Pediatric Sleep Medicine

Judith A. Owens MD MPH

Boston Children's Hospital
Harvard Medical School

18th Annual Sleep Medicine CME Course

18th Annual Sleep Medicine CME Course

Pediatric Sleep Medicine

Judith A. Owens MD MPH
Boston Children's Hospital
Harvard Medical School

Boston Children's Hospital
Until every child is well

HARVARD MEDICAL SCHOOL

Learning Objectives

- To review the clinical presentation and management of childhood insomnia, including behavioral interventions and melatonin use
- To list the key features of and treatment strategies for restless legs syndrome, periodic limb movement disorder and restless sleep disorder in the pediatric population
- To outline the key features characterizing arousal disorders/parasomnias in children

Clinical Presentation and Management of Pediatric Insomnia

ICSD-3-TR : Chronic Insomnia Disorder*

- The patient reports, or the *patient's parents or caregiver observes*, one or more of the following:*
  - Difficulty initiating sleep.
  - Difficulty maintaining sleep.
  - Waking up earlier than desired.
  - *Resistance going to bed on appropriate schedule*
  - Difficulty sleeping *without parent or caregiver intervention*
- The reported sleep/wake complaints cannot be explained purely by inadequate opportunity (i.e., enough time allotted for sleep) or inadequate circumstances (i.e., the environment is safe, dark, quiet, and comfortable) for sleep

*≥3x/week for ≥ 3 mths

ICSD-3-Tr: Chronic Insomnia Disorder

- The patient reports, *or the patient's parents or caregiver observes*, one or more of the following related to the nighttime sleep difficulty:
  - Fatigue/malaise
  - Attention, concentration, or memory impairment
  - Impaired social, family, occupational, or *academic performance*
  - Mood disturbance/irritability
  - Daytime sleepiness
  - *Behavioral problems (e.g., hyperactivity, impulsivity, aggression)*
  - Reduced motivation/energy/initiative
  - Proneness for errors/accidents
  - Concerns about or dissatisfaction with sleep

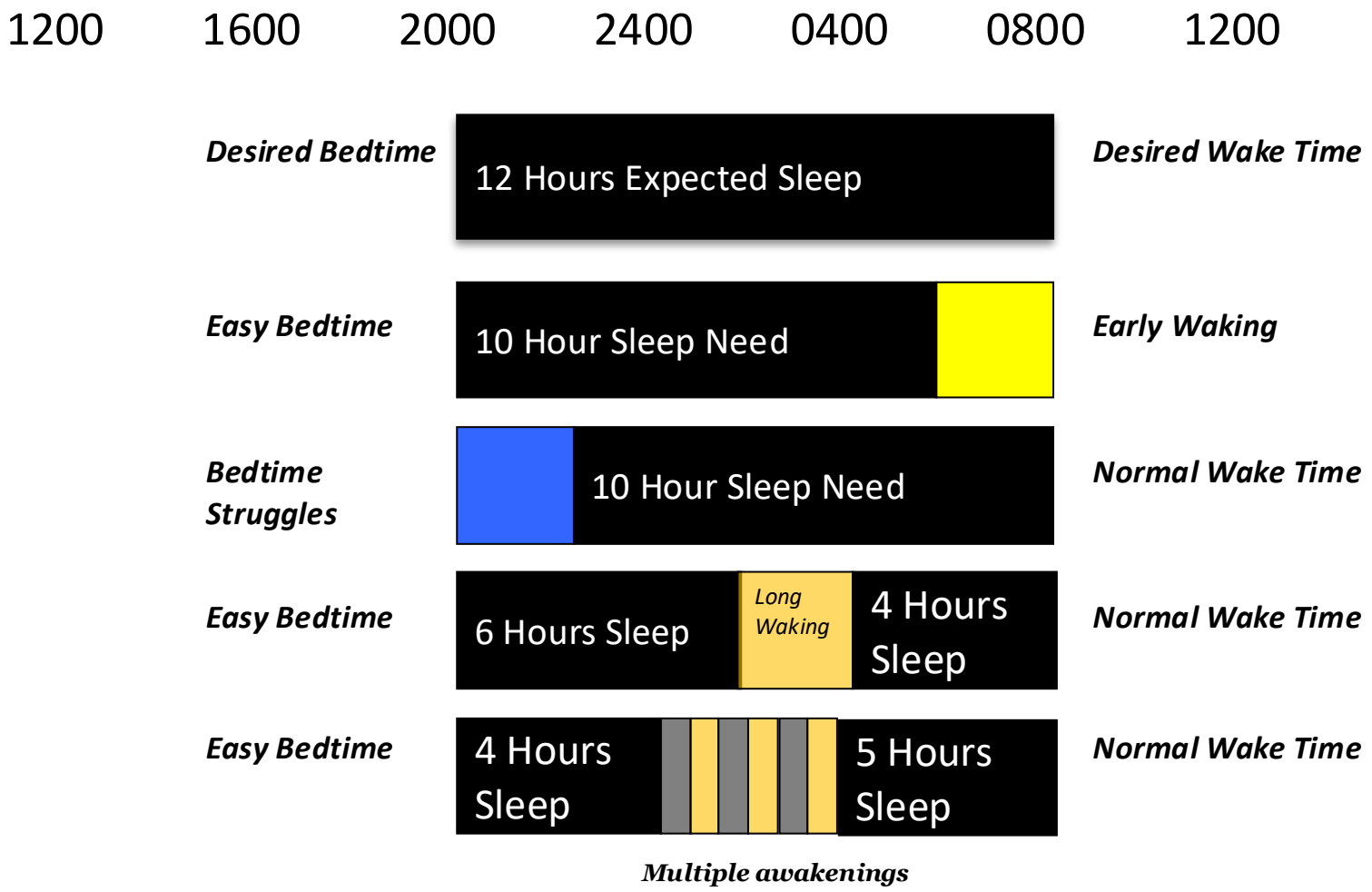
Behavioral Insomnia of Childhood: ICSD-2 Definition

