

SLEEP AND THE NEUROENDOCRINE SYSTEM: IT'S ABOUT TIME!

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DISCLOSURES

I receive salary support through research agreements from Eisai Inc and Levo Therapeutics to the Children's Hospital of Philadelphia unrelated to the current topic.

OBJECTIVES

- Provide a background about sleep.
- Discuss the relationship between sleep and the neuroendocrine system.
- Discuss common sleep disorders in childhood and adolescence and treatment recommendations.



SLEEP: WHAT AND WHY

- Humans spend 1/3 of their lives sleeping.
- It is an active state for your brain.
- Affects almost every type of tissue and system in the body – from the brain, heart, and lungs to metabolism, immune function, mood, and disease resistance.
 - ✓Sleep Quantity
 - ✓Sleep Timing
 - ✓Sleep Quality

Aminoff, Boller, & Swaab, 2011

<https://www.ninds.nih.gov/disorders/patient-caregiver-education/understanding-sleep>

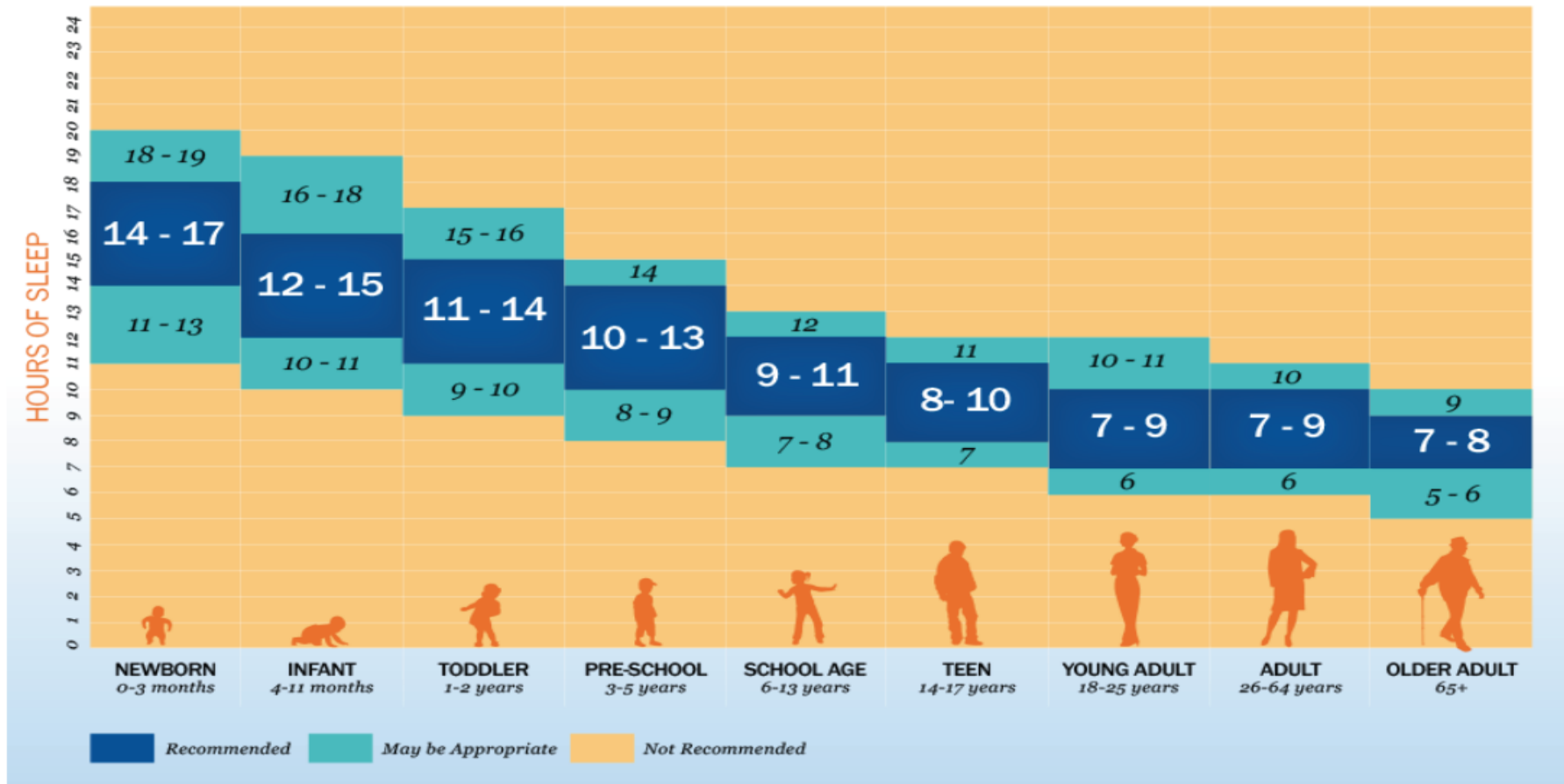
WHAT IS “NORMAL” SLEEP?

