Obstructive sleep apnea: recent advances and future trends

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• Sleep physiology
• Historical aspects
• Clinical profile
• Polysomnography
• Management
• Recent advances
• Future directions
Sleep physiology

- Sleep is a period of bodily rest with reduced awareness of the environment
- Two phases of sleep – REM, NREM
- NREM and REM sleep bouts alternate with each other throughout the night (average cycle length is 90 mins)
REM sleep

- Rapid eye movements
- Generalized hypotonia of muscles
- Irregular rate and depth of respiration
- Marked suppression of hypothalamic regulation of homeostasis
NREM sleep

- Normal muscle tone
- Regular respiration
- Four stages of NREM sleep based on EEG
  - Stage 1- small amplitude high frequency waves resembling awake state
  - Stage 4- large amplitude and lowest frequency waves approaching REM
EEG record

Awake — Low Voltage — Random, Fast

Drowsy — 8 to 12 cps — Alpha Waves

REM Sleep (D Sleep) — Low voltage — Random, Fast

Stage 1 — 3 to 7 cps — Theta Waves

Stage 2 — 12 to 14 cps — Sleep Spindles and K Complexes

Delta Sleep (S Sleep) — 1/2 to 2 cps — Delta Waves
Functions of sleep

• “Restoration of body” – as metabolic and energy demands are reduced. But what is restored?
• NREM - replenishes cerebral glycogen stores
• REM – restoration of depleted noradrenergic neurons
• Consolidation of memory and improved learning !!
Resp effects of NREM sleep

- depresses activity of respiratory pump muscles
- markedly depresses activity of airway dilator muscles → upper airway obstruction
- resultant decreased ventilation causes PaCO2 to rise by 5-6 mmHg
- fall in PaO2 in sleep does not affect healthy individuals.
- causes significant hypoxemia in COPD patients who may require supplemental oxygen during sleep not during waking hours.
• CO₂ Apnea threshold increased during NREM sleep.
• Awake AT is 20 mmHg, increases to 40 mmHg in NREM.
• In hypoxic patients who may be hypocapnic during NREM there are increased chances of having central sleep apneas (CSA).
• upper airway obstruction due to reduced tone of dilator muscles may cause OSA usually stage 1,2 of NREM.
Reduced CO$_2$ responsiveness

- Due to reduced CO$_2$ sensitivity of central chemo receptors (change in membrane properties of neurons)
- Reduced activity of respiratory motor neurons due to withdrawal of excitatory effects of wakefulness on these neurons.
- Contribute to the hypoventilation that occurs during sleep
Resp effects of REM sleep

- Profound atonia all muscles
- Thoracic muscles are more depressed than abdominal muscles
- Irregular respirations result but average ventilation changes little compared to wakefulness
Resp effects of REM sleep

- Increased upper airway obstruction due to hypotonia of dilator pharyngeal muscles
- Considerable suppression and disorganized activity of diaphragm
- OSA episodes and oxygen desaturation are longer and more severe than NREM
Cardiovascular effects of REM

- Marked fluctuations in sympathetic outflow
- Bidirectional changes in HR and BP
- Sinus bradycardia, sinus arrest have been reported
- Adverse cardiac events such as arrhythmia, Ac MI, sudden death may occur in pt with CAD
Pharyngeal muscles

- affecting hyoid: geniohyoid, sternohyoid (XII)
- affecting tongue: genioglossus (XII)
- affecting palate: tensor palatini levator palatini (V)
- Nuclei receive inputs from respiratory centres (ventral medulla) – phasic vs tonic
- Most impt stimulus is negative intrapharyngeal pressure during inspiration → contraction keeps pharynx open during inspiration
Pharyngeal airway

• Patency depends on balance of forces that tend to collapse (negative intraluminal pressure and extraluminal pressure) and the contraction of dilator muscles

• Transmural press ($P_{tm}$) = $P_{lumen} - P_{tissue}$

• Closing pressure is $P_{tm}$ at which the pharynx collapses

• $P_{Critical}$ — at which airflow ceases completely

• Normal: $-8 \text{ cm H}_2\text{O}$ OSA: $> 0 \text{ cm H}_2\text{O}$
Other factors

- Role of lung volume in airway size – OSAHS airways have greater dependence on lung volumes
- Decreased FRC with sleep may lead to pharyngeal collapse and increased airflow resistance
- Instability of resp control - contribute to compromised airway patency in some cases
Progression of OSA

