# 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 night (average cycle length is 90 mins)

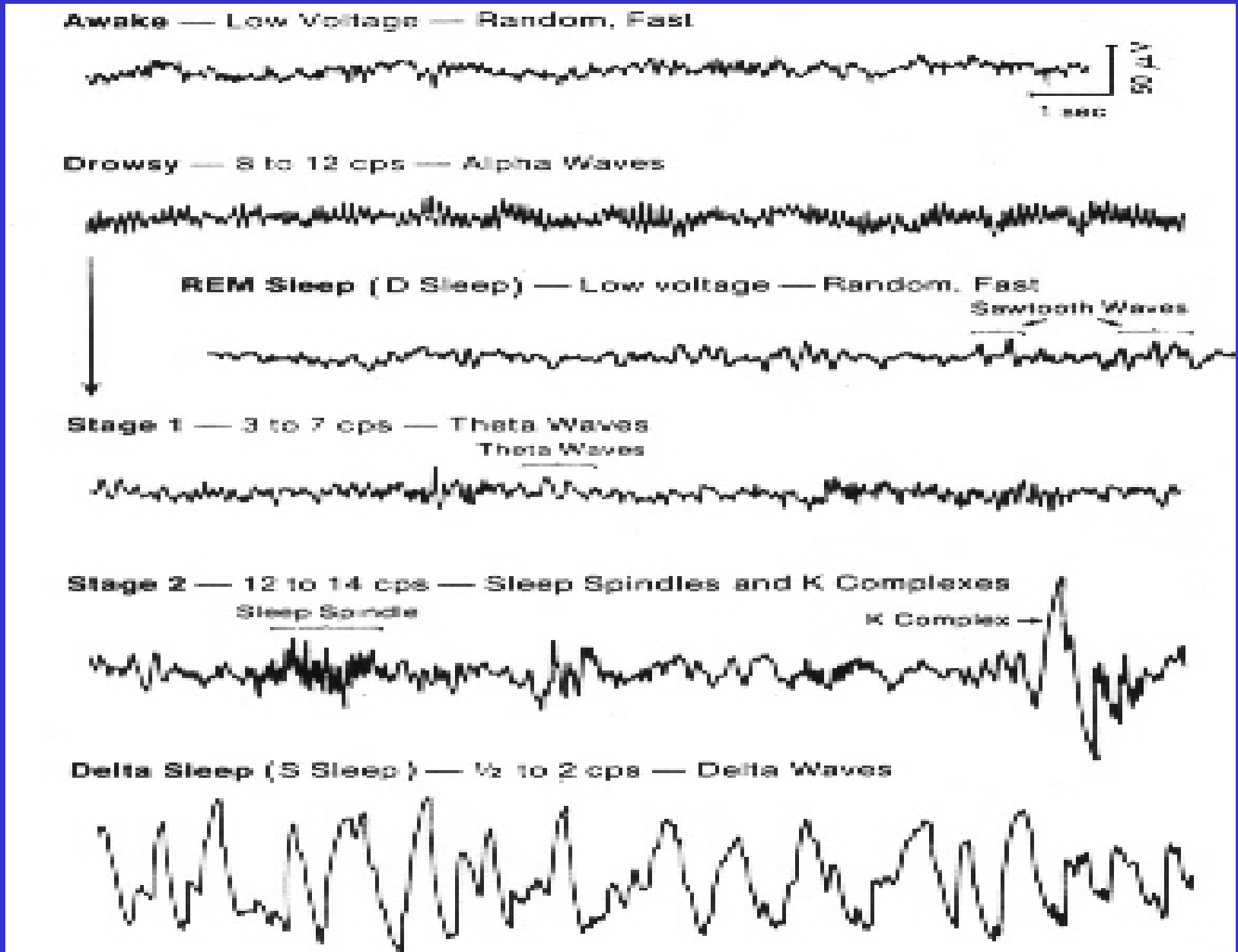
# REM sleep

- 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
50 μV
1 sec
Drowsy — 8 to 12 cps — Alpha Waves
REM Sleep (D Sleep) — Low voltage — Random, Fast
Sawtooth Waves
Stage 1 — 3 to 7 cps — Theta Waves
Theta Waves
Stage 2 — 12 to 14 cps — Sleep Spindles and K Complexes
Sleep Spindle
K Complex
Delta Sleep (S Sleep) — ½ 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.

- $CO_2$ 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 cm $H_2O$ OSA: > 0 cm $H_2O$

# 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 alNeth 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 hypersomnolence

# 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)

Atypical presentation

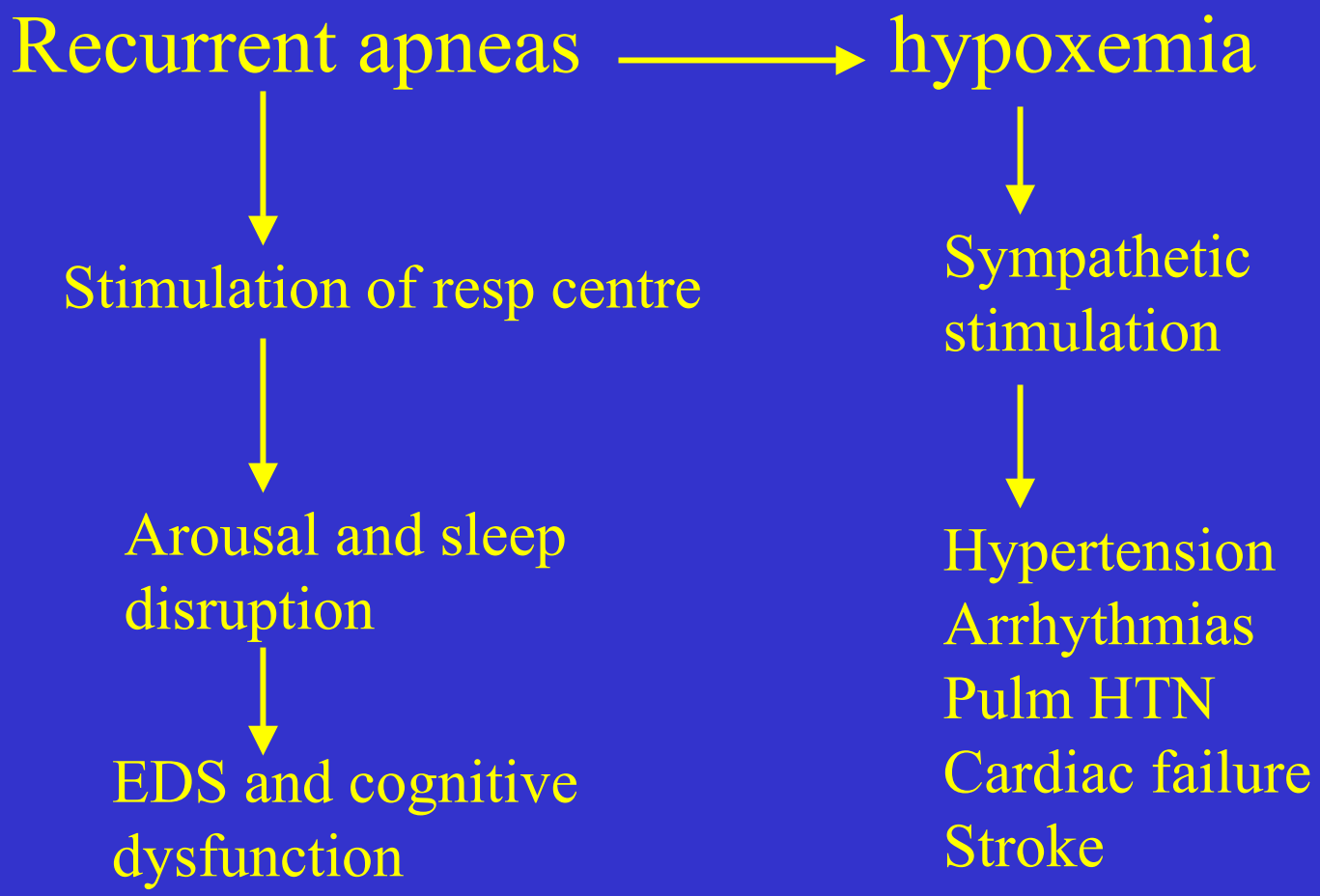
**Table 1** How OSAHS might present to non-sleep specialists

