

Consequences of OSA

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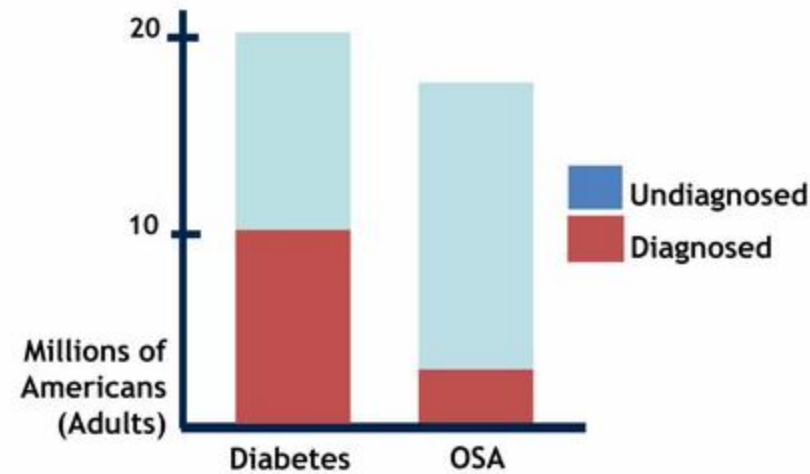
This presentation is an educational material for students of the JLF UK in Martin - elective subject Sleep Related Disorders of Breathing and was created based on resources of teachers working at the JLF UK in the past and present, who have participated in teaching the subject.

Prof. MUDr. Miloš Tatár PhD
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OSA is a Largely Undiagnosed Epidemic

- 18 million suffer (prevalence similar to Diabetes)
- 85% have not been diagnosed

Diabetes and OSA Prevalence is Similar



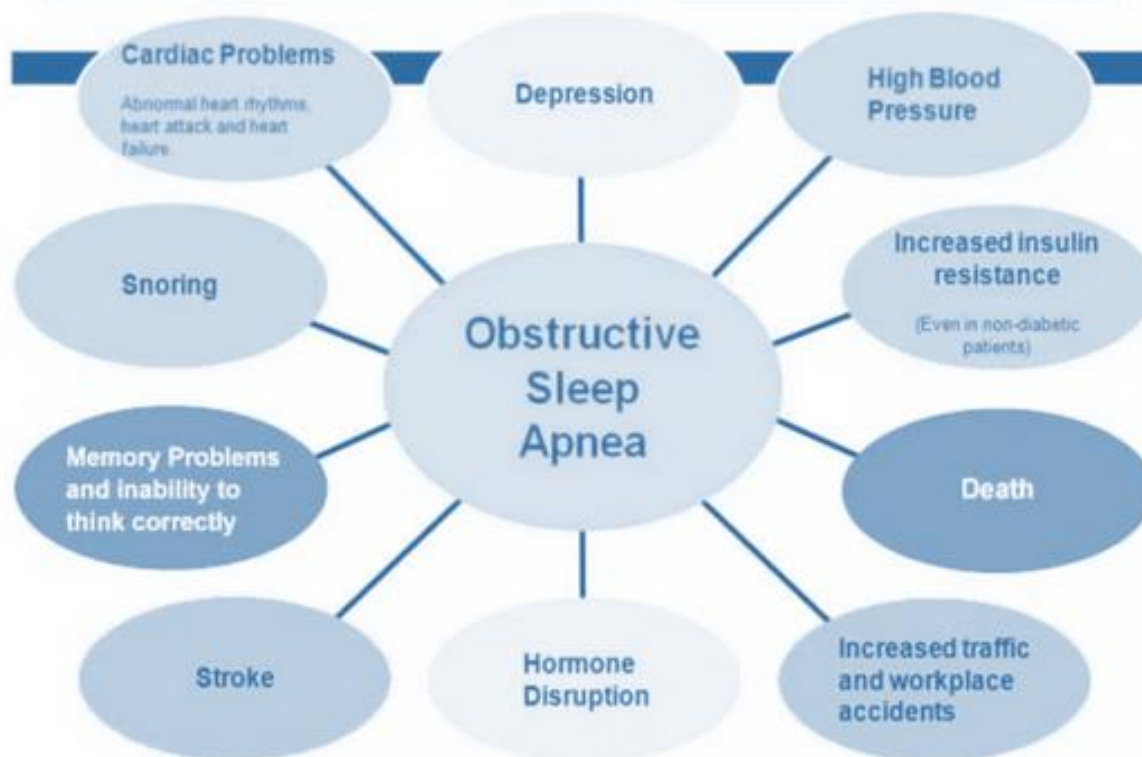
Young 2002, 1997

Sleep related breathing disorders have significant consequences

- Health consequences (onset and progression of secondary diseases)
- Social and psychological wellbeing
- Economic/Financial
- Health consequences are caused by combination of apnoe, desaturation, arousals (sympathetic system activation and thoracic pressure oscillations especially in OSA (not in central apnoe)
 - peracute (e.g. sudden cardiac death)
 - acute (e.g. arrhythmia)
 - chronic (e.g. pulmonary and systemic hypertension)

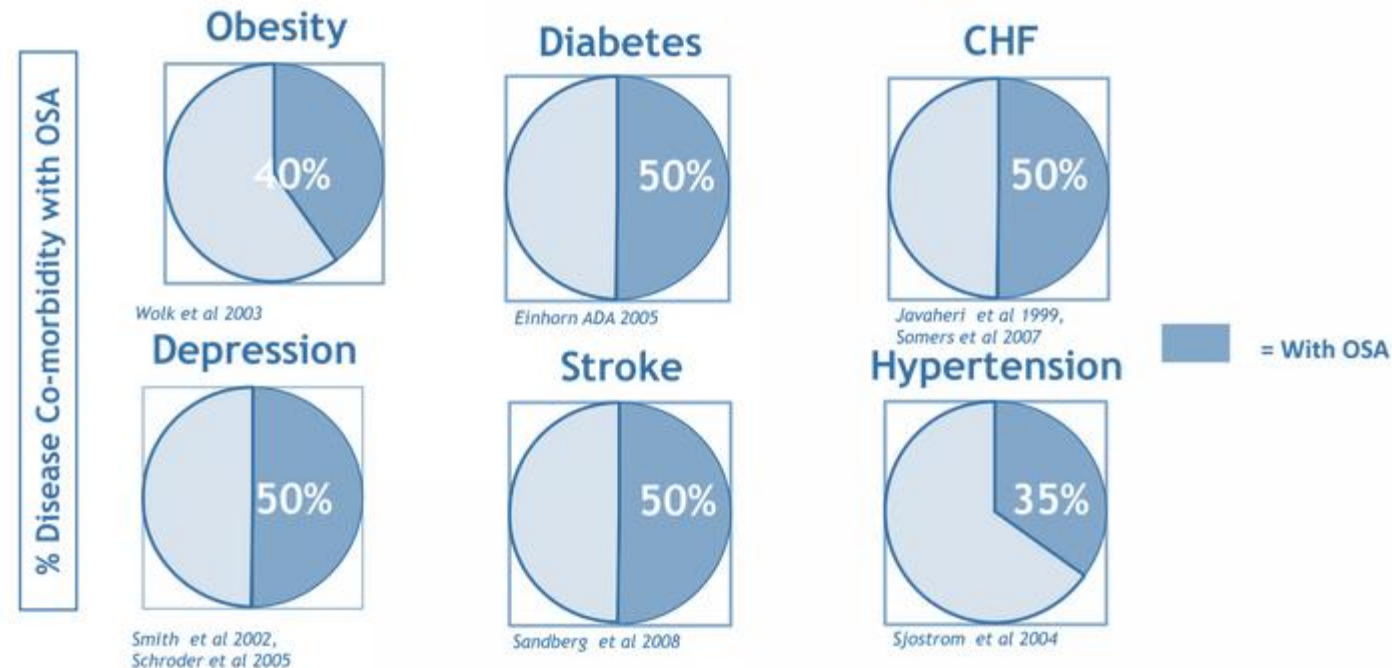
Snoring and Sleep Apnea

What are the effects?



OSA Increases Co-Morbid Health Risks

- OSA is an independent risk factor for HTN & Type II DM



- Left undiagnosed, OSA increases risk of stroke by 2X, risk of fatal cardiovascular events by 5X, and risk of serious vehicular accidents

Sources: Yaggi et al, NEJM 2005; Young et al, Sleep 2008; Teran-Santos, NEJM 1999

Sleep related breathing disorders manifestations

intermittent snoring
evidence of interrupted breathing (apnoe)
interrupted sleep
excessive daytime fatigue
morning headache
problems with concentration and memory
depression
night time sweating
nykturia
dry mouth and throat in the morning
weight gain

Consequences of OSA

- Sleep disorders – fragmentation and interrupted sleep cycles
- Hypoxemia and hyperkapnia
- Changes of cardiovascular function
 - changes of the heart rate: brady-, tachycardia
 - reduced cardiac output
 - **systemic hypertension**
 - pulmonary hypertension
- Changes in the function of central nervous system
- Changes in the function of endocrine system

Neuropsychologic consequences

- Frequent sleep interruption
 - change in the sleep architecture → insufficient sleep
- Abnormal sleep architecture
 - excessive daytime sleepiness: social problems, work performance problems in positions requiring high attention and focus (microsleep while driving – accidents)
- Abnormal mental functions
 - decreased concentration and general lack of interest
 - reduced cognitive functions (memory, creativity...)

