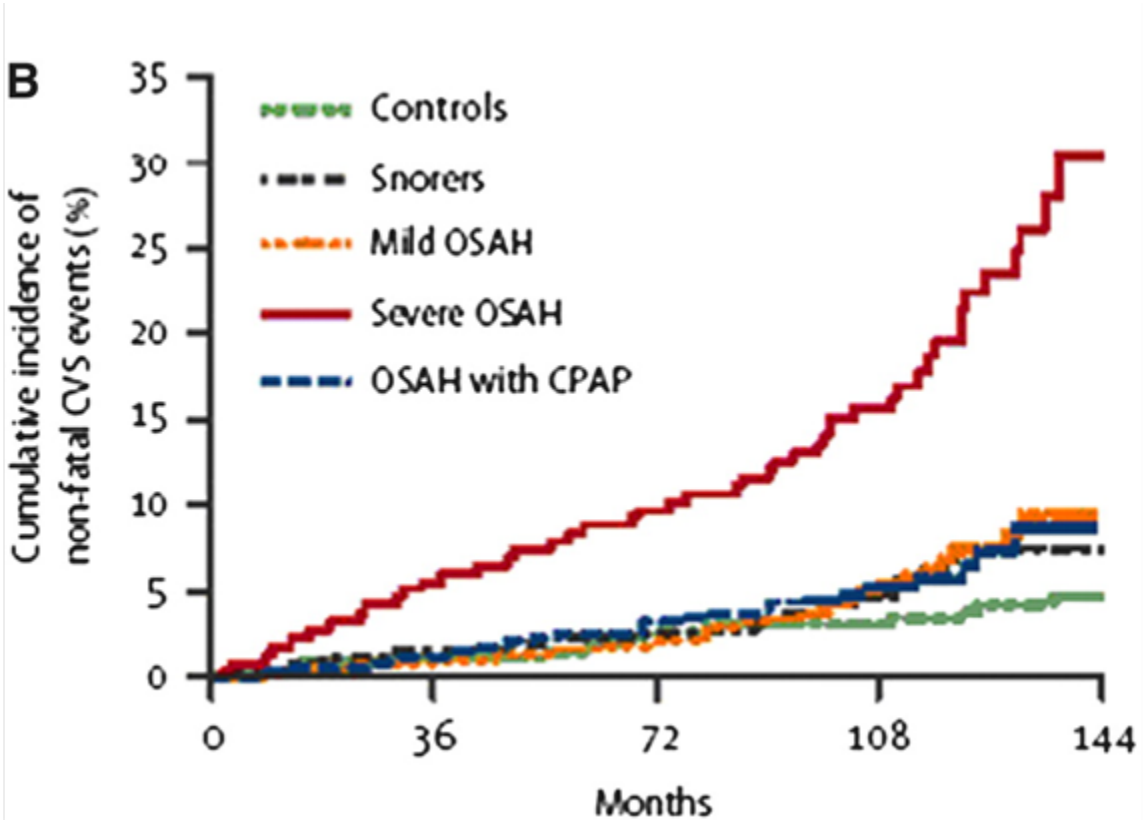
Sharma SK et al. N Engl J Med 2011;365:2277-2286

Men with Fatal CV Events (More than 10 Years Follow-up)



