

# SLEEP DISORDERS IN SMITH-LEMLI-OPITZ SYNDROME

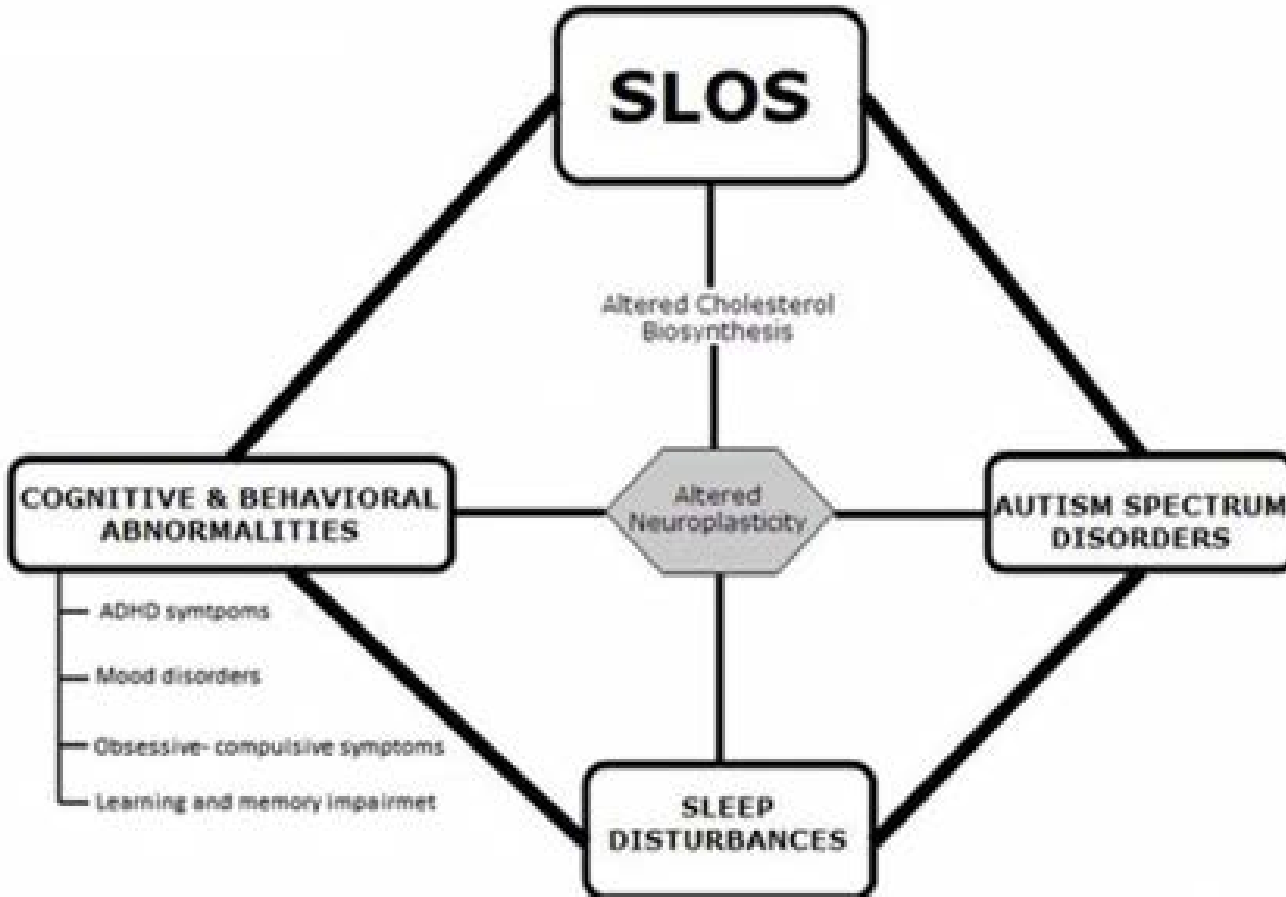
## Diagnosis and Treatment

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# OVERVIEW

- Etiology
- Prevalence
- Insomnia
- Sleep Apnea
- Restless Legs Syndrome/Periodic Limb Movement Disorder

