Sleep, 'the golden chain': 
Assessment & Treatment of Sleep Problems

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Disclosures

• We have no financial relationships to disclose.
• This presentation will include discussion of off-label pharmacologic treatment.

Improved identification of sleep problems

Brief physiology of sleep

Background, Definitions & Physiology: a quick review

• What is sleep and why is it important?
  • Still debated theory!
  • New research emerging often
  • Sleep duration and symptoms of psychiatric disorders

• Energy conservation and allocation
  • Metabolism, growth and immune function- flu vaccine/rhinovirus
  • Higher brain functions: synaptic plasticity, memory consolidation and creative insight

Speaker Introduction

Bridget Gramkowski has been a certified pediatric nurse practitioner in primary care for more than a decade, working in both primary care and school-based health centers. She is currently practicing in pediatric neurology. She is also faculty and clinical placement coordinator for the primary care PNP program at the University of California, San Francisco.

Victoria Keeton has been a certified pediatric nurse practitioner in primary care for more than 15 years and practices in both community pediatrics and school-based health centers in the San Francisco Bay Area. She is also faculty and specialty coordinator for the primary care PNP program at the University of California, San Francisco, and is currently a PhD candidate at the University of California, Davis, Betty Irene Moore School of Nursing.

Learning Outcomes

1. Summarize the prevalence of both behavioral and physiologic sleep problems in pediatric populations
2. Discuss health consequences of poor sleep and the common diagnoses leading to prescription of medicines
3. Identify the medical conditions and pharmacologic treatments contributing to poor sleep.
4. Review the latest evidence-based guidelines and resources available to primary care providers for the delivery of comprehensive sleep health
5. Understand how PNP's can utilize partners within their communities to properly assess and treat sleep problems

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  • Higher brain functions: synaptic plasticity, memory consolidation and creative insight
Sleep: Universally recognized as important in all cultures throughout time

ANCIENT GREEK:
HYPNOS, THEIR GOD OF SLEEP AND DREAMS, HAD THE POWER TO REMOVE ALL PAIN, SUFFERING AND SORROW.

THOMAS DECKER 1610:
"DO NOT CONSIDER WHAT AN EXCELLENT THING SLEEP IS...THAT GOLDEN CHAIN THAT TIES HEALTH AND OUR BODIES TOGETHER."

TRADITIONAL CHINESE MEDICINE
YIN / YANG THEORY OF SLEEP "YIN" ENERGY OF THE BODY IS COOLING, CALMING AND RESTORATIVE. IMBALANCE = INSOMNIA.

Sleep physiology

How melatonin is made:
Tryptophan (amino acid) 
5-Hydroxytryptophan 
Serotonin 
N-acetylserotonin 
Melatonin final product

Sleep Stages: 60 (newborn) or 90 minute cycles

NREM: Non Rapid Eye Movement - 3 levels of NREM sleep, distinguished by brainwaves, limb movements, eye movements [identified on EEG]
NREM1: Transitional, first stage, 3-6% of total sleep, easily aroused.
NREM2: Low voltage, harder to arouse. Sleep spindles, thought to represent memory consolidation, lower body temp and no eye movement. Longest time spent here!
NREM3: Slow wave sleep (SWS) first third of night, most relaxed and hardest to awaken. This is where most Growth Hormone is released - 70%. Theory: NREM/SWS=MSK recovery. Deprivation leads to excessive fatigue.
REM: Paralysis of striated muscles except: muscles controlling eye movements & breathing. Mixed frequency brain wave activity = similar to when awake. RR, HR, and BP increase to near waking levels.

Normal Sleep Architecture:
Cyclical pattern of sleep as it shifts between the different sleep stages

Abnormal Sleep Architecture:
Hypnogram of adult with depression
### Sleep: Definitions of measures

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
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<tbody>
<tr>
<td>Sleep latency</td>
<td>Period of time between bedtime and onset of sleep</td>
</tr>
<tr>
<td>Sleep duration</td>
<td>Time to sleep; note that self-report overestimates duration measured by actigraphy</td>
</tr>
<tr>
<td>Sleep quality (PSQI)</td>
<td>Composite of 7 components, (1) sleep duration, (2) sleep disturbance, (3) sleep latency, (4) daytime dysfunction due to sleepiness, (5) sleep efficiency, (6) overall sleep quality, and (7) sleep medication use.</td>
</tr>
<tr>
<td>Sleep arousal</td>
<td>An abrupt change from “deeper” stage of non-REM (NREM) sleep to a “lighter” stage, or from NREM sleep toward wakefulness, with the possibility of awakening as the final outcome.</td>
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<tr>
<td>Sleep efficiency</td>
<td>Time asleep / (total time in bed - time to fall asleep)</td>
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</tbody>
</table>