• Severity of apnea known to worsen over time
• Roughly AHI doubles every decade
• Wisconsin sleep study AHI increased 2.6 to 5.1 /h over 8 years
• Accelerated by obesity: 10% weight gain caused 32% increase in AHI
• Vibration induced trauma and edema of soft tissues of upper airways and pharyngeal muscle dysfunction responsible for progression
Historical aspects

• 1918 - Sir William Osler first proposed the relationship between obesity and Pickwickian syndrome
• 1956 - Burwell et al first described alveolar hypoventilation with extreme obesity caused Pickwickian syndrome
• 1966 - Gastaut et al demonstrated the occurrence of recurrent apneas in sleep by polysomnography and suggested, sleep disruption was the cause of daytime sleepiness
Sleep apnea

- Apnea is cessation of airflow for at least 10 seconds
- OSA- apnea with continued respiratory efforts
- CSA- airflow and resp efforts are absent
- Mixed- starts as central but becomes obstructive in the same episode
Hypopneas

- Decrement of airflow of 50% or more accompanied by fall of 4% in oxygen saturation or EEG evidence of arousal
- Produces the same pathophysiological changes as apnea
- Oxyhemoglobin desaturation maybe less severe than apnea episodes
OSAHS

- Recurrent episodes of obstructive apnea or hypopnea associated with both excessive daytime sleepiness and night-time symptoms
- Apnea hypopnea index (AHI) on polysomnography > 5/h
- Usually not hypercapnic when awake (PaCO$_2$ < 45 mmHg) when compared with Obesity Hypoventilation Syndrome.
- Recent study: 17% OSA were hypercapnic
  
  Resta et al Neth Med J 2000
Underlying causes

- Skeletal abnormalities
- Soft tissue abnormalities - pharyngeal/nasal
- Craniofacial disorders
- Endocrine
- Obesity
- Genetic
Clinical profile

- Snoring
- Witnessed apneas
- Nocturnal choking
- Excessive daytime sleepiness (EDS)
- Personality changes
- Nocturia
- Automobile accidents
Snoring

- affects bed partner/family and neighbors !!
- common in population: 35-45% men, 15-28% women have habitual snoring
- most freq symptom of OSA 70-95%
- only 6% OSA pts do not report snoring
- ¾ patients who deny snoring are found to snore during objective assessment
EDS

- Assessed by Epworth sleepiness scale (ESS) subjective questionnaire
- Has poor correlation with severity of OSA
- Inputs from bed partner are useful
- Exclude lethargy, exhaustion, shift work, drug intake, sleep related movement disorder, depression, narcolepsy and idiopathic hypersomnia
Apneas

- Reported in 6% normal population
- Females less likely to report apneas
- Nocturnal panic or choking episodes
- Cause considerable distress
- Exclude PND, nocturnal asthma, Cheyne Stokes respiration and acute stridor (usually last longer)
### Table 1: How OSAHS might present to non-sleep specialists

<table>
<thead>
<tr>
<th>Profession</th>
<th>Presentation</th>
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<tbody>
<tr>
<td>Cardiologist</td>
<td>Hypertension, Left ventricular hypertrophy, Nocturnal angina, Myocardial infarction, Atrial fibrillation, Bradycardia, Heart failure, Cor pulmonale, Increased pulmonary artery pressure</td>
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<tr>
<td>Psychiatrist</td>
<td>Depression, Anxiety, Behavioural problems, Acute delirium</td>
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<td>Neurologist</td>
<td>Refractory epilepsy, Stroke, Impaired rehabilitation post stroke, Headache on waking</td>
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<tr>
<td>Anaesthetist</td>
<td>Difficult intubation, Sensitivity to opioid analgesia and sedation</td>
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<tr>
<td>Urologist</td>
<td>Witnessed apnoea during recovery, Nocturia, Impotence, Erectile dysfunction</td>
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<tr>
<td>Endocrinologist</td>
<td>Hyperthyroidism, Acromegaly, Diabetes</td>
</tr>
<tr>
<td>ENT surgeon</td>
<td>Snoring, Sore throat, Hoarse voice</td>
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<tr>
<td>Gastroenterologist</td>
<td>Oesophageal reflux, Polycythaemia</td>
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<tr>
<td>Haematologist</td>
<td>Nocturnal shortness of breath, Respiratory failure</td>
</tr>
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</table>

