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Advocate Christ Medical Center, Oak Lawn, IL
## Conflict of Interest Disclosures for Speakers

1. I do not have any relationships with any entities **producing, marketing, re-selling, or distributing** health care goods or services consumed by, or used on, patients, OR

2. I have the following relationships with entities **producing, marketing, re-selling, or distributing** health care goods or services consumed by, or used on, patients.

<table>
<thead>
<tr>
<th>Type of Potential Conflict</th>
<th>Details of Potential Conflict</th>
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<tbody>
<tr>
<td>Grant/Research Support</td>
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<tr>
<td>Consultant</td>
<td>Served on advisory committee to AASM Scoring Manual Editorial Board for developing criteria for scoring sleep/wake in infants 0-2 months of age and wrote an evidence-based review of this. I received no financial support for this.</td>
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<td>Speakers’ Bureaus</td>
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<tr>
<td>Financial support</td>
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<tr>
<td>Other</td>
<td>Wrote article on special considerations for polysomnography in children for up-to-date; receive royalties for this.</td>
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3. The material presented in this lecture has no relationship with any of these potential conflicts
Objectives of Talk

1) Appreciate the crucial role of sleep in early brain development and network connectivity;
2) Know how to score Wakefulness, NREM, REM and Transitional Sleep in infants 0 to 2 months of age using the AASM Sleep Scoring Rules;
3) Learn what we know, do not know, and need to know about normative PSG data in infants
4) Recognize which infants need PSGs and why.
Infants Sleep for Brain
Sleep is the Major “Work” of Infants

- Piaget thought play was the major ‘work’ of children, but it is sleep for neonates and infants;
- Sleep is principal behavior state of infancy and early childhood, same period in which rapid advances in growth, cognition and behavior occur.

Piaget J. Play, dreams, and imitation in childhood. 1951
REM Sleep Plays Crucial Role in Early Brain Development

- Infants at term sleep 14 to 18 hours per 24, 50% of it in REM sleep; preterm spent 80% of sleep time in REM sleep;
- Time course of development (and decline) of REM sleep in humans corresponds with critical periods of brain maturation.

- Hypothesis: brain stem mechanisms that produce REM sleep provide ascending stimulation to forebrain to promote brain development when wake-related stimulation is low

Delta Brushes (DBs) Reflect Sculpting of Brain Networks and Sensory Maps in Sleep

- Premature infants move and twitch far more than term, and much more than adults do when sleeping.
- These myoclonic twitches of skeletal muscles (often tens of thousands per day) are neither random nor purposeless;
- Proprioceptive feedback from twitching limb triggers delta brushes in appropriate regions of developing somatosensory cortex;
- Similar mapping of auditory, touch, pain and smell correlates with delta brush activity.

DBs play central role in early topographic mapping of different regions of cerebral cortex.

Premature Infants Sleep Better in Womb Than in Neonatal ICU

- Preterm infants in NICU have less TST and more NREM sleep compared to fetuses of similar age sleeping in womb.

Sleep disturbed by handling, noise, light, underlying disease processes, abnormal day-night cycles, pain, drug effects.

Neonatal ICU Sleeping Challenges

• 5-10 dB sounds disrupt sleep premature infants in their incubators (more often average noise 50 dB);\(^1\)
• Pain problematic: REM sleep decreased within 1 h after pain regardless of intervention (oxycodone or glucose);\(^2\)
• Drugs disturb sleep phenobarbital, fentanyl, methylxanthine, caffeine, steroids = less REM sleep, more wake and hyperactivity).\(^3\)

Better to Sleep in Utero Till Term

• Study comparing sleep/wake transitions in infants born premature (PT, <37 weeks GA) compared to those born term;
  – PT infants who had more immature sleep patterns, sleep stage shifts, and greater amounts of T had poorer developmental outcomes on Bayley II at 6 months;
  – Longer periods of sustained sleep, more REM sleep time better cognitive outcomes.

Hands-On Provider Care Disturbs Sleep/Wake Cycling in Neonates

• Reviewed video-PSG data for 25 medically stable infants (mean GA 39 ± 2 weeks) regarding effect of handling on sleep/wake cycling:
  – Neonates spent 27% (65 min) out of a 4-h recording being handled (1/3 by sleep techs); only 50% had a complete sleep/wake cycle during this;
  – Arousals occurred in 57% of contacts with sleeping infants;
  – Desaturation, hypopneas, and apneas occurred with 20%, 16% and 8% of contacts with sleeping infants;
  – Hypopneas were most likely to occur following contact with infants in REM sleep (28%).

Sleep/Wake Transitions in Infants Predict Later Neurodevelopment

Study 1: Outcome age 5

- Longitudinal study of sleep/wake transition patterns in 143 preterm infants (mean age 31.8 weeks);
- NREM sleep/wakefulness $\rightarrow$ greater neonatal neuromaturation, less negative emotionality, and better verbal, symbolic and executive competences at age 5;
- REM sleep and cry, short episodes of REM and NREM sleep $\rightarrow$ poorer outcomes.