### Epidemiology of childhood insomnia worldwide:

Varies with cultures and regions:

- 10% Vietnam/Thailand
- 25%-30% USA/Australia
- 75% China/Taiwan

(Esposito, 2019)

### Benefits of Sufficient Sleep

- Learning and memory processing
- Growth and healing of body tissues
- CNS system repair
- Maintain energy balance
- Emotional regulation
- Regulate activity/behavior

Better sleep in kids generally means better sleep for parents!

### Sleep = cognition + growth + health

Adequate sleep for age improves:

- Learning, attention & memory
- Physical Growth and healing of body tissues
- CNS system repair
- Maintain energy balance
- Emotional regulation
- Regulate activity/behavior

Inadequate sleep increases incidence of:

- Affective disturbance/behavioral issues
- Cognitive function
- School problems
- Depression
- Health Problems

(AAP Sleep Guidelines; Tham, et al, 2017)

### Improved identification of sleep problems:

Developmental Approaches to Sleep Assessment & Common Sleep Challenges across the Pediatric Age Span

### Development of Sleep Patterns in Infancy

- Maturation of biological rhythms
- Melatonin levels low until about 12-16 weeks
- Cortisol secretion begins to follow cycles of day and night
- Progression of caloric need and ability to retain calories
- Acquisition of skills to cope with physiologic sleep arousal

(Bathory, et al, 2017)
Sleeping “Through the Night”
- Definition: 5 consecutive hours after midnight
- 50% by 6 months, 90% by 12 months
- Normal to awaken every few hours
- By 12-14 lbs, babies can sleep longer
- No evidence that solid foods help prolong sleep
- Developmental stage affects sleep
- All babies are different! All families are different!

Common Sleep Challenges in Infants
- Daytime – nighttime reversal
- Only sleeps while held
- GER
- Frequent waking
- Weaning from nighttime feeds
- Refuses to nap
- Won’t sleep in a crib

Sleep Patterns in Toddlerhood
- Typical pattern is 12-14 hours/night
- 1-2 naps of 30-120 min
- May transition from crib or bed-sharing to own bed
- Should have minimal night wakings

Common Sleep Challenges in Toddlers
- Weaning from the breast/bottle
- Climbing out of crib/bed
- Won’t sleep alone
- Nap refusal
- Sleep “regression”
- Triggers include illness, travel, stress, change in routine

When to Worry/Refer: Infants and Toddlers
- Signs or suspicions of apneic episodes
- Severe GER
- Dental caries
- Signs of postpartum depression/anxiety

Sleep Patterns in Early Childhood and School Age
- Typical pattern is 11-12 hours in early childhood, decreasing to 9-10 hours in later years
- May still need 1 nap until about 5 years
- Begin to consistently stay dry overnight between 4-8 years
- May have fears of the dark, monsters, etc.
Common Sleep Challenges in EC/School Age

- Won't sleep alone
- Nap refusal but still seems sleep deprived
- Snoring/OSA
- Fears

<table>
<thead>
<tr>
<th>Night Terrors</th>
<th>Nightmares</th>
</tr>
</thead>
<tbody>
<tr>
<td>Younger</td>
<td>Older</td>
</tr>
<tr>
<td>Usually during first third of night</td>
<td>Usually during last half of night</td>
</tr>
<tr>
<td>Appears awake but does not remember</td>
<td>Remembers graphic details</td>
</tr>
<tr>
<td>Does not accept comfort</td>
<td>Accepts comfort</td>
</tr>
<tr>
<td>Rapid return to sleep</td>
<td>Slow return to sleep</td>
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</table>

When to Worry/Refer: EC/School Age

- Snoring or loud open-mouthed breathing accompanied by gasping/choking
- Behavior issues with reports of poor sleep habits or frequent disruptions
- Fears/nightmares so significant that lead to persistent insomnia

