SLEEP-WAKE DISORDERS AND EATING DISORDERS

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How is your sleep? Assessment tool

✓ Check if any of the following apply to you:

- ❑ **Snore loudly**
- ❑ **You or others have observed that you stop breathing or gasp for breath during sleep**
- ❑ **Feel sleepy or doze off while watching TV, reading, driving or engaged in daily activities**
- ❑ **Have difficulty sleeping 3 nights a week or more (e.g. trouble falling asleep, wake frequently during the night or wake too early and cannot get back to sleep)**
- ❑ **Feel unpleasant, tingling, creeping feelings or nervousness and the urge to move in your legs when trying to sleep**
- ❑ **Interruptions to your sleep (e.g., nighttime heartburn, bad dreams, pain, discomfort, noise, sleep difficulties of family members, light or temperature)**

National Sleep Foundation

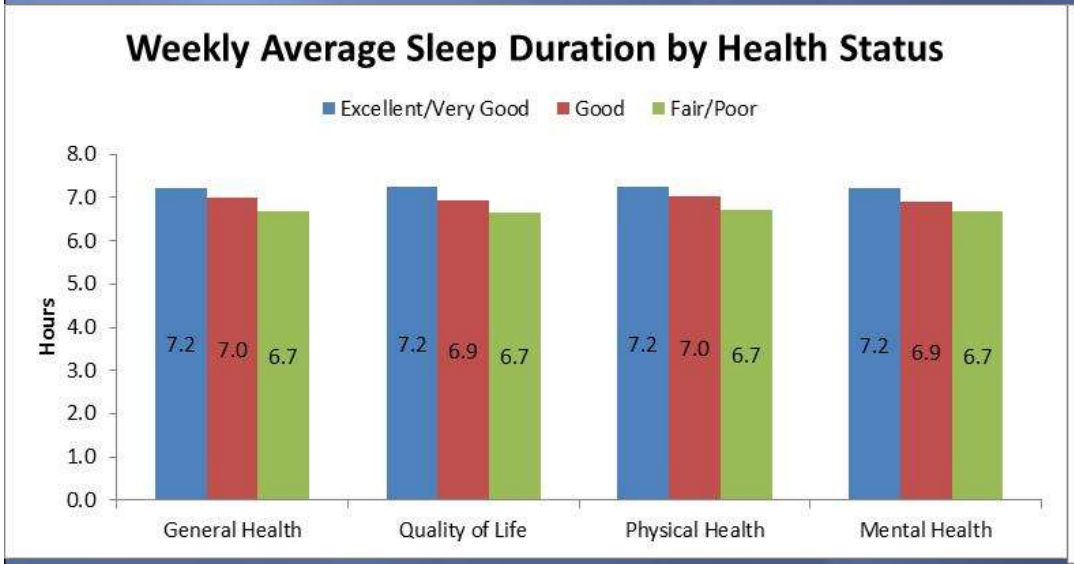
Outline

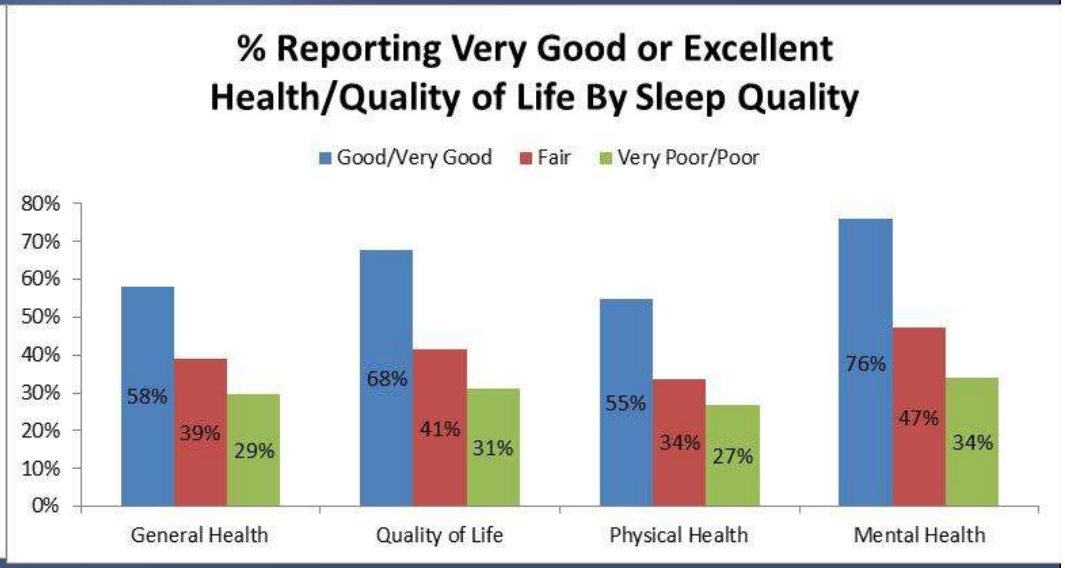
- Epidemiological data
- Physiology of sleep
- Dyssomnias
- Parasomnias

Sleep and General Health

Longer sleep duration and better sleep quality were associated with better health:

- those who rate their sleep quality more highly were also more likely to rate their health and quality of life as very good or excellent (all p<0001);
- those who rated their health and quality of life highly reported getting more sleep -- getting approximately 30-34 minutes more sleep (all p<.001).