Study 2: Outcome 18 months

- Prospective follow-up study of 65 infants born premature. Recorded actigraphy, sleep diaries, and structured observation:
  - Poor sleepers (31) in neonatal period exhibited poorer attention and distractability at 4 and 18 months than those well slept.

Strategies to Improve Sleep/Wake Cycling in NICU

• Sleep with ear muffs;
• Reduce noise and handling;
• Train staff to differentiate REM sleep from W;
• Treat pain to skin-to-skin contact and/or glucose (rather than oxycodone);
• Lights out 7 pm to 7 am.
Technical Aspects of Recording Neonatal/Infant Sleep Studies (How)
Neonatal/Infant Sleep Studies

- At UNM we record 5-8 infant PSGs a year;
- These are inpatient studies recorded more often in neonatal ICU, sometimes in pediatric ICU or ward.
- 1-5 neonatal video-EEGs a week (continuous for therapeutic hypothermia and status epilepticus).
What You Need to Know To Order, Record and Read a Neonatal/Infant PSG

• **Clinical history:** DOB, Age, indication for PSG, APGAR scores, occurrence of SZs, desaturations, hypoxia, hypercapnia, ALTE, GER, infection, genetic abnormalities.

• **Medication/treatment:** therapeutic hypothermia, **morphine**, barbiturates, caffeine, benzodiazepines, warming blankets, ECMO, CPAP, bubble CPAP, high flow O2, O2 via NC;
  - Amounts, dosages, time of administration, serum levels if known.

• Tech needs to provide detailed observations supplemented by **video:** awake/asleep, on ventilator, O2, CPAP, in incubator, feeding, loud noises, nursing care, respiratory rate, body temperature, SpO2, HR, therapy trials.
## Crucial to Know: Conceptional Age (CA) of An Infant When Reading their PSG

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
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<tbody>
<tr>
<td>Gestational Age (GA)</td>
<td>Weeks infant was in uterus</td>
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<tr>
<td>Legal Age</td>
<td>Age in weeks since birth</td>
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<tr>
<td>Conceptional Age or Corrected Age (CA)</td>
<td>GA + legal age in weeks</td>
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<tr>
<td>Prematurity</td>
<td>GA &lt; 37 weeks</td>
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<tr>
<td>Full term</td>
<td>Birth at GA of 37-42 weeks</td>
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Conceptional Age (CA) Crucial

• Infant’s CA crucial for interpreting normalcy, immaturity or abnormality of a neonatal or infant PSG (or EEG);

• Brain and EEG develop and mature at a similar rate independent of whether the infant is in utero or post-delivery;

• Except when stressed, or in situations involving encephalopathy, seizures, or medication-related factors, PSG infants ≤ 6 months reflects developmental age of the brain.

PSG of a healthy low-risk premature infant born at 32 weeks GA when 8 weeks old should resemble that of a normal 40 weeks GA infant born 2 days earlier.
Neonatal/Infant PSG EEG Montage

- Because rudimentary sleep spindles first appear over Cz (vertex) 43-48 weeks CA and often asynchronous, best to display C3-Cz, Cz-C4 help detect early and asynchronous sleep spindles for scoring stage N.
UNM Neonatal/Infant PSG Montage

- EOG, L and R;
- EEG frontal, central, occipital referenced to contralateral mastoid
- Cz-C3, Cz-C4 to recognize asymmetric and midline sleep spindles
- Chin EMG, EKG, R-R interval, L and R Ant. Tib
- Nasal pressure, orothermal sensor, Chest RIP, Abd RIP, SUM Rip, SpO2, pulse waveform, etCO2, capnogram, tcCO2, and video

- Real time observations and detailed documentation of behaviors by the sleep technologist during collection (and focused video).
Often Need to Reduce EOG and Chin EMG Distances When Recording Very Small Infants

- **Gentler electrodes:** use neonatal EKG electrodes made of hydrocolloids for EKG, chin EMG, and EOG.
- **EEG sensitivity:** often need 10-15 $\mu$V/mm;
- **EOG** electrode distance from eyes reduced from 1 to 0.5 cm.
- **Chin EMG** electrodes often need to be reduced from 2 to 1 cm and use 2-3 $\mu$V/mm sensitivity.
- **EKG:**
  - **Modified lead II:** electrodes R and L anterior chest wall;
  - **Alternative lead I:** electrodes R and L arms permits recording EKG + arm movements.
Would a 4-hour Nap Study Suffice?