Stages of Sleep

- Non-rapid eye movement (NREM) sleep
 - N1: Transition from sleep to wake (2-5% of night)
 - N2: Sleep onset (45-55% of night)
 - N3: Slow wave sleep/deep sleep (3-23% of night)
 - Energy is restored
 - Increased blood supply to muscles
 - Tissue growth and repair
 - Hormones released for growth and development
 - Decreases by 40-50% from early childhood to adolescence
- Rapid eye movement (REM) sleep
 - Brain is active (dreaming occurs)
 - Body immobile
- Cycles lengthen over childhood
 - 50 minutes in infancy → 90-110 minutes by school age
- Arousals are NORMAL!



RECOMMENDED SLEEP DURATION



 NATIONAL SLEEP FOUNDATION

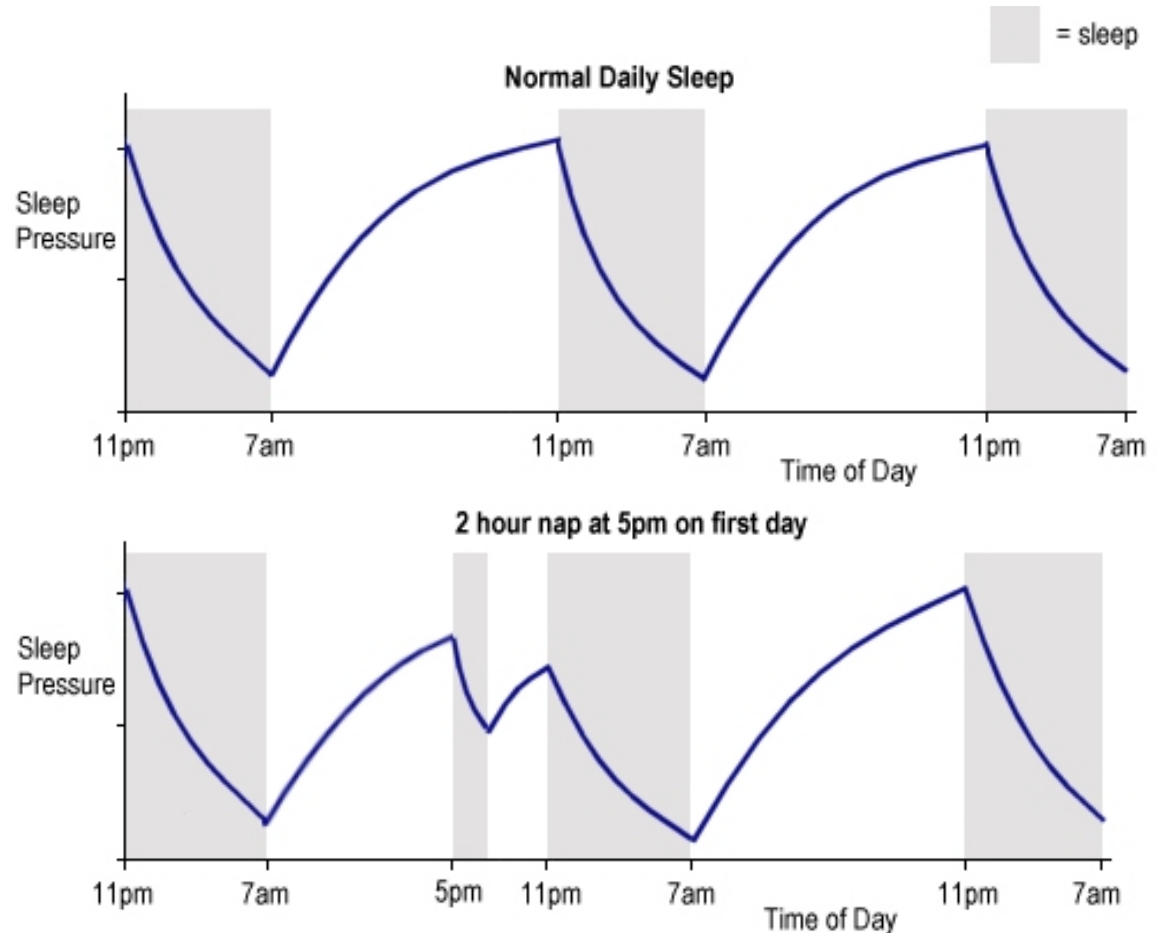
TWO PROCESS MODEL

- **Homeostatic sleep drive (Process S)**
 - Pressure to sleep (e.g., adenosine build up)
 - Depends on hours awake and hours of sleep
 - Sleep loss tolerance increases over childhood
- **Circadian Pacemaker (Process C)**
 - Time-keeper
 - External Cues
 - Melatonin
 - Cortisol



