

HYPERSOMNIA

Solving the Mystery of the Sleepy Patient

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Medical Director

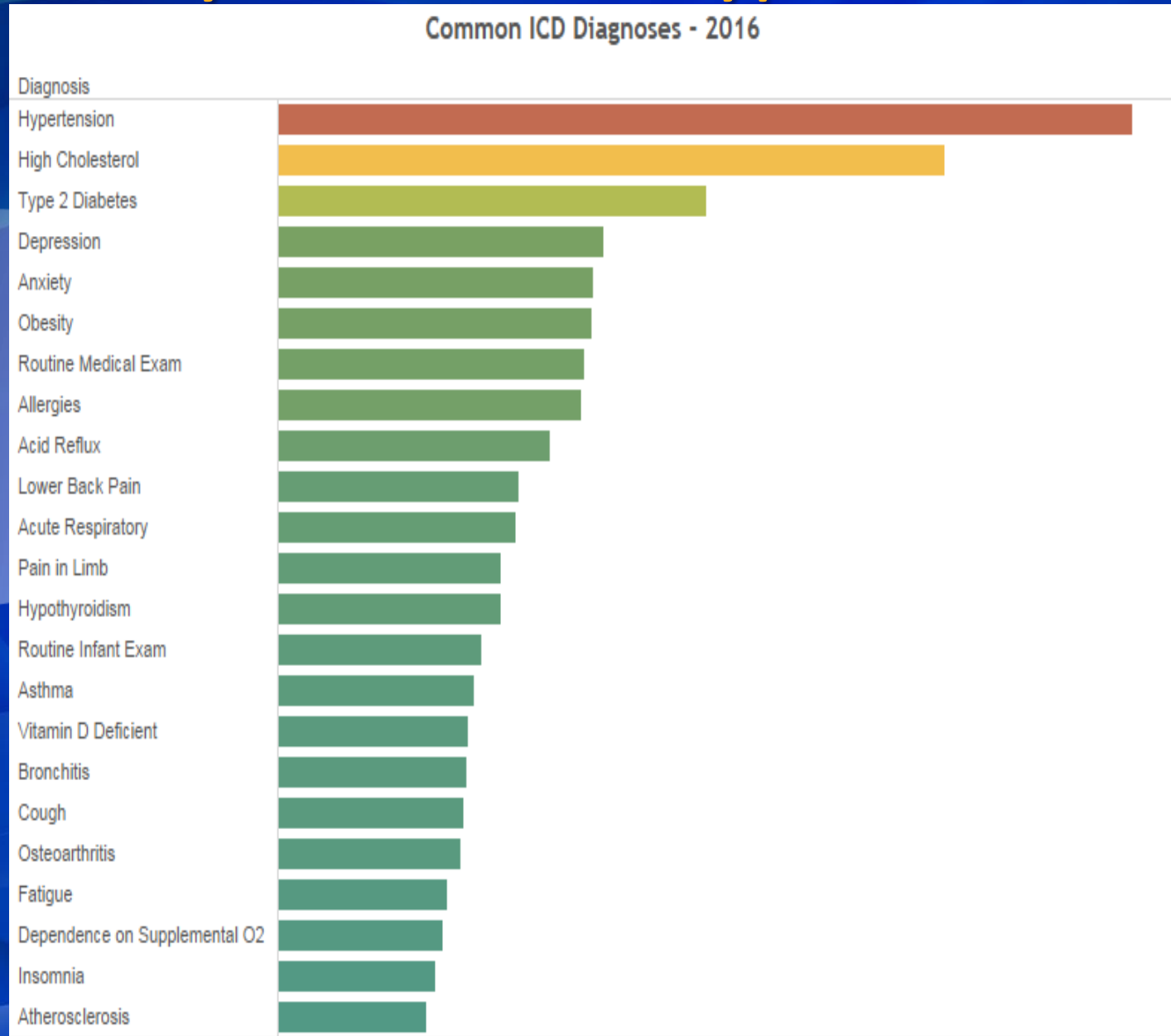
Presbyterian Westside Sleep Disorders Center

OBJECTIVES

- Learn tips for determining whether a patient has hypersomnia vs. fatigue
- Review the most common causes of hypersomnia
- Learn a framework for categorizing types of hypersomnia
- Learn the basic work up for hypersomnia
- Know what to refer



Why Talk About Hypersomnia?



FATIGUE

“I’m always sooooo tired!”

Is it a LACK OF ENERGY?



Or is it SLEEPINESS?



Is it LACK OF ENERGY?

- Desire for “rest” (but maybe not sleep)
- May be acute or chronic
- Mental/Emotional
 - Depression
 - Anxiety
 - Stress
- Physical
 - Chronic Illness
 - Medications
 - TSH/CBC/B12/CMP/Vit D?

Is it LACK OF ENERGY?

Fatigue is a lack of energy, a feeling of mental, emotional and physical exhaustion. It doesn't go away after sleep. Cure MS

#curems

Fatigue is different than being tired. When you are tired, you know that if you can just get some sleep you will feel better, but fatigue is still there when you wake up, it stays with you all day. It is a lack of energy, a feeling of mental, emotional and physical exhaustion

Facebook Page
FlourishMS Support



Is it SLEEPINESS?

Drowsiness

- The intermediate state between alert wakefulness and sleep.