| | Presentation |
|---|---|
| Cardiologist[87] | Hypertension |
| | Left ventricular hypertrophy |
| | Nocturnal angina |
| | Myocardial infarction |
| | Arrhythmias, particularly bradyarrhythmias |
| | Heart failure |
| | Cor pulmonale |
| | Increased pulmonary artery pressure |
| Psychiatrist[88] | Depression |
| | Anxiety |
| | Behavioural problems |
| | Acute delirium |
| Neurologist[89–92] | Refractory epilepsy |
| | Stroke |
| | Impaired rehabilitation post stroke |
| | Headache on waking |
| Anaesthetist[93–95] | Difficult intubation |
| | Sensitivity to opioid analgesia and sedation |
| | Witnessed apnoeas during recovery |
| Urologist[96–98] | Nocturia |
| | Impotence |
| | Erectile dysfunction |
| Endocrinologist[99] | Hypothyroidism |
| | Acromegaly |
| | Diabetes |
| ENT surgeon[100] | Snoring |
| | Sore throat |
| | Hoarse voice |
| Gastroenterologist[101] | Oesophageal reflux |
| Haematologist[102] | Polycythaemia |
| Respiratory physician[103–105] | Nocturnal shortness of breath |
| | Respiratory failure |

# 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



# 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

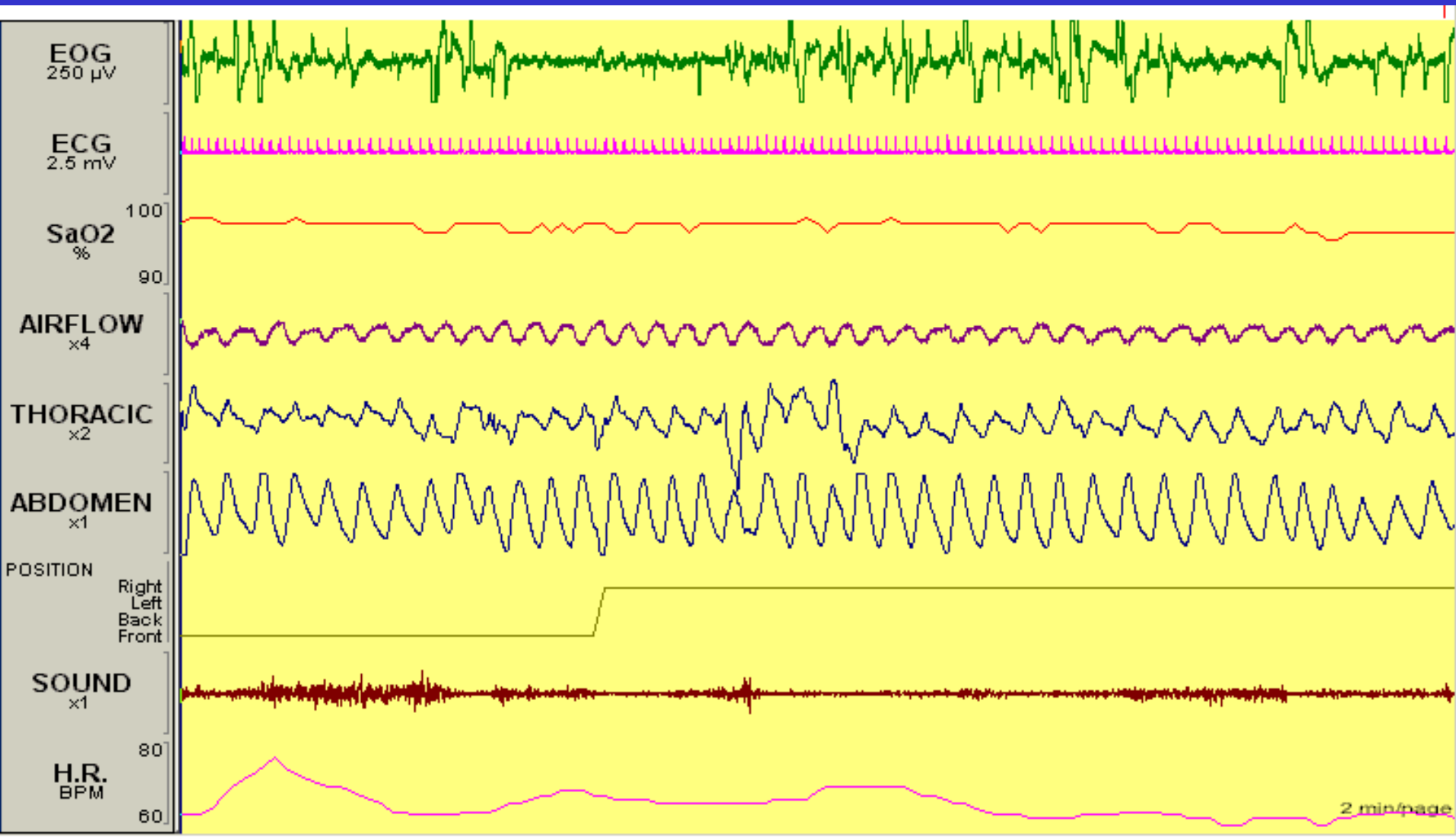
# AASM Classification

| Level | 1 | 2 | 3 | 4 |
|---|---|---|---|---|
| Parameters | min x7 EEG+ | min x7 EEG+ | min x 4 | min x1 |
| Body postn | monitor | possible | possible | no |
| Leg movts | EMG | optional | optional | no |
| Personnel | yes | no | no | no |
| Interventn | possible | no | no | no |