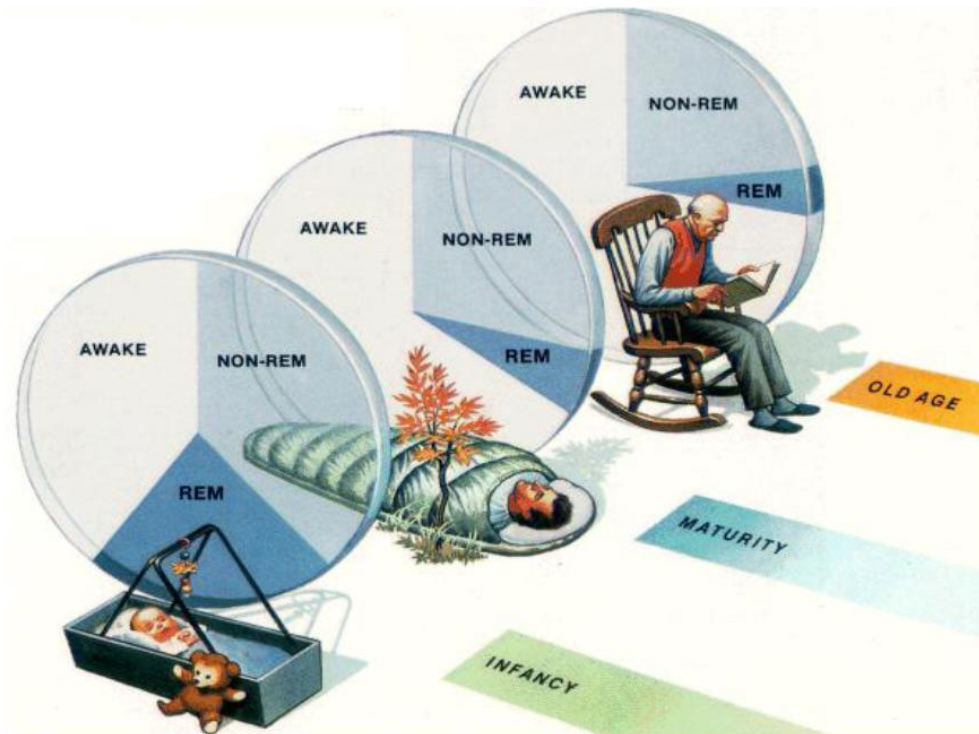
- **Social consequences**

- increased risk of accidents
- limited professional activities
- limited social functions
- marital dysharmony

- **Economic consequences**

- increased cost of unrecognized OSA
- various compensations (accidents etc.)

Sleep fragmentation and REM rebound



REM – rapid eye movement

Paradoxical sleep

Active brain in paralyzed body

Vivid, bizzare, illogical dreams

Increased metabolism (20%)

Muscle paralysis, brain directs movement that is not realized

Increased HR and RR

After deprivation – anxiety, irritability, tremor, slurred speech

Deprivation compensation - total

NonREM

SWS – slow wave sleep

Orthodox sleep

Resting brain in moveable body

Decreased metabolism (10-30%)

Somnambulism

Somnilokvia

Without eye movement

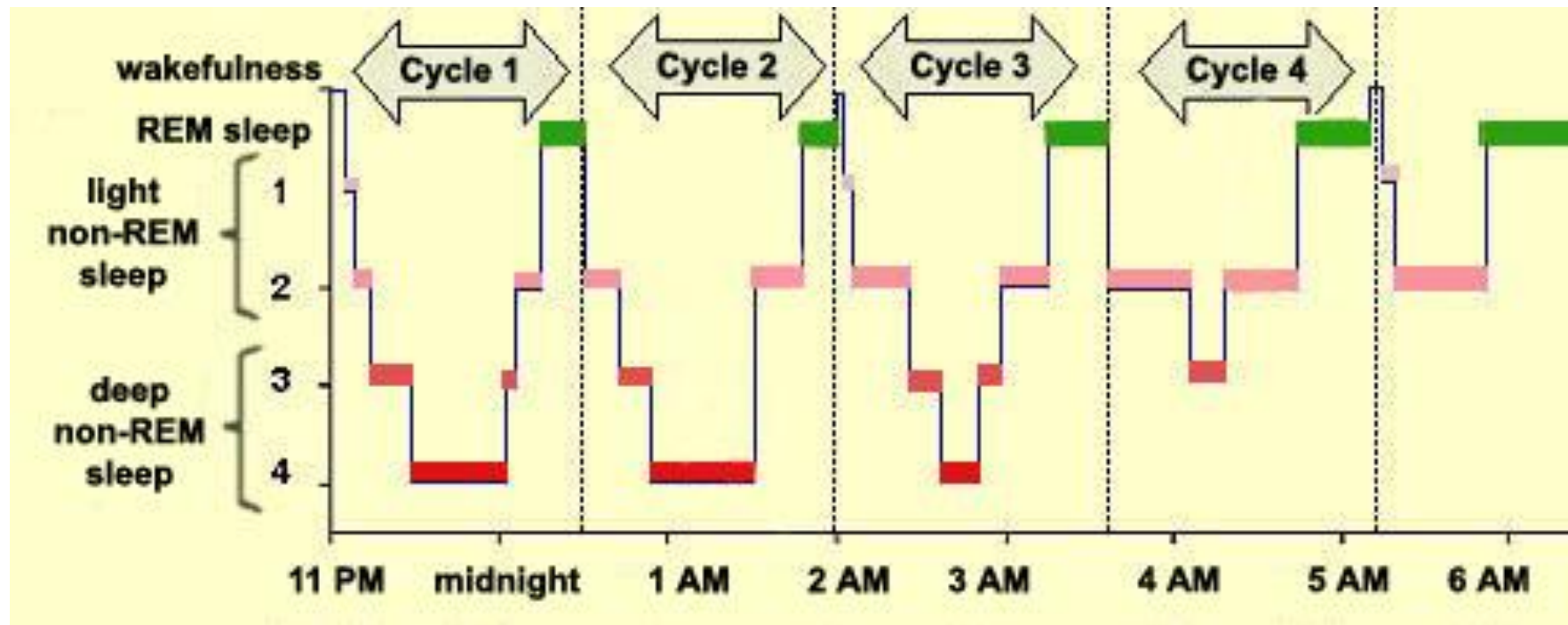
Decreased HR and RR

EEG – increased voltage, slow waves

Logically coherent thoughts

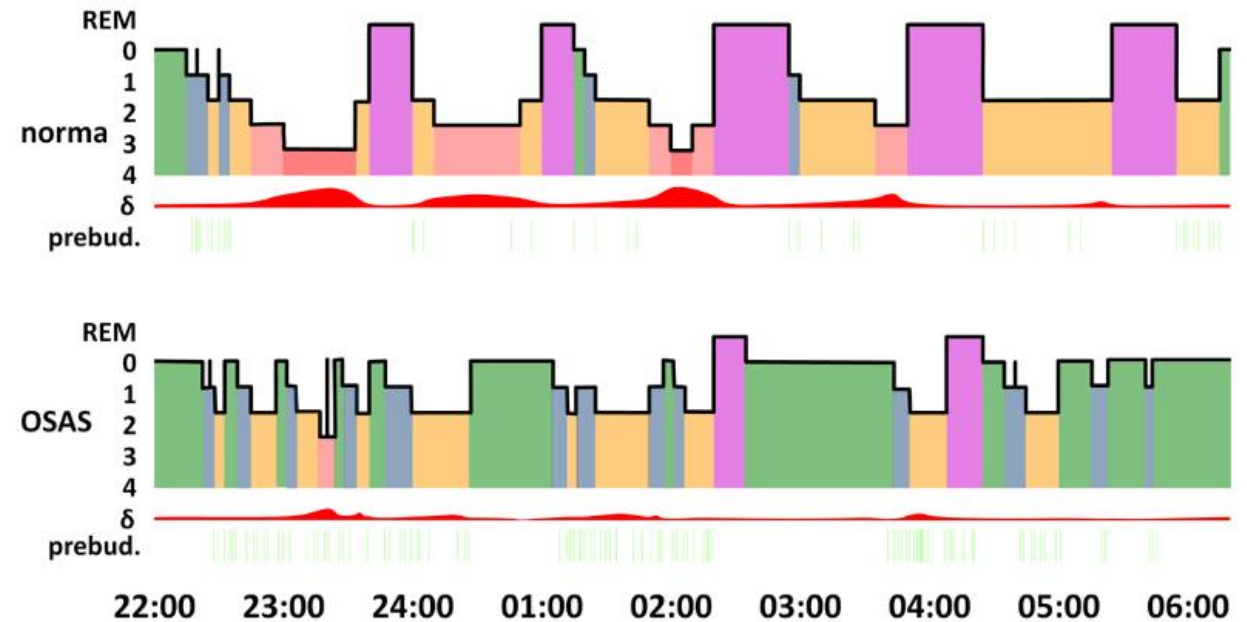
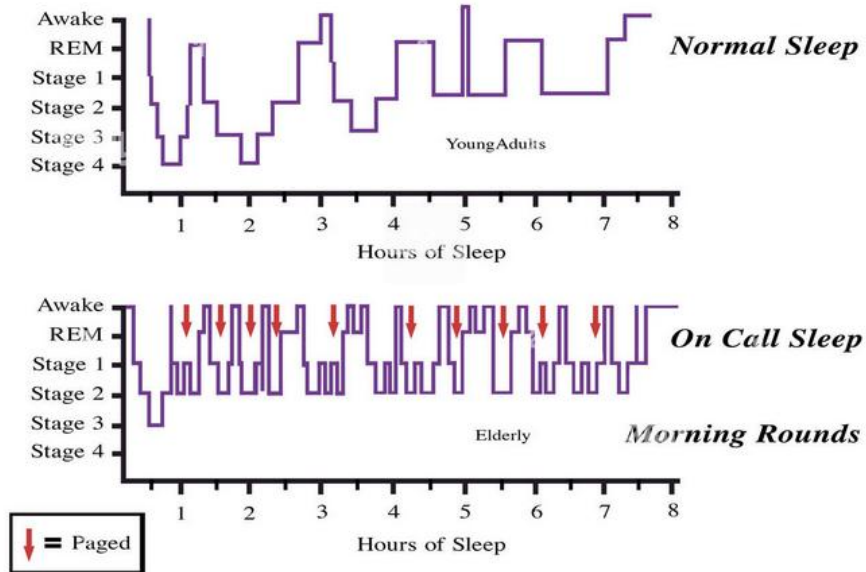
Deprivation compensation - partial

Comparison of normal and fragmented sleep pattern



Comparison of normal and fragmented sleep pattern

Sleep Fragmentation Affects Sleep Quality



Sleep fragmentation and REM rebound

Sleep is necessary to organism revitalization – either by its duration as well as cyclic pattern and potential for full rest (presence of deep sleep)

