Disclosures

- I am NOT receiving direct or indirect payment from any other commercial entity for honorarium, travel or other expenses
Educational Objectives

- To describe the two process model of sleep regulation
- To identify people at risk for obstructive sleep apnea
- To name insomnia treatments
Weather forecast for tonight:

dark.

Forecast

1. Sleep neurobiology
2. Obstructive sleep apnea
3. Insomnia
4. Hypersomnia
5. RLS
6. Summary
Sleep

- Species specific behavior characterized by a state of immobility with greatly reduced responsiveness.
- Distinguished from coma or anesthesia by its rapid reversibility.
- Additionally, when sleep is prevented, the body tries to recover the lost amount.

Slegel JM, Nature, 2005
Species Specific Behavior

Average Daily Sleep Totals

- Giraffe: 1.9 hours
- Elephant: 2.5 hours
- Human: 8.0 hours
- Chimpanzee: 9.7 hours
- Bottle-nosed Dolphin: 11.4 hours
- Rabbit: 13.1 hours
- Brown Bat: 15.8 hours
- Tiger: 19.9 hours
2 Process Model Of Sleep Regulation

- **A** = spontaneous wake time at 6 am
- **B** = afternoon siesta time
- **C** = beginning of the wake maintenance zone
- **D** = habitual sleep onset time
- **E** = 4 am, body temperature minimum, about 2 hours before spontaneous wake time at 6 am (when sleep load has been fully dissipated).

- The dark underscore bar = sleep time.
### AASM Sleep Needs by Age

<table>
<thead>
<tr>
<th>Age</th>
<th>Sleep Need</th>
</tr>
</thead>
<tbody>
<tr>
<td>Newborn to 2 months</td>
<td>12 hrs to 18 hrs</td>
</tr>
<tr>
<td>3 months to 1 year</td>
<td>14 hrs to 15 hrs</td>
</tr>
<tr>
<td>1 to 3 years</td>
<td>12 hrs to 14 hrs</td>
</tr>
<tr>
<td>3 to 5 years</td>
<td>11 hrs to 13 hrs</td>
</tr>
<tr>
<td>5 to 12 years</td>
<td>10 hrs to 11 hrs</td>
</tr>
<tr>
<td>12 to 18 years</td>
<td>8.5 hrs to 9.25 hrs</td>
</tr>
<tr>
<td>Adult (18+)</td>
<td>7 hrs to 9 hrs</td>
</tr>
</tbody>
</table>
Functional Neuroanatomy of Wakefulness & Sleep

A. Ascending Wakefulness/Arousal Promoting Regions
- Basal forebrain
- Lateral hypothalamic area
- Tubermammillary nuc
- Substantia nigra & ventral tegmental area
- Dorsal raphe nuc
- Locus coeruleus nuc
- Reticular formation
- Thalamus

B. Slow Wave Sleep Promoting Regions
- Ventrolateral preoptic area
- Tubermammillary nuc
- Substantia nigra & ventral tegmental area
- Dorsal raphe nuc
- Locus coeruleus nuc
- Laterodorsal tegmental & pendunculopontine areas

C. REM Sleep Promoting Regions
- Tubermammillary nuc
- Dorsal raphe nuc
- Locus coeruleus nuc
- REM-active cells in the laterodorsal tegmental & pendunculopontine areas

Taber K. J Neuropsychiatry Clin Neurosci. 2006
Sleep Consolidates Memory
Sleep & Hormones

Hormone production is affected by sleeping
Brainstem Respiratory Centers
Respiratory Drive
# Chemoreceptors

<table>
<thead>
<tr>
<th>Sensor Type</th>
<th>Location</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central</td>
<td>pH-sensitive membrane bound proteins</td>
<td>Ventrolateral medulla</td>
</tr>
<tr>
<td>Peripheral</td>
<td>Glomus cells sensitive to PaO2, pH, and PaCO2 sensitive</td>
<td>Carotid body, aortic body</td>
</tr>
</tbody>
</table>
Lung and Airway Mechanoreceptors