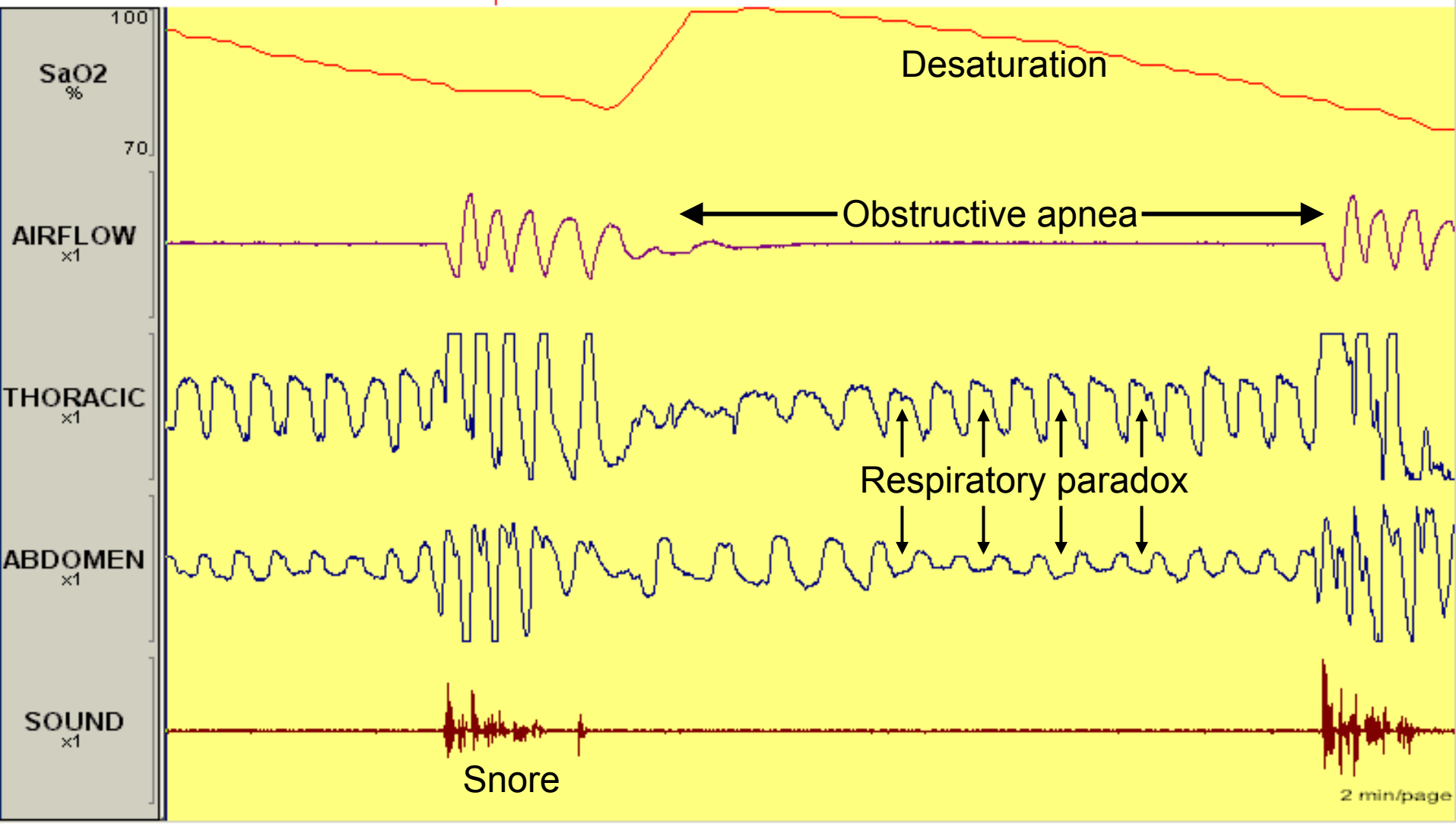
# PGI sleep lab

- 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)