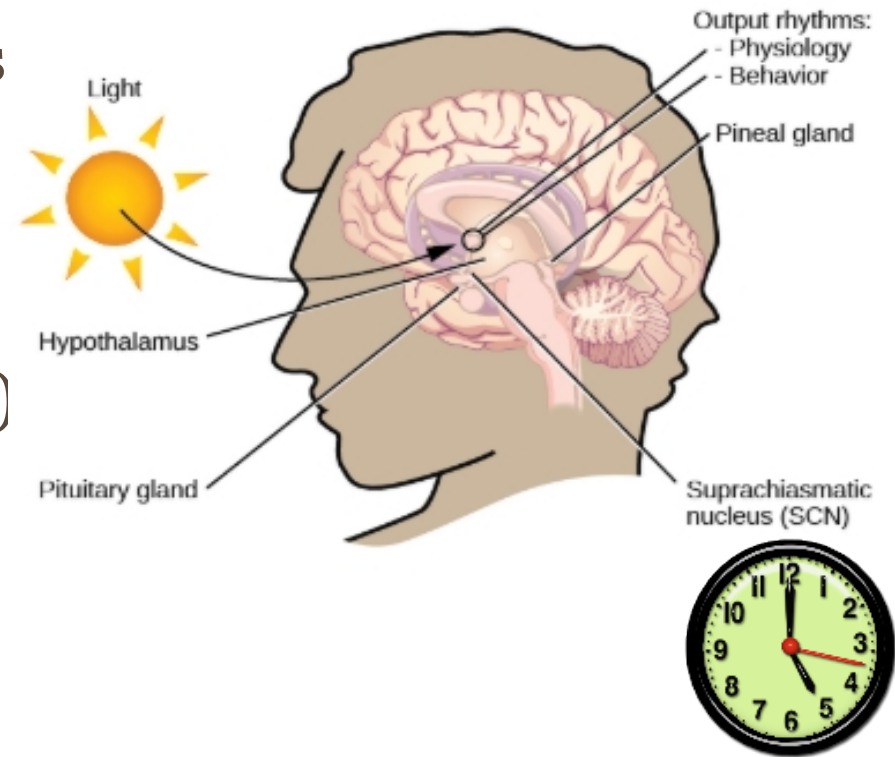
PROCESS S: SLEEP HOMEOSTASIS

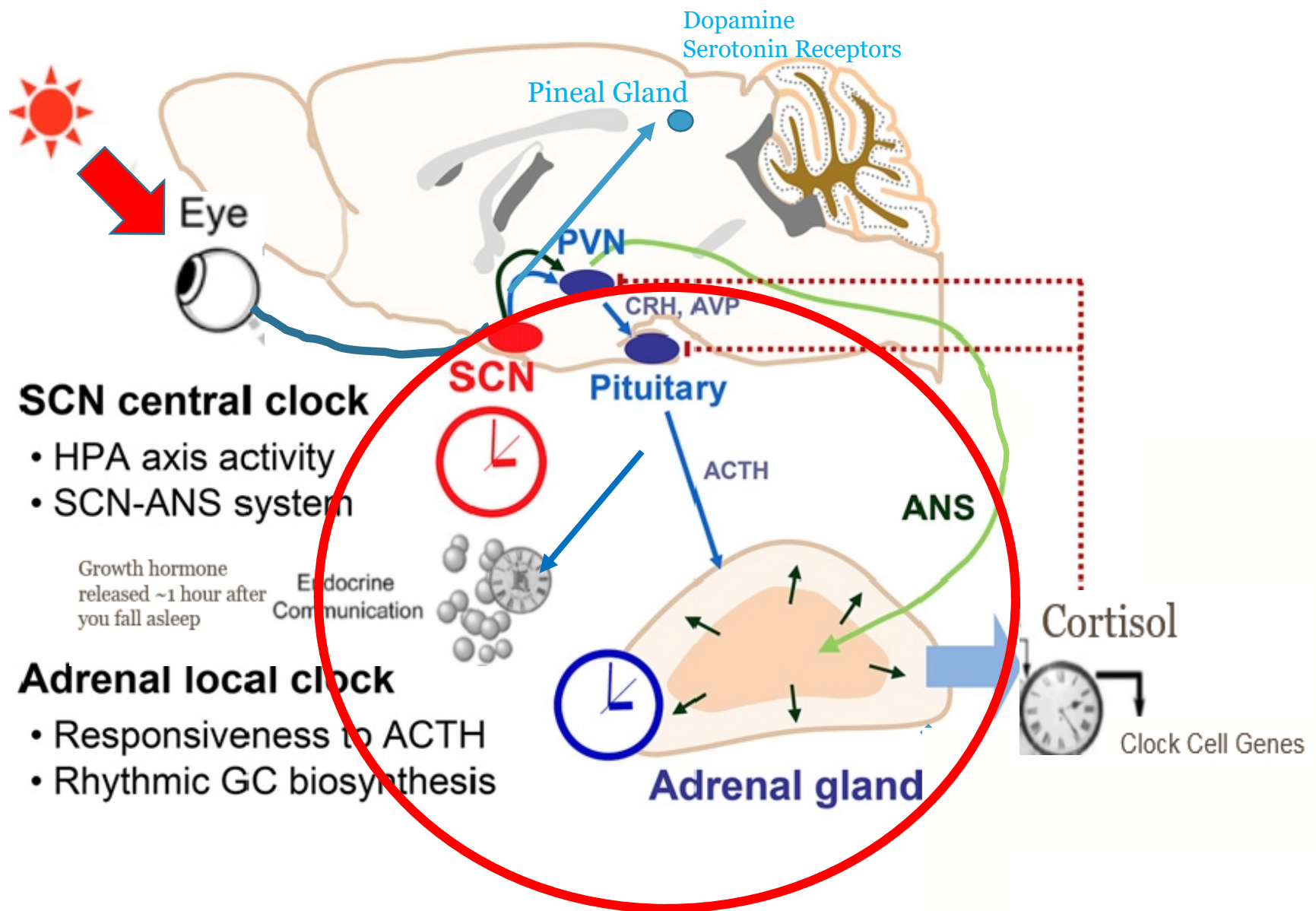
- Naps decrease homeostatic