



Saturday, August 3, 2019

Breakout Session B8 • 1:30-2:30pm • Grand Ballroom C

Sleep in Children with CHARGE Syndrome

Susan Wiley, MD, Cincinnati Children's Hospital Medical Center
Christine Heubi, MD, Cincinnati Children's Hospital Medical Center

Presenter Information

Susan Wiley is a developmental-behavioral pediatrician with clinical and research interests in children who are Deaf/Hard of Hearing with complex developmental and medical needs. She is the co-director of the CHARGE clinic at Cincinnati Children's Hospital Medical Center. She is a member of the cochlear implant team and has worked with the Ohio Center for DeafBlind Education and American Academy of Pediatrics on topics related to children who are Deaf/HH and Deaf/HH Plus.

Christine Heubi is a pediatric ear, nose, and throat physician with board certification in sleep medicine and otolaryngology. She takes care of children with upper airway obstruction, tracheostomy tube dependence, obstructive sleep apnea, insomnia, and circadian rhythm disorders. Her research is focused on sleep disorders in special populations, including children with CHARGE syndrome. She works in collaboration with Dr. Susan Wiley, co-chairperson of the CHARGE clinic at Cincinnati Children's Hospital, to improve the quality of life in children with CHARGE syndrome. Most recently, she and Dr. Wiley presented at the annual CHARGE meeting held in Cincinnati in July, 2018 for both professionals and parents.

Presentation Abstract

Sleep problems in CHARGE syndrome are estimated to occur in 59% of patients, and can be related to anxiety and behavioral concerns. Caregiver well-being has been found to suffer in children with CHARGE syndrome and sleep problems. Recommendations need to be made once identification of the underlying issues is determined. Sleep issues in children with CHARGE will be discussed including: (1) medical issues (night time feedings or treatments, obstructive sleep apnea, circadian rhythm disorder, pain), (2) visual impairment, (3) hearing loss, (4) environmental factors. Successful behavioral and environmental interventions will be described, as well as when further medical evaluation and treatment is needed. The use of light therapy and supplementation with melatonin will be reviewed as it applies to clinical improvement in certain patients. Attention will also be given to the evaluation and management of sleep disordered breathing and upper airway obstruction. Case presentations will be used as examples for the work-up and management of children with CHARGE who have sleep problems.

Learning Objectives

- Identify sleep problems in children with CHARGE syndrome.
- Describe the work-up and management of sleep disorders in children with CHARGE syndrome.
- Discuss special considerations in this population including the impact of visual impairment, circadian rhythm disorders, and sleep disordered breathing.

Sleep in Children with CHARGE syndrome

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Pediatric Otolaryngologist
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August 2019



Overview

- Background
- General sleep hygiene
- Focused topics in sleep
 - Chronobiology
 - Role of sleep study
 - Insomnia



What do we know?

- Most behavioral sleep information is within the general population
- There are some studies of sleep difficulties in specific developmental disabilities, children with vision impairment, and specific syndromes
- Medical Publication query of CHARGE syndrome and sleep
 - 4 articles, two on OSA, two broader studies, both from Dr. Hartshorne's group



Sleep problems in CHARGE syndrome using Self- and Parent Report Measures

- 53 individuals with CHARGE 13 and older, recruited from Perkins and International CHARGE Syndrome Conference
 - Sleep apnea in 25%
 - **59% with sleep difficulties**
 - Sleep problems were correlated with anxiety, self-injury, "conduct" and autistic features

Hartshorne N, Hudson A, MacCuspie J, Kennert B, Nacarato T, Hartshorne T, Blake K. Quality of Life in Adolescents and Adults with CHARGE Syndrome Am J Med Genet Part A 170A:2012–2021.



Impact of sleep problems in children and families with CHARGE syndrome

- Via CHARGE Foundation participation, surveys mailed to 102 parents of children with CHARGE, 6-18 years.
- 89/102 returned surveys (exceptional return rate)
 - Malaise inventory (mother's mental well-being)
 - The Developmental Behavior Checklist (behavior problems in individuals with intellectual disabilities)
 - The Sleep Disturbance Scale for Children (categorizes type of sleep problem)

Hartshorne T, Heussler H, Dallor AN, Williams GL, Papadopoulos D, Brandt K. Sleep disturbances in CHARGE syndrome: types and relationships with behavior and caregiver well-being Developmental Medicine & Child Neurology 2009; 51: 143–150.