# ETIOLOGY OF SLEEP PROBLEMS



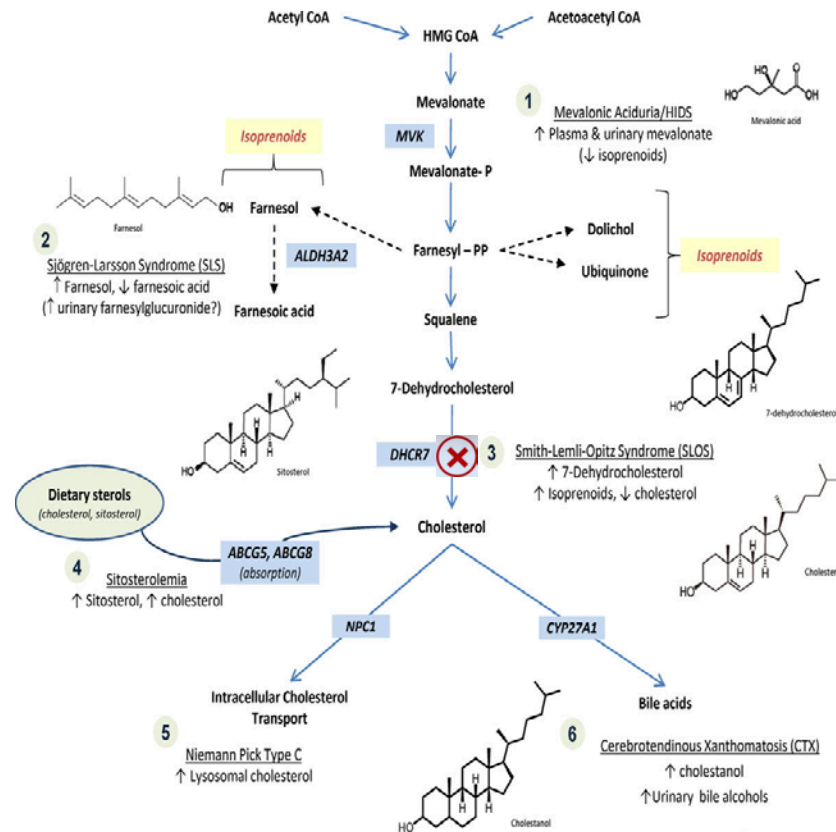
(Diaz-Stransky & Tierney, 2012)

# ALTERED CHEMICAL BIOSYNTHESIS

○ SLOS is characterized by deficiency of 7-dehydrocholesterol reductase

○ Cholesterol synthesis disruption

- Increased 7-dehydrocholesterol
- Increased isoprenoids
- Decreased cholesterol



(Svoboda et al, 2012)