- Sleep Onset Association subtype
  - Falling asleep is an extended process that requires special conditions
  - Sleep-onset associations are highly problematic or demanding
  - In the absence of the associated conditions, sleep onset is significantly delayed or sleep is otherwise disrupted
  - Nighttime awakenings require caregiver intervention for the child to return to sleep

Behavioral Insomnia of Childhood: ICSD-2 Definition

- Limit Setting subtype
  - The child has difficulty initiating or maintaining sleep
  - The child stalls or refuses to go to bed at an appropriate time or refuses to return to bed following a nighttime awakening
  - The caregiver demonstrates insufficient or inappropriate limit setting to establish appropriate sleeping behavior in the child

Too Much Time In Bed



Behavioral Interventions for Insomnia in Children

Extinction

- Elimination of parental attention as a reinforcer for undesired behaviors (e.g., crying)
- *Unmodified extinction* ("cry it out" or "cold turkey" approach): parents put the child to bed at a designated bedtime, and then ignore protest behaviors such as tantrums until a preset time the next morning
  - Effective but poorly tolerated by many parents

Extinction

- *Graduated extinction* ("sleep training, checking, controlled crying, Ferber method"): variety of techniques in which parents are typically instructed to ignore bedtime crying and tantrums for specified periods of time
- Involve gradual shaping of appropriate behaviors and fading of interventions

Bedtime Fading

- Temporarily delay of bedtime to match child's natural fall asleep time and promote rapid sleep initiation;
  - Bedtime then moved earlier by small increments (ie, 15 minutes) over successive nights ("fading") until pre-established bedtime goal is achieved

Treatment Issues

- Ensure readiness for sleep: “drowsy but awake”
- Time interval between checks fixed or variable
- Avoid reinforcement during checks
- Gates/physical barrier
- Common for crying/protest to briefly intensify 2nd or 3rd night (“extinction burst”)
- Intermittent/non-consistent use of behavioral plans is the most common reason for treatment failure

Melatonin in the US: The Landscape

- Dietary supplement: little FDA oversight
  - FDA considers supplements "safe until proven otherwise"
  - Clinical trials not required
  - Must meet label content +/- 10%
- Marketing issues

Extent of Melatonin Use (USA)

- Recent survey study of caregivers (2024)[1]:
  - Among children ages five to nine, 18% had been given melatonin in the previous 30 days
    - Elementary school students and preteens had used melatonin for median lengths of 18 and 21 months, respectively
  - Nearly 6% of preschoolers ages one to four had taken melatonin in the previous month
    - Preschoolers who used melatonin had been taking it for a median length of a year
- In comparison, only 1% of U.S. caregivers overall reportedly gave their children melatonin in 2017-18[2]