• 2013 study compared 4-h nap to overnight PSG in 34 infants ≤ 6 months:
  – All had SDB on both studies (AHI 37/h, OAHI 20/h, CAI 7/h);
  – Among infants <2 months no significant difference in diagnostic yield they have REM sleep in day (mean REM latency 25 minutes and %REM sleep in 4 h nap = 37%);

• UNM approach:
  – Prefer night (quieter), often diagnose first 4 hours then try interventions (positioning, O2, CPAP, NP tube, high flow O2).

Kahlke PE et al. Sleep Medicine 2013;14:177-82.
• Demographics of Neonatal/Infant Sleep Studies: **Who** is Being Referred, **Where** and **Why**?
Prevalence of Apnea in Otherwise Healthy Term Infants Rare: 1 in 1,000

- Recent large database analysis of 2.6 million healthy term (>37 weeks GA) newborn discharges in US.
- Isolated apnea diagnosed in 2,034 healthy FT newborns (1 in 1,000).
- Additional 478 FT newborns had apnea + hypoxia and/or bradycardia.

Total prevalence of immature or benign apnea 1/1000 healthy term infants. Apnea in FT infants stayed 1.4 days longer and had $653 greater costs.

**Retrospective Review**  PSG on 104 Infants ≤ 52 weeks CA  Inpatient U of New Mexico 2007-2017

<table>
<thead>
<tr>
<th>Symptom/sign</th>
<th>Percent</th>
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<tbody>
<tr>
<td>Nocturnal desaturation</td>
<td>67%</td>
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<tr>
<td>Persistent hypoxemia worse sleep</td>
<td>35%</td>
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<tr>
<td>Perioral cyanosis</td>
<td>16%</td>
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<tr>
<td>Snoring</td>
<td>10%</td>
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<tr>
<td>Stridor</td>
<td>5%</td>
</tr>
<tr>
<td>Failure-to-thrive</td>
<td>3%</td>
</tr>
<tr>
<td>Apparent Life-threatening event (ALTE)</td>
<td>3%</td>
</tr>
</tbody>
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Wolfe K, Grigg-Damberger M, unpublished data

**Demographics All subjects (n = 104)**

- **Mean Gestational Age at Birth (weeks)**: 37.9 weeks GA
- **Mean Age at first Sleep Study (weeks)**: 2.4 weeks
- **Location of Study**: 2/3 NICU; 1/3 Pediatric ICU

Most infants were 40-47 weeks CA
Symptoms Prompting PSG Order?

- Desaturations were the most common indication for PSG in both infants with and without comorbidities.
- 81% of the 102 infants had one or more comorbidity associated with sleep apnea;
- Feeding problems were a common indicator.
- Snoring was a complaint in only 6% (and these old with mean age 46 weeks CA)
Comorbidities Often Present

- Prader-Willi syndrome
- Chiari 2
- Achondroplasia
- Pierre Robin Sequence
- Congenital myotonic dystrophy type 1
- Neonatal myasthenia
- Central congenital hypoventilation syndrome
- Craniofacial syndromes
HOW TO SCORE INFANTS 0-2 MONTHS USING THE 2018 AASM MANUAL RULES
Sleep and Wakefulness
Scored Infants 0-2 Months

- Wakefulness (W);
- REM Sleep (R);
- NREM Sleep (N);
- Transitional (T) sleep.

AASM Scoring Manual Version 2.5
Important Concepts for Scoring Sleep in Neonates and Young Infants

1. Eyes open best determinant of Wakefulness
2. Sleep onsets more often REM sleep till 2-3 months post-term
3. Regularity or irregularity of respiration single most reliable PSG characteristic when scoring infant PSGs
4. Chin EMG often unreliable as marker for REM sleep
5. Infant behaviors far more important for identifying sleep/wake states than EEG (especially when they are stressed)
5 Steps for Scoring an Infant PSG

- Eyes open?
- Respiration regular or irregular?
- Rapid eye movements?
- Chin tone present or absent?
- EEG trace alternant or continuous?
Regularity/Irregularity of Respiration
Is Single Most **Useful** PSG Characteristic Scoring Infant PSGs

- **Regular respiration** = epoch in which respiratory rate varies < 20 breaths/minute (and characteristic of NREM sleep).

- **Irregular respiration** = respiratory rate > 2 breaths per minute (characteristic of REM sleep and Wakefulness)

Anders et al. thought regularity of respiration usually determined by visual inspection: If more precise measurement needed, measure longest and shortest respiratory cycles in an epoch → extrapolate respiratory rates for each of these in a minute.
Sleep Onsets More Often REM Sleep Until 2-3 Months Post-Term

- Transitions from W to T to R difficult to determine without visual observations made by sleep technologist at bedside;
- By 44-48 weeks CA, more sleep onsets maybe stage N; REM latencies at this age may be < 8 minutes or > 16 minutes.

Chin EMG in Infants Often Unreliable

• Chin EMG:
  – Inappropriately present 20% of REM sleep epochs;
  – Inappropriately absent 15-20% of NREM epochs.