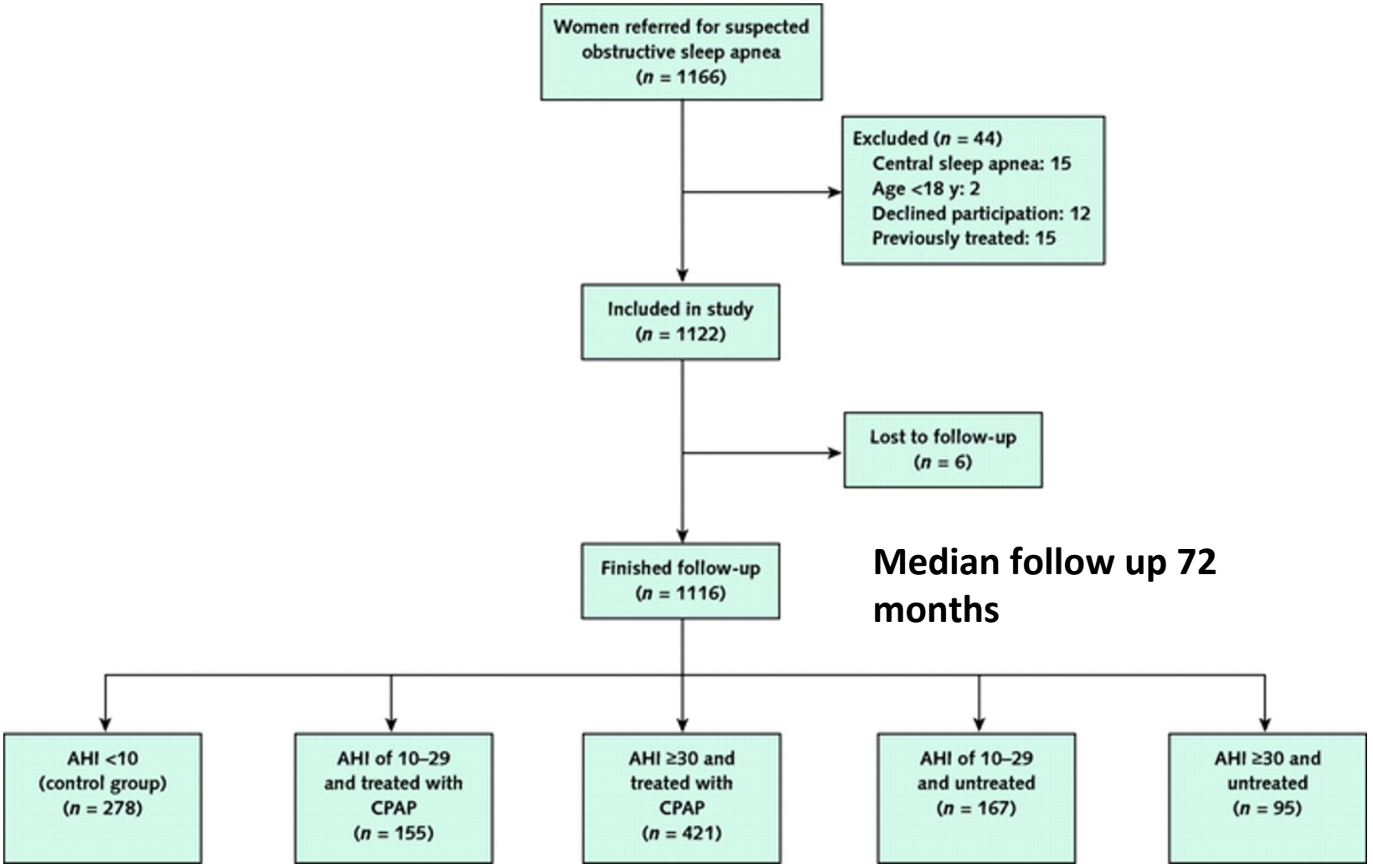
(Marin JM et al. Lancet 2005;365:1046-53)

Men with Non-fatal CV Events (More than 10 Years Follow-up)



(Marin JM et al. Lancet 2005;365:1046-53)

CV Mortality in Women with OSA with or without CPAP Treatment

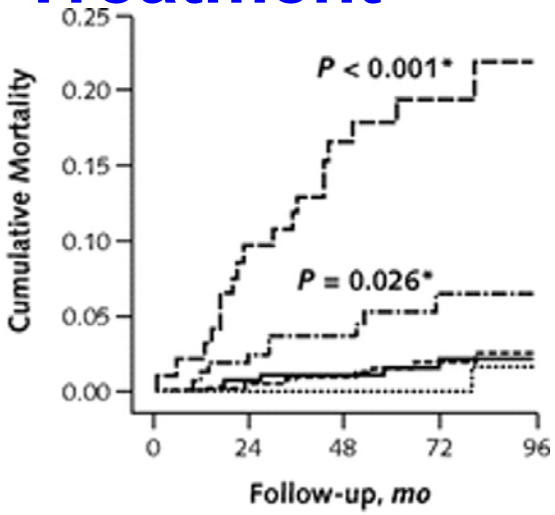


Median follow up 72 months

Campos-Rodriguez F et al. Ann Intern Med 2012;156:115-122

Annals of Internal Medicine

CV Mortality in Women with OSA with or without CPAP Treatment



Patients at risk, *n*					
AHI <10 (control group)	277	255	198	102	23
AHI of 10–29 and treated with CPAP	155	140	102	55	18
AHI ≥30 and treated with CPAP	419	381	280	148	48
AHI of 10–29 and untreated	166	146	102	49	12
AHI ≥30 and untreated	93	78	55	28	7

— AHI <10
····· AHI of 10–29 and treated with CPAP
---- AHI of 30 and treated with CPAP
–·– AHI of 10–29 and untreated
– – – AHI of 30 and untreated

Campos-Rodriguez F et al. Ann Intern Med 2012;156:115-122

Annals of Internal Medicine

CV Mortality in Women with OSA with or without CPAP Treatment

- **Severe OSA is associated with cardiovascular death in women and adequate CPAP treatment may reduce this risk**

Campos-Rodriguez F et al. Ann Intern Med 2012;156:115-122

Adherence to CPAP Therapy

- **The use of CPAP > 6 hours decreases sleepiness, improves daily functioning, and restores memory to normal levels**
- **Adherence to CPAP therapy is defined as greater than 4 hours of nightly use**
- **46 to 83% of patients with obstructive sleep apnea have been reported to be nonadherent to treatment.**

