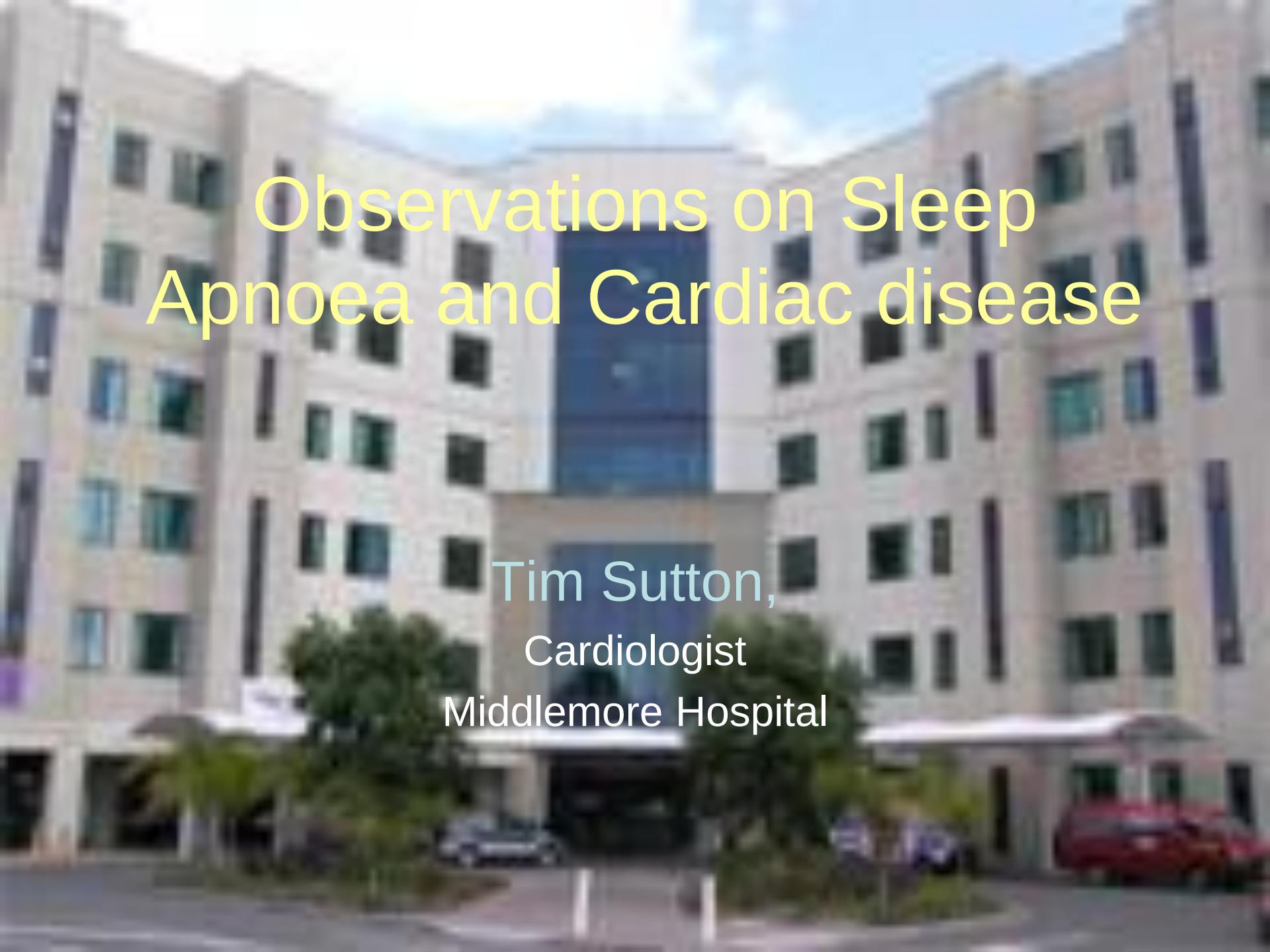


A photograph of a large, modern, multi-story hospital building with a central glass facade and many windows. The building is surrounded by some greenery and a parking lot with a few cars. The sky is blue with some clouds.

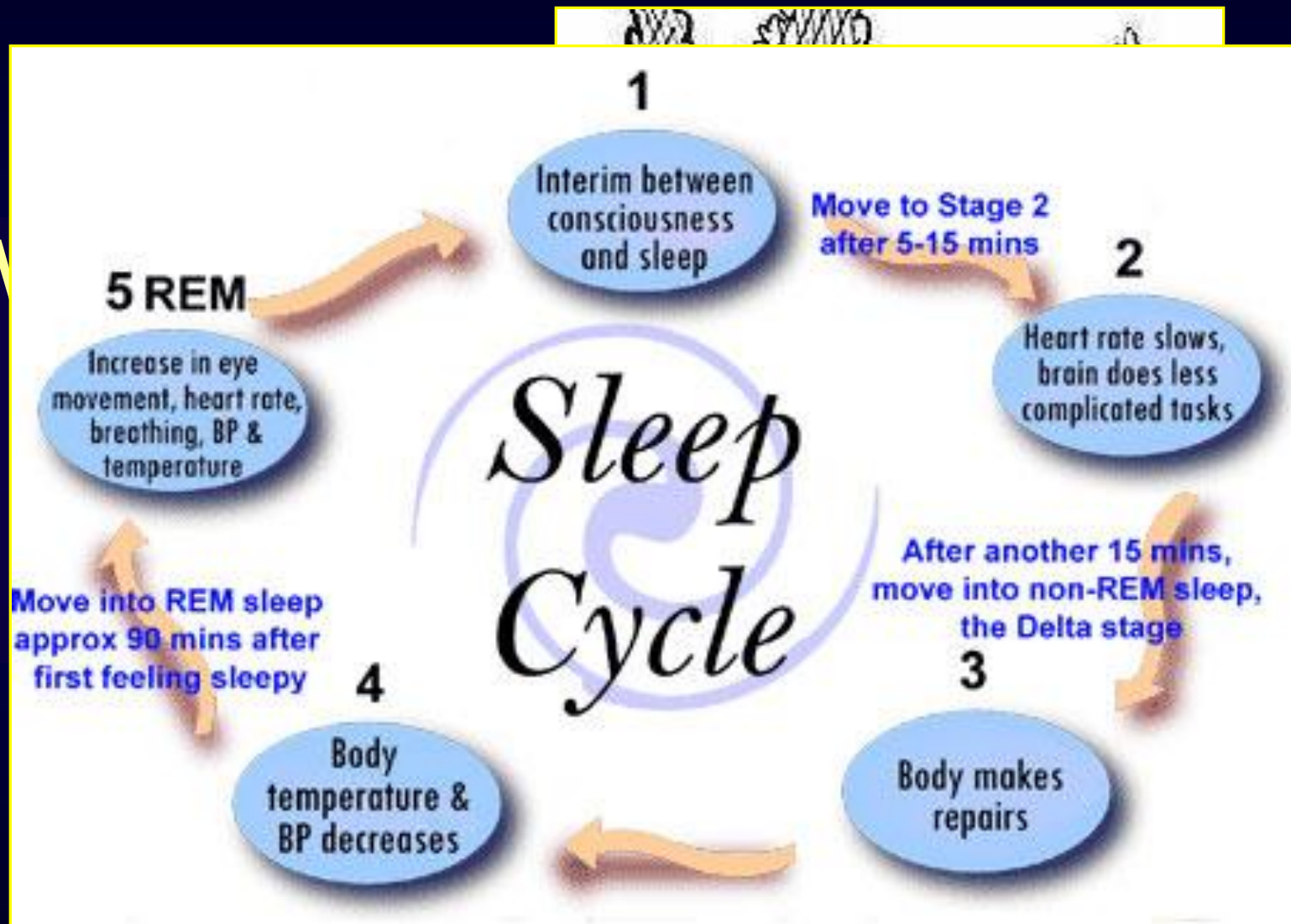
Observations on Sleep Apnoea and Cardiac disease

Tim Sutton,
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What is sleep?