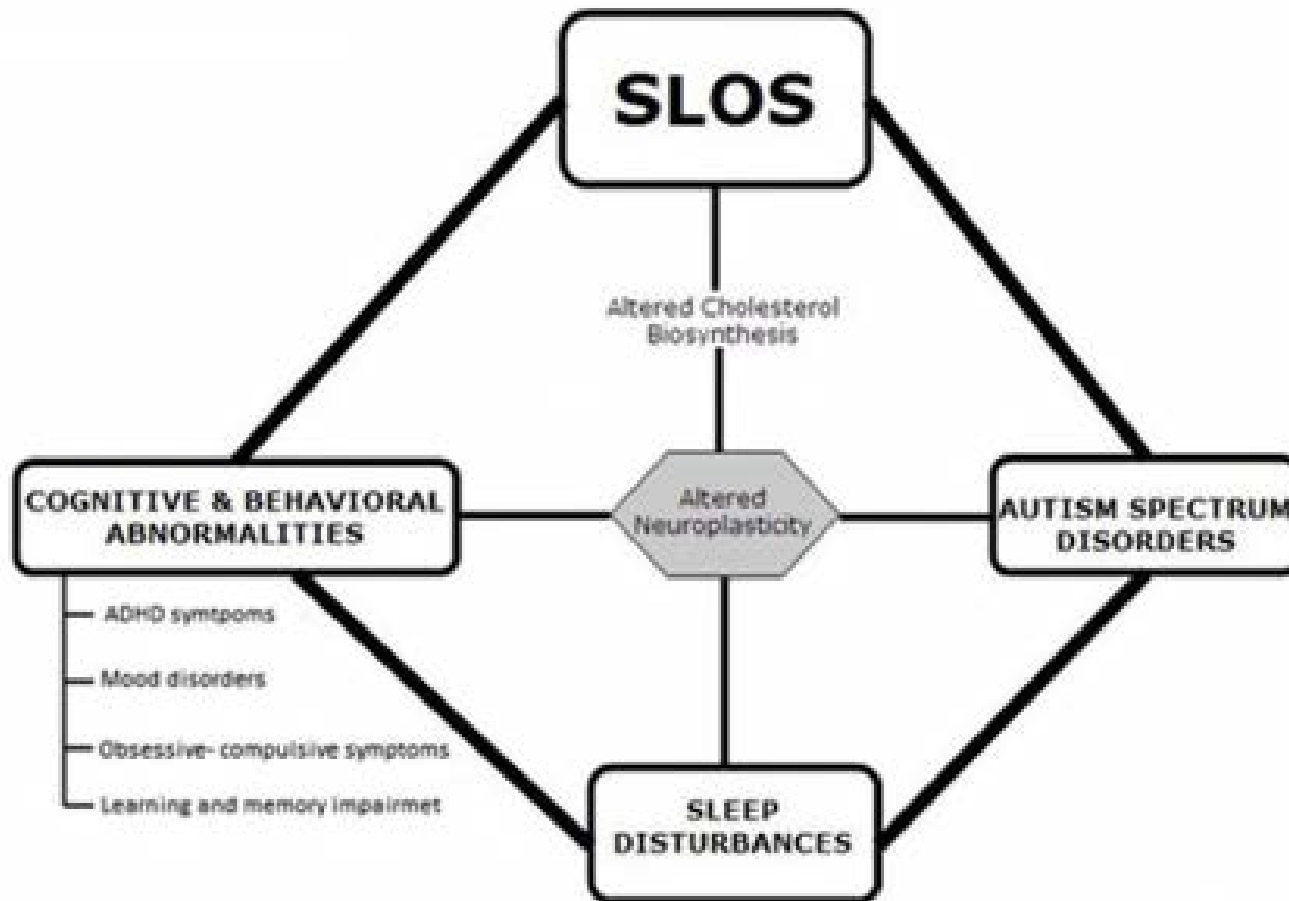
# ALTERED CHEMICAL BIOSYNTHESIS

- ◉ Freeman et al (2016) measured biomarkers of cholesterol synthesis (7-DHC, 8-DHC, cholesterol, mevalonic acid)
- ◉ Parents of 20 children completed the Children's Sleep Habits Questionnaire
- ◉ Association between biomarkers and parent-reported sleep problems (sleep onset delay, sleep duration, total sleep disturbance)
- ◉ Cholesterol deficiency and cholesterol precursor accumulation may impact sleep

# ALTERED CHEMICAL BIOSYNTHESIS

- Cholesterol synthesis increases at night time and decreases during the day
- Cholesterol plays a vital role in myelination of the central nervous system
- Individuals with SLOS
  - reduced capability to synthesize and transport cholesterol
  - Reduced ability to produce and repair myelin of CNS
  - Prevent recuperation from restful sleep and worsening of sleep disturbance over time
- Cholesterol supplementation may improve behavior (and sleep) (Nwokoro et al, 1997)

# ETIOLOGY OF SLEEP PROBLEMS



(Diaz-Stransky & Tierney, 2012)

# ETIOLOGY OF SLEEP PROBLEMS

## ⦿ ADHD

- Difficulty falling asleep and staying asleep
- Restlessness at night

## ⦿ Mood Symptoms

- Depression: excessive daytime sleepiness, difficulty falling asleep and staying asleep
- Anxiety: difficulty falling asleep and staying asleep