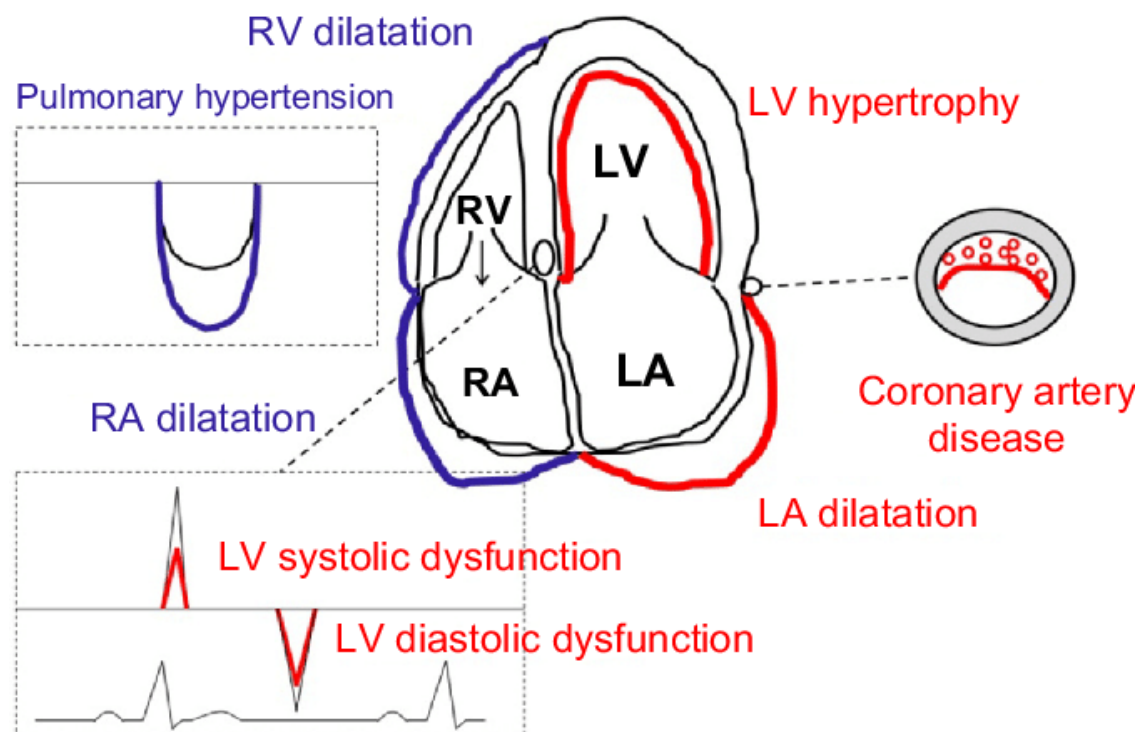
In an OSA patient the cyclic pattern disappears, many arousal reaction following apnoea are present that do not allow reaching deeper stages of sleep

Proportion of shallow NREM sleep increases, deep sleep is often completely absent, missing REM

REM as well as other sleep stages represent biological necessity and if its lacking, the brain favours it whenever possible - REM rebound

REM rebound represents prolongation, increased frequency, and depth of REM sleep that is observed after a period of sleep deprivation and is being reached faster than usual

Cardiac consequences



Pulmonary hypertension and disorders of right ventricle function

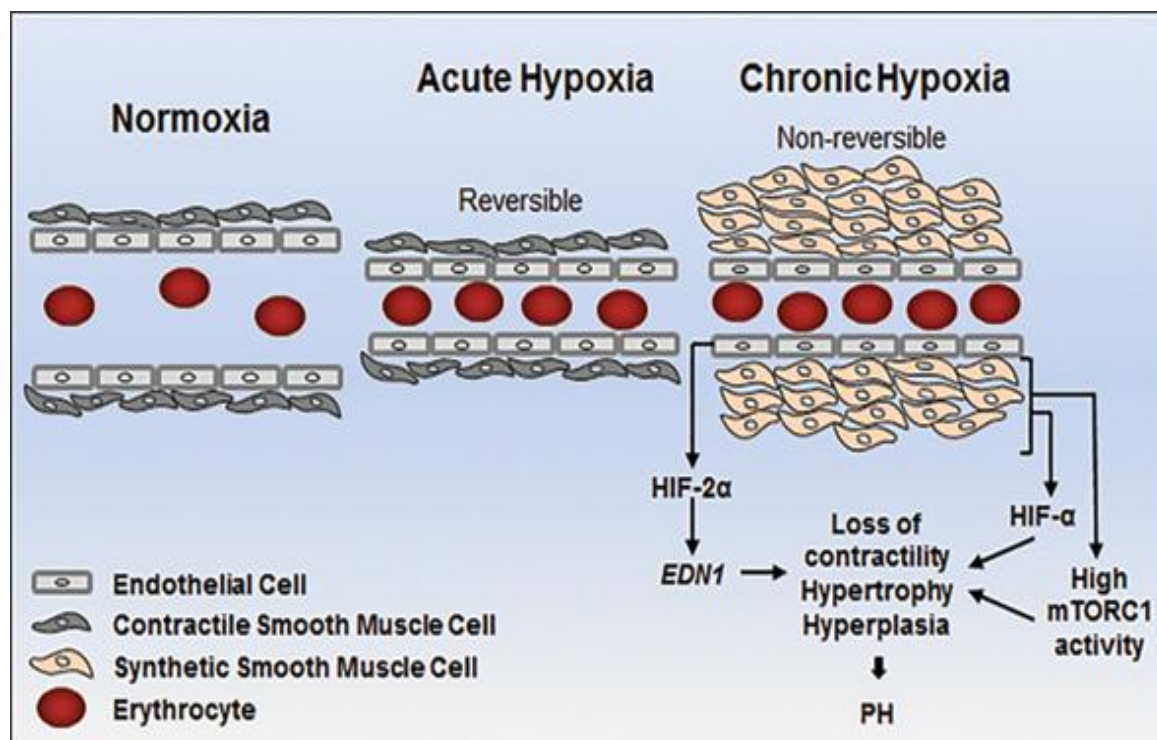
- Pulm. circulation is physiologically low-pressure, low-resistance and capacious
- Resembles venous circulation in many aspects
- Therefore, right ventricle has lower afterload compared to LV
- Pulmonary perfusion is regulated by PaO_2 , to be adequate to ventilation (V/Q ratio)

- **Repeated desaturations and hypercapnea during the night**

Hypoxemia leads to vasoconstriction in pulmonary circulations (functional increase in resistance), later morphologically fixed (remodelling of pulmonary arterial wall)

- pulmonary hypertension → RV strain → insufficiency due to increased afterload
- potentiated by muscle hypoxia due to present desaturations

Pulmonary hypertension and disorders of right ventricle function

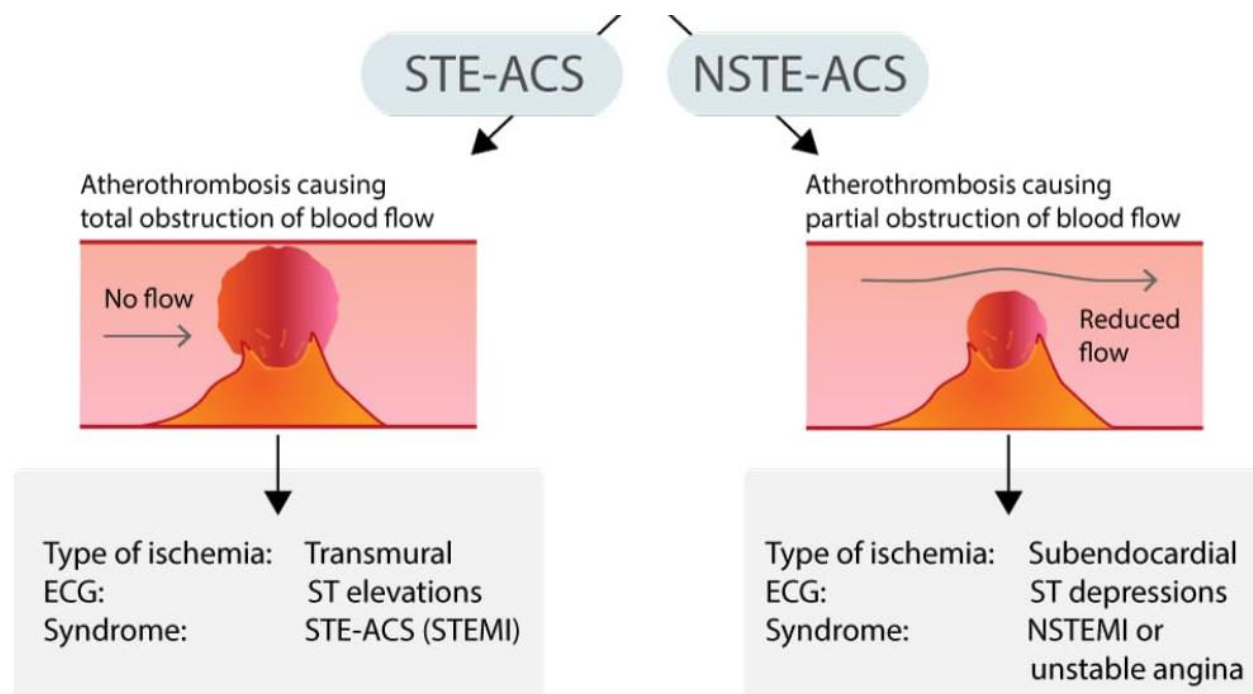
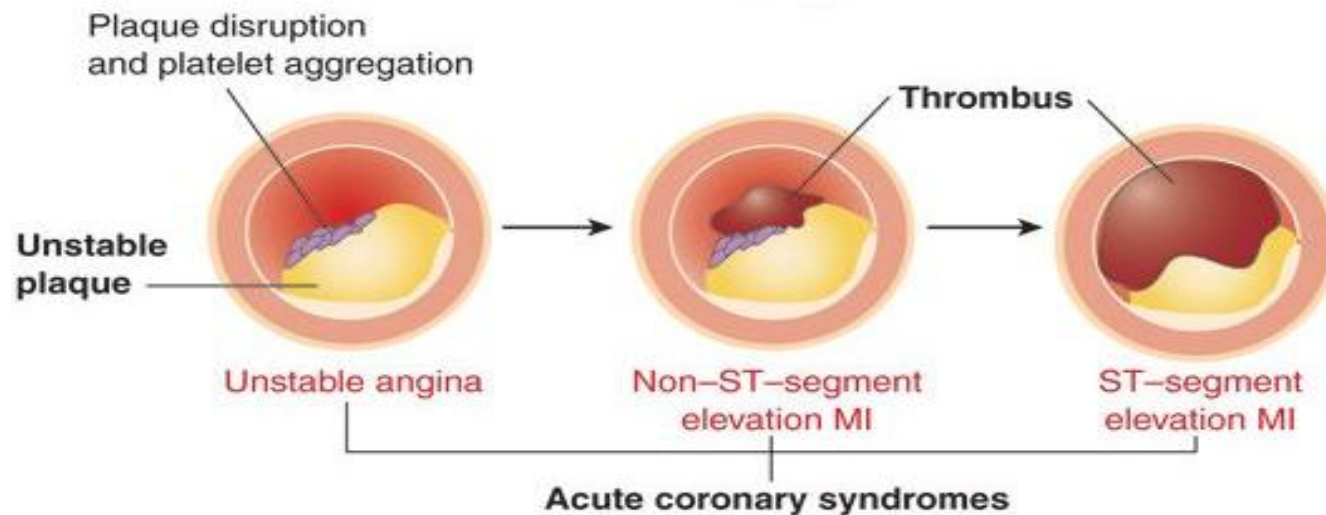


