

# Sleep: Foundation for Health, Well-being, Performance and Learning

- Stephen Nelson, MD, PhD, FAACPDM, FAAN, FAAP, FANA
- Professor of Pediatrics, Neurology, Neurosurgery and Psychiatry
- Epileptologist
- Section Head, Tulane University School of Medicine
- CHNOLA Pediatric Neurology

# Disclosure slide

All opinions are mine, and are based on my knowledge, training and expertise. I do not represent Tulane University, CHNOLA, the AAP, or any other organization with these opinions.

It is my obligation to disclose to you (the audience) that I am on the Speakers Bureaus for BioMarin and Supernus. However, I acknowledge that today's activity is certified for CME credit and thus cannot be promotional. I will give a balanced presentation using the best available evidence to support my conclusions and recommendations. I do not intend to discuss an unapproved/investigative use of a commercial product/device in my presentation.

# Development of Sleep

- Overall quantity of sleep and temporal organization of sleep stages evolves continuously from infancy through adolescence.
- By 27 to 28 weeks postconceptional age, can distinguish wake and sleep (80% active (rapid eye movement [REM]) sleep - irregular respiratory pattern, intermittent EMG activity, and low-voltage mixed-frequency EEG activity).
- By full term (40 weeks), active sleep decreases to ~50% of total sleep time, with the rest as quiet (nonREM) sleep.
- Sleep spindles and K complexes (maturation of thalamocortical activity) appear by 2 - 3 months.
- By 4 to 6 months, quiet sleep differentiates into N1, N2, and N3 sleep stages (lighter to deeper sleep).

# Development of Sleep

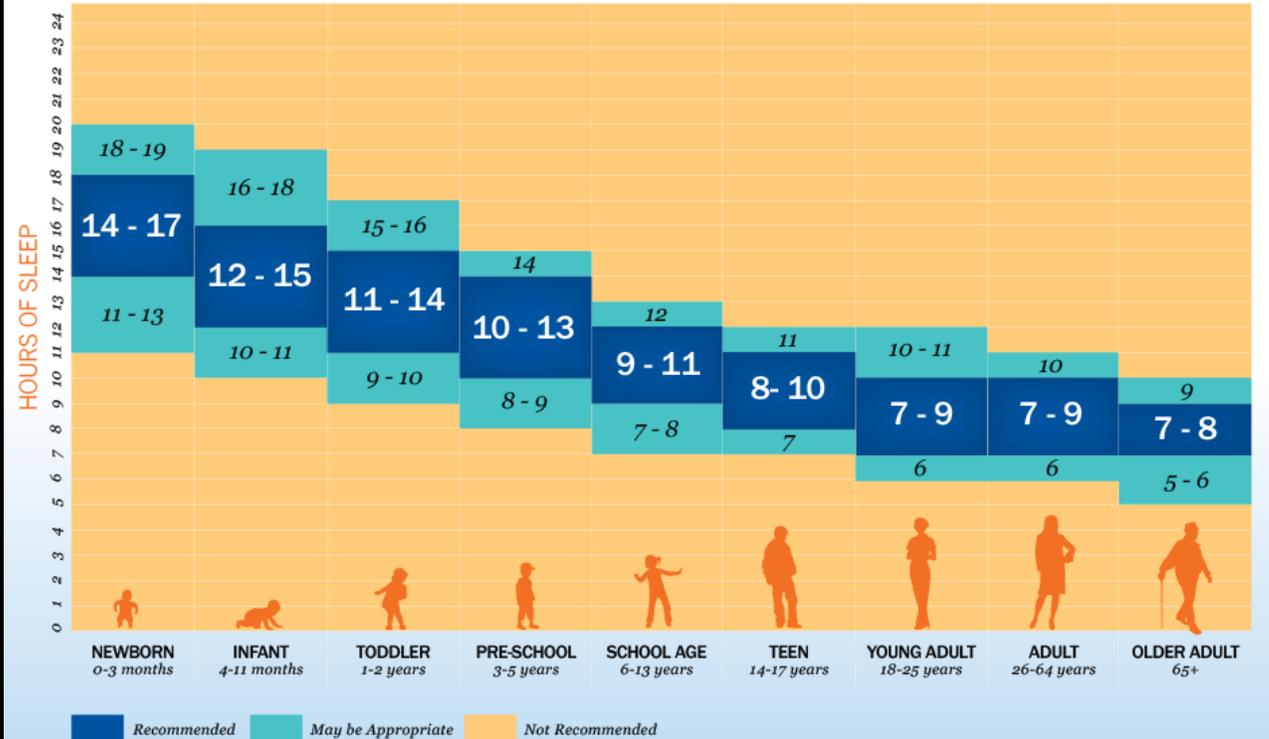
- Sleep stage N3: generalized 0.5 Hz to 4 Hz slow-wave activity
- Occurs predominantly in the first third of the night
- Children have large amounts of N3 sleep due to release of growth hormone and the consolidation of explicit memories
- Short-term memories stored in the hippocampus become consolidated into long-term memories in the neocortex during the N3 sleep stage by replay of short-term memory events
- REM sleep: by the age of 3 years, only ~20% - 25% of sleep