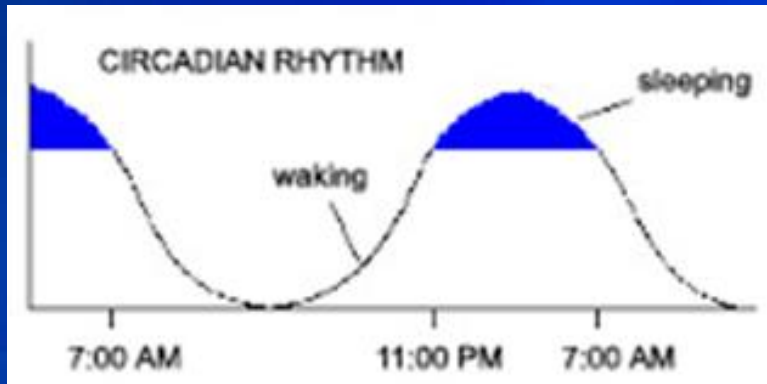


Sleep Propensity

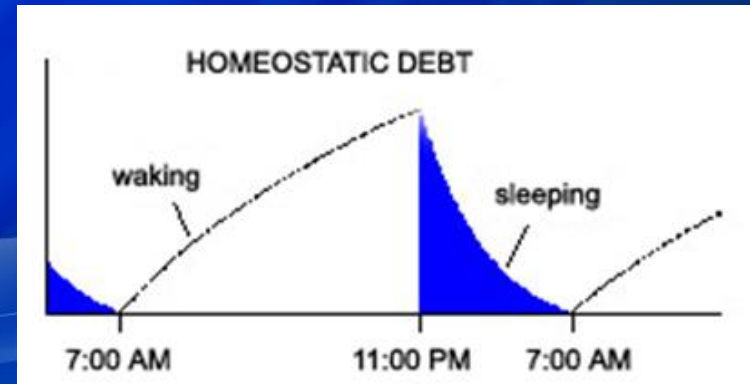
- The probability, ease or speed of making the transition from alert wakefulness, through drowsiness, to sleep under a given set of circumstances.
- Sleep propensity is what **Excessive Daytime Sleepiness (EDS)** relates to.

Sleep Propensity

**Circadian Rhythm
Highs and Lows
(Process C)**

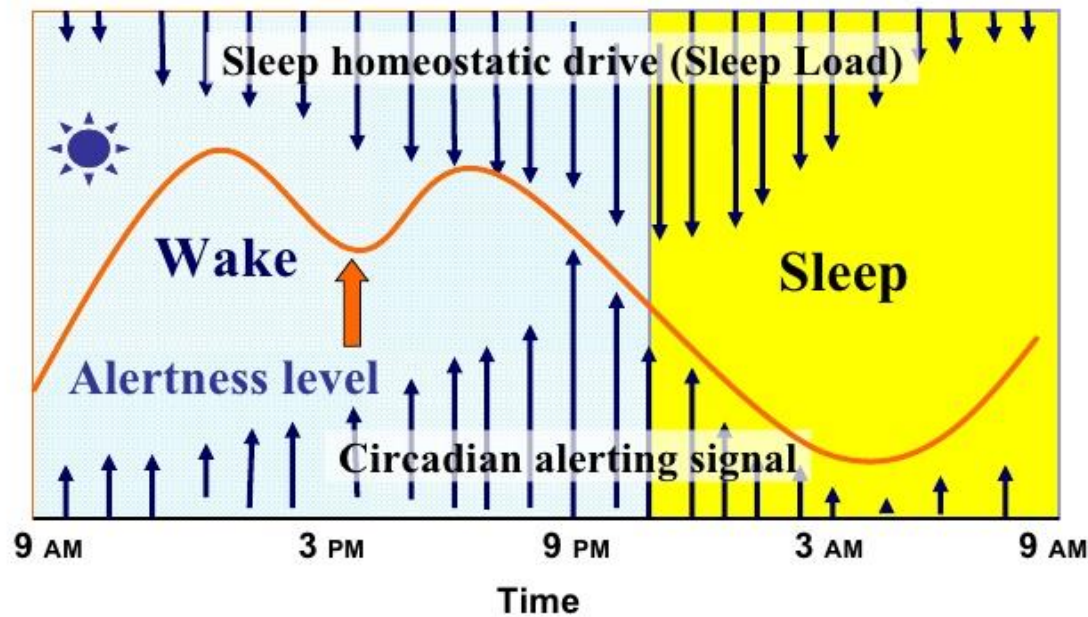


**Homeostatic Process
Length of Time Awake
(Process S)**



Sleep Propensity

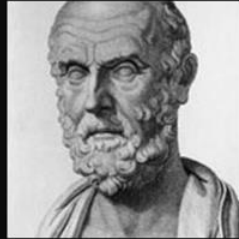
Circadian Rhythms and Sleep



When is “sleepy” too sleepy?



We know that being too sleepy is bad



Sleep and watchfulness, both of them, when immoderate, constitute disease.

~ Hippocrates

AZ QUOTES



Even where sleep is concerned, too much is a bad thing.

(Homer)

izquotes.com

When is “sleepy” too sleepy?

Excessive Daytime Sleepiness (EDS)

- The inability to remain fully awake during the wakefulness portion of the sleep/wake cycle



When is “sleepy” too sleepy? -----attempts to quantify it-----

- There are a multitude of different scales out there
- ESS
 - Epworth Sleepiness Scale
- ESS-CHAD
 - Epworth Sleepiness Scale for Children and Adolescents

SLEEPINESS?