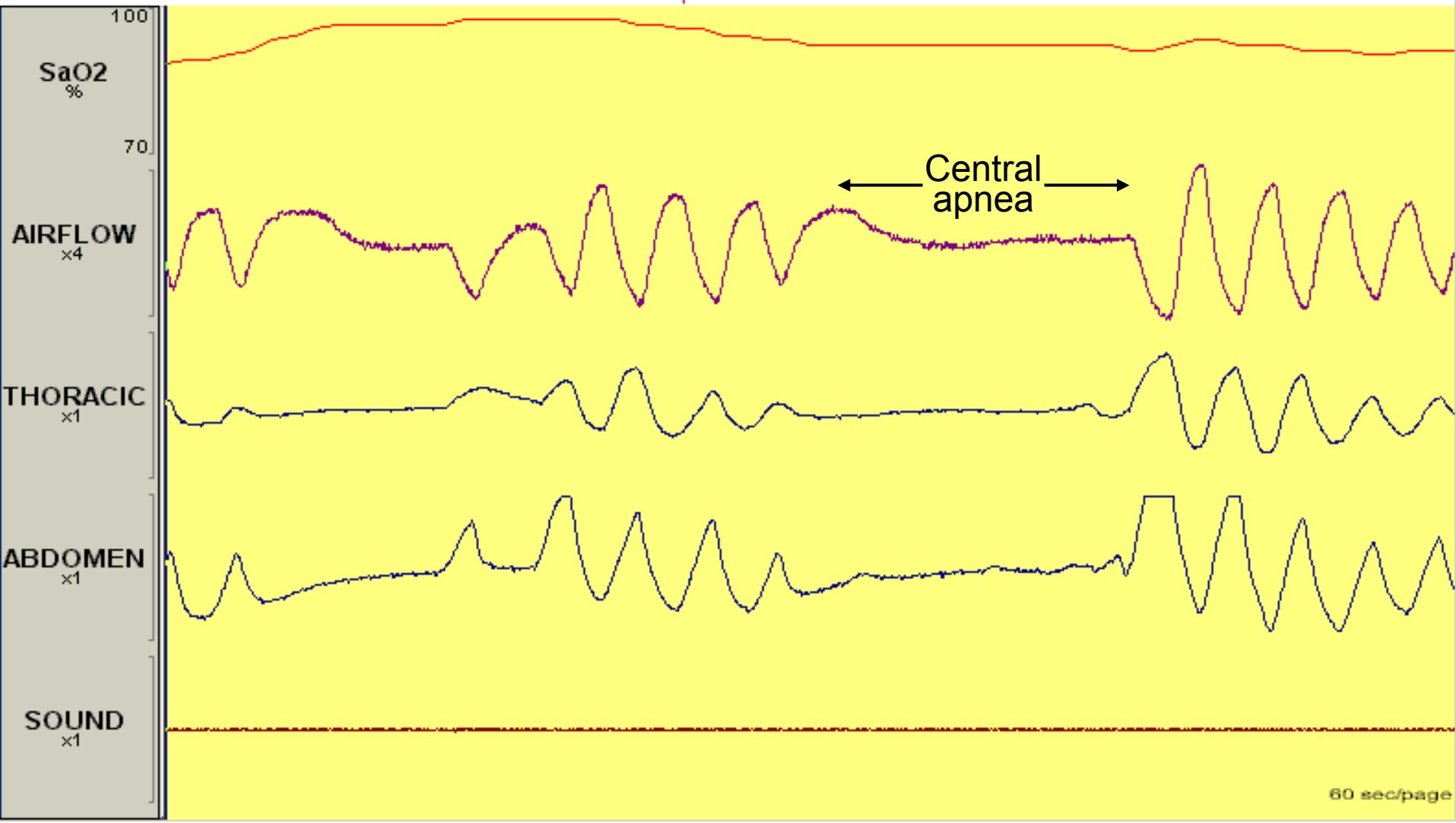
# Normal Sleep Study



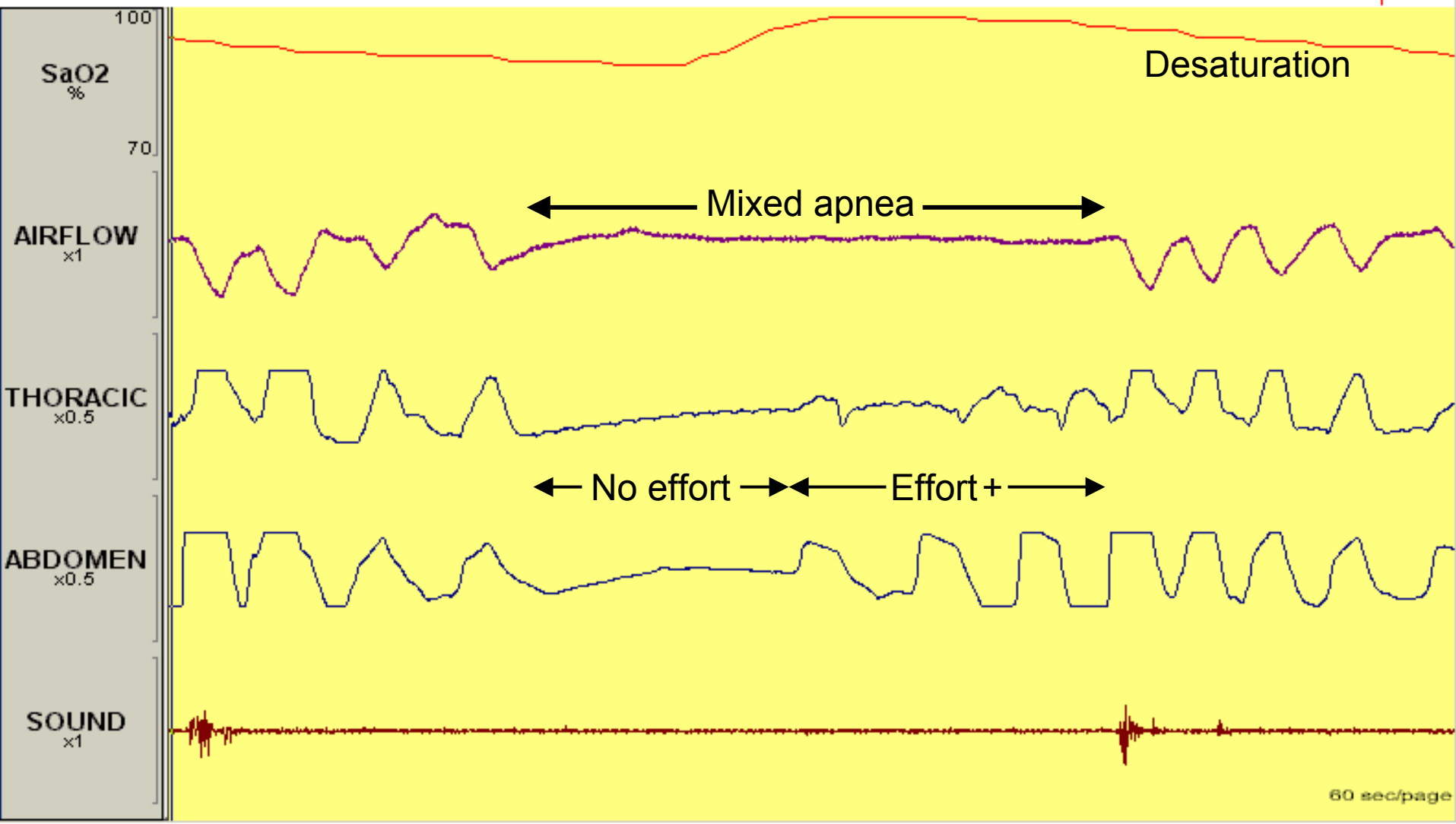
# Obstructive apnea: Complete cessation of airflow despite efforts to breathe



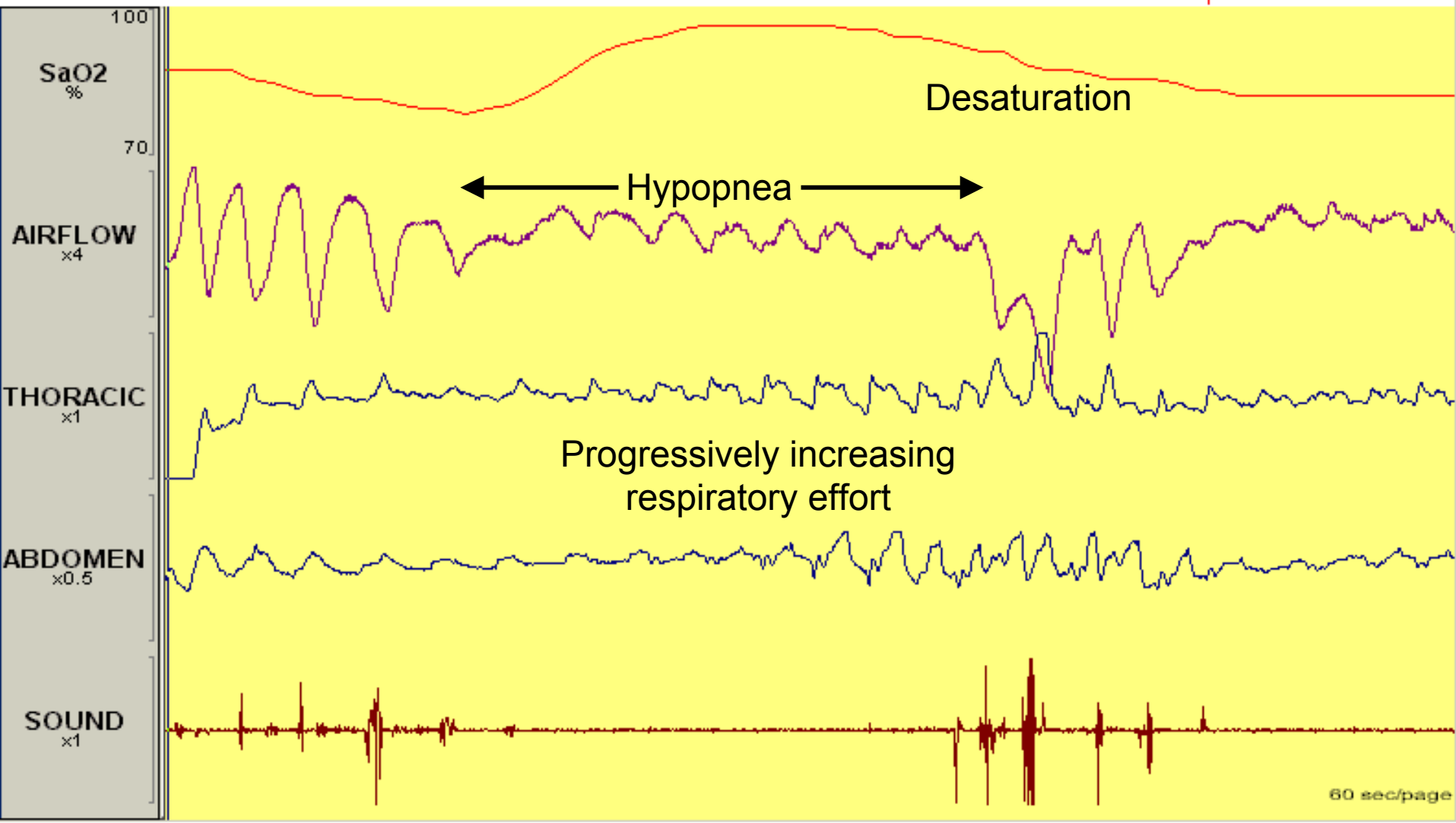
# Central apnea: Complete cessation of respiratory effort and airflow