# Sleep Changes

- < 3 months old, infants transition directly from wake to REM sleep.
- > 3 months old, transition wake into non-REM sleep, with REM sleep occurring ~1.5 – 2 hours after initial sleep onset.
- Elementary school age - usually become sleepy ~2000-2030
- Transition from prepuberty to puberty, melatonin is released later, with delay in the sleep onset ~2230-2300, leading to later wake-up time.
- Also, melatonin secretion declines w/ advancing Tanner stage, boys > girls.
- Easy to understand why most teenagers want to sleep in and are chronically sleep deprived.

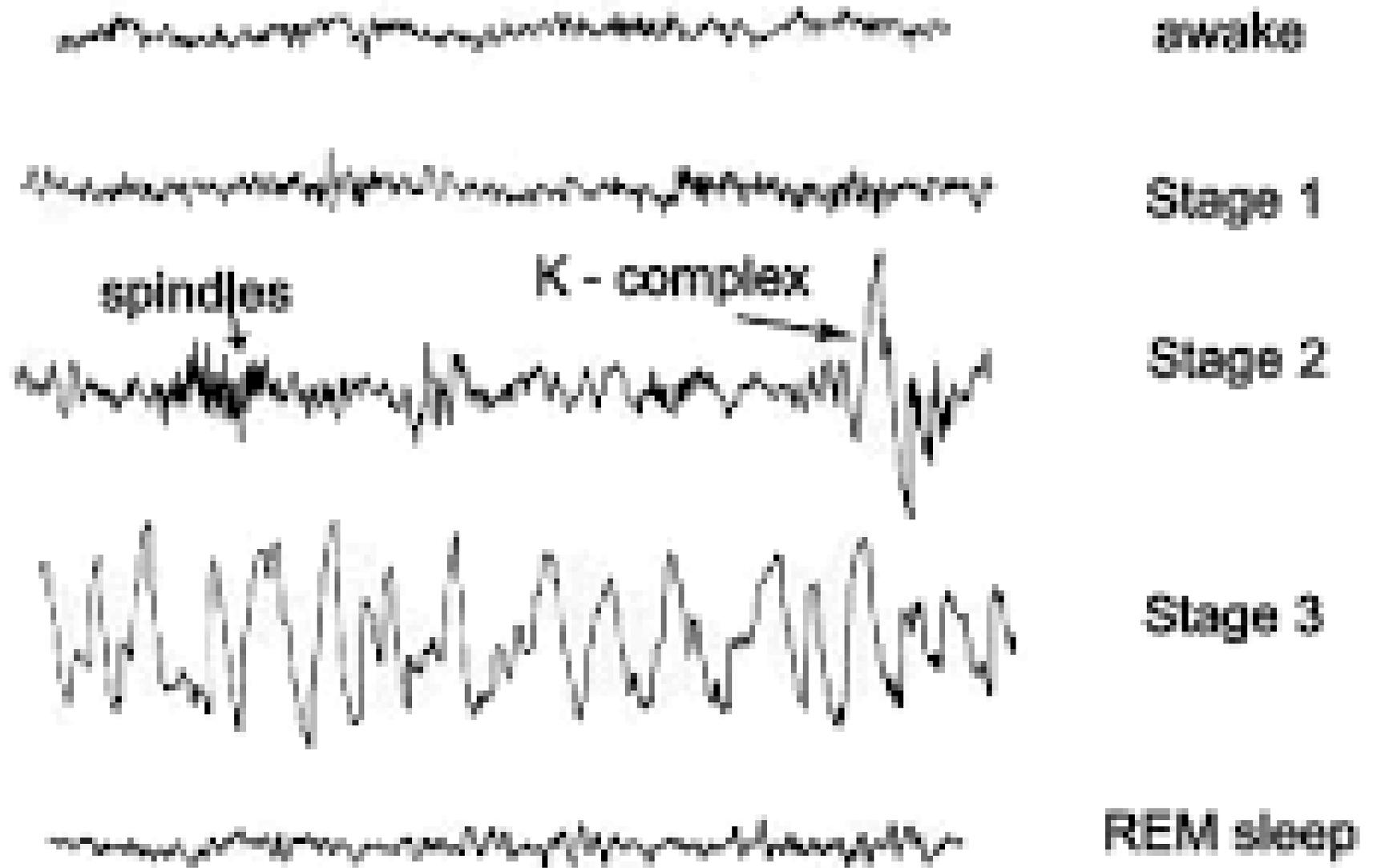
# SLEEP DURATION RECOMMENDATIONS

How much sleep do we need?

