Screening, Diagnosis and Treatment of Sleep Disordered Breathing (SDB)

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Disclosures

• I have no disclosures at this time
Objectives

• Sleep Physiology
• Cost of Obstructive Sleep Apnea
• Evaluation and Assessment for OSA
• Making the diagnosis, choosing the proper testing
• Troubleshooting the barriers to successful treatment
• The role of the sleep medicine consultant
Overview

• What is sleep?
  • A reversible behavioral state of perceptual disengagement from and unresponsiveness to the environment.

• What is sleep good for?
  • Memory Consolidation
  • Energy Conservation
  • Brain Restoration
  • Protective Behavioral Adaptation
    • avoid exposure to predators
  • Immune Function
Normal Sleep and Ventilation

- **Sleep Stages**
  - Non-REM Sleep
    - Stage 1
    - Stage 2
    - Slow wave sleep
  - Stage REM

- **Sleep Architecture**
  - 4 to 5 cycles per night
  - SWS predominated in the second half of the night
  - Stage REM is longer as the night progresses.

**Hypnogram** - a recording of a normal nights sleep, displayed here as a chart

- 11 pm
- 7.30 am
- Note the short periods of waking through the night

Sleep stages:
- 1
- 2
- 3
- 4

Hours
Sleep Physiology

• Autonomic Nervous System
  • NREM: ↓ Sympathetic Activity, ↑ Parasympathetic
  • REM: ↓↓ Sympathetic, ↑↑ Parasympathetic

• Respiratory System
  • Decreased in PaO2 and SaO2

• Cardiovascular System
  • NREM: ↓ HR ↓ CO ↓ BP
  • Tonic REM: ↓↓ HR ↓↓ CO ↓↓ BP
  • Phasic REM: ↑ HR ↑ CO ↑ BP
  • BP ~ 10% lower while sleeping

• GI System
  • ↓ Swallowing, Salivary production and esophageal motility

• Renal System
  • ↓↓ Urine output

• Endocrine System
  • ↑ GH ↑ Prolactin ↑ PTH ↑ Testosterone
  • ↓ Cortisol ↓ Insulin ↓ TSH

• Musculoskeletal
  • Hypotonia/Atonia and inhibition of deep tendon reflex

• Thermoregulation
  • Core body temp lowest 2 hours prior to waking up
  • Circadian Pattern
What can go wrong?

• **Apnea** - Literally means “no breath”.

• **Obstructive Apnea**
  - **APNEA**: Cessation of respiration that lasts at least 10 seconds, due to obstruction in the upper airway, that may be associated with arousal and/or desaturation.
  - **HYPOPNEA**: shallow breathing in which the air flow in and out of the airway is less than half of normal--usually associated with oxygen desaturation.

• **Central Apnea**
  - Pause in respiratory activity due to failure to initiate the breath. (IE- no obstruction is present.)
Types of Sleep Apnea

Central | Obstructive | Mixed

Respiratory flow

Respiratory effort

O₂ sat
In the Starling resistor model, the collapsible segment of the tube is bound by an upstream and downstream segment with corresponding upstream and downstream pressures (Pus and Pds) and resistances (upstream resistance pressure and downstream resistance; data not shown). See text for further explanation (adapted in part from Gleadhill et al\textsuperscript{19}). Vimax = maximal inspiratory flow; Rus = upstream resistance.

Cost
Who is at risk for developing sleep apnea?

• Nearly 90% of cases of OSA are undiagnosed

• Only 10% of primary care physicians ask about OSA in standardized patient interviews (OSCE)

• In a mid-western middle age work force
  • AHI>5  9%W and 24%M
  • OSA  2%W and 4%M

• **Asian** - maxillofacial factors of more importance

• **Woman** - Lower BMI greater symptoms at lower AHI

• **Familial** - increased risk of both snoring and sleep apnea

Young et. al NEJM 328(17):1230-5 Apr 29,1993
Redline S. et al AJRCCM 151(3 Pt 1):682-7, Mar 1995

AJRCCM 2002 165: 1217-1239
Sleep 2004 27:1518-1525
US Prevalence of OSA

US OSAS prevalence is estimated at 3-5%; prevalence of moderate-severe OSA is estimated at 6.5-8.5%.

