CARDIOVASCULAR CONSEQUENCES OF OSA

Richard Goodstein DO FCCP
Haggin Pulmonary & Sleep Medicine

Conflict of Interest Disclosures
Speaker:

[✓] 1. I do not have any potential conflicts of interest to disclose, **OR**

[ ] 2. I wish to disclose the following potential conflicts of interest

Type of Potential Conflict	Details of Potential Conflict
Grant/Research Support	
Consultant	
Speakers' Bureaus	
Financial support	
Other	

[ ] 3. The material presented in this lecture has no relationship with any of these potential conflicts, **OR**

[ ] 4. This talk presents material that is related to one or more of these potential conflicts, and the following objective references are provided as support for this lecture:

1.
2.
3.

As a way of introduction…I am…

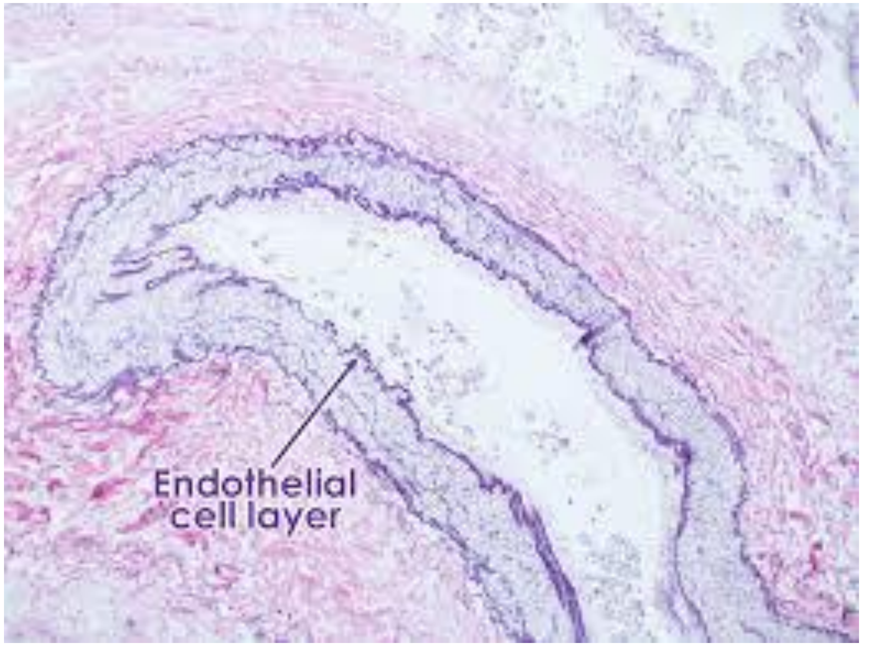
UNTREATED OSA

METABOLIC SYNDROME (OSA)

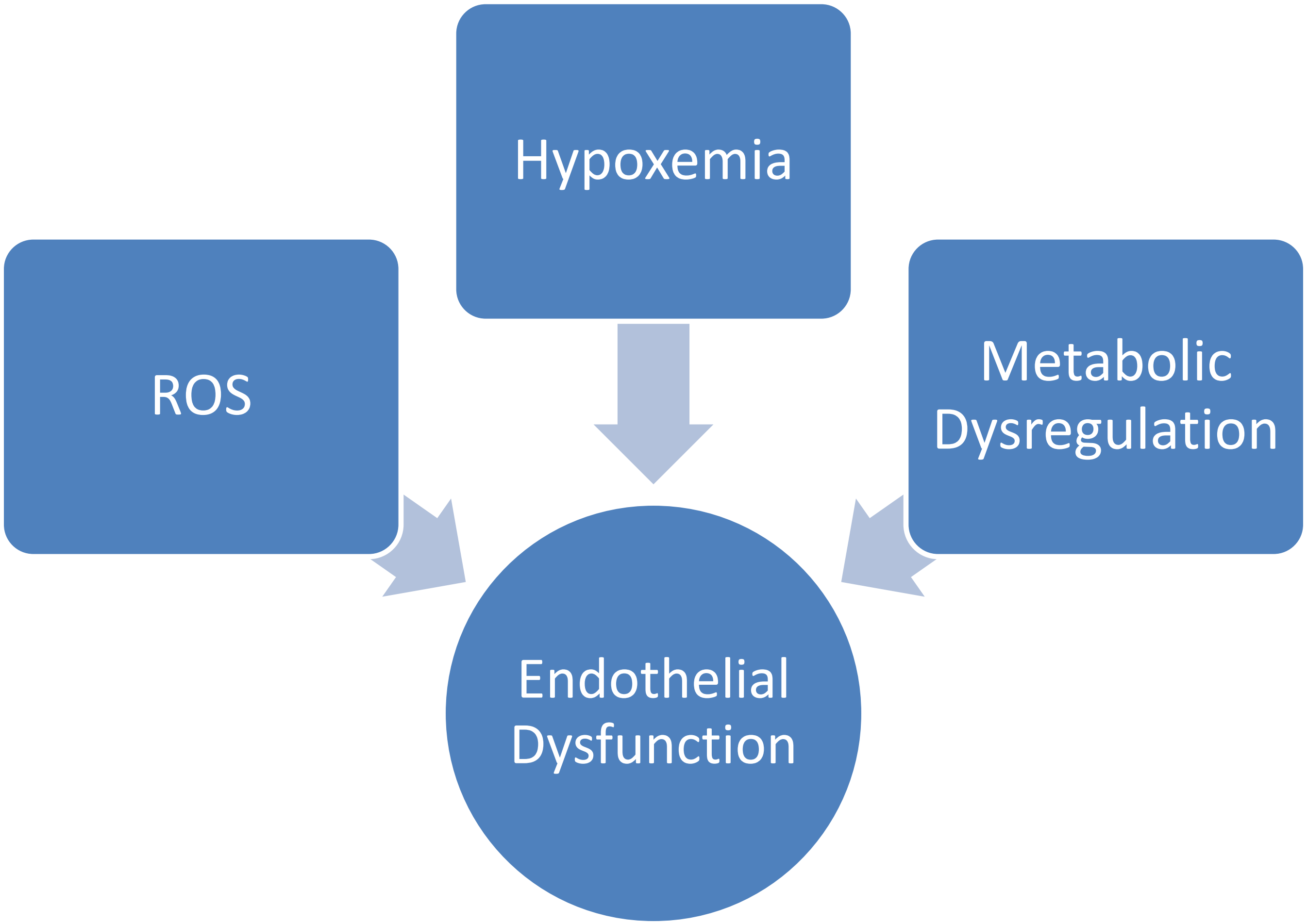
- OBESITY
- HYPERTENSION
- INSULIN RESISTANCE
- LIPID ABNORMALITIES
- HYPERURICEMIA
- INFLAMMATORY STATE

OSA AS AN INFLAMMATORY PROCESS

Endothelium



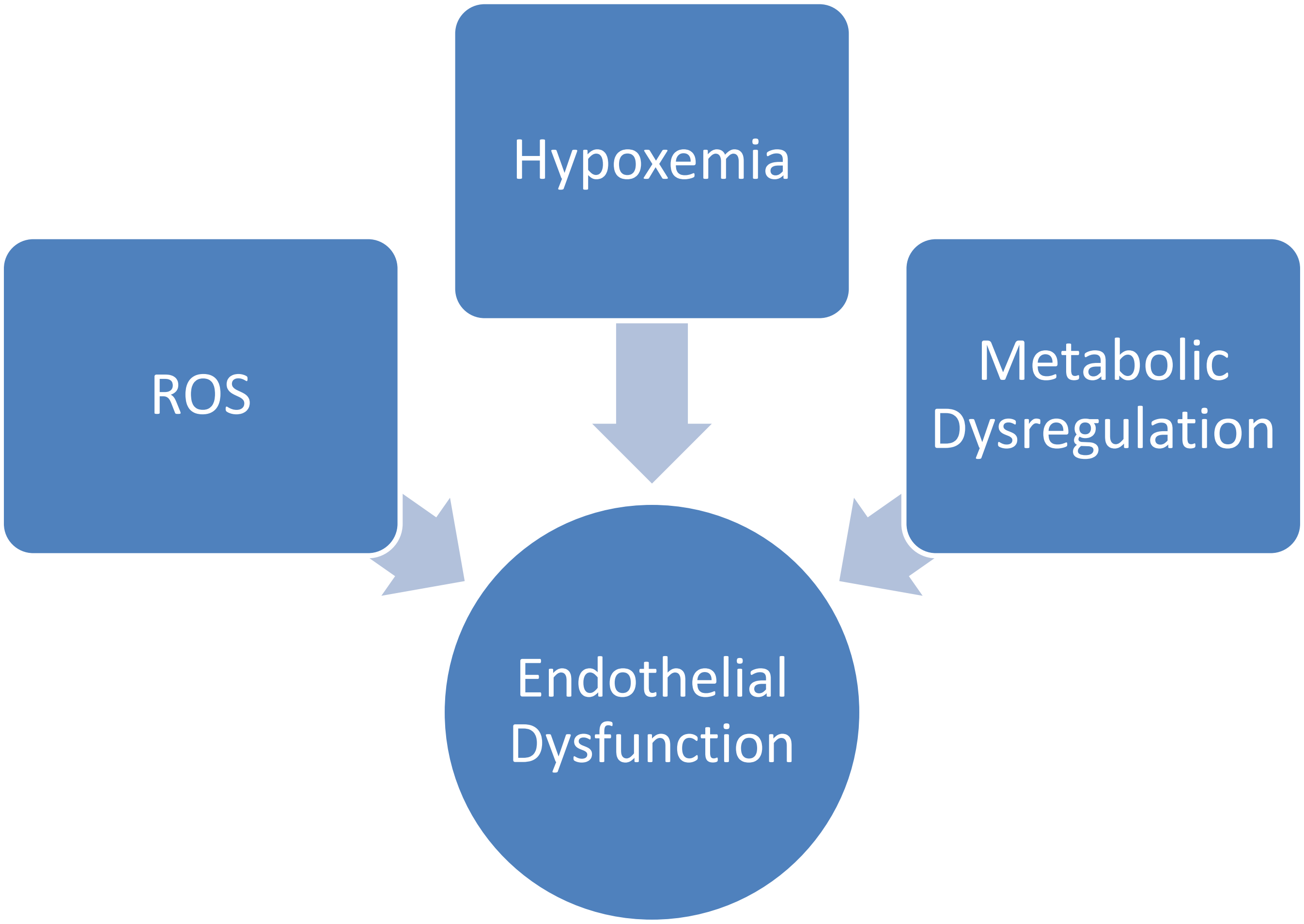
Endothelial Dysfunction



Hypoxemia

- High versus Low frequency cyclic hypoxemia
- Reoxygenation with increased ROS
- Altered reduction oxidation capacity(NADPH)
- Bradycardia
- Primary vascular insult