“a naturally recurring state of relatively suspended sensory and motor activity, characterized by total or partial unconsciousness and the inactivity of nearly all voluntary muscles”

What is a Sleep Cycle?



The Phases of non REM Sleep

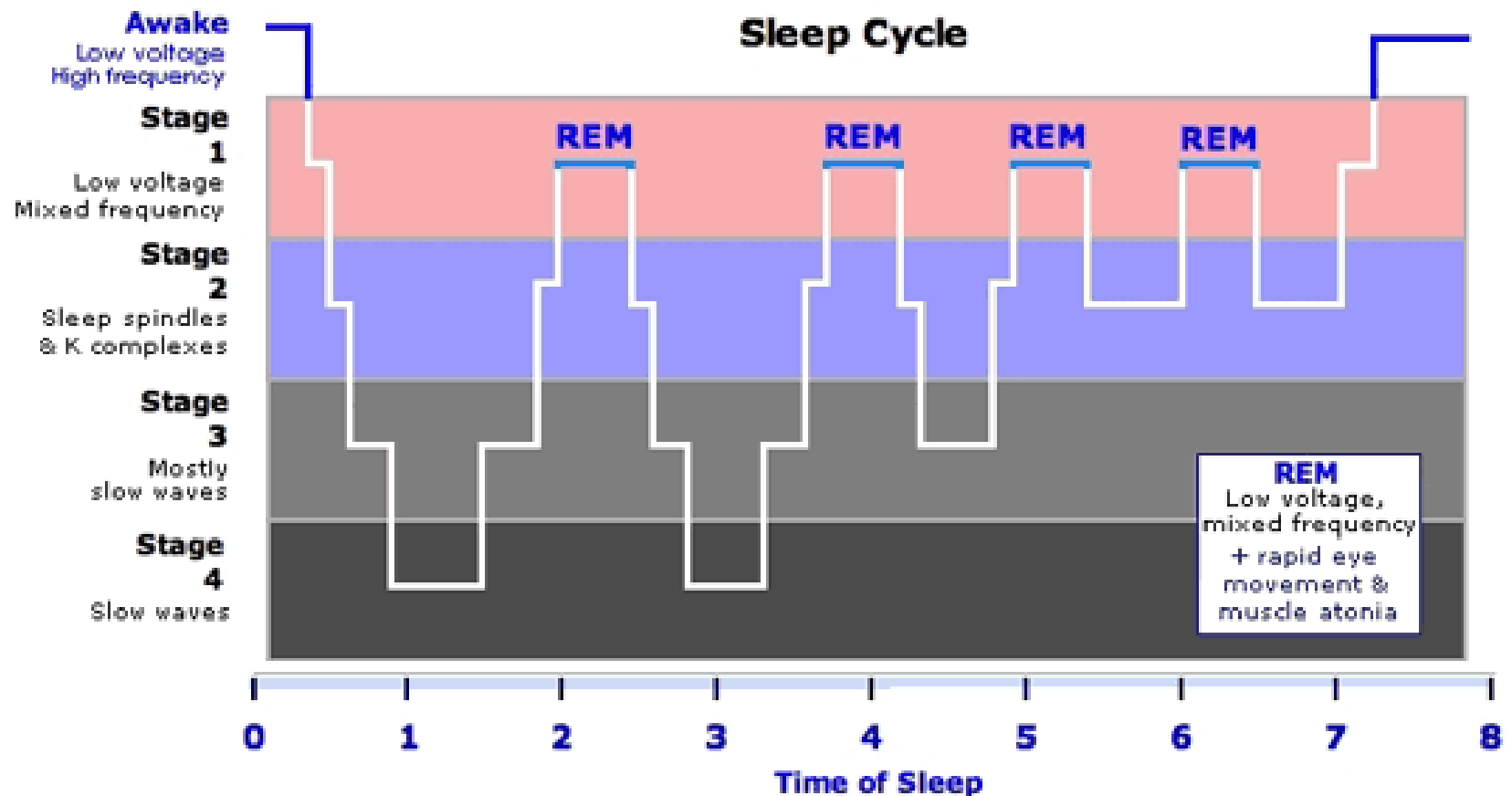
- Stage 1 *(Falling asleep)*
 - Brain waves and muscle activity begin to slow down
- Stage 2 *(Light Sleep)* 45-55%
 - Eye movements stop
 - Brain waves become slower - bursts of rapid waves (sleep spindles), with spontaneous periods of muscle tone mixed with periods of muscle relaxation.
 - The heart rate slows
 - Body temperature decreases

The Phase of REM sleep

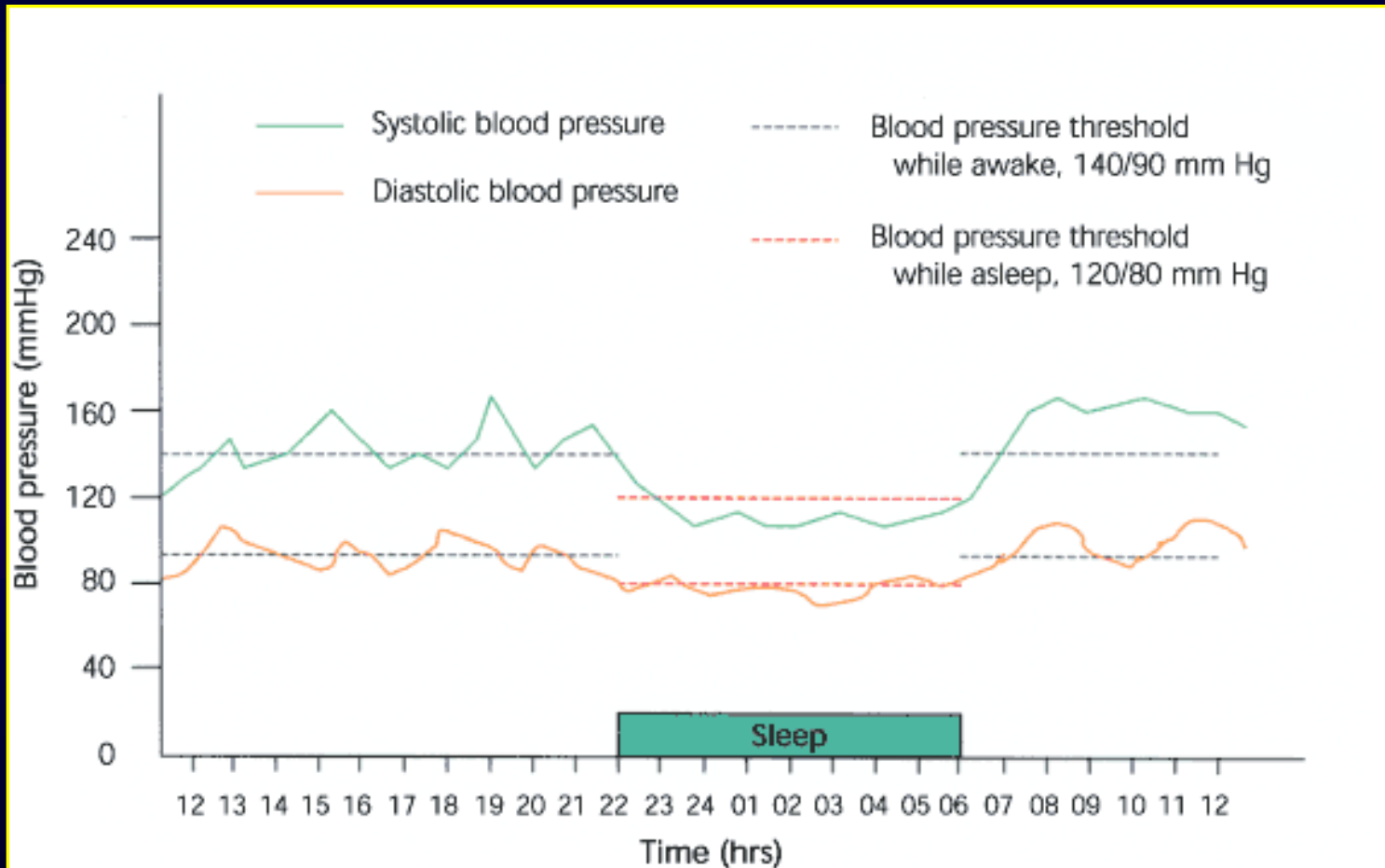
Active period of sleep (20-25%)