Public health costs
- Clear link established between moderate-severe OSA (AHI ≥ 15) and co-morbidities (e.g., treating OSA reduces CVD outcomes)
- We assume diagnosis/treatment and hidden healthcare costs apply to all people with moderate-severe OSA (which includes those with OSAS)

Public safety costs
- Limited published data on extent of self-reported sleepiness underestimation?
- We have chosen to estimate non-healthcare costs for the population with people with OSAS only

<table>
<thead>
<tr>
<th>Age group</th>
<th>Prevalence of OSAS Percent</th>
<th>Prevalence of AHI ≥ 15 Percent</th>
<th>Population in age group Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 30</td>
<td>1.5-2.51</td>
<td>~3.41</td>
<td>41</td>
</tr>
<tr>
<td>30-60</td>
<td>2.5-4.51</td>
<td>~5.5-7.51</td>
<td>42</td>
</tr>
<tr>
<td>60+</td>
<td>4.5-9.51</td>
<td>~19-211</td>
<td>17</td>
</tr>
</tbody>
</table>

1. Scaled to take into account prevalence growth drivers (obesity and age)
2. One traffic accidents study suggests ~25% of people underestimate their sleepiness.

Prevalence of sleep-disordered breathing in the general population: the HypnoLaus Study

A Sleep-disordered breathing

B Sleep apnoea syndrome

Heinzer et al Lancer Resp Med 2015 3:310-318
Untreated OSA – Major Economic Cost

Economic cost of unmanaged moderate-severe OSA in the US estimated between ~$65B and $165B

Estimated annual economic cost of OSA/OSAS in the US

$ Billions

<table>
<thead>
<tr>
<th>Public health costs</th>
<th>Public safety costs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosis and treatment</td>
<td>2-10</td>
</tr>
<tr>
<td>Hidden health-care costs</td>
<td>45-80</td>
</tr>
<tr>
<td>Traffic accidents</td>
<td>10-40</td>
</tr>
<tr>
<td>Workplace accidents</td>
<td>5-20</td>
</tr>
<tr>
<td>Loss of productivity</td>
<td>5-15+</td>
</tr>
<tr>
<td>Other</td>
<td>Unknown</td>
</tr>
<tr>
<td>Total</td>
<td>67-165+</td>
</tr>
</tbody>
</table>

- MD visits, polysomnography diagnostic, CPAP device, CPAP titration, and disposables
- Incremental medical costs of co-morbidities and OSAS-linked traffic/workplace accidents
- All nonmedical traffic accident costs related to OSAS (e.g., lost wages, property damage)
- All nonmedical, nonmotor vehicle workplace accident costs associated with OSAS
- Cost of OSAS-driven absenteeism (poor on-the-job performance not estimated)
- Societal costs of disrupted lives (e.g., family turmoil, increased divorce, child development)

SOURCE: Academic papers, expert interviews, market reports
Sleep Apnea is Associated with significant Co-morbidities

- Cardiovascular Complications
- Neuro-cognitive Complications
- Metabolic Complications
Type II Diabetes and OSA

• 40% of people with OSA have diabetes, the incidence of new diabetes in patients with OSA is unknown

• In patients with diabetes, the prevalence of OSA may be as high as 23% and the prevalence of some form of SDB may be as high as 58%.

• OSA may effect the glycemic control of patients with type 2 diabetes
OSA and Cardiovascular Disease

• Primary HTN: Prevalence 35%
• Drug resistant HTN: 65-80% prevalence
• Heart Failure: 21-37% Prevalence
• Atrial Fibrillation: OSA present 5x more likely
• Coronary Artery Disease: 30% Prevalence
• Stroke: 60% prevalence
Sleep Disorder Breathing and Mortality: Wisconsin Sleep Cohort (n=1396)

- Baseline AHI category
- All-cause mortality Hazard Ratio (95% CI)
- Cardiovascular mortality Hazard Ratio (95% CI)

<table>
<thead>
<tr>
<th>Category</th>
<th>Hazard Ratio (95% CI)</th>
<th>Hazard Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>None: 0 - &lt; 5</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>Mild: 5 - &lt; 15</td>
<td>1.4 (0.7, 2.6)</td>
<td>1.3 (0.4, 4.1)</td>
</tr>
<tr>
<td>Moderate: 15 - &lt; 30</td>
<td>1.7 (0.7, 4.1)</td>
<td>1.5 (0.3, 7.3)</td>
</tr>
<tr>
<td>Severe: ≥30</td>
<td>3.8 (1.6, 9.0)</td>
<td>5.2 (1.4, 19.2)</td>
</tr>
</tbody>
</table>

*Hazard ratios adjusted for age, age², sex, body mass index, and body mass index²

Sleep 2008 31: 1071-1078
Evaluation and Assessment for OSA
OSA: Complaints

- Day time sleepiness/fatigue
- AM Headache
- Vivid Dreams
- Insomnia
- Hyperactivity
- Memory and learning impairments
- Snoring
- Unrefreshing sleep
OSA: Physical Exam

- Neck size greater than 17.5 inches (men)
- Weight greater than a BMI of 30.
- Pharynx Thick side walls
- Uvula Long
- Soft palate Low
- Tonsils Large
- Nasal Obstruction

Mallampati classification

Class I = visualization of the soft palate, uvula, anterior and posterior pillars
Upper Airway Anatomy
What is the Epworth Sleepiness Scale?