*Figure from Anders T, Emde R, Parmelee A. UCLA Brain Information Service, 1971.
Four Different Infant Sleep EEG Patterns
But Only One Specific To Sleep State

Trace alternant  High Voltage Slow  Mixed  Low Voltage
Let’s Summarize the Sleep Patterns

a) NREM Sleep with continuous HVS EEG, regular respiration, chin EMG tone present, and no eye movements

b) REM Sleep with continuous Mixed EEG, irregular respiration, low chin EMG, and rapid eye movements

c) NREM Sleep with discontinuous TA EEG, regular respiration, chin EMG tone present, and no eye movements

d) REM Sleep with continuous LVI EEG, irregular respiration, low chin EMG and rapid eye movements
- Discontinuous EEG pattern alternating runs of bilaterally symmetrical synchronous 50-150 µV 1-3 Hz delta activity lasting 3-8 seconds which alternate with interburst intervals (IBIs) of 25-50 µV 4-7 Hz theta activity;
- IBIs: duration ↓ and amplitude increases with ↑ CA (5-6 sec 37 weeks CA, 2-4 sec at 40, and 1-2 sec 42 weeks);
- TA first seen 37 weeks CA, disappears by 44 weeks replaced by HVS.
High Voltage Slow (HVS) EEG Pattern
Primarily NREM Sleep, Rarely REM Sleep

- Continuous symmetrical synchronous high voltage (50-150 $\mu$V) 1-3 Hz delta which often has an occipital or central predominance;
- Usually by 44 weeks CA (up to 46 weeks) TA replaced by HVS
Mixed (M) EEG Pattern

Present R after W, Sometimes W, Rarely N

- Continuous irregular synchronous symmetrical low amplitude (<50 µV) 5-7 Hz theta intermixed with occasional >100 µV 2-4 Hz slow waves.
Low Voltage EEG Pattern
Typically Seen after Period of NREM, or in W

- Continuous irregular centrally predominant 25-50 $\mu$V 4-7 Hz activity intermixed with occasional 1-3 Hz delta of similarly low amplitude
Transitional Sleep Common

Seems reasonable for neonates and young infants to exhibit state dissociations where markers of one sleep state intrude into other;
When unsure which sleep state, score T.
Scoring Stage Transitional (T)

- Depending on how strictly stage T is defined, 10-15% or 20-40% of 30-sec epochs of sleep in 0-2 months can be scored as T;
- T sleep contains physiological markers of a different sleep state (discordant).
- T sleep most often occurs in transitions to sleep:
  - Especially W to REM sleep (less of R to N) and following arousals or awakenings.
AASM Criteria for Scoring Stage T

Only 1 PSG characteristic is discordant

Score N, R or W

> 2 PSG Characteristics are discordant

Score T

- 3 NREM + 2 REM or 2 REM + 3 NREM

- Percentage of T sleep ↓ with ↑ infant maturation;
- AASM Goal: improve inter-scorer reliability.
Transitional Sleep (Stage T)

- 30-second epoch showing discontinuous trace alternant EEG, no eye movements and regular heart rate suggestive of stage N, but irregular respiration and body movements suggestive of stage R.
Ready, Set, and Go to Score!
Score Sleep Stages in 30-second Sequential Epochs from Lights Out to Lights On

1) Assign a stage to each epoch (W, T, R, N);
2) If 2 or more stages coexist, assign stage comprising greatest portion of epoch;
3) Score sleep onset as the first epoch of sleep (often REM sleep until 2-3 months post-term);
4) Sleep and wakefulness in infants 38 to 48 weeks CA are scored based on:
   a) Behavioral observations;
   b) Regularity or irregularity of respiration; and
   c) EEG, EOG, and chin EMG pattern.

AASM Scoring Manual Version 2.2
Best Strategy: Score Infant Sleep EEG as Continuous or Discontinuous

• Because trace alternant or sleep spindles only specific patterns for a particular sleep stage (NREM) and HVS, M, LVI continuous and contain more (or less) delta; all too hard;

• AASM Scoring Manual Editorial Board said why not just score EEG as continuous or discontinuous in infants?

Our techs first score Wake based on behavior; then score REM based on irregular respiration and eye movements.
1. **Score epochs as stage W** if either a, b, or c present majority of epoch:
   a. Eyes wide open (for majority of epoch);
   b. Vocalization (whimpering, crying) or actively feeding;
   c. All of the following are met:
      • Eyes are open intermittently;
      • REMs or scanning eye movements;
      • Sustained chin EMG tone with bursts of muscle activity;
      • Irregular respiration;
      • EEG: LVI or M.

