

Sleep Disorders in Women

Milena Pavlova, M.D.

Department of Neurology, Brigham and Women's Hospital

Associate Professor, Harvard Medical School

Medical Director, Faulkner Sleep and EEG Testing Center

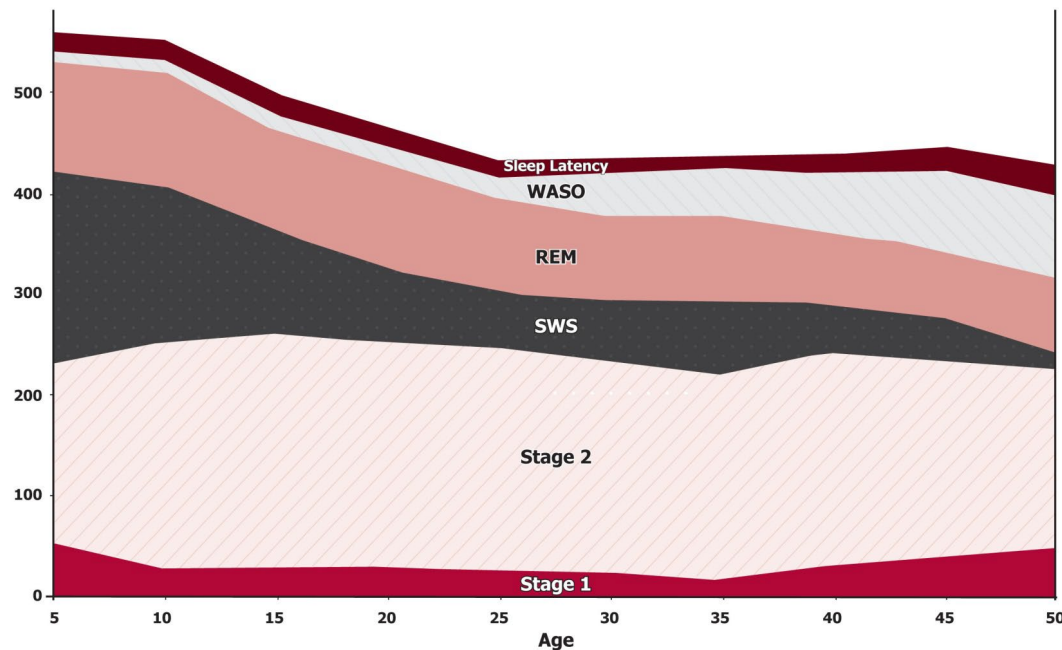
Disclosures

- Jazz pharma
- Biomobie inc.

Overall gender considerations

- Women are more susceptible to comorbidities
 - Migraine
 - Anxiety
 - Depressive disorders
- Insomnia symptoms are more frequent in women
- Reproductive hormones affect sleep
- Evaluation and treatment should consider time (reproductive age, pregnancy, menopause)

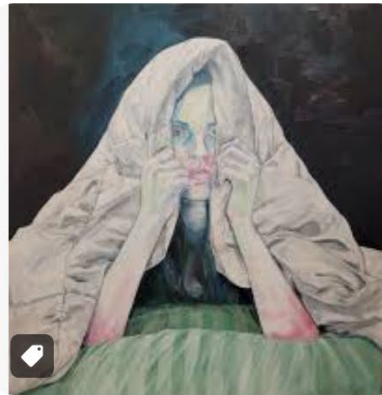
Developmental meta-analysis of sleep architecture of men and women



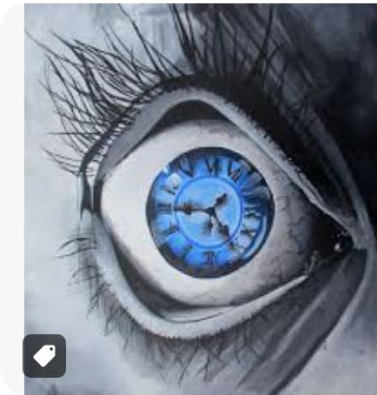
- 3577 subjects, 5 - 80 y/o - meta-analysis
- PSG and actigraphic data.
- Age-related findings:
 - increase of sleep latency,
 - increased percent Stage 1 and Stage 2
 - Decrease in REM sleep.
- larger effect sizes were observed in women for
 - total sleep time (TST),
 - sleep efficiency,
 - percentage of Stage 1 sleep,
 - REM latency.
- → women more 'vulnerable' to age related sleep changes



Artist Christine Mercer...
Insomnia Painting / a ...



Singulart · In stock
Insomnia by Joanna Aslani...



Pictorem.com · In stock
Insomnia - Marietou Biteye



Widowcranky
Presentiment Of Insomnia – Sergey ...



Saatchi Art · In stock
Insomnia Painting by En



DeviantArt



Art of Gabriel



Artsv



Reddit



Art of Gabriel

Gender differences in insomnia

- A meta-analysis - insomnia prevalence - from 13 studies, women had
 - a significantly higher prevalence of insomnia (OR = 1.58, 95% CI: 1.35, 1.85, $p < 0.0001$)*
 - greater levels of pre-sleep arousal**
- Working middle-aged women - ruminating and worrying about daily tasks at night
- More stress induced by the competing demands of paid work and unpaid domestic labor which may also restrict time that can be allocated toward adequate sleep***

*Zeng, et al. Front. Psychiatry 11, 577429. doi: 10.3389

**El Rafihi-Ferreira et al., 2022

***Sidani et al., 2019

Comorbid, hormonal, and genetic polymorphism

- Women are two to three times as likely to be diagnosed with depression and/or anxiety over the course of their lifetime when compared to men*
- Gender specific risk –
 - premenstrual dysphoric disorder,
 - postpartum depression,
 - postmenopausal depression and anxiety*
- Polymorphisms in the serotonin-linked polymorphic region (5HTTLPR) may also play a role in the depression and anxiety gender gap
- variation in ovarian hormone levels esp. decreases in estrogen**

*Wang et al., 2021

**Vigod and Stewart, 2009

Social factors

- A survey by the World Health Organization (WHO) found that more than one in ten women endorse experiencing perceived gender discrimination
- Perceived gender discrimination was significantly associated with higher depression scores even after adjusting for poverty, social support, and gender inequality*
- Societal disparities, such as economic reliance, limited decision-making authority, contradictory gender expectations, unequal distribution of domestic duties, and instances of violence that women bear disproportionately to men

Recognizing sleep disorders

- Chief complaint “I can’t sleep”
 - “I haven’t slept since...”
 - “I was never a good sleeper”
 - “I fall asleep, but keep waking up every hour”
- Chief complaint: “ I fall asleep when I should not”

Culprits

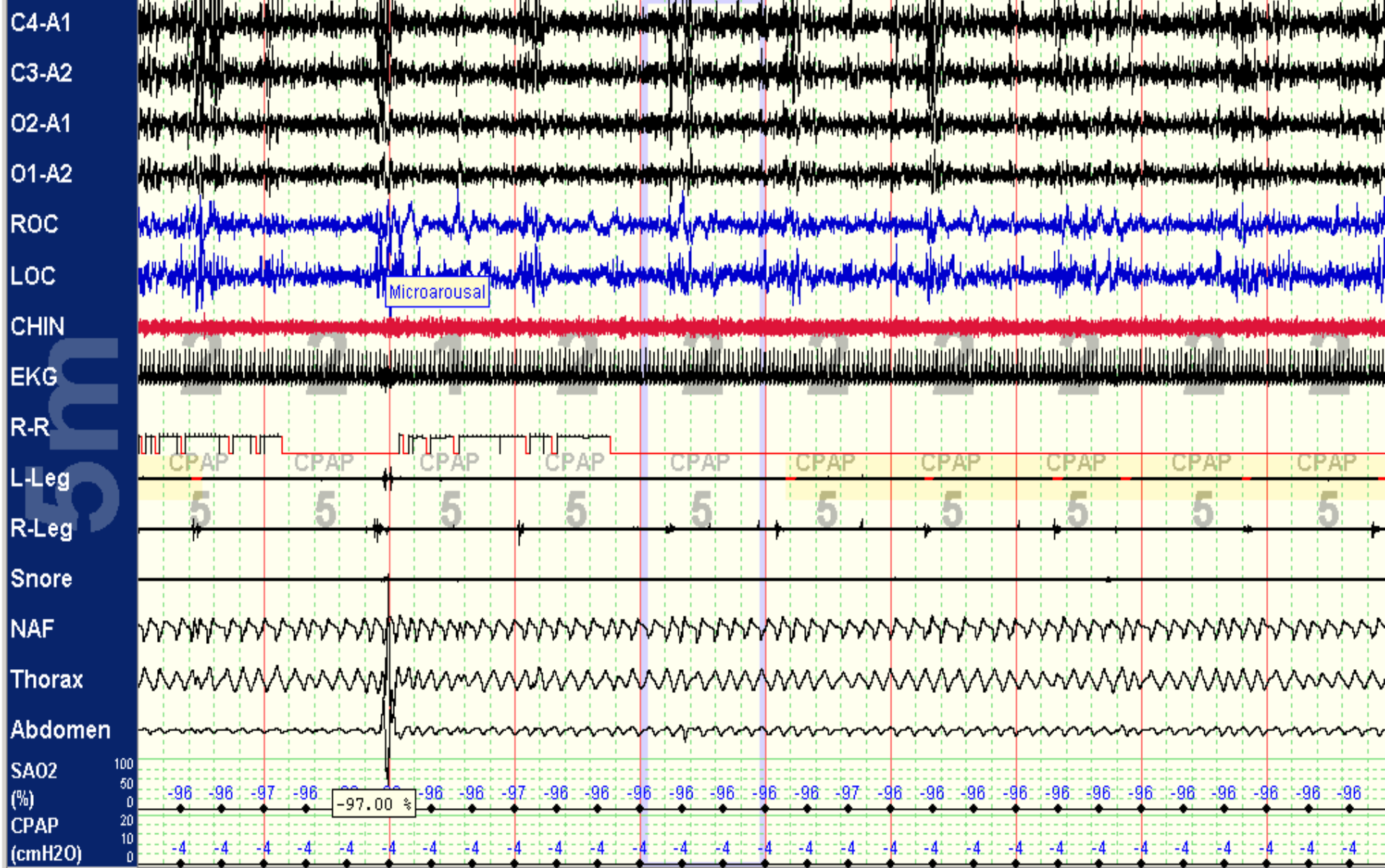
- Medications/substances
 - Caffeine, alcohol, illicit
 - ADD medications, some antidepressants, some BP medications
- A medical/neurological disorder
 - Hyperthyroidism, anemia, bipolar disorder
- A primary sleep disorder
 - RLS,
 - circadian rhythm disorder
 - Parasomnia/ RBD
- Medications/substances
 - Anxiolytics, neuroleptic, antidepressants, antihypertensive,
- A medical/neurological disorder
 - Hypothyroidism, Parkinson’s disease
- A primary sleep disorder
 - OSA, PLMS, RBD
 - Narcolepsy, Idiopathic hypersomnia