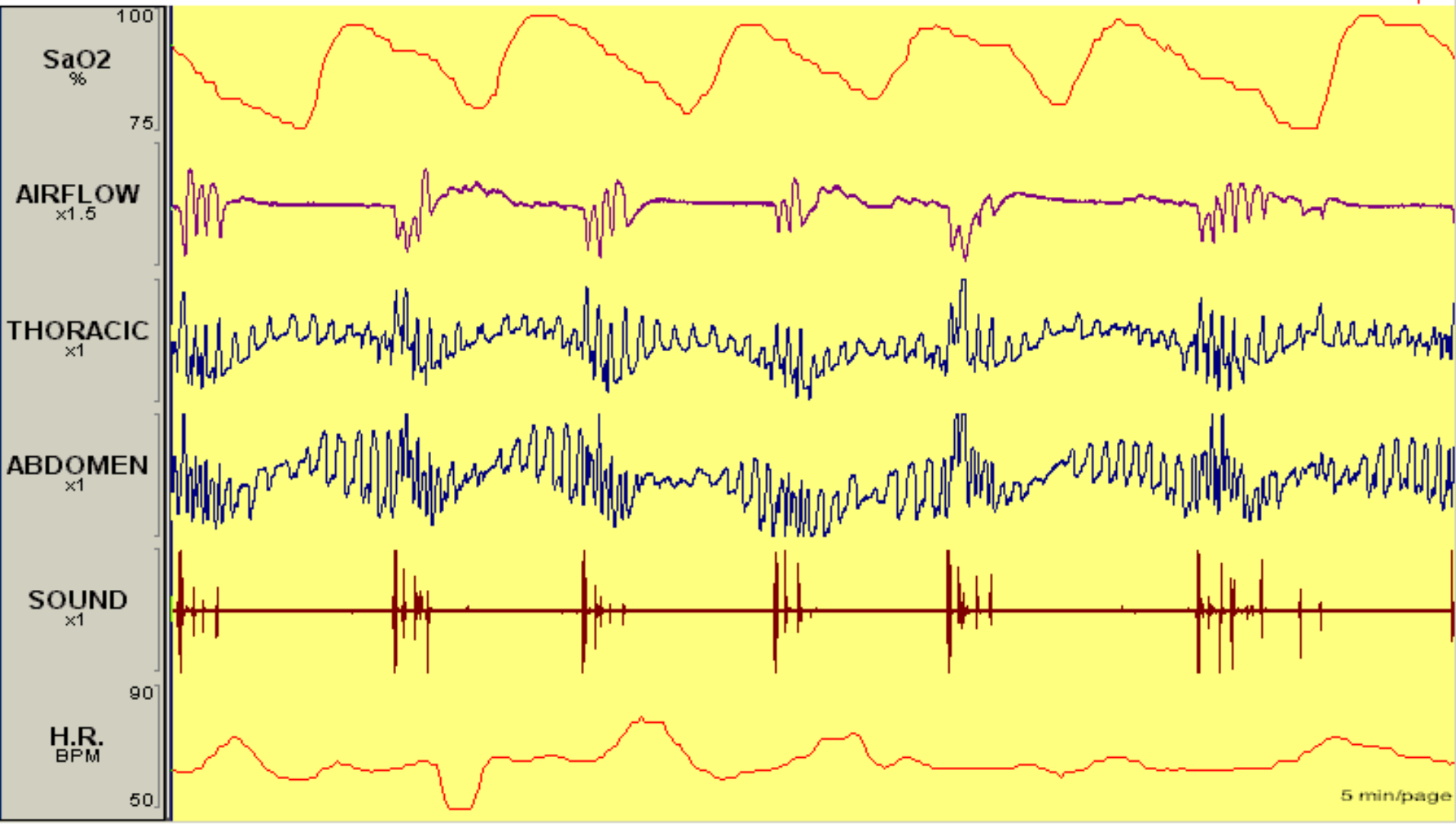


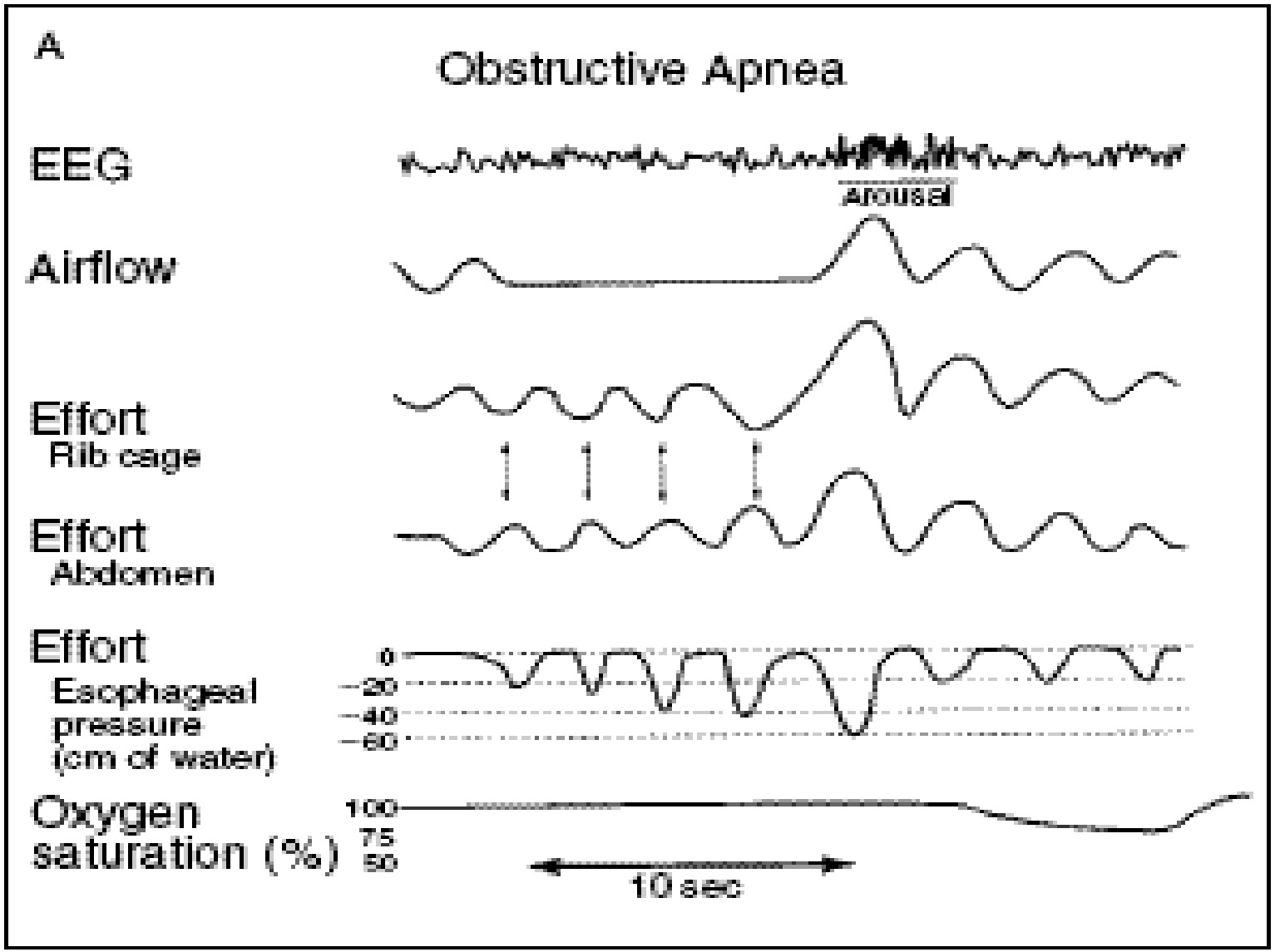
# Mixed apnea: Complete cessation of airflow with gradual increase in respiratory effort after an initial absence