Endothelial Dysfunction

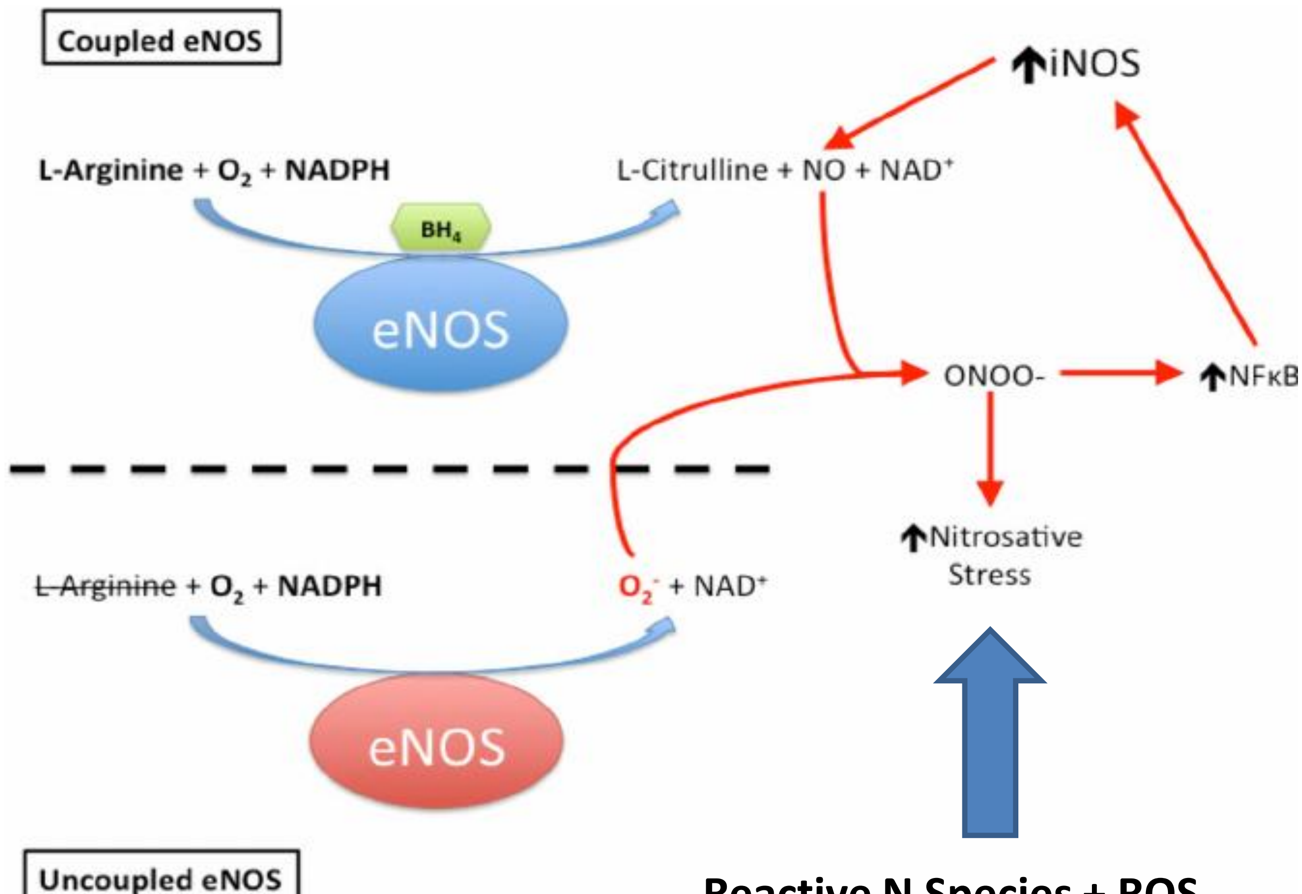


Endothelial Cell…Function Follows Form

Intact Endothelial Cell

- Endothelial Nitrous Oxide synthetase (eNOs)…cyclic GMP….vasodilatation
- Dismutase…Reactive Oxygen Species metabolism
- On exposure to L-arginine stimulates Inducible Nitrous Oxide Synthetase (iNOs)

Oxy-Nitrosative Stress

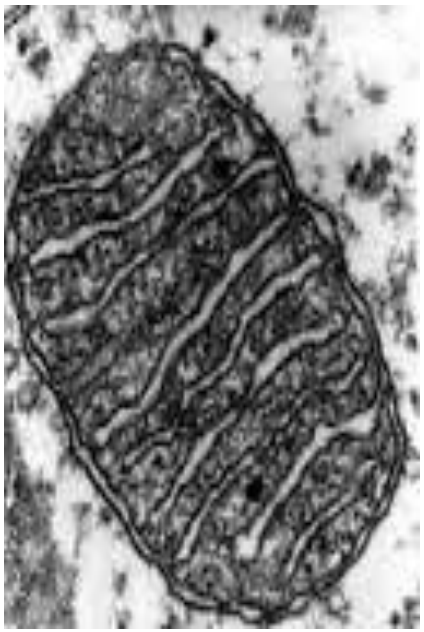


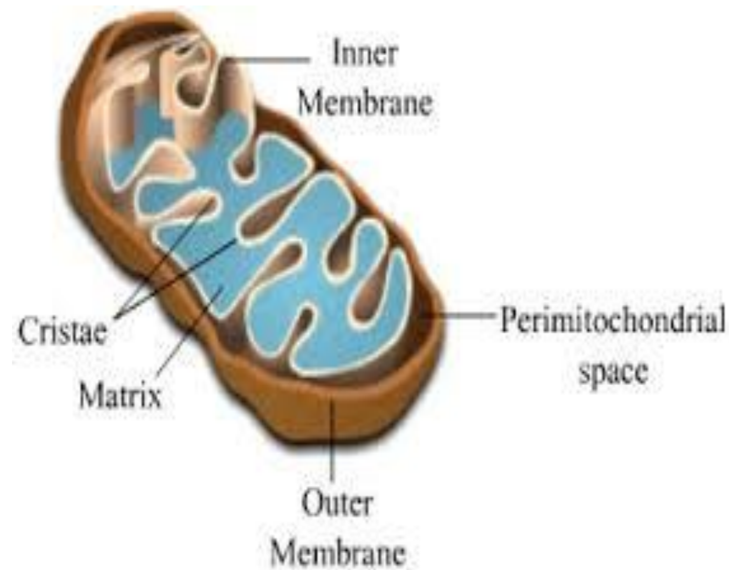
Reactive N Species + ROS

Oxy-Nitrosative Stress

- OONO taken up by endoplasmic reticulum of mitochondria
- Cell dysfunction
- Cell death…especially vascular/renal cells

Mitochondria





ELECTRON GRADIENT. PROTON INFLUX. ATP SYNTHESIS

Mitochondria produce energy (ATP) through an Electron Transport Chain (ECT). Mitochondia may also serve as a "sensing" organ to counter hypoxia !