Weaver TE and Grunstein RR. Proc Am Thorac Soc 2008; 5: 173-178

Interventions to Improve CPAP Adherence

- **Humidification of the Airway**
- **Machine Design**

  Bilevel CPAP, auto-CPAP(developed to vary and optimize the level of CPAP through the night), or flexible CPAP (alternates airway pressure between exhalation and inhalation on a breath-by-breath basis to improve patient comfort).
- **Behavioral Interventions**

  Cognitive behavioral therapy

Weaver TE and Grunstein RR. Proc Am Thorac Soc 2008; 5: 173-178

Medical Therapy: Pharmacologic Agents

- Serotoninergic agents (fluoxetine, paroxetine, mitrazapine)
- REM sleep suppressant therapy (protriptyline, clonidine)
- Ventilatory stimulants [methyl xanthine derivatives, opioid antagonists (naloxone), doxopram, nicotine]
- Hormone treatment (medroxyprogesterone and estrogen)
- Endocrinological disorders (thyroid hormone replacement, Growth hormone suppressant)
- Wake promoting agents (modafinil)

Wake Promoting Agents (Modafinil)

- **Despite treatment with CPAP, many patients demonstrate residual sleepiness**
- **Modafinil is a wake-promoting agent which has been approved for the treatment of narcolepsy**
- **In a randomized, double blind, placebo-controlled parallel group trial, modafinil (200 mg/day week 1 and then 400 mg/day weeks 2-4), significantly improved daytime sleepiness, but no effect on AHI**
- **Adult patients with OSA having excessive somnolence despite well treated with CPAP**

(Pack Al et al. Modafinil as adjunct therapy for daytime sleepiness in obstructive sleep apnea. Am J Respir Crit Care Med 2001; 164: 1675–81)

Medical Therapy:

- **Supplemental oxygen**

  Supplemental nocturnal oxygen therapy improves oxygen saturation levels but does not improve airway patency.

- **Therapies intended to improve nasal patency**

  Patients with OSA and coexisting rhinitis may benefit from the use of nasal corticosteroids.

- **Positional therapies**

  Lateral positioning therapy has been found to improve AHI

Surgical Treatment

- **Procedures for nasal obstruction**
  Septoplasty
  Turbinectomy
  Radiofrequency ablation of turbinates
- **Reduction of soft palate redundancy**
  Uvulopalatopharyngoplasty
  Uvulopalatal flap
  Laser assisted uvulopalatoplasty
  RF ablation of the soft palate with adenotonsillectomy

Surgical Treatment

- **Reduction of the bulk of the tongue base to prevent hypopharyngeal or retrolingual obstruction**

  Genioglossal advancement

  Hyoid suspension

  Distraction osteogenesis

  Tongue RF ablation

  Lingualplasty

  Maxillomandibular advancement

Hypoglossal Nerve Stimulation (HGNS)

- 30 middle-aged patients with OSA who could not tolerate CPAP
- Implantation of a neurostimulator and respiration sensing lead under GA
- Stimulating lead is placed on the hypoglossal nerve to stimulate the nerve during inspiration
- Progressive increase in inspiratory airflow with increasing stimulation intensity, producing opening of the airway

(Schwartz AR et al. Am J Respir Crit Care 2011(10.1164rccm.201109-1614OC)


Thank you

Epworth Sleepiness Scale

Name: _____ Today's date: _____

Your age (Yrs): _____ Your sex (Male = M, Female = F): _____

How likely are you to doze off or fall asleep in the following situations, in contrast to feeling just tired?

This refers to your usual way of life in recent times.

Even if you haven't done some of these things recently try to work out how they would have affected you.

Use the following scale to choose the **most appropriate number** for each situation:

0 = would **never** doze
1 = **slight chance** of dozing
2 = **moderate chance** of dozing
3 = **high chance** of dozing

It is important that you answer each question as best you can.

Situation	**Chance of Dozing (0-3)**
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	

THANK YOU FOR YOUR COOPERATION

Stanford Sleepiness Scale

Degree of Sleepiness	Scale Rating
Feeling active, vital, alert, or wide awake	1
Functioning at high levels, but not at peak; able to concentrate	2
Awake, but relaxed; responsive but not fully alert	3
Somewhat foggy, let down	4
Foggy; losing interest in remaining awake; slowed down	5
Sleepy, woozy, fighting sleep; prefer to lie down	6
No longer fighting sleep, sleep onset soon; having dream-like thoughts	7
Asleep	X

Below three indicated sleep debt, need more sleep

Diagnosis:
Assessment Of Sleepiness

- **Subjective**
  - **Epworth sleepiness scale (ESS)**
  - **Stanford sleepiness scale (SSS)**
- **Objective**
  - **Multiple sleep latency test (MSLT)**
  - **Maintenance of wakefulness test (MWT)**