Impact of sleep problems in children and families with CHARGE syndrome

- 57.5% had a high score (above cut-off) on sleep measure
- Highest sleep problems were in the categories of:
 - Initiating and maintaining sleep
 - Sleep disordered breathing (snoring, OSA)
 - Sleep-wake transition
- Higher scores among those with more significant vision impairment and hearing loss
- Not particularly elevated in
 - Disorders of arousal
 - Excessive somnolence
 - Sleep hyperhydrosis

Hartshorne T, Heussler H, Dallor AN, Williams GL, Papadopoulos D, Brandt K. Sleep disturbances in CHARGE syndrome: types and relationships with behavior and caregiver well-being Developmental Medicine & Child Neurology 2009; 51: 143–150.



Sleep problems

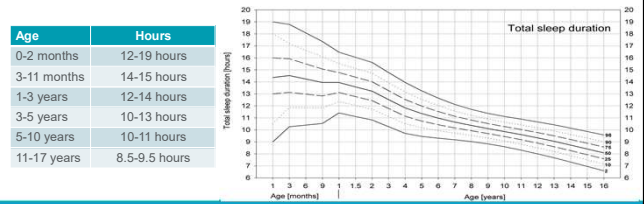
- For children with difficulties initiating and maintaining sleep, this was associated with (not necessarily causal, but related to each other) Parent Well-being
- Behaviors associated with sleep problems
 - Self-absorbed behaviors
 - Disruptive behaviors
 - Trends seen in anxiety and social difficulties

Hartshorne T, Heussler H, Dallor AN, Williams GL, Papadopoulos D, Brandt K. Sleep disturbances in CHARGE syndrome: types and relationships with behavior and caregiver well-being *Developmental Medicine & Child Neurology* 2009, 51: 143-150.



How much sleep do TD children need?

- Age-dependent and to some degree individually variable



Iglowstein et al., 2003, p. 304



Sleep hygiene

- Sleep hygiene is not about cleanliness, but health habits that promote good sleep

SLEEP HYGIENE
If you are having trouble sleeping, this is a list of things you should try to improve your sleep hygiene and the quality of your sleep.

- Stick to a sleep schedule always even on weekends.
- Exercise is great, but not too late in the day.
- Avoid caffeine and nicotine.
- Avoid alcoholic drinks before bed.
- Avoid large meals and beverages late at night before going to bed.
- Don't take naps after 3 p.m. Keep power naps less than 1 hour.
- Relax before bed.
- Take a hot bath before bed.
- Have a good sleeping environment. Get rid of anything in your bedroom that might distract you from sleep.
- Have the right sunlight exposure.
- Don't lie in bed awake. If you find yourself still awake after staying in bed for more than 20min, get up and do a relaxing activity until you feel sleepy.
- Adopt Good Sleeping Postures.
- See a doctor if you continue to have trouble sleeping.



Good Sleep Habits



- Timing
 - A bedtime when the child is not tired doesn't tend to get a child to fall asleep sooner (bedtime vs time that a child fell asleep), consistent schedule
- Environment
 - Where the child falls asleep, lighting, temperature
- Bedtime routine
 - Keep it relatively short (30 minutes)
 - Includes calming activities rather than stimulating activities to allow transition to fall asleep



Sleep Associations

- What is happening at time of sleep onset
- Very important in younger children
- Parent/adult presence/co-sleeping?
- Environmental (door open/closed; lighting)
- Feeding
- Rocking



Slide content from Kelly Byars, PhD



What about for children with CHARGE Syndrome?

- In CHARGE syndrome, there can be numerous factors which impact sleep:
 - Medical Issues (Night-time feedings, night-time treatments, Obstructive Sleep Apnea, poorly managed pain)
 - Vision Impairment (which can impact melatonin production)
 - Hearing Loss (with lights out, may lose comfortable level of environmental awareness)
 - Environmental Factors (alarms, night-time nursing)



Modifiable factors

- Medical Issues
 - Ask hospital providers to respect night-time routine, when possible keep lights out/dim at night
- Vision Impairment
 - Night-light, consider melatonin if VI significantly impacting light perception
- Hearing Loss
 - Take off amplification after asleep, night-light
- Environmental Factors
 - Maintain day and night cues
 - Train night nurses about bedtime routine and strategies to minimize sleep disruption



What do we know?