- Sitting and reading
- Watching TV
- Sitting inactive in a public place (e.g., a theater or a meeting)
- As a passenger in a car for an hour without a break
- Lying down to rest in the afternoon when circumstances permit
- Sitting and talking to someone
- Sitting quietly after a lunch without alcohol
- In a car, while stopped for a few minutes in traffic

Choosing the right test for the right patient
# Types of Sleep Studies

<table>
<thead>
<tr>
<th>Sleep test</th>
<th>Description</th>
<th>Personnel</th>
<th>Required signals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type I</td>
<td>In-lab PSG</td>
<td>Attended</td>
<td>Minimum of 7 signals; EEG, EOG, EKG, chin EMG, respiratory flow and effort, pulse oximetry</td>
</tr>
<tr>
<td>Type II</td>
<td>Portable PSG</td>
<td>Unattended</td>
<td>Same as above</td>
</tr>
<tr>
<td>Type III</td>
<td>4-channel portable study</td>
<td>Unattended or attended</td>
<td>Minimum of 4 signals; pulse oximetry, EKG/HR, 2 channels of respiratory airflow or movement</td>
</tr>
<tr>
<td>Type IV</td>
<td>Continuous recording of 1-2 signals</td>
<td>Unattended</td>
<td>Pulse oximetry or respiratory flow</td>
</tr>
</tbody>
</table>

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OSA: Diagnosis - Polysomnogram

8 hour over night study

- EEG - 6 leads
- EOG (EYE) - 2 leads
- EKG - 2 leads
- Leg movement - 2 leads
- Respiratory flow - nasal/ oral sensor
- $O_2$ saturation - finger pulse oximetry
- Abdomen and Thoracic strain gauges.
Home Portable Sleep Studies

Apneas/Hypopneas

HDI 34.5

Hypopneas

Obs

Mix

Cen

AAD 35.0

Hypopneas 20.0s / CPAP: 0

Oxygen Saturation

Epoch: 4
Max: 94% Min: 91%

Body Position

Epoch: 4
Body Position: Left Side
Is HST Inferior to PSG?: The HOME PAP Study

• Compared HST vs. lab PSG for OSA diagnosis and PAP treatment
• Multicenter RCT
• Patients randomized to lab PSG (1-2 sleep studies) vs. home-based type III testing followed by AutoPAP with transition to fixed pressure to CPAP after 1 week based on 90% pressure

Is HST Inferior to PSG?: The HOME PAP Study

• Conclusions: HST for both diagnosis and treatment of moderate-to-severe OSA is not inferior to lab PSG
  • Acceptance of PAP therapy (87%)
  • Titration pressures (10-11 cwp)
  • Effective titrations (85%)
  • Time to treatment
  • ESS score (14.6 to 8.7 before and after in both arms)

• Study showed HST saved on average $47,000

• In lab PSG
  • Administrative costs
  • Over head costs

• Costs in the “real world”
  • Missing mild OSA
  • Higher failures due to cognitive issues

Ambulatory Management of OSA: VA Study

• Compared OSA diagnosis and PAP treatment with HST vs. lab PSG
• Multicenter (VA) RCT and Non-inferiority study

Lab Pathway

• How is CPAP attained?
  • 1-2 sleep studies needed depending on the ability to perform a “split night” study

Home Testing Pathway

• How is CPAP attained?
  • Auto CPAP used
  • Fixed pressure set at 90% pressure
  • If AHI on auto CPAP was >10, the patient sent back to lab for a formal titration study

Ambulatory Management of OSA: VA Study

• Superiority
  • Functional Outcomes of Sleep Questionnaire (FOSQ) improvement was statistically better in the home group compared to the lab group
  • QoL was better for both groups after CPAP

• Compliance
  • No significant difference between groups

### Types of Portable Sleep Testing

#### Type 2 Studies
- Can diagnose all conditions but requires a highly trained tech which is costly
- Less stage 1 sleep
- Could be used in hospitalized patients
- More convenient for research subjects
  - *Sleep Heart Health Study*
  - *Sleep Action for Health in Diabetes*