## ⦿ OCD

- Difficulty falling asleep

## ⦿ Autism

- Difficulty falling asleep and staying asleep



# PREVALENCE OF SLEEP PROBLEMS IN SLOS

- 18 subjects ages 2-31 years
- Questionnaires
  - Intake Demographic Form
  - Pediatric Sleep Questionnaire
    - Symptoms associated with sleep-related breathing disorders
    - Periodic Limb Movement of Sleep scale
  - Pediatric Daytime Sleepiness Scale
    - 8 items to assess excessive sleepiness

(Zarowski et al, 2011)

# PREVALENCE OF SLEEP PROBLEMS IN SLOS

- Health problems related to sleep
  - Hypotonia (66.7%)
  - Attention problems (11.1%)
  - Emotional problems (22.2%)
  - Tonsil hypertrophy (77.8%)
  - Obesity (11.1%)

# PREVALENCE OF SLEEP PROBLEMS IN SLOS

TABLE II. Prevalence of Sleep Problems in Patients With SLO

	% Yes
<b>Nighttime and daytime breathing</b>	
Does the family member with SLO snore?	50.0
Have heavy or labored breathing?	11.1
Have trouble breathing, or struggle to breathe?	11.1
Breathe through the mouth during the day?	50.0
Sleep with the mouth open?	66.7
Dry mouth on waking in the morning?	27.8
Occasionally wet the bed?	77.8
Become sweaty?	27.8
<b>Sleep behaviors</b>	
Get out of bed for any reason?	44.8
Grind his or her teeth at night?	38.9
Talk during sleep (sleep talking)?	33.3
Woken up screaming during the night?	61.1
Have difficulty falling asleep at night?	61.1
Time to fall asleep >30 min?	61.1
Rock his or her body when going to sleep?	38.9
Wake up more than twice a night on average?	44.4
Trouble falling back asleep if he or she wakes up at night?	66.7
Wake up early and have difficulty going back to sleep?	61.1
Goes to bed change a lot from day to day?	27.8
<b>Daytime behaviors</b>	
Feeling unrefreshed in the morning?	38.9
Sleepiness during the day?	44.4
Feels sleepy during the day	28.2
Appears sleepy during the day?	66.7
Take a nap during the day on most days?	55.6
Does not seem to listen when spoken to directly?	55.6
Has difficulty organizing tasks and activities?	66.7
Is easily distracted by extraneous stimuli?	38.9
Fidgets with hands or feet or squirms in seat?	66.7
Is "on the go" or often acts as if "driven by a motor"?	38.9
Interrupts or intrudes on others?	50.0

(Zarowski et al,  
2011)

# WHY ARE SLEEP PROBLEMS CHALLENGING FOR CLINICIANS?

- #1 Families do not ask their doctor for help



Howard County Mom Hub

February 11 at 9:05 PM · 📷

Sleep question. And if you don't agree with Cry it Out that's fine but please keep scrolling... Has anyone done full Extinction for CIO? My LO will be one next week. She has been nursed since birth and has slept through the night four times in her entire life. She... See More



Howard County Mom Hub

October 2, 2018 at 12:48 PM · 📷

Anyone experience [sleep](#) regression with an almost 3 year old? I have twins who have slept through the night since they were 4 months old. Now one of them screams constantly unless myself or my husband are physically in the room and our bedtime routine takes about an... See More



Howard County Mom Hub

May 5 at 2:32 PM · 📷

Dear Moms This is my first post regarding a [sleep](#) question for my 16 month old baby. I am now trying to [sleep](#) train him and transitioning him from Co-sleeping in the bed to crib. I understand that I am very late and should have done it much earlier. My question to you is are... See More



