Sleep Disorders Update

Ronald J. Servi DO FCCP
Adjunct Assistant Professor
Department of Pulmonary Medicine
University of Texas MD Anderson Cancer Center
Banner MD Anderson Cancer Center
Gilbert, AZ
Question #1

• Signs and symptoms of sleep disorders poorly predict disease severity.
  • A. True
  • B. False
Question #2

• Appropriate therapy for sleep disorders is dependent on severity
  • A. True
  • B. False
Question #3

- Sleep disorders can lead to increased morbidity from the cardiovascular consequences, increased risk of motor vehicle accidents and, as a result, increased mortality
  - A. True
  - B. False
Function of Sleep

- If sleep does not serve an absolutely vital function, then it is the biggest mistake the evolutionary process ever made.

Allan Rechtschaffen
Coeditor of the Standard Sleep Scoring System
Sleep Stage: Ontogeny
Total Sleep Requirement

![Histogram of Total Sleep Requirement](image)
A Good Nights Rest

Adults typically require 7-9 hours of sleep a night.

<table>
<thead>
<tr>
<th>NREM (75% of night)</th>
<th>Sleepers first enter NREM (non-rapid eye movement), which is composed of Stages 1-4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 1</td>
<td>Lightly asleep</td>
</tr>
<tr>
<td>Stage 2</td>
<td>Onset of sleep; detached with environment, normal breathing and heart rate, and body temperature decreases</td>
</tr>
<tr>
<td>Stages 3/4 Slow Wave</td>
<td>Deepest and most restorative sleep; blood pressure and breathing rate decrease, regain energy, and release hormones for growth and development</td>
</tr>
<tr>
<td>REM (25% of night)</td>
<td>Rapid eye movement. Provides energy to brain and body. Brain is active and dreams occur in this stage. Muscles shut down as body becomes immobile and relaxed. Breathing and heart rate may become irregular.</td>
</tr>
</tbody>
</table>

Let Sleep Work for You! Brochure from National Sleep Foundation, Jan 2003
Sleep History

• Activities prior to sleep onset
• Sleep environment
• Sleep onset
• Awakenings during sleep
• Sleep duration
• How much do you feel rested
Sleep History

• Behavior During Sleep
  • Snoring
  • Movement
  • Legs
  • Parasomnia
Sleep History

- Naps
  - How often
  - What time
  - How long
- Cataplexy, Hypnogagic Hallucinations, Sleep Paralysis
### Epworth Sleepiness Scale (ESS)

<table>
<thead>
<tr>
<th>Situation</th>
<th>Chance of dozing (0-3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sitting and reading</td>
<td>0 1 2 3</td>
</tr>
<tr>
<td>Watching television</td>
<td>0 1 2 3</td>
</tr>
<tr>
<td>Sitting inactive in a public place—for example, a theater or meeting</td>
<td>0 1 2 3</td>
</tr>
<tr>
<td>As a passenger in a car for an hour without a break</td>
<td>0 1 2 3</td>
</tr>
<tr>
<td>Lying down to rest in the afternoon</td>
<td>0 1 2 3</td>
</tr>
<tr>
<td>Sitting and talking to someone</td>
<td>0 1 2 3</td>
</tr>
<tr>
<td>Sitting quietly after lunch (when you've had no alcohol)</td>
<td>0 1 2 3</td>
</tr>
<tr>
<td>In a car, while stopped in traffic</td>
<td>0 1 2 3</td>
</tr>
</tbody>
</table>

**Total Score**

0 = would never doze  
1 = slight chance of dozing  
2 = moderate chance of dozing  
3 = high chance of dozing

ESS total score \( \geq 10 \) indicates possible excessive daytime sleepiness or sleep disorder.
Differential

• Too little time in bed
  • Insufficient Sleep Syndrome

• Impaired Sleep Quality
  • Sleep Disordered Breathing
  • Restless Leg Syndrome (PLMS)
  • Insomnia
  • Non-restorative Sleep
Differential

• Intrinsic Sleepiness
  • Narcolepsy
  • Idiopathic CNS Hypersomnolence

• Circadian Rhythm Disorder
  • Shift Work Syndrome
  • Advanced Sleep Phase
  • Delayed Sleep Phase
Differential

• Medical-Psychiatric Comorbidity
  • Cardiopulmonary Disease
  • Fibromyalgia
  • Mood disorders
  • Alcohol
  • Drugs
  • Medications
Differential

• Medical evaluation of fatigue
  • Anemia
  • Hypothyroid
  • Cancer
  • AIDS
  • Rheumatological Evaluation
Polysomnography
Why Get a Sleep Study?

