Circadian Rhythm Sleep Disorders

by

Peter Mansbach, PhD

President, Circadian Sleep Disorders Network

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Overview

• Introduction
• Circadian Rhythm Sleep Disorders
  – DSPS
  – Non-24
• Diagnosis
• Treatment
• Research Issues
• Circadian Sleep Disorders Network
Circadian Rhythms

• 24 hours 10 minutes on average
• *Entrained* to 24 hours (*zeitgebers*)
• Suprachiasmatic nucleus (SCN) – the master clock
• ipRGC cells (intrinsically photosensitive Retinal Ganglion Cells)
Circadian Rhythm Sleep Disorders

• Definition
  – A circadian rhythm sleep disorder is an abnormality of the body’s internal clock, in which a person is unable to fall asleep at a normal evening bedtime, although he is able to sleep reasonably well at other times dictated by his internal rhythm.

• Complaints
  – Insomnia
  – Excessive daytime sleepiness

• Inflexibility

• Coordination with other circadian rhythms
Circadian Sleep Disorder Subtypes*

- Delayed Sleep-Phase Syndrome (G47.21**)
- Non-24-Hour Sleep-Wake Disorder (G47.24)
- Advanced Sleep-Phase Syndrome (G47.22)
- Irregular Sleep-Wake Pattern (G47.23)
- Shift Work Sleep Disorder (G47.26)
- Jet Lag Syndrome

* From The International Classification of Sleep Disorders, Revised (ICSD-R)
** ICD-10-CM diagnostic codes in parentheses
Definition of DSPS

from *The International Classification of Sleep Disorders, Revised* (ICSD-R):

- Sleep-onset and wake times that are intractably later than desired
- Actual sleep-onset times at nearly the same daily clock hour
- Little or no reported difficulty in maintaining sleep once sleep has begun
- Extreme difficulty awakening at the desired time in the morning, and
- A relatively severe to absolute inability to advance the sleep phase to earlier hours by enforcing conventional sleep and wake times.
Definition of DSPS

Delayed Sleep Phase Disorder is a disorder in which a person’s sleep occurs much later than desired. He finds it difficult to impossible to fall asleep until very late at night, and therefore difficult to wake up until very late in the morning or even afternoon.
Normal and Delayed Sleep Phases

- Example of a Normal Sleep Phase
- Example of a Delayed Sleep Phase
Circadian Rhythm Sleep Disorders – TWO Factors

• Not entrained to day/night cycle
• Inflexible
  – This is the part people don’t understand
Biological Markers

- Melatonin level (timing)
  - DLMO (Dim Light Melatonin Onset)

- Core body temperature

- Cortisol level
<table>
<thead>
<tr>
<th>Sleep Disorder</th>
<th>Number of Americans</th>
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<td>Narcolepsy</td>
<td>150,000</td>
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</table>

represents 75,000 Americans
Snooze Alarm
Sleeping in Hallway
Sleep Study
(not me)
“For decades I worked day jobs after sleeping 3:30 to 7:30 a.m., catching up on weekends.... That worked as long as youthful resilience lasted. Next step was adding a "nap" 5 to 10 p.m. Wreaks havoc with the social life, but it kept me my job for years.

“If you can't be normal, you're not good enough. You learn to apologize, make excuses, tell lies. No one understands.... “
"I just can't help thinking that I'd have no problem being awake and alert if I were to simply follow my own natural sleep cycle. The only problems I would face are unemployment and nearly no social life."
Circadian Sleep Disorders

Sleep Periods

Example of a Normal Sleep Phase

Example of a Delayed Sleep Phase

Example of an Advanced Sleep Phase

Example of an Irregular Sleep-Wake Pattern

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Definition of Non-24

Non-24-hour Sleep-Wake Disorder (Non-24 for short) is a disorder in which an individual falls asleep later and later each day, eventually rotating all the way around the clock.
Non-24-Hour Sleep-Wake Disorder

Example of Progression of Sleep Periods
### Incidence

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represents 75,000 Americans

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Living with Non-24

• Sleeping on a 24 hour schedule
  – periods of insomnia alternating with good sleep

• Sleeping on your body’s schedule
  – sleep time rotates around the clock
  – may be unpredictable
“Ever since I became Non-24, I constantly have to beg people to change their schedules, or try to be pleasing and unobtrusive while I quietly ask if they have another time available. It's affected my relationships with all: family, who don't believe it in it; friends, who can never find a slot to talk to me, let alone get together, and have finally stopped trying; doctors, next to impossible to schedule.... When I can't meet the world’s demands, I am deemed selfish or weak or lazy or depressed.... I could be fine with me. But the world is not fine with me, and that makes me not fine.