Atypical presentation
Classification of severity

- **Sleepiness**
  - Mild: unwanted sleepiness or involuntary sleep episodes occur during activities that require little attention
  - Moderate: unwanted sleepiness or involuntary sleep episodes occur during activities that require some attention
  - Severe: unwanted sleepiness or involuntary sleep episodes occur during activities that require active attention

- **Sleep related obstructive breathing events (apnoea, hypopnoea, and respiratory effort related arousals):**
  - Mild: 5–15 events/hour of sleep
  - Moderate: 15–30 events/hour of sleep
  - Severe: >30 events/hour of sleep
Consequences

Recurrent apneas → hypoxemia

- Stimulation of resp centre
  - Arousal and sleep disruption
    - EDS and cognitive dysfunction
  - Sympathetic stimulation
    - Hypertension
    - Arrhythmias
    - Pulm HTN
    - Cardiac failure
    - Stroke
Clinical assessment

- Diagnosis may be wrong in 50% cases
- Loud snoring + witnessed apneas identified OSAHS with sensitivity 78% and specificity 67%
- Neck circumference <37cm, >48 cm are associated with low and high risk of OSA
- Obesity (BMI>30) independent risk factor but ~50% cases are not obese
Polysomnography

- EEG
- EOG
- EMG
- ECG
- Oronasal airflow
- Pulse oximetry
- Respiratory efforts
- Snoring
- Position
- Leg movements
PSG

- Full PSG is “gold standard” for diagnosis of OSA
- Time consuming, expensive, req trained technician and hosp admission
- Criteria used by observers to define hypopnea lead to wide differences in RDI
- AHI correlated poorly with EDS and did not predict long term morbidity/mortality
## AASM Classification

<table>
<thead>
<tr>
<th>Level</th>
<th>1</th>
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<th>4</th>
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<td>Parameters</td>
<td>min x7 EEG+</td>
<td>min x7 EEG+</td>
<td>min x 4</td>
<td>min x 1</td>
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<tr>
<td>Body postn</td>
<td>monitor</td>
<td>possible</td>
<td>possible</td>
<td>no</td>
</tr>
<tr>
<td>Leg movts</td>
<td>EMG</td>
<td>optional</td>
<td>optional</td>
<td>no</td>
</tr>
<tr>
<td>Personnel</td>
<td>yes</td>
<td>no</td>
<td>no</td>
<td>no</td>
</tr>
<tr>
<td>Interventn</td>
<td>possible</td>
<td>no</td>
<td>no</td>
<td>no</td>
</tr>
</tbody>
</table>
PGI sleep lab

- Name: Compumedics, Australia
- Type: Level III (except EEG & EMG)
- No of cases studied ~55
- CPAP: ~15 patients
- Drawbacks - lack of EEG leads to error in calculated AHI (bed time vs sleep time)
Normal Sleep Study

- EOG 250 μV
- ECG 2.5 mV
- SaO2 %
- AIRFLOW x4
- THORACIC x2
- ABDOMEN x1
- POSITION Right, Left, Back, Front
- SOUND x1
- H.R. BPM

2 min/page
Obstructive apnea: Complete cessation of airflow despite efforts to breathe

- Desaturation
- Obstructive apnea
- Respiratory paradox
- Snore
Central apnea: Complete cessation of respiratory effort and airflow
Mixed apnea: Complete cessation of airflow with gradual increase in respiratory effort after an initial absence.
Hypopnea: Reduction in airflow compared to baseline, associated with desaturation.

Hypopnea:

Progressively increasing respiratory effort.

Desaturation:
Obstructive Apnea

EEG

Airflow

Effort
  Rib cage

Effort
  Abdomen

Effort
  Esophageal pressure (cm of water)

Oxygen saturation (%)

100
75
50

10 sec
Obstructive Hypopnea

EEG

Airflow

Effort
   Rib cage

Effort
   Abdomen

Effort
   Esophageal pressure (cm of water)

Oxygen saturation (%)

- Arousal

100
75
50

10 sec
Upper-Airway Resistance

- EEG
- Airflow
- Effort
  - Rib cage
  - Abdomen
- Effort
  - Esophageal pressure (cm of water)
- Oxygen saturation (%)

Arousal

10 sec
Role of monitoring sleep

- Sleep assessed by EEG, EOG & EMG
- Detects arousal, micro-arousal with apneas
- Various studies showed arousal index had no relation with EDS
  
  *Drinnan et al AJRCCM 1998*

- Electrophysiological analysis did not alter the diagnosis in 200 cases of OSAHS established accurately with AHI.