- There are a multitude of different scales out there

- ESS

- Epworth Sleepiness Scale

- ESS-CHAD

- Epworth Sleepiness Scale for Children and Adolescents

- Whether someone is awake or asleep at any particular time depends not only on the time of day, how long they have been awake, the duration and quality of their previous sleep, but also on many other variables, including what they are doing at the time “ their posture and activity, both physical and mental, and the environmental stimulation to which they are subjected (Johns, 2010). Simply to lie down rather than stand up increases one’s likelihood of falling asleep – the change of posture increases one’s sleep propensity at the time.

ESS

- Self-administered questionnaire
- 8 questions which include 8 different activities
- Rate 0-3 (no chance to high chance), their usual chances of dozing off while engaged in those activities
- The ESS score (the sum of 8 item scores, 0-3) can range from 0 to 24.
- The higher the ESS score, the higher that person's sleep propensity or their daytime sleepiness.
- Takes 2-3 minutes to answer.

Epworth Sleepiness Scale

8 Questions – Self Administered

Interpretation of the ESS (DS = Daytime Sleepiness)

Epworth Sleepiness Scale

How likely are you to doze off or fall asleep in the following situations?
Use the following scale to choose the most appropriate number:

	0 no chance	1 slight chance	2 moderate chance	3 high chance
Sitting and reading	0	1	2	3
Watching television	0	1	2	3
Sitting inactive, in a public space	0	1	2	3
Lying down to rest in the afternoon when circumstances permit	0	1	2	3
Sitting and talking to someone	0	1	2	3
Sitting quietly after a lunch without alcohol	0	1	2	3
As a passenger in car for an hour without a break	0	1	2	3
In a car, while stopped for a few minutes in traffic	0	1	2	3

Total Score:

- **0-5 Lower Normal DS**
- **6-10 Higher Normal DS**
- **11-12 Mild EDS**
- **13-15 Moderate EDS**
- **16-24 Severe EDS**

Epworth Sleepiness Scales

ESS

Epworth Sleepiness Scale

Name: _____ Today's date: _____

Your age (Yrs): _____ Your sex (Male = M, Female = F): _____

How likely are you to doze off or fall asleep in the following situations, in contrast to feeling just tired?

This refers to your usual way of life in recent times.

Even if you haven't done some of these things recently try to work out how they would have affected you.

Use the following scale to choose the **most appropriate number** for each situation:

- 0 = would **never** doze
- 1 = **slight chance** of dozing
- 2 = **moderate chance** of dozing
- 3 = **high chance** of dozing

It is important that you answer each question as best you can.

Situation	Chance of Dozing (0-3)
Sitting and reading _____	
Watching TV _____	
Sitting, inactive in a public place (e.g. a theatre or a meeting) _____	
As a passenger in a car for an hour without a break _____	
Lying down to rest in the afternoon when circumstances permit _____	
Sitting and talking to someone _____	
Sitting quietly after a lunch without alcohol _____	
In a car, while stopped for a few minutes in the traffic _____	

THANK YOU FOR YOUR COOPERATION

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ESS-CHAD

Epworth Sleepiness Scale for Children and Adolescents
ESS-CHAD

Your name: _____ Today's date: _____

How old are you? _____ (years) Boy? () or Girl? () tick one space

Over the last month, how likely have you been to fall asleep while doing the things that are described below (activities)?

Even if you haven't done some of these things in the last month, try to imagine how they would have affected you.

Use the following scale to choose one number that best describes what has been happening to you during each activity over the last month. Write that number in the box below.

- 0 = would **never** fall asleep
- 1 = **slight chance** of falling asleep
- 2 = **moderate chance** of falling asleep
- 3 = **high chance** of falling asleep

It is important that you answer each question as best you can

Activities	Chance of falling asleep (0 - 3)
Sitting and reading _____	
Sitting and watching TV or a video _____	
Sitting in a classroom at school during the morning _____	
Sitting and riding in a car or bus for about half an hour _____	
Lying down to rest or nap in the afternoon _____	
Sitting and talking to someone _____	
Sitting quietly by yourself after lunch _____	
Sitting and eating a meal _____	

Thank you

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Name: _____ Date: ____/____/____ Hospital No: _____ Date of Birth: ____/____/____

In contrast to just feeling tired, how likely are you to doze off or fall asleep in the following situations? Even if you have not done some of these things recently, try to work out how they would affect you. Use the following scale to choose the most appropriate number for each situation.

Situation ☒ Please tick box	0 No chance of dozing	1 Slight chance	2 Moderate chance	3 Definitely would doze
Sitting and reading	☐	☐	☐	☐
Watching TV	☐	☐	☐	☐
Sitting inactive in a public place (e.g. Theatre or a meeting)	☐	☐	☐	☐
As a passenger in a car for an hour without a break	☐	☐	☐	☐
Lying down to rest in the afternoon when circumstances permit	☐	☐	☐	☐
Sitting and talking to someone	☐	☐	☐	☐
Sitting quietly after lunch without alcohol	☐	☐	☐	☐
In a car, while stopped for a few minutes in traffic	☐	☐	☐	☐

- Hypersomnia, or EDS, is usually a symptom of a condition.
- According to the National Sleep Foundation, up to 40% of people have some symptoms of hypersomnia from time to time.