Sleep Patterns in Adolescence

- Increased growth = increased need for sleep
- Changes in natural-wake sleep cycle at onset of puberty/delayed release of melatonin
- Environmental Barriers
  - Homework, extracurriculars, jobs
  - Early school start time
  - Caffeine consumption
  - Backlit screens decrease endogenous melatonin, delay sleep
- Social Media:
  - = inadequate sleep quantity/quality, & daytime sleepiness
  - = sleep disturbance & depression, regardless of content

Common Sleep Challenges in Adolescence

- Not enough sleep!
- Excessive screen time leads to prolonged bed time
- Insomnia, may lead to developing poor sleep hygiene
- Sleep-related Breathing Disorders

When to Worry/Refer: Adolescence

- Snoring or loud open-mouthed breathing accompanied by gasping/choking
- Behavior issues with reports of poor sleep habits or frequent disruptions
- Persistent sleep disruption associated with sx of depression, anxiety, PTSD or other mental health conditions

Improved identification of sleep problems

Sleep Assessment
Assessment of Sleep: History-Taking

- Most sleep problems are diagnosed via history or screening tools
  - Also polysomnography for sleep-related breathing d/o, restless legs syndrome
  - Variety of screening tools/questionnaires exist, e.g.:
    - BEARS
    - Pittsburgh Sleep Quality Index (PSQI)
    - Children’s Sleep Habits Questionnaire (CSHQ)
    - Sleep Disturbance Scale for Children (SDSC)
  - Includes thorough past medical and family history
  - Also remember to assess for social determinants that may impact sleep environment or quality of sleep

BEARS Prompts for Sleep Assessment

- Bedtime problems - going to bed or falling asleep
  - Environment, limit setting, fears, restless legs
  - Excessive daytime sleepiness
  - Duration of sleep, school performance, meds, caffeine/substances
  - Awakenings during the night
  - Sleep-related breathing, environment, enuresis, family hx, mental health
  - Regularity and duration of sleep
  - Routines, times, naps, limits, screen time
  - Snoring
  - Chronic allergic rhinitis, craniofacial anatomy, pausing/gasping/choking

Physical exam

- Weight/BMI
- General energy level, nourishment
- Affect
- Nasal turbinates
- Dorsopharynx
- Tonsillar hypertrophy
- Erosion of teeth
- Macroglossia
- High-arched palate
- Thyroid
- Neurodevelopment
- Integument
- Scars/sx of self harm
- Hair loss
- Lanugo

Improved identification of sleep problems

Sleep disorders & health conditions that directly impact sleep

Common Sleep Problems: Parasomnias

REM
- Nightmares
- Sleep Paralysis (adolescence)
- Nocturnal enuresis

NREM
- Confusional arousals (2-5YO)
- Somnambulism (4-8 YO)
- Night terrors (18M-8YO)
- Nocturnal enuresis
  - Hx: snoring, parasomnias, restless sleep?

REM
- Sleep-related rhythmic movement disorder* <5YO
- Benign sleep myoclonus of infancy <5YO
- Sleep starts (hypnic jerks)
- Hypnagogic foot tremor

NREM
- Sleep-related rhythmic movement disorder* <5YO
- Sleep-related bruxism history
- Periodic limb movement disorder (PLMD) 5/hour (polysomnography required)
- Hypnagogic foot tremor

* disorder if interference with sleep, injury occurs, or impacts functioning in daytime
Common Sleep Problems: falling asleep

Criteria for Restless Leg Syndrome:
1. Legs = urge to move + unpleasant sensation
2. Begin or worsen during inactivity
3. Relieved by movement
4. Occur exclusively or predominantly in the evening or night
5. Rule out other medical or behavioral condition

- Diagnosed by History: Family History, ADHD, no numbness
- Labs: ferritin levels

Pediatric Insomnia: 20-30% of children

Insomnia defined:
1. Sleep latency longer >30 min
2. Insufficient sleep for age/development
3. Poor sleep consolidation
   - Despite time and opportunity
   - & leading to functional impairment

Behavioral Causes:
- Behavioral insomnia of childhood
- Psycho-physiologic (conditioned) insomnia

Conditions & history relevant to sleep

Chronic Conditions:
- Neurologic
- Gastrointestinal
- Genetic syndromes
- Sickle Cell
- Atopic dermatitis
- Pulmonary
- Obesity
- Obstructive sleep apnea
- Visually impaired
- Juvenile idiopathic arthritis
- Diabetes
- Migraine/Headache