  *Douglas et al Lancet 1992*
Problems in hypopnea

- Air flow detection by thermistors cannot reliably detect hypopneas
- **Nasal pressure sensor** connected via prongs are more sensitive in detecting hypopneas
- Nasal obstruction produces false elevations
- Resp inductance plethysmography (RIP) semi-quantitative assessment of ventilation and hypopnea
- Recommended by AASM task force  *Sleep 1999*
Role of oximetry

- Desaturations are common with apnea, but can be absent in hypopneas, upper airway resistance syndrome (UARS).
- Oxygen desaturation index (ODI) – 4% desaturation is considered significant by most authors (3% and 5% are also used).
- \( CT_{90} \) – cumulative percentage of time \( SpO_2 \) was below 90% is a useful index of severity (\( CT_{90} > 1\% \) indicates SA).
Level 4 study: Dual parameter record

Figure 2. Pattern of Oxygen Saturation in a Patient with Severe Sleep Apnea.
Oximetry

• As a screening test for OSA sensitivity of 69% and specificity of 97%  
  *Lee CL Clin Chest Med 2003*

• To confirm OSA in cases with high clinical suspicion

• To exclude OSA in snorers with low clinical suspicion

• ODI 4- has been shown to be best variable predicting benefit from CPAP  
  *Schlosshan et al Thorax 2004*
Problems with oximetry

- Dyshemoglobininemia
- Hypotension, hypothermia
- Poor attachment / disconnection
- Recording artifacts in obese
Split night study

- **1st part** – diagnosis of OSA
- **2nd part** – CPAP titration
- Value in patients with EDS as therapy with CPAP will be well accepted.
- AHI > 40/h over first 2 hours proceed to CPAP titration
- Not recommended for mild to moderate OSA without daytime sleepiness

*Chesson AL et al, Sleep 1997*
Home studies

- Portable unattended sleep studies at home are yet to be standardized against the full PSG
- Most devices do not monitor sleep stage and cannot distinguish OSA and CSA
- Prone to tech failures
- Data should be manually analyzed by physician
- Not recommended at present

*Christopher KL et al Clin Chest Med 2003*
Diagnostic role of APAP device

- Automatic positive airway pressure devices have built-in sensors to detect upper airway obstruction and airflow.
- Detects apnea, hypopnea, snoring and appropriately delivers positive pressure to overcome the obstruction.
- Does not detect sleep hence AHI may be erroneous.
- Can be used for diagnosing cases with high clinical suspicion.
- Requires to be validated against full PSG.
Clinical decision algorithm

• Adjusted neck circumference predict the clinical probability OSA and guide evaluation & management

• Add  +4 for hypertension
   +3 for snoring
   +3 for Choking episodes

• <43 cm  low clinical probability
  43-48cm  intermediate
  >48 cm  high probability

Patient with suspected sleep apnea

Clinical probability of a positive test for sleep apnea

Low (adjusted neck circumference, <43 cm)

Daytime symptoms

None or mild

Conservative treatment

Moderate to severe

Polysomnography readily available

No

Portable monitor

RDI <5

Daytime symptoms

None or mild

Conservative treatment

Polysomnography

Moderate to severe

Trial of CPAP

RDI, 6–30

Daytime symptoms

None or mild

Conservative treatment

RDI >30

Trial of CPAP

Intermediate or high (adjusted neck circumference, 43–48 cm and >48 cm, respectively)

Daytime symptoms

None or mild

Conservative treatment

Polysomnography

Moderate to severe

Trial of CPAP

AHI <5

Daytime symptoms

None or mild

Conservative treatment

AHI, 5–30

Daytime symptoms

None or mild

Conservative treatment

AHI >30

Daytime symptoms

Moderate to severe

Trial of CPAP

Conservative treatment

Check for other causes (insufficient sleep, circadian-rhythm abnormality, narcolepsy, periodic limb movement disorder)
Management

• Conservative measures
• Continuous Positive airway pressure
• Medications
• Oral appliances
• Surgery
• Miscellaneous
Indications of treatment

• Daytime sleepiness and its consequences
• Cardiovascular morbidity and mortality
• Snoring
• Difficulty in deciding treatment occurs in asymptomatic case with severe OSA and symptomatic case with low AHI
Behavioral therapy

• Weight reduction
  – Effective in short term
  – Recurrence may occur despite wt loss