Causes of Hypersomnia

Sleep Disorders

- Behaviorally induced insufficient sleep syndrome
- Obstructive Sleep Apnea
- Periodic Limb Movements of Sleep
- Narcolepsy
- Idiopathic Hypersomnia
- Recurrent hypersomnia

Other

- Metabolic syndromes
- Toxic or infectious disease processes
- Drugs that suppress CNS alerting systems

Neurologic Processes

- Niemann-Pick type C disease
- Prader-Willi
- Myotonic dystrophy
- Parkinson disease
- Alzheimer's disease
- Cervical spine or whiplash injury
- Multiple sclerosis
- Vascular disorders
- Encephalitis
- Lesions/tumors of thalamus, hypothalamus or brain stem
- Traumatic Brain Injury

Select causes of hypersomnia

- Insufficient Quantity
 - Behaviorally induced insufficient sleep syndrome
- Insufficient Quality
 - Obstructive Sleep Apnea
 - Periodic Limb Movement Disorder
- Central Origin (?Insufficient Circuitry?)
 - Narcolepsy
 - Recurrent Hypersomnia
 - Idiopathic Hypersomnia

Select causes of hypersomnia

- Insufficient Quantity
 - Behaviorally induced insufficient sleep syndrome



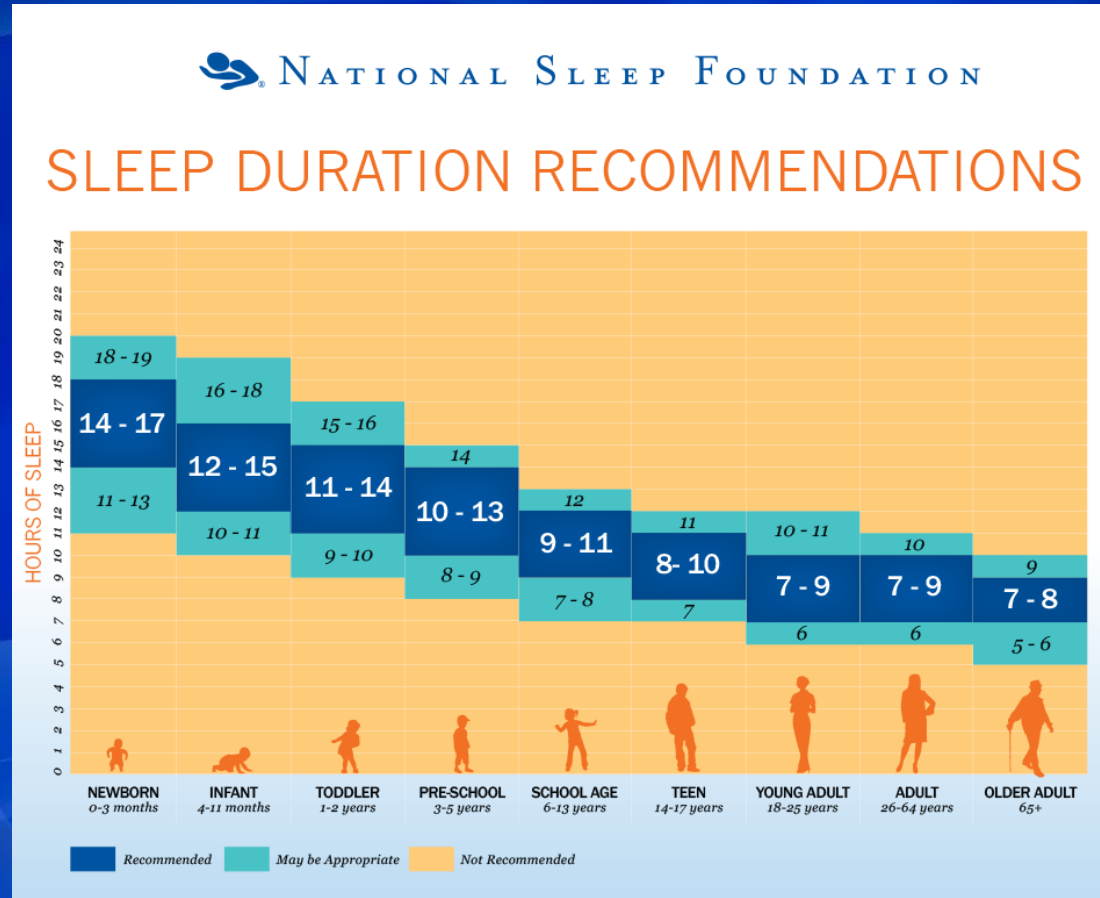
Insufficient Quantity - Sleep Restriction

- How Much Do We Need? Depends on who you are!
- Sloths in captivity may sleep 15-20 hours/day!



Insufficient Quantity - Sleep Restriction

- How Much Do We Need? **Age, Individual Variation**



SLEEPFOUNDATION.ORG | SLEEP.ORG

Hirshkowitz M, The National Sleep Foundation's sleep time duration recommendations: methodology and results summary, Sleep Health (2015), <http://dx.doi.org/10.1016/j.sleh.2014.12.010>

Insufficient Quantity - Sleep Restriction

How Much Do We Get?

Hands up
if you didn't
get enough
sleep last
night!



How Much Do We Get?