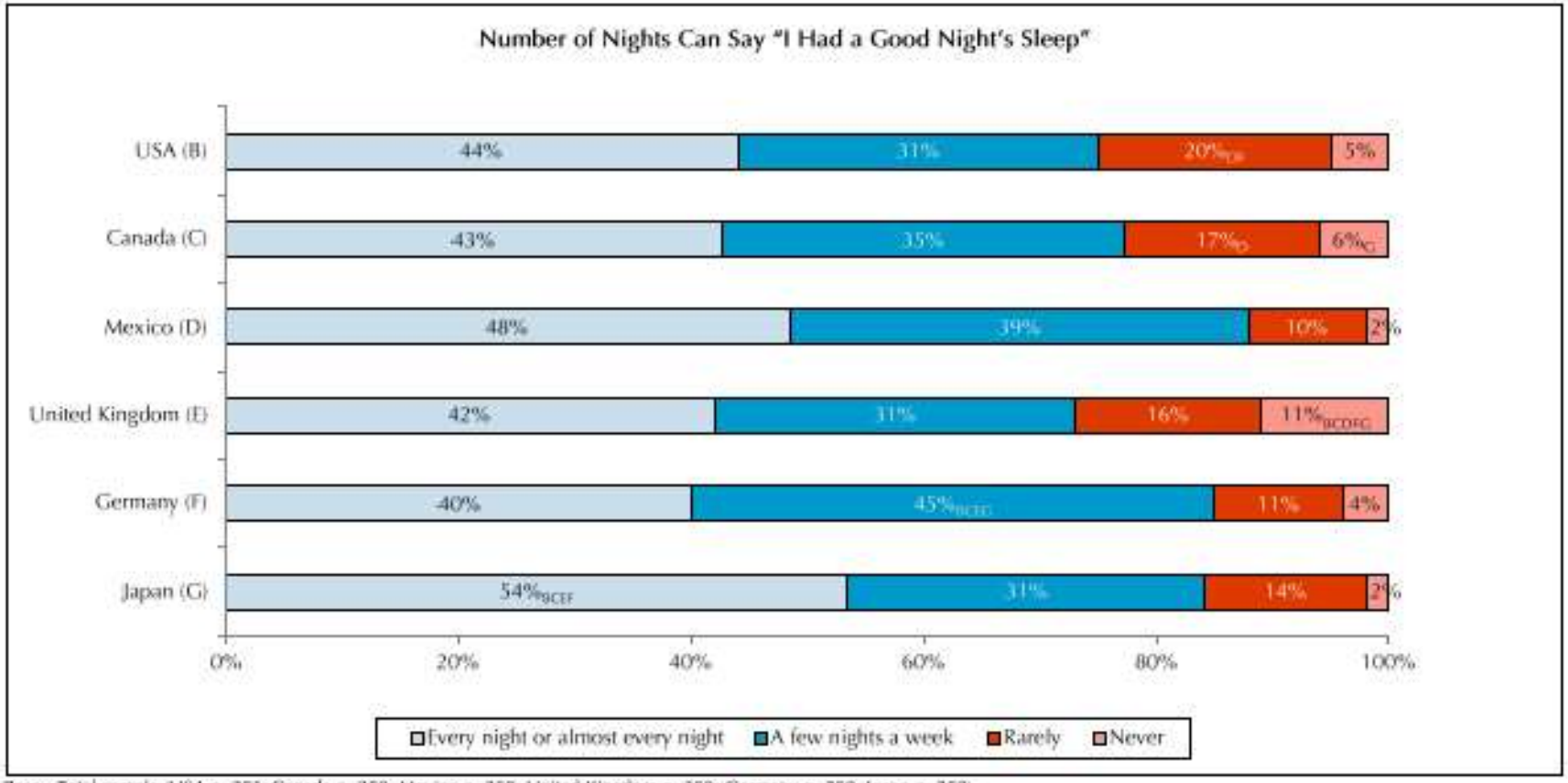


National Sleep Foundation, 2015

Sleep Habits (continued)

All respondents surveyed were asked how often they can say "I had a good night's sleep," using a scale of every night or almost every night, a few nights a week, rarely or never.

- More than one-half (54%) of those interviewed in Japan said they can say "I had a good night's sleep" every night or almost every night. This is significantly higher than all other countries surveyed with the exception of Mexico.
- Interestingly, 11% of those in the United Kingdom mentioned they can never say "I had a good night's sleep". This is significantly higher than all other countries surveyed.



Base= Total sample (USA n=251; Canada n=250; Mexico n=250; United Kingdom n=250; Germany n=250; Japan n=250)
Letters indicate significant differences at the 95% confidence level.
Q9

Impact on work, social life and health status

- ✓Missed work or events or errors at work;
- ✓The intimate relationship affected because of being too sleepy;
- ✓Problems in the relationship due to their or their partner's sleep disorders;
- ✓Driving drowsy;
- ✓Other psychiatric /somatic medical conditions.

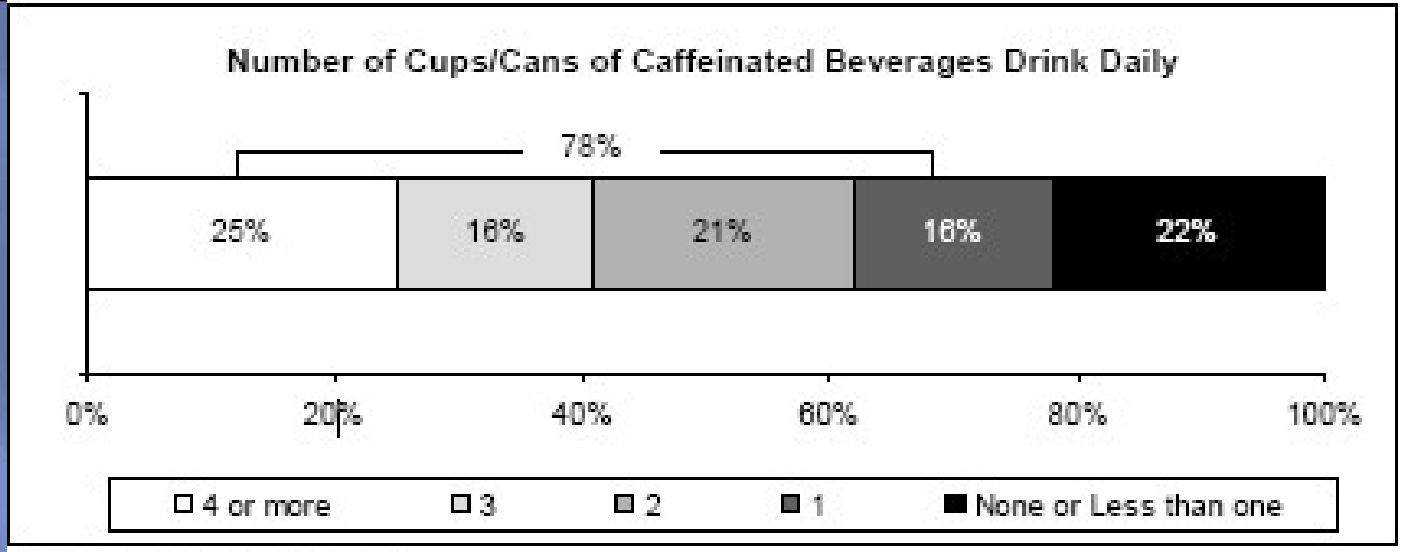
Those interviewed were asked the impact of not getting enough sleep on different aspects of their life. The percentages below represent those who stated that not getting enough sleep has an impact on the specific area of their life:

- In general, those interviewed in Japan cited not getting enough sleep has significantly less impact on certain aspects of their life as compared to the other countries interviewed.

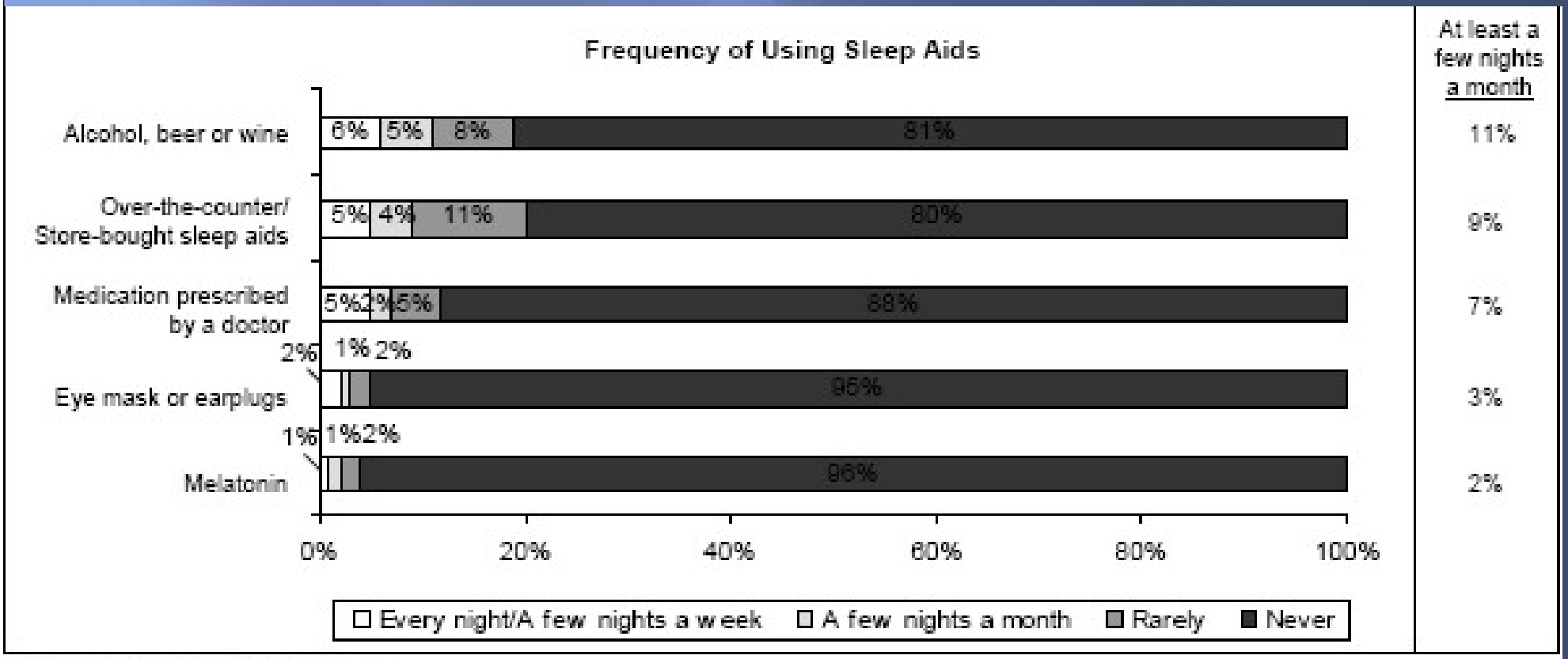
Impact of "Not Getting Enough Sleep" - Those who say they do not get adequate sleep						
	USA (B)	Canada (C)	Mexico (D)	United Kingdom (E)	Germany (F)	Japan (G)
Net: Any impact n =	(66)	(70)	(84)	(42)	(67)	(86)
Work productivity	59%	69%	69%	69%	64%	59%
Social life or leisure activities	78$_{CFG}$	68$_{G}$	58$_{G}$	74$_{G}$	58$_{G}$	40
Family life or home responsibilities	76$_{G}$	71$_{G}$	70$_{G}$	67	66	51
Mood	84	78	85$_{G}$	86$_{G}$	87$_{G}$	71
Intimate relations	56$_{G}$	47$_{G}$	40$_{G}$	50$_{G}$	45$_{G}$	13
Health	73	66	74	67	64	62