NEJM 2005;353(19):2042-2055
Weir, Lopez-Barneo, Buckler and Archer

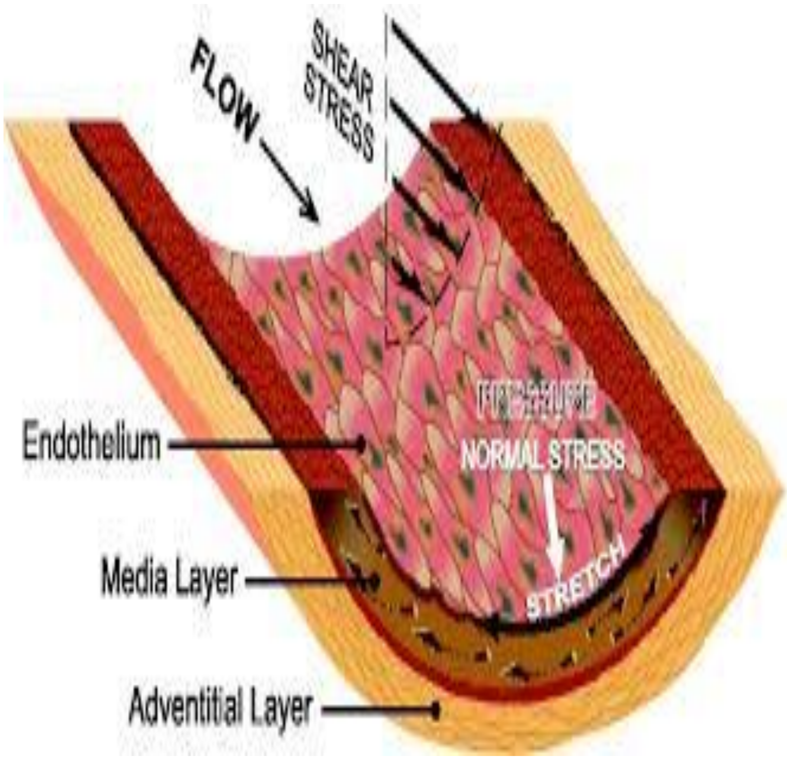
Oxy-Nitrosative Stress

- **OONO taken up by endoplasmic reticulum of mitochondria**
- **Cell dysfunction**
- **Cell death…especially vascular/renal cells**

Metabolic Dysregulation

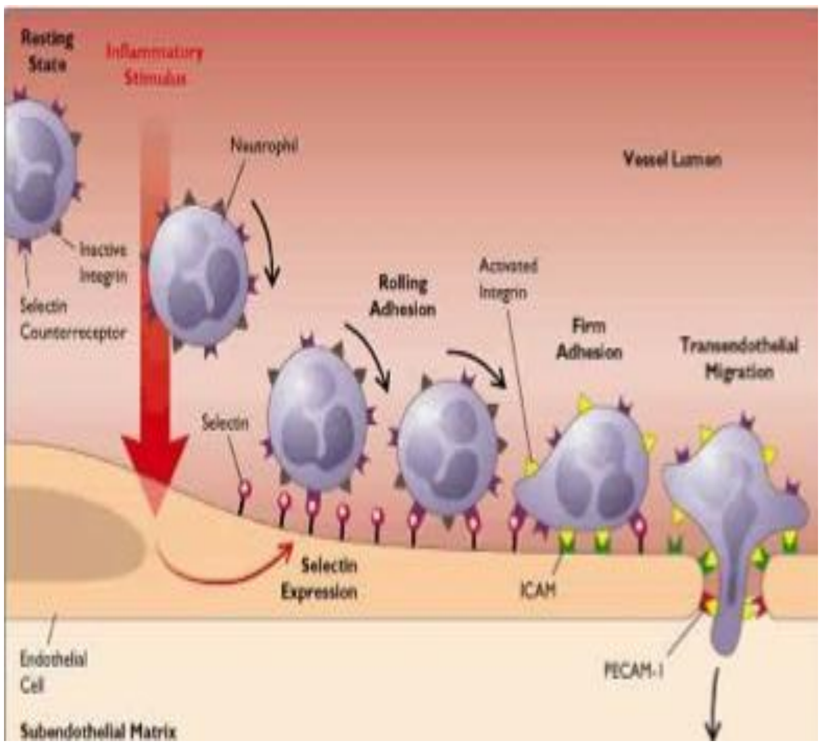
- Leptin…increased weight/altered insulin receptors
- Cytokines…IL-6 …TNF …PMNs …Platelet activation …C-reactive protein
- Decreased Peroxidase / Superoxide Dismutase(SOD) and NADPH
- Increased oxygen radicals…O3/OH-/H2O2
- Increased P-selectin

Endothelial Dysfunction



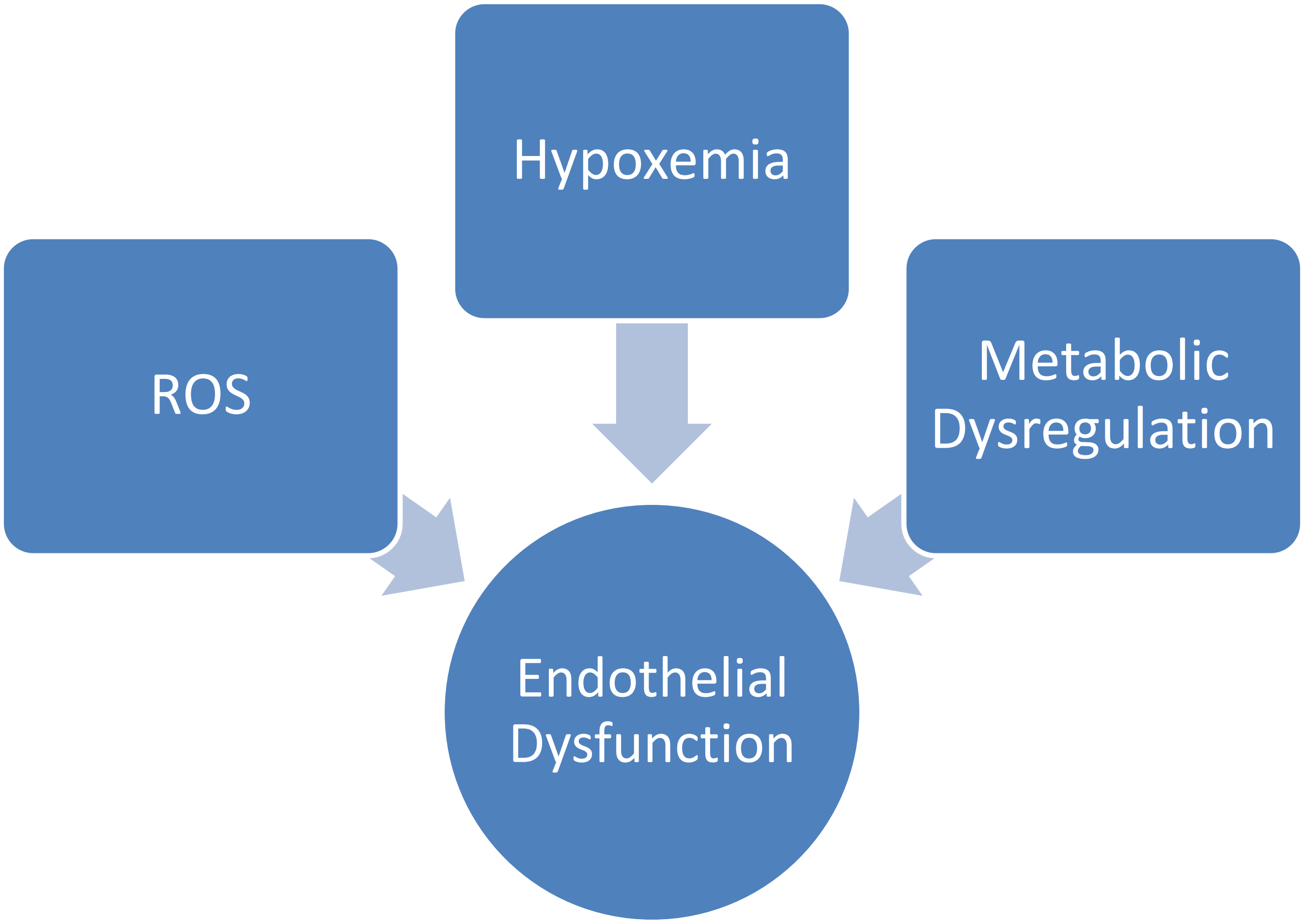
- **Shear Effect**
- **P Selectin (increased vascular adhesion molecules)**
- **Increased cytokines(IL-6 and TNF alpha)**
- **Increased programmed cell death (apoptosis)**
- **Hypercoaguability**

P-Selectin



- Up-regulates ICAMs
- Up-regulates VCAM
- Increases PMN "rolling"
- Cell-cell adhesion (hyaluronidase) breakdown
- PMN invasion

Endothelial Dysfunction

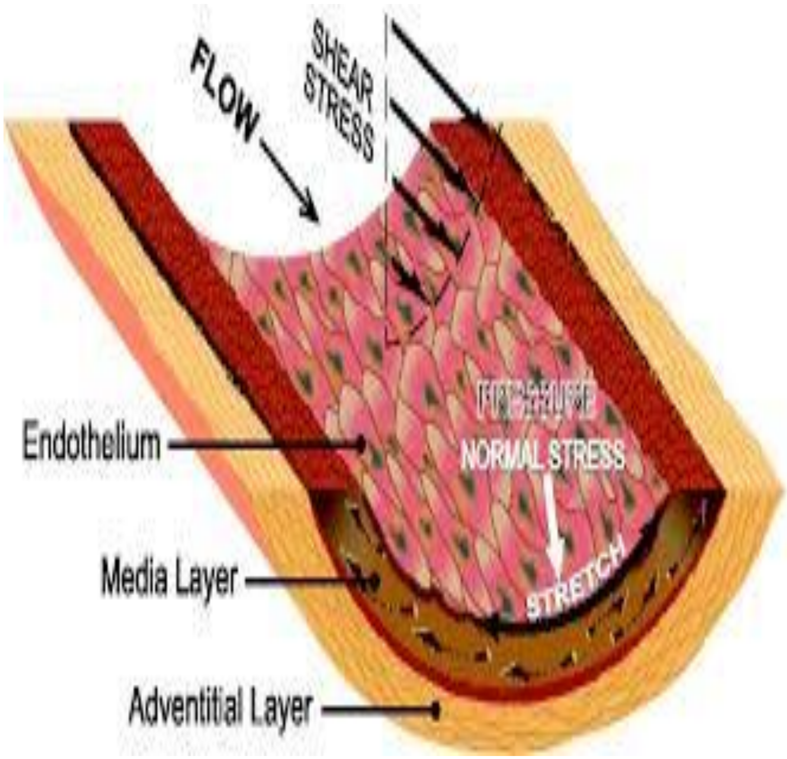


Cell Death (Apotosis)