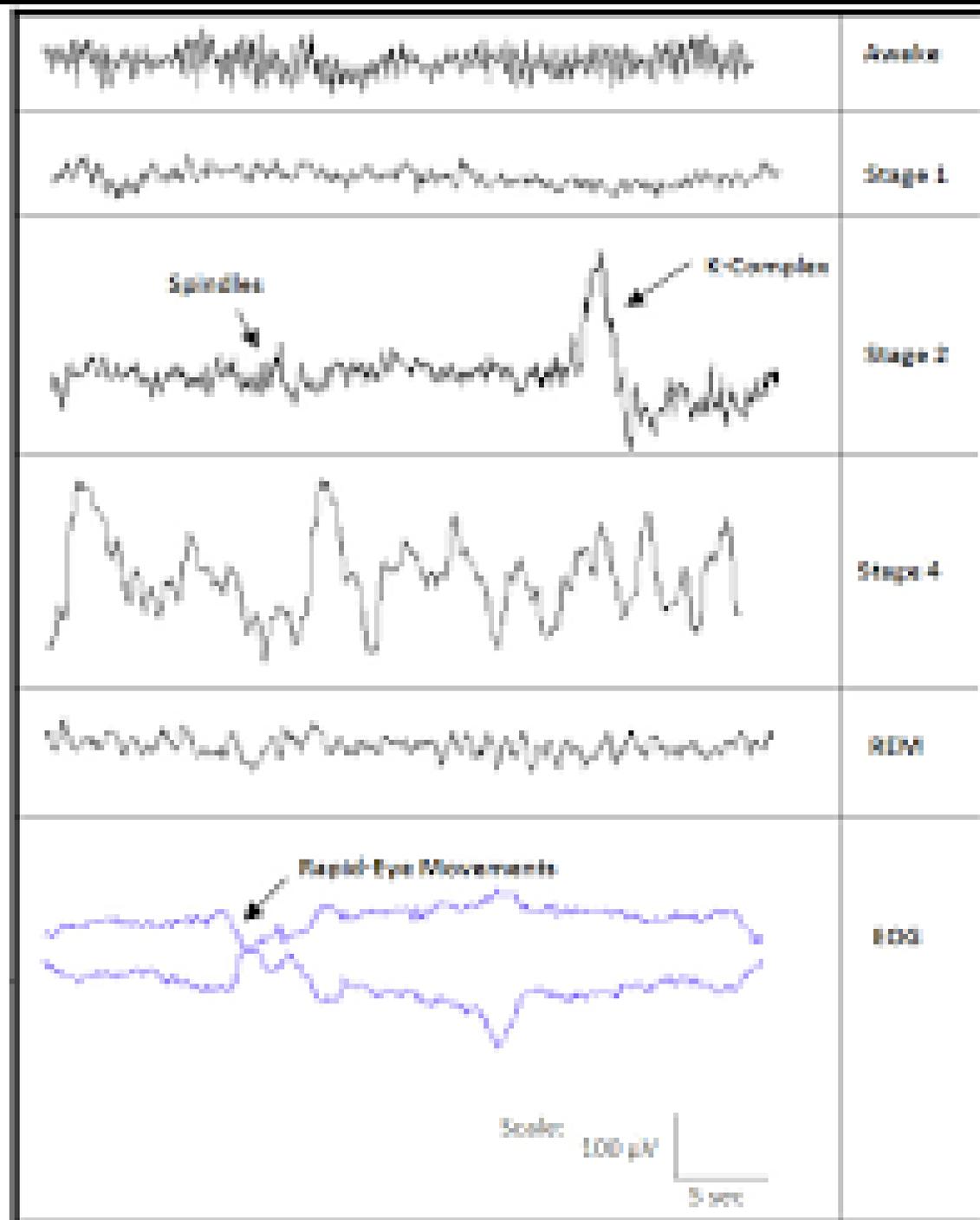


SLEEPFOUNDATION.ORG | SLEEP.ORG

# Stages of sleep

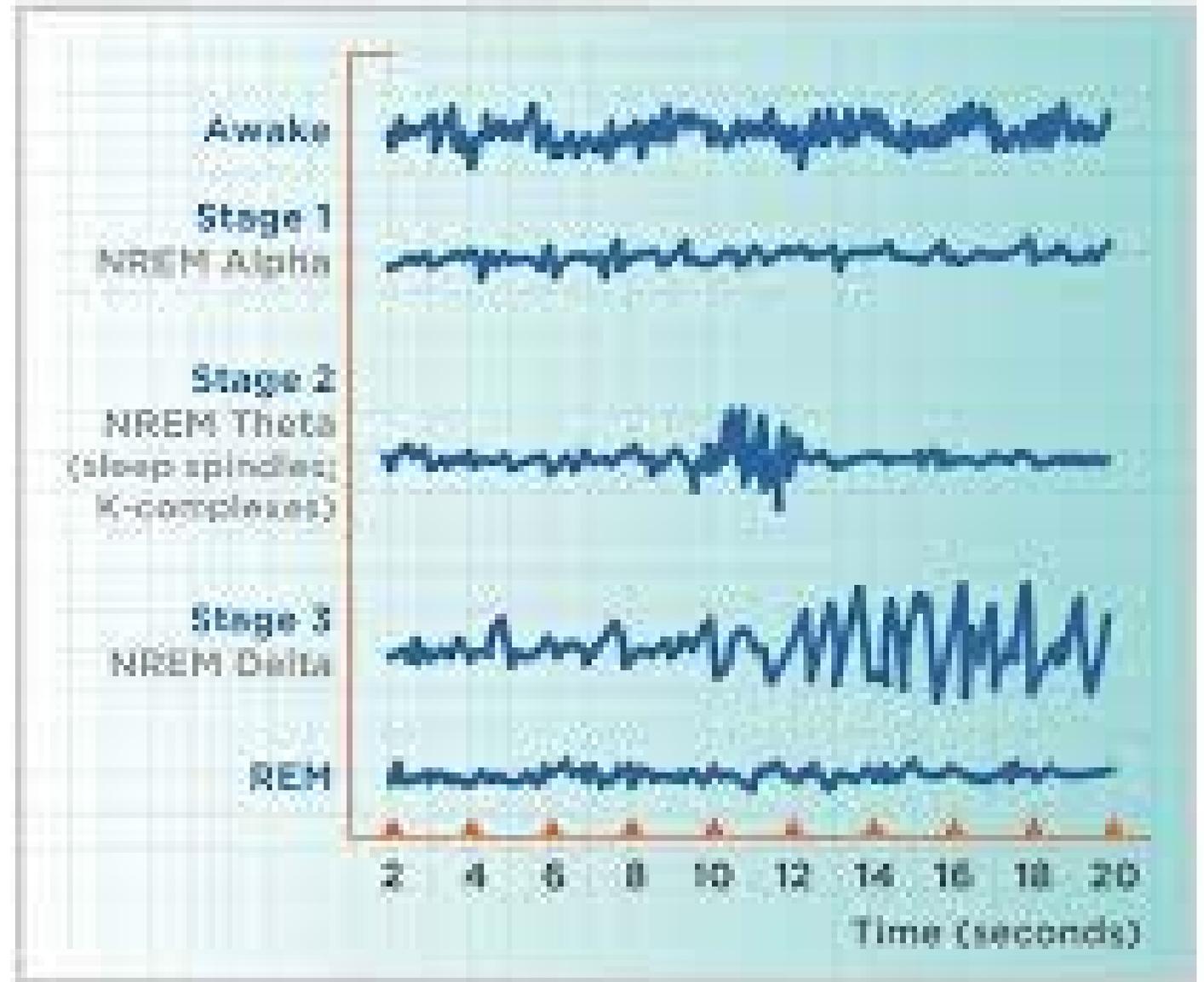


# Stages of Sleep

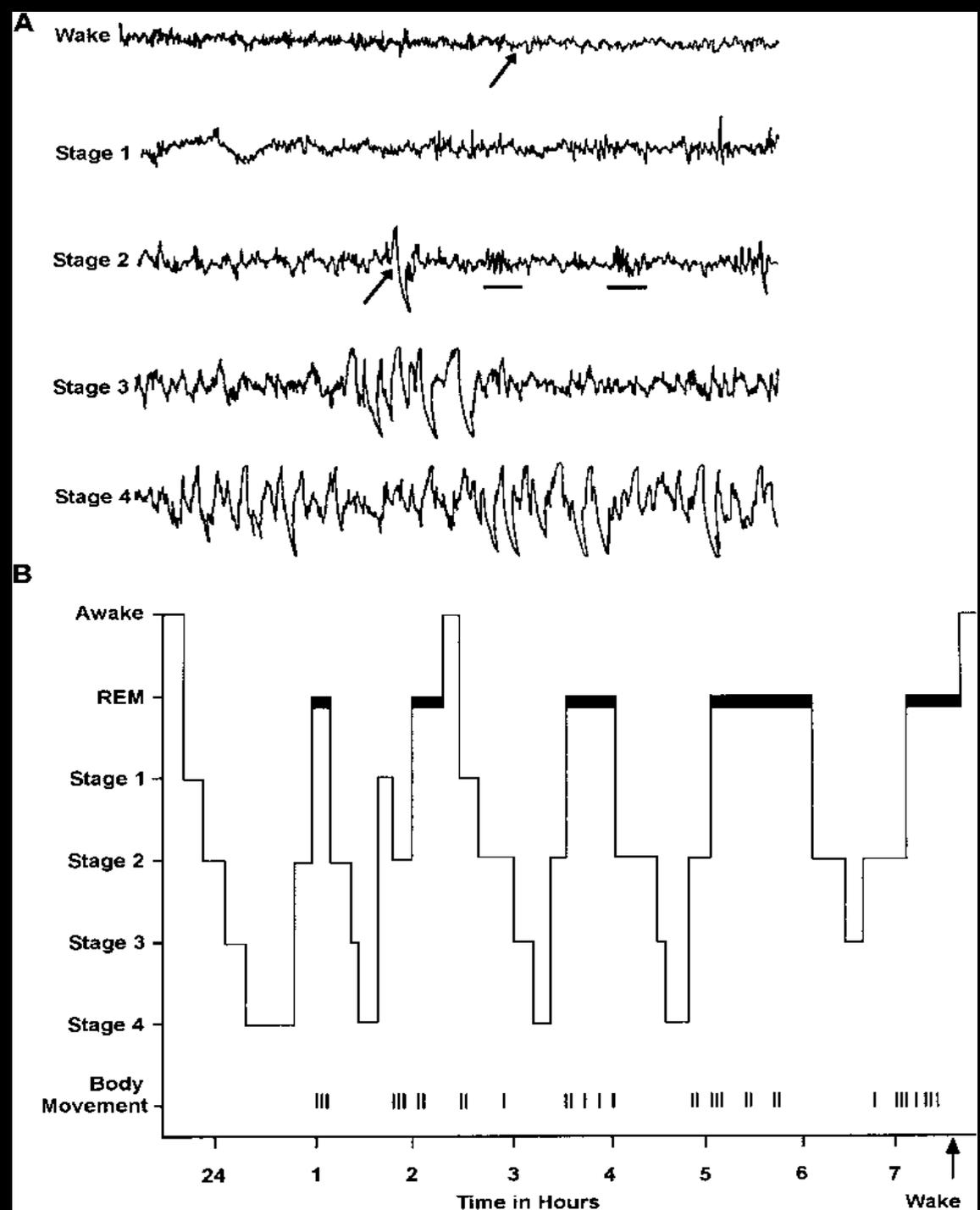


# Stages of Sleep

## EEG RECORDINGS DURING SLEEP



# Stages of Sleep



# Sleep history

- Sleep environment, bedtime and approximate sleep-onset time
- Sensation of discomfort: in the extremities (restless legs syndrome [RLS]); intrusive thoughts or worries (anxiety); snoring or periods of observed apnea and restless sleep (obstructive sleep apnea [OSA]); unusual nighttime events (parasomnias, seizures)
- Daytime sleepiness: hypersomnia disorders, mood disturbances, and medications

# Sleep examination

- Height, weight, and body mass index (BMI)
- Presence of craniofacial anomalies, tonsillar hypertrophy and whether the oral airway is crowded
- Examination of the anterior nasal passages
- Auscultation of the heart and lungs