National Sleep Foundation, 2013

Impact on work, social life and health status
- substance abuse



Base = Those answering (n=1,498)
Q46

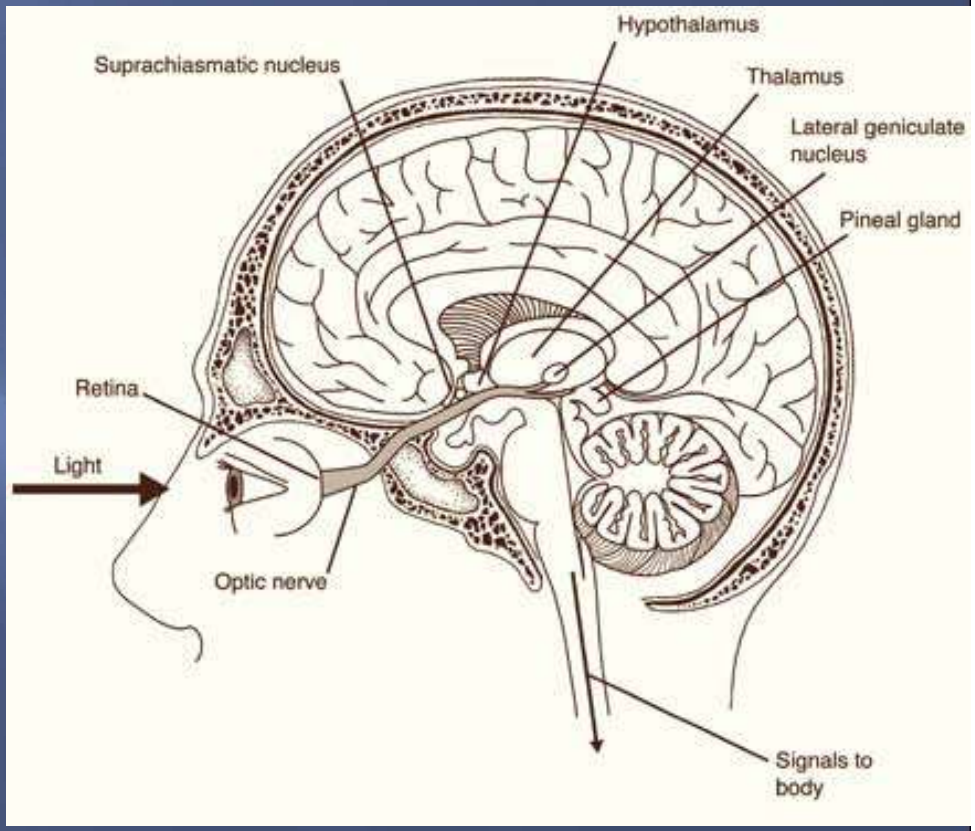


Base = Those answering (n=1,458-1,503)
Q32a-e

Circadian rhythms

- Cyclical changes—like fluctuations in
  - body temperature,
  - hormone levels,
  - sleep

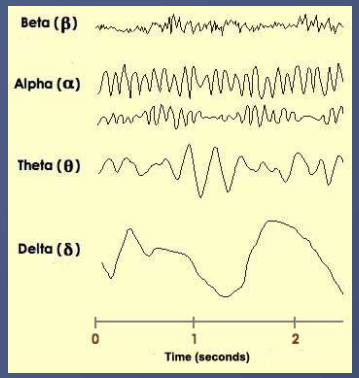
  —that occur over a 24-hour period, driven by the brain's biological "clock."



- These internal 24-hour rhythms in physiology and behavior are synchronized to the external physical environment and social/work schedules.

In humans, light is the strongest synchronizing agent and melatonin is main chemical transmitter in SCN (suprachiasmatic nucleus).

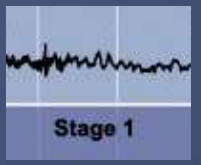
The Stages of Sleep



NREM sleep - a reduction in physiological activity.

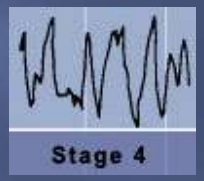
As sleep gets deeper, the brain waves as measured by EEG get slower and have greater amplitude, breathing and heart rate slow down, and blood pressure drops.

- Stage 1 - drowsiness or transition from being awake to falling asleep; **alpha and theta waves**.



- Stage 2 - light sleep during which eye movements stop; **theta waves, sleep spindles, K complexes;**

- Stages 3 and 4 (slow wave sleep, SWS) - **delta waves** interspersed with smaller, faster waves.



REM sleep - an active period of sleep.

- Brain waves are fast and desynchronized.
- Breathing becomes more rapid, irregular, and shallow.
- Heart rate increases and blood pressure rises.
- Eyes move rapidly in various directions and limb muscles become temporarily paralyzed.
- Most dreams occur.

Sleep Architecture - The Right Mix of Sleep

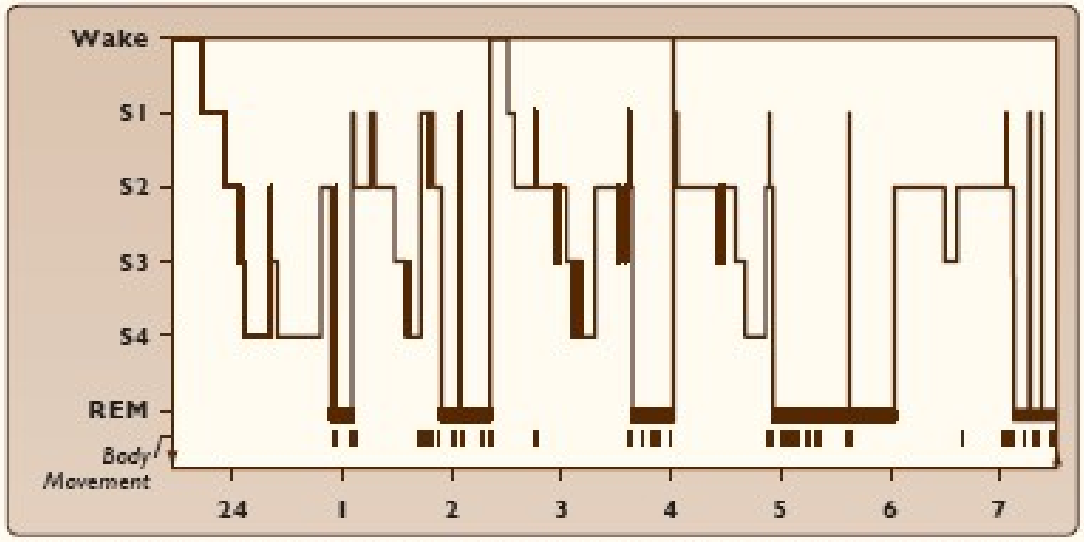
A complete sleep cycle consists of NREM and REM cycles that alternate every 90 to 110 minutes and is repeated four to six times per night.