#### Type 3 Studies
- Pt can do their own setup
- Pros:
  - Diagnose CSA vs. OSA
- Cons:
  - No EEG: Cannot determine wake vs. sleep
  - Cannot be used to diagnose restless leg syndrome or narcolepsy
Types of Portable Sleep Testing

• Over 30 type 2 and 3 monitors are currently marketed
  • It should not be assumed that the monitors are equivalent, even if they’re in the same class

• No studies to date have compared portable monitoring devices head-to-head; it’s unknown which combination of signals have the best sensitivity and specificity

• Technology changes have not been controlled for
  • Thermal flow vs. pressure transducer

Contraindications to HST

- Neuromuscular disease (ALS, MD, PD)
- Stroke with respiratory complications
- Epilepsy
- NYHA III or IV heart failure (EF <45%)
- Moderate-severe pulmonary disease with nocturnal O₂ use or daytime hypercapnea
- Super obesity (BMI >45)
- Another known sleep disorder (narcolepsy, parasomnia, central sleep apnea)
Picking your OSA test

• Home Sleep Testing
  • High Pre-test Probability
  • No significant cardiovascular co-morbidities

• Split Night Polysomnogram
  • High Pre-test Probability
  • Interested in PAP therapy
  • Need to expedite diagnosis and treatment (Symptomatic)

• Diagnostic Polysomnogram
  • Intermediate Pre-test probability
  • Unable to perform home sleep testing
  • Cardiovascular co-morbidities
Troubleshooting the barriers to successful treatment
# Positive Airway Pressure

## Types of Home Nocturnal Positive Airway Pressure Devices

<table>
<thead>
<tr>
<th>Type of Device</th>
<th>Pressure Delivery</th>
<th>Indication</th>
<th>Mechanism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Continuous Pressure</td>
<td>Unchanged through the night</td>
<td>OSA</td>
<td>Prevents upper airway obstruction</td>
</tr>
<tr>
<td>Bilevel Pressure</td>
<td>Separate inspiratory and expiratory pressure</td>
<td>1) OSA</td>
<td>In OSA may increase patient comfort and compliance</td>
</tr>
<tr>
<td>Auto Pressure</td>
<td>Delivered pressure changes breath to breath</td>
<td>1) Estimating CPAP requirements in OSA 2) Improving OSA patient comfort and compliance</td>
<td>Measurement of changes in flow are compensated for by increased pressure delivered on a breath to breath basis</td>
</tr>
</tbody>
</table>
CPAP Compliance

![Graph showing CPAP Compliance over hours of nightly CPAP use with different scales for different measures: FOSQ, ESS, MSLT.](image-url)
CPAP Compliance
CPAP Compliance

3 hours of CPAP

4 hours of CPAP
Long term Cardiovascular Outcomes

A

Cumulative incidence of fatal CVS events (%)

- Controls
- Snorers
- Mild OSAH
- Severe OSAH
- OSAH with CPAP

B

Cumulative incidence of non-fatal CVS events (%)

- Controls
- Snorers
- Mild OSAH
- Severe OSAH
- OSAH with CPAP

Controls 264 262 259 258
Snorers 377 372 361 232
Mild OSAH 403 401 392 264
Severe OSAH 235 229 221 167
OSAH with CPAP 372 364 361 229

Lancet 2005 365: 1046-1053
PAP is not an easy therapy to tolerate

- Restrictive sleep
- Dry mouth
- Skin Irritation
- Sinus congestion
- Claustrophobia
- Fragmented sleep secondary to leak
CPAP Adherence and CV Outcomes
SAVE Trial

Improving Adherence and Compliance

Compliance Summary

<table>
<thead>
<tr>
<th>Data Range</th>
<th>2/18/2018 - 3/19/2018 (30 days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days with Device Usage</td>
<td>25 days</td>
</tr>
<tr>
<td>Days without Device Usage</td>
<td>5 days</td>
</tr>
<tr>
<td>Percent Days with Device Usage</td>
<td>83.3%</td>
</tr>
<tr>
<td>Cumulative Usage</td>
<td>4 days 13 hrs. 10 mins. 7 secs.</td>
</tr>
<tr>
<td>Maximum Usage (1 Day)</td>
<td>7 hrs. 35 mins. 49 secs.</td>
</tr>
<tr>
<td>Average Usage (All Days)</td>
<td>2 hrs. 26 mins. 22 secs.</td>
</tr>
<tr>
<td>Average Usage (Days Used)</td>
<td>4 hrs. 19 mins. 36 secs.</td>
</tr>
<tr>
<td>Minimum Usage (1 Day)</td>
<td>1 hr. 9 mins. 18 secs.</td>
</tr>
<tr>
<td>Percent of Days with Usage &gt;= 4 Hours</td>
<td>56.0%</td>
</tr>
<tr>
<td>Percent of Days with Usage &lt; 4 Hours</td>
<td>50.0%</td>
</tr>
<tr>
<td>Total Blow Time</td>
<td>5 days 9 hrs. 33 mins. 49 secs.</td>
</tr>
</tbody>
</table>