- PROGRAMMED
- INDUCIBLE

Inducible Apotosis

Endothelial Dysfunction



- **Shear Effect**
- **P Selectin (increased vascular adhesion molecules)**
- **Increased cytokines(IL-6 and TNF alpha)**
- **Increased programmed cell death (apoptosis)**
- **Hypercoaguability**

Thrombus Formation

- Shearing Effect

- Increased VWF
- Increased collagen

- Platelet activation
- Decreased anti-coagulants (Protein C)

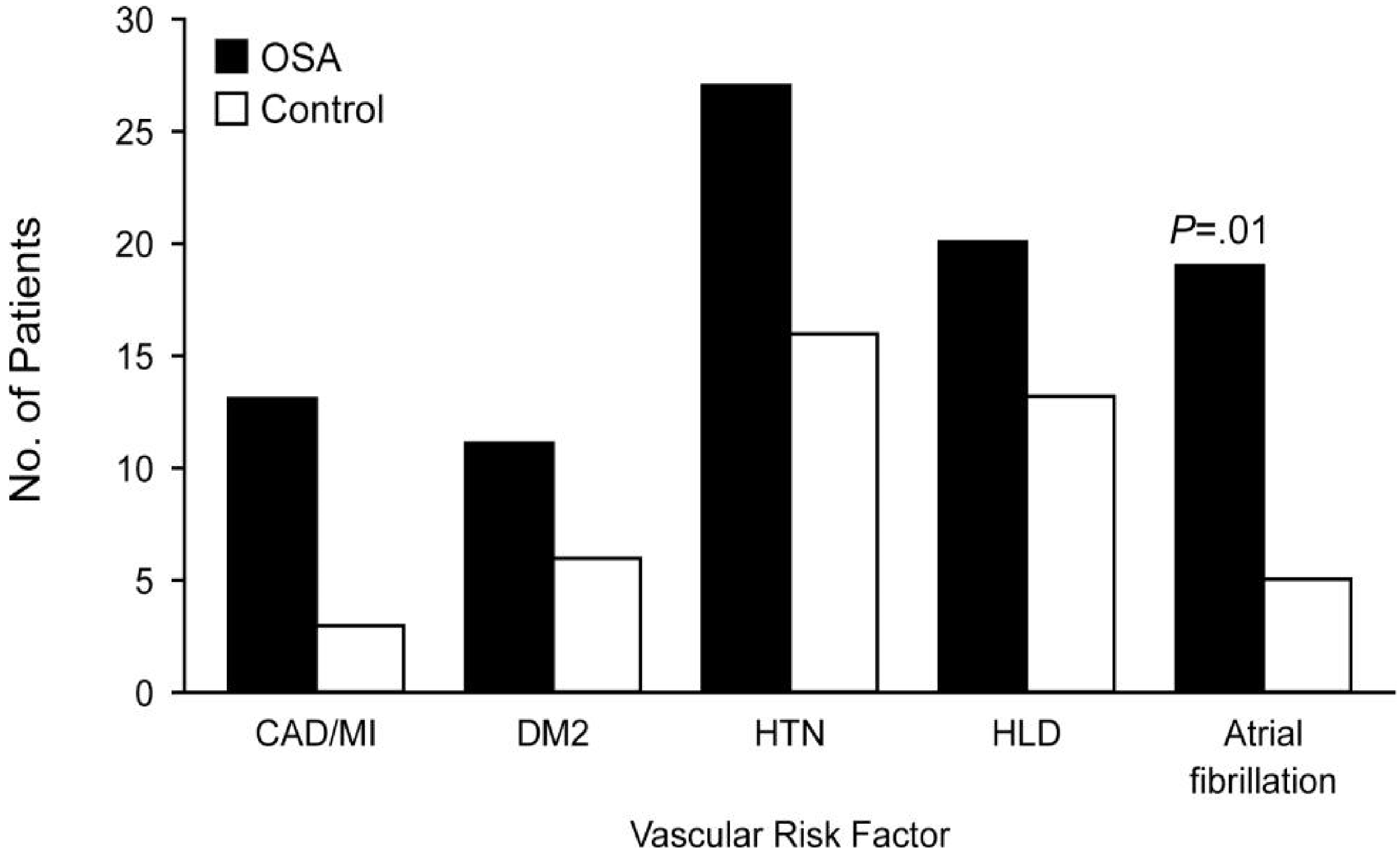
OSA and Cardiovascular Disease

- OSA

- Increased Sympathetic Activity
- Oxidative Stress
- Systemic Inflammation

- CAD
- Hypertension
- CVA

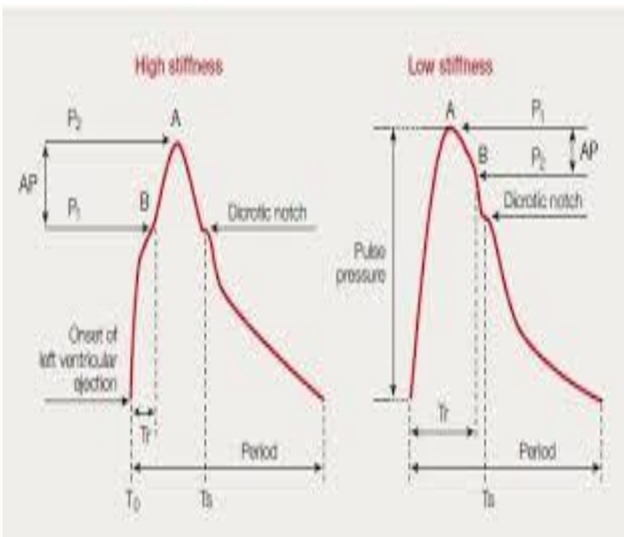
OSA RISK PROFILE



HYPERTENSION IN OSA

- **Sympathetic Activation…catecholamines**
- **Intermittent Hypoxia**
- **Renal Affects…Altered cortical perfusion and Renin-Angiotensin Axis**
- **Transthoracic Pressure**
- **Arterial " Stiffness"**

ARTERIAL STIFFNESS



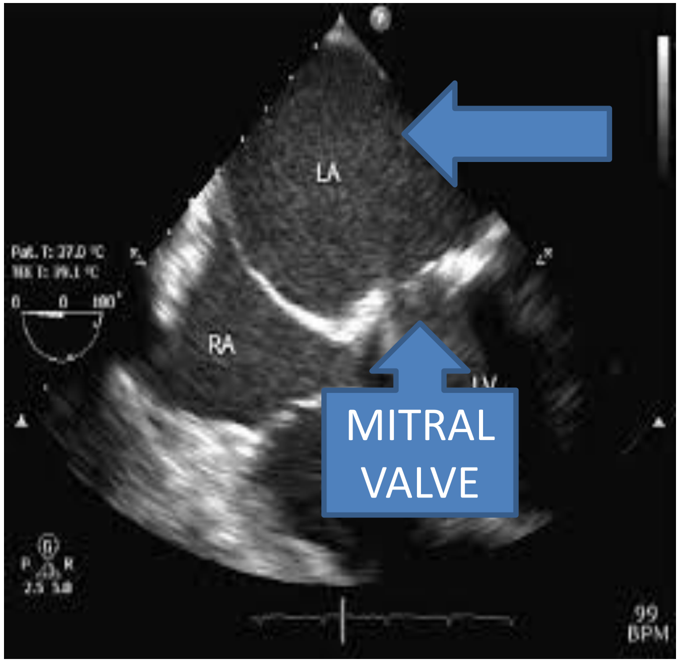
- Increased " wear and tear " on artery
- Collagen deposition
- Increased work for LV
- Early physiologic marker of Atherosclerosis and OSA