(The length of each cycle averages 50 minutes for a full-term newborn, increasing to approximately 90 minutes by adolescence.)

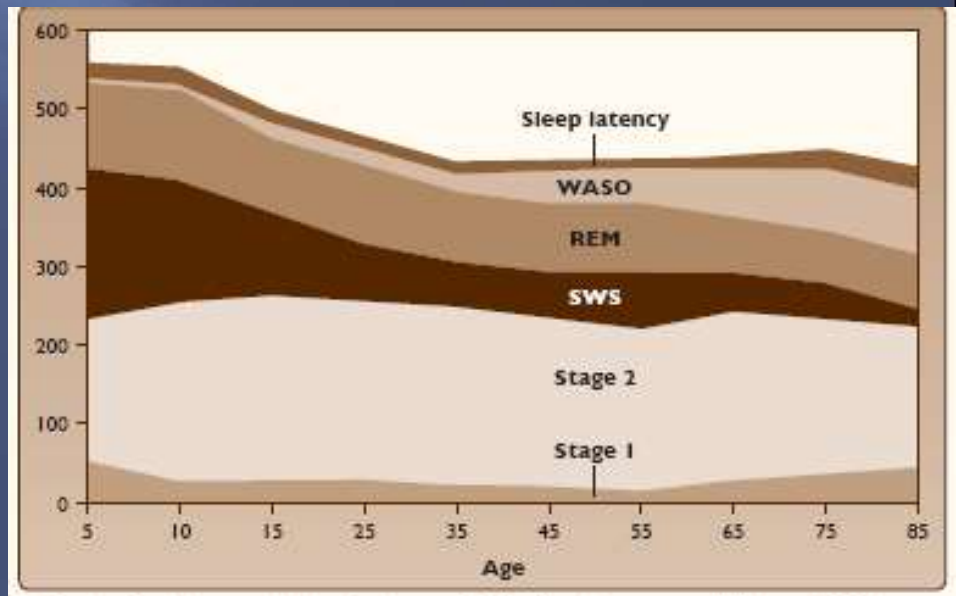
As the night wears on, REM periods increase in length while the amount of slow wave sleep decreases.

The sleep architecture also varies over the course of a lifetime.

Progression of sleep stages during a single night in a normal young adult.



Progression of sleep stages during a single night in a normal young adult. Reprinted from Principles and Practice of Sleep Medicine, Kryger M, Roth T, Dement WC, 4th ed, Normal Human Sleep An Overview. Carskadon M, Dement WC, p18 ©2005 with permission from Elsevier



Time (in minutes) for sleep latency and wake time after sleep onset (WASO), and for rapid eye movement (REM) sleep and NREM sleep stages 1, 2, and slow wave sleep (SWS). (Ohayon M, Carskadon MA, Guilleminault C, et al; Meta-analysis of quantitative sleep parameters from childhood to old age in healthy individuals: Developing normative sleep values across the human lifespan. Sleep 2004;27:1255-1273). Permission granted by the Associated Professional Sleep Societies, LLC, April 2006. Reprinted from Principles and Practice of Sleep Medicine, 4th ed, Kryger M, Roth T, Dement WC, Normal Human Sleep An Overview. Carskadon M, Dement WC p19 ©2005 with permission from Elsevier

ICSD - International classification of sleep disorders

TABLE 1] ICSD-3 Major Diagnostic Sections

Section
Insomnia
Sleep-related breathing disorders
Central disorders of hypersomnolence
Circadian rhythm sleep-wake disorders
Parasomnias
Sleep-related movement disorders
Other sleep disorders

ICSD= *International Classification of Sleep Disorders.*

DSM-5 – sleep-wake disorders

- Insomnia disorder
- Hypersomnolence disorder
- Narcolepsy
- Breathing-related sleep disorders
  - Obstructive sleep apnea hypopnea
  - Central sleep apnea
    - Idiopathic central sleep apnea
    - Cheyne-Stokes breathing
    - Central sleep apnea comorbid with opioid use
  - Sleep-related hypowentilation
- Circadian rhythm sleep-wake disorder
  - Delayed sleep phase type
  - Advanced sleep phase type
  - Irregular sleep -wake type
  - Non-24-hour sleep-wake type
  - Shift work type
  - Unspecified type

DSM-5 – sleep-wake disorders

- Parasomnias
  - Non-rapid eye movement sleep arousal disorders
    - Sleepwalking type
    - Sleep terror type
  - Nightmare disorder
  - Rapid eye movement sleep behavior disorder
- Restless legs syndrome, limb movement disorder
- Substance/medication-induced sleep disorder

How to measure sleep?

National Sleep Foundation

Sleepiness Diary

Sleepiness can interfere with a person's productivity, safety and overall quality of life. This diary enables you to record how sleepy you are and how difficult it is to stay awake during your day. You can compare this to how much you slept during the night and how much you napped during your day. To record for a second week, please use the tables on the reverse side of this sheet.

WEEK OF: _____

The faces on the scale below represent different levels of sleepiness from being wide awake ("0") to falling asleep ("4"). At the times indicated on the chart, record with a "0, 1, 2, 3 or 4" for each day which face most represents how you feel at the given time.