pressure making going to sleep at night challenging.



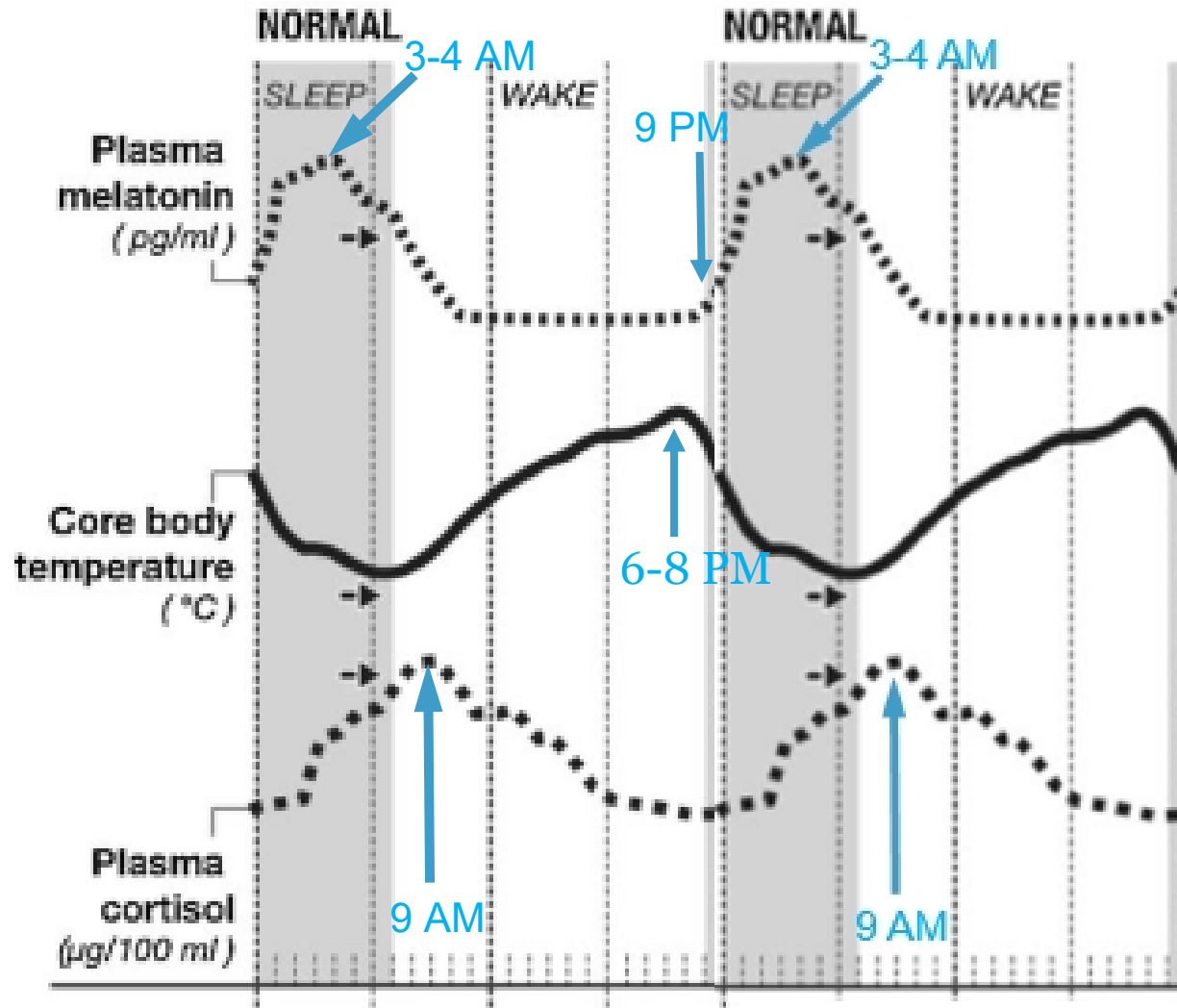
CIRCADIAN PACEMAKER (PROCESS C)