<table>
<thead>
<tr>
<th>Sensor Type</th>
<th>Location</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stretch</td>
<td>Myelinated afferent fibers sensitive to pressure</td>
<td>Airway smooth muscle and extrapulmonary airway</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Increased firing by elevated bronchial transmural pressure; afferent transmission via vagus nerve</td>
</tr>
<tr>
<td>Irritant</td>
<td>Myelinated afferent fibers stimulated chemically by nitrogen dioxide, sulfur dioxide, ammonia, inhaled antigens</td>
<td>Airway epithelial cells</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cough, bronchoconstriction, apnea and glottal closure</td>
</tr>
<tr>
<td>Unmyelinated C fibers</td>
<td>Unmyelinated afferent fibers and local receptors stimulated by chemical irritants</td>
<td>Lung interstitium and alveolar walls</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Vagal afferent signal causing irritation, burning and choking sensations; localized vasodilation and mucosal swelling</td>
</tr>
</tbody>
</table>
# Chest Wall Mechanoreceptors

<table>
<thead>
<tr>
<th>Sensor Type</th>
<th>Location</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Joint</td>
<td>Receptors responding to deep pressure, stress or change in position</td>
<td>Joint capsules and associated ligaments</td>
</tr>
<tr>
<td>Muscle spindle</td>
<td>Stretch-sensitive nerve fibers imbedded in muscles</td>
<td>Muscle fibers of intercostal and abdominal wall muscles</td>
</tr>
<tr>
<td>Tendon organs</td>
<td>Branched nerve endings respond to stretch</td>
<td>Tendons</td>
</tr>
</tbody>
</table>
Control of Ventilation

Emotional stimuli acting through the limbic system

Peripheral chemoreceptors \( O_2 \downarrow, CO_2 \uparrow, H^+ \uparrow \)

Higher brain centers (cerebral cortex—voluntary control over breathing)

Respiratory centers (medulla and pons)

Stretch receptors in lungs

Central chemoreceptors \( CO_2 \uparrow, H^+ \uparrow \)

Receptors in muscles and joints

Wakefulness drive to breathe

Receptors for touch, temperature, and pain stimuli

Respiratory Physiology: Understanding the Control of Ventilation
Eckert, Danny J., Principles and Practice of Sleep Medicine, Chapter 16, 167-173.e4
Copyright © 2017 Copyright © 2017 by Elsevier, Inc. All rights reserved.
Obstructive Sleep Apnea (OSA) Prevalence

- 1 billion people worldwide\(^1\)
- 26% of general US population\(^{15}\)
- 20-25% of middle-aged adults\(^{11}\)
- Prevalence increasing\(^{11}\)
  - Obesity
  - Age
  - Awareness

http://dx.doi.org/10.1016/S2213-2600(19)30198-5
Obesity
Age and OSA

https://www.researchgate.net/figure/Prevalence-of-a-high-risk-for-obstructive-sleep-apnea-according-to-age-and-sex-High-risk_fig1_324807640

https://www.quora.com/How-old-is-the-average-American
Definition: Apnea

- A drop in breathing airflow by $\geq 90\%$ of baseline for at least at least 2 breath cycles in children or 10 seconds in adults.

- Obstructive apnea: present inspiratory effort throughout the entire duration of the event.

- The AASM Manual for the Scoring of Sleep and Associated Events 2.5 2018
- www.aasmnet.org
Definition: Hypopnea

- Decrease in the nasal pressure excursions by ≥ 50% of baseline for at least at least 2 breaths in children or 10 seconds in adults associated with an arousal, awakening or ≥4% desaturation

- The AASM Manual for the Scoring of Sleep and Associated Events 2.5 2018
- www.aasmnet.org
Definition: RERA and Hypoventilation

- Respiratory effort-related arousals (RERA’s)
- Decrease in the nasal pressure excursions by < 50% of baseline
- Nasal pressure waveform flattening
  - snoring
  - noisy breathing
  - elevation in the end-tidal CO₂
  - visual evidence of increased work of breathing for at least at least 2 breaths