Auto-CPAP Summary (Phillips Respironics)

| Auto-CPAP Mean Pressure | 11.1 cmH2O |
| Auto-CPAP Peak Average Pressure | 12.1 cmH2O |
| Average Device Pressure <= 40% of Time | 12.8 cmH2O |
| Average Time in Large Leak Per Day | 48 secs |
| Average AHI               | 2.8 |

Compliance Report

<table>
<thead>
<tr>
<th>Usage</th>
<th>05/29/2018 - 08/27/2018</th>
</tr>
</thead>
<tbody>
<tr>
<td>Usage days</td>
<td>90/90 days (100%)</td>
</tr>
<tr>
<td>&gt;4 hours</td>
<td>90 days (100%)</td>
</tr>
<tr>
<td>&lt;=4 hours</td>
<td>0 days (0%)</td>
</tr>
<tr>
<td>Usage hours</td>
<td>623 hours 56 minutes</td>
</tr>
<tr>
<td>Average usage (total days)</td>
<td>6 hours 57 minutes</td>
</tr>
<tr>
<td>Average usage (days used)</td>
<td>6 hours 57 minutes</td>
</tr>
<tr>
<td>Median usage (days used)</td>
<td>7 hours 2 minutes</td>
</tr>
</tbody>
</table>

S9 AutoSet

<table>
<thead>
<tr>
<th>Serial number</th>
<th>231132000868</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mode</td>
<td>CPAP</td>
</tr>
<tr>
<td>Elt pressure</td>
<td>11 cmH2O</td>
</tr>
<tr>
<td>EPR</td>
<td>Fulltime</td>
</tr>
<tr>
<td>EPR level</td>
<td>2</td>
</tr>
</tbody>
</table>

Therapy

<table>
<thead>
<tr>
<th>Leaks - U/min</th>
<th>Median: 0.2</th>
<th>95th percentile: 1.9</th>
<th>Maximum: 5.6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Events per Hour</td>
<td>AI: 0.4</td>
<td>HI: 1.3</td>
<td>AH: 1.7</td>
</tr>
<tr>
<td>Apnea Index</td>
<td>Central: 0.2</td>
<td>Obstructive: 0.1</td>
<td>Unknown: 0.0</td>
</tr>
</tbody>
</table>

Usage - hours

Graph showing usage hours from 2018-2019.
Other Treatment Options

• Oral Appliance Therapy
  • Over 20+ types of devices
  • Typically used for mild to moderate OSA in patients with no CV risk factors
  • Average cost ~$830
  • No way to monitor adherence
  • Meta-analysis: Oral appliance therapy is efficacious in ~50% of all patients with OSA

Sleep 2006 29: 244-262
Other Treatment Options

- Upper Airway Stimulation
  - INSPIRE therapy
  - Unilateral hypoglossal nerve stimulation
  - Sensing lead placed between internal and external intercostal muscles to detect ventilation

Other Treatment Options

• ADHERE TRIAL
  • Multicenter registry of patient with UAS
  • Six month follow-up showed improvement in both AHI and ESS
  • Average use 6.6 ± 2.4 hours

Boon J Oto Head Neck 2018 159(2): 379-385
Summary

• Incidence and prevalence of OSA has increased over the last 20 years and will continue to increase in the future with the ongoing obesity crisis, leading to increased healthcare costs
• Transition of diagnosis from in lab PSG to home sleep testing
• Improved cardiovascular outcomes associated with CPAP treatment
• Randomized controlled trials do not demonstrate a favorable treatment response, but this is confounded by poor adherence to therapy in those trials
• Not all patients respond to PAP therapy and have to explore other treatment options
When to call for help?

Suspected OSA
- Primary care referral
  - Sleep specialist
    - Diagnostic sleep study

~50% CPAP fail
- CPAP titration study
  - CPAP recommendation
    - Sleep specialist
    - Sleep specialist
  - Other therapies
    - Sleep specialist

Sleep specialist

Oral appliance recommendation
- Dental visits/acclimatization
  - ~50% sub-therapeutic response

Carberry et al, CHEST 2018 153(3) 744-755
Thank You

Questions??