Patient A

- A 23- year-old pregnant, otherwise healthy middle school teacher (woman) complains of difficulty falling asleep.
- She describes that during the summer, she enjoyed normal sleep, with somewhat variable bedtime, but often 1-3 am and wake-time at 9-11 am and felt fully energetic.
- During the school year, she needs to get up at 6 am for work.
- She uses several alarms on of which requires for her to take out her phone and take a picture
- She feels exhausted
- She is mostly on her feet during the day
- Despite the exhaustion, when she comes home from work, has difficulty sitting and resting.
- She describes that at rest, she gets uncomfortable, indescribable urge to move her legs, needs to get up and pace around.
- This continues in the evening and bed-time hours, and she keeps re-positioning, “like a fish out of water”
- Exam is normal and appropriate for gestational age, except for slightly decreased hematocrit.

RLS

- Unpleasant, very uncomfortable sensations
- Rest – when they occur
- Getting up and walking makes them better
- Evening predominance



RLS and pregnancy

- Up to 20%!
- Usually second-third trimester
- Most resolve within ~1 month postpartum
- highly associated with iron deficiency anemia
- First line treatment options include gentle exercise, such as yoga
- Iron replacement
- In severe cases, additional pharmacotherapy may be considered after the first trimester on a case by case basis

RLS/PLMD treatment

- Fe supplementation if indicated
 - ferritin levels are <50-75 mcg/mL or
 - Transferin saturation <20%
 - Can be oral (Fe+vit C) or IV
 - In pregnant women – can be if ferritin <100
- Gabapentin/gabapentin enacarbil
- Dopamine-agonists(pramipexole, 0.5–0.75 mg; ropinirole, 4 mg; rotigotine, 3 mg)
- The dose of dopamine agonists should be kept low to avoid augmentation
- Opiates – late in the disease for more severe situations
- Benzodiazepines – sometimes helpful with caution

Patient A – 1 month postpartum

- The patient is now 1 month postpartum
- She has been told to “sleep when the baby sleeps”
- She is unable to do that
- RLS is resolved, but she feels she sleeps in “bits and pieces”
- She has difficulty concentrating and is afraid she will drop the baby or forget something important and some disaster will happen.
- She is still on maternity leave, entirely concentrated on baby-care,
- has stopped her habitual exercise (running, tennis, and Pilates)

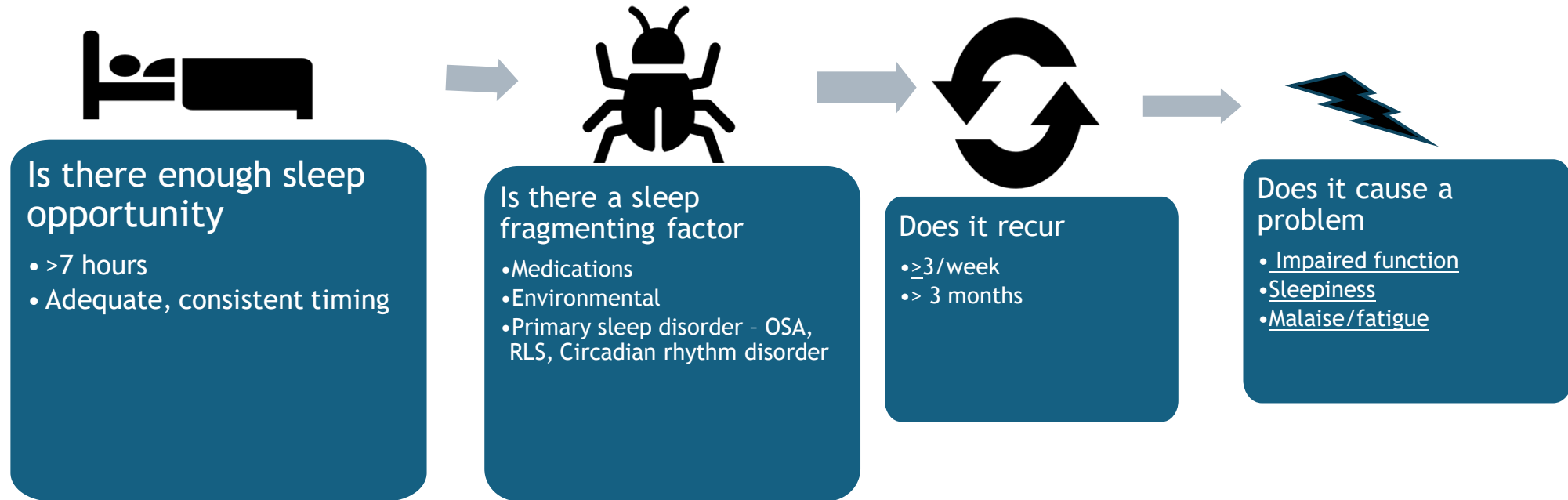
Complaints

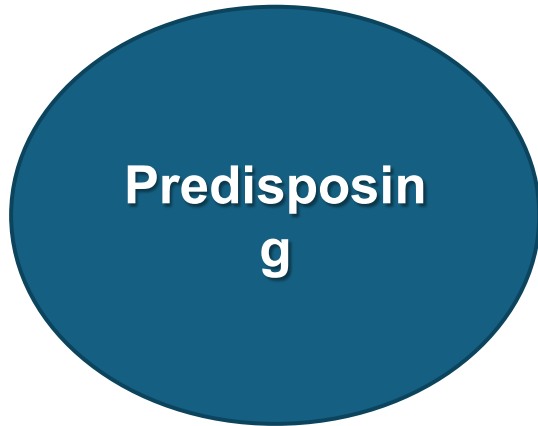
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 - “I was never a good sleeper”
 - “I fall asleep, but keep waking up every hour”
- Chief complaint: “ I fall asleep when I should not”
 - TV/passive
 - Working/interacting
 - **Driving**
 - Standing

Culprits

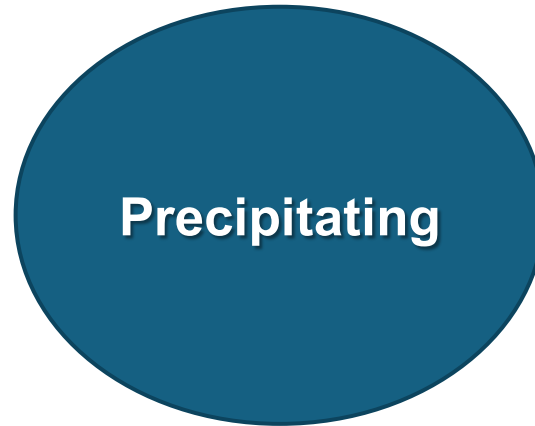
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Chronic insomnia