1Hartstein et al 2024; 2Stierman et al 2020

Melatonin: What You See May Not Be What You Get

- FDA study: Chromatography analysis random sample of 110 *pediatric marketed* melatonin supplements
  - Gummies, liquid, tablets, capsules, other edibles
- Content ranged from 0-667% of label
  - Gummy: 0-195% (50% >label); liquid 38-486%; other edibles (100%>label)
  - Overage: no evidence significant degradation over 12 mths; no correlation expiration date/melatonin content
- “Adult” labeled products (12%) marketed to children on product website
  - Some co-formulated with herbals, other supplements, vitamins
- Majority child-proof packaging; include recommendation to consult healthcare provider

Pawar et al 2024

The US Pediatric Melatonin Landscape

- Safety concerns
  - Poison center calls: Increased 530% 2012-2021
  - ED visits: Melatonin ingestions increased 421% 2009-2020
  - <50% of caregivers consult provider before giving melatonin to their child (including for children ages 0-36 mths); often for unsupported indications
- Commercial influence
  - Social media (40% of TikTok videos contained misinformation)
  - Unsubstantiated indications, delivery systems
- All of the above contribute to caregiver and healthcare provider lack of confidence → overuse, underuse and misuse of melatonin

Melatonin Recommendations

- Studies support use of melatonin for special needs pediatric populations (children with autism, neurological disorders; ADHD)
- Very limited data supports use in healthy typically developing children with insomnia; but can be useful ONLY if:
  - A thorough sleep evaluation identifies insomnia
  - It is combined with behavioral interventions and healthy sleep practices
- Melatonin should be used only under the care of a medical professional
- Melatonin should NOT be used in children under age 2 years

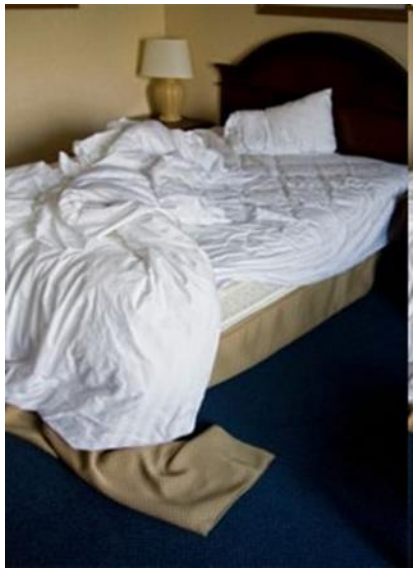
Melatonin Recommendations

- Immediate release melatonin should be used ONLY for sleep onset insomnia
- In countries where melatonin is available over-the-counter, ONLY pharmaceutical grade (USP Verified Mark*) melatonin should be recommended
- A number of over-the-counter medications contain melatonin (like “nighttime” cough syrups for children and “relaxation aids”)

*A USP Verified Mark indicates that the product was produced in a facility following the Good Manufacturing Practice (GMP) standards. These products meet some product quality control measures, including containing the amount of an ingredient on the label without harmful levels of specific contaminants. However, this is a voluntary program, and only four melatonin products, all with either 3 mg or 5 mg of melatonin, have received the USP Verified Mark

Pediatric RLS/PLMD/RSD

- Overall evidence regarding risk factors for and the epidemiology, genetics, and natural history of both disorders in the pediatric population remains relatively sparse compared to that in adults



Pediatric RLS

- Symptoms of RLS may start as early as 6 -12 months of age (pedaling, kicking, slapping legs accompanied by distress)
- Subjective symptoms of a “need” to move and dysesthesias occur primarily in the legs, but arm sensations have been reported to be common in children (although are rarely the only complaint).
- A significant percentage of children report prominent daytime symptoms while inactive
- Frequent presenting complaints by caregivers of children with RLS include bedtime resistance and difficulty falling asleep

Pediatric RLS

- Impairments in mood, daily activities including academic/work performance, and energy are common in children with RLS
- Neurobehavioral symptoms such as inattention and hyperactivity may be the presenting complaints in pediatric patients
  - In one study, 64% of pediatric patients with RLS had one or more comorbid psychiatric disorders; mood disturbances in 29% patients, anxiety disorders in 12% patients, and behavioral disturbances in 11%

Epidemiology

- “REST” study in the US and the UK found a prevalence of “definite” RLS in about 2% of both 8- to 11-year-olds and 12- to 17-year-olds; this represents some 980,000 school-aged children in the United States
  - One-quarter to one-half of these children and adolescents had moderate to severe symptoms, largely in adolescents
- Another much smaller study in 12- to 20-year-olds found a prevalence of RLS of 8%
- Because a definitive diagnosis requires PSG, there are fewer data regarding the prevalence of PLMs and PLMD in childhood
  - Prevalence of PLMI>5 is 5-27% in sleep clinic referral populations