Wide open eyes most crucial determinant of W in infant
Notes About Scoring Stage W

Transient eye closures especially when crying.
A 30-second epoch of sleep best scored as Stage W (40 weeks CA). Tech noted eyes open, moving head and crying; EEG = Mixed; REMs+, Chin EMG+, Irreg respiration, + movement and muscle artifact.
Wake/Sleep Transitions in Infants

- Sustained eye closure = best physiological marker of drowsiness in infant this age:
  - AASM scoring rule = if infant’s eyes are closed > 3 minutes, the infant is considered asleep;
- Transition to sleep characterized by:
  - Relative immobility;
  - Absence of focused attention;
  - Intermittent eye closure.

- Sleep onsets are typically REM sleep (often preceded by a few epochs best scored as stage T);
- EEG change: may see increase in amplitude of theta and delta activity especially over frontal regions.
Full-term infant R-N-R sleep cycle begins with REM sleep onset, note “typical” cycle of EEG patterns and sleep states.
Neonatal Sleep Cycling

- Polyphasic sleep cycles last 50-60 minutes interrupted by awakening for feeding and care every 3-4 h;
- With a given REM-NREM-REM sleep cycle, R sleep lasts 10-45 (mean 25) minutes, N 20 minutes and T sleep 10 minutes;
- Stage N after first period of stage R often begins with HVS for 3-5% of cycle, then a longer period of TA for 25%;
- Stage T (10-15% of TST on good day) occur most often at sleep onset, stage shifts especially from R to N and following arousals.
AASM Rule for Scoring Stage R

- Score R sleep in epochs with \( \geq 4 \) including irregular respiration AND rapid eye movements (REMs):
  - a. Low chin EMG (for the majority of the epoch);
  - b. Eyes closed with at least one rapid eye movement (concurrent with low chin tone);
  - c. Irregular respiration;
  - d. Mouthing, sucking, twitches or brief head movements;
  - e. EEG exhibits a continuous pattern without sleep spindles.
Definite Stage R

: Note +REMs, EEG Continuous Mixed; Chin EMG low, Respiration Irregular.
Important Notes Scoring Stage R

- Epoch of **definite** stage R required to begin scoring R;
- Rapid eye movements can be single or occur in clusters;
- Chin EMG unreliable: chin often preserved in R (15% of R epochs);
- Irregular respiration and heart rates especially during phasic REM sleep when REMs more prevalent.

AASM Scoring Manual Version 2.5
REM sleep

- **Audio**: Sighs, sobs
- **Eyes**: closed or slightly opening and closing; May open during REM;
- **Motor**: sporadic, appears in bursts 5-60 s; Muscle tone low between movements;
- **Face**: smiles, grimaces, frowns, bursts of sucking movements, small twitches, sighs and sobs..

AASM Rule for Continuing to Score Stage R

- Continue to score epochs as stage R which follow an epoch of definite R in the absence of rapid eye movements if ALL of the following are present:
  a) EEG continuous LVI or M without sleep spindles or TA
  b) Chin muscle tone low majority of epoch
  c) No intervening arousal.

AASM Scoring Manual Version 2.5
AASM Rule for Scoring Stage N

• Score stage N if ≥ 4 of following present, including regular respiration for majority of epoch:
  1. Eyes closed with no eye movements;
  2. Chin EMG tone present;
  3. Regular respiration (post sigh respiratory pauses may occur);
  4. Trace alternant (TA), High Voltage Slow (HVS) or sleep spindles present;
  5. Reduced movement relative to W.
Stage N

EEG discontinuous TA, no eye Movements, + chin EMG, regular respiration.
High Voltage Slow (HVS) in Stage N

Trace Alternant (TA) in Stage N
Baby Awakens from NREM Sleep

**NREM sleep**

*Audio:* Sighs  
*Eyes:* closed;  
*Motor:* Little or none; startles; continuous tonic levels; low motion;  
*Face:* Episodes of rhythmic mouth movements; sucking;

**Arousals:**
- *Eyes:* open eyes; fixed and focused;  
- *Motor:* head and hand movements; motion shows different intensity.

**Wakefulness**

*Audio:* crying, fussing;  
*Eyes:* open, focused, no rapid eye movements, scanning;  
*Motor:* head and arm movements; orientation response; motor tone high or low;  
*Face:* no smile or frown; in quiet wake, relaxed.  

CAVEAT: Do not mistake for SZs: sucking and puckering mouth movements and/or dysconjugate eye movements common in newborns when awake.
Notes About Scoring **Stage N**

- Regularity of respiration most reliable PSG characteristic for scoring stage N in infants this age;
- Chin EMG is variable in stage N, generally lower than W and higher than in R;
  - Chin EMG tone preserved 80 to 85% of epochs of N sleep; its presence useful, its absence not;
  - Stage N can still be scored with low EMG tone if at least four other criteria for stage N including regular respiration are met.
Sleep Spindles Suggest Stage N

- Appear as early 3-9 weeks post-term in both infants born preterm and term;
- First appear over midline central (Cz, vertex) and shift from side to side (C3, C4);
- 3 longitudinal studies using EEG, PSG and MEG confirm sleep spindles are usually present by 2 months post-term.