Average American Sleeps:

- 6.9 h on weekdays
 - 68% sleep < 8h on weekdays
- 7.5 h on weekends
 - 39% sleep < 7h on weekends

Kids:

- <45% age 6-17 are getting ≥ 9 h
- <33% age 12-14 are getting ≥ 9 h
- 56% age 15-17 are getting 7h

Insufficient Quantity - Sleep Restriction

Reports of “falling asleep during the day and frequent sleep attacks”:

- 5-10% of young and middle-aged adults
- 20-30% of elderly

If you short yourself 1 hour per night every day:

- 365 hours of sleep debt by the end of the year



Consequences of Sleep Restriction

Behavioral/Mood

Physiologic



Behaviorally induced insufficient sleep syndrome

- Hx sleep deprivation
- May be a result of social or work-related factors
- Especially common in adolescents and shift workers
- Attempts to “catch up” on sleep on the weekends
- Pt may have neurocognitive impairment due to insufficient sleep time
- **TREATMENT:**
 - behavioral modification
 - aka “sleep more”

Select causes of hypersomnia

- Insufficient Quality
 - Obstructive Sleep Apnea
 - Periodic Limb Movement Disorder

Obstructive Sleep Apnea



- Most prevalent sleep-breathing disturbance
- Repetitive obstruction of the upper airway
 - Often results in O₂ desaturation and arousals from sleep
 - Closure may be total or partial
- **24% of men and 9% of women** in the general population
- May be associated with :
 - excessive daytime sleepiness
 - unrefreshing sleep
 - poor concentration/memory

Obstructive Sleep Apnea



- Decreased quality of life increased incidence of:
 - coronary artery diseases
 - hypertension
 - congestive heart failure
 - cerebrovascular accidents
 - gastroesophageal reflux disease
- **Avg life span of pt with untreated OSA is 58 years, versus avg life span of 78 yr for men and 83 yr for women.**

Quick OSA Screen – STOP BANG

STOP-BANG Questionnaire

- S – Snoring: Do you snore loudly?
- T – Tired: Do you feel tired, sleepy during daytime?
- O – Observed: Has anyone observed you stop breathing during sleep?
- P – Blood Pressure: Are you being treated or had you been treated for hypertension?
- B – BMI: Body mass index > 35
- A – Age: Age over 50 years
- N – Neck: Neck circumference greater than 40 cm
- G – Gender: Male gender

Low Risk : Yes to 0 - 2 questions

Intermediate Risk : Yes to 3 - 4 questions

High Risk : Yes to 5 - 8 questions

Periodic Limb Movement Disorder (PLMD)

- Periodic Limb Movements of Sleep (PLMS): found in 5% of >30yo, and nearly 50% of >65yo.
- Involuntary, repetitive limb movements:
 - Occur at periodic intervals, usually 20–40 seconds apart.
 - PLMS are similar to a Babinski.
- Excessive leg movements reported by bed partner
- PLMS related to (but should not be confused with) Restless Legs Syndrome.
 - 80% of those with RLS will have PLMS
 - Only 20% of those with PLMS will have RLS

Periodic Limb Movement Disorder (PLMD)

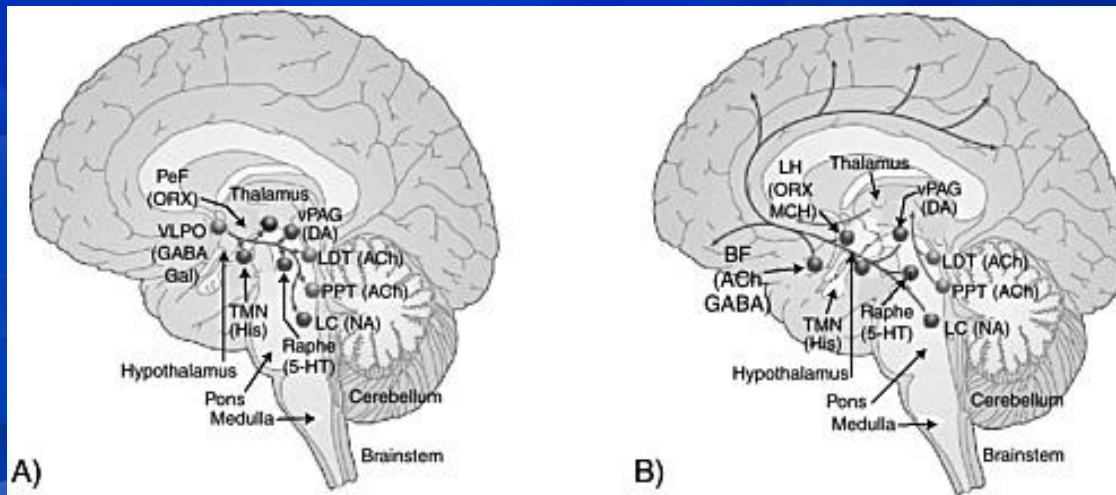
- With PLMD:
 - The PLMS cause repeated partial arousal or awakening.
 - Pts usually does not know the cause of their EDS
 - Pts may complain of EDS, as well as difficulty falling and/or staying asleep.
- Exacerbated by: TCAs, SSRIs, stress, sleep deprivation, caffeine, and alcohol.
- PLMD treatments: dopamine agonists (eg ropinirole, pramipexole), anticonvulsants (gabapentin), benzodiazepines (clonazepam), possibly muscle relaxants.