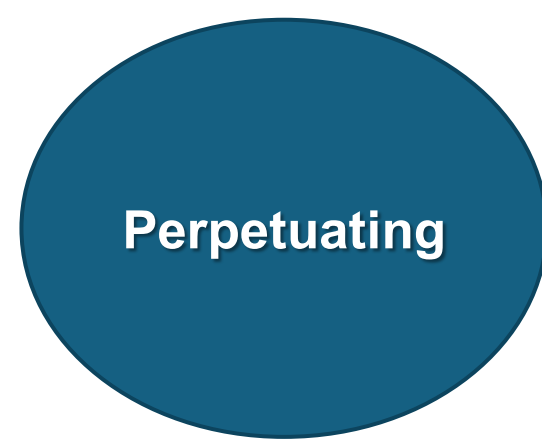




Inherited



Major stress
Illness
Other
physiologic
change



Maladaptive behaviors, such as:

- Rumination
- Anxiety about not being able to fall asleep
- Substance use – caffeine to counteract the resulting fatigue, alcohol at bedtime

Treatment of insomnia

- Counseling:
 - Sleep hygiene
 - Cognitive behavioral therapy
 - Relaxation techniques
- Medications:
 - Benzodiazepines
 - Other hypnotics
 - Melatonin agonist
 - Antidepressants
 - Others

Good Sleep Rules

- Determine time in bed – most need 7-9 hrs of sleep, do not stay in bed longer
- Use bed for **sleep/intimacy** only
- Turn clock, so it is not visible from the bed
- Naps, if taken at all, should be early afternoon at latest
- Schedule regular wake times
- Allow ample amount of light during the day
- Allow dimmer light in the evening
- Moderate or limit caffeine - last intake at noon
- Limit alcohol – best not close to bedtime

Medications for insomnia

- Benzodiazepines
 - Lorazepam, temazepam, oxazepam
- Other hypnotics
 - Zolpidem, zaleplon, eszopiclone
- Melatonin agonists
 - Ramelteon,
- Orexin antagonist
 - Suvorexant, Lemborexant, Daridorexant
- Antidepressants
 - Mirtazapine, trazodone, amitriptyline, etc.
- Others

Benzodiazepines

- Advantages:
 - Cheap and ubiquitous
- Problems:
 - Excessive sedation
 - High frequency of falls, esp. in elderly – due to nonselective GABA effects
 - Hypotension
 - Tend to lose efficacy after longer use
 - Muscle relaxant effect
 - Significant cognitive effects
 - Long term cognitive effects.

Other hypnotics

- Zolpidem, Zolpidem XR, Intermezzo (zolpidem ultrashort acting, 3mg)
- Zaleplon
- Eszopiclone
- Advantages
 - some are very short acting (Intermezzo, Zaleplon)
 - Some are FDA approved for chronic insomnia treatment (eszopiclone, zolpidem CR).
- Problems
 - Common side effects – parasomnia, over-sedation, etc.
 - Some also have a potential to lose efficacy

Antidepressants

- Trazodone, Mirtazapine, Amitriptyline, low dose doxepine
- Advantages
 - More suitable for long-term use
 - May have advantages when combining treatment of insomnia and pain (e.g. amitriptyline)
- Problems
 - Anticholinergic side effects – dry mouth constipation, etc.
 - Orthostatic hypotension

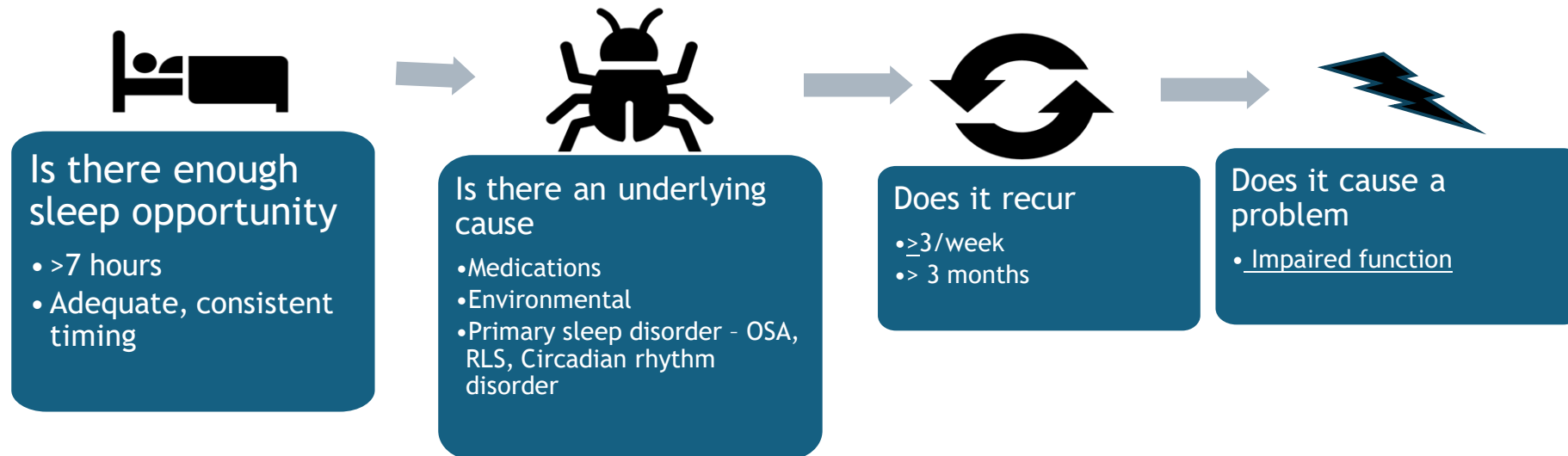
Others

- Antihistamines
- Melatonin
- Melatonin agonist
- Orexin antagonist
- Other substances

Patient

- A 23 year old woman presents with sleepiness and asks if she may have narcolepsy
- She describes predominantly difficulty waking up for work.
- Symptoms intensified after she finished college and started job with a stable daytime schedule
- Besides sleepiness, she has had sleep paralysis on several occasions
- Sleep schedule:

Diagnosing hypersomnia



Central hypersomnia

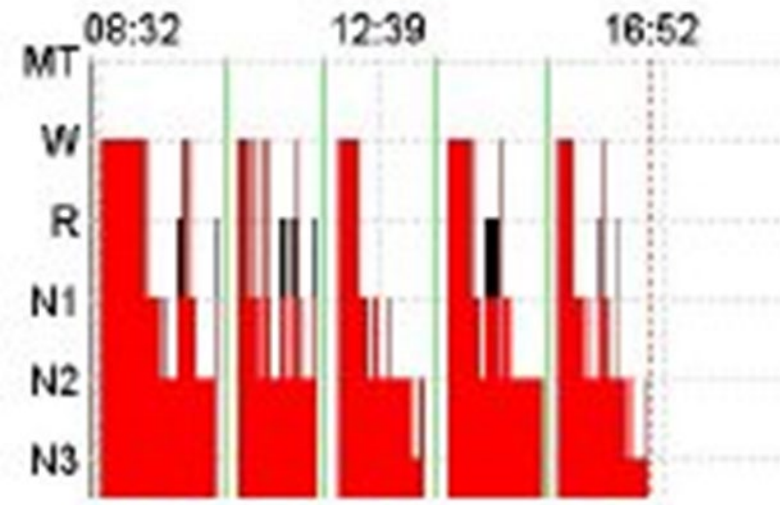
- Narcolepsy type 1 (with cataplexy)
- Narcolepsy type 2 (no cataplexy)
- Idiopathic hypersomnia
 - With long sleep time
 - Without long sleep time
- Recurrent hypersomnia

Narcolepsy – disorder of REM regulation

- ▶ Classic symptoms
 - ▶ Sleepiness
 - ▶ Sleep paralysis
 - ▶ Hypnagogic hallucinations
- ▶ Cataplexy in narcolepsy type 1 –
 - ▶ loss of muscle tone typically with positive emotions (laughing/telling a joke, surprise, can be anger)
 - ▶ Can be mild or unilateral
 - ▶ Can be more severe
- ▶ Naps are short and refreshing
- ▶ HLA associations - DQB1*0602
- ▶ Orexin – low in CSF type 1

Diagnosis

- Clinically
- Objective documentation - MSLT
 - on the day after a PSG
 - 5 nap opportunities x 20 min
 - short sleep latency (<8 min.)
 - ‘SOREM’: ≥ 2 naps containing REM
 - or REM in one nap and a REM latency on the preceding PSG <15 min.
- HLA typing
- CSF measurement of hypocretin