ATRIAL FIBRILLATION

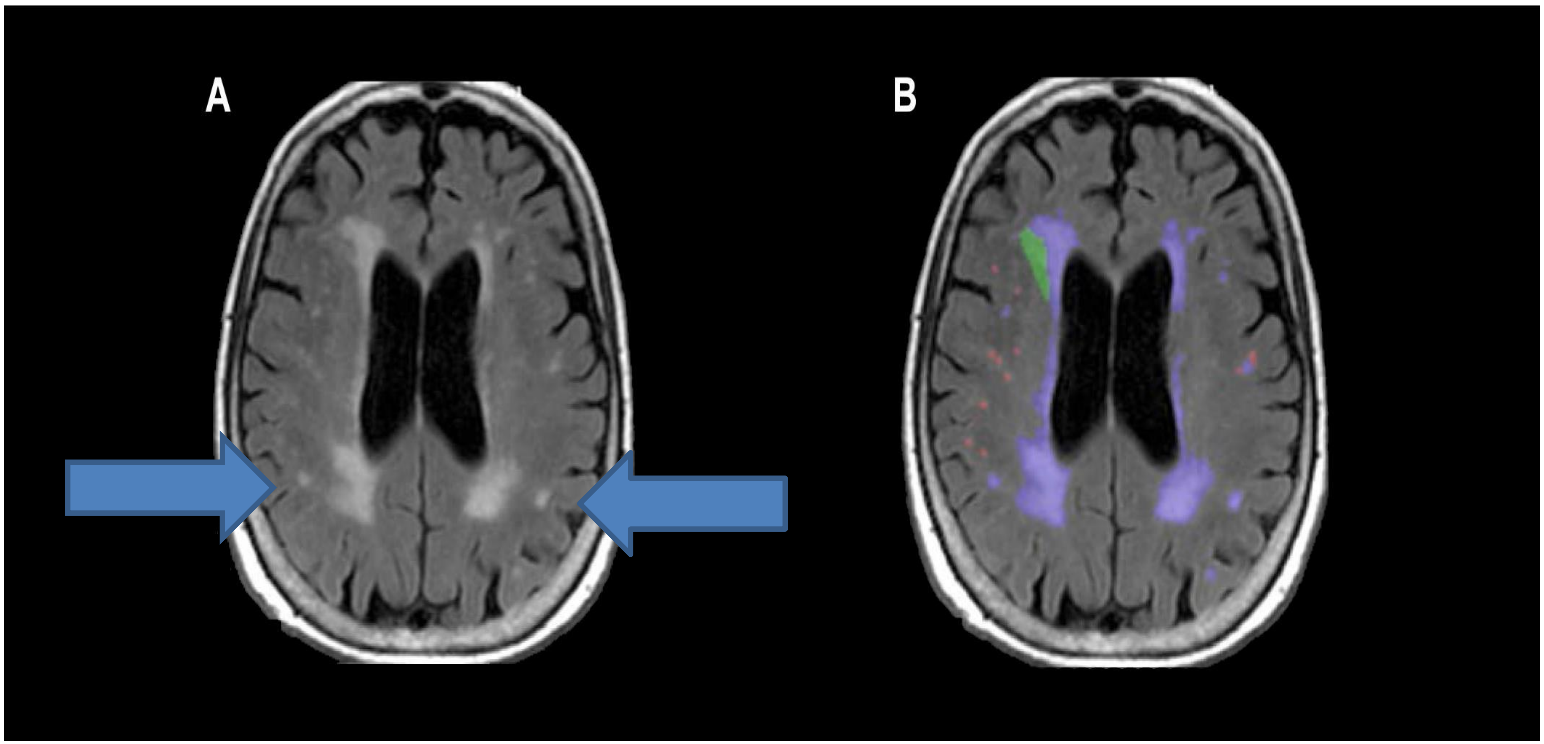
J Cardiovascular Electrophysiol 1995: 6:69-74
Levy, Novella , Ricard & Paganelli

- AF 4% of adults > 60yo
- 25-62% are PAF
- In cryptogenic CVA extended monitoring 19% PAF within 72 hours of CVA