Stage N  HVS + Sleep Spindles (47 Weeks CA)

Sleep spindles first appear over Cz, often shift from side to side (C3 to C4)
Infants This Age **Arousals** Can Cause EEG Flattening (Decrements)

- If EEG background is HSV then stimulus provokes abrupt attenuation lasting 10 s;
- If LVI with prominent theta, then stimulus often elicits generalized delta activity lasting up to 15 seconds;
- Isolated generalized myoclonic jerks can be seen as an infant wakes from sleep, not to be mistaken for seizures.
Sleep in Infants 41 to 45 Weeks CA

41-44 weeks CA

- Low voltage mixed frequency EEG seen in W and R;
- Delta brushes gradually disappear by 44 weeks CA;
- On occasion in W, broad biphasic lambda waves in occipital regions bilaterally coincident with visual fixation;
- IBIs brief (typically 2-4 sec) and IBI amplitudes >50 μV; by 44 weeks IBIs have “filled in”, trace alternant replaced by CSWS.

45 + weeks CA

- First appearance of sleep spindles in NREM sleep;
- When first seen, 12-14 Hz over midline (Cz) spreading to left or right (C3 or C4) regions;
- Not well synchronized at his age.
- R sleep onsets until 3 months term;
- Dominant posterior rhythm (3-4 Hz) first seen 3 months.
- 43-48 weeks CA sleep cycles average 60 minutes; ~50% NREM, 50% REM;
- By 44-48 weeks more sleep onsets are NREM (REM latencies <8 or >16 min);
- All neonatal EEG patterns gone by 52 weeks.
NIGHTMARE: SCORING RESPIRATORY EVENTS 0-2 MONTHS
Reality Test: Guidelines Needed for Abnormal Respiratory Events and AHI in Infants

- Limited evidence and no consensus for pathological apnea in preterm and term infants;
- 2 respiratory pauses in infants = 3 s in neonates; 5 s in infants 5 to 6 months old;
- Others report need bradycardia (>10%, <100 bpm) or desaturation (<85%) needed to score as abnormal;
- Short central apneas (2-10 sec) probably normal at all ages;
- Longer respiratory pauses → more likely to cause decreases in SpO2, lung volume, HR, changes in blood flow to brain, skin, gut.

How abnormal a neonatal PSG who cares?
- Surgical therapies recommended based on how severity of OSA;
- History of apnea of prematurity associated with decreased arousal from sleep first few months of life.
What Do We Know About Respiratory Events and Breathing During Sleep in Infants < 2 Months?

- Healthy newborns and infants < 2-3 months old have more apneas than older children (most of these are central apnea);
- Majority central apneas (CA) usually last ≥ 3 and < 10 sec;
  - Most CA seen in stage R, after a sigh breath or a body movement, and transition W to sleep;
  - CA >20 sec are rare (especially pathologic if bradycardia and/or desaturation < 80%);
  - Upper range CAI 1-month-old 45/h; 30/h for 2-month-olds?
- Obstructive and mixed apneas rare in normal infants:
  - Apneas lasting > 10 sec usually mixed apneas;
  - Upper range for OAI and MAI < 1.0/h of sleep.

Normative PSG Respiratory Data Quite Different in Infants 0-2 Months

- Respiratory rates during sleep age 1 month median 40/min (range 33-54); 2-12 months 29 (range 22-43).
- Respiratory rates of 40-50 breaths/min in sleeping neonates may be normal in absence of other signs;
  - Young infants have many brief desaturations with lower limit of normal for desaturations <80% are 15/h for day 1, 41/h for day 4, and 15/h day 39 following birth;
  - 48% of desaturation events were associated with concomitant apnea day 1, increasing to 94% at age 6 months.

Pathological Apnea in Term Infant?

- Pathological apnea = cessation of respiratory effort or airflow for 20 s or shorter when accompanied by bradycardia or hypoxemia;
- Not evidence-based and lacks parameters for degree of bradycardia or hypoxemia to make it clinically significant.
- CHIME study arbitrarily defined extreme apnea an event lasting > 30 sec;
- Mixed apnea (central apnea followed by airway obstruction) most frequent type of longer apnea in PT infants.
- Apnea of prematurity usually resolves spontaneously by 40-44 weeks PMA.