- Sleep-related hypoventilation
  - >25% of the total sleep time with a CO₂ > 50 mm Hg

- The AASM Manual for the Scoring of Sleep and Associated Events 2.5 2018
- www.aasmnet.org
# Diagnosis

- **Prevalence**
  - 14% of men
  - 5% of women

- **Clinical**
  - Symptoms
  - Signs

- **Polysomnography = gold standard**
  - Laboratory
  - Home
Clinical Symptoms

- Witnessed apneas
- Loud Snoring
- Gasping/choking at night
- Excessive sleepiness not explained by other factors
- Non-refreshing sleep
- Total sleep amount
- Nocturia
- Morning headaches
- Decreased concentration
- Memory loss
- Decreased libido
- Irritability
- Sleep fragmentation
- Maintenance insomnia
Clinical Signs

- Neck circumference (> 17 inches in men, > 16 inches in women)
- Body mass index (BMI) ≥ 30 kg/m²
- Modified Mallampati score of 3 or 4
- Retrognathia
- Lateral peritonsillar narrowing
- Elongated/enlarged uvula
- High arched/narrow hard palate
- Nasal abnormalities (polyps, deviation, valve abnormalities, turbinate hypertrophy)
- Overjet
- Tonsillar hypertrophy
- Macroglossia
Eyes

- “Floppy eyelids”
- Blood shot conjunctiva
- Non-arteritic anterior optic ischemic neuropathy
- Glaucoma, open angle
Maxillo-Mandibular Findings

- Male gender
- Older age
- Retrognathia
- Receding chin
- “Buck teeth”
Crowded Oropharynx
Clinical Symptoms in Children

- Frequent snoring (≥3 nights/wk)
- Labored breathing during sleep
- Gasps/snorting noises/observed episodes of apnea
- Sleep enuresis (especially secondary enuresis = > 6 months of continence)
- Learning problems
- Nocturnal diaphoresis

- Sleeping in a seated position or with the neck hyperextended “sword swallowing position”
- Cyanosis
- Headaches on awakening
- Daytime sleepiness
- Attention-deficit/hyperactivity disorder

Clinical Signs in Children

- Underweight or overweight
- Tonsillar hypertrophy
- Adenoidal facies
- Micrognathia/retrognathia
- High-arched palate
- Failure to thrive
- Hypertension

“Sword swallowing position”
Adenoid Facies

- Sunken eyes
- Narrow pinched nostrils
- Open mouth
- High arched palate
- Crowded / protruding teeth
- Dull mask like face
- Everted upper lip
- Loss of nasolabial fold
- Rhinorrhea
High Arched Palate
Physical Exam
Practical Adult OSA Screening

STOP BANG Questionnaire

1. **Snoring**
   Do you snore loudly (louder than talking or loud enough to be heard through closed doors)?

2. **Tired**
   Do you often feel tired, fatigued or sleepy during daytime?

3. **Observed**
   Has anyone observe you stopping breathing during your sleep?

4. **Blood Pressure**
   Do you have or are you being treated for high blood pressure?

5. **BMI**
   BMI more than 35kg/m²?

6. **Age**
   Age over 50 years old?

7. **Neck circumference**
   Neck circumference greater than 40 cm (15.75”)?

8. **Gender**
   Male gender?

High risk of OSA –’yes’ to three or more items

Chung. Anesthesiology. 2008
Definition: Polysomnography

- Simultaneous recordings of multiple physiologic signals during sleep, including:
  - Electroencephalogram (central, occipital)
  - Electromyogram (chin, tibialis)
  - Electrooculogram (right, left)
  - Electrocardiogram
  - Snoring microphone
  - Nasal/Oral Airflow (thermistor, pressure)
  - Thoracic Effort
  - Abdominal Effort
  - SaO2
  - Capnography
  - Body Position / video