0 1 2 3 4

	Mon	Tues	Wed	Thurs	Fri	Sat	Sun
Morning (6am-12pm) Time:_____							
Afternoon (12am-6pm) Time:_____							
Evening (6pm-12am) Time:_____							
Night (12am-6am) Time:_____							

The three statements on the left in the table below represent difficulties staying awake. For each day of the week, record how frequently during the day you experience this level of sleepiness:

0= Not at all 1= Occasionally 2 =Some of the time 3=Most of the time 4=All of the time

	Mon	Tues	Wed	Thurs	Fri	Sat	Sun
I fought off/ignored a need to sleep							
I dozed off/fell asleep without meaning to							
I needed caffeine or another stimulant drug to stay awake							

For each day below, record how much you slept the previous night and how much time you spent napping during your day in hours (___Hrs.) and minutes (___Min.). Then, enter your total sleep time.

	Mon	Tues	Wed	Thurs	Fri	Sat	Sun
Hours/Minutes spent sleeping last night	____Hrs. ____Min.	____Hrs. ____Min.	____Hrs. ____Min.	____Hrs. ____Min.	____Hrs. ____Min.	____Hrs. ____Min.	____Hrs. ____Min.
Hours/Minutes spent napping last night	____Hrs. ____Min.	____Hrs. ____Min.	____Hrs. ____Min.	____Hrs. ____Min.	____Hrs. ____Min.	____Hrs. ____Min.	____Hrs. ____Min.
TOTAL	____Hrs. ____Min.	____Hrs. ____Min.	____Hrs. ____Min.	____Hrs. ____Min.	____Hrs. ____Min.	____Hrs. ____Min.	____Hrs. ____Min.

For each day, note the hours you slept and compare this to your level of sleepiness recorded on the sleepiness scales. While sleepiness is most often caused by not getting enough sleep, for some people it may be the result of a sleep disorder or other condition. If you are concerned, share this chart with your doctor to talk about your sleep.

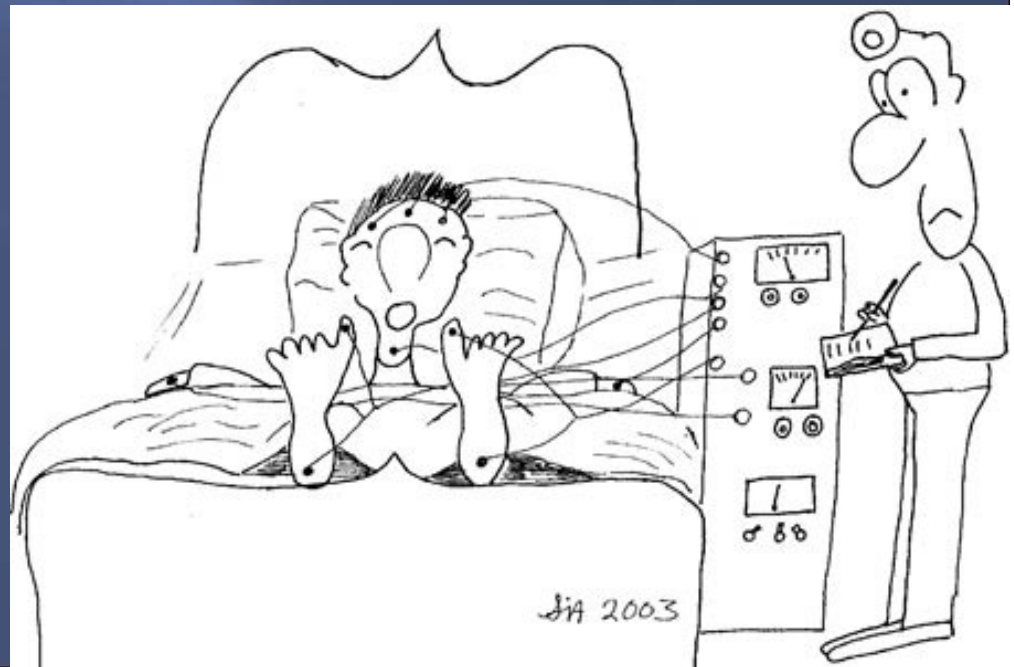
Polysomnography

Polysomnography or **PSG** is a multi-parametric test used in the study of sleep; the test result is called a polysomnogram.

The PSG monitors many body functions including:
- brain (EEG),
- eye movements (EOG),
- muscle activity (EMG),
- heart rhythm (ECG)

and
- breathing function
  (pulse oxymetry)

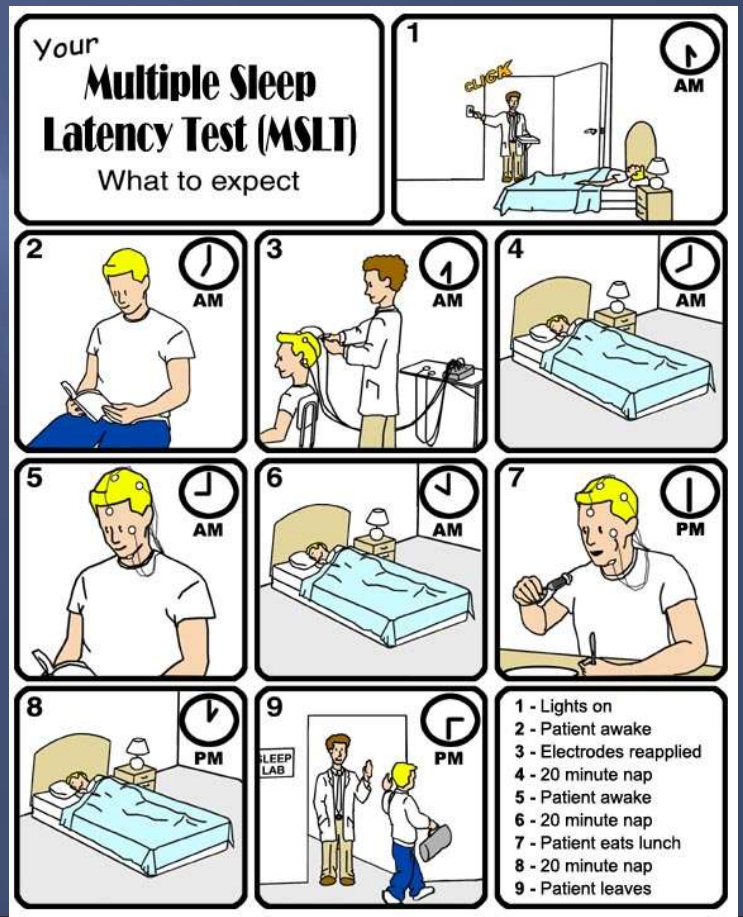
or
- respiratory effort during sleep
  (nasal and oral airflow).