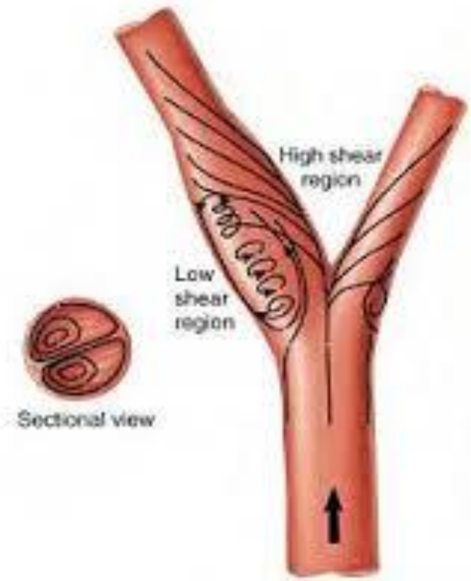
ATRIAL FIBRILLATION IN OSA

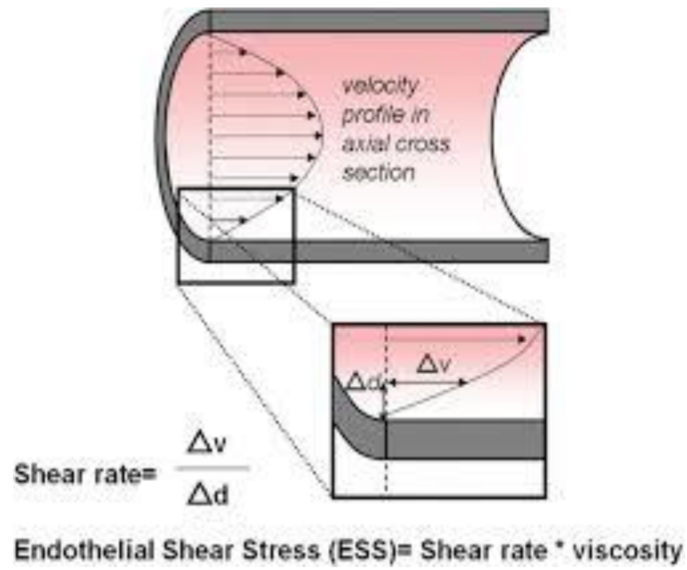


NEUROVASCULAR CONSEQUENCES

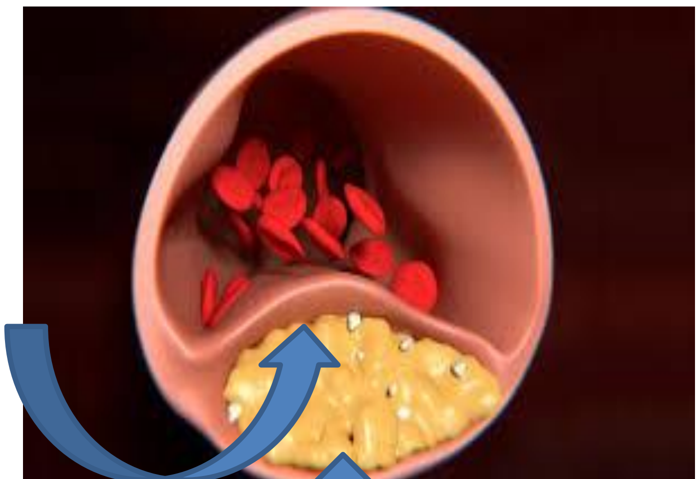


ACOUSTIC TRAUMA



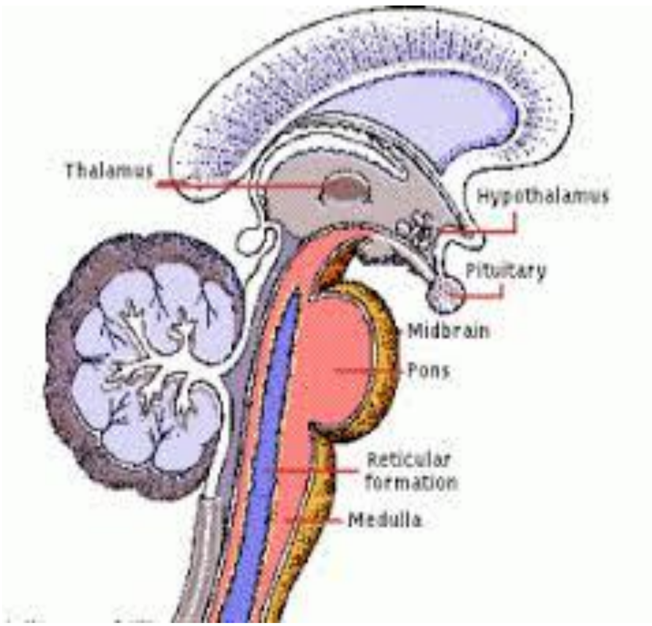


CAROTID ARTERY DISEASE



SUB-INTIMAL DEPOSITION

CEREBRO-MICROVASCULAR

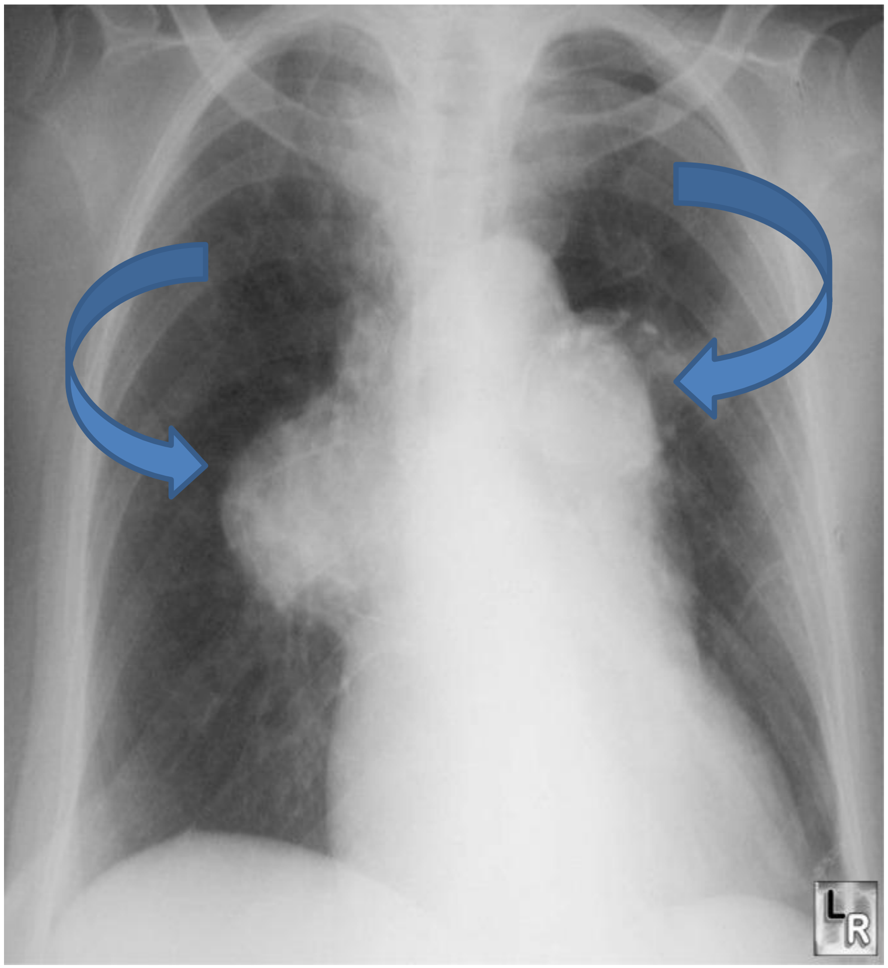


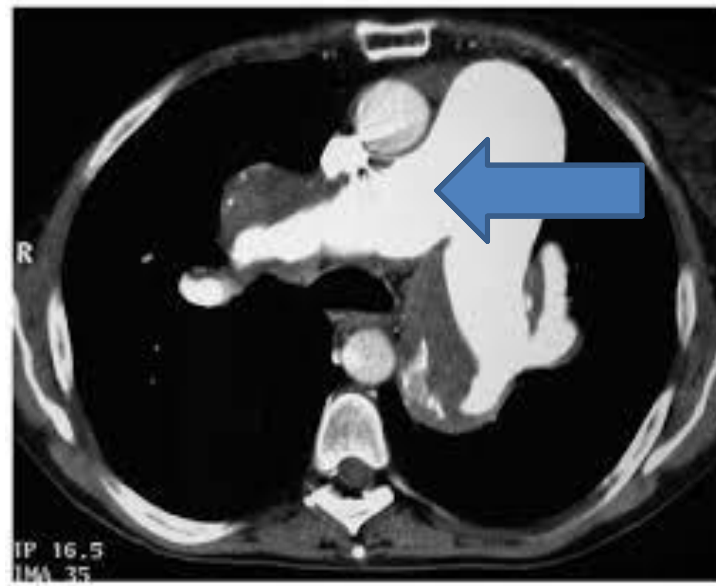
- **Microvascular**
- **Decreased CO**
- **Metabolic (DM2) Neuropathy**

RESPIRATORY INSTABILITY

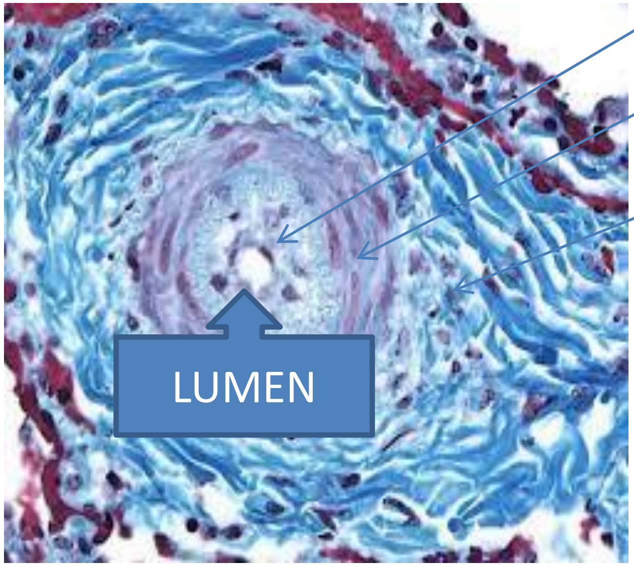
1. **CSA**
2. **Progression of CVD**

Pulmonary Artery Hypertension





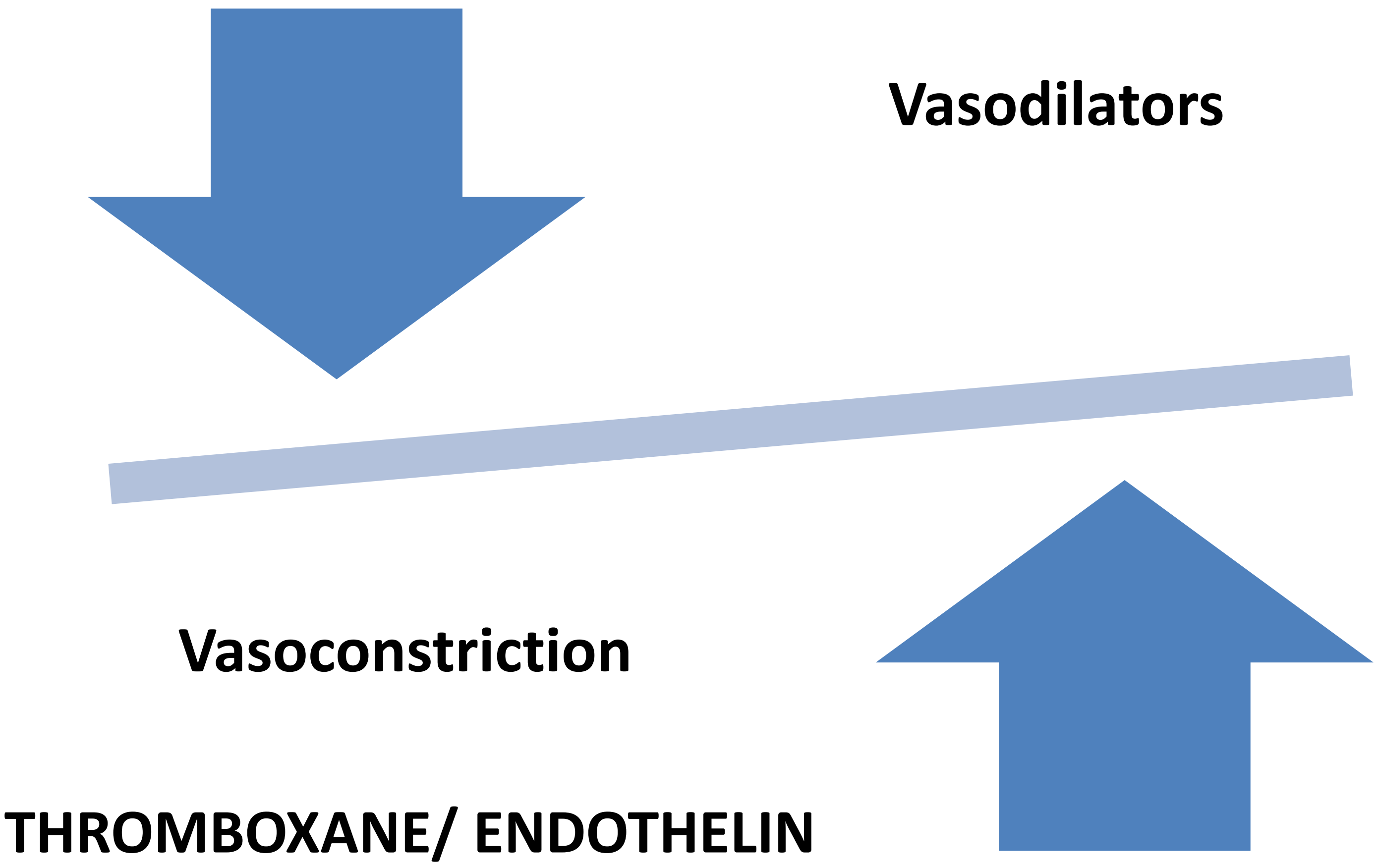
Pulmonary Artery Hypertension



- Endothelial Thickening
- Muscularization
- Increased Adventita

- ALL OF WHICH CAN BE THE RESULT OF UNTREATED OSA WITH HYPOXEMIA !!