AASM. Scoring Manual Version 2.5. 2018
Home Sleep Apnea Test

PAT – cpt code 95800

Type 3 – cpt code 95806
Home Sleep Apnea Test Contraindications

- Severe pulm disease
- BMI > 40
- Narcotic analgesic use
- Raynaud's
- Neuromuscular disease
- Stroke
- CHF
- Inability to cooperate
- Lack of dexterity
- Asymptomatic patients
- Individuals suspected of having other sleep disorders
- Identification of individuals working in safety-critical occupations
- Pediatric populations
Classification According to Severity - Adults

**Chicago Criteria**

- **Severe**
  - $RDI \geq 30 / \text{hour}$

- **Moderate**
  - $RDI \approx 29.9 / \text{hour}$

- **Mild**
  - $RDI \approx 14.9 / \text{hour}$

- **Variant of normal**
  - $RDI < 5 / \text{hour}$
Classification According to Severity - Children

- Not straight forward
- Several factors to be considered:
  - Apnea hypopnea frequency over hour of sleep (AHI / RDI)
  - Length of apneas / hypopneas
  - Degree of hypoventilation
  - Degree of hypoxemia
  - Clinical presentation

Classification according to AHI / RDI
- Mild: >1.5 but < 5 / hour
- Moderate: ≥5 but < 10 / hour
- Severe: ≥ 10 / hour
Treatment Options for OSA in Adults

- Positive Airway pressure
- Surgery
- Oral appliances
- Weight loss
- Oral Pressure therapy (Wynx®)
- Hypoglossal nerve stimulation (Inspire®)
- Didgeridoo playing
- Positional therapy (Zzoma®, Rem-A-Tee®, Night Shift®)
- Nasal expiratory resistance device (NERD) - Provent® / Theravent®
- Elastic stockings in venous insufficiency
- Anaerobic exercise
- Hormonal therapy in hypothyroidism and acromegaly
CPAP: 1st line therapy for adults with OSA

- Best for moderate to severe OSA
- Minimizes excessive daytime sleepiness
- Helps hypertension
- Reduces cardiovascular morbidity and mortality
- Improves safe driving
- Lowers post-operative respiratory complications

McDaid C. Sleep Med Rev. 2009
Modalities of PAP

- Fixed continuous positive airway pressure (CPAP)
- Auto-CPAP
- Bilevel PAP – spontaneous vs timed modes
- Auto-Bilevel PAP
- Adaptive positive pressure servo ventilation (APPSV)
- Volume Assured Pressure Support (AVAPS)
Oral Appliances

- Open / dilate the airway
  - repositioning the mandible
  - Increases upper airway muscle tone
  - Stabilize the tongue position

- Mild to moderate OSA
  - Oral appliance preference over CPAP
  - CPAP not tolerated / failed

- Supine predominant have most benefit

- American Academy of Dental Sleep Medicine
  - www.aadsm.org

Ramar K. JCSM. 2015
Selected Surgical Procedures

- **Otolaryngology**
  - Tracheotomy
  - Uvulopalatopharyngoplasty (UPPP)
  - Genioglossus advancement (GGA)
  - Hyoid advancement
  - Radiofrequency ablation (RFA)
  - Hypoglossal nerve stimulation (Inspire®)

- **Oral Surgeon**
  - Mandibulomaxillary advancement (MMA)
  - Maxillomandibular expansion

- **Minimally Invasive Surgeon**
  - Gastric bypass, Roux en-Y
  - Gastric sleeve
  - Lap Banding
Therapeutic Considerations in Children

- Surgery
- Positive airway pressure
- Orthodontic procedures
- Medical therapy
- Behavioral therapy
- Orofacial myofunctional therapy (OMT)
Adenotonsillectomy

- **STANDARD: 1st Line Therapy in Children**
  - ± Inferior nasal turbinates RFA
  - AHI ≥ 5 / hour (age ≥ 2 years)
  - ≈ 80% cure rate

- **Complications (18 – 34%)**
  - Pain
  - Anxiety
  - Dehydration
  - Anesthetic complications
  - Hemorrhage
  - Infection
  - Postoperative respiratory difficulties
  - Velopharyngeal incompetence
  - Nasopharyngeal stenosis
  - Death