- Intense brain activity - brain waves are fast and desynchronized, similar to those in the waking state.
- Breathing more rapid, irregular, and shallow
- Eyes move rapidly in various directions and limb muscles become temporarily paralyzed
- Heart rate increases
- Blood pressure rises.

So in one night....



So what happens to Blood Pressure Overnight?

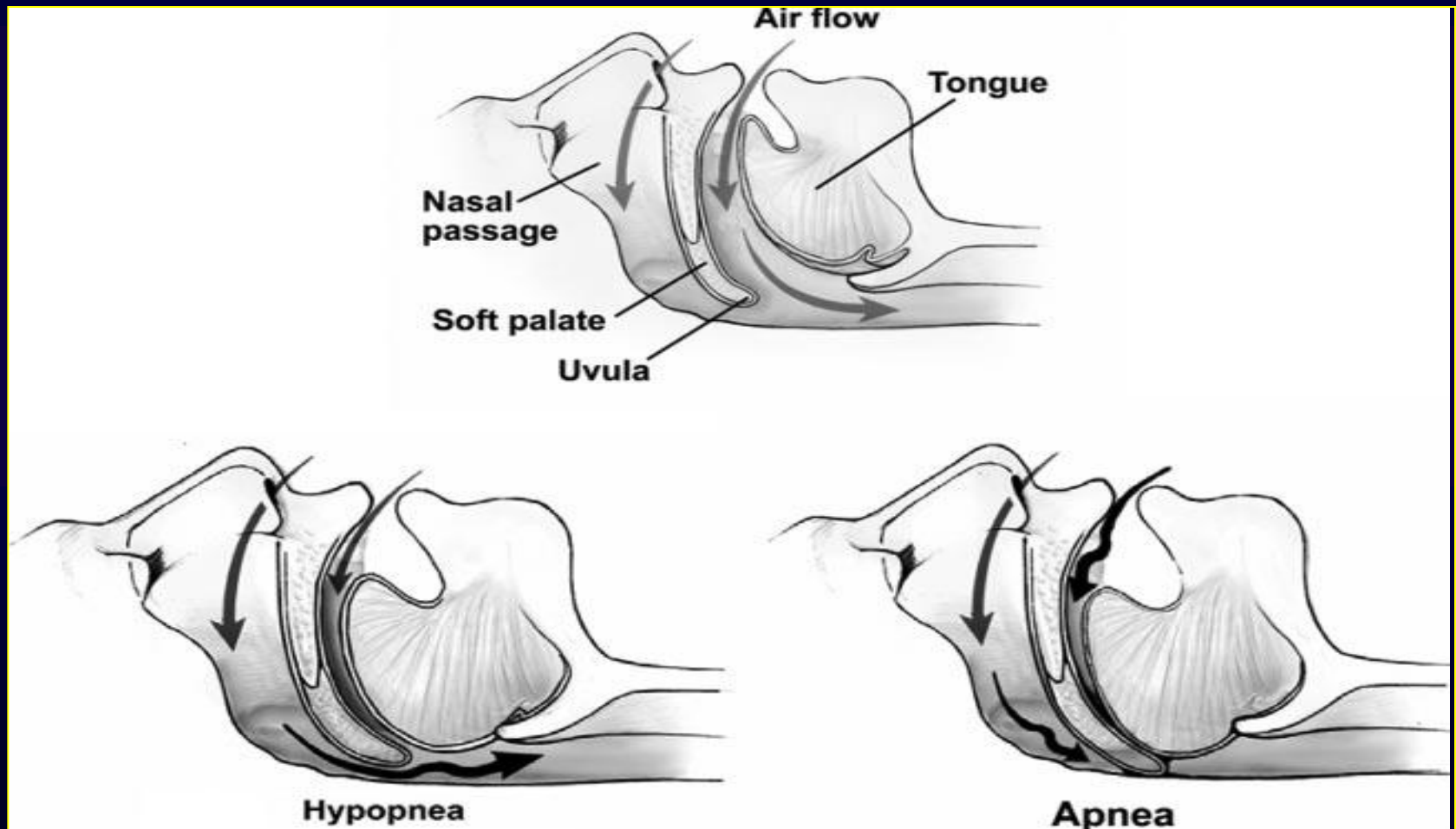


Sleep Apnoea Terminology

- **Apnoea** : a decrease in the peak thermal airflow sensor by 90% or greater of baseline for 10 seconds or longer.
- **Hyponoeas** : a decrease in a nasal pressure airflow sensor excursion by 30% or greater of baseline for 10 seconds or longer with a 4% or more O₂ desaturation A 50% or more decrease in nasal pressure excursion for 10 seconds or longer with either a 3% or more O₂ desaturation or an arousal
- **Apnoea / Hyponoea Index (AHI)** : Number of event in 1 hour
- **Respiratory Effort-Related Arousal (RERA)** : a sequence of breaths lasting at least 10 seconds characterized by increasing respiratory effort or flattening of the nasal pressure waveform leading to an arousal from sleep when the sequence of breaths does not meet criteria for an apnea or hypopnea."
- **Respiratory Disturbance Index (RDI)** : is the number of RERAs per hour plus the number of apneas and hypopneas

Obstructive Sleep Apnoea (OSA)

Respiratory effort maintained, but no airflow due to obstruction of airway



Upper Airway – Mechanical Factors

Tube like structure...