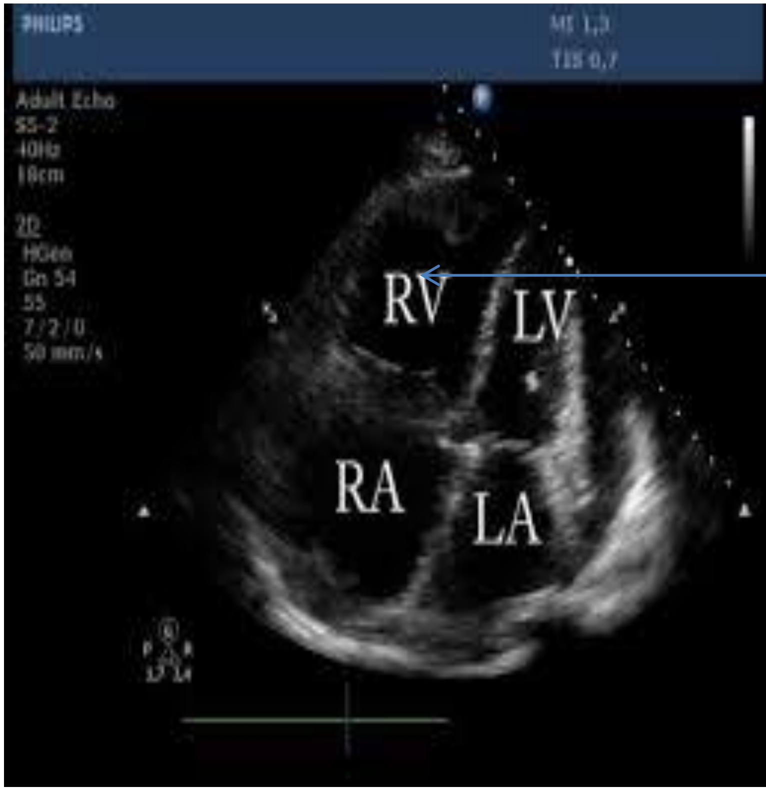
Pulmonary Vaso-reactivity

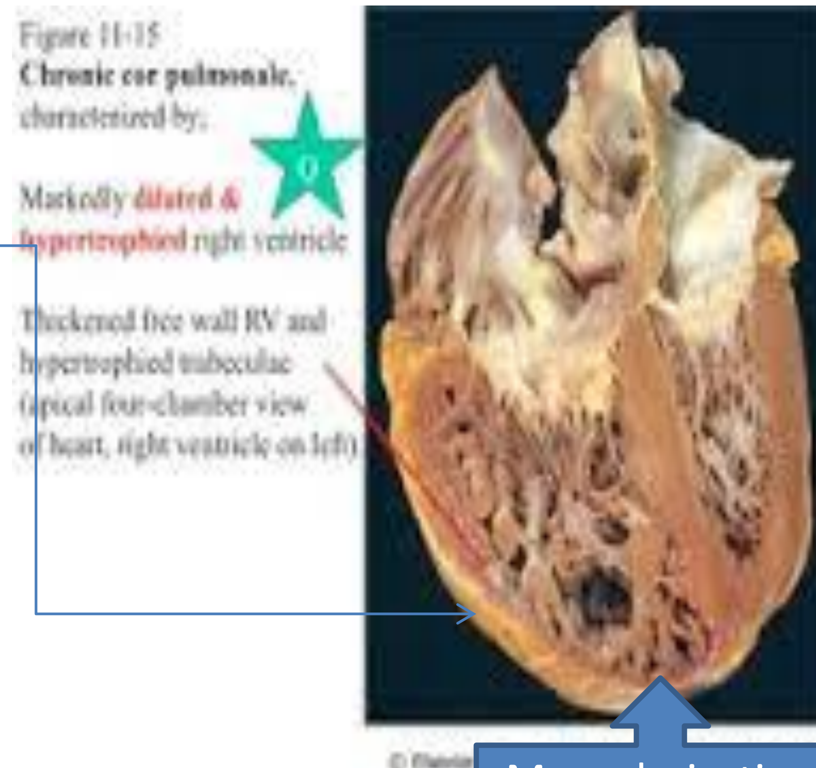


“Pulmonary Artery hypertension begets Pulmonary Artery Hypertension”

Robbins Textbook of Pathology

Cor Pulmonale





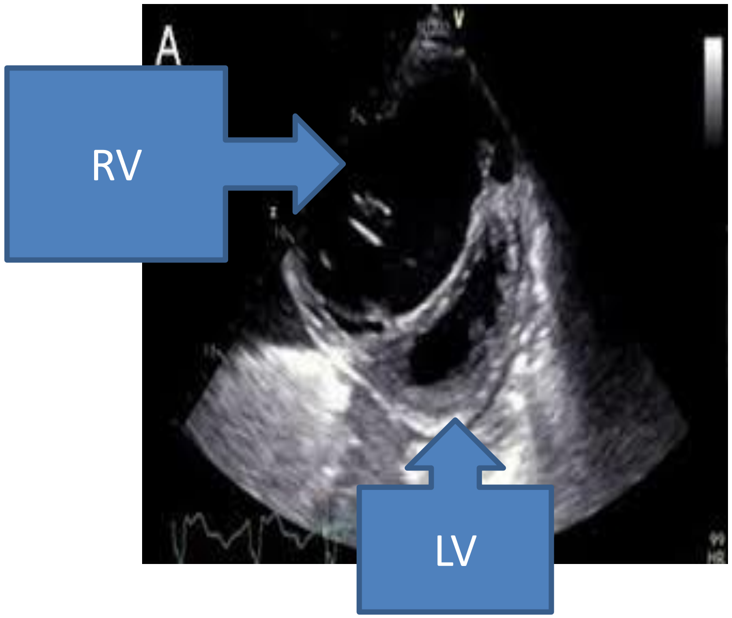
Muscularization of RV

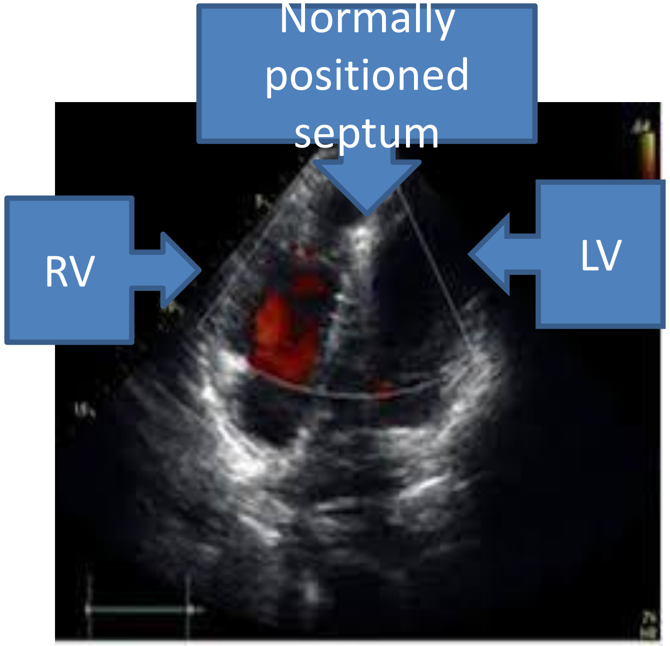
NOTE THE DIFFERENCE IN RV VERSUS LV
RV > LV . RA > LA !

Cor Pulmonale

- Centripetal Obesity
- Peripheral edema
- Lower extremity venous stasis
- Gynecomastia
- ? Ascites (Anasarca)
- JVD
- Thready peripheral pulse

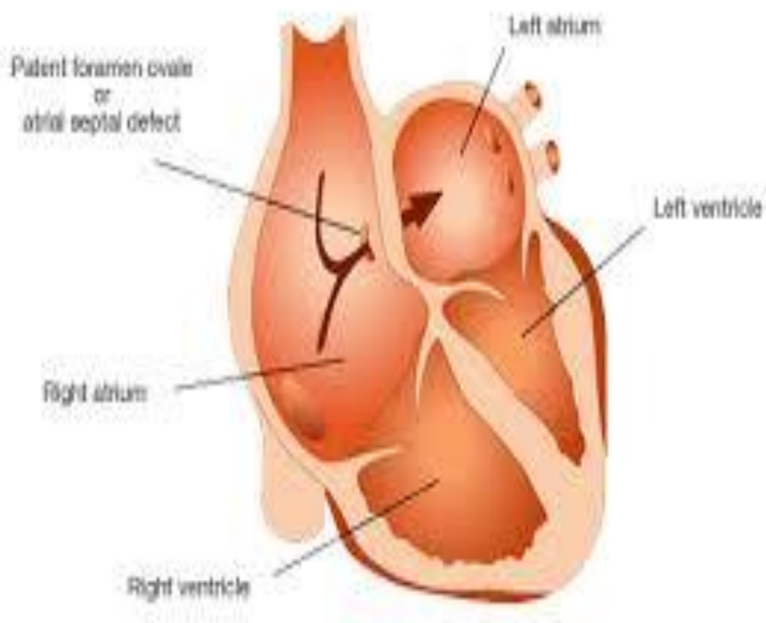
Ventricular Interdependence





Septum assumes a “D” shape Compressing the LV . Creating outflow obstruction !

Patent Foramen Ovale (PFO)



- **Increased incidence in PAH**
- **Most common Congenital ASD**
- **Right-to-Left Shunt**
- **Paradoxical Embolus**
- **Increased Aa gradient; Shunt**

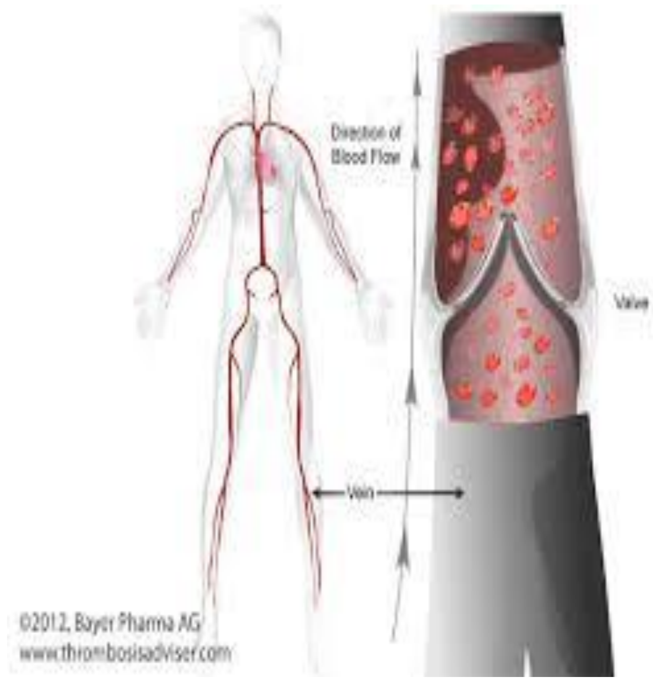
OSA and PE

- Each 10u increase in AHI increases risk 45%
- Obesity ….venous stasis and sedentarism
- Obesity increases risk by 60%
- OSA + PE requires more Warfarin than PE without OSA. Increased D Dimers.
- Increased coaguability and decreased fibrinolysis

WHY ?