- Suprachiasmatic nucleus (SCN)
 - Master Clock
 - Regulates pituitary hormones
 - Signals the pineal gland to secrete melatonin
- *Zietgebers* (Time-Keepers)
 - **Light/dark**
 - Social activities/habits
 - Meals





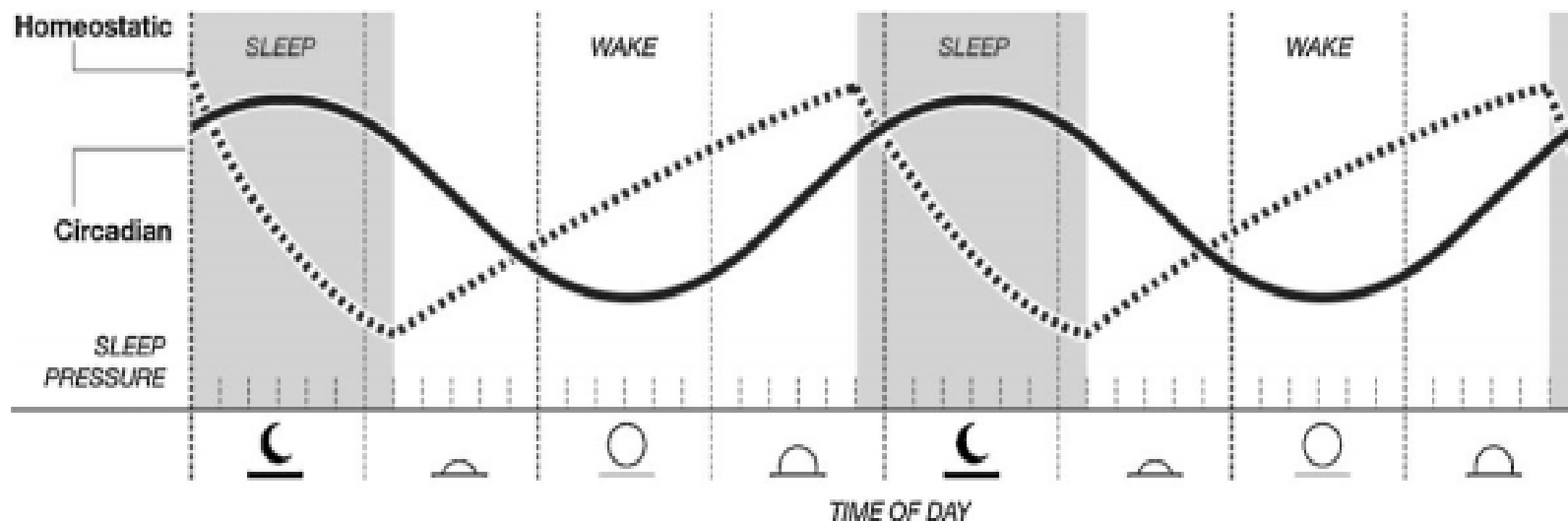
PROCESS C: CIRCADIAN RHYTHM



TWO PROCESS MODEL

- S and C work together to regulate and consolidate sleep

Two-process model of sleep regulation

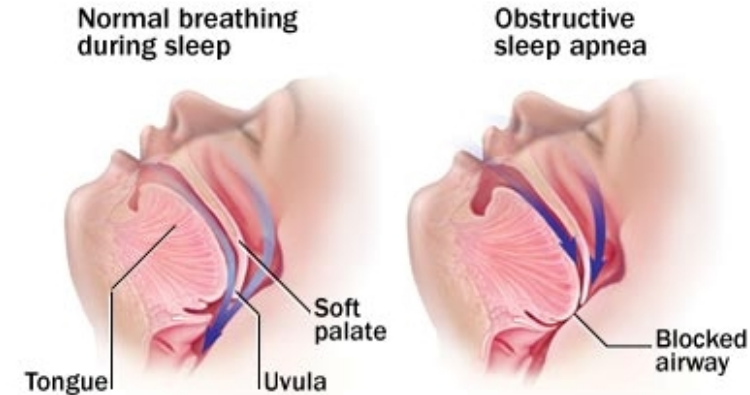


SLEEP DISORDERS & TREATMENTS



OBSTRUCTIVE SLEEP APNEA SYNDROME

- **Obstructive sleep apnea (OSA)**
 - 1-4% of all children
 - **Snoring**, pauses in breathing, gasping,
 - Hyperactivity, difficulty paying attention, irritability, learning problems
 - Requires sleep study to diagnose
 - Higher risk if presence of:
 - Enlarged tonsils and adenoids
 - **Obesity**
 - Acromegly
 - Prader Willi
 - Low muscle tone
 - Hypothyroidism