Extrinsic

- Jaw

Intra-mural

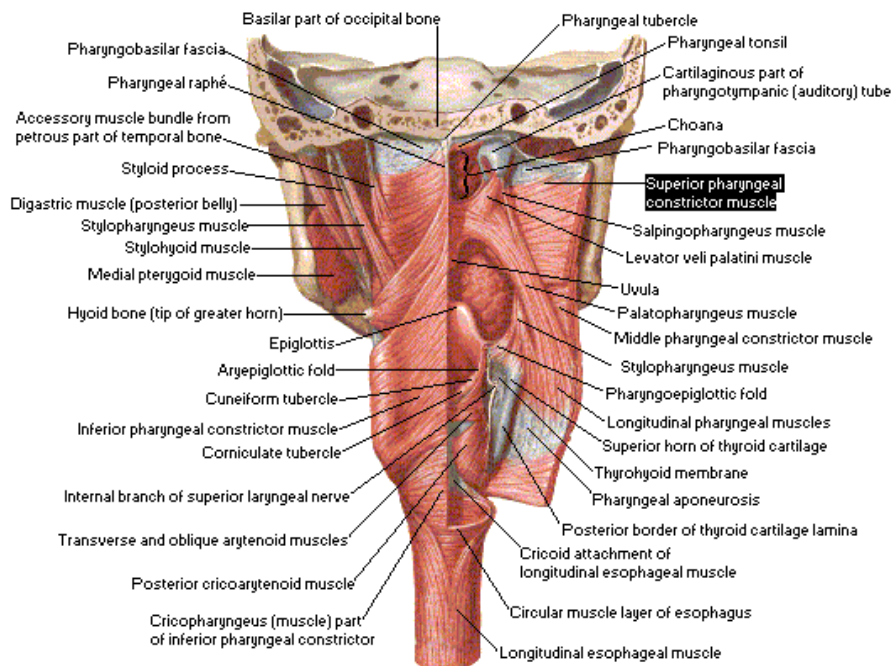
- Oedema / pharyngeal adipose tissue

Intraluminal

- Tongue
- Tonsils

Upper Airway – Neuromuscular factors

Muscles of Pharynx
Partially Opened Posterior View



- Muscles maintain pharyngeal patency (negative pressure reflex)
- Reduced pharyngeal muscle activity in sleep
- Local traumatic sensory neuropathy

Infra pharyngeal issues

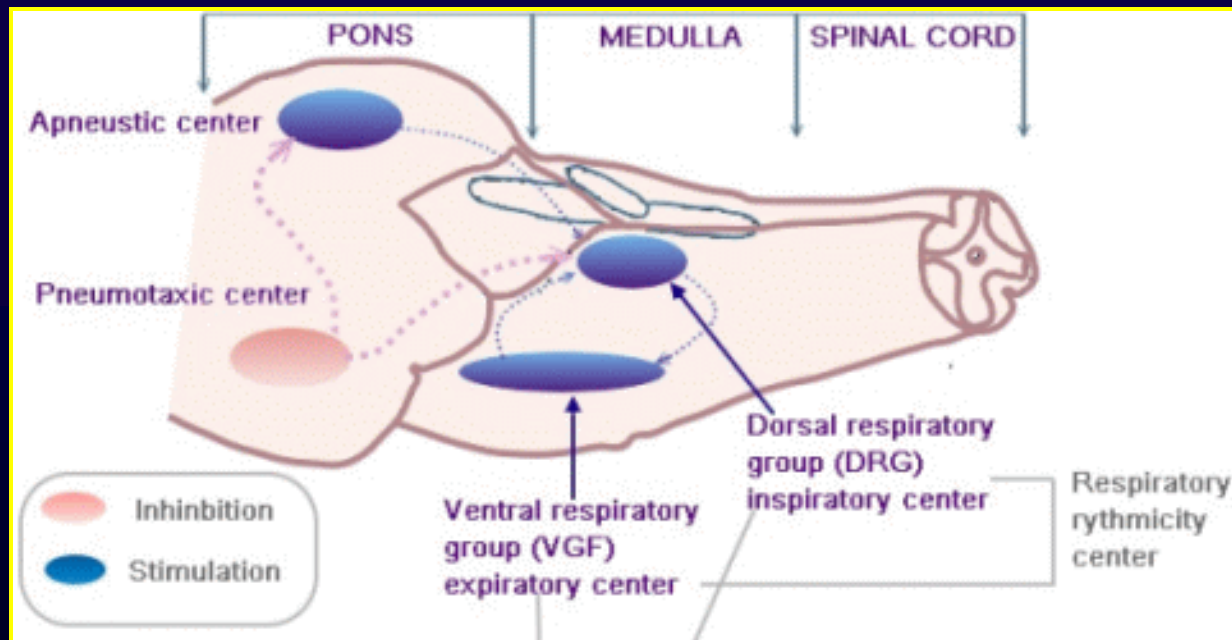
Supine

- Less efficient use of muscle of respiration
 - Chest wall
 - Diaphragm
- Increased effort of breathing
 - Lifting chest wall and tissues
 - Displacing abdominal tissue

Supra pharyngeal

Central input

- Hypoxaemic / hypercapnoeic sensitivity
- Autonomic nervous system



Central Sleep Apnoea (CSA)

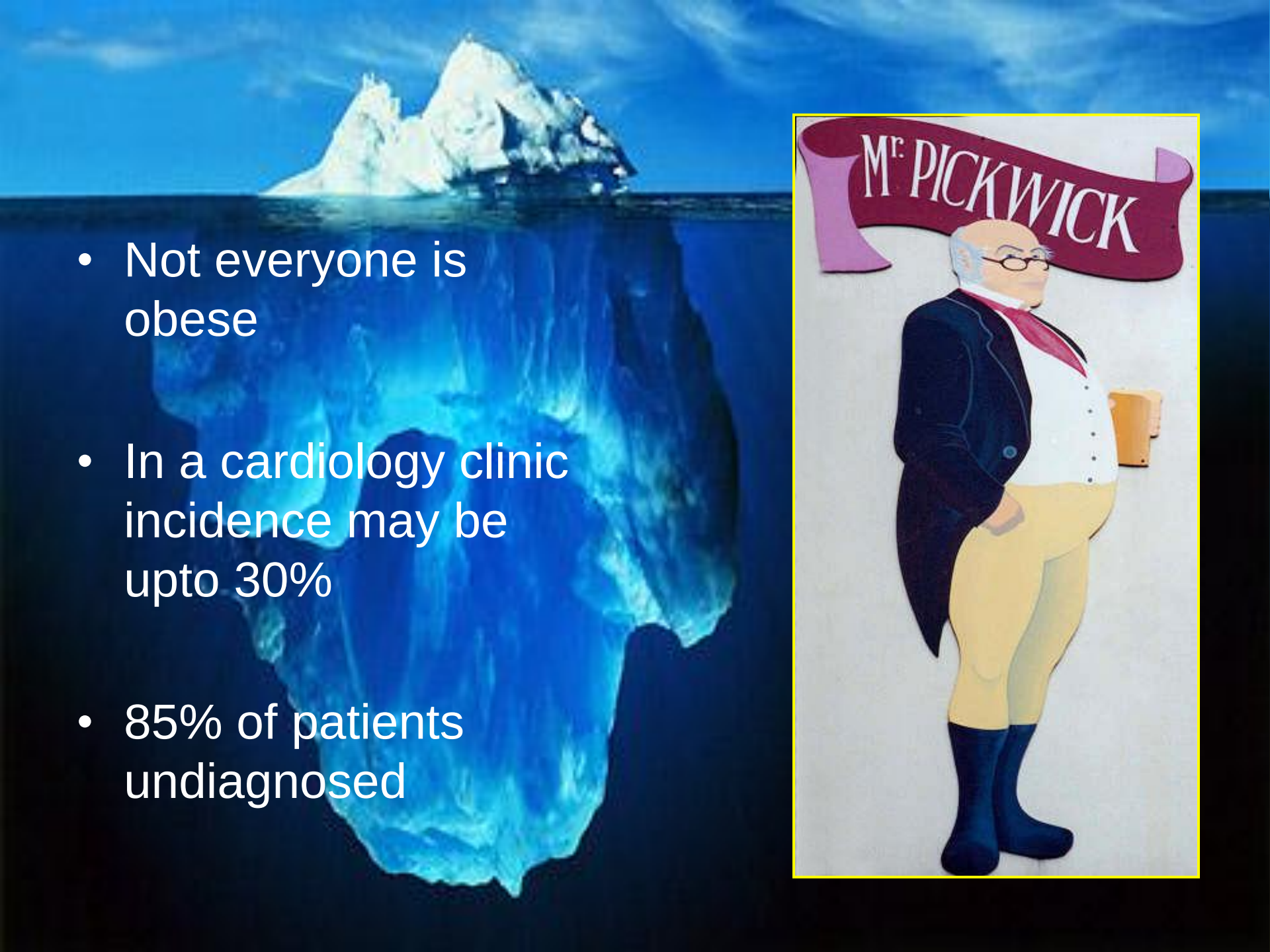
- Loss of central ventilatory drive
- Manifests as an apnoea with no respiratory effort
- Often has overlap with OSA
- Common in heart failure