- Intermittent hypoxia….Increased oxidative stress
- Inflammatory effects….Endothelial effects
- Altered venous flow….Stasis
- Increased platelet activation…Aggregation and clumping
- Decreased fibrinolytic effect

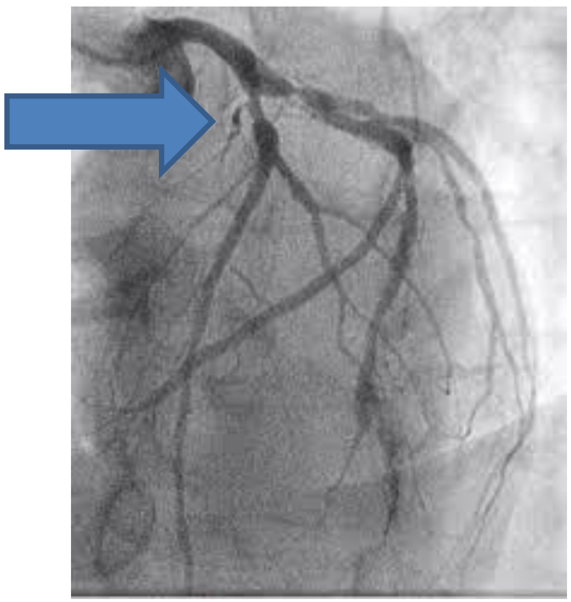
Venous Valves

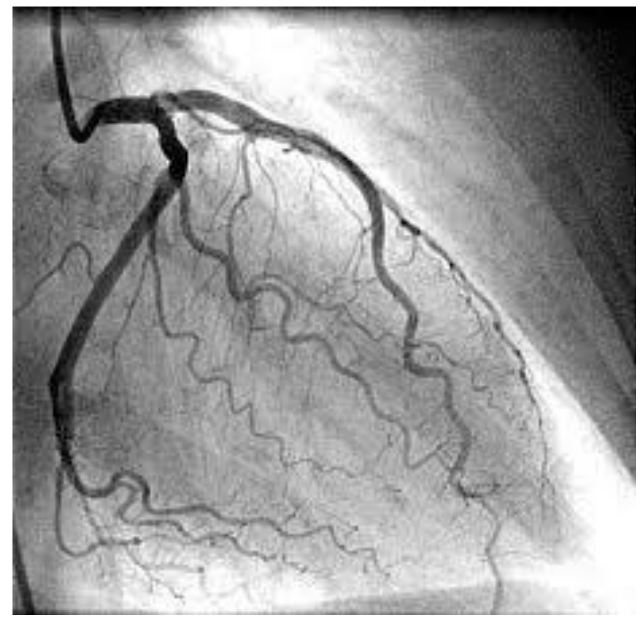


WHY ?

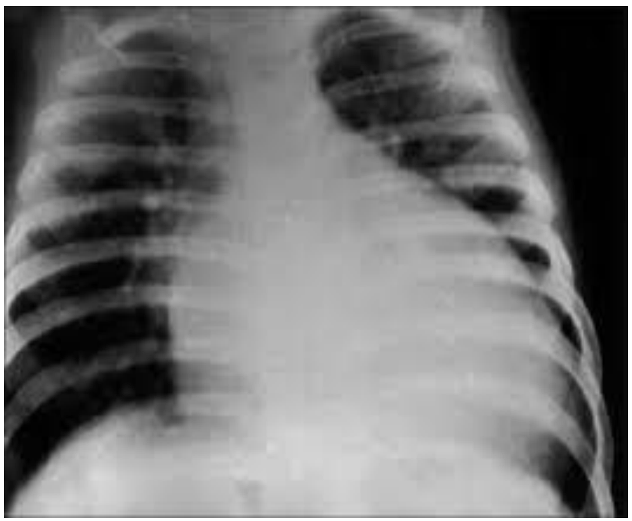
- Intermittent hypoxia….Increased oxidative stress
- Inflammatory effects….Endothelial effects
- Altered venous flow….Stasis
- Increased platelet activation…Aggregation and clumping
- Decreased fibrinolytic effect

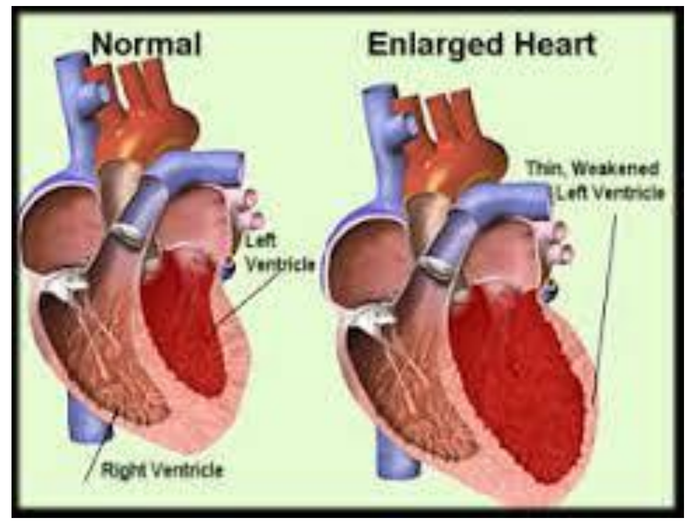
CORONARY ARTERY DISEASE IN OSA



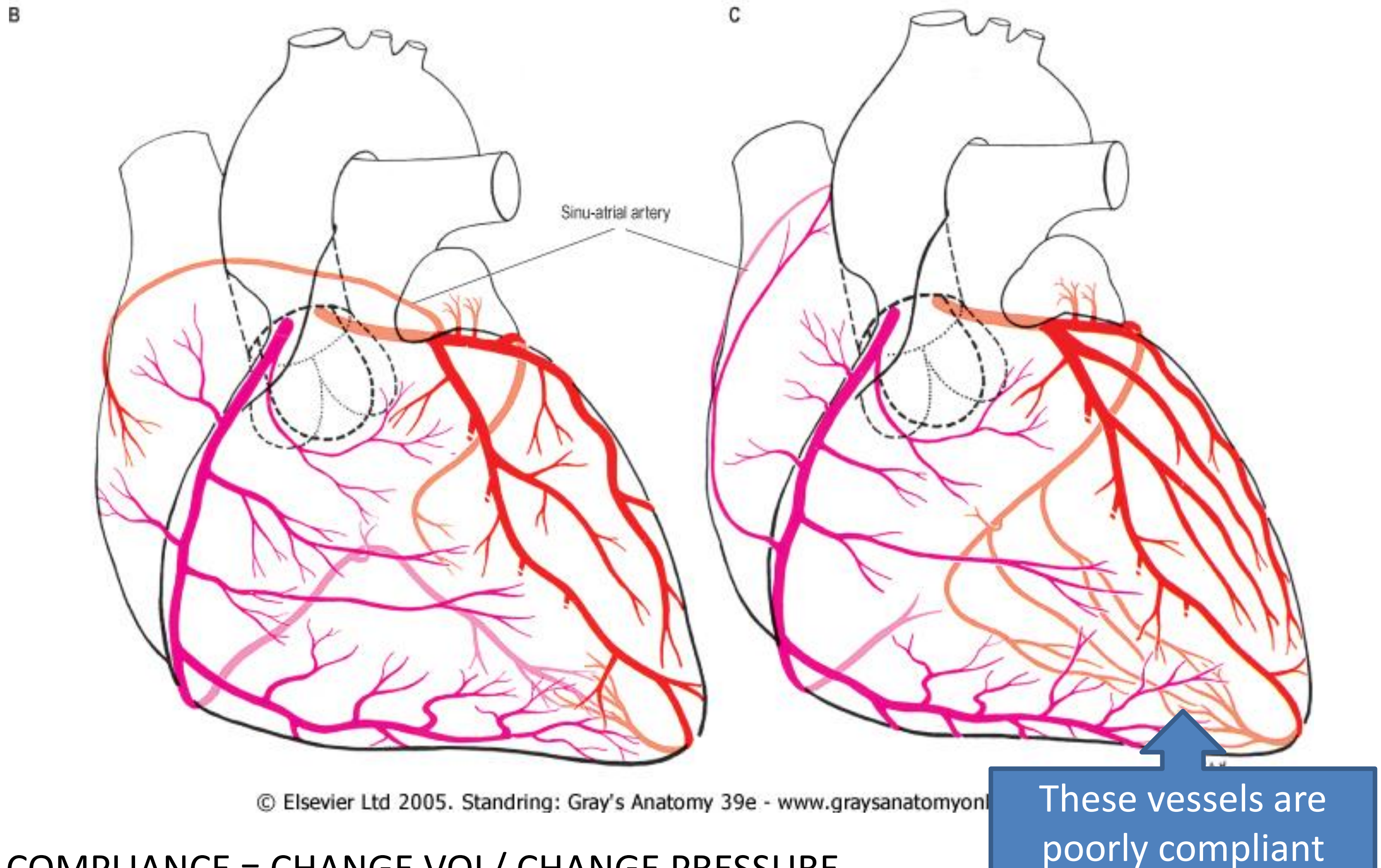


EFFECTS OF CARDIOMEGALY ON MYOCARDIAL PERFUSION





CORONARY ARTERY



COMPLIANCE = CHANGE VOL/ CHANGE PRESSURE

SUBENDOCARDIAL INFARCTION

SUDDEN DEATH….
ISCHEMIC/ARRTHYMOGENIC

SUDDEN DEATH

- GENERALLY REM RELATED
- EARLY AM
- REM …PREDOMINANTLY PARASYMPATHETIC
- OSA…SYMPATHETIC SURGE

Treatment (CPAP/ BiPAP) Works !

“ADMIRAL, I FIND YOUR LACK OF FAITH…DISCONCERTING”
LORD VADER

I AM DONE !