Mental Health:
- Depression & anxiety

Acute or Historical events:
- History of pediatric stroke
- Concussion/TBI
- Pain
- Cough
- Cancer survivor

Chronic conditions and sleep

- Asthma-bronchospasm can disrupt both REM and SWS leaving children with symptoms of sleep deprivation
- Cough-On actigraphy, the presence of nocturnal cough is associated with a shorter total sleep time, lower sleep efficiency, and longer time spent in WASO (CF, asthma, acute viral illnesses)
- Duodenal ulcers- 3-20x more acid secretion in REM than those without ulcers
- A large, systematic review and meta-analysis of adults without CF identified a relative risk for all-cause mortality of 1.06 annually for every one hour reduction in total sleep time from 7 hours (67).

Cystic Fibrosis Severity and Sleep

Sleep Efficiency Compared to Illness Severity

Sleep with Co-occurring Conditions

Neurologic Conditions: high rates of sleep problems

Neuro-developmental disorders:
- Autism 3.9%
- Cerebral Palsy 4.1%
- Mott Syndrome 87.4%
- Angelman Syn 22.6%
- Williams Syn 37%
- Smith-Magenis syndrome 9%

Heterogeneous and disease specific
Multiple genes identified

All impact sleep for child and family-consider long term effect on caregiver
ASD, ADHD & Sleep

ASD: dysregulated neurotransmitters + genetics
ADHD: behavior + hyperactivity + stimulant Rx

Behavioral based insomnia
Hyperactivity and ODD
Sleep disordered breathing
Periodic limb movement/restless leg syndrome

Sleep disturbances associated with ADHD:

(Siddhur, et al, 2016; Tsai, Hsu & Huang, 2016)

Sleep Elevated BMI

Elevated BMI as Cause of Sleep Disruption

- ↑ risk for obstructive sleep apnea, GERD & IBS
- Visceral adiposity = ↑ pro-inflammatory cytokines
- ↑ fat/↓ fiber diet affects hormones & circadian rhythm
- Vitamin D deficiency impacts sleep regulation?

Elevated BMI as Result of Sleep Disruption

- ↑ consumption of high glycemic/caloric foods
- ↑ eating in response to external cues
- ↑ insulin & cortisol
- Leptin resistance & ↑ ghrelin?
- ↑ screen & sedentary time
- ↓ melatonin?

(Soria et al, 2017; Muscogiuri, et al, 2019)

Best practices in behavioral treatment

- Once regains birth weight, don’t awaken to feed
- Keep night feedings “uninteresting”
- Keep light exposure to a minimum at night and during naps
- 3-4 months, allow for brief night awakenings without intervening
- Establish bedtime routines early
- “Sleep Training” principles:
  - Start putting down while awake to allow self-soothing to sleep
  - Encourage good daytime naps, but not too late in the day
  - Consider use of comfort object (~9 mos or older)
  - NO SCREENS!

Promoting Healthy Sleep Early

Infants and Young Children
- Quiet play after 5 PM
- Bath, music, massage, books
- Teach self-soothing for night waking after 4 mos old
- Music or white noise
- Darkened room during sleep
- Create a visual sleep schedule
- Consistency!

Older Children and Adolescents
- Regular bedtimes all week
- All screens turned off 30 minutes before bedtime
- No TV, computers or other screens in bedroom
- Keep Reading!!
- Bathroom before bed

Additional wellness interventions

- Limit/eliminate afternoon/evening caffeine
- Mindfulness, meditation, guided imagery (several apps available)
- Deep breathing and progressive muscle relaxation
- Gratefulness – three good things that happened today
- Sleep mood tracking
- Journaling, “re-write” nightmares
- “Worry dolls”
- Weighted blankets
Cognitive Behavioral Therapy

- Brief Behavioral Treatment for Insomnia:
  - 4-week design by American Academy of Sleep Medicine
  - Sleep restriction and stimulus control
  - Sleep diary
  1) Sleep diary: total sleep+30m
  2) Stimulus control: sleep only in bed
  3) Fixed wake time
  4) Only in bed for 20 min: trying to sleep: get up do something relaxing
  5) Titrate bedtime up or down by 15 minutes

(American Academy of Sleep Medicine, 2020)

Best practices in pharmacologic treatment:
All off label, all expert opinion

1. Medications that impact sleep
2. Nutraceuticals: melatonin, tryptophan, food sources
3. OTC-antihistamines
4. Prescribed

Pharmacologic agents & sleep

All of the following drugs are known to cause difficulty sleeping: central nervous system (CNS) stimulants, respiratory medications, decongestants, hormones, and psychotropics.