Etiology

- Genetics: In the “REST” study, 70% and 80% of children with “definite” RLS had at least one biological parent with RLS and 16% had both parents affected
- Lower ferritin levels (defined as <50 ng/mL) are found in some 70% to 75% of children with RLS
  - Acute phase reactant; may be elevated during illness
  - Consider iron and transferrin, TIBC levels
  - Levels impacted by fasting/TOD, iron-rich foods
- Children with ADHD may also be more likely to have low serum ferritin levels *and RLS*
- Low vitamin D levels also linked

Diagnosis

- The child must describe the RLS symptoms in his or her own words
  - The diagnostician should be aware of the typical words children and adolescents use to describe RLS
  - Language and cognitive development determine the applicability of the RLS diagnostic criteria, rather than age
- In children in particular, caregiver reports of leg movements during sleep lack adequate sensitivity or specificity
- The diagnosis of PLMD requires a minimum number of limb movements per hour (>15/hr in adults and, based on pediatric normative data, >5/hr in children)

In Their Own Words…

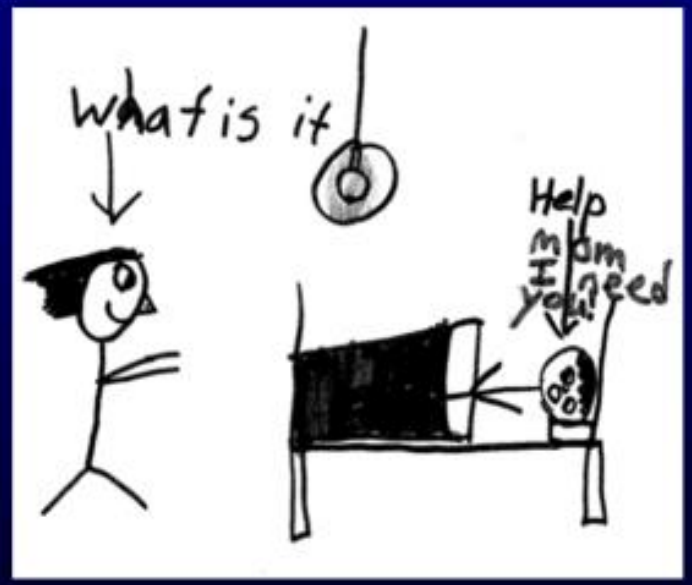
Study: 33 children 6-17yo with definite RLS and parent interviewed by pediatric sleep specialists

- Need/have to move/kick
- Pain/hurt
- Un/can't get comfortable
- Bugs/ants crawling
- Weird/funny feelings
- Tingling
- Nails/pins/needles
- Wiggly
- Itchy
- Tightening
- Restless
- Shaky
- Fizzing/bubbles
- Pulling/tugging

Picchetti et al, Jl Child Neurol 2011

And Pictures…

"They (my legs) like feel weird, and they want to kick" *7 yo boy*



"OK, I'm in bed, and my legs really, really hurt. So I say, help, Mom, I need you."

7 yo boy

RLS/PLMD in Children: Treatment AIMS

- **A** voidance
  - Drugs which exacerbate RLS TCAs, SSRIs, antihistamines, antiemetics
  - Caffeine, nicotine, alcohol
- **I** ron supplementation
- **M** uscles
  - Increase physical activity
  - Counter-stimulation (rubbing), massage, application heat/cold
  - Muscle relaxation, biofeedback
- **S** leep
  - Regular sleep schedule
  - Adequate amount for age
  - Good sleep hygiene (bedtime routine, relaxation)

Restless Sleep Disorder (RSD): Essential Diagnostic Criteria

- A complaint of “restless sleep” is the core diagnostic feature of RSD and must be present
  - ≥3X/week for ≥3 mths
- This is typically reported by a parent, caregiver, or bed partner
- Sometimes “restless sleep” is reported by the patient, based on the observations of others or the condition of the bed upon awakening
- Differentiation of a sign or symptom (restless sleep) from a disorder (restless sleep disorder)

RSD Essential Diagnostic Criteria

- The visible body movements, involve *large muscle groups of the whole body, all four limbs, arms, legs, or head* during sleep
  - Frequent repositioning
  - Disruption of the bedsheets
  - Falling out of bed
- Total body movements on video-PSG 5/hr
- Significant impairment in function
- Associated with low ferritin levels
  - Iron therapy