Multiple Sleep Latency Test (MSLT)

- Used to measure the time it takes from the start of a daytime nap period to the first signs of sleep, called **sleep latency**.
- It can be used to test for narcolepsy, to distinguish between physical tiredness and true excessive daytime sleepiness, or to see if breathing disorder treatments are working. Its main purpose is to serve as an objective measure of sleepiness.

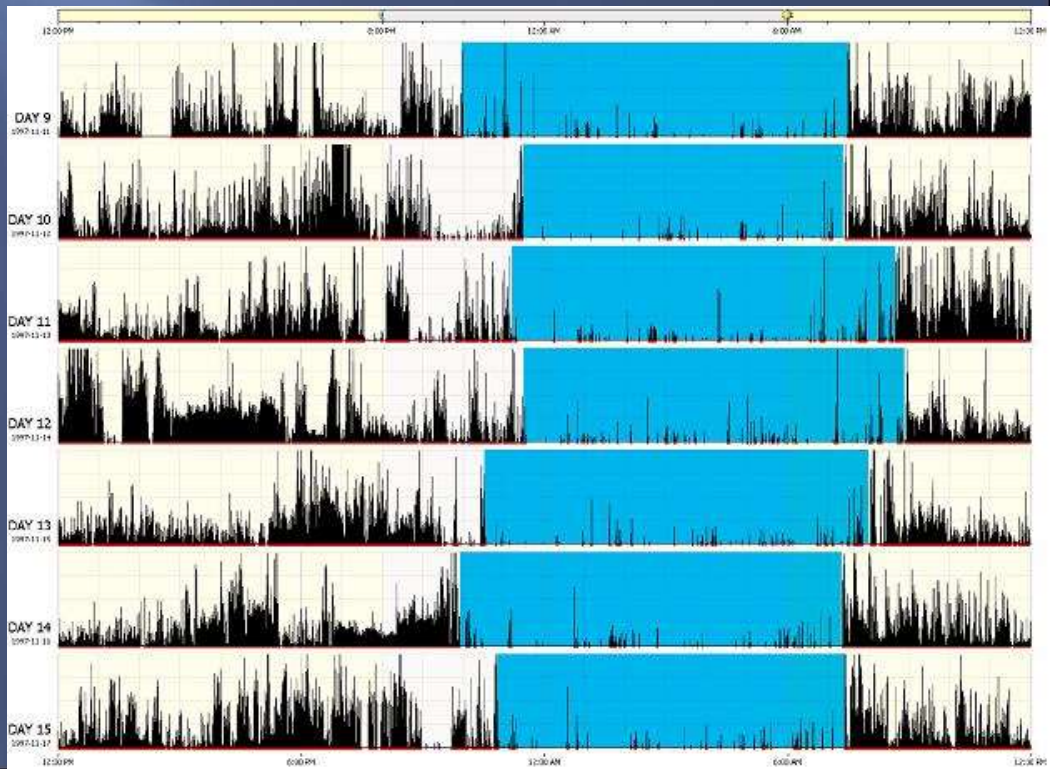
  - The test consists of four or five, twenty minute nap opportunities that are scheduled about two hours apart. The test is often done following an overnight sleep study. During the test, things such as the patient's brain waves, EEG, muscle activity and eye movements are monitored and recorded. The entire test normally takes about 7 hours.



Actigraphy

Actigraphy uses a portable device worn around the wrist like a watch to record movement over extended periods, making it highly useful to study sleep patterns and circadian rhythms.