Disorders of left ventricle function

- Insufficiency:
 - Temporary/permanent systemic AH represents increased afterload (pressure overload)
 - Ventricle reacts to increased afterload by concentric hypertrophy
 - Hypertrophy – intended as compensatory mechanisms – begins to represent a problem
 - Decreased perfusion in simultaneously increased demands to O_2 delivery by hypertrophic LV
 - Decreased diastolic function (disturbance in relaxation and decreased compliance of LV wall)
 - Decreased contractility

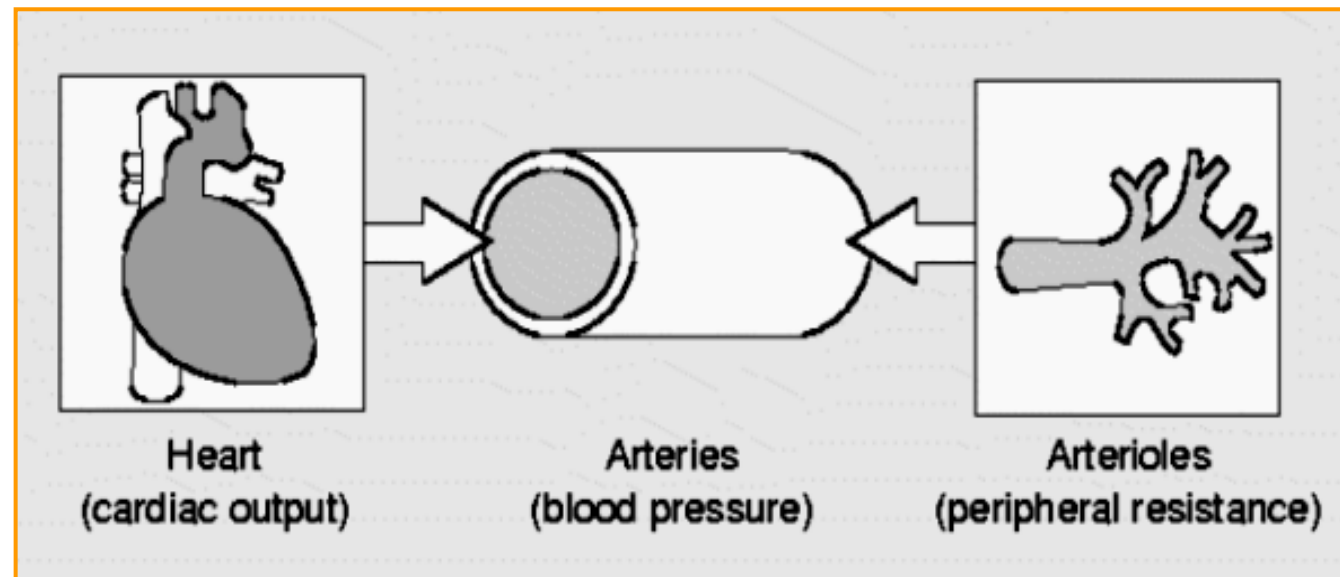
Ischemia and myocardial infarction

- MI does not happen in otherwise healthy individual, just because they have OSA !!! There must be also some other factors which are usually risk factors for both conditions (e.g. obesity) and/or some degree of stenosis of coronary arteries in subjects with general cardiovascular risk factors (age, sex, obesity, hyperlipidemia, smoking...)
- subcritical occlusion of coronary artery + obstruction (collapse) of the upper airways
 - hypoxemia → increased activity of the SNS → increased myocardial O_2 consumption
 - ↓ of intrathoracic pressure → ↓ of ejection fraction → ↓ coronary perfusion



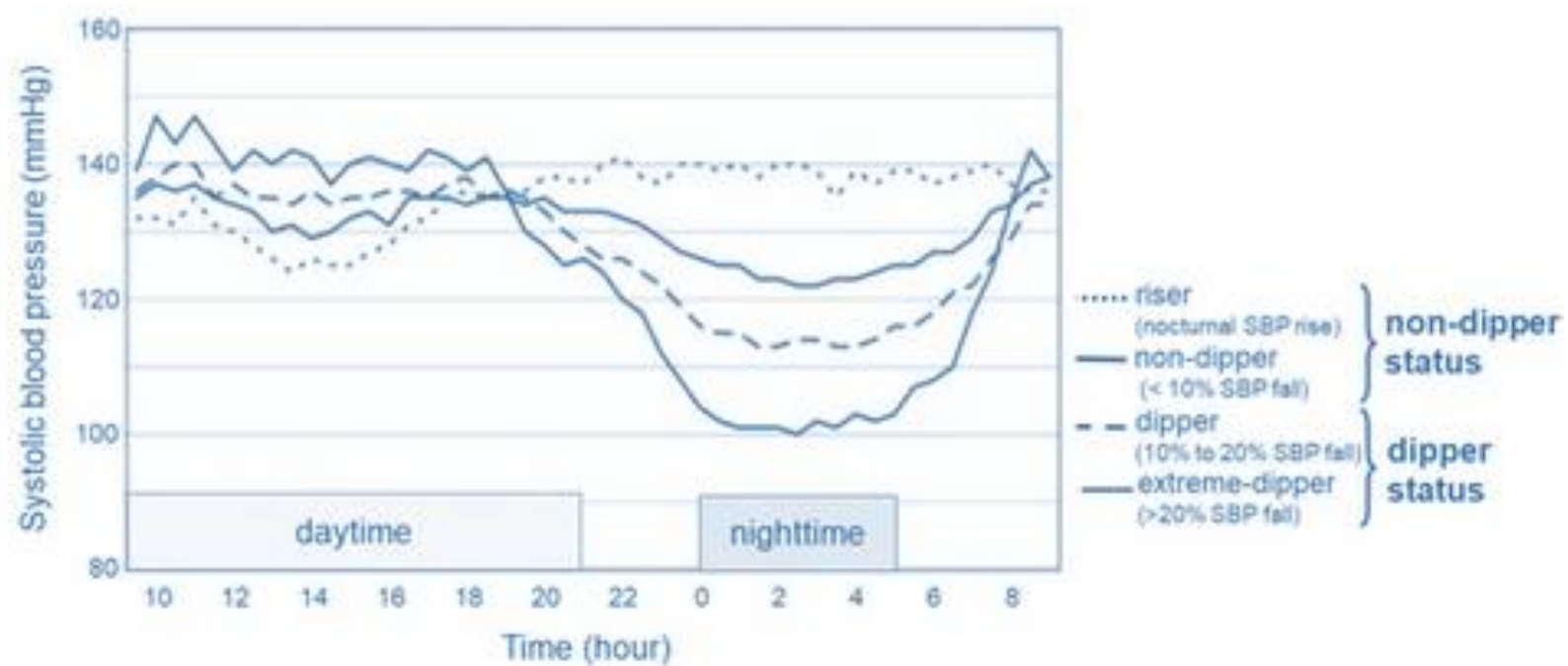
Secondary hypertension

- Determinants of blood pressure are cardiac output and peripheral vascular resistance
- Blood pressure is a lateral pressure on the vessel wall and it determines organ perfusion (via MAP) and regulatory functions of the endothelium
- Increased values of blood pressure (hypertension) have consequences for the heart, brain, vessels, kidneys, retina, this increasing morbidity and mortality



Main pathomechanisms of hypertension in OSA

- Effect of hypoxemia and hyperkapnia on sympathetic activity
- Decreased sensitivity of baroreflex mechanism
- Impact of intrathoracic pressure fluctuations on sympathetic/parasympathetic function in OSA
- Generalized stress caused by multiple arousals and sleep interruptions
- Changes in the function of endothelial cells and remodelling of arterial wall due to hypoxemia and increased sympathetic tone:
 - ROS, endothelin, angiotensin
 - reduced production of NO
- **Secondary hypertension in OSA is non-deeper non-responder type of hypertension**



Disturbances of the heart electrophysiology

- Each of the arousals represents strong stimulus for the activation of SNS, which is associated with tachycardia and high risk of tachyarrhythmias such as SVPB, VPB, SVT, VT, a-fib or a-flutter
- Also bradycardia may result from intense stimulation of the vagus nerve
 - negative intrathoracic pressure and its oscillations stimulate vagus nerve, which has inhibitory effect on production and conduction of impulses

Mechanisms of arrhythmia in OSA

Direct

- hypoxia/hyperkapnia
- sympathetic/parasympathetic NS
- changes of intrathoracic pressure