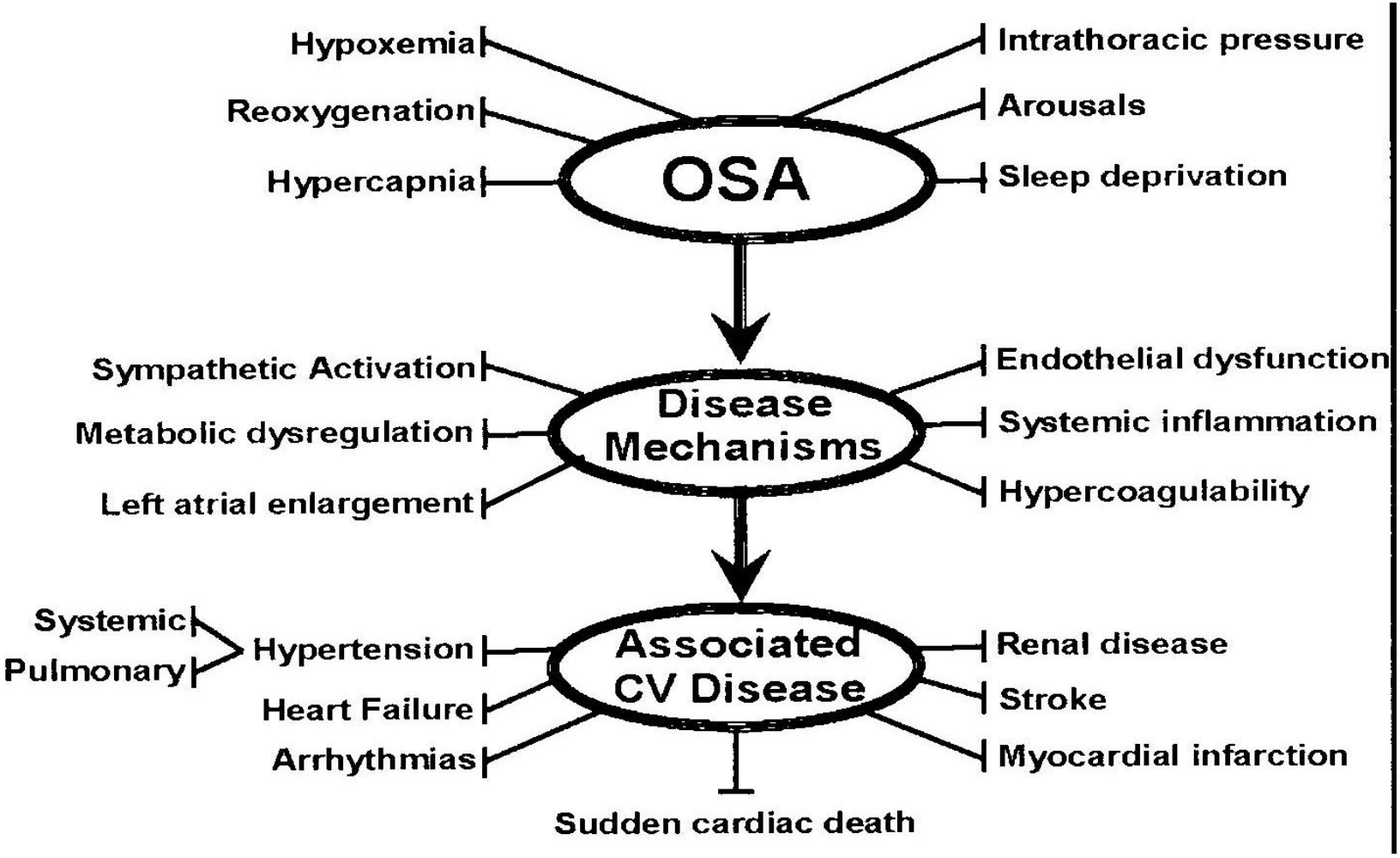
Pathophysiology During Sleep

- Chemoreflex sensitivity and response to hypoxia, hypercapnia and apnea
- Apnea-induced bradycardia
- Baroreflex activation
- Variations in intrathoracic pressure