Periodic Limb Movements of Sleep

- video

Select causes of hypersomnia

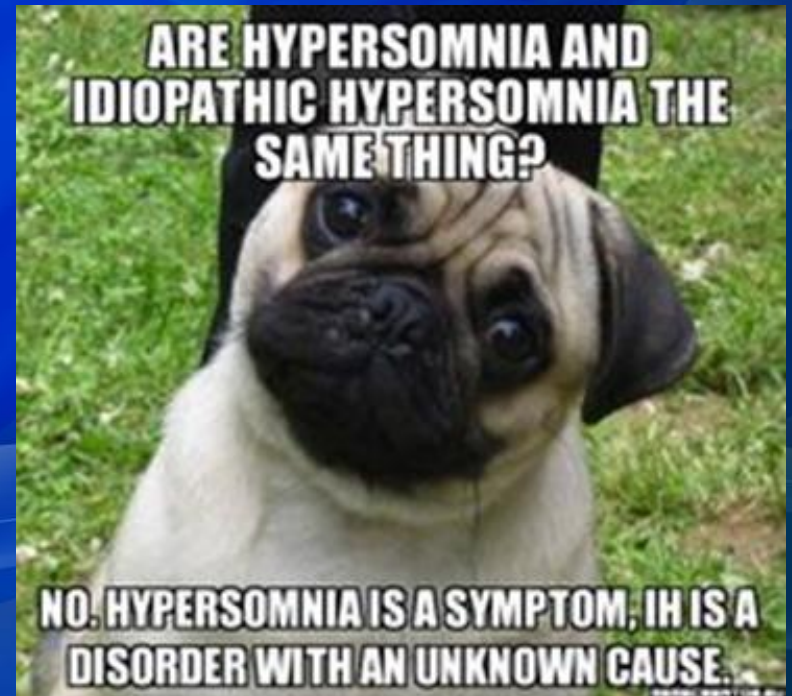
- Central Origin (?Insufficient Circuitry?)
 - Idiopathic Hypersomnia
 - Recurrent Hypersomnia
 - Narcolepsy
- Neuropathology within the Sleep-Wake circuitry of the brain



Central Origin

Idiopathic Hypersomnia

- With/Without Long Sleep Time
 - With - ≥ 10 hr sleep/night
 - Without – >6 & <10 hr sleep/night
- Non-refreshing sleep; difficulty waking up
- Naps are not refreshing
- Laborious morning or end-of-nap arousals
- Almost daily EDS for at least 3 months



Idiopathic hypersomnia



- Exact prevalence unknown
 - Est WITH long sleep time (>10h/d) 1/10,000 - 1/25,000
 - Est WITHOUT long sleep time 1/11,000 - 1/100,000
- Male=Female
- Usually stats before age 25yo

Idiopathic hypersomnia



- First described in 1950s
- Not well understood and other causes of hypersomnia have to be r/o'd
- Etiology is ??????????
 - ?abnormal melatonin secretion
 - ?circadian dysfunction
- Often has negative social & professional impact

Central Origin

Recurrent Hypersomnia

- Kleine-Levin Syndrome

Kleine-Levin Syndrome (KLS)

- Type of Recurring Hypersomnia
- EDS lasts 2days to 4wks
- Occurs at least once/yr (almost never >15mo in between)
- During active episode sleep needs drastically increase (>12hr in 24)
- Also known as “Sleeping Beauty Syndrome”



Kleine-Levin Syndrome (KLS)

- Rare (1 in 1 million)
- Peak age at initial presentation is 2nd decade of life
 - But literature reports cases from age 4yo-80yo
- Men > women (2:1)
- No clear heritability or genetic susceptibility
- Normal alertness, cognitive functioning, & mental status between attacks
- **Hypersomnia + hyperphagia + hypersexuality**
- Cognitive abnormalities: feeling of unreality, confusion, hallucinations.
- Abnormal behavior such as irritability, aggression, odd behavior

KLS

- Precipitating factor reported in 9 of 10 pts
 - Infection or high fever is most common complaint
 - Stress, etoh, travel, sleep deprivation
 - <15% can identify a prodromal event to account for recurrent episodes
- Recurrence becomes less frequent, less severe, & shorter duration as time passes
- CT/MRI normal but SPECT shows reduced perfusion of thalamus during active episode and normal when symptoms resolved
- Limited response to tx with: valproic acid, lithium, amantadine, or lamotrigine
- Modafinil decreases the duration of episode but doesn't change recurrence

Kleine-Levin Video

video

Menstrual-related hypersomnia

- Type of Recurring Hypersomnia
- Very rare
- May occur:
 - At menarche
 - During menstruation alone
 - During menstruation in conjunction with other factors such as etoh use or a bout of influenza
- Recurrent EDS lasting 2d – 4wk
- Recur at least 1x/yr
- Normal alertness, cognitive functioning, & mental status in between episodes
- ? Triggered by progesterone
- Possibly tx with OCPs

Central Origin

Narcolepsy

- Narcolepsy -
 - With Cataplexy (Type 1)
 - Without Cataplexy (Type 2)
- Inability to regulate sleep-wake cycles
 - Sleep intrudes on wakefulness and wakefulness intrudes on sleep
- Name comes from a combination of the Greek words narké (“numbness”) and leptos (“seizure”)

Narcolepsy

- Prevalence 25 - 50 per 100,000 people
- Male=Female
- Mean age onset = mid-20s
- Bimodal peak occurrences 15yo and 35yo
- Narcolepsy with cataplexy>>>without cataplexy
- Exclude hypersomnia from systemic disease, drugs/meds, CNS trauma/disease
- 1st degree relatives of pts with narcolepsy have 1-2% risk of developing the disorder