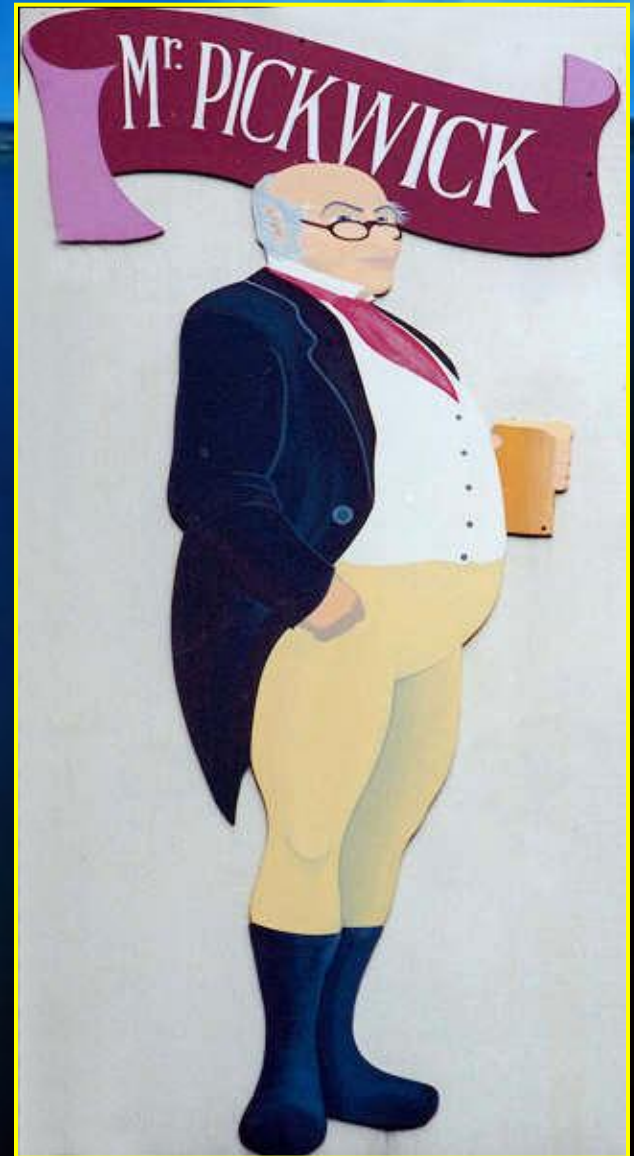
Symptoms

- Awake feeling dissatisfied with sleep
- Fatigue
- Early morning headache
- Nocturnal arousals – wake up choking / no clear reason
- Irritability / change of character
- Loss of libido / impotence
- Spouse reports snoring / apnoeas

Epidemiology

- Incidence (US) :
 - 1:5 people mild OSA
 - 1:15 moderate or severe OSA
- Male gender: OR 2
- Obesity (BMI >30)
- Age
- Untreated : increased risk of CV mortality

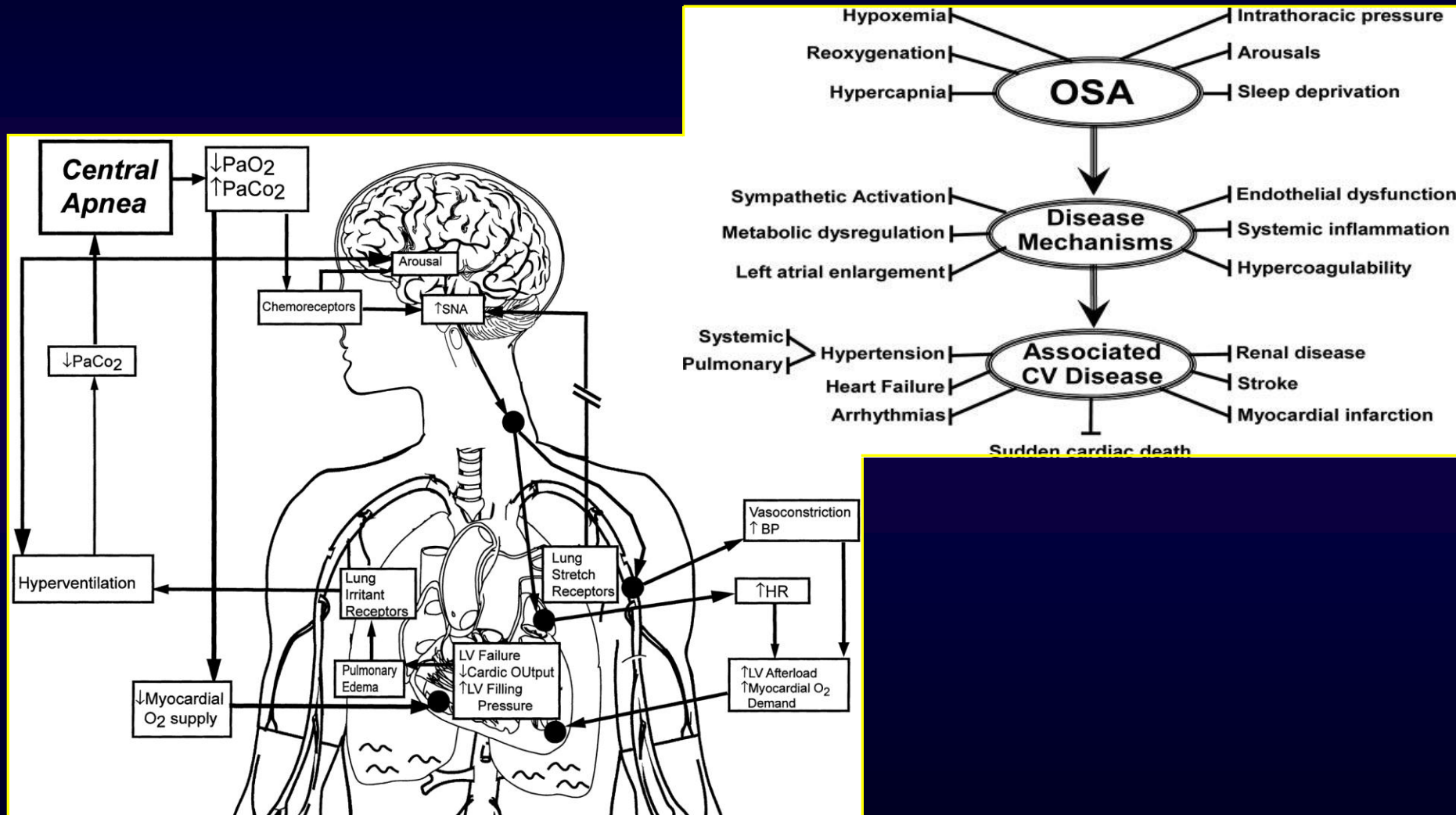
- 
- An iceberg floating in the ocean. The tip of the iceberg, which is above the water, is relatively small and jagged. The much larger part of the iceberg is submerged underwater, illustrating the concept of hidden or undiagnosed issues.
- Not everyone is obese
 - In a cardiology clinic incidence may be upto 30%
 - 85% of patients undiagnosed