# Excessive Daytime Sleepiness

- Worldwide prevalence in childhood and adolescence 4% - 20%.
- Underestimated since often either not asked or diagnosed with another condition (such as ADD or daydreaming)
- Failure to address can lead to impaired academic performance and reduced safety (driving, employment)

# Excessive Daytime Sleepiness

- Circadian Rhythm Sleep-Wake Disorders:
  - Delayed Sleep-Wake Phase
  - Advanced Sleep-Wake Phase
  - Irregular Sleep-Wake Rhythm
  - Non-24-Hour Sleep-Wake Rhythm
  - Shift Work
  - Jet Lag
- Risk factors: Mental illness, vision impairment, cognitive impairment, genetic, environmental
- All treated with combination of light therapy, melatonin and sleep hygiene

# Excessive Daytime Sleepiness

- Environmental
  - Illicit substances
  - Inadequate sleep hygiene
  - Over-the-counter medicines
  - Prescription medicines
- Inadequate Sleep Hygiene: most common etiology in adolescents

# Inadequate Sleep Hygiene

- Common habits:
  - Mentally activating activities such as watching TV in the 1 - 2 hours before bed
  - Use of electronic devices or cell phones
  - Caffeine, tobacco, or substance use at night
  - Exercising or showering close to bedtime
  - Eating or drinking during the night
  - Daytime napping
- Most common activity when unable to sleep - use of electronics

# Childhood Insomnia

- Behavioral insomnia of childhood
  - Related to sleep-onset associations
  - Related to inadequate limit-setting by parents
- Psychophysiologic (conditioned) insomnia
- Transient sleep disturbances

# Types of Behavioral Insomnia of Childhood

- Sleep-onset association type - child's dependency on a specific activity/behavior/ stimulation, typically objects or settings, for initiating sleep or returning to sleep following an awakening that when absent significantly delay sleep onset
- Limit-setting type - behaviors of stalling or refusing to go to bed attributable to inadequate limit setting by the parent or caregiver
- Mixed hybrid type - features of both
- Some degree of bedtime resistance or insomnia are common in children
- Sleep disorder -  $\geq 3$  times per week, persist  $\geq 3$  months, and result in significant impairment of functioning in the child, parent(s), or family

# Insomnia Related to Sleep-Onset Associations

- Generally one of prolonged night waking that results in insufficient sleep
- Infant or child has learned to fall asleep only under certain conditions or has specific sleep associations that typically require parental intervention, such as being rocked or fed, which are usually readily available at bedtime
- During the night, when the child experiences the type of brief arousal that normally occurs at the end of each 60- to 90-minute sleep cycle, or awakens for other reasons, not able to get back to sleep ("self-soothe") unless those same conditions are available, and so "signals" the caregiver by crying (or coming into the parents' bedroom if the child is no longer in a crib) until the necessary associations are provided
- Avoided or attenuated by practice of putting the infant or child to bed while drowsy but still awake, starting at approximately three months of age
- Transition objects – good and bad

# Insomnia Related to Inadequate Parental Limit-Setting

- Active resistance, verbal protests, and repeated demands at bedtime ("curtain calls") rather than night wakings
- If sufficiently prolonged, the sleep onset delay may result in inadequate sleep
- Some children present with nighttime fears characterized by fearful behaviors (eg, crying, clinging, or leaving the bedroom to seek parental reassurance), but these are a manifestation of bedtime stalling rather than anxiety
- Develops from a caregiver's inability or unwillingness to set consistent bedtime rules and enforce a regular bedtime
- In some cases, however, the child's resistance at bedtime reflects an underlying problem in falling asleep caused by other factors, such as asthma, medication use, or other medical conditions; a sleep disorder, such as restless legs syndrome or anxiety; or a mismatch between the child's intrinsic circadian preferences ("night owl") and parental expectations

# Insomnia Related to Excessive "Time in Bed"

- Not a "formal" subtype of insomnia, but useful in clinical practice
- Children whose parent-set time in bed exceeds their sleep needs, resulting in prolonged bedtime struggles, night wakings, or early morning awakening (or some combination of all three)
- Solution is to reduce the "sleep window" to match sleep, typically by delaying bedtime and/or advancing wake time
- Can be done incrementally, eg, delaying bedtime by 15 minutes every few nights until the target sleep window is achieved
- Ferber method