Things that can impact sleep that aren't related to CHARGE

- **Trouble falling asleep** (taking a long time to fall asleep, difficulties with self-soothing, state regulation)
 - Does your child have a way to self-sooth or regulate their state?
 - Is it too early?
 - Building a sleep routine
- Not wanting to go to bed (**refusal, resistance**, I want to stay up with everyone else)
 - Is it too early?
 - Behavioral approach to incentive going to bed on time, getting up less frequently
 - Rewards for staying in bed (one extra book at night, small reward)
- Night-time worries
 - Consider communication level, specific fear (dark, use a night light), develop social stories, books (or use monster spray)



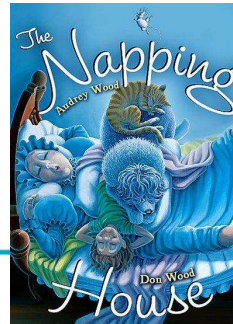
What do we know?

Things that can impact sleep that aren't related to CHARGE

- **Sleep association** (I need something specific to fall asleep and when I rouse a bit at night, I need that same thing to fall back asleep)
 - Sleep hygiene and bedtime routines, helping child learn how to fall asleep on their own
- **Waking up** at night and having a hard time falling back asleep or wanting to stay up for a while to play (as if I just had a nap rather than being bedtime)
 - Sleep association can contribute to this problem
- **Night mares** (child remembers them)
 - Reassurance, dream-catcher, talking through the dream
- **Night-terrors** (appear awake and screaming, often at same time each night, has no memory of the event the next day)
 - Child doesn't remember these, usually occur around the same time each night, can try waking up an hour before they occur to disrupt the sleep cycle



So what's the big deal with Sleep



- If your child is not sleeping, you are probably not sleeping either
- And if there are other kids in the house, it's likely that they are not sleeping



Focused Topics in Sleep

- Importance of sleep history
- Circadian rhythm disorders
- Visual impairment and sleep
- Sources of sleep disruption
- Other considerations
 - Medications for insomnia



Sleep History

- Bed time and wake time
 - Ask about routine to determine sleep hygiene
 - Use of electronics and/or stimulating behaviors
- Daytime sleepiness and napping
 - School performance
 - Mood
- Sleep environment
 - Medical equipment
 - Darkness level
- Sleep disordered breathing
 - Snoring, choking/gasping, snorting, apnea, pauses
- Restless sleep
 - Daytime symptoms of achy legs
- Parasomnias (sleep talking, walking, sleep behaviors)
 - Important in consideration of sleep medications



Chronobiology

- Sleep logs for 2 weeks
 - Total sleep time
 - Sleep acquisition
 - Identify sleep phase disorder
 - Delayed sleep phase disorder
 - Free running circadian disorder
 - Autonomic dysregulation
- Actigraphy can also be employed

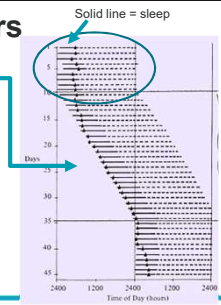
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<http://yoursleep.aasmnet.org/pdf/sleepdiary.pdf>



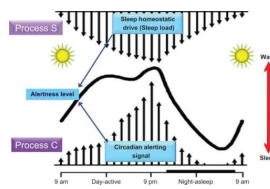
Circadian rhythm disorders

- Free running circadian disorder
- Delayed sleep phase disorder
 - Later bed time
 - Normal propensity as adolescent
 - Can be managed with light and melatonin
- Time spent in ICU/hospital
- Autonomic dysregulation



Impact of Visual Impairment on Sleep

- Sleep mediated by
 - Process S: DRIVE for sleep
 - Process C: Circadian rhythm "clock"
 - Modulated in part by light
 - Light suppresses melatonin
- Blind individuals report more sleep disturbances than sighted individuals
 - Lack of entrainment by light
 - Abnormal timing of melatonin release
 - Greater incidence of a free-running circadian rhythm



Light exposure

- Newer evidence that some blind individuals retain cells for photic circadian entrainment
 - 16 visually blind individuals exposed to bright light and melatonin measured for suppression
 - 50% were responsive to light
- **Why is this important?**
 - Important not to disregard sleep hygiene instructions in regard to light exposure
 - Black out shades in bedrooms
 - Early morning light exposure for 30 minutes
 - Natural light preferred
 - In some case, light boxes are helpful
 - Discontinue device and TV at least 1 hour before bedtime (blue light)
 - Keep electronics out of bedroom

Hull JT, Czeisler CA, Lockley SW. Suppression of melatonin secretion in totally visually blind people by ocular exposure to white light. *Ophthalmology*. 2018 Epub ahead of print.