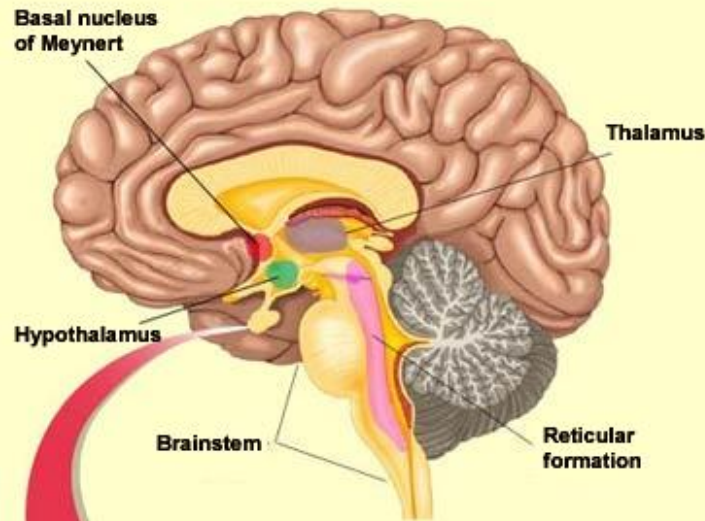
Narcolepsy -- Classic Tetrad + 1

- EDS (≥ 3 months)
 - Sleep Attacks – inadvertent and irresistible urge to sleep that appears without warning
- Cataplexy (75%) (loss of muscle tone triggered by laughter or strong emotion)
- Hypnagogic hallucinations (50-60%)
- Sleep paralysis (50-66%)
- (Fragmented sleep)

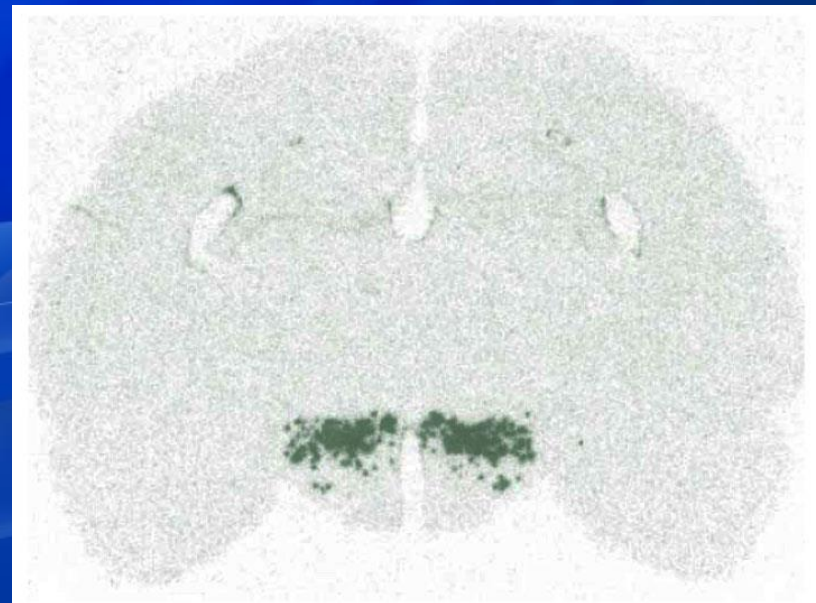
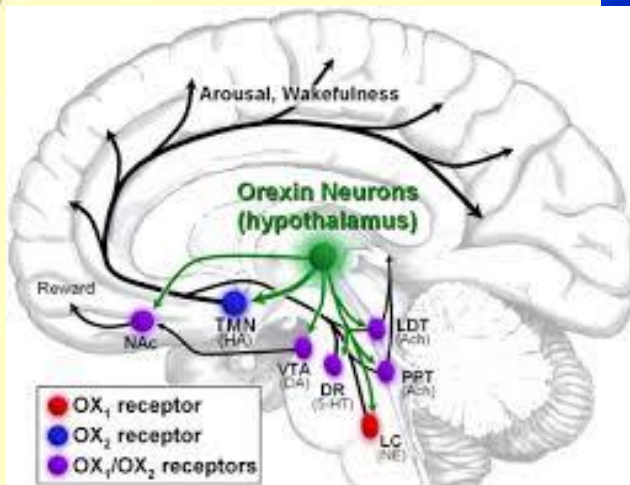
Narcolepsy with cataplexy

- EDS and episodic loss of muscle tone
 - Identified 1877
- Genetic basis
 - Human Leukocyte Antigen (HLA) types
 - HLA-DR2 Japanese population with narcolepsy
 - HLA-DQB1*0602 African Americans and Caucasians who have narcolepsy with cataplexy
 - 90% of pts with narcolepsy w/ cataplexy test +
 - But 12-34% of the general population has this allele
- Hypocretin/Orexin pathway
 - neuropeptide that regulates arousal, wakefulness, and appetite

Narcolepsy with cataplexy

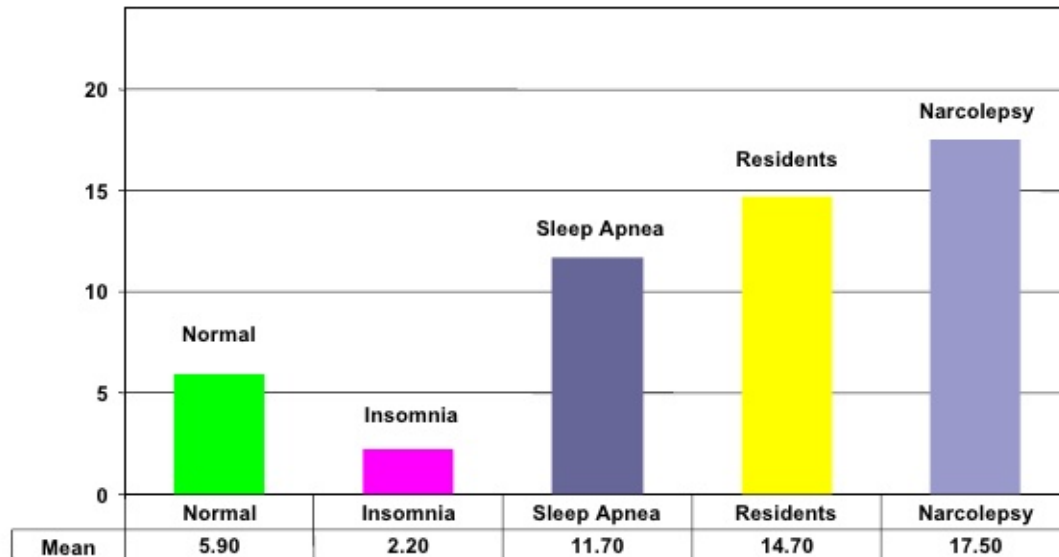


- 70,000 orexin producing neurons in lateral hypothalamus
- Project from to neurons and brain regions that modulate wakefulness.