Most common arrhythmias in OSA

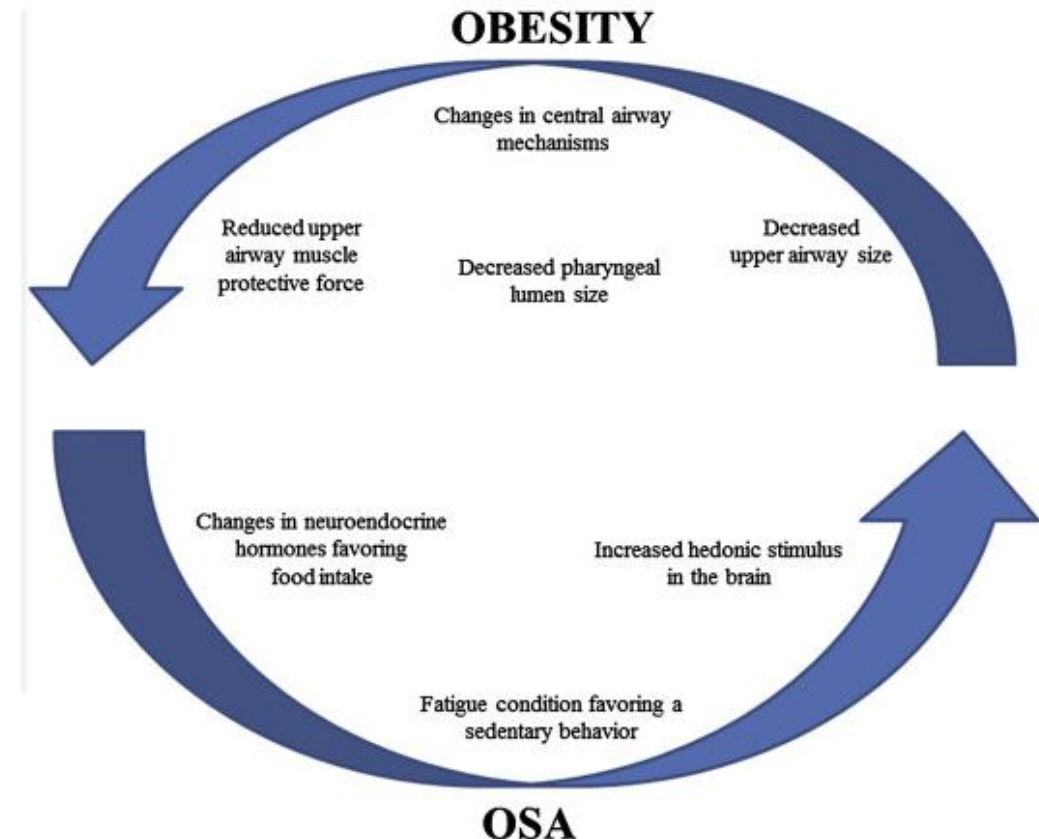
- Sick sinus syndrome
- A-fib
- V-tach

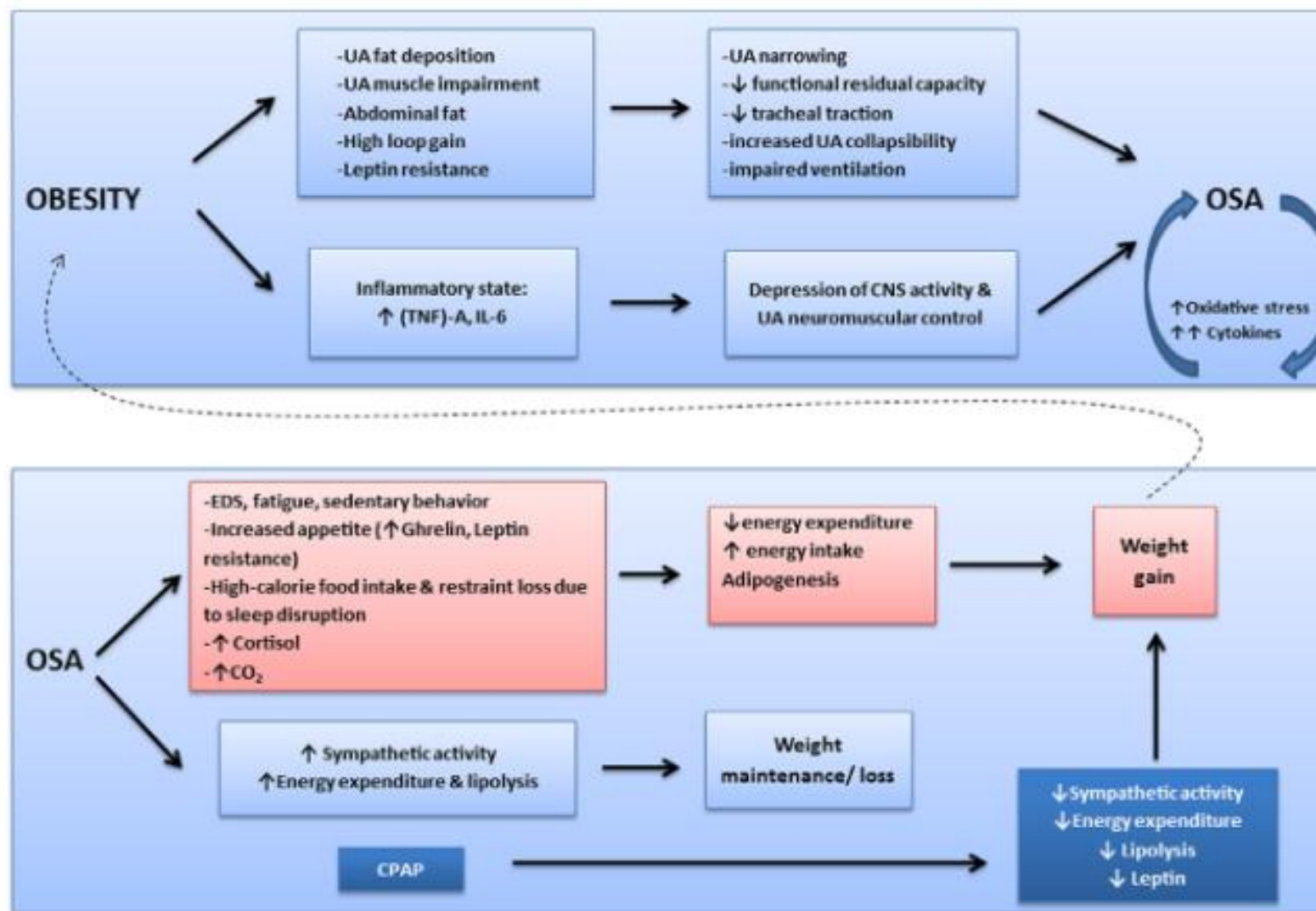
Indirect

- Onset and progression of cardiovascular diseases e.g. hypertension or chronic heart failure, which lead to the heart remodelling thus increasing the risk of onset of arrhythmogenic substrate

Obesity and OSA

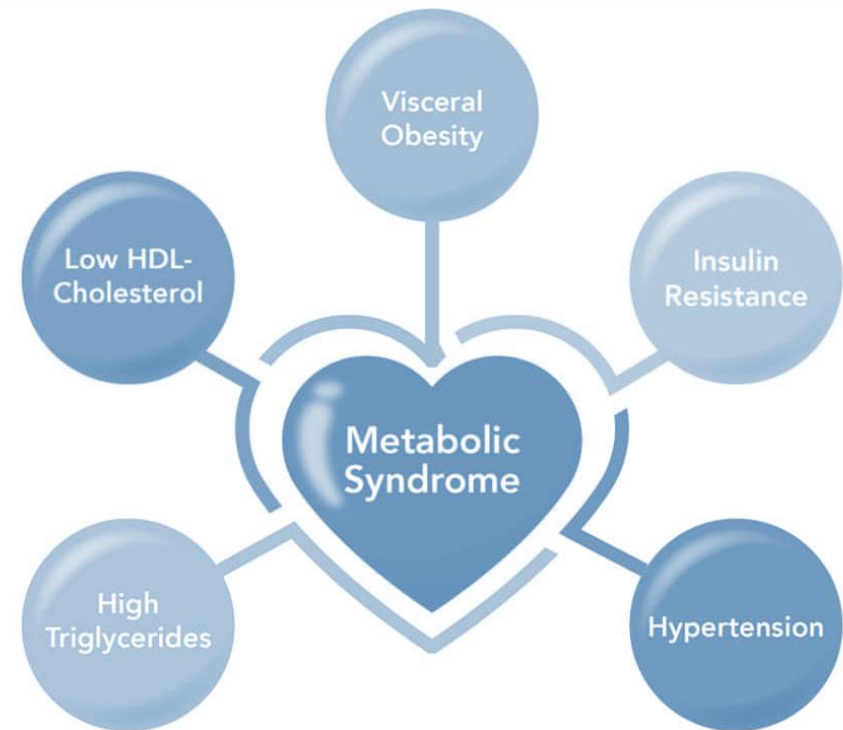
- Obesity – fat neck type is a strong risk factor for OSA development
- As well as visceral fat accumulation that increases diaphragm position
- On the other hand OSA patients have a tendency to weight gain
 - Ghrelin secretion impairment
 - Increased cortisol production
 - Metabolic syndrome association