CHALLENGE: NO Accepted Criteria How Many Apneas and Hypopneas Are Abnormal in Infants, 0-2 Months

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<th>OSA Severity Criteria Children?</th>
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<tr>
<td>Probably &gt; 2 obstructive apneas and hypopneas per h of sleep abnormal in children &gt; 2 years old;</td>
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<tr>
<td>Severity grading for OSA in children &gt; 1-2 years and adolescents is:</td>
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<tr>
<td>▪ Mild: 2 to &lt;5/h</td>
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<tr>
<td>▪ Moderate: 5 to &lt;9/h;</td>
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<td>▪ Severe: ≥10/h;</td>
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<td>▪ Very Severe: &gt;20-24/h;</td>
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<td>▪ How many severe in REM? 20, 30, 40, 50/h?</td>
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<thead>
<tr>
<th>Apnea Severity Criteria Infants?</th>
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<tr>
<td>Many more central apneas in healthy infants &lt; 2-3 months than in older children:</td>
</tr>
<tr>
<td>✓ Mean Central Apnea Index (mean number of central apneas per hour of sleep): abnormal &gt; 45/h 1-month-old and &gt;30/h 2-months old.</td>
</tr>
<tr>
<td>▪ Obstructive and mixed apneas rare in normal infants:</td>
</tr>
<tr>
<td>✓ Apneas lasting &gt; 10 sec usually mixed apneas;</td>
</tr>
<tr>
<td>✓ Upper range for OAI and MAI &lt; 1.0/h of sleep.</td>
</tr>
</tbody>
</table>

Their Sleep Apnea Often Severe

- PAOHI 76/h; CAI: 42/h
- MAI: 10/h
- Baseline SpO2 Sleep 85-89%; nadir SpO2 57% with a 10-sec OH;
- tcCO2 55 Torr;
- Trials of placing nasopharyngeal tube, prone or lateral position, with or without O2 did not improve SDB.

- 24-day-old now 42 weeks CA infant with Pierre Robin Sequence, mandibular micro- and retrognathia, U-shaped cleft palate, bifid anterior tongue and tight lingual frenulum
Obstructive Apneas Last 5.7 to 8.4 Sec Cause Desats from 87% to 67%

42 weeks CA, 24-day-old female infant with Pierre Robin Sequence on ½ L supplemental oxygen went on to have mandibular distraction.
Same Infant, Age 8 Months After Mandibular Distraction and Cleft Palate Repair

- Obstructive sleep disordered breathing now only mild (PAOHI) 4.8/h of sleep, worse in REM sleep (21/h REM sleep vs. 4/h NREM sleep); SpO2 < 88% 1 min.
Studies Show OA and MA Very Rare in Healthy Infants (<1/h TST)

Level 3 PSG Recorded at Home in 37 Healthy Term Infants at 1-Month-Old

Frequency of Obstructive Apneas According to Age (N = 1023 Healthy Infants)

- Found marked fall in AHI, CAI and OMAHI when cardiorespiratory PSG repeated at age 3 months.

- Mean OAI 0.3/h with mean duration 5.5 (3-13 sec);
- Mean MAI 0.1/h with mean duration 8 (3.5-15 sec);
- Frequency of OA and MA decreased markedly after 8 weeks post-term.

Central Apnea (CA) Very Frequent First 6 Months of Life: Typically Last > 3 to < 10 sec

- Highest CAI (at sea level) in first 5 weeks of life (median CAI 8/h sleep); CAI 6-12 months median 6.4/h in REM and 1.7/h in NREM. Frequency CA declines after first year of life.

Longest Apneas Often Mixed Type

42 weeks CA
Runs of Periodic Breathing (PB) Common in Infants < 3 Months But Typically Less than 5% of the TST

PB often 1-2% of sleep time, Brockmann et al. proposed cutoffs for normal of <9% TST age 1 month, <4% age 3 months.
Nasal CPAP or High Flow NC Feasible in Hospitalized Infants But No Way Home

• But if an infant for some reason needs PAP therapy to go home, not FDA approved;
• Worse yet, can you guarantee it will do what it is supposed to do what it is suppose do and be used as it “right” at home?
• Reality in NM: no way home.
LIMITED NORMATIVE DATA FOR SLEEP ARCHITECTURE AND APNEA
# Level 3 Home PSG
in 37 Healthy Term Infants at 1-Month-Old

<table>
<thead>
<tr>
<th>Indices (n/h)</th>
<th>Median</th>
<th>95&lt;sup&gt;th&lt;/sup&gt; Centile</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central Apnea Index (CAI per TST)</td>
<td>4.1</td>
<td>24.2</td>
</tr>
<tr>
<td>Obstructive Apnea Index (OAI)</td>
<td>0.8</td>
<td>2.2</td>
</tr>
<tr>
<td>Mixed Apnea Index (MAI)</td>
<td>0.1</td>
<td>0.7</td>
</tr>
<tr>
<td>Hypopnea Index (HI)</td>
<td>0</td>
<td>0.7</td>
</tr>
<tr>
<td>Central apnea after sighs index</td>
<td>0.9</td>
<td>4.0</td>
</tr>
<tr>
<td>Apnea-Hypopnea Index (AHI)</td>
<td>4.1</td>
<td>26.4</td>
</tr>
<tr>
<td>Pediatric Obstructive Mixed AHI (POMAHI)</td>
<td>0.9</td>
<td>3.4</td>
</tr>
<tr>
<td>Periodic Breathing (PB) % of TST</td>
<td>1.1%</td>
<td>8.9%</td>
</tr>
</tbody>
</table>