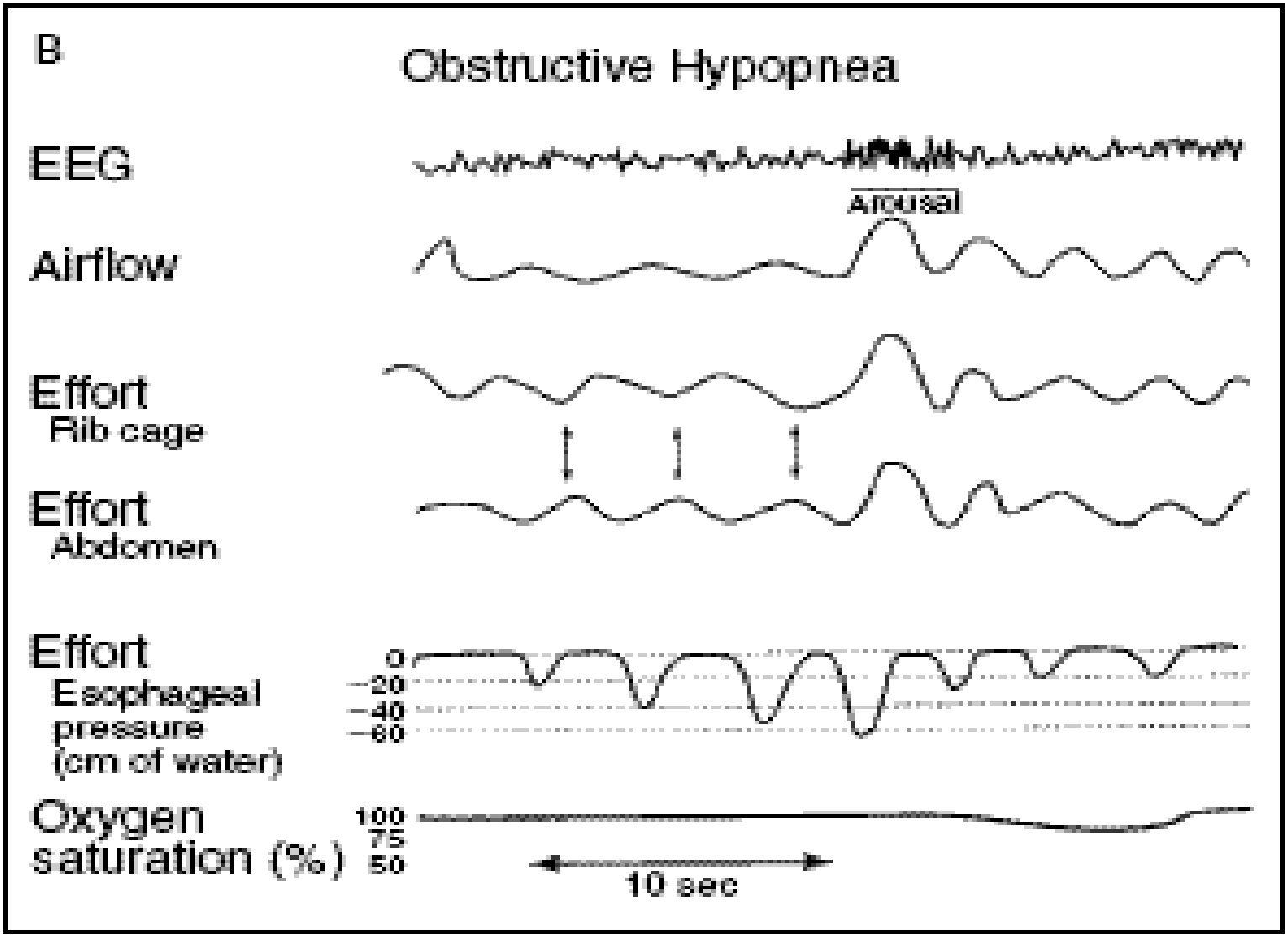


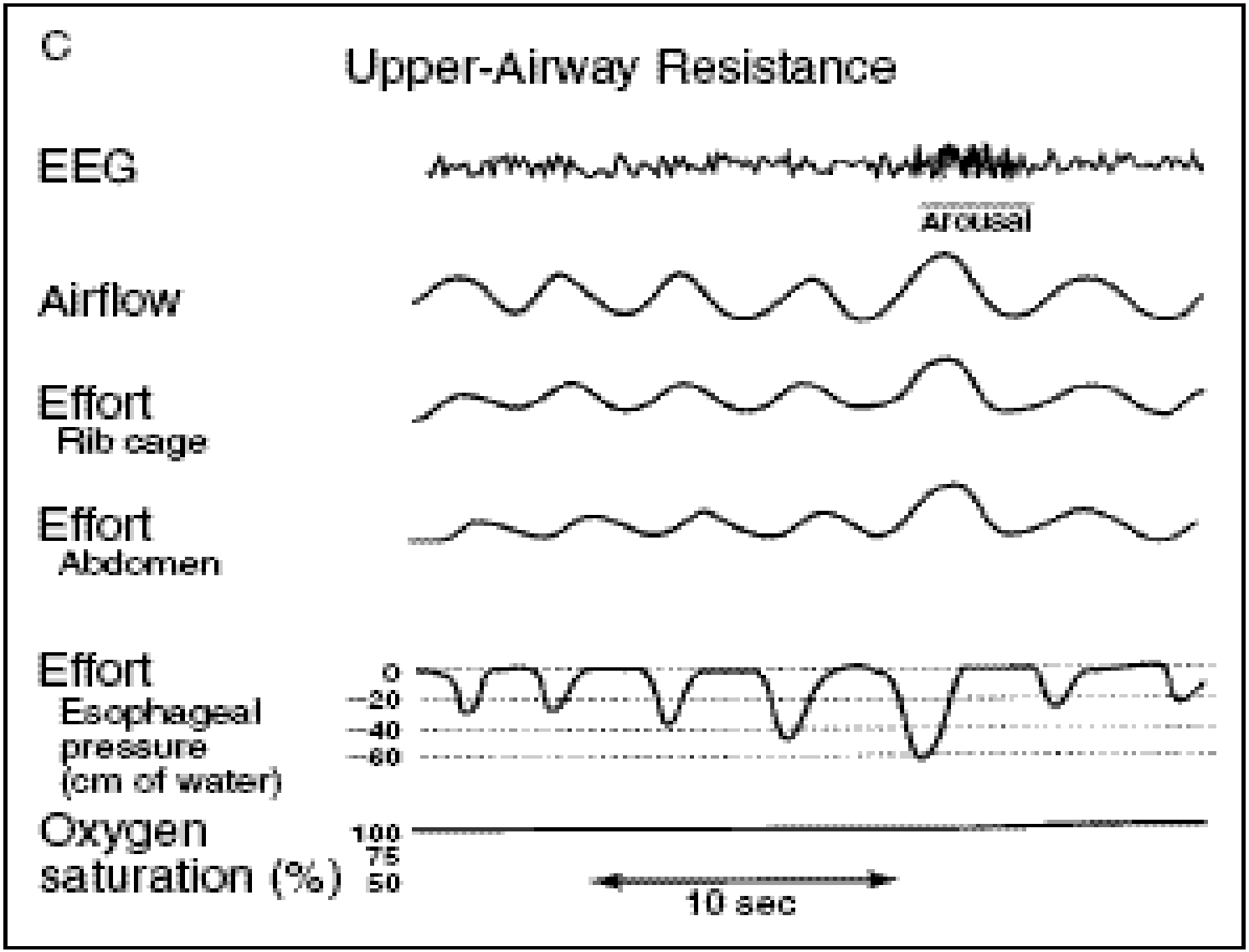
# Hypopnea: Reduction in airflow compared to baseline, associated with desaturation




100
SaO2
%
75
AIRFLOW
x1.5
THORACIC
x1
ABDOMEN
x1
SOUND
x1
90
H.R.
BPM
50
5 min/page


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