# Psychophysiological (Conditioned) Insomnia

- Characterized by anxiety specifically about falling or staying asleep due to heightened physiologic and emotional arousal related to sleep and the sleep environment.
- Frequently arises from a combination of predisposing such as genetic vulnerability, medical disorders, or psychiatric conditions
- Precipitating factors may include acute stress and perpetuating factors may include poor sleep habits, caffeine use, or inappropriate daytime napping
- Fight Club

# Transient Sleep Disturbances

- Can occur in a child with previously normal sleep
- A period of night wakings, for example, can be the result of a stressful life event and is usually self-limited
- Disruption of sleep schedule while travelling can cause jet lag
- Many illnesses also can disturb sleep
- Can become chronic if parents respond in ways that reinforces the night wakings and foster inappropriate sleep habits

# Childhood Insomnia is common

- Prevalence 20 – 30% worldwide
- Infants and toddlers: Night wakings in 25 – 50%; bedtime resistance 10 – 15% toddlers
- Preschool-aged children: 15 – 30% have difficulties falling asleep and/or night wakings
- Middle childhood: 15% bedtime resistance and > 10% sleep-related anxiety (ie, psychophysiologic [conditioned] insomnia)
- Adolescents: > 10% have a history of significant insomnia
- Children with neurodevelopmental (such as Autism or intellectual disability) and psychiatric disorders (ie, depression, anxiety, ADHD) are at particularly high risk for sleep disturbances – medications vs disorder

# Intrinsic vs Extrinsic Factors

- Intrinsic factors (those that are inborn or unique to the child and predispose to sleep problems) include temperament, medical issues, circadian preferences ("night owl" versus "morning lark"), neurodevelopmental disabilities, anxiety disorders, etc.
- Would include sleep disorders and sleep disordered breathing
- May vary over lifetime in severity and frequency

# Intrinsic vs Extrinsic Factors

- Extrinsic factors (environmental stimuli or caregivers' response) that precipitate or perpetuate the problem include characteristics of the parents/caregiver that interfere with their ability to set clear limits both during the day and at bedtime due to mental illness, emotional stress, distraction by other responsibilities, long work hours, etc.
- In some cases, a "mismatch" arises between parental expectations and normal developmental trajectory of sleep behaviors arises
- Environmental factors may contribute to poor limit-setting or negative sleep-onset associations, such as sharing a bedroom, noise, poor temperature setting, etc.

# Intrinsic vs Extrinsic Factors

- Usually a combination of both
- Twin studies demonstrated that 26% variance in sleep duration due to genetic effects and 66% due to shared environmental effects
- Additionally, daytime sleep duration was influenced more by environmental factors, and nighttime sleep duration was largely genetic

# Treatment – Behavior Modification

- Bedtime routines
  - Systematic ignoring (or "extinction") and its variants
  - Bedtime fading
  - Positive reinforcement
- 
- Highly effective (>80%) short- and long-term
  - No detrimental effects reported

# Bedtime routines

- Helpful for all manifestations of behavioral insomnia (bedtime resistance, prolonged sleep onset, and night wakings)
- Should last ~20 - 45 minutes and include 3 - 4 soothing activities
- Transition objects
- To bed awake
- Appropriate amount of time in bed based on age
- Appropriate time in bed based on age

# Sleep Times by Age

- Infants (4 – 12mo) 12 – 16 hours w/ naps
  - Toddlers (1 -2yo) 11 – 14 hours w/ naps
  - Children (3 – 5yo) 10 – 13 hours w/ naps
  - Children (6 – 12yo) 9 – 12 hours (NO NAPS)
  - Teens (13 – 18yo) 8 – 10 hours (NO NAPS)
- 
- Time of sleep onset shifts later with age (circadian clock)
  - Individual variation in time and amount of sleep
  - Routine maintains circadian rhythm

# Systematic ignoring

- Targets sleep onset insomnia or night waking (demands presence of parent to fall asleep)
- Unmodified extinction - put child to bed and leave in bed until set time, and ignore any crying
- Graduated extinction – gradually increased time prior to checking on child, and incorporate positive reinforcement

# Bedtime fading

- Addresses problems with insomnia at sleep onset
- “Mismatch” between the set bedtime and the child's fall asleep time
- Initial bedtime set to coincide w/ natural sleep onset time
- Circadian preference is then gradually modified by setting the bedtime earlier or later over a period of several weeks
- Also addressing excess time in bed that results in difficulty falling asleep, prolonged night wakings, or early morning waking
- Setting the bedtime later - "sleep window" approximates sleep needs