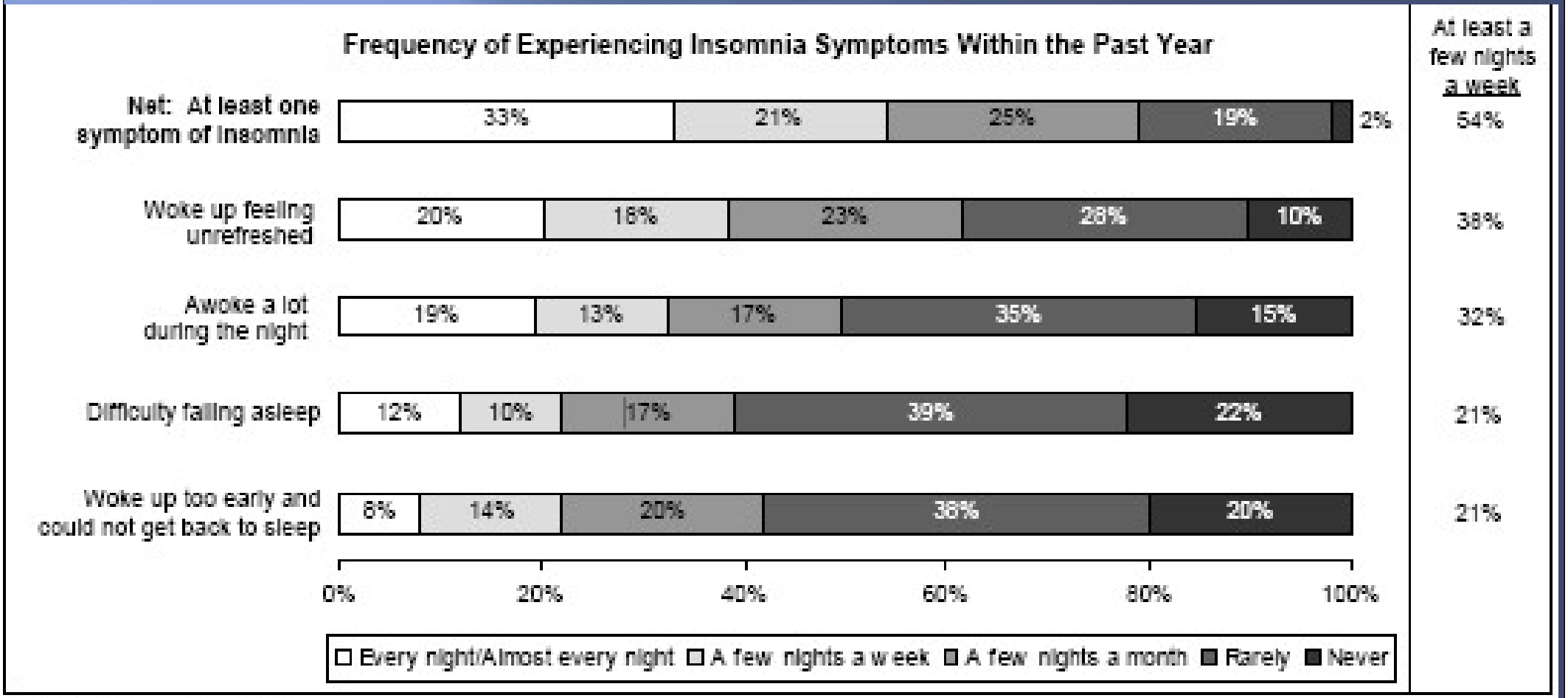
Distinguishing primary insomnia from circadian rhythm disorders and identifying paradoxical insomnia is useful, particularly in those patients who are refractory to treatment. This study provides an indirect objective measure of sleep and wake time.



Insomnia - decreased sleep efficiency or decreased total hours of sleep, with some associated decrease in productivity or well-being

- Initial insomnia - difficulty falling asleep, with increased sleep latency (time between going to bed and falling asleep); frequently related to anxiety disorders.
- Middle insomnia - difficulty maintaining sleep; decreased sleep efficiency is present, with fragmented unrestful sleep and frequent waking during the night; may be associated with medical illness, pain syndromes, or depression.
- Terminal insomnia (early morning wakening) - patients consistently wake up earlier than needed; frequently associated with major depression.

Prevalence of insomnia symptoms



Base = Total sample (n=1,506)
Don't know/Refused = <1 to 1%
Q14a-d

Complicated nature of insomnia

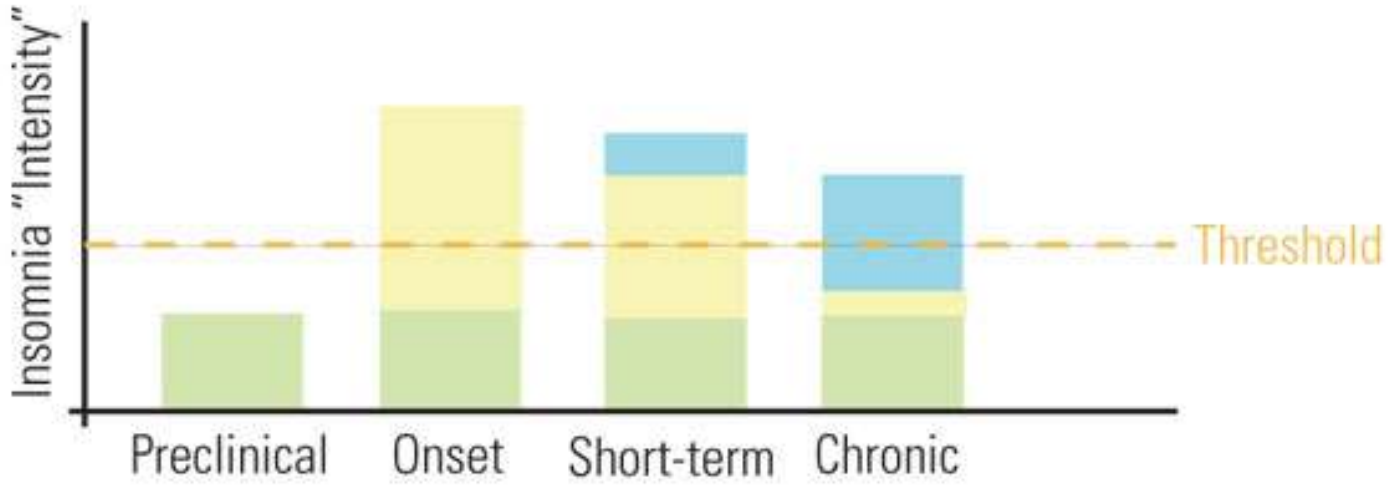
FIGURE

A MODEL OF CHRONIC INSOMNIA[2-4]

Predisposing Factors
- Biologic traits
- Psychological traits
- Social factors

Precipitating Factors
- Medical illness
- Psychiatric illness
- Stressful life events

Perpetuating Factors
- Excessive time in bed
- Napping
- Conditioning



Erman MK. *Primary Psychiatry*. Vol 14, No 7. 2007.

Insomnia disorder

A. A predominant compliant of dissatisfaction with sleep quantity or quality, associated with one (or more) of the following symptoms:
   1. Difficulty initiating sleep.
   2. Difficulty maintaining sleep…
   3. Early-morning awakening with inability to return to sleep.

B. The sleep disturbance causes clinically significant distress or impairment in social, occupational, educational, academic, behavioral, or other