Iron Therapy for RLS/PLMD

- Oral ferrous fumarate or sulfate
- Tablet or liquid: 3-6 mg/kg of elemental iron/day x 3 months
  - Take with 200mg vitamin C on an empty stomach
  - Avoid calcium containing foods
  - May be effective in every other day dosing
- GI absorption may be lower at higher baseline levels (50-75ng/ml)
- Goal is ferritin above 50ng/ml (75-100?) in children

Iron Therapy for RLS/PLMD

- Consider in:
  - Moderate to severe RLS,
  - Serum ferritin is ≤ 100 µg/l with TSAT% < 45
  - Oral iron treatment failure: intolerance or lack of efficacy.
  - A condition that blocks oral iron absorption or makes response unlikely
  - Oral but not IV iron contraindication.
  - Clinical need for a more rapid response than with oral iron.
- IV: Ferric carboxymaltose; low molecular wgt dextran
- Pre-treat with IV diphenhydramine?
- Evaluate clinically 6-12 weeks after IV iron and adjust any other RLS treatments as indicated

NREM Disorders of **Arousal**

Disorders of Arousal: ICSD-3-TR

- Recurrent episodes of incomplete awakening
- Inappropriate or absent responsiveness to efforts of others to intervene, redirect
- Limited (e.g., a single visual scene) or no associated cognitive or dream imagery
- Partial or complete amnesia for the episode
- The disturbance is not better explained by another current sleep disorder, medical disorder, mental disorder, or medication/substance use

Disorders of Arousal: General Features

- Combine clinical features of:
  - Sleep state (high arousal threshold, unresponsiveness to external stimuli)
  - Awake state (ambulation, vocalizations)
- Typically emerge out of slow wave sleep (80% NREM stage 3; 20% NREM stage 2)
- Usually occur within first 3 hours of sleep; rare during naps

Disorders of Arousal: General Features

- Generally occur 1-3 times per month
- Can last minutes to 45 minutes
- Confusion, disorientation
- Can be induced in susceptible individuals (e.g., sudden noises)
- Familial component
- Decrease with increasing age

Triggers/Risk Factors

- Exacerbation by factors increasing SWS, sleep fragmentation
- Sleep deprivation rebound increase SWS
- Sleep schedule changes, unfamiliar environment
- ETOH, caffeine
- Medications (especially for sleepwalking)
  - BZD receptor agonists, antidepressants
  - Strongest evidence zolpidem, sodium oxybate
- Stress/Illness
- Sleep disordered breathing
- RLS/PLMD

Sleep Terrors

- Sleep Terrors reported in 1-6% of children <7yrs
- Peak prevalence in preschool children; usual disappearance by adolescence
- Frequency: often highest at onset; often higher (> once a week) with younger onset
- Characteristics:
  - Dramatic, extreme terror
  - Eyes open
  - Autonomic response (pupils dilated, flushed, sweating, tachycardia, tachypnea)
  - Agitated appearance, screaming; inconsolability
  - Parasomniac choking (rare)

Sleepwalking

- Regular sleepwalking reported in 13-17% in children 5-12y
  - Peak prevalence at 10 years; school aged children
- Genetics: 47% with one parent; 61% with both
- Confused/dazed appearing and rarely agitation
- Variable behaviors

  Complex and coordinated movements: getting dressed, unlocking a door

  Bizarre behaviors: urinating in wastebasket

  Automatic movements

  Impaired judgment
- SAFETY concerns: climbing out of windows, leaving the house, self-injury with cuts, bruises

Confusional Arousals

- Prevalence: 17% in children aged 3-13 years; 3-4% in adults > 15 yrs; lifetime 18%
- Generally infant, toddlers, young children
- Often occurs with or precedes ST, SW
- Child appears disoriented, unresponsive and no recall
- Tends to last few minutes, remains in bed
- May be triggered by external environmental stimuli
  - Also reported in morning with forced wakings
- Accompanied by odd behaviors
  - Sitting up, thrashing, agitated/combative

Disorders of Arousal: Management

- Parental reassurance, education
- Safety precautions (window and door locks, alarms, monitors; secure sharp objects)
- Avoid triggers/exacerbating factors (result in sleep fragmentation, increased SWS)
- Stress reduction; relaxation
- Scheduled awakenings: consider for frequent episodes
- Pharmacotherapy rarely needed; SWS suppressants (off-label)

Thank You!

judith.owens@childrens.harvard.edu