Pathophysiology During Wakefulness

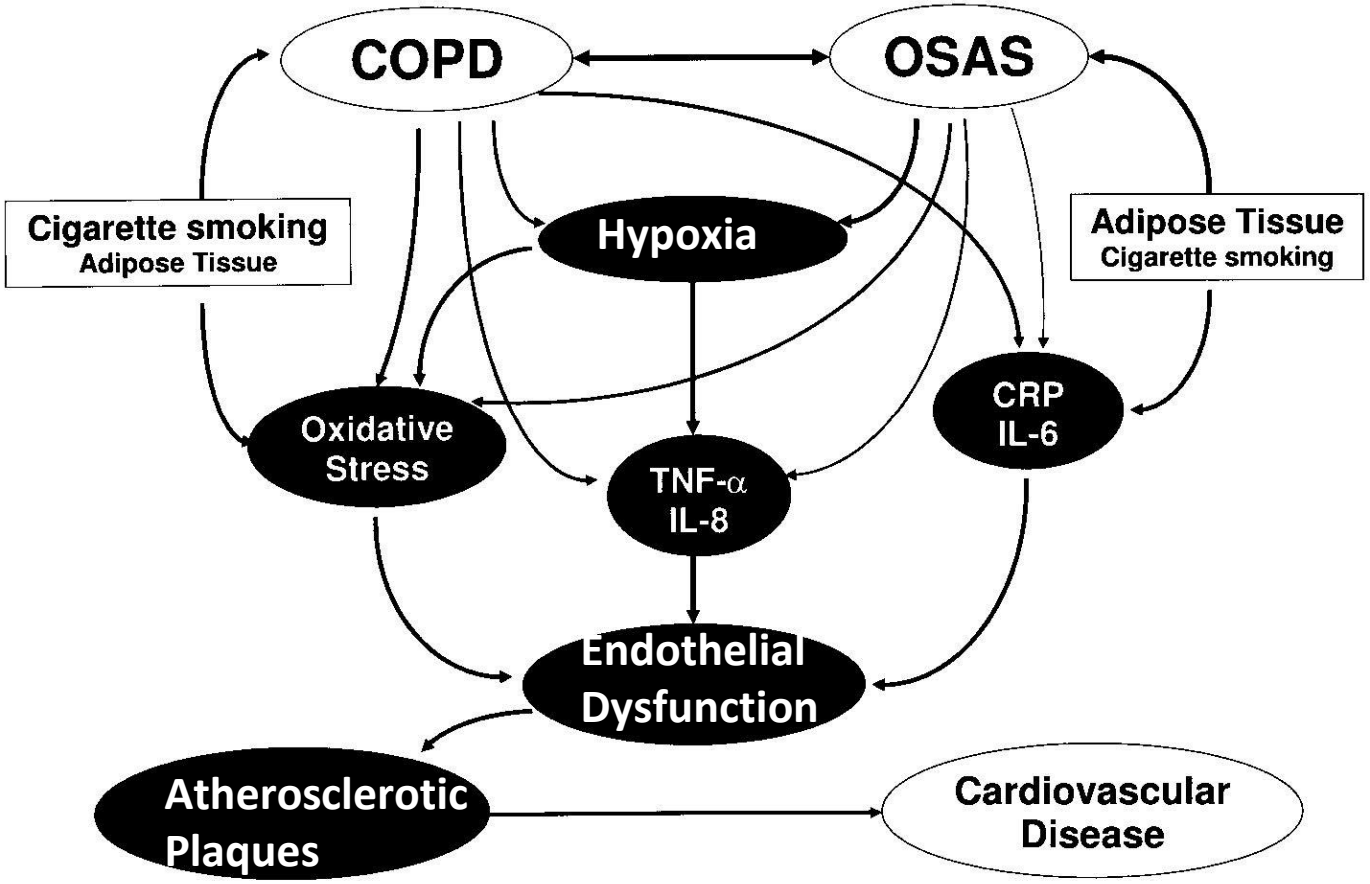
- **Sympathetic activity and impaired cardiovascular variability**
- **Vascular dysfunction**
- **Systemic inflammation**
- **Metabolic dysregulation**

Pathophysiological Components of OSA, CV Disease Mechanisms and Associated CV Diseases



AHA 2008 Scientific Statement: Sleep Apnea and Cardiovascular Disease

COPD and OSAS: Overlapping Molecular Mechanisms of Systemic Inflammation



(McNicholas WT. Am J Respir Crit Care Med 2009; 180: 692-700)