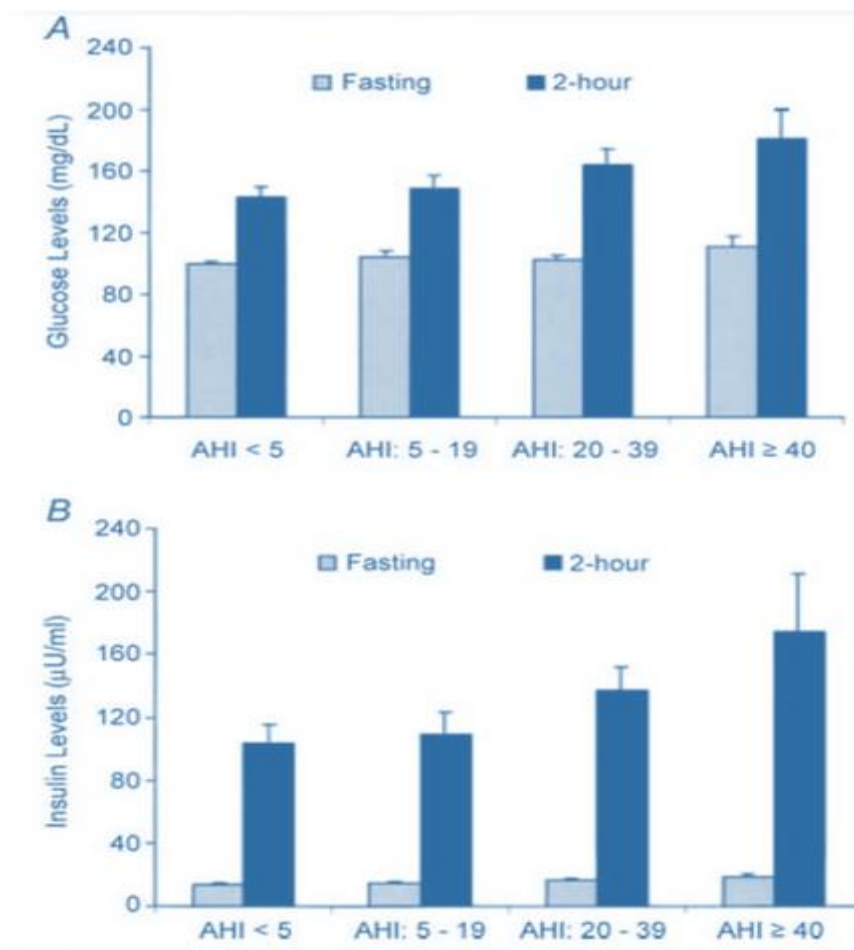




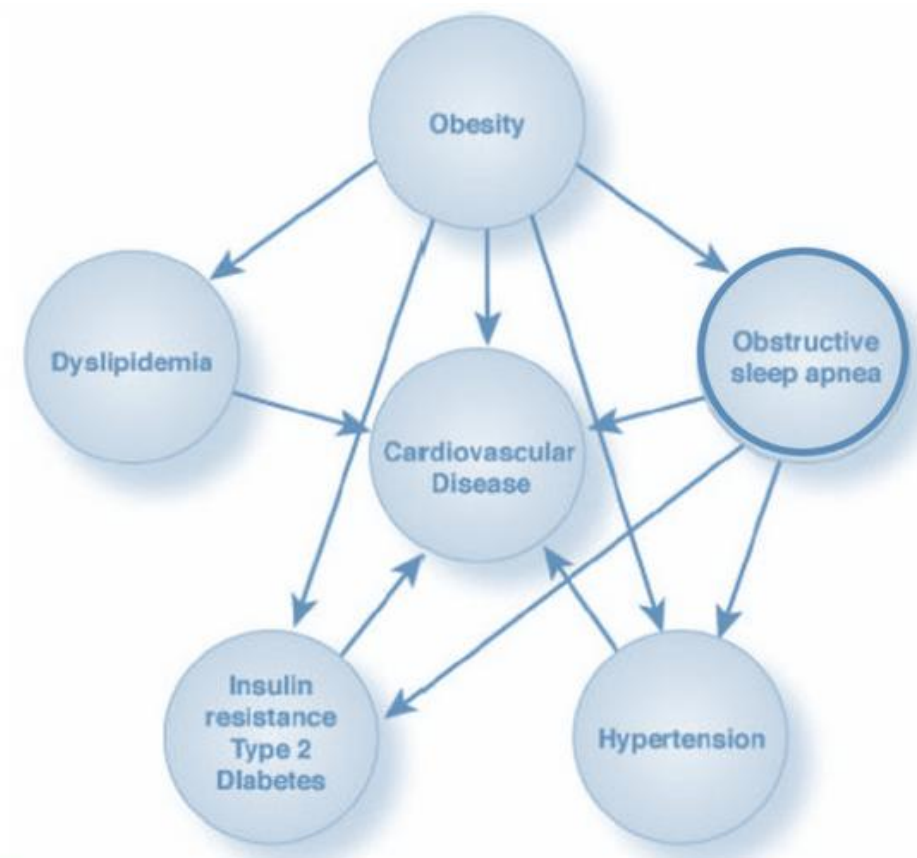
Syndrome Z

- **Metabolic syndrome and OSA association**
- Fasting hyperglycaemia
- Hyperlipidaemia and dyslipidaemia
- Hyperinsulinaemia
- Insulin resistance
- (Hirsutism)
- Central type obesity (apple)



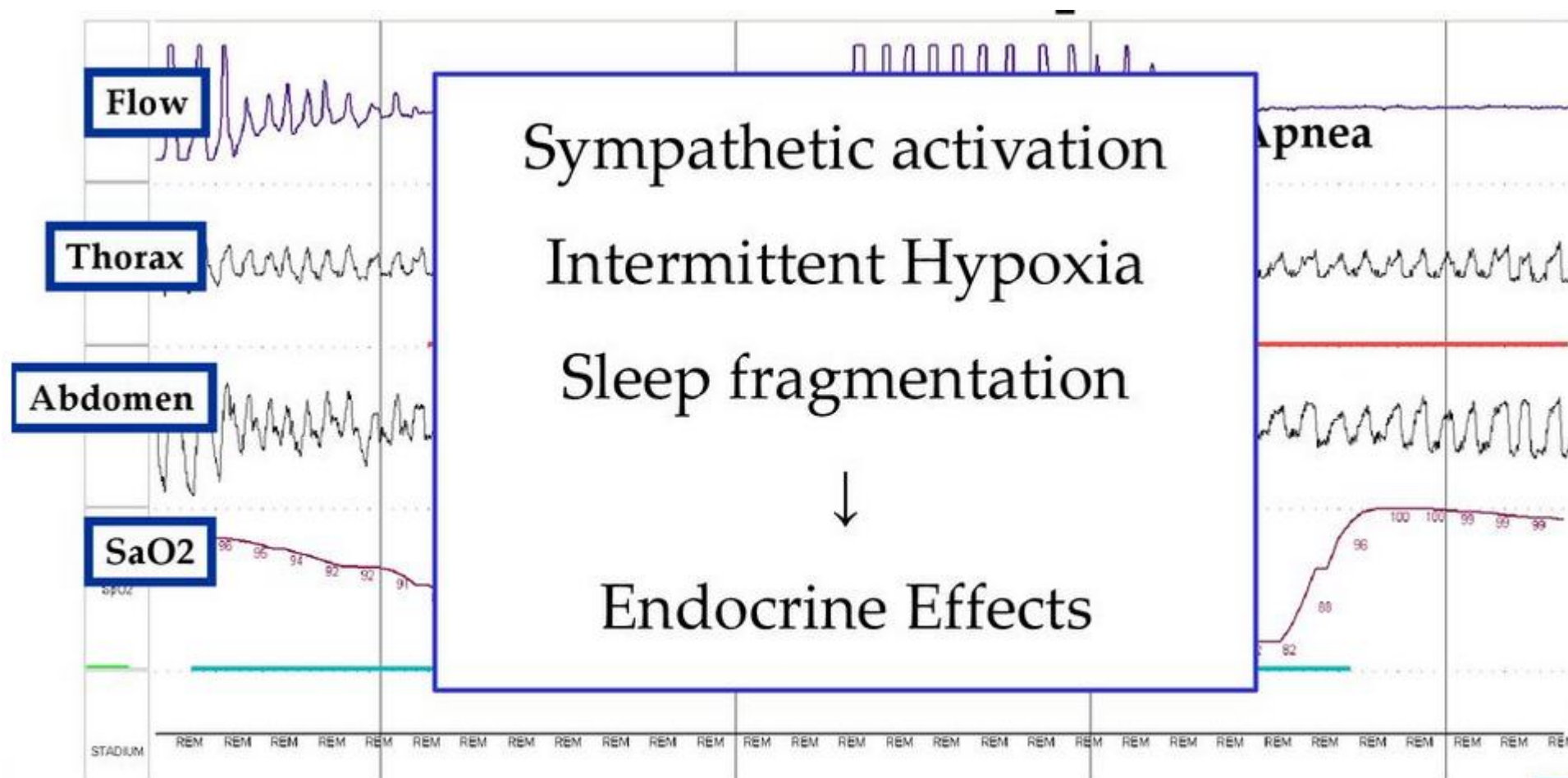


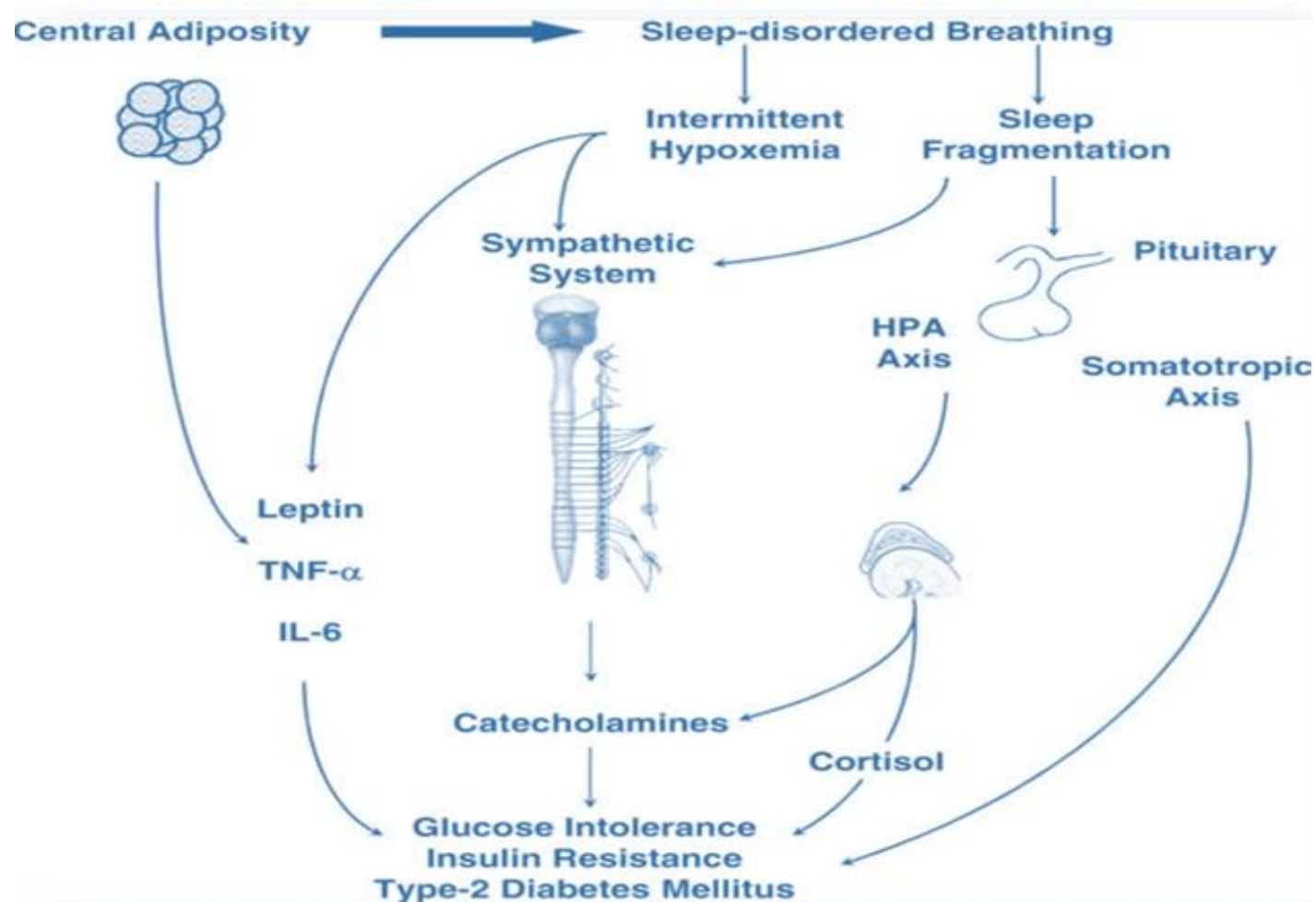
Glucose and insulin levels increase in proportion with OSA severity