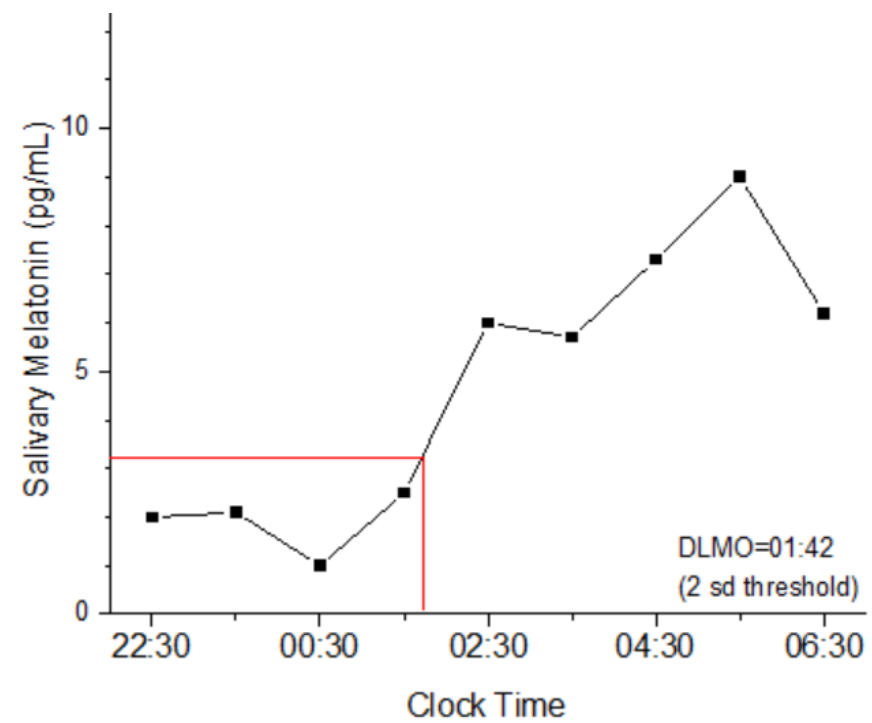
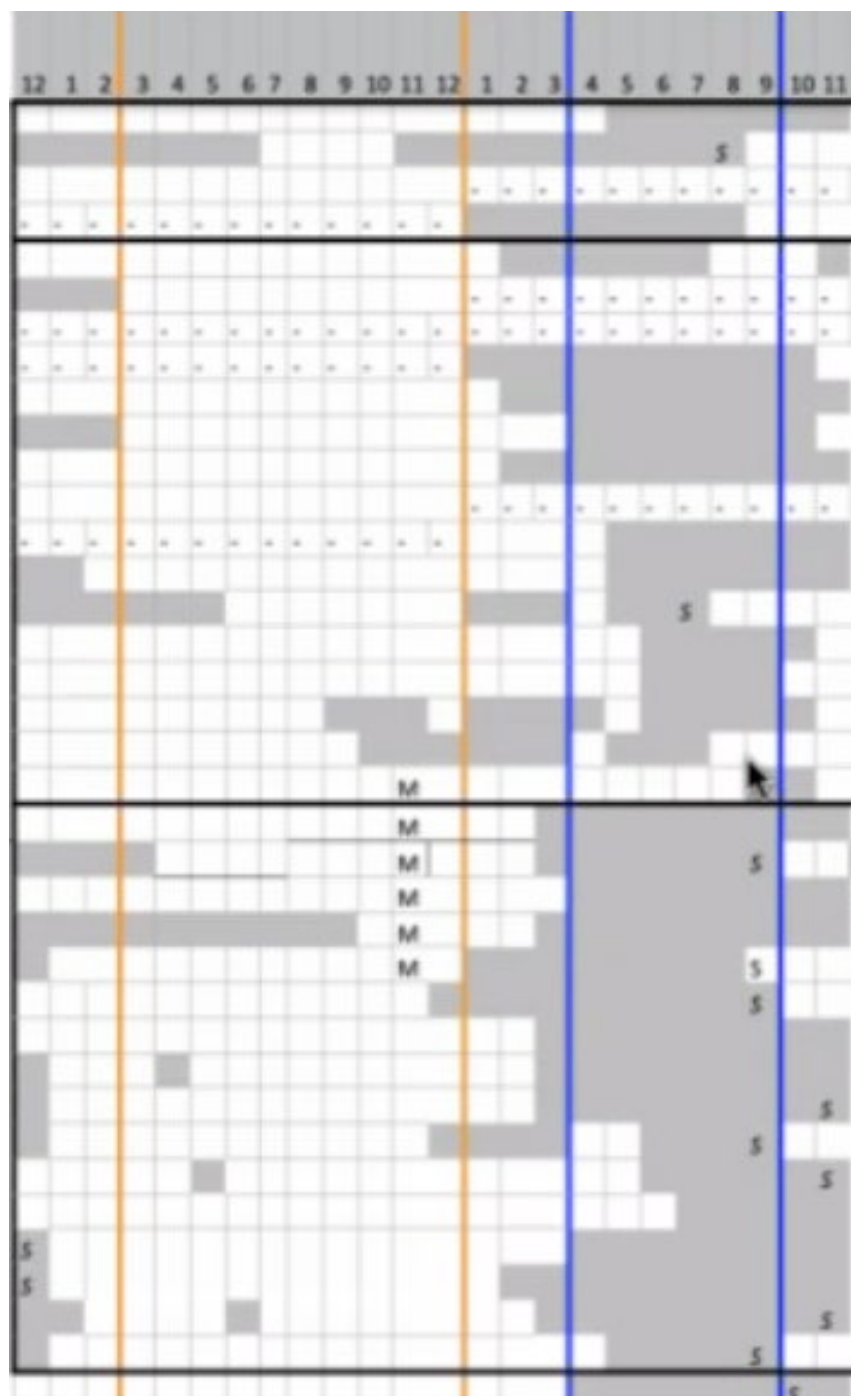


Other causes of hypersomnia

- Secondary to medical, neurological, psychiatric disorder or medications
- Recurrent (Kleine-Levin syndrome, menstruation-related hypersomnia)
- Posttraumatic
- Post-viral
- Idiopathic

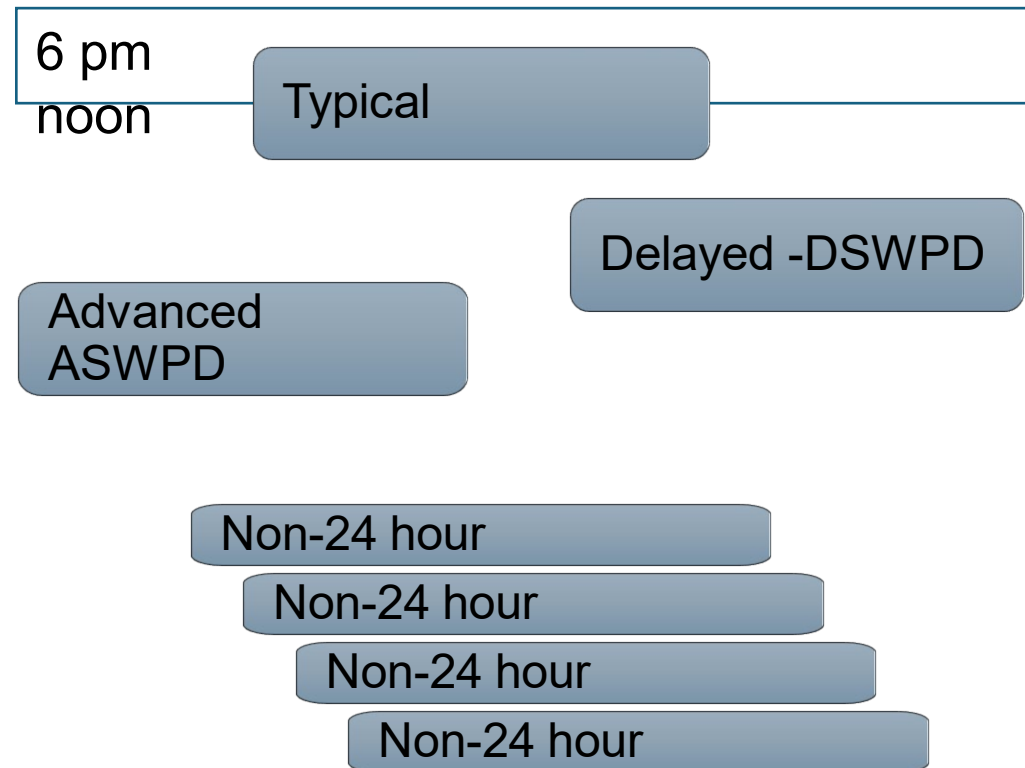
Idiopathic Hypersomnia

- Presentation: long, non-refreshing naps
- With long sleep time
- Without long sleep time
- MSLT criteria: sleep latency <8 minutes, no SOREM
- Treatment often challenging



Recognizing circadian rhythm disorders

- Delayed sleep wake phase disorder
- Advanced sleep wake phase disorder
- Irregular sleep wake phase disorder
- Non-24 hour



Diagnosing circadian rhythm sleep wake disorders

- Sleep log
- Actigraphy
- Melatonin measurements –
dim light melatonin onset time

TWO WEEK SLEEP DIARY



INSTRUCTIONS:

1. Write the date, day of the week, and type of day: Work, School, Day Off, or Vacation.
2. Put the letter "C" in the box when you have coffee, cola or tea. Put "M" when you take any medicine. Put "A" when you drink alcohol. Put "E" when you exercise.
3. Put a line (l) to show when you go to bed. Shade in the box that shows when you think you fell asleep.
4. Shade in all the boxes that show when you are asleep at night or when you take a nap during the day.
5. Leave boxes unshaded to show when you wake up at night and when you are awake during the day.