Narcolepsy EDS

Epworth Sleepiness Scale



Sleepiness in residents is equivalent to that found in patients with serious sleep disorders.

Mustafa and Strohl, unpublished data. Papp, 2002

cataplexy

- Sudden, involuntary loss or decrease of muscle tone
 - Last few seconds to few minutes
- Most commonly precipitated by strong emotion
 - Usually laughter, elation, surprise
- May be profound or subtle
 - Profound
 - Generalized atonia (falls/injury)
 - Subtle muscle weakness
 - Slurring of speech
 - Buckling of knees
 - Jaw dropping
 - Head nodding

cataplexy

- Present in 50% of pts at dx
- About 40% will progress and have cataplexy later in the course of their disease
- Most will experience 1st episode w/in 10 yr of onset of EDS.

Cataplexy Video

video

Sleep paralysis

- Inability to move while totally aware of one's surroundings
- Either at arousal or sleep onset
- Rarely lasts more than a few minutes
- Occurs in 2/3 of patients with narcolepsy



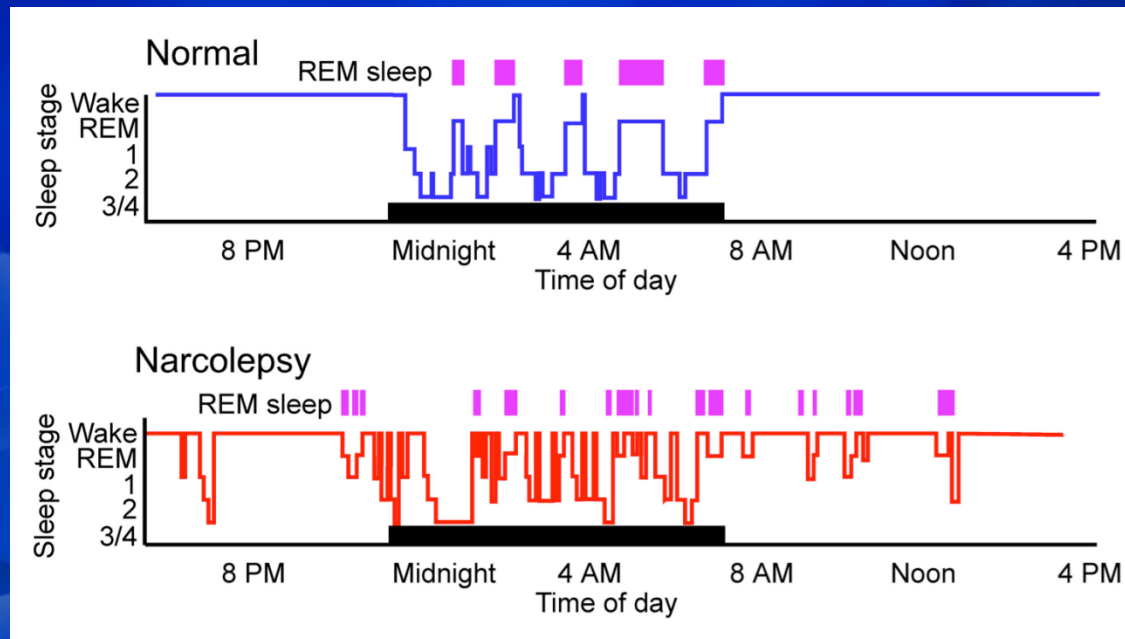
Hypnagogic/hypnopompic hallucinations

- Simple or complex visual hallucinations
- Could be auditory or tactile
- Occur at sleep transitions (falling asleep or waking up)
- Experienced by 2/3 of pts with narcolepsy



Disturbed night time sleep

- Vivid dreams
- Sleep fragmentation due to multiple arousals
- Early morning awakenings
- Nocturnal eating
- Unrefreshing nocturnal sleep



Pathophysiology

- Hypocretin/Orexin pathway and it's ability to regulate sleep and wakefulness
- CSF levels of hypocretin-1
- Hypothalamic hypocretinergic cell dropout in pts with narcolepsy with cataplexy
- Naps are usually refreshing

Diagnosis

- Multiple Sleep Latency Test
 - Overnight psg with at least 6hr (without other causes for EDS)
 - Five 20 minute nap opportunities (at 2hr intervals)
 - Mean Sleep Latency ≤ 8 min
 - 2 or more Sleep Onset REM Periods (SOREMPs)
- CSF hypocretin level < 110 pg/mL
- HLA typing???

Diagnosing Hypersomnia

- Polysomnogram (PSG) aka Sleep Study
- Multiple Sleep Latency Test (MSLT)

QUESTIONS?



- Learn tips for determining whether a patient has hypersomnia vs. fatigue
- Review the most common causes of hypersomnia
- Learn a framework for categorizing types of hypersomnia
- Learn the basic work up for hypersomnia
- Know what to refer