Orthodontic Treatment

- Non-invasive maxillary mandibular distraction

- Mandibular advancement
  - Villa MP. Sleep Breath. 2012

- Complements surgical therapy
  - Shot SR. Curr Opin Otolaryngol HNS. 2011
Orofacial Myofunctional Therapy (OMT)

- Improves snoring
- Improves OSA severity in children and adults
- Speech therapy
- Airway Gym App
- Youtube

De Felicio DM. Nat Sci Sleep. 2018
Weight loss in the obese child

- Family effort / involvement
- Multidisciplinary
- Socioeconomic analysis
- Close follow up

Jebelle, H. Obese Rev. 2019
CPAP in Children

- First line therapy for severe OSA persistent after TA, and possibly primary treatment in obese children

- Adequate effectiveness and adherence is possible
  - Marcus CL. Pediatrics 2006

- CPAP pressures change over time in children (growth and development)

- High flow nasal cannula (air 20 LPM via NC)
  - McGinley B. Pediatrics 2009
Medical Therapy

- **Intranasal Steroids (budesonide)**

- **Montelukast**

- **Intranasal Steroids + Montelukast**
Chronic Insomnia

- Sleep disturbance > 3 months
  1. Difficulty in initiating sleep
  2. Difficulty in maintaining sleep
  3. Waking up earlier than desired
- Adequate opportunity and circumstances for sleep
- Daytime disturbances

  - International Classification of Sleep Disorders 3rd Edition. AASM. 2014
Age and Gender on Insomnia

Insomnia across the life span

% Reporting insomnia

15-19  20-99  30-39  40-49  50-59  60-69  >70

Males  Females

Based on data and adapted from Olbyon MM, Castel M, Sullivan SM. How a general population perceives its sleep and how this relates to the complaint of insomnia. Sleep 2006; 29(6):715-723, 1997.
Initial Evaluation

- Insomnia history
- Identify / rule out sleep comorbidities
- Review past history
  - Medical / psychiatric
  - Pharmacological
  - Social / occupational / family
- Physical exam
- Diagnostic tests
Diagnostic Tests

- Insomnia / sleep questionnaires
- Psychiatric screening
- Sleep logs (diary)
- Actigraphy
- Polysomnogram – not standard
- Serologic / imaging – not standard
Goals of Therapy

- ↑ sleep quality / time
- ↓ insomnia-related daytime impairment
- Formation of a positive and clear association between the bed and sleeping
- ↓ sleep related psychological distress
Patient Centered Therapeutic Plan

- Therapeutic Choice
  - Pharmacological
  - Behavioral w or w/o hypnotic tapering
  - Both*

- Patient readiness to start Rx

- Sleep diaries
OTC Medications

- Alcohol
- Valerian
- Melatonin
- Diphenhydramine
- Cyclobenzaprine
- Hydroxyzine