SAMPLE ENTRY BELOW: On a Monday when I worked, I jogged on my lunch break at 1 PM, had a glass of wine with dinner at 6 PM, fell asleep watching TV from 7 to 8 PM, went to bed at 10:30 PM, fell asleep around Midnight, woke up and couldn't get back to sleep at about 4 AM, went back to sleep from 5 to 7 AM, and had coffee and medicine at 7:00 in the morning.

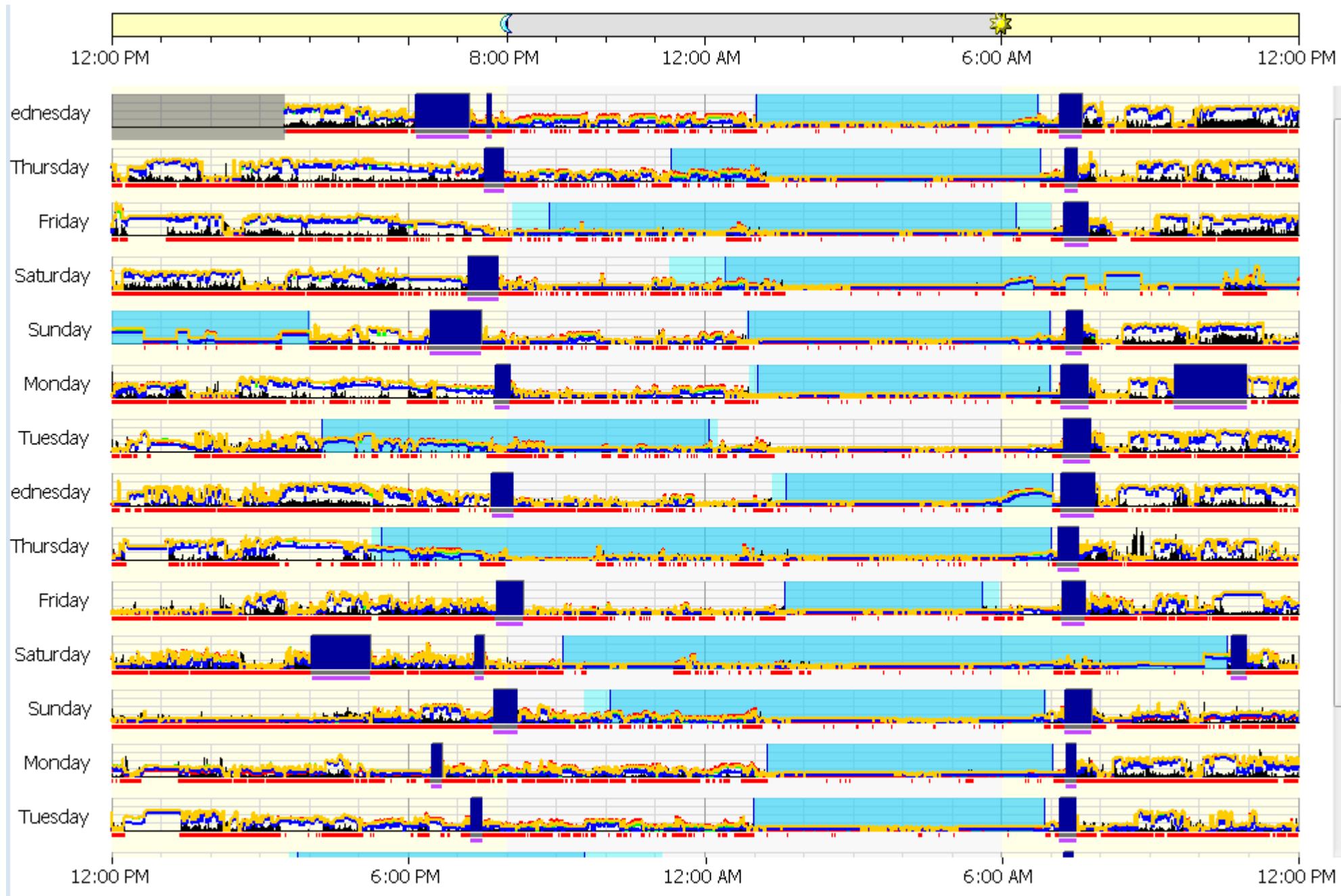
Today's Date	Day of the week	Type of Day Work, School, Off, Vacation	Noon	1PM	2	3	4	5	6PM	7	8	9	10	11PM	Midnight	1AM	2	3	4	5	6AM	7	8	9	10	11AM
sample	Mon.	Work		E					A				l									M	C			