Other Sources of Sleep Disruption

- OSA
- Central sleep apnea
- Non-apneic hypoxemia
- Hypoventilation
- Periodic limb movements of sleep (PLMs)



Obstructive Sleep Apnea (OSA) in Children

- Seen in 1-3% of the population
- Episodes of partial or complete airway obstruction during sleep
 - Can be associated with decrease in oxygen saturation (hypoxemia) and/or arousal
 - Also can see carbon dioxide retention (hypoventilation)
- Risks factors: enlarged tonsils and adenoids, obesity, **craniofacial anomalies**, neuromuscular disorders



OSA in Children

- Muscle relaxation during sleep leads to narrowing and collapse



Why do we worry about OSA?

- Sleep disruption
 - Worsen or exacerbate behavioral problems during the day
- Increased cardiovascular disease, systemic hypertension, and pulmonary hypertension
- Associated with higher rate of diabetes, abnormal glucose metabolism



Sleep Disordered Breathing and CHARGE

- 1 year old with CHARGE syndrome
 - Frequent nighttime awakenings, did not sleep longer than 3 hours
 - Snoring
 - Stopped breathing during sleep
 - Mouth breathing by day
 - Daytime somnolence
 - Behavioral concerns
- Sleep study at 18 mos showed obstructive sleep apnea (OSA)
 - Treated with continuous positive airway pressure (CPAP), but did not tolerate
 - Tracheostomy was discussed
 - Adenotonsillectomy (T&A) performed with resolution of symptoms
 - Behavioral concerns persisted

Trider CL, Blake K. Obstructive sleep apnea in a patient with CHARGE syndrome. Case Reports in Otolaryngology 2012.



OSA and CHARGE Syndrome

1. Adolescent and adult issues in CHARGE syndrome
 - 45 minute interview of both parents and/or individual with CHARGE syndrome (30 patients)
 - Sleep apnea reported in 13 (43%)
2. Understanding OSA in children with CHARGE syndrome
 - Questionnaires given to parents of 51 children
 - Previous diagnosis of OSA in 65%

1. Blake KD, Salem-Hartshorne N, Daoud MA, Gradstein J. Adolescent and adult issues in CHARGE syndrome. Clinical Pediatrics 2005; 44:151-159.
2. Trider CL, Corsten G, Morrison D, Helfner M, Davenport S, Blake K. Understanding obstructive sleep apnea in children with CHARGE syndrome. Int J Ped Otorhinolaryng 2012; 76:947-953.



Is this overlooked in CHARGE syndrome?

- Sleep medicine is a relatively new field
- Not a concern for children with a tracheostomy in place
- Many parents may feel this is just how their child sleeps
- May be dealing with many medical problems, sometimes life threatening, that are dealt with first
- Many **health consequences of OSA** are seen in children with CHARGE syndrome
 - Behavioral problems, failure to thrive, cardiac problems



Screening for OSA

- Following symptoms merit referral to ENT or sleep for sleep study
 - Snoring > 3nights per week
 - Apnea
 - Snorting/gasping and/or choking during sleep
 - Unusual sleep positions
 - Restless sleep
 - Daytime somnolence
 - Napping
 - Easily falls asleep in car, when TV on
 - Mood in morning



Diagnosis of OSA

- Gold standard for diagnosis is overnight polysomnography (PSG) = **SLEEP STUDY**
- Pediatric sleep lab preferred
- 2nd respiratory therapist to assist with hook-up
- HST is not recommended for children
- Home oximetry is not reliable

Also important in evaluation for decannulation (downsize to 2.5/3.0 capping study).