Feren et al. 2006
## FDA Approved Hypnotics

<table>
<thead>
<tr>
<th>Generic</th>
<th>Trade Name</th>
<th>Mechanism of Action</th>
<th>Dose (mg)</th>
<th>Metabolic enzymes</th>
<th>Half-life (hours)</th>
<th>Tmax (hours)</th>
<th>DEA Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estazolam</td>
<td>ProSom</td>
<td>BzRA</td>
<td>1, 2</td>
<td>CYP3A4</td>
<td>10-24</td>
<td>0.5-6</td>
<td>IV</td>
</tr>
<tr>
<td>Flurazepam</td>
<td>Dalmate</td>
<td>BzRA</td>
<td>15, 30</td>
<td>CYP3A4 (probable)</td>
<td>47-100</td>
<td>0.5-1</td>
<td>IV</td>
</tr>
<tr>
<td>Temazepam</td>
<td>Restoril</td>
<td>BzRA</td>
<td>7.5, 15, 22.5, 30</td>
<td>Conjugation with glucuronic acid</td>
<td>3.5-18.4</td>
<td>1.2-1.6</td>
<td>IV</td>
</tr>
<tr>
<td>Triazolam</td>
<td>Halcion</td>
<td>BzRA</td>
<td>0.125, 0.25</td>
<td>CYP3A4</td>
<td>1.5-5.5</td>
<td>2</td>
<td>IV</td>
</tr>
<tr>
<td>Quazepam</td>
<td>Doral</td>
<td>BzRA</td>
<td>7.5, 15</td>
<td>CYP3A4 (minor: CYP2C9, CYP2C19)</td>
<td>39-73</td>
<td>2</td>
<td>IV</td>
</tr>
<tr>
<td>Zolpidem</td>
<td>Ambien</td>
<td>BzRA</td>
<td>5, 10</td>
<td>CYP3A4, CYP2C9</td>
<td>1.4-4.5</td>
<td>1.6</td>
<td>IV</td>
</tr>
<tr>
<td>Zolpidem CR</td>
<td>Ambien CR</td>
<td>BzRA</td>
<td>6.25, 12.5</td>
<td>CYP3A4, CYP2C9</td>
<td>2.8</td>
<td>1.5</td>
<td>IV</td>
</tr>
<tr>
<td>Zolpidem SL*</td>
<td>Intermezzo</td>
<td>BzRA</td>
<td>1.75, 3.5</td>
<td>CYP3A4, CYP2C9</td>
<td>1.4-3.6</td>
<td>0.5-1.25</td>
<td>IV</td>
</tr>
<tr>
<td>Zaleplon</td>
<td>Sonata</td>
<td>BzRA</td>
<td>5, 10, 20</td>
<td>Aldehyde oxidase (minor: CYP3A4)</td>
<td>1</td>
<td>1</td>
<td>IV</td>
</tr>
<tr>
<td>Eszopiclone</td>
<td>Lunesta</td>
<td>BzRA</td>
<td>1, 2, 3</td>
<td>CYP3A4, CYP2E1</td>
<td>6</td>
<td>1</td>
<td>IV</td>
</tr>
<tr>
<td>Ramelteon</td>
<td>Rozerem</td>
<td>MtRA</td>
<td>8</td>
<td>CYP1A2 (minor: CYP2C, CYP3A4)</td>
<td>1-2.6</td>
<td>0.75</td>
<td>n/a</td>
</tr>
<tr>
<td>**Tasimelteon</td>
<td>Hetioz</td>
<td>MtRA</td>
<td>20</td>
<td>CYP1A2, CYP3A4</td>
<td>1.3 ± 0.4</td>
<td>0.5 to 3</td>
<td>n/a</td>
</tr>
<tr>
<td>Doxepin</td>
<td>Silenor</td>
<td>H1Ant</td>
<td>3, 6</td>
<td>CYP2C19, CYP2D6 (minor: CYP1A2, CYP2C9)</td>
<td>15.3-31</td>
<td>3.5</td>
<td>n/a</td>
</tr>
<tr>
<td>Suvorexant</td>
<td>Belsoma</td>
<td>OX1R &amp; OX2R (Ant)</td>
<td>5, 10, 15, 20</td>
<td>CYP3A</td>
<td>12</td>
<td>1.5-2</td>
<td>IV</td>
</tr>
</tbody>
</table>
Half Life Matters

Cognitive Behavioral Therapy for Insomnia (CBTI)

- Non-pharmacological & psychological Rx
- 3 components:
  - Educational
  - Cognitive
  - Behavioral
- Aimed to modify behaviors & cognitions that perpetuate insomnia
Effectiveness

- 70-80% of insomniacs benefit
- Effective: primary & comorbid
- Large therapeutic effect ~50%
  - Sleep onset latency
  - Subjective quality of sleep
- Moderate for other sleep parameters
“I am Tired” – What do People Mean?