• Signs and symptoms poorly predict disease severity
• Therapy dependent on severity
• Failure to treat leads to:
  • Increased morbidity
  • Motor vehicle crashes
  • Mortality
• Other causes of daytime sleepiness
What Test Should be Used?

• Laboratory full night polysomnography (PSG)
  • Split night studies

• Home diagnostic systems
  • Oximetry to full PSG
Full Night In Laboratory Polysomnography

• Pro
  • Full set of variables obtained
  • Equipment problems can be repaired
  • Technician can address problems

• Con
  • Cost and Accessibility
  • Patient sleeps away from home
Split Night In Laboratory Polysomnography

- **Pro**
  - Reduced cost
  - Patient *may* be studied only once
  - Reduces time to treatment initiation

- **Con**
  - Diagnostic time may be inadequate
  - Treatment time limited
  - Difficult decisions required of technicians
Oximetry

• Pro
  • Inexpensive
  • Simple to perform
  • Little patient discomfort
  • Widely available

• Con
  • Interpretation not standard
  • Poor sensitivity – missed diagnosis
  • Specificity controversial
Home Study

• Pro
  • Potentially less expensive
  • Patient sleeps at home

• Con
  • Generally fewer signals are recorded
  • Equipment cannot be adjusted
  • Technician cannot assist patient
Diagnosis of Sleep Apnea

- In laboratory polysomnography
  - Gold standard
  - Assess severity
  - Initiate treatment
Diagnostic Testing

• Polysomnogram
  • Routine study
  • Split Study for CPAP titration in OSA
• MSLT – Multiple Sleep Latency Test
  • How quickly do you fall asleep?
• MWT – Maintenance of Wakefulness Test
  • Can you stay awake in a sleep conductive environment?
Polysomnogram

- Overnight Study
- Sleep Stage: EEG
- EKG
- Abdominal / Chest Movement
- Airflow / SaO2
- Position
- Costs about $600-$1200
Polysomnogram:
What to Look for in a Study

- Total Sleep Time
- Time in Supine Position / REM sleep
- Apnea – Hypopnea Index
- Time with Sa02 below 90% (> 3 min)
- Leg Movement Arousal Index
- Arrhythmias
Multiple Sleep Latency Test

• Evaluation for Objective Measurement of Sleepiness and Narcolepsy
• 5 naps during the day
• 9am, 11 am, 1 pm, 3 pm, 5 pm
• Done the day after PSG
• Allow sleep for 15 minutes
• Sleep Latency
• REM Latency (if seen it’s abnormal)
Maintenance of Wakefulness Test

• Measure of ability to stay awake
• 5 trials
• Stay awake 45 minutes in dark, quiet room
• Truck Drivers, Airplane Pilots
• Assessment of Therapy
Narcolepsy

• An overwhelming urge to sleep
• Sleep wake cycle reversed 16 hours sleep and 8 hours of wakefulness
• As common as Cystic Fibrosis
• Often misdiagnosed as depression
Narcolepsy

• Normal overnight PSG
• 5 minute sleep latency and 2 sleep onset REM
• Daytime Sleepiness
• Cataplexy
• Hypnogagic Hallucinations
• Sleep Paralysis
• Fragmented Sleep
Management of Narcolepsy

- Patient and family education
- Sleep hygiene
- Napping
- Safety issues
- Medications
Narcolepsy: Rx Cataplexy/EDS