Who might have OSA

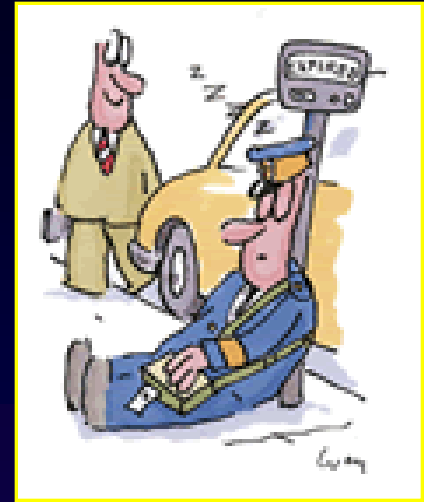
- Patients with:
 - Nocturnal angina
 - Drug resistant hypertension
 - Paroxysmal AF (especially nocturnal)
 - Heart failure
 - Metabolic syndrome type risk factors
 - “syncope” whilst driving

How might OSA contribute to CVD?



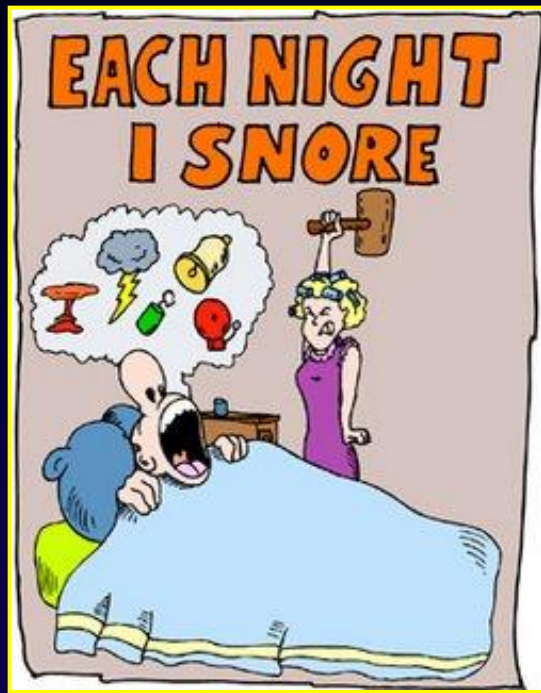
Epworth Sleepiness Score (measure of daytime sleepiness)

What do you think the chances of you falling asleep in these situations is...



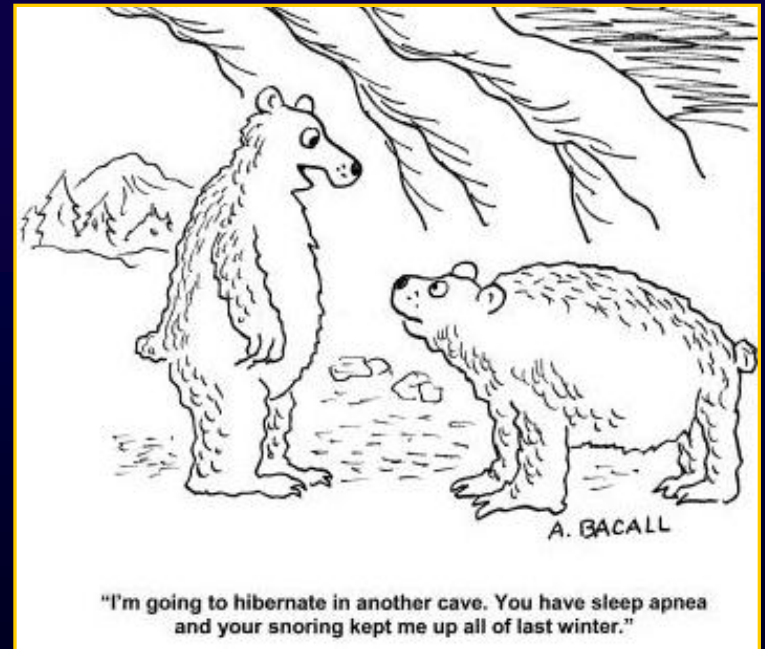
- After lunch, without alcohol
- During conversation
- Whilst driving in slowly moving traffic
- In the afternoon if circumstances permit
- Whilst reading
- Whilst watching TV
- In a public place / meeting
- As a passenger on an car journey longer than 1 hour

Score between 0 and 3



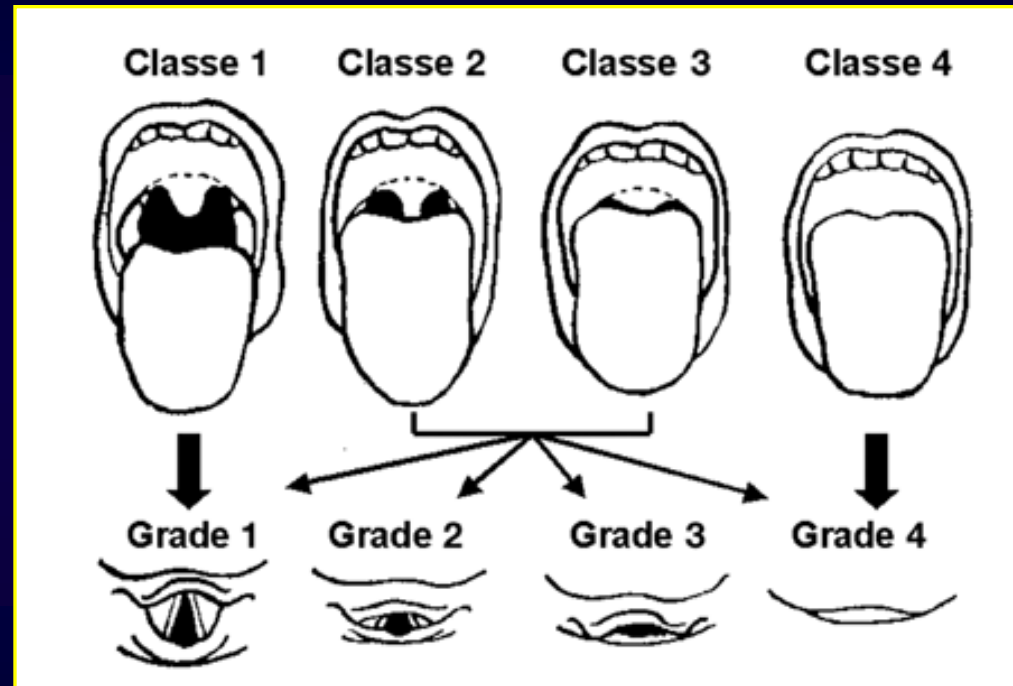
Marital disharmony

...