Howard County Mom Hub

October 2, 2018 at 2:41 PM · 📷

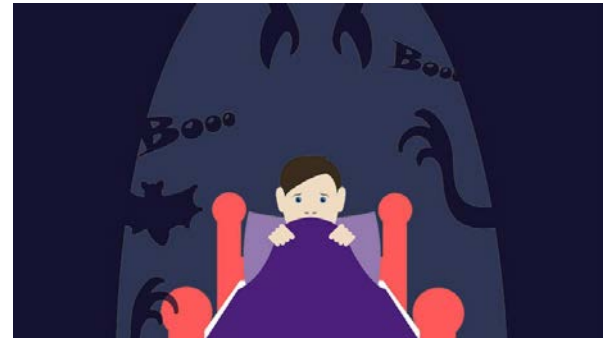
I have an 8 day old who refuses to [sleep](#) in his bassinet and will only [sleep](#) when I'm holding him. Does anyone have any suggestions on what my husband and I can do to help him be more inclined at night...

- #2 Doctors do not ask patients about their sleep
  - Many training programs do not require sleep education.
  - Doctors are not trained in behavioral interventions for sleep
- #3 Sleep medication trials in children are limited



# INSOMNIA

- ◉ Difficulty falling asleep, staying asleep, or waking up too early
- ◉ Behaviors that interfere with sleep:
  - worrying about falling asleep
  - trying too hard to fall asleep
- ◉ Tension about sleep
- ◉ Daytime problems:
  - difficulty functioning
  - often tired, moody, irritable



(Mindell & Owens, 2003)



Parents

14 hrs · ⚙️



Sounds about right! 😊



PARENTS.COM

**New Parents Are In for 6 Years of Bad Sleep, Study Says**

# SLEEP STRATEGIES

- ◉ Environmental
- ◉ Behavioral
- ◉ Medication





# ENVIRONMENTAL INTERVENTIONS

## ○ Light

- Dim light in the early evening
- No electronics or TV an hour before bedtime
- Lights out at bedtime
- Black out curtains

## ○ Sound

- White noise, nature sounds, classical music
- Maintain all night long

## ○ Comfort items

## ○ Temperature

## ○ Consistent sleep schedule

## ○ Avoid caffeine



# BEHAVIORAL INTERVENTIONS

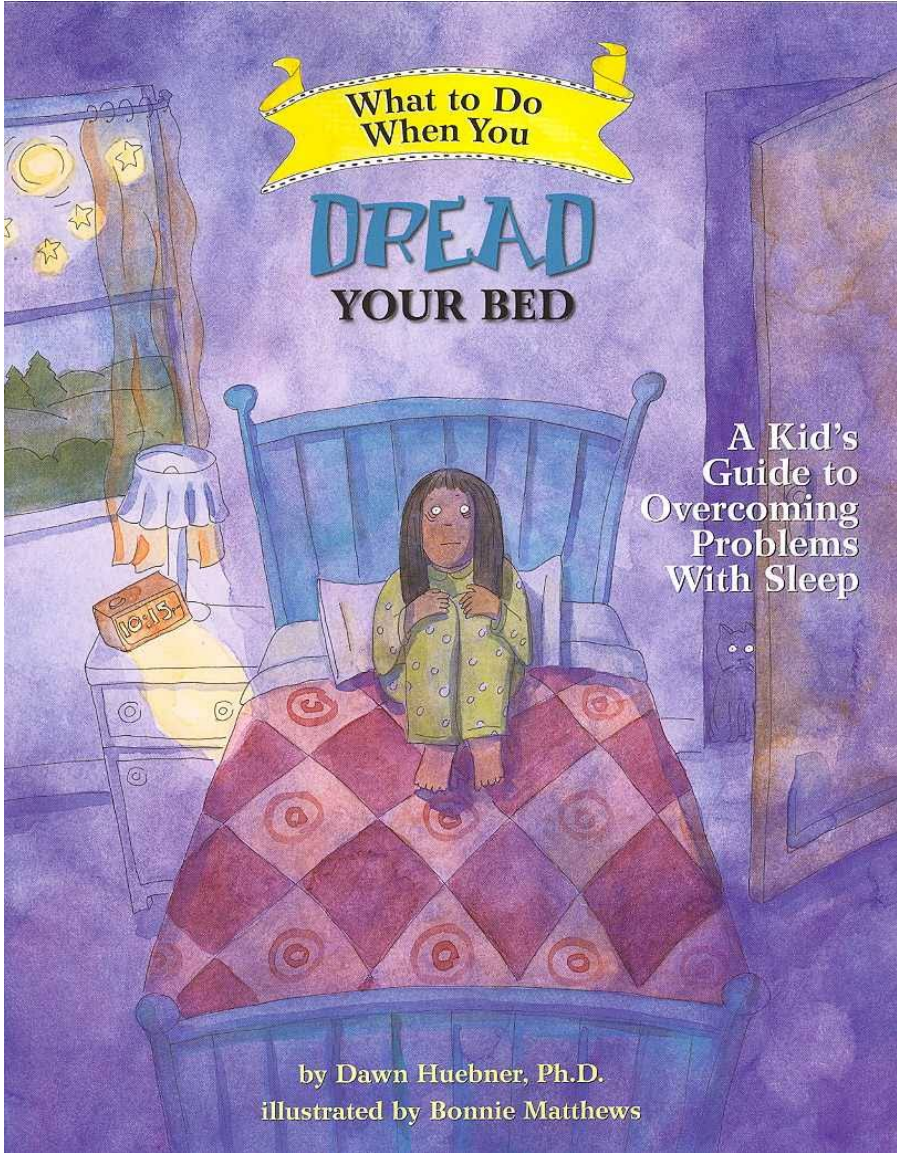
- Provide opportunity for physical activity in the early evening
- Establish a bedtime routine
- Bedtime fading
- Neutral responding
  