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


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

# 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

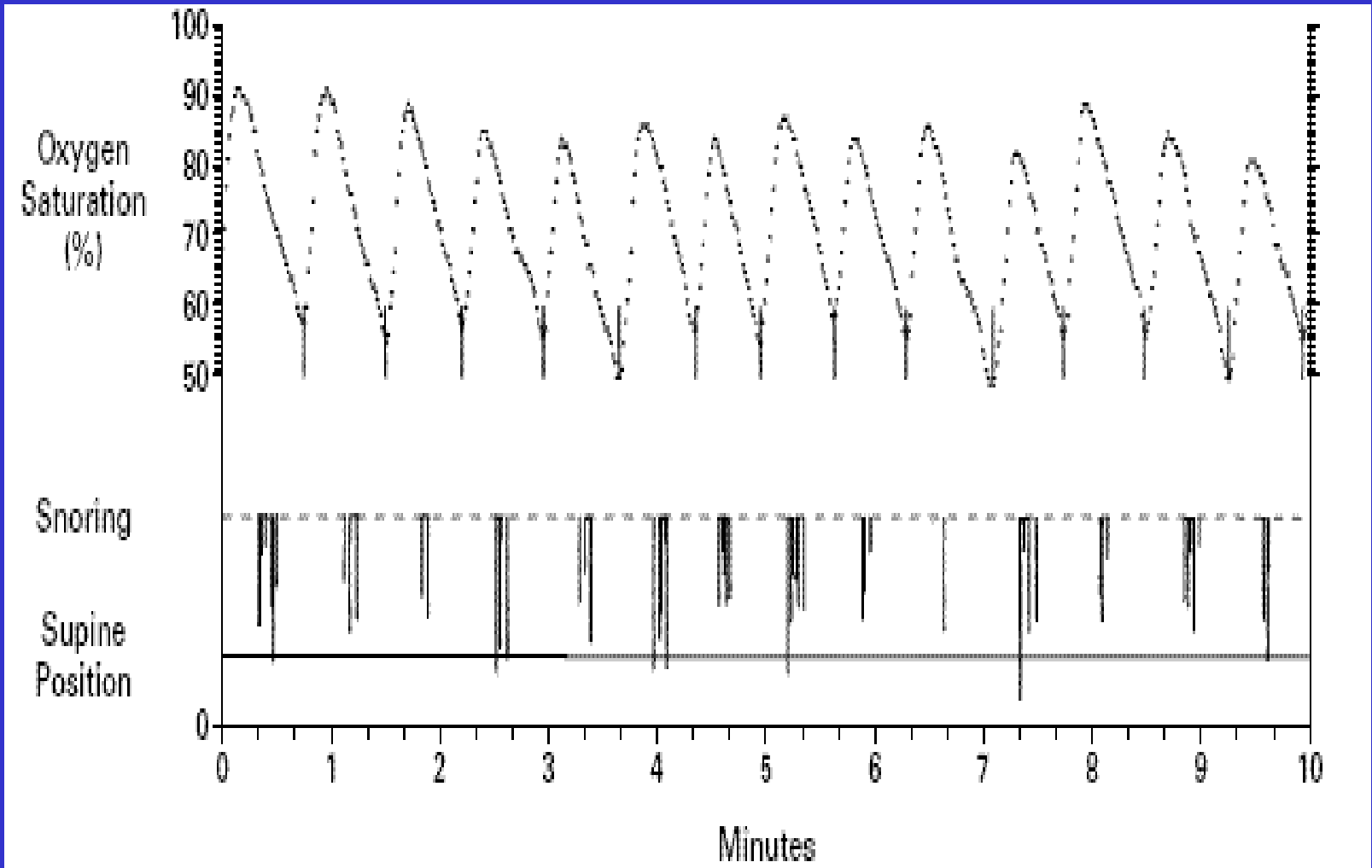



Figure 2. Pattern of Oxygen Saturation in a Patient with Severe Sleep Apnea.