Parish JM, Chest 2009

Combination of metabolic syndrome and OSA was named syndrome Z

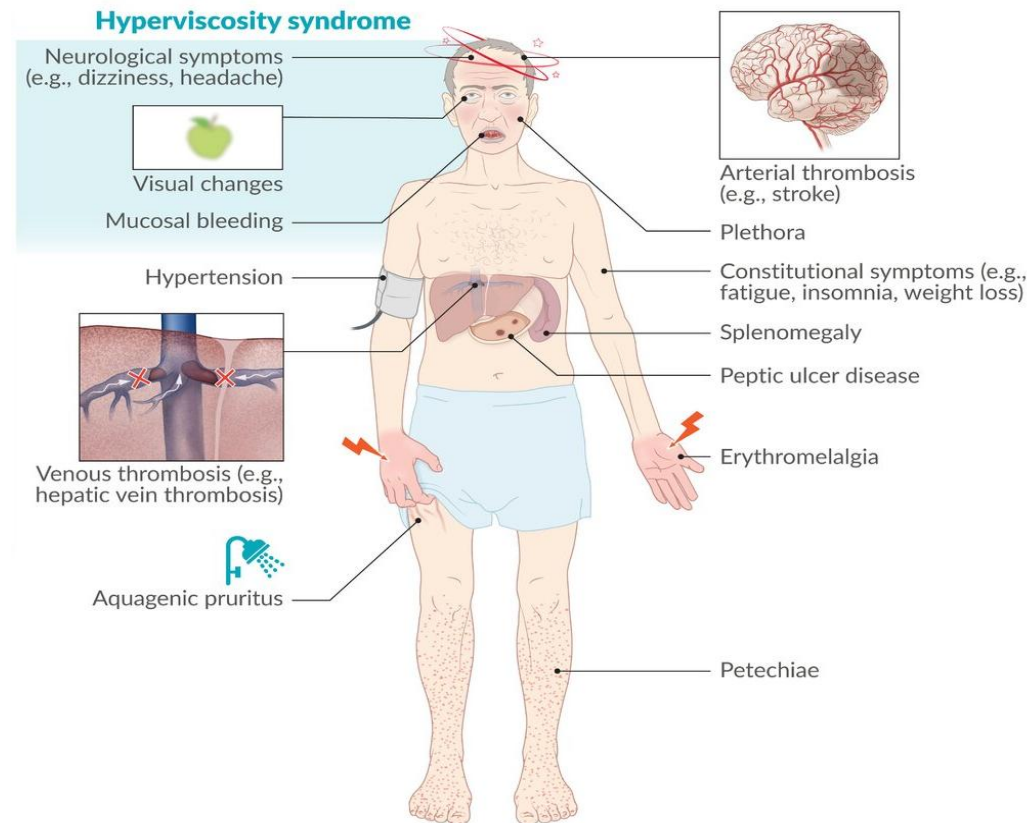




Haematologic complications

• Polycythaemia

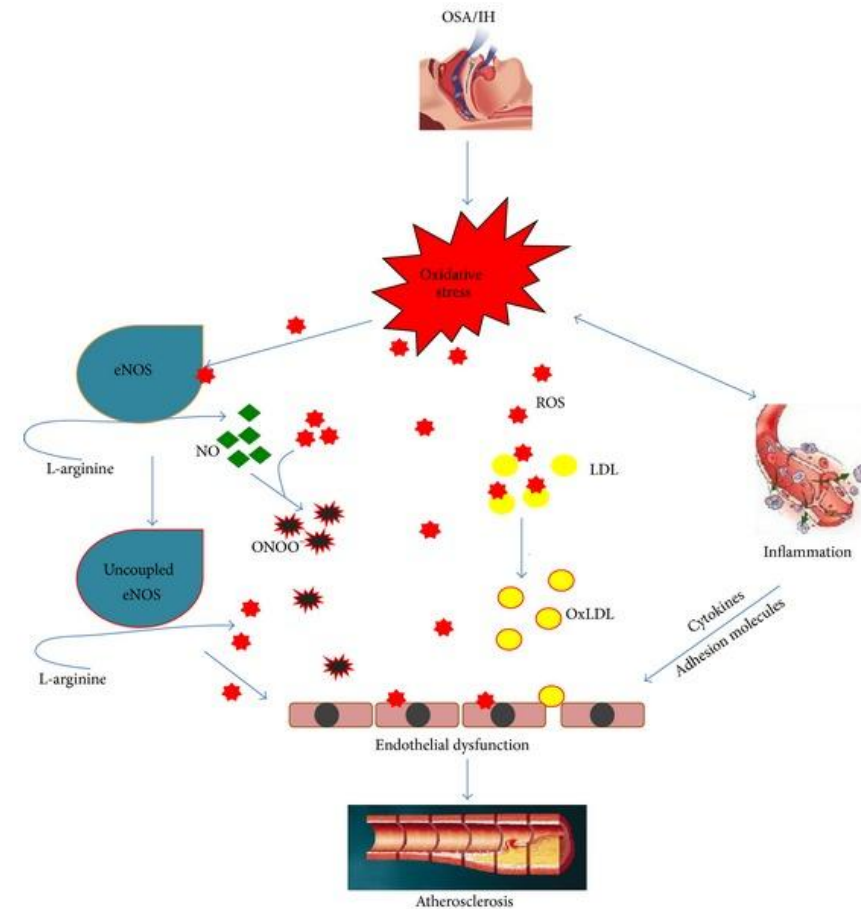
- repeated night desaturations → increased EPO production
- overlap syndrome – SAS + chronic obstructive pulmonary disorders → EPO



- **Increased coagulation**

Activation of endothelial cells by repeated desaturations

Increased activity of sympathetic NS



Endocrine complications

Sleep fragmentation leads to impaired hormone release

- Hormones with significant diurnal rhythm
- Decreased STH release leads to absence of its lipolytic effect and can contribute to obesity development
- Increased ghrelin secretion increases appetite and stimulates food intake
- Increased ANP secretion leads to nocturia – also contributes to inadequate night rest
- Increased cortisol release – stress hormone contributing to obesity
- Disorder in sex hormone release
 - decreased testosterone production in men → erectile dysfunction, decreased libido
 - decreased levels of oestrogen and increased testosterone in postmenopausal women predisposes to OSA
- Altered melatonin production
- Hypothyroidism – risk factor of OSA development

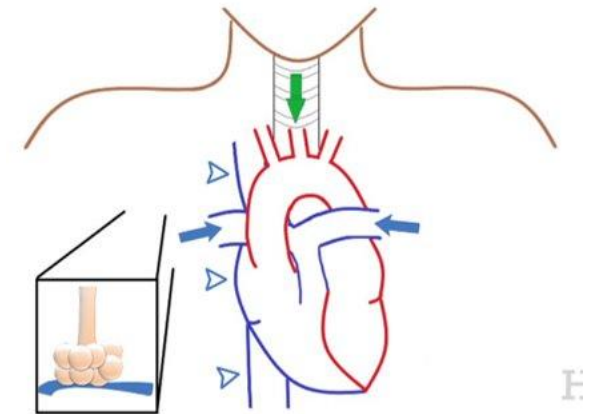
Effect of mechanical ventilation on hemodynamics

Right ventricle

Decreased preload – by positive pressure of the ventilator, decreases venous return

Increased afterload – positive pressure opens alveoli and generates pressure on the capillary – thereby increasing vascular resistance. Increased pulmovascular resistance increases afterload of the right ventricle

Some patients with right ventricle failure might not tolerate/deteriorate on positive pressure ventilation



Effect of mechanical ventilation on hemodynamics

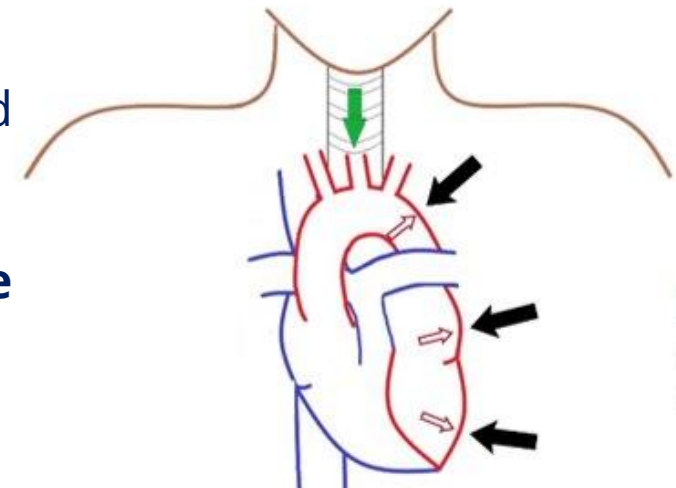
Left ventricle

Decreased preload – by positive pressure applied by the ventilator

Decreases afterload to left ventricle by the effect of transmural pressure (red and black arrows)