week 1

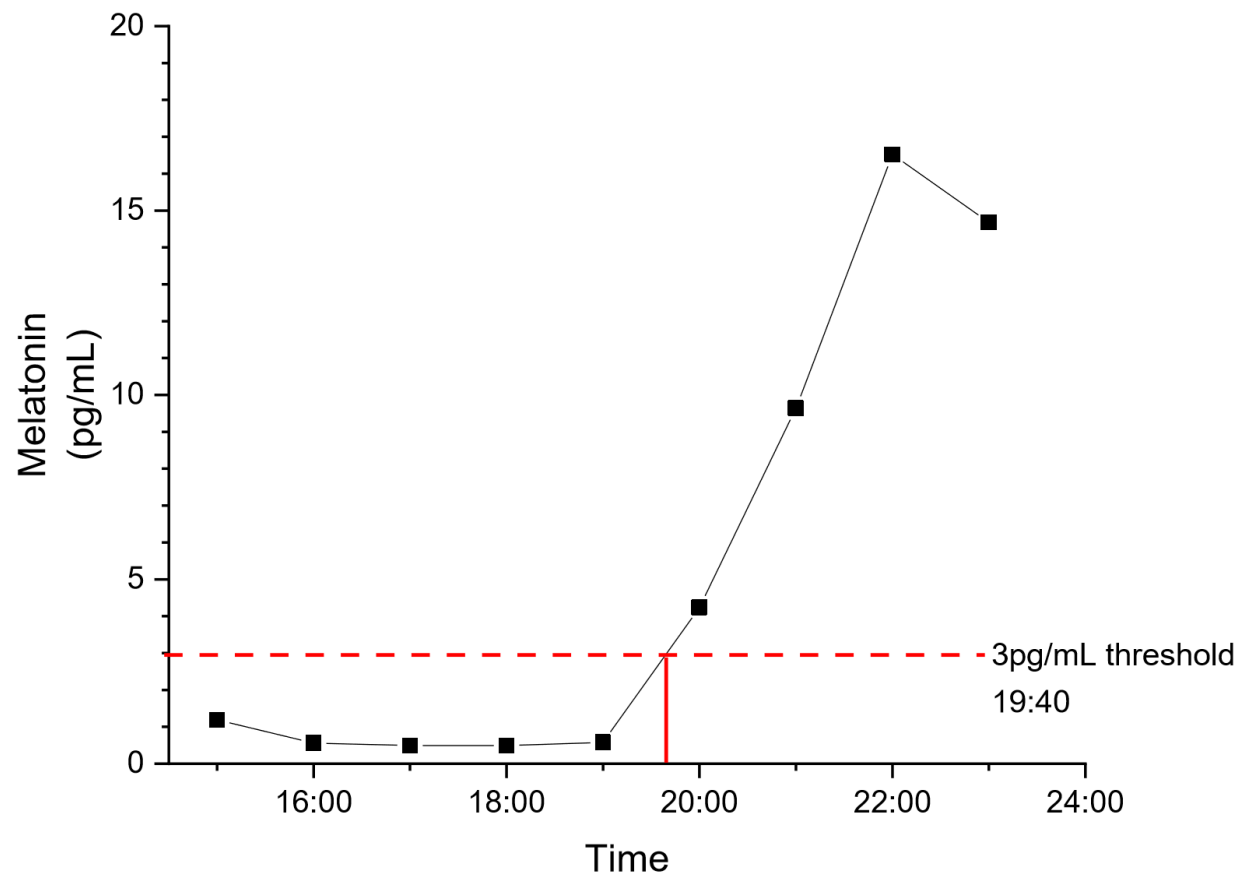
week 2

Activity/sleep patterns

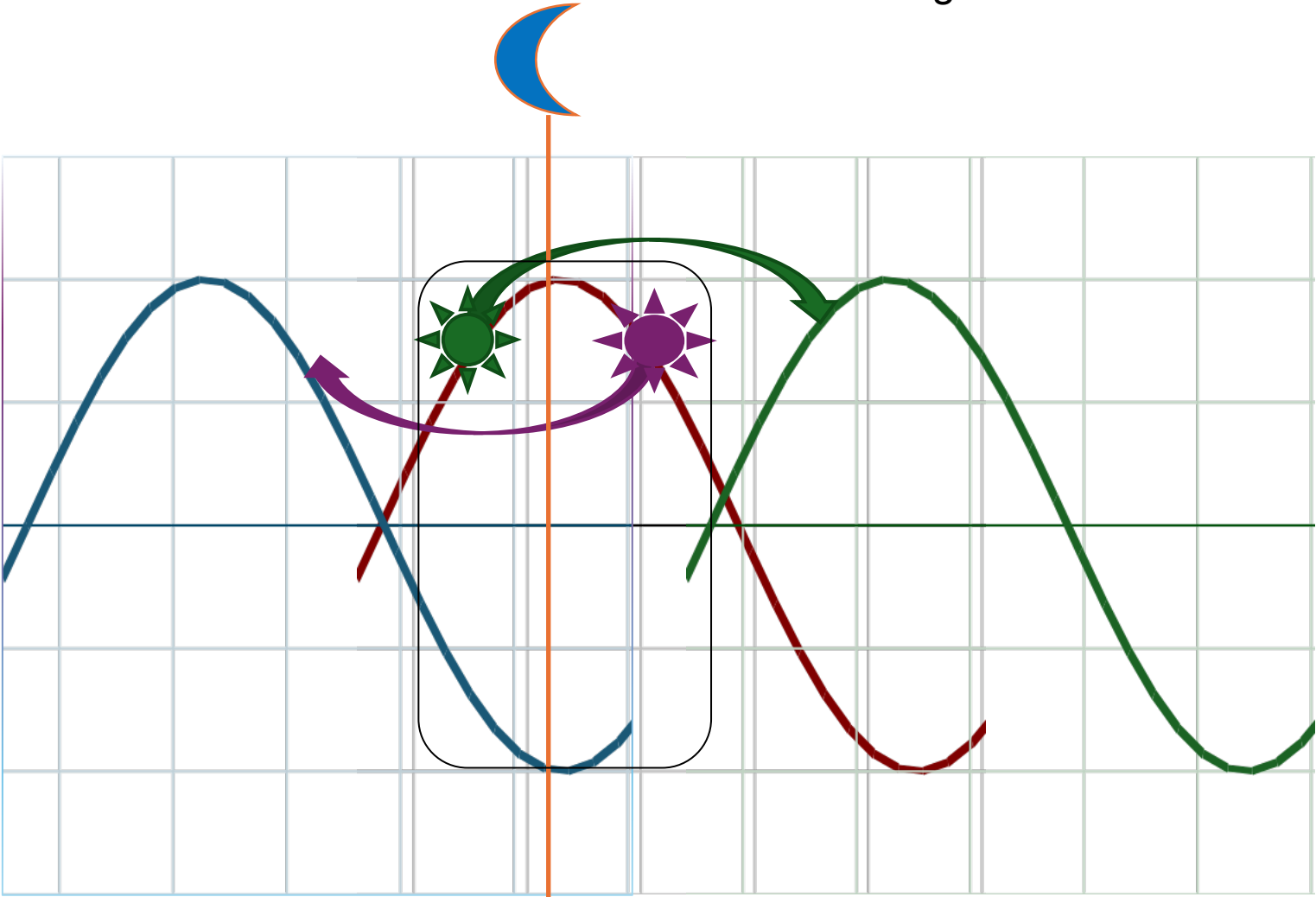




DLMO



Light treatment



Core body temperature minimum

Treatment of circadian rhythm disorders

- Timed light exposure
- For delayed sleep phase - Melatonin 0.5 mg taken 1 hr before required sleep onset time
 - Example – pt scheduled wake time is 6 am, needs 8 hrs sleep.
Instructions:
 - – melatonin, 0.5 mg at 9 pm
 - Low light levelt 9-10 pm (candle light level)
 - Bedtime – 10 pm
 - Wake – 6 am
 - Bright/blue light – 6 am
- Other help – re-timer glasses, potentially other hypnotics or stimulants

Patient C

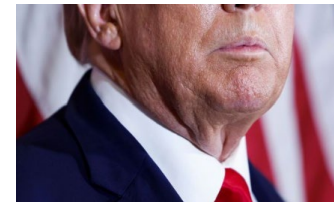
- A 66 year old woman presents with very fragmented sleep
- She is tired during the day and sometimes is drowsy during the day
- During the 2020 pandemic, she changed lifestyle (used to be an avid swimmer in indoor pool at her gym) and has gained >30 lb
- She reports significant snoring
- Sometimes wakes up gasping

Recognizing sleep disorders

- Obstructive sleep apnea
 - Large neck
 - Small chin
 - Crowded upper airway
- Common symptoms
 - Asleep in the waiting room
 - Overall sleepiness/fragmented sleep
 - Concentration difficulties
 - High blood pressure



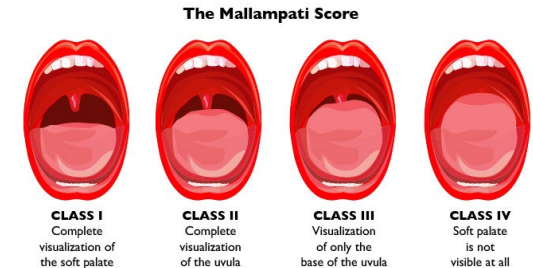
Small chin



Large neck

Obstructive Sleep Apnea

- Snoring/apneas/gasping upon awakening
- Insomnia – particularly in women,
- Sleep fragmentation
- Nonspecific symptoms
 - Morning headache, better over the course of the day
 - Panic attacks at night
 - Attention deficits,
 - Mood disturbance
 - Others – nocturia, night sweats, erectile dysfunction, etc.
 - Aggravation of other disease (e.g. recurrent seizures in a previously controlled epilepsy pt; new seizures in late adulthood)
- Aggravated by alcohol, sedatives, and supine sleep position
- Exam hint – do you see the uvula?

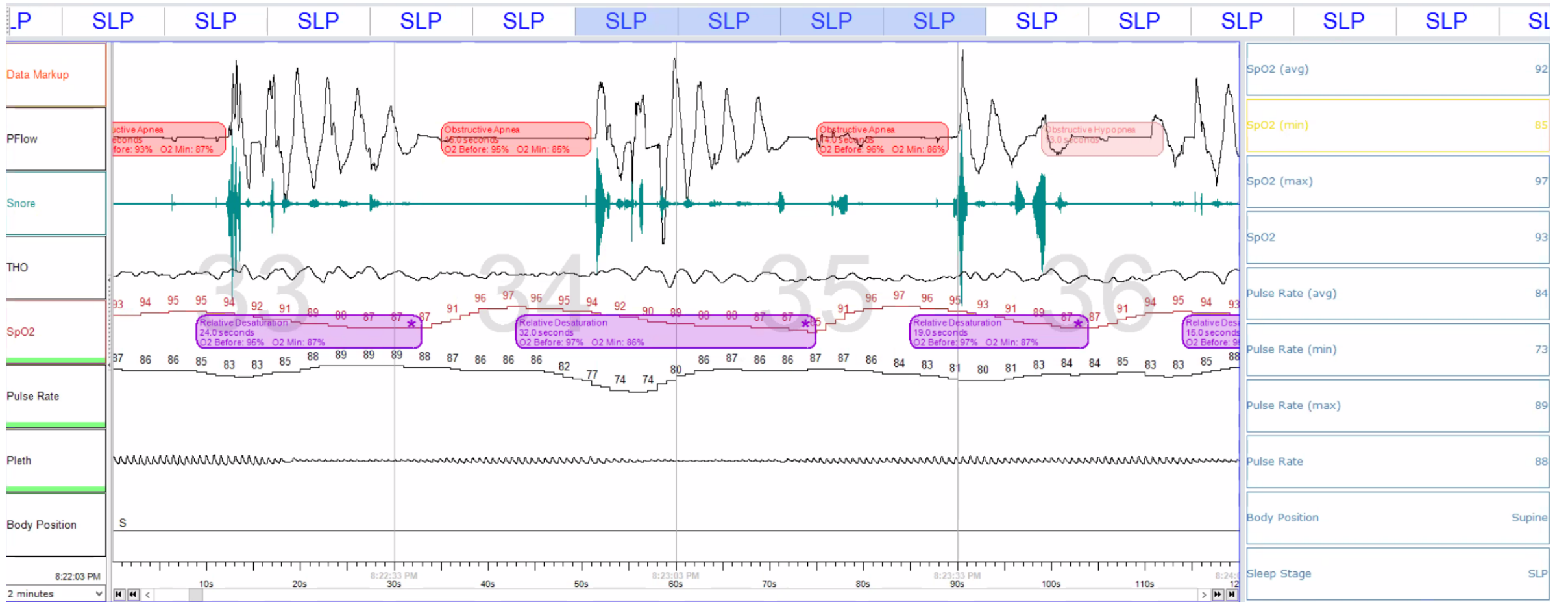


Screening for OSA (STOP BANG)