 - Craniofacial differences



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TREATMENT

- Adenoid and Tonsil Surgery
- Positive Airway Pressure (CPAP & BPAP)
- Weight Loss
- Other Oral Maxillary Surgeries
- Orthodontics



→ Neuroendocrine Considerations:

- Treat underlying neuroendocrine condition
 - Hypothyroidism, compression of optic nerve, hormone deficiencies, etc
- Certain tumors in the brain
 - Craniopharyngioma
- Treatment of OSA can improve overall function in children with neuroendocrine dysfunction

INSOMNIA

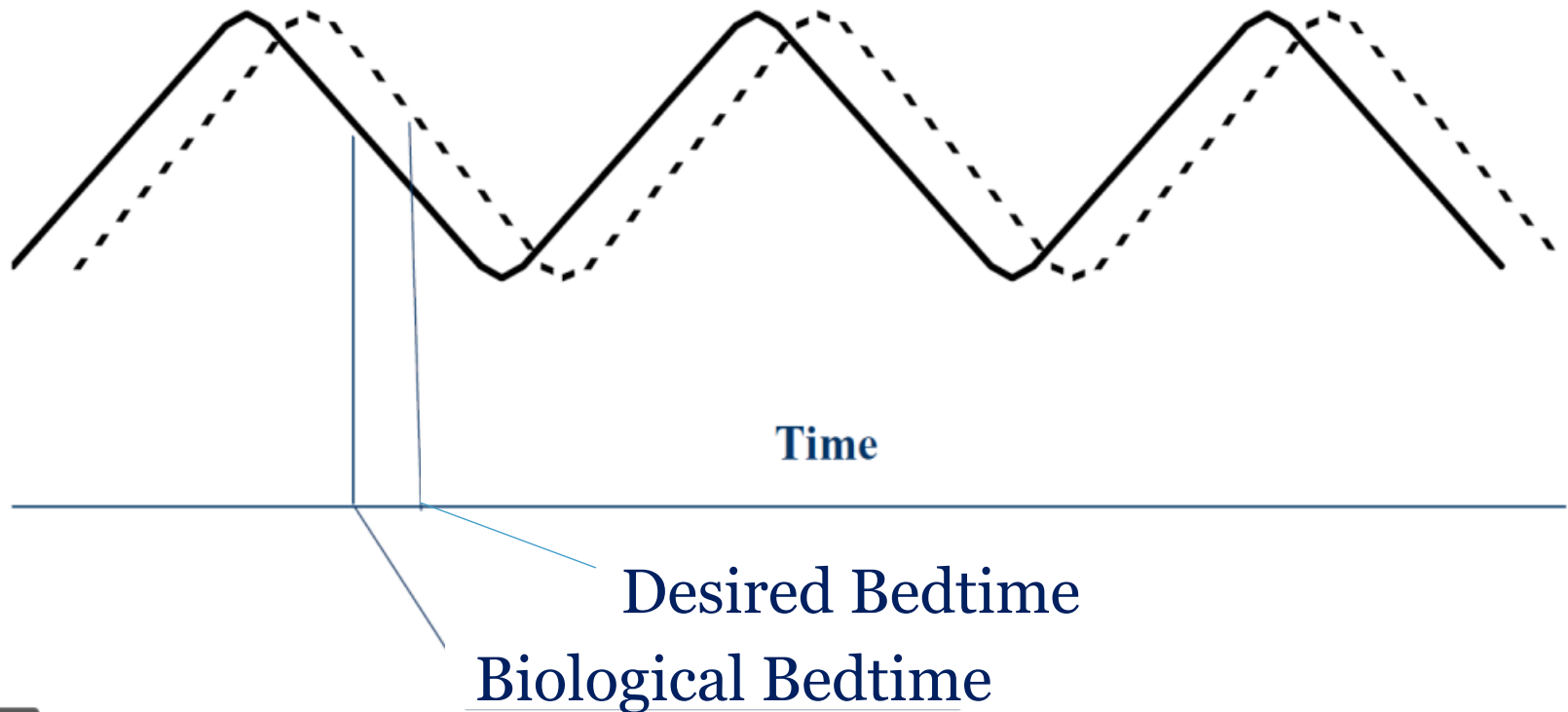
- Difficulty falling/staying asleep or early morning waking
 - 3 nights per week for 3 months or more
 - Occurs despite adequate sleep opportunity
 - Not explained by/occur exclusively in context of another sleep disorder
- Sleep-related worries and hyperarousal at bedtime
- Daytime sleepiness/fatigue