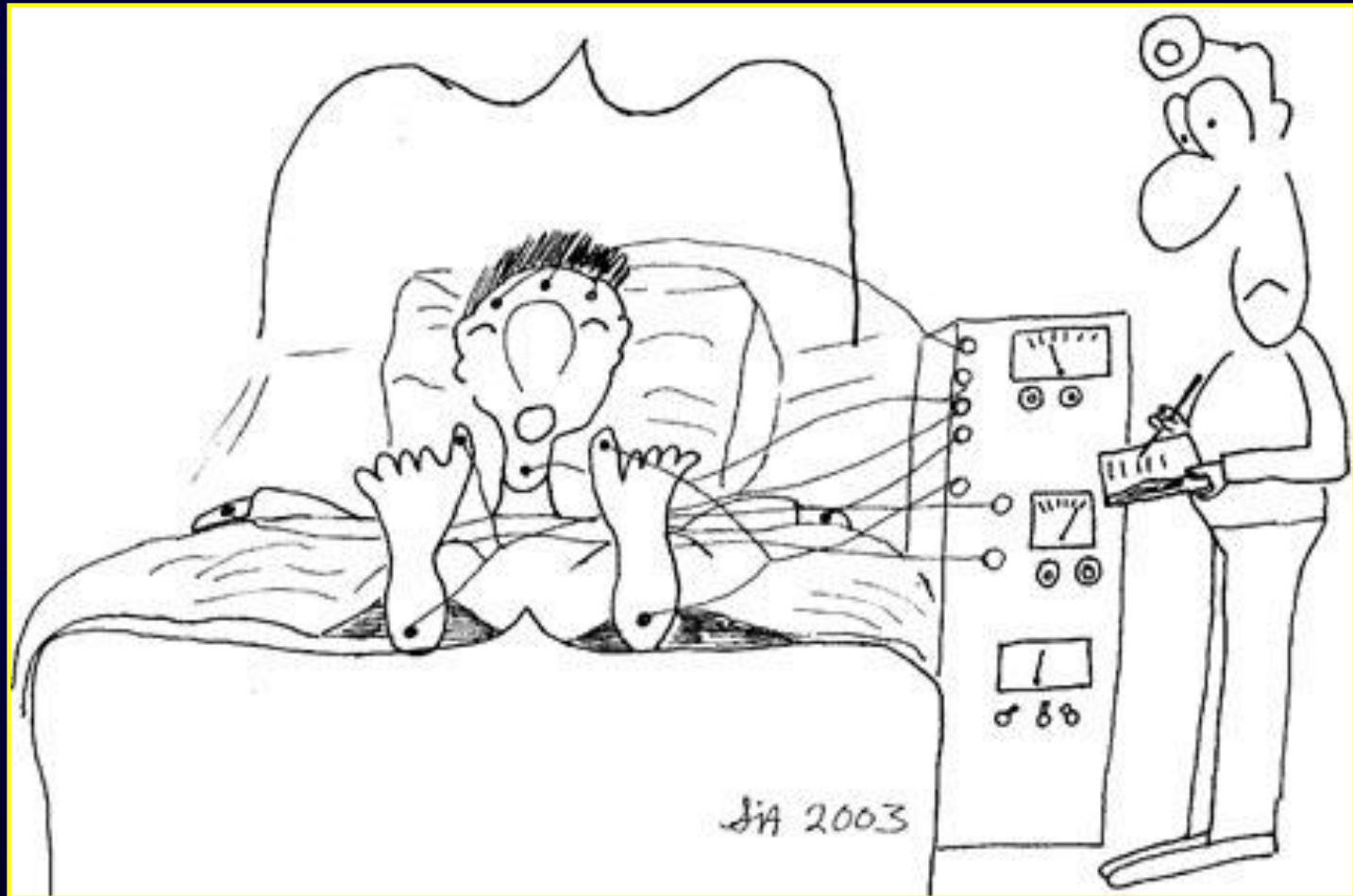


Examination

- BMI
- Neck circumference
- Pharyngeal assessment



Investigations: Polysomnography



Screening test (at home)

Overnight Oximetry

- Airflow
- Oxygenation

Embletta Study

- Respiration
- Airflow
- Oxygenation
- Heart rate
- Body position

To diagnose Obstructive Sleep Apnoea

Need greater or RDI > 15 events per hour

Or

AHI or RDI greater than or equal to 5 and less than or equal to 14 events per hour with documented symptoms of excessive daytime sleepiness, impaired cognition, mood disorders or insomnia, or documented hypertension, ischemic heart disease, or history of stroke

Determination of Sleep Disordered Breathing

Mild : Sleepiness present only when sedentary or when attention is required. May not be present every day.

Severity : Mean O₂ sat $\geq 90\%$

Symptoms : predominantly Sleepiness

Minor impairment of social or occupational function.

Epworth Sleepiness Scale result in region of 12.

Mild : Frequency of obstructions ≤ 5

Mild : $AHI / RDI \leq 5$

Moderate : Daily sleepiness that occurs when minimally active and a moderate degree of attention (e.g., driving, attending meetings or

Moderate : Degree of desaturation – Minimum and maximum mean oxygen saturation $15 - 30\%$

Epworth Sleepiness Scale in region of 13-17.

Severe : Frequency of obstructions ≥ 15

Severe : $AHI / RDI \geq 15$

Severe : Sleepiness during active tasks or tasks that require significant attention. E.g. include driving, conversation, eating or walking.

OSA and Hypertension

- 50% of patient with OSA are hypertensive
- 30% of patients with OSA have hypertension
- Normotensive patients with OSA have an increase risk of developing hypertension – correlates with AHI
- Drug resistant hypertension: - 50-80% of patients reported to have sleep apnoea

Nocturnal “Hypertension”

- Loss of “Dipper” response on 24 hour ambulatory blood pressure monitor
- Consider OSA – may be a contributing factor. OSA more prevalent in this group.

Potential Mechanisms for Hypertension

- Intermittent hypoxaemia
- Chemoreceptor stimulation
- Sympathetic activation
- Renin- angiotensin system activation

So does treatment lower BP

- Not in normotensive / well pharmacologically treated patients
- Can see a moderate reduction of BP (mean 7-10mmHg in daytime and 10-12mmHg in nocturnal BP) in
 - More severe OSA
 - Difficult to control hypertension
 - Good compliance with CPAP

Bradyarrhythmias in OSA

- Bradyarrhythmias
 - Mediated by prolonged apnoea and hypoxaemia – enhanced vagal tone
- Profound bradyarrhythmias – 10% in presence of an otherwise electrically normal heart.
- Tend to occur during REM sleep and are associated with worse hypoxaemia

So...

- In those with nocturnal AV block / sinus node dysfunction, but normal daytime conduction CPAP treats bradyarrhythmias
- In the pacemaker population:
 - Upto 60% may have OSA
 - Upto 70% for those with AV block

Atrial arrhythmias...

- Does OSA cause AF?
- OSA patients have more atrial tachyarrhythmias
- AF is more common post op in patients with OSA
- Post cardioversion for AF, untreated OSA associated with a 82% risk of recurrence of AF at 1 year
- Does AF impact on thromboembolic risk?