# 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

- Dyshemoglobinemia
- Hypotension ,hypothermia
- Poor attachment / disconnection
- Recording artifacts in obese

# Split night study

- I$^{st}$ part – diagnosis of OSA
- II$^{nd}$ 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 ,Sleep1997*

# 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*

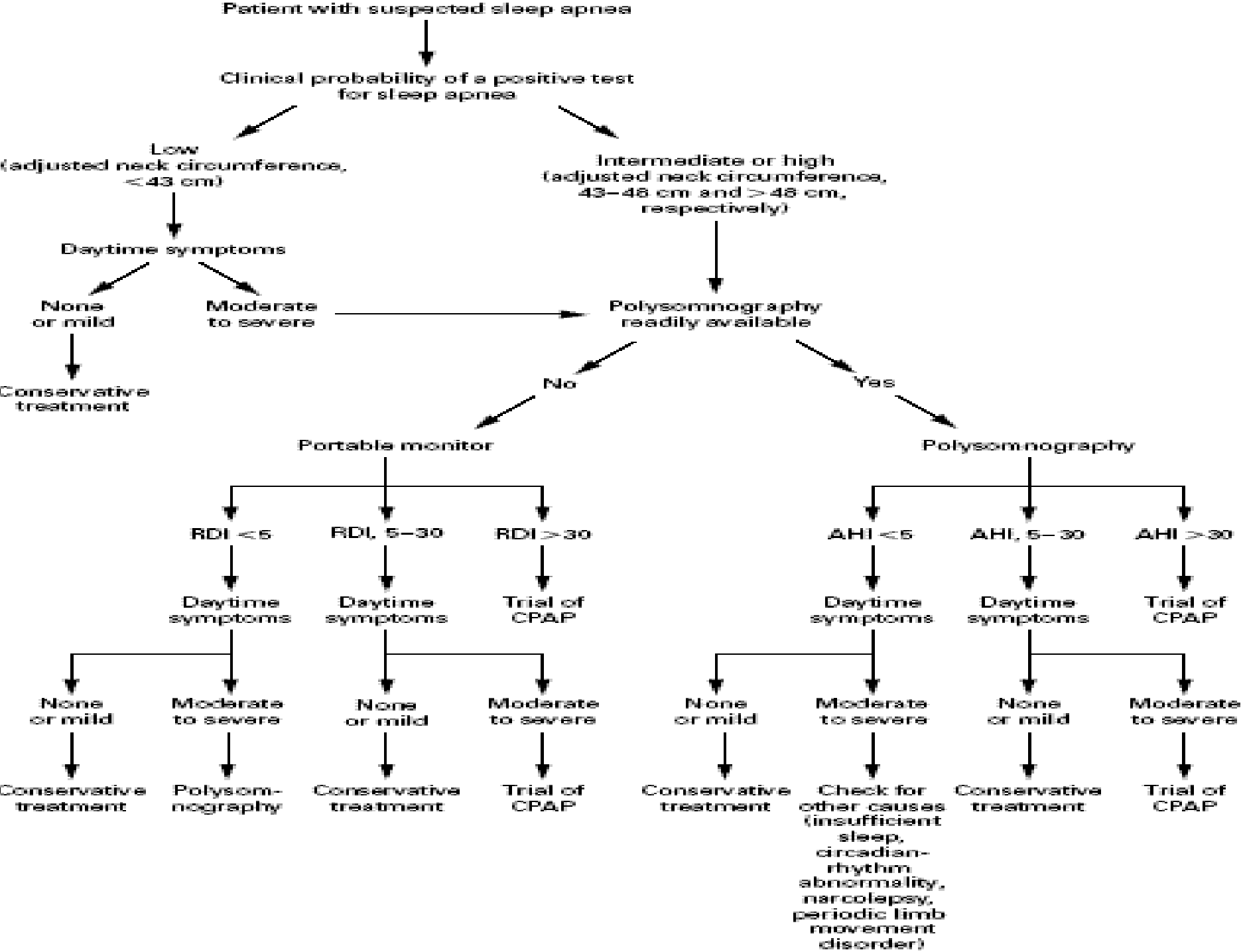
# Diagnostic role of APAP device

- 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

*Flemmons WW, N Engl J Med 2002*


Patient with suspected sleep apnea
Clinical probability of a positive test for sleep apnea
Low (adjusted neck circumference, <43 cm)
Intermediate or high (adjusted neck circumference, 43–48 cm and >48 cm, respectively)
Daytime symptoms
None or mild
Moderate to severe
Conservative treatment
Polysomnography readily available
No
Yes
Portable monitor
Polysomnography
RDI <5
RDI, 5–30
RDI >30
AHI <5
AHI, 5–30
AHI >30
Daytime symptoms
Daytime symptoms
Trial of CPAP
Daytime symptoms
Daytime symptoms
Trial of CPAP
None or mild
Moderate to severe
None or mild
Moderate to severe
None or mild
Moderate to severe
None or mild
Moderate to severe
Conservative treatment
Polysom-nography
Conservative treatment
Trial of CPAP
Conservative treatment
Check for other causes (insufficient sleep, circadian-rhythm abnormality, narcolepsy, periodic limb movement disorder)
Conservative treatment
Trial of CPAP

# 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)

*Strollo PJ, Clin Chest Med 2003*

# 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 cardiovasccular endpoints
- May be assoc with reduction in mortality

*Roux FJ et al Clin Chest Med 2003*

# 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.

- Behavioral
  - Weight loss
  - Avoidance of alcohol and sedatives
  - Avoidance of sleep deprivation
  - Nocturnal positioning
- Medical
  - First-line therapy
    - Positive pressure through a mask
  - Second-line therapy
    - Oral appliance
  - Other
    - Fluoxetine or protriptyline
    - Thyroid hormone (in hypothyroid patients)
    - Nocturnal oxygen
- Surgical
  - Upper-airway bypass
    - Tracheostomy
  - Upper-airway reconstruction
    - Uvulopalatopharyngoplasty
    - Genioglossal advancement
    - Maxillomandibular advancement

# 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