- Referral to behavioral specialist



What to Do  
When You

# DREAD YOUR BED

A Kid's  
Guide to  
Overcoming  
Problems  
With Sleep



by Dawn Huebner, Ph.D.  
illustrated by Bonnie Matthews

# ACTIGRAPHY



# MEDICATIONS

- Melatonin
- Clonidine
- Guanfacine
- Hydroxyzine
- Mirtazapine
- Gabapentin
- Clonazepam
- Trazodone
- Ambien
- Lunesta



# SLEEP APNEA

## ○ Obstructive Sleep Apnea

- Loud snoring
- Pauses in breathing or gasping for air
- Morning headaches
- Daytime sleepiness
- Sweating during sleep
- Bedwetting

## ○ Central Sleep Apnea

- Pauses in breathing
- Daytime sleepiness



# DIAGNOSIS

- ⦿ Physical exam
  - Enlarged tonsils
  - Floppy airway
  - Low tone
- ⦿ Polysomnogram (sleep study)
- ⦿ Desensitization



# INTERVENTION

- ◉ Tonsillectomy and adenoidectomy
- ◉ CPAP/BiPAP
- ◉ Dental device
- ◉ Weight loss





# RESTLESS LEGS SYNDROME/ PERIODIC LIMB MOVEMENT DISORDER

- ◉ Restless during sleep
- ◉ Leg pain at night or during the day at rest
- ◉ Unable to sit still
- ◉ Etiology: Anemia, poor diet, dopamine antagonists



# TREATMENT OF RLS/PLMD

- Iron supplementation
- Dopamine agonists



# WHEN IS A REFERRAL TO SLEEP CLINIC WARRANTED?

- ◉ Behavioral and environmental strategies have been exhausted
- ◉ Child has undesired side effects to medication
- ◉ PCP is not comfortable with further management
- ◉ A sleep study is recommended and abnormal



# WHAT HAPPENS AT A SLEEP CLINIC APPOINTMENT?

- ◉ Information obtained about the child's sleep by a clinician (MD or NP) and a psychologist
- ◉ Child is examined by the clinician
- ◉ Behavioral/environmental recommendations made by the psychologist
- ◉ Medical tests and medication recommendations provided by the clinician
- ◉ Sleep study results reviewed with the family

# HOW TO REACH OUT

- ◉ Kennedy Krieger Institute Intake line  
443-923-9400
- ◉ [SleepPatientInfo@kennedykrieger.org](mailto:SleepPatientInfo@kennedykrieger.org)
- ◉ Admin: Jovida Walker  
443-923-0580