Ventricular Arrhythmias

- Nocturnal incidence upto 65% - during apnoeas vs upto 10% in normal individuals
 - More frequent in patient with more severe OSA / extensive cardiac comorbidities
- CPAP does reduce the incidence of ectopics
- NSVT associated with respiratory disturbance (2% patients)

OSA and Pulmonary Hypertension

- Reported incidence varies – 20-40%
- Generally relatively mild
- More prevalent in those with daytime hypoxaemia / hypercapnoea
- Therapeutic CPAP brings about a drop in daytime PAP
- Hypoxaemia causes a rise in PA pressure
 - Those with PHT have a higher degree of hypoxic vasoreactivity

Cardiac Structural changes in OSA

- Left heart
 - Left atrial dilatation
 - LVH – initial interventricular septum then more global
 - Diastolic dysfunction
- Right heart
 - RV dilatation and hypertrophy
 - Mild elevation of PAP

SA and Heart Failure

Does sleep apnoea cause heart failure?

- Diastolic – probably
- Systolic – unknown

Upto 50% of patient with CHF have sleep apnoea
Do patients with heart failure often have

*BUT CSA is predominant
sleep apnoea?*

- Unquestionably at least 2 :1

How is SA bad for systolic function?

Enhanced sympathetic tone

Elevation of LV afterload

- Blood pressure
- Obstructive events increase LV transmural pressure

Hypoxia

- Elevation of RV afterload (hypoxia)
- Myocardial supply / demand mismatch

Does CPAP helps in CHF and SA?

- Improves EF (slightly)
- Improves effort tolerance (slightly)
- Mild neurohormonal deactivation
- No clear proof of general survival benefit as yet

OSA and Coronary disease

- Upto 2 fold greater incidence vs “non coronary subjects”
- Along with co-existent of risk factors physiological stressors of SA
- 1/3 patients with severe OSA experience asymptomatic nocturnal ST depression
- Observational data suggest increase risk of MACE in those with CVD and OSA

Treatment options: Weight loss



“What fits your busy schedule better, exercising one hour a day or being dead 24 hours a day?”

Avoid exacerbating factors

- Alcohol
- Sedatives

Treatment options: Positional therapy

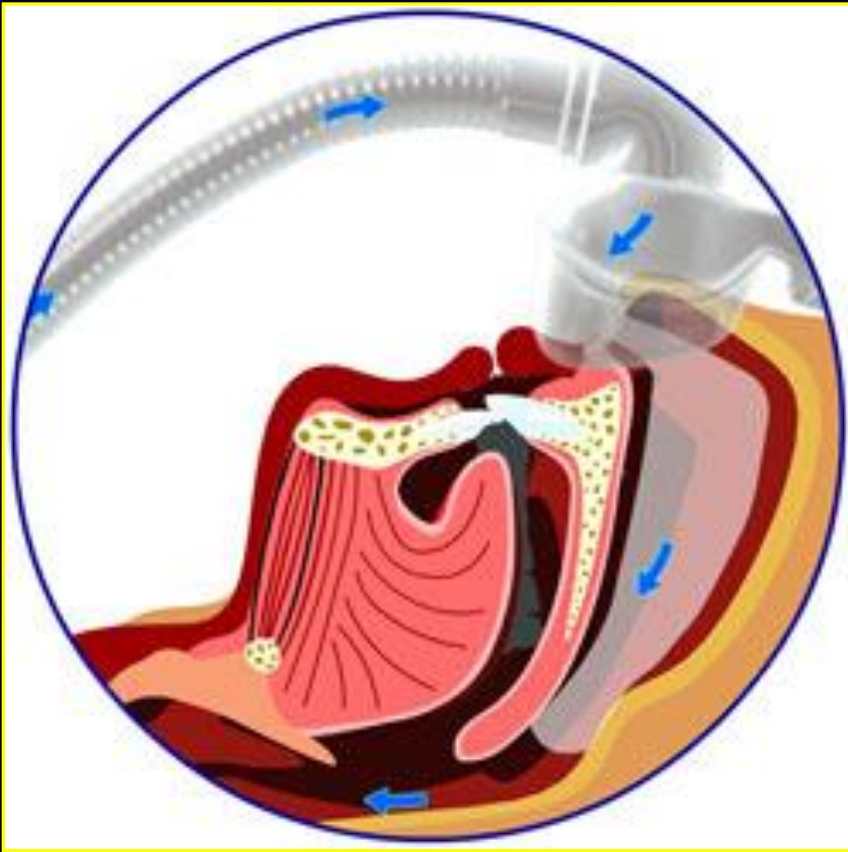


Treatment options: Oral appliances



Treatment options: CPAP

(Continuous positive airways pressure)



Does CPAP work?



Potential problems

Machine

- Noise
- Pressure / humidity settings

Mask

- Air leak
- Contact abrasions

Nasal cavity

- Rhinitis
- Dryness

Other

- Aerophagia
- Mouth breathing



Surgery

- Uvulopalatopharyngoplasty
- Tonsillectomy
- Tracheostomy

In summary



- Sleep apnoea is endemic in our patients
- Many are undiagnosed
- In selected patients intervention is effective
- Remember to ask

- We are learning a lot through observation
- Small trials have shown therapeutic effect
- Need more data though



Sleep Apnea Cardiovascular Endpoint Study

www.savetrial.org

PROTOCOL

An investigator-initiated and conducted, collaborative, phase III, multi-centre, open label, randomised, controlled trial of continuous positive airway pressure for the treatment of obstructive sleep apnea to prevent cardiovascular disease

- A large-scale, prospective, multi-centre, open label, parallel group, randomised controlled trial of
 - CPAP + usual care **versus** usual care alone
 - In patients with
 - diagnosed OSA (moderate-severe) and
 - established CV disease (cerebrovascular or coronary disease)

Eligibility Criteria: Inclusion

1. Age 45 and 75 years
2. Established Coronary or Cerebrovascular disease
 - Previous MI ≥ 90 days; or
 - Stable angina or unstable angina (clinical event ≥ 30 days); or
 - PTCA and/or stent ≥ 90 days; or
 - CABG >1 year; or
 - Previous stroke ≥ 90 days; or
 - Minor disabling stroke ≥ 7 days; or
 - Previous TIA ≥ 7 days & < 1 year
3. Moderate OSA (≥ 4 O2 dip rate ≥ 12 h on ApneaLink)
4. Informed consent

Exclusion Criteria

1. Medical conditions making patient unsuitable for the study eg severe disability or significant memory disorder
2. Any planned coronary revascularization procedure in the next 6 months
3. Severe respiratory disease
4. Heart failure (NYHA categories III-IV)
5. Subarachnoid haemorrhage
6. Other household member enrolled in SAVE or using CPAP

Exclusion Criteria

- 7. Prior use of CPAP treatment for OSA**
- 8. Increased risk of a sleep-related accident (driver occupation, fall-asleep or 'near miss' accident in previous 12 months, Epworth >15)**
- 9. Severe nocturnal desaturation**
- 10. Cheyne-Stokes respiration**

Outcomes

Primary

- Composite of cardiovascular events
 - CV death, myocardial infarction, stroke, and hospital admission for one of heart failure, unstable angina or TIA

Secondary

- Separate types of cardiovascular events
- Revascularisation procedures
- New onset AF, diabetes
- Daytime sleepiness, quality of life, mood

SAVE