- Xyrem (Sodium Oxybate)
  - Gamma hydroxybutate (GHB)
  - Drug of abuse
  - Dose twice during night: sleep onset and 3 hours later
  - Improves Cataplexy and EDS
Narcolepsy: Rx Stimulants

- Provigil (Modafinil)
  - 100 and 200 mg tablets
  - Up to 400 mg
  - Once a day
  - Headache, Nausea, Insomnia
Narcolepsy: Rx Stimulants

• Ritalin (Methylphenidate)
  • 5, 10, and 20 mg tabs
  • Usually 30 mg/day, up to 90 with care
  • Every 4 hours as needed
  • Nervousness, Rash, Insomnia, CV Effects
Restless Legs Syndrome (RLS) and Periodic Limb Movement Disorder (PLMD)

• RLS is a symptom
• PLMS is an EMG finding
• RLS and PLMS frequently overlap
• Neither is necessary nor sufficient to make the diagnosis of the other
Restless Legs Syndrome (RLS)

- Uncomfortable leg sensations
- Worse at night
- Worse with inactivity: relieved with activity
- Associated motor hyperactivity
Periodic Limb Movement Disorder (PLMD)

- Stereotypic, repetitive movements of the legs (or arms)
- During sleep / inactivity
- Every 20-40 seconds
- May be associated with arousals from sleep
- Occur in minimum clusters of 4
Patient Complaints With RLS

- Sleep disturbances
- Difficulty falling asleep and staying asleep
- Need to walk around ("nightwalkers")
- Daytime sleepiness
Associated Conditions

• Neuropathies, myelopathies, and radiculopathies
• Pregnancy
• Anemia (iron deficiency)
• Chronic renal failure
• Folate / B12 deficiency
• Medications (tricyclics, SSRI’s, caffeine)
• Obesity
• Hypothyroidism
Restless Legs Syndrome (RLS) and Periodic Limb Movement Disorder (PLMD)

- Check ferritin, replace if level is < 45
- Consider renal failure and diabetes
- Encourage exercise.
- Abstinence from caffeine, nicotine, and alcohol
- Validate and support
Restless Legs Syndrome (RLS) and Periodic Limb Movement Disorder (PLMD)

- Dopamine agonists
  - Carbidopa / Levodopa, Pergolide, Pramipexole
- Anticonvulsants
  - Gabapentin
- Benzodiazepines
  - Clonazepam, Temazepam
- Opioids
  - Oxycodone, Methadone
Sleep Disordered Breathing

- Central Sleep Apnea
- Primary Snoring
- Obstructive Sleep Apnea
  - Upper Airway Resistance Syndrome
  - Obesity-Hypoventilation Syndrome
  - Pickwickian Syndrome
Obstructive Sleep Apnea: Pathophysiology

- Abnormal collapse of airway
- Repetitive arousals
- Sleep fragmentation
- Oxygen desaturation
- Recurrent and strenuous effort to breathe against closed glottis
Sleep Disordered Breathing

• Apnea
  • Cessation of airflow ≥ 10 seconds

• Hypopnea
  • Decreased airflow ≥ 10 seconds associated with:
    • Arousal
    • Oxyhemoglobin desaturation
### Apnea Patterns

<table>
<thead>
<tr>
<th>Airflow</th>
<th>Obstructive</th>
<th>Mixed</th>
<th>Central</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory effort</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Obstructive Apnea

![Diagram showing various measurements related to obstructive apnea, including EEG, airflow, abdominal effort, rib cage effort, Pes effort, and arterial oxygen saturation (SaO2).]
Central Apnea

- EEG
- Airflow
- Effort (Rib Cage)
- Effort (Abdomen)
- Effort (Pes)
- \( \text{SaO}_2 \)

\[ \text{Arousal} \]

10 sec
Mixed Apnea

- EEG
- Airflow
- Effort (Rib Cage)
- Effort (Abdomen)
- Effort (Pes)
- \( \text{SaO}_2 \)

Arousal

10 sec
Obstructive Hypopnea

- EEG
- Airflow
- Effort (Rib Cage)
- Effort (Abdomen)
- Effort (Pes)
- \( \text{SaO}_2 \)

\[ \text{Arousal} \]