# Napping

- Napping is natural in younger aged children
- Napping should be avoided in older children, teens and adults
- There should be  $\geq 4$  hours between sleep periods
- Naps that are too close together, too long in duration, or too close to bedtime can result in insomnia
- Napping often used to “refresh” because of poor sleep habits, but just perpetuates the issue

# Positive reinforcement

- Start small with goals
- Multiple small rewards more effective than fewer larger rewards
- Rewards should be immediate
- Do not combine with negative reinforcement

# Treatment – Behavior Modification

- Positive effects include improvements in daytime behavior such as crying, irritability, detachment, self-esteem, or emotional well-being
- Also improvements in parental well-being with effects on mood, stress, and marital satisfaction
- Vast majority of sleep disturbances in children can be successfully managed with behavior therapy alone
- Medications should be considered only when appropriately implemented behavioral interventions have not been effective and furthermore should always be combined with behavior therapy

# Insomnia in Older Children and Adults

- Psychophysiologic (conditioned) insomnia
  - Anxiety around difficulty falling or staying asleep
- Delayed sleep-wake phase disorder
  - Teenagers/young adults - circadian rhythm slightly longer than 24 hours
  - Results in delay in sleep and wake time relative to the desired or required sleep schedule

# Sleep Hygiene

- Regular sleep-wake schedule
- Avoid light-emitting devices at least one hour before bedtime
- Use the bed only for sleep, get out of bed if unable to fall asleep
- Restrict time in bed to actual time asleep
- Relaxation techniques and cognitive-behavioral strategies to reduce anxiety
- Avoid caffeine especially in afternoon/evening
- Exercise daily, but not within 2 – 3 hours of bedtime
- Exposure to sunlight and lights during am/day
- Evaluate temperature, noise, light, setting of sleep

# Medications

- Vast majority of sleep disturbances are successfully managed with behavior therapy alone
- Reasonable to consider medications **as an adjunct to behavioral therapy when:**
  - Children with medical, psychiatric disorders, or neurodevelopmental disorders
  - Behavioral strategies alone have been persistently unsuccessful
  - Sleep problem results in significant family disruption or safety risks

# Melatonin

- Synthetic form of the hormone produced by the pineal gland
- Retinal fibers to the suprachiasmatic nucleus in the hypothalamus prevent natural release when exposed to light
- Better for sleep onset insomnia rather than sleep maintenance
- Dose timing is important and depends on clinical use
  - Several hours before bedtime for circadian rhythm effects
  - Shortly before bedtime for sleep-onset insomnia
- NOT FDA APPROVED
- CONTENT OF PRODUCTS VARIES WIDELY
- DOSING – MORE IS NOT BETTER

# Anti-histamines

- Diphenhydramine, cyproheptadine, hydroxyzine, etc.
- Paradoxical response
- Poor sleep quality
- NOT FDA APPROVED FOR TREATMENT OF SLEEP
- Anti-cholinergic side effects
- Tolerance develops
  
- May be useful for short-term use, but generally NOT RECOMMENDED
- May be useful if treating co-morbid condition

# Anti-depressants

- Some can be very sedating such as Amitriptyline, Trazadone, Quetiapine, etc.
- NOT FDA APPROVED FOR SLEEP
- Best if co-morbid condition
- Suppress REM sleep
- May have residual daytime side effects
- May have multiple side effects or increase risk for other co-morbid disorders

# Benzodiazepines

- GABA receptor agonists
- Can be effective when used to treat co-morbid condition that impacts sleep such as anxiety, seizures, or RLS/PLMS
- Tolerance and addiction can develop
- Can depress respirations
- Can interact with other medications or drugs (such as alcohol)
- May have daytime sedation effects or impair function

# Nonbenzodiazepine receptor agonists

- Abrupt withdrawal with prolonged use (>2 weeks) may be associated with rebound
- Black box warning: Complex sleep-related behaviors (eg, sleepwalking or sleep driving), hallucinations
- Little empirical evidence of efficacy in children or teens
- May be used for short time in teens or adults

# Alpha-2 adrenergic agonists

- NOT FDA APPROVED FOR SLEEP
- Narrow therapeutic window
- May be option with co-morbid ADHD
- Guanfacine has longer half-life than Clonidine (maintenance vs onset)

# AVOID

- Chloral hydrate – no longer available in the US

Questions?