Core Components of Metabolic Syndrome

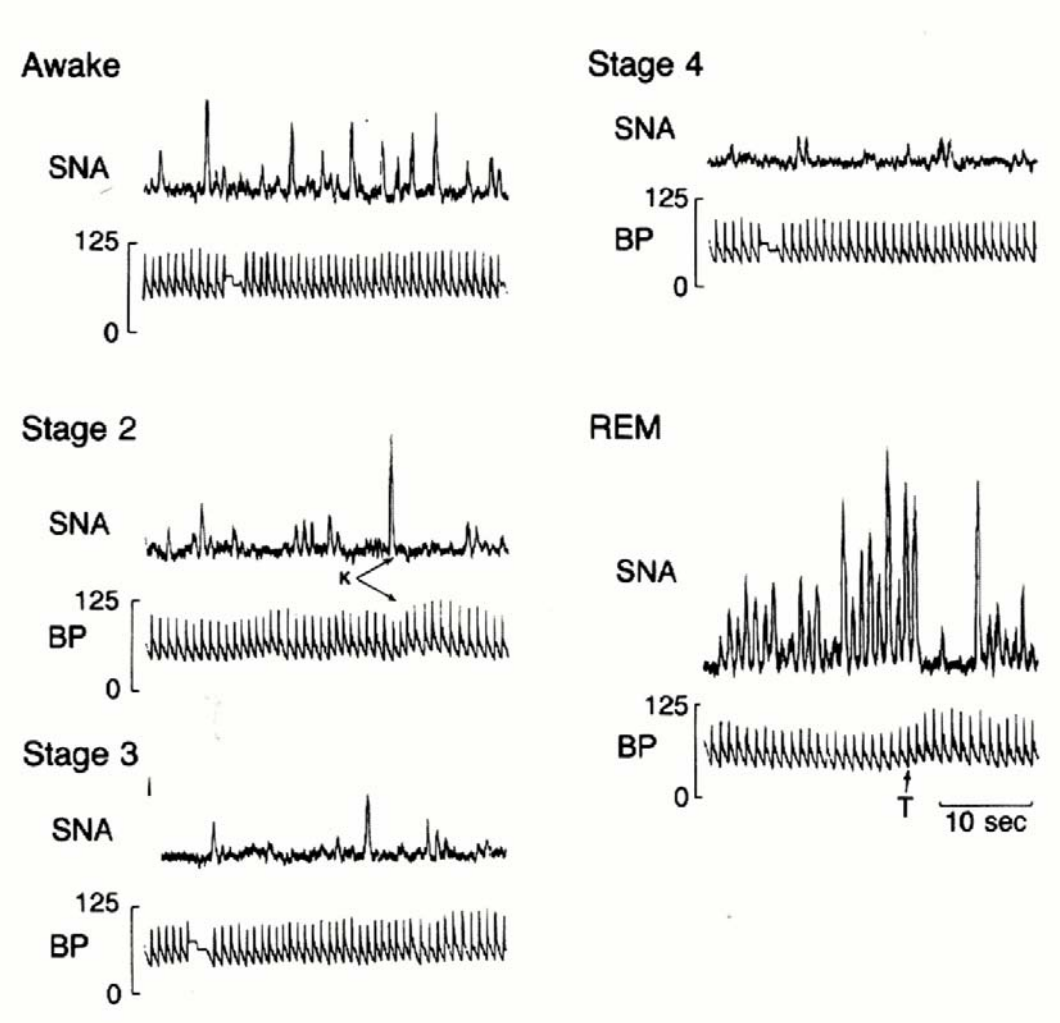
- **Obesity**
- **Insulin resistance**
- **Hypertension**
- **Dyslipidemia**

(Tasali E and Ip MSM. Proc Am Thorac soc 2008; 5: 207-217)

Normal Sleep

- **NREM- 85% of sleep**
  - **↓ Sympathetic Nervous system activity, Heart rate, Blood Pressure, Cardiac output, SVR, Metabolic rate**
  - **↑ Parasympathetic activity**
- **REM-15% of sleep**
  - **Intermittent surges in sympathetic activity**

Recordings of Sympathetic-Nerve Activity (SNA) and Mean Blood Pressure (BP) in a Single Subject while Awake and while in Stages 2, 3, 4, and REM Sleep



Somers, V. K. et al. N Engl J Med 1993;328:303-307

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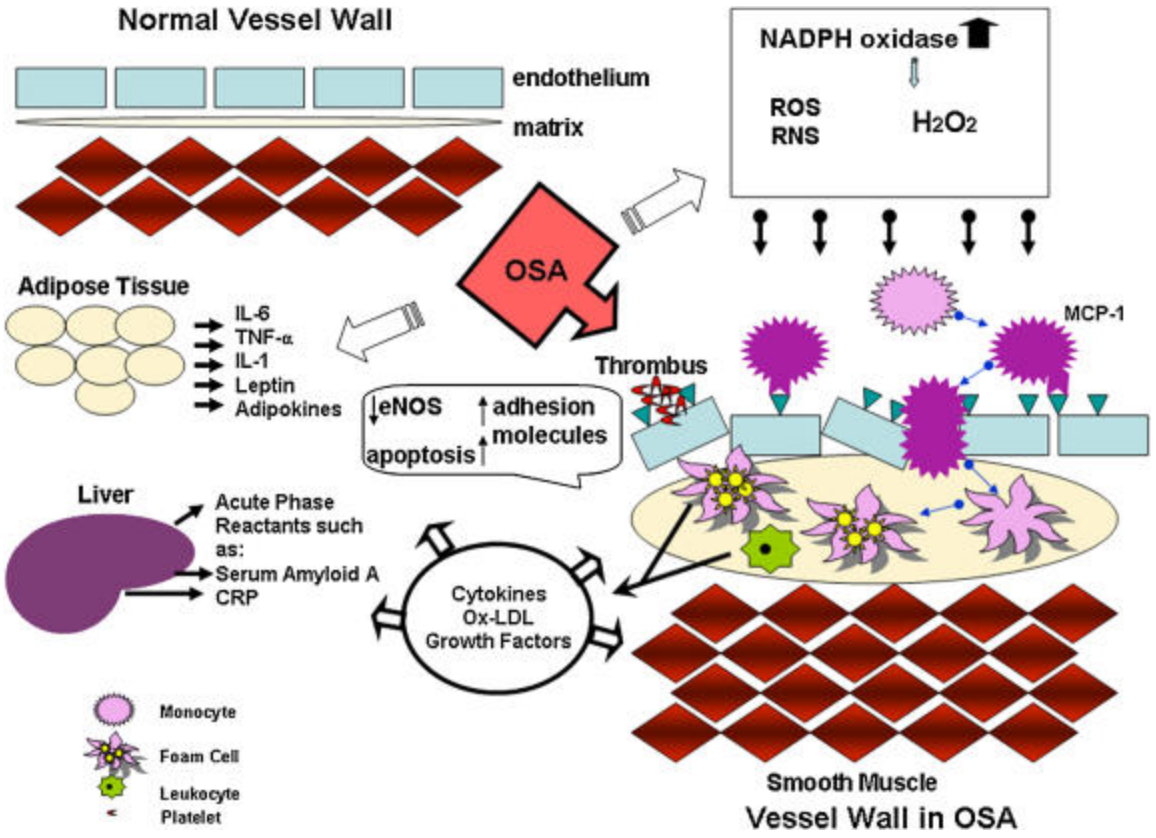
Complex Sleep Apnea