Infants Age 1 Month Had Much Higher AHI, C-AHI, O-AHI, and % TST Periodic Breathing Than When Older

<table>
<thead>
<tr>
<th></th>
<th>Group 1  (n =106)</th>
<th>Group 2  (n = 89)</th>
<th>Group 3  (n = 61)</th>
<th>Group 4  (n = 25)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age</td>
<td>1.0 ± 0.3 mo</td>
<td>3.6 ± 0.5 mo</td>
<td>6.6 ± 0.6</td>
<td>13.2 ± 1.9</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>AHI (/h TST)</td>
<td>21</td>
<td>12</td>
<td>7.4</td>
<td>3.1</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Central AHI (/h TST)</td>
<td>12.4</td>
<td>8.3</td>
<td>5.5</td>
<td>2.3</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Obstructive AHI (/h TST)</td>
<td>6.8</td>
<td>3.5</td>
<td>0.9</td>
<td>0.5</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Periodic breathing (% TST)</td>
<td>2 (0-22)</td>
<td>0.9 (0-16)</td>
<td>0.2 (0-3)</td>
<td>0 (0-5.5)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>AH duration (sec, range)</td>
<td>6.1 (4.8-7.2)</td>
<td>6.0 (5.0-7.4)</td>
<td>6.2 (4.8-8.8)</td>
<td>6.8 (5.3-8.4)</td>
<td>NS</td>
</tr>
</tbody>
</table>

HIGH ALTITUDE DATA

### Level 2 Home PSG in 84 Healthy 44-48 Weeks CA Infants

<table>
<thead>
<tr>
<th>PSG Value (norm)</th>
<th>Mean ± 2 SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Time in Bed (TIB)</td>
<td>719 ± 82 minutes</td>
</tr>
<tr>
<td>Total Sleep Time (TST)</td>
<td>477 ± 59 minutes</td>
</tr>
<tr>
<td>Stage R</td>
<td>37 ± 7%</td>
</tr>
<tr>
<td>Stage N</td>
<td>42 ± 5%</td>
</tr>
<tr>
<td>Stage T</td>
<td>22 ± 6%</td>
</tr>
<tr>
<td>Awakening Index</td>
<td>8.5 + 2.1/h</td>
</tr>
<tr>
<td>Arousal Index</td>
<td>19.3 + 3.7/h</td>
</tr>
<tr>
<td>Mean Apnea-hypopnea Index (AHI)</td>
<td>13.7 + 14.1/h;</td>
</tr>
<tr>
<td>Obstructive apnea hypopnea index (OAHI)</td>
<td>OAHI 0.0 + 0.0/h</td>
</tr>
<tr>
<td>3% Oxygen desaturation index (ODI)</td>
<td>20.9 + 16.9/h</td>
</tr>
</tbody>
</table>


How Sleep Architecture and Arousals Change with Age from 1 to 13 Months

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (n = 106)</th>
<th>Group 2 (n = 89)</th>
<th>Group 3 (n = 61)</th>
<th>Group 4 (n = 25)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age</td>
<td>1 mo</td>
<td>3.6 mo</td>
<td>6.6 mo</td>
<td>13 months</td>
</tr>
<tr>
<td>Sleep Efficiency</td>
<td>80%</td>
<td>88%</td>
<td>89%</td>
<td>84%</td>
</tr>
<tr>
<td>Percent TST spent in R Sleep</td>
<td>53%</td>
<td>50%</td>
<td>27%</td>
<td>24%</td>
</tr>
<tr>
<td>Percent TST in N Sleep</td>
<td>46%</td>
<td>50%</td>
<td>73%</td>
<td>76%</td>
</tr>
<tr>
<td>Arousal Index</td>
<td>19</td>
<td>15</td>
<td>11</td>
<td>10</td>
</tr>
<tr>
<td>Resp Ar Index</td>
<td>1.6</td>
<td>1.2</td>
<td>0.6</td>
<td>0.1</td>
</tr>
</tbody>
</table>

Note how percentage of time in NREM sleep increases from 46% at 1-month-old to 76% at 12 months; Arousal index especially respiratory arousal indexes fall in the same period.

What We Still Need to Know…

- Effects of poor sleep, sleep disordered breathing, hypoxia and/or hypercarbia on neurodevelopmental outcomes in infants born premature (especially those spending days or months in NICU);
- Normative respiratory data infants 0-2 months;
- Long-term effects of treatments for apnea of prematurity and hypoxemia in premature infants.
- Optimizing sleep in preterm infants in neonatal ICU.
Thanks for Your Attention
Hope Not Too Much Information for You.
OTHER REFERENCES