- Snoring ?
 - Do you Snore Loudly (loud enough to be heard through closed doors or your bed-partner elbows you for snoring at night)?
- Tired ?
 - Do you often feel Tired, Fatigued, or Sleepy during the daytime (such as falling asleep during driving or talking to someone)?
- Observed ?
 - Has anyone Observed you Stop Breathing or Choking/Gasping during your sleep ?
- Pressure ?
 - Do you have or are being treated for High Blood Pressure ?
- Body Mass Index more than 35 kg/m²?
- Age older than 50 ?
- Neck size large ? (Measured around Adams apple)
 - For male, is your shirt collar 17 inches / 43cm or larger?
 - For female, is your shirt collar 16 inches / 41cm or larger?
- Gender = Male ?
- Yes on >3 questions – moderate to high risk of OSA

Home Sleep Test

- Three channels minimum
- No measure of sleep available
- Adequate for objective confirmation of obstructive sleep apnea
- Negative test does not rule out obstructive sleep apnea
- Cannot evaluate PLMS, RBD or other movement disorders or the possibility of nocturnal seizures



Active Apnea
6.0 seconds
O2 Before: 93% O2 Min: 87%

Obstructive Apnea
46.0 seconds
O2 Before: 95% O2 Min: 85%

Obstructive Apnea
17.0 seconds
O2 Before: 96% O2 Min: 86%

Obstructive Hypopnea
3.0 seconds
O2 Before: 93% O2 Min: 87%

Relative Desaturation
24.0 seconds
O2 Before: 95% O2 Min: 87%

Relative Desaturation
32.0 seconds
O2 Before: 97% O2 Min: 86%

Relative Desaturation
19.0 seconds
O2 Before: 97% O2 Min: 87%

Relative Desaturation
15.0 seconds
O2 Before: 94% O2 Min: 85%

8:22:03 PM

8:22:33 PM

8:23:03 PM

8:23:33 PM

8:24:03 PM

2 minutes

10s

20s

30s

40s

50s

60s

70s

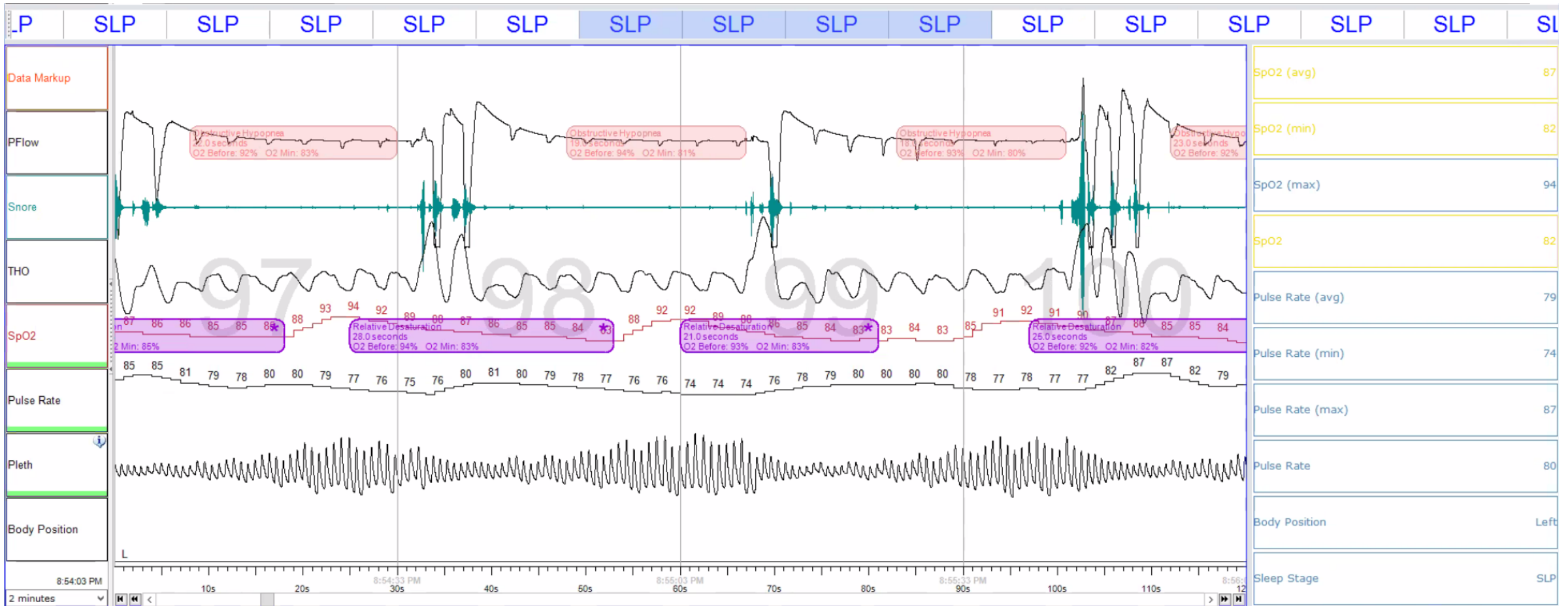
80s

90s

100s

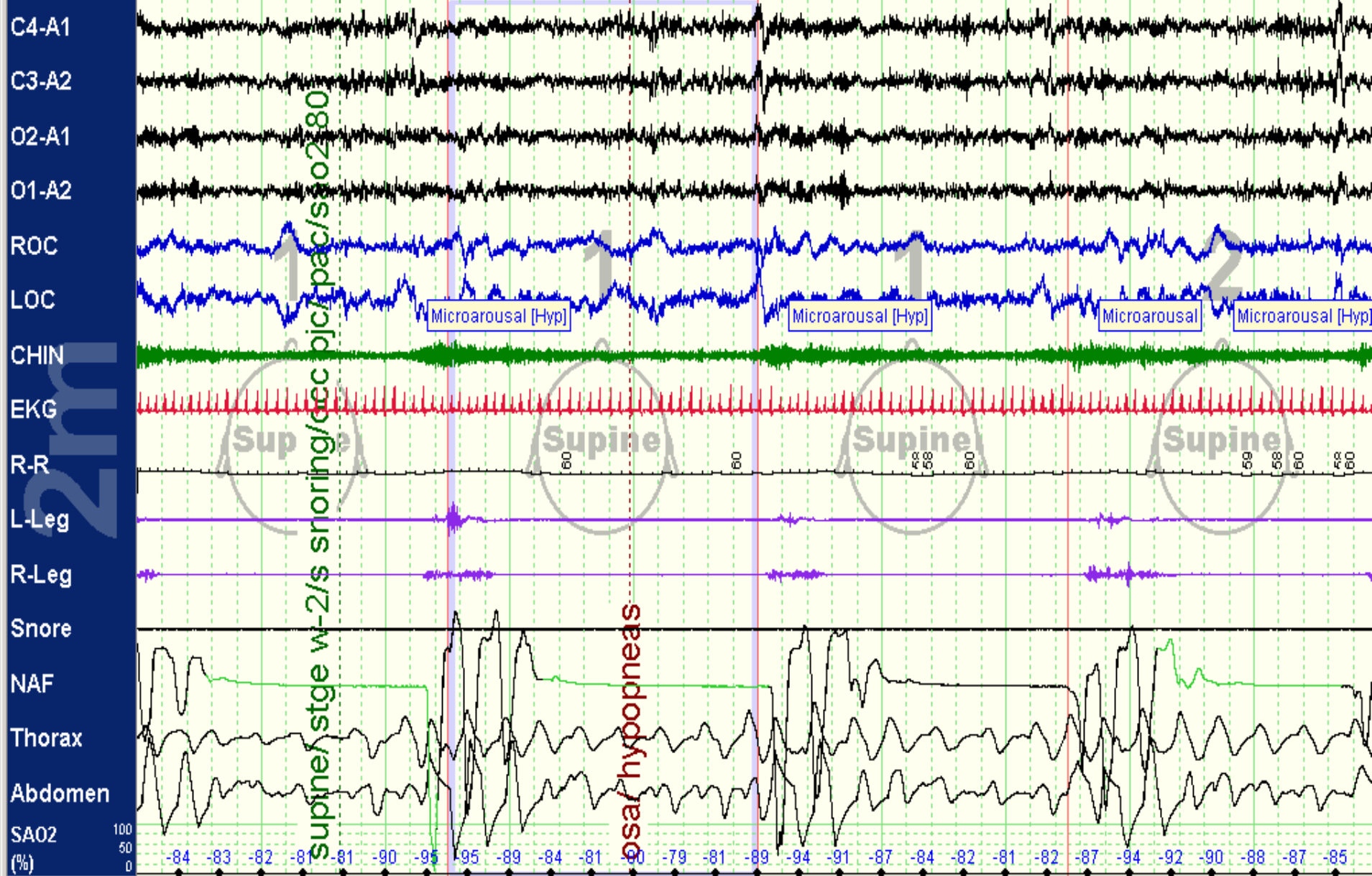
110s

120s



PSG - polysomnogram

- Gold standard for overnight evaluation of sleep
- Performed in a sleep laboratory
- Continuous video monitoring allows direct observation and in some circumstances – treatment
- Screens for a variety of sleep disorders
- Allows a good evaluation of
 - Obstructive sleep apnea
 - Central sleep apnea
 - Periodic limb movements of sleep
 - REM sleep behavior disorder
 - Overall sleep architecture
- Convenient
- More expensive than HST