• Positional therapy
  – 50-60% have positional apnea in supine postn
  – Sleep with head end elevated & lateral postn
  – Posture alarm, balls in backpack to train
Pharmacologic measures

- Protriptiline
- SSRI
- Medroxyprogesterone
- Thyroid hormones*
- Acetazolamide
- Modafinil*

Currently no drugs are recommended as alternative to CPA P
Role of nocturnal oxygen

- Unable to accept CPAP (esp increased risk of vascular complications)
- Elderly patients (>80 years)
- Mentally retarded (Down’s Syndrome)
- Hospitalized patients (before stabilization)

**CPAP**

- Treatment of choice
- Acts as pneumatic splint to keep UA open
- Improves the airway obstr in 70-80 %
- Administered via nasal mask /pillow
- Mouth leak – chin strap or oronasal mask used
- Effective pressure ($P_{eff}$) which abolishes apnea, hypopnea, snoring, airflow limitation and arousals determined by titration study.
CPAP

- Reduced nocturnal sleep disturbances
- Improved nocturnal oxygenation
- Improved sleep architecture
- Improves EDS & cognitive function
- Improves cardiovascular endpoints
- May be assoc with reduction in mortality

CPAP

- Mask intolerance: claustrophobia
- Nasal congestion, dryness
- Discomfort
- Noise
- Compliance depends on symptom relief
  Vary from 50-80%
- Median use 3-5 h/night
CPAP

- **Inadequate pressure** - may rarely be fatal, may allow patient to go into REM sleep where airway muscles and resp muscles are severely depressed
- Can cause cardiac arrhythmia and hypoventilation in cases with cardiac diseases
- **Excessive pressure** - discomfort can interfere with sleep, and can precipitate episode of CSA

*Attarian HP Postgraduate Medicine 2002*
Role of BiPAP

- Intolerance to CPAP
- Coexisting OSA and COPD
- Coexisting OSA and OHS
- Persistent Right heart failure
Role of APAP

- Overall results are similar to conventional CPAP
- Mean pressure lower than CPAP
- Compliance and preference slightly better
- Cost 1.5-3 times the conventional device
- Not recommended to be used in OSA complicated by OHS or CSA
- Comorbid diseases
- High level of CPAP >15 cm
Problems with APAP

• Leaks are interpreted as apnea / hypopnea
• Some cases may develop CSA after changing to APAP (mechanism ?) hence cases likely to have CSA are excluded
  – Stroke
  – COPD / Resp failure
  – Cardiac failure
Role of oral appliances

- Two types of devices
  - Tongue advancing device
  - Mandibular repositioning device

- Improve airway patency by enlarging the airway and improving the muscle tone
- Devices are not as effective as CPAP
- Useful for patients with simple snoring
- OSA cases who do not tolerate or fail CPAP
Oral appliances

Tongue advancing device

Mandibular repositioning device
Role of surgery

- Adenoidectomy/tonsillectomy/septoplasty (for specific cases)
- Uvulopalatopharyngoplasty
- Genioglossus advancement with hyoid myotomy
- Maxillomandibular advancement recommended in those intolerant of CPAP
- Tracheostomy
Table 2. Interventions for Sleep Apnea.

<table>
<thead>
<tr>
<th>Behavioral</th>
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<tbody>
<tr>
<td>Weight loss</td>
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<tr>
<td>Avoidance of alcohol and sedatives</td>
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<tr>
<td>Avoidance of sleep deprivation</td>
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<td>Nocturnal positioning</td>
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<thead>
<tr>
<th>Medical</th>
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<tr>
<td>First-line therapy</td>
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<tr>
<td>Positive pressure through a mask</td>
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<tr>
<td>Second-line therapy</td>
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<td>Oral appliance</td>
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<tr>
<th>Other</th>
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<tr>
<td>Fluoxetine or protriptyline</td>
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<td>Thyroid hormone (in hypothyroid patients)</td>
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<td>Nocturnal oxygen</td>
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<td>Tracheostomy</td>
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<tr>
<td>Upper-airway reconstruction</td>
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<tr>
<td>Uvulopalatopharyngoplasty</td>
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<tr>
<td>Genioglossal advancement</td>
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<tr>
<td>Maxillomandibular advancement</td>
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Future directions

• definition of hypopnea
• Ideal cut off between normal and SA
• Role of unattended sleep study
• APAP devices in diagnosis of OSA
• Role of Modafinil with CPAP
• SSRI in mild OSA
THANK YOU