Obstructive Index

- oAHI: Average number of apneas and hypopneas per hour
 - APNEA: complete obstruction
 - HYPOPNEA: partial obstruction
- AHI takes into account CSA

| | Pediatric | Adult |
|--------------|-----------|-------|
| Normal | <1 | <5 |
| Mild OSA | 1-5 | 5-15 |
| Moderate OSA | 5-10 | 15-30 |
| Severe OSA | >10 | >30 |



Special Considerations in CHARGE Syndrome

- Non-apneic hypoxemia
 - Increased time with O2 saturation level less than 92%
 - Not associated with respiratory events
 - May be associated with cardiac disease
- Low oxygen desaturations can be seen in patient with aspiration
 - Also in chronic lung disease



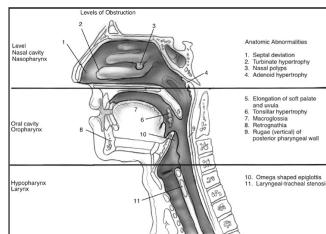
Treatment of OSA

- AAP clinical guideline: Adenotonsillectomy is recommended as the first line treatment of patients with adenotonsillar hypertrophy.
- Mild OSA managed medically with Flonase and Singulair
- Continuous Positive Airway Pressure (CPAP)
 - Need full cooperation of parents
 - May need to try multiple masks
 - Work on desensitization
- Supplemental O2 can be used, typically only in infants
- Tracheostomy in rare, severe cases
- Repeat sleep study needed with any intervention

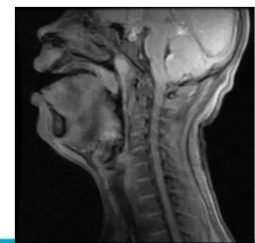
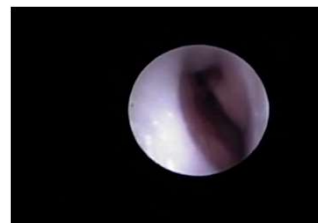


Persistent OSA after Adenotonsillectomy

- Nasal
- Nasopharyngeal
- Retropalatal
- Retroglossal
- Hypopharyngeal
- Supraglottis/laryngeal



Evaluate for Site of Obstruction



DISE: Drug Induced Sleep Endoscopy



Periodic Limb Movements of Sleep (PLMs)

- Treatment indicated if index >5 per hour with history of restless sleep
 - Some night to night variability
- Check CBC, ferritin
 - If ferritin <50, start iron supplementation
 - Re-check labs in 3-4 months
- Other medical treatment options can also be considered

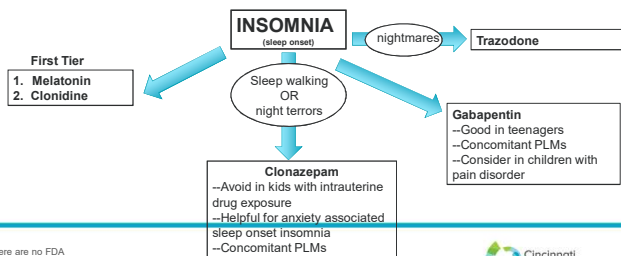


Other Considerations

- Caregiver well-being
- Comprehensive evaluation is often needed
 - Value of developmental pediatrician, sleep provider, and sleep psychologist
 - Evaluate and treat for any “treatable conditions”
 - Role of pain management
 - Behavioral and medical management of insomnia



Some Sleep Medications to Consider

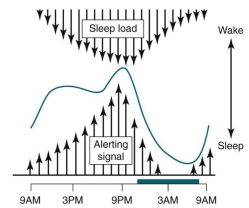


There are no FDA approved medications for insomnia in children.



Why not Diphenhydramine?

- Children sometimes have paradoxical hyperactivity and lack of sleep when given diphenhydramine
- Often due to incorrect timing of administration
- Circadian surge of alertness or “second wind” occurs in evening
 - If medication given at that time, children become disinhibited and hyper, remain awake
- Tolerance is very common
- Long term cognitive issues (increased risk of dementia)



Insomnia. In: Berry R, ed. *Fundamentals of Sleep Medicine*. 2012.



Additional Medications

- Mirtazapine—anti-depressant
- Suvorexant—orexin receptor antagonist
- Zolpidem—non-benzo, benzo receptor agonist



Medications with common side effect of impacting sleep

| Promotes wakefulness | Promotes sleep/somnolence |
|----------------------|---------------------------|
| Albuterol nebs | Alpha agonists |
| Stimulants | Anticonvulsants |
| Diphenhydramine* | Psychotropic medications |
| Beta Blockers | |



Summary

- Sleep issues are common in patients with CHARGE
- Role of sleep specialist, developmental pediatrician, and sleep psychologist
 - Importance of sleep diary
 - Optimize sleep hygiene
 - Consider chronobiology and light exposure
- Treat OSA, PLMs, and pain
- Determine role of medications for insomnia



Thank you to the families who have helped guide our understanding and improve our ability to give care

Questions:
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