Treating OSA

- C&E: Discussion of diagnosis, severity, and implication
 - Mild OSA (AHI \leq 15/hr) – consideration of symptom severity and comorbidities
 - Moderate OSA (AHI 15-30/hr.) – needs treatment, many options: PAP, oral appliances, surgical options
 - Severe (>30/hr.) needs treatment, PAP, some surgical options, including hypoglossal nerve stimulator. Dental devices may not be sufficient
 - All: discussion of aggravating factors
 - Temporary – alcohol, muscle relaxants
 - Longer term – weight gain



OSA - PAP treatment – follow-up



Hours of use - Medicare requires >4hrs, >70%



Residual AHI <5/hr



Pressure – auto



Leak

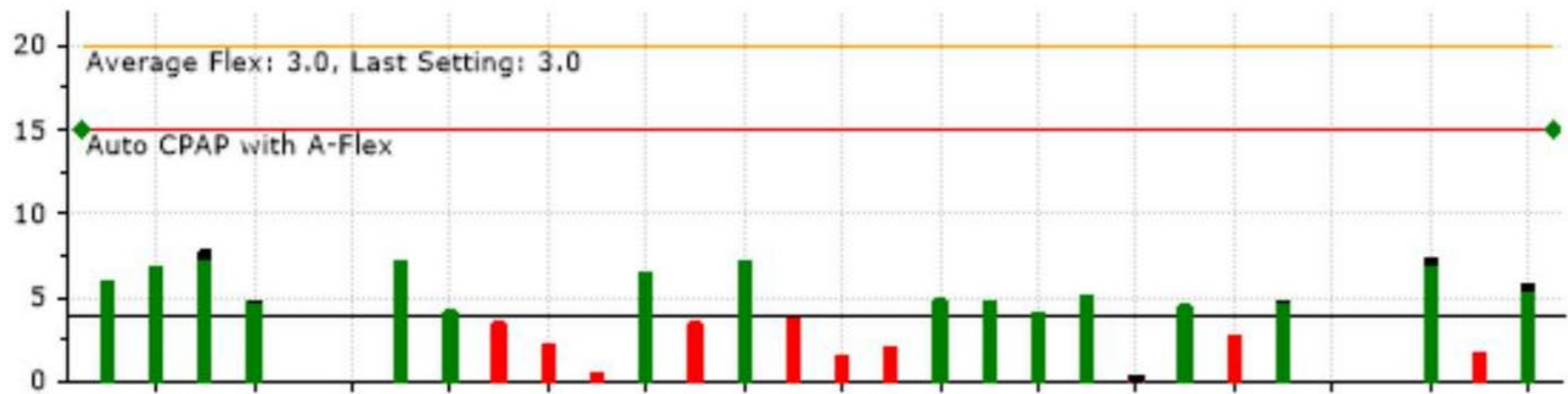


Periodic breathing



Humidification, settings etc.

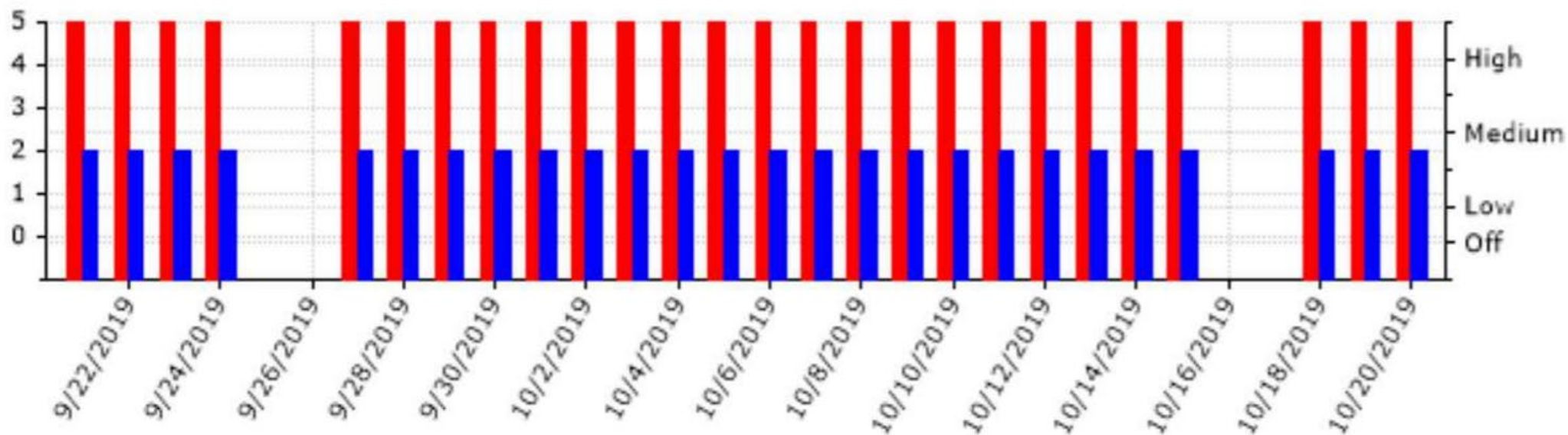
Hours of Usage



Device Humidification Settings

Heated Tube Temperature

Heated Tube Humidity Level



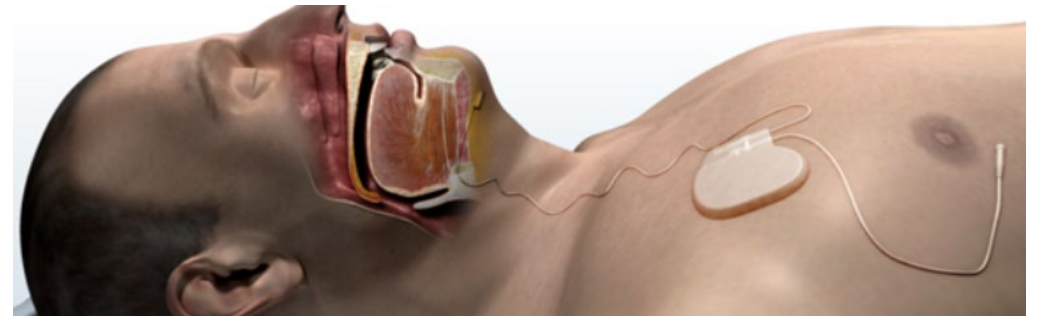
Days with Device Usage	26 days
Days without Device Usage	4 days
Percent Days with Device Usage	86.7%
Cumulative Usage	4 days 16 hrs. 17 mins. 45 secs.
Maximum Usage (1 Day)	7 hrs. 19 mins. 36 secs.
Average Usage (All Days)	3 hrs. 44 mins. 35 secs.
Average Usage (Days Used)	4 hrs. 19 mins. 8 secs.
Minimum Usage (1 Day)	3 mins. 50 secs.
Percent of Days with Usage >= 4 Hours	53.3%
Percent of Days with Usage < 4 Hours	46.7%
Total Blower Time	4 days 17 hrs. 50 mins. 51 secs.

Auto-CPAP Summary

Auto-CPAP Mean Pressure	4.6 cmH2O
Auto-CPAP Peak Average Pressure	5.8 cmH2O
Average Device Pressure <= 90% of Time	5.9 cmH2O
Average Time in Large Leak Per Day	23 secs.
Average AHI	2.7

OSA – alternatives to PCPAP

- BiPAP
- ASV
- OAT
- Surgical
 - Hypoglossal nerve stimulation therapy
 - Other surgical options



LGBTQ+ and sleep

- LGBTQ+ adolescents are more likely to report short sleep duration in comparison to their heterosexual peers*
- LGBTQ+ adults also have a higher likelihood of experiencing disordered sleep**
- Bisexual adults have a 1.4 times greater relative risk of developing sleep difficulties compared to heterosexual adults***

*Dai et al., 2019

**Patterson and Potter, 2020

***Duncan et al., 2018