- Dyspnea or dyspnea on exertion
  - Difficulty breathing
- Fatigue
  - Decreased energy levels
  - i.e.: after running a marathon, depression
- Excessive daytime sleepiness
  - Increased propensity to fall asleep
  - 24 hour sleep deprivation
National Sleep Foundation
Sleep in America Poll 2008

A Day in the Life of a Typical American Worker

- Wake Time: 5:00 AM
- Commute Time: 7:45 AM
- Work Day: 8:09 AM
- Commute Time: 5:04 PM
- Time Before Bed: 5:27 PM
- Time in Bed: 10:53 PM

- American’s work day: 9 hours and 28 minutes
- Time spent in bed: 6 hours and 55 minutes
- Total sleep time: 6 hours and 40 minutes

www.sleepfoundation.org
Effects of Sleep Deprivation on the Brain

A. Resting Awake State

Increased CBF

D. Sleep Deprived

Decreased CBF
Sleepiness Accumulates Over Time

Experiments on chronic restriction of sleep from 1-2 weeks reveal cumulative increases in lapse rates in a sleep-dose response manner.


Behavioral Management of Hypersomnia

- Sleep extension
- Scheduling short naps (15-30 minutes)
- Sleep hygiene
- Adherence to stimulants
- Positive airway pressure in SDB
- Timed light
- Exercise
Hypersomnia: Pharmacological Treatment

- Caffeine
- Modafinil / Armodafinil
- Methylphenidate
- Amphetamines
- Solriamfetol
- Pitolisant
Sodium Oxybate

- Orphan drug FDA approved for cataplexy and sleepiness in narcolepsy.
- Not the illegal “date rape drug”
- Acts on GABA
- Contraindicated if alcoholic, taking sedating medications or opioids – *Respiratory Depression / Death*
- Extreme caution if depressed due to suicidal ideation
- Watch for cardiac, hepatic or renal pathology due to high sodium content
RESTLESS LEGS SYNDROME (RLS)
Diagnostic Criteria for RLS

**Mnemonic**

- Urge to move
- Rest induced
- Gets better with activity
- Evening and night accentuation
- Not caused by other conditions

Wijemanne S. *Sleep Med.* 2015
Medications Worsening RLS

- Antihistaminergic agents
- SSRIs / SNRIs
- TCA's
- Mirtazapine
- Atypical antipsychotics
- Antiemetic agents
- Amphetamines / methylphenidate
- Alcohol
- Caffeine
- PPI’s (interfere with iron absorption)

Hoque. JCSM. 2010
Non Pharmacological Therapy

- Try before prescribing medications
- Mild to moderate physical activity
- Hot baths
- Engrossing mental activity (eg, video games, solitaire)
- Schedule sedentary activities in the morning (eg, movies, long plane flights)
- Exercise or housework later in the day
- Avoid triggers (caffeine, alcohol)
RLS Pharmacological Therapy

FDA Approved Options

- Dopaminergic agonists (most widely used)
- Reduce RLS symptoms and PLM’s
  - Ropinirole (Requip)
  - Pramipexole (Mirapex)
  - Rotigotine transdermal (Neupro)
- Gabapentin Enacarbil (Horizant)

Non-FDA Approved Options

- Other dopaminergic drugs (levodopa)
- Calcium channel alpha-2-delta (α2δ) ligands
  - Gabapentin, gabapentin enacarbil, pregabalin
- Opioids
- Clonazepam
- Iron
Dopamine Drugs: Possible Side Effects

- **Augmentation**
  - Worsening of RLS after starting a medication to treat RLS
  - Is a medication effect and dose dependent
  - Progressively earlier onset of symptoms
  - More intense
  - Increasing requirement of drug

- **Sleepiness**
  1. Sleepy soon after med
  2. Sleepy all day
  3. Not sleepy, but suddenly sleepy when sedentary

- **Compulsive Behavior**
  - Shopping, eating, gambling, sexual activities, thoroughness, tidiness
Summary

- Sleep is a natural but complex biological process
- History and physical are the key of uncovering sleep pathology
- OSA is prevalent, serious and has many solutions
- Clarify the word “tired” with your patient
- Medications affect sleep
- Insomnia is treated without and with medication
- Medications used to treat RLS can have serious side effects
Thank You