“I feel so isolated. I am desperate for social contact.”
"What is hardest is explaining non-24 to new acquaintances, for example someone you might meet at a party. It tends to derail the whole social process. The inability to remain employed has an even more profound effect on my social life. It's not something people accept when you look healthy."
Possible Causes

- Long intrinsic circadian period
- Lack of sensitivity to light
- Oversensitivity to light
- Lack of melatonin
- Long elimination time of melatonin
- Deficiencies in ipRGC cells
- Longer time from temperature minimum to waking
- Difference in tolerance to phase mismatch
Diagnosis

- Patient Reporting
- Sleep Log or Chart
- Actigraph
- Polysomnogram (PSG)
  - Watch the timing!
- MSLT Interpretation
- Biological Markers? Not yet
# Sleep Chart – DSPS Patient

## Sleep Diary

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<tr>
<th>Name:</th>
<th>Birth Date:</th>
<th>Physician:</th>
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<td>Diary started on:</td>
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<td>Remarks / Notes:</td>
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<td>Medications used:</td>
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**Instructions:** In the table above, use ‘S’ to indicate your sleep hours and ‘U’ to indicate hours when you were awake.

[www.FreePrintableMedicalForms.com](http://www.FreePrintableMedicalForms.com)
Sleep Chart – Non-24 Patient

### Sleep Diary

<table>
<thead>
<tr>
<th>Name:</th>
<th>Birth Date:</th>
<th>Physician:</th>
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**Diary started on:**

**Remarks / Notes:**

**Medication used:**

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#### Instructions:

- Use "S" to indicate your sleep hours and "U" to indicate hours when you were awake.

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Actigraph – Non-24 Patient
Diagnosis

- Patient Reporting
- Sleep Log or Chart
- Actigraph
- Polysomnogram (PSG)
  - Watch the timing!
- MSLT Interpretation
- Biological Markers? Not yet
Core Body Temperature (CBT) Rhythm
Treatments

- Sleep Hygiene
- Sleeping pills (no help)
- Chronotherapy (risky)
- Light therapy - in the morning
- Light restriction (“dark therapy”) in the evening
- Melatonin
Sleep Hygiene

• Comfortable bedroom, dark, quiet
• Go to bed at same time, get up at same time every day
  – particularly important with circadian rhythm disorders
• Avoid caffeine within 6 – 8 hours of bedtime
• Avoid alcohol near bedtime
• Avoid light, computers, phone, TV before bedtime
• Avoid exercise within 3 hours of bedtime
• Avoid naps in the evening
Treatments

• Sleep Hygiene
• Sleeping pills (no help)
• Chronotherapy (risky)
• Light therapy - in the morning
• Light restriction ("dark therapy") in the evening
• Melatonin
Phase Response Curve (PRC)

St. Hilaire et al “Human Phase Response Curve (PRC) to a 1-hour pulse of bright white light” (2012)
1 hour 8000 lux light pulse, normal sleepers
Scatter in PRC data

St. Hilaire et al “Human Phase Response Curve (PRC) to a 1-hour pulse of bright white light” (2012)
1 hour 8000 lux light pulse, normal sleepers
Light Therapy

- Standard procedure
- Phase Response Curve (PRC)
- Individual variability
- Timing issue when starting therapy
- How fast to shift?
- Success Rate
Treatments

- Sleep Hygiene
- Sleeping pills (no help)
- Chronotherapy (risky)
- Light therapy - in the morning
- Light restriction ("dark therapy") in the evening
- Melatonin
Phase Response Curve for Melatonin

Burgess, HJ et al “Human phase response curves to three days of daily melatonin 0.5 mg versus 3.0 mg” (2010)
Reasons for Failure

- DLMO shift ≠ subjective well-being
- Shift work ≠ DSPS or Non-24
  - CRSD may involve impairments
- Short term success ≠ long term
- Lack of synchronization with other body rhythms
- Sleep deprivation may lessen effect

- Partial success?
The Myth of the Good Night’s Sleep

The myth

The reality
Research Issues

• Different underlying causes
  – Tailoring therapy to cause

• Therapy parameters
  – Time, brightness, color, dose, etc
  – Testing on patients, not normal sleepers
  – Test combined light and dark therapy
  – Long term and subjective improvement
  – Can light therapy harm eyesight?

• Better diagnostic tests
• Incidence data
• Comorbidities
Circadian Sleep Disorders Network is a nonprofit organization dedicated to improving the lives of people with chronic circadian rhythm disorders.

We aim to increase awareness within the medical community and among the general public, to provide emotional support and practical ideas for people living with these disorders, to encourage research into circadian rhythms, and to advocate for accommodations in education and employment for people with circadian rhythm sleep disorders.
Thank You!

Visit us at: CircadianSleepDisorders.org

shortcut: csd-n.org

(don't forget the hyphen!)

Email me at: peter@csd-n.org