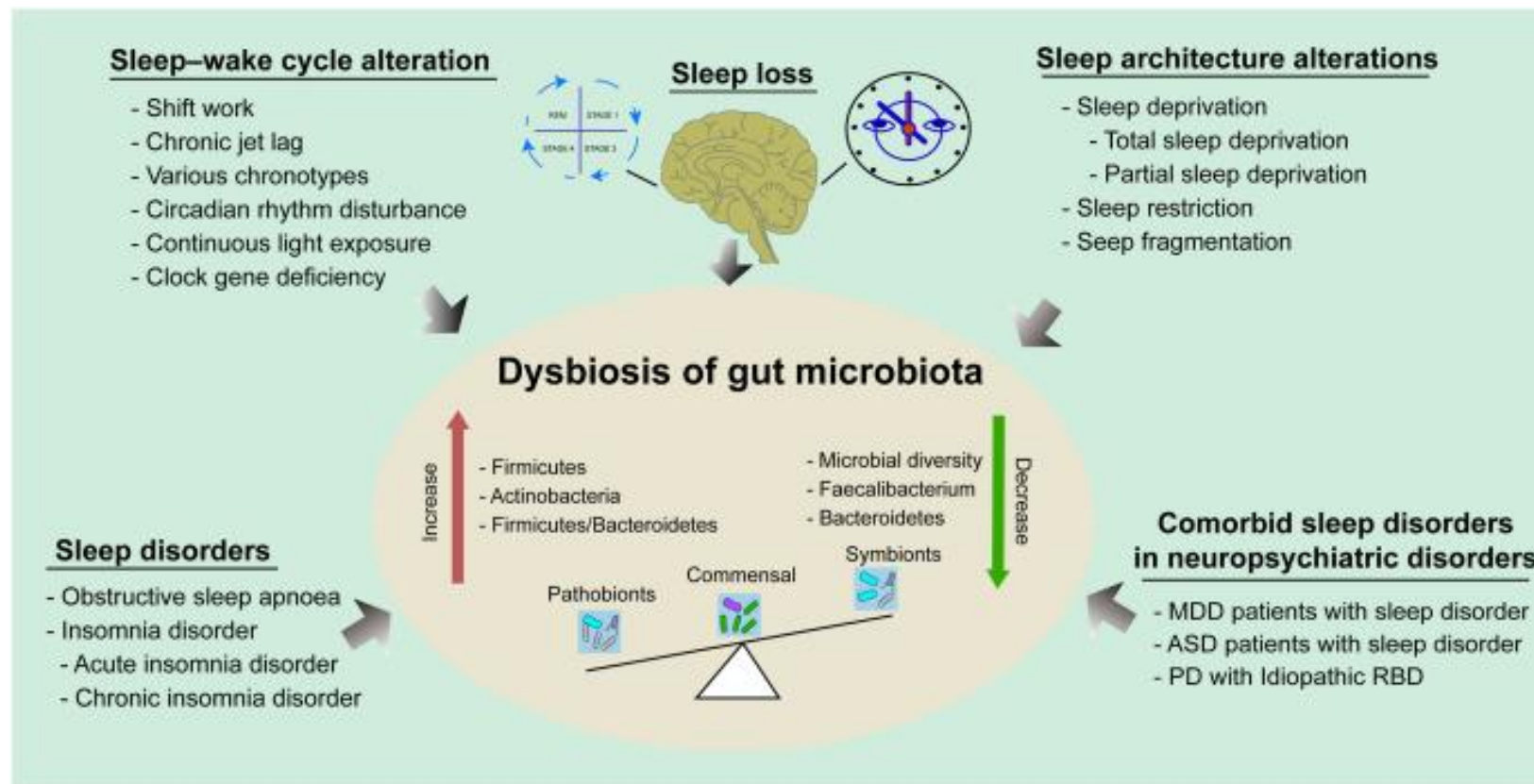
positive pressure (black arrows) decreases transmural pressure gradient and so it decreases afterload

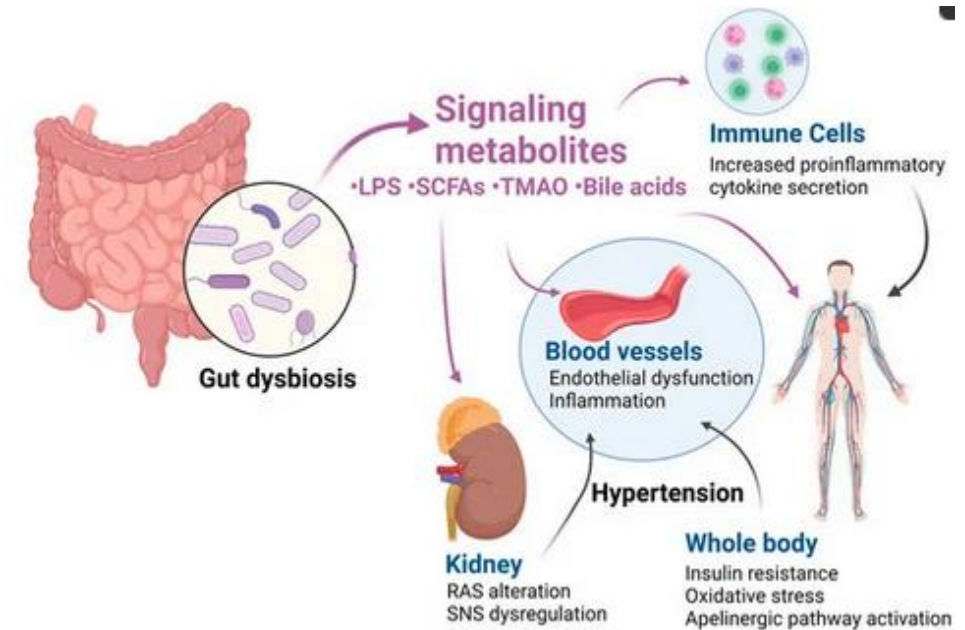
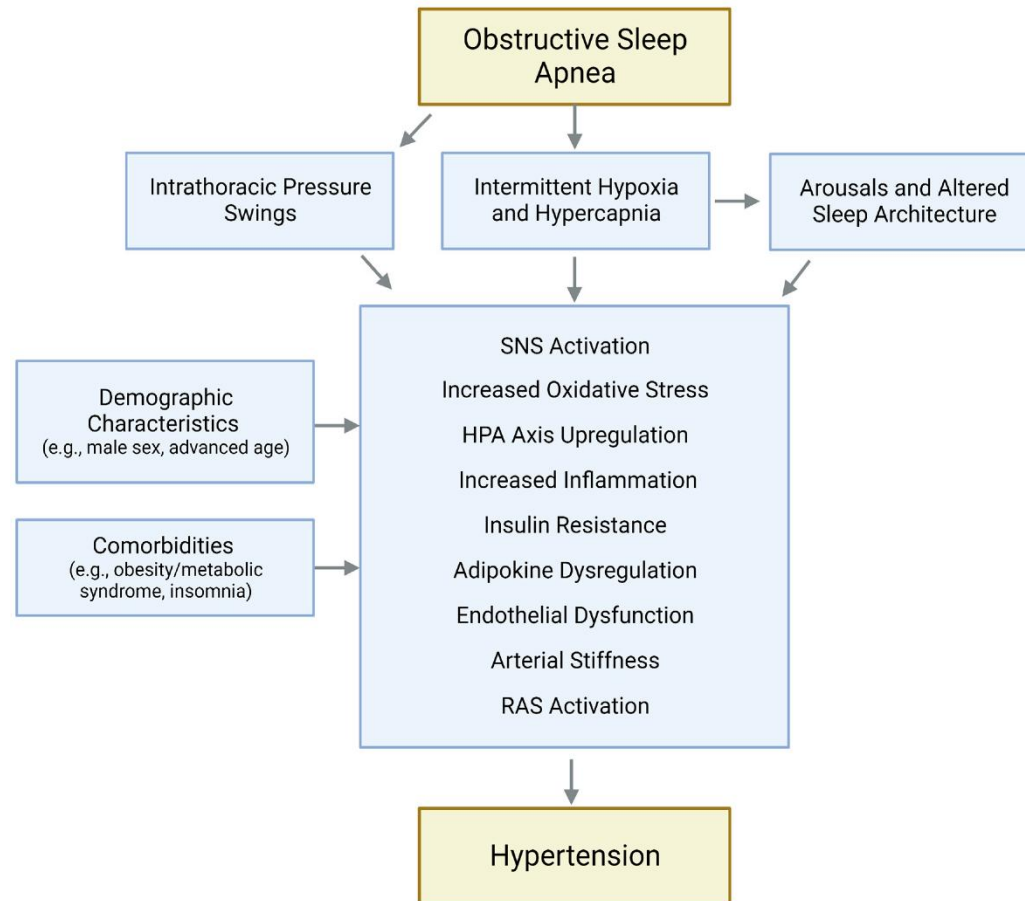
Patients with left ventricle failure might benefit from positive pressure ventilation

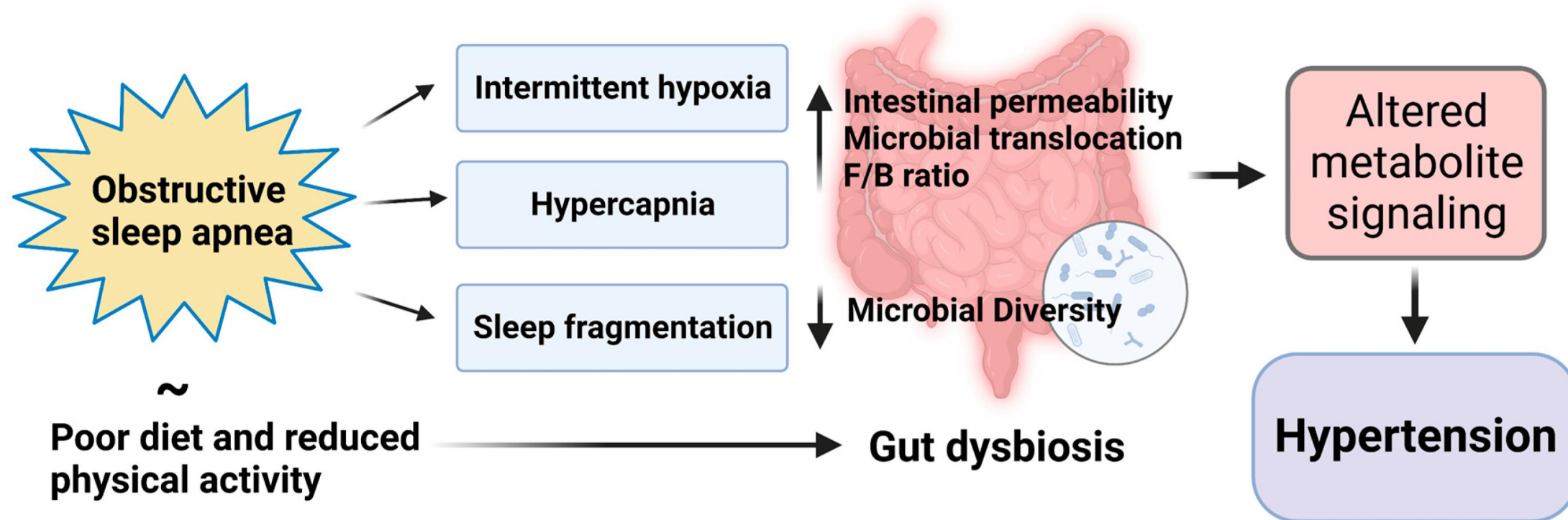


Microbiome complications

Disturbed sleeping pattern and microbiome







Majority of complications disappear after CPAP treatment

It confirms the causality between OSA and mentioned complications