CIRCADIAN RHYTHM DISORDERS

- **Delayed Sleep-Wake Phase Disorder**
 - Significant delay as evidenced by inability to fall asleep and difficulty awakening at a desired or required clock time.
 - If allowed to choose own schedule, normal sleep period.
 - Lack of correspondence between body clock and social clock
 - Early school start times; social expectations; occupational
- **Non-24 Hour Sleep-Wake**
 - Can't entrain a 24 hour light dark/clock times.
 - Usually a progressive delay and then have daytime sleepiness and nighttime insomnia.
 - Usually occurs when completely blind (but not always).

CIRCADIAN DISORDERS

— Circadian Rhythm - - Desired Sleep/Wake Schedule



8.50 in

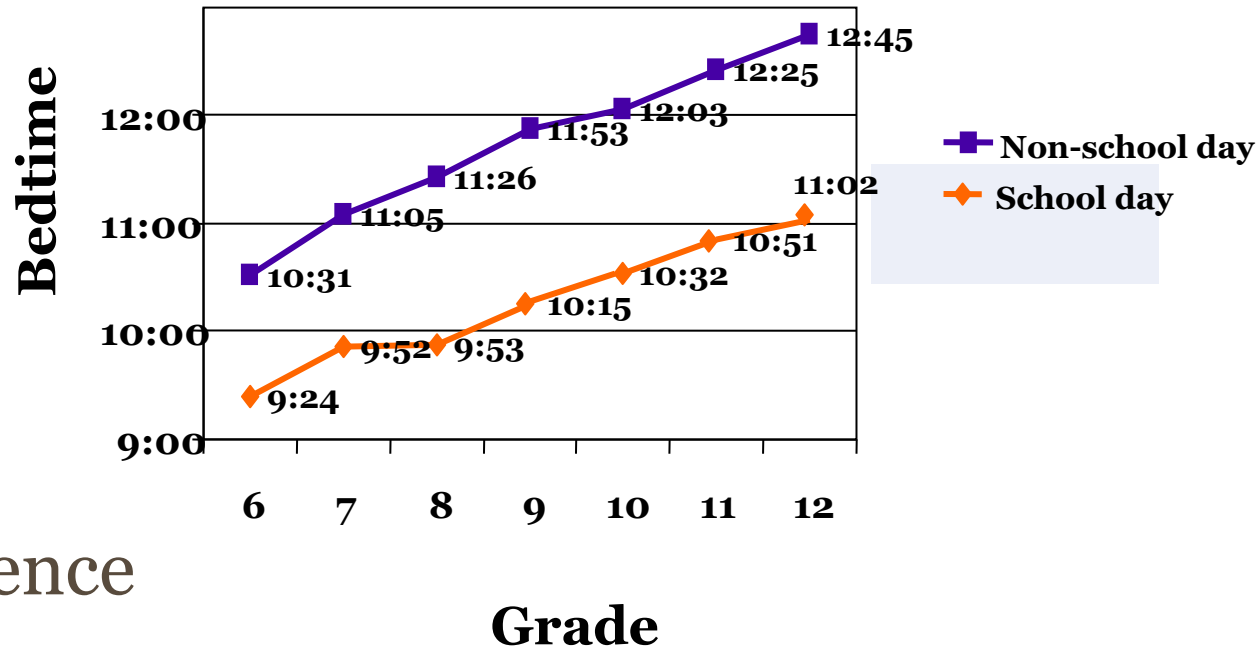
CAUSES



- Behaviors and Habits:
 - Sleep Hygiene
 - Schedule
 - Stress
- Medical:
 - Hyperthyroidism, Cushing's disease, optic nerve chiasm compression, pain, certain tumors, blindness, cancer, diabetes, asthma, gastroesophageal reflux disease (GERD), surgical or radiation treatments.
- Medications
 - Caffeine, nicotine, alcohol, steroids, and many, many others.
- Behavioral Health Conditions:
 - Depression, anxiety, PTSD, and many others

CAUSES OF CIRCADIAN

- Adolescent shift
- Social Jet Lag
- Genetics
- Circadian Preference
 - Larks and Owls



CIRCADIAN DISORDERS

Sleep Diary

Name: Sleepy Teen

Dob: / /

Date Started: / /

Date Ended: / /

List Medications:

	Midnight												Noon													
Day	6p	7	8	9	10	11	12	1	2	3	4	5	6	7	8	9	10	11	12	1	2	3	4	5	Comments	
Mon																										
Tues																										
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TREATMENT: SLEEP HYGIENE

- Keep your bedtime and wake time consistent from day to day, including weekends.
- Do not do any other activities in bed except sleep.
- Make your bedroom comfortable (cool and dark) for sleep and only use it for sleep.
- Create a relaxing consistent bedtime routine, such as taking a warm shower, reading (a book) or listening to soft music.
- Limit electronics 1 hour prior to bedtime.
 - No electronics in the bedroom.
- Avoid or limit naps.
- Avoid caffeine.