Complex Sleep Apnea is a form of sleep apnea in which central apneas persist or emerge (CAI >5) during attempts to treat obstructive events with nCPAP or

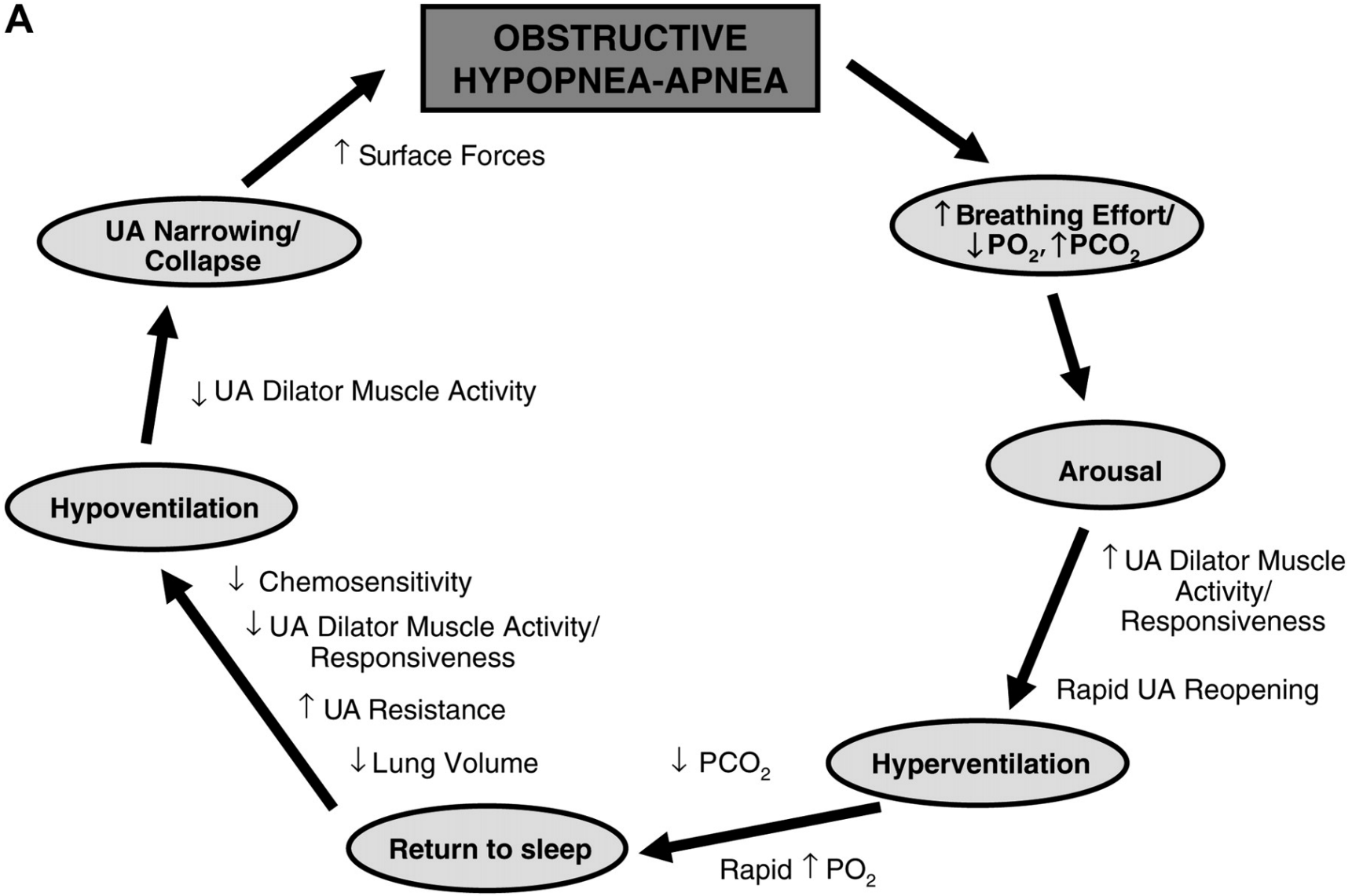
Bilevel PAP.