Impact of stimulants on sleep

Meta-analysis:
- Longer Sleep Latency*
- Shorter Sleep Duration
- Worse Sleep Efficiency

(Kidwell et al., 2015)

Activating properties of Antidepressant Medications

- Treatment-emergent insomnia clinical trials: SSRI was 17% VS 9% placebo
- Sleep Impact of activating ATC: decrease SWS, REM and continuity

<table>
<thead>
<tr>
<th>Medication</th>
<th>Insomnia</th>
<th>Drowsiness</th>
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<tbody>
<tr>
<td>Fluoxetine</td>
<td>10-33%</td>
<td>5-17%</td>
</tr>
<tr>
<td>Sertraline</td>
<td>12-28%</td>
<td>2-15%</td>
</tr>
<tr>
<td>Escitalopram</td>
<td>7-14%</td>
<td>4-13%</td>
</tr>
<tr>
<td>Citalopram</td>
<td>15%</td>
<td>18%</td>
</tr>
<tr>
<td>Paroxetine</td>
<td>11-24%</td>
<td>15-24%</td>
</tr>
</tbody>
</table>

(Wichniak et al, 2017; Lexicomp, 2020)

Clinical consideration of sleep medications

- What we don’t know: efficacy, side effects, safety... RISK/BENEFIT profile?
- Tolerance/addiction potential, daytime sleepiness/sedation
- Short term or Lasting improvement? Discontinuation?
- Medications are not a substitute for sleep interventions, adjunct only... remember your first line is behavioral for all sleep problems
Nutraceuticals
Non-regulated supplements

Over the Counter Medicine:
Not FDA approved for children, off label
Lexicomp (2020): “Insomnia; occasional:
Note: Evaluation of sleep hygiene and use of non-pharmacologic (ie, behavioral) treatment are preferred treatments; medications may be used as adjunct treatment (Owens 2005).”
“Limited data available for <12 years”

Prescribed Medications for
sleep: Not FDA approved for children, off label

Prescribed Medications for
sleep:
November 2019 Review of Adult Evidence Concluded:
1. Non-pharmacological interventions are preferable for safety
2. CBT effective first-line therapy for adults with insomnia followed by other behavioral interventions.
3. Short courses of pharmacological interventions can supplement
   ➢ No evidence on appropriate duration

“Comparative effectiveness and safety of pharmacological and non-pharmacological interventions for insomnia: an overview of reviews” Rios et al. Systematic Reviews 2019

Nutraceuticals- Melatonin
Highest food sources: Tart Montmorency Cherries (red) & milk

Pros
• Caregiver acceptance
• Well tolerated
• Widely available
• Evidence for genetic syndromes/neurologic conditions
• Give clear timing for dosing

Cons
• FDA does not regulate
• Range of 0.37%-466% of labelled concentration in OTC products
• Long-term use unknown
• Avoid direct from animal sources due to risk of viral contamination
• Cytochrome P450: drug interactions

1st Generation Antihistamines – off-label use in children
MOA: Antihistamine, crosses BBB inversely agonizes H1 in CNS
ex: diphenhydramine (Benadryl) & doxylamine (Unisom)

Pros
• Rapid onset and relative short t1/2 life
• Caregiver acceptance
• Well tolerated
• Widely available
• Low cost & liquid formulations

Cons
• Not evidence based
• Tolerance
• Interacts with other anticholinergics
• SIDE EFFECTS: paradoxical excitation, morning sleepiness, cognitive impact & anticholinergic reactions
Summary Points

- Sleep issues in children and adolescents range from common to complex, and all may impact health outcomes.
- Several chronic conditions and medications impact sleep in children.
- A thorough history and physical, including medical, mental health and social factors is essential to diagnosing disordered sleep.
- Behavioral treatment remains the mainstay of management for sleep disruption and sleep disorders.
- Pharmacotherapy, including the use of nutraceuticals, is not FDA-approved for treatment of sleep disorders in children.
- Recommendations for pharmacotherapy to supplement behavior therapy for sleep disorders should be evidence-based and include patient/family education about benefits and risks.

“Gratefulness is described as a felt sense of wonder, thankfulness, and appreciation for life (Emmons & Shelton, 2002, p. 460)

Questions?

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References


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