TREATMENT: INSOMNIA

- **Stimulus Control:**

- Sleeping is only for the bed, the bed is only for sleeping
- No clock watching
- Get out of bed and do something boring (e.g., reading a physical book) if can't sleep 15-20 minutes.

- **Sleep restriction**

- Traditional (calculate with diary and actigraphy if possible)
- Adaptation (later bedtime, consistent wake time, no naps)
- Under the care of a professional.

- **Cognitive Behavioral Therapy for Insomnia (CBTi)**

- Cognitive Restructuring
- Stress Management: Relaxation techniques
- Addressing underlying psychiatric concerns (anxiety and depression)

- **Check medications**

TREATMENT: DELAYED SLEEP WAKE PHASE

- Consistent bed and wake times—even on weekends
- Bright light exposure in the morning
 - Natural light exposure
 - Light box
 - 20 to 30 minutes
 - 2,500 to 10,000 lux
- Avoid bright light in the evening
- Sunglasses in the late afternoon
- No screen time in the evening
- No napping
- No electronics 60 minutes before bedtime
- Phase Advancement, Chronotherapy, and Sleep Restriction *under the care of a professional.*



SLEEP MEDICATIONS

- Melatonin
 - Not regulated by the FDA; Look for USP Verification label
 - Rarely used in isolation
 - For sleep initiation:
 - 3-6 mg, 30-60 minutes before bedtime
 - For shifting circadian phase shift:
 - 1.5-2mg 2 hours prior to habitual bedtimes
 - 3-5 mg at 6-7 pm (with comorbid psychiatric condition)
- Other medications: Off-label in children
 - Clonidine and Trazodone
 - Psychiatric Medications
 - Rarely used; always under close supervision with specialist

CHOP SLEEP CENTER

- Interdisciplinary Sleep Clinic
 - Physicians Boarded in Sleep Medicine
 - Pulmonary, Neurology, Psychiatry, Family
 - Clinical Psychologists
 - Respiratory Therapists
 - Nurse Practitioner
- **Main, KOP, Virtua**
- **215-590-3749 for appointments**
- **<https://www.chop.edu/centers-programs/sleep-center>**
- Sleep Lab
 - Physician Referral

RESOURCES

- <https://www.sleepfoundation.org/>
- <https://kidshealth.org/en/parents/sleep.html>
- <http://sleepeducation.org/essentials-in-sleep>

THANK YOU! QUESTIONS?