Putative Alterations in the Normal Vessel Wall with OSA



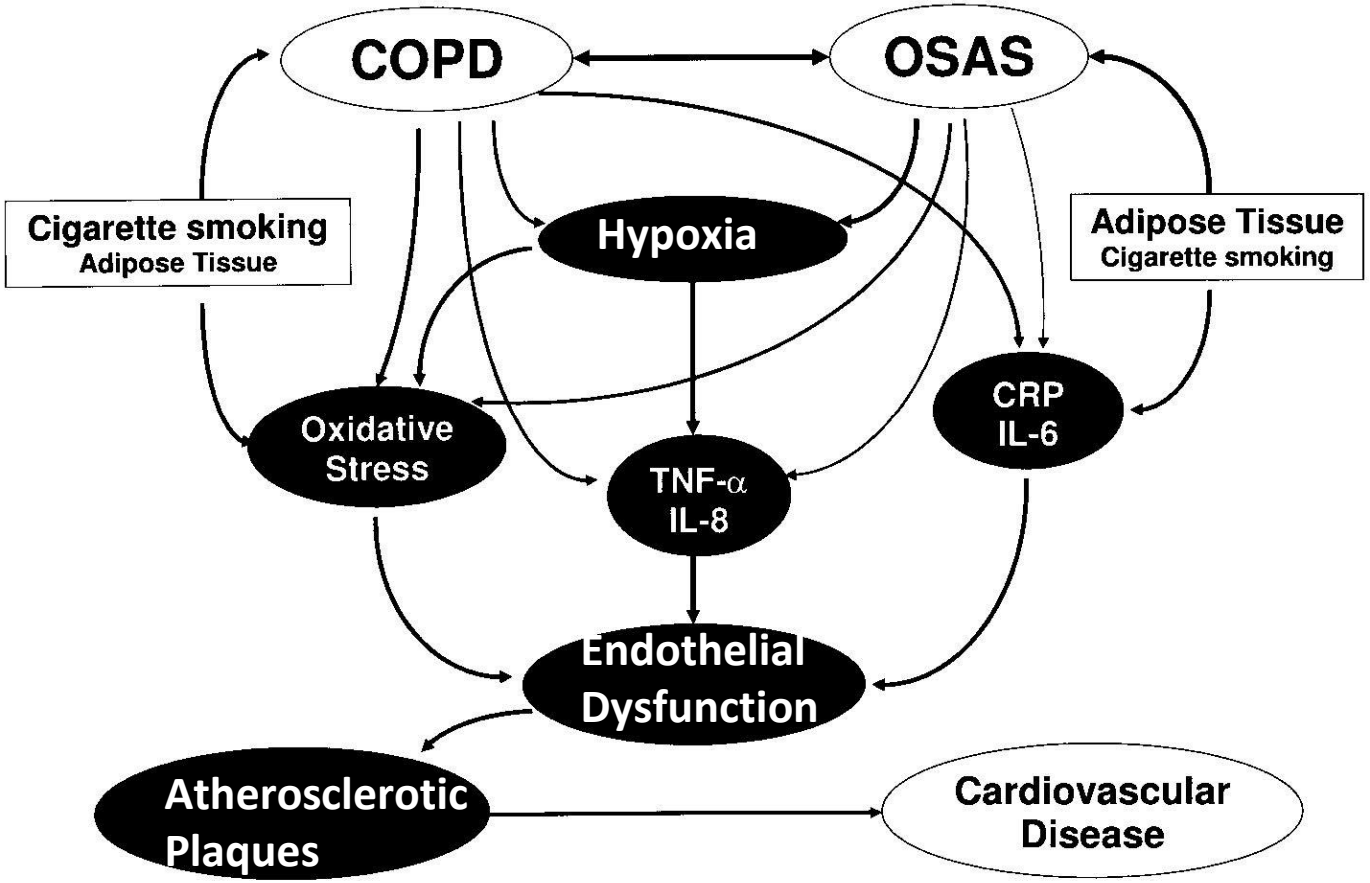
(Gozal D and Gozal LK. Am J Respir Crit Care Med 2008; 177: 369-379)

Pathophysiological Sequences in OSA



(Eckert DJ et al. Proc Am Thorac Soc 2008;5:144-153)

COPD and OSAS: Overlapping Molecular Mechanisms of Systemic Inflammation



(McNicholas WT. Am J Respir Crit Care Med 2009; 180: 692-700)