10 sec
Upper Airway Resistance Syndrome

- EEG
- Airflow
- Effort (Rib Cage)
- Effort (Abdomen)
- Effort (Pes)
- SaO$_2$

10 sec

Arousal
Measures of Sleep       Apnea Frequency

• Apnea Index
  • Number apneas per hour of sleep

• Apnea/Hypopnea Index (AHI)
  • Number apneas + hypopneas per hour of sleep
Obstructive Sleep Apnea

- Apnea/Hypopnea Index = Disordered breathing events / hour of sleep
  - AHI > 5 Abnormal
  - AHI > 12 Clinical Significant
  - AHI > 25 Severe
- Positional Effect
- REM Effect
OSA Symptoms

- Snoring
- Observed Apnea
- Daytime Sleepiness
- Restless Sleep
- Morning Headache
- Sore Throat
Consequences of Sleep Apnea Syndrome

Sleep
- Loss of airway tone
  - Airway obstruction
    - Hypoxia
      - Hypercapnia
        - Acidosis
    - Arousal
      - Increase in airway tone
        - Patent airway

Arrhythmia
- Systemic hypertension
- Chronic hypercapnia
- Pulmonary hypertension
- Cor pulmonale

Cardiovascular stressors

Daytime sleepiness
- Impaired cognition

Fragmented sleep

OSA: Mortality

  • Odds ratio of mortality 4.9 compared to no treatment in severe OSA.

• He, et al. Chest 1988
  • Severe Untreated OSA has 40% Mortality

• Lavie, et al. Sleep 1995
  • Observed to expected mortality ratio in patients under 70 years was 3.33
Cardiovascular Conditions Associated With OSA

- Hypertension
- Arrhythmias
- CHF
- Stroke
- CAD
- Pulmonary Hypertension
Obstructive Sleep Apnea

- Treatment
  - Behavioral
    - Weight Loss
    - Alcohol Avoidance
    - Sedative Avoidance
    - Smoking Cessation
    - Naps
Obstructive Sleep Apnea

• Treatment
  • CPAP
    • Optimal Pressure
    • Positional Effect
    • Trouble Shooting
      • Mask Fit
      • Humidification
      • Smart CPAP Systems
      • Atrovent Nasal Spray
Obstructive Sleep Apnea

- Surgical Treatments
  - Mandible Advancement
  - UPPP
  - Maxiofacial Surgery
  - Tracheostomy
## Pharmacokinetics of Hypnotics

<table>
<thead>
<tr>
<th>Agent (Brand Name)¹-⁴</th>
<th>Recommended Dose (mg)</th>
<th>Half-life (h) (range)</th>
<th>Risk of Residual Sedation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Long-acting</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Flurazepam HCl (Dalmane®)</td>
<td>15 or 30</td>
<td>47-100*</td>
<td>High</td>
</tr>
<tr>
<td>Quazepam (Doral®)</td>
<td>7.5 or 15</td>
<td>39-73*</td>
<td>High</td>
</tr>
<tr>
<td><strong>Intermediate-acting</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Estazolam (ProSom™)</td>
<td>0.5, 1, or 2</td>
<td>10-24</td>
<td>Medium</td>
</tr>
<tr>
<td>Temazepam (Restoril®)</td>
<td>7.5, 15, or 30</td>
<td>3.5-18.4</td>
<td>Medium</td>
</tr>
<tr>
<td><strong>Short-acting</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Triazolam (Halcion®)</td>
<td>0.125 or 0.25</td>
<td>1.5-5.5</td>
<td>Low</td>
</tr>
<tr>
<td>Zolpidem (Ambien®)</td>
<td>5 or 10</td>
<td>1.4-4.5</td>
<td>Low</td>
</tr>
<tr>
<td>Zaleplon (Sonata®)</td>
<td>5 or 10</td>
<td>1.0</td>
<td>Minimal</td>
</tr>
</tbody>
</table>

*Includes active metabolite(s).

2. SONATA (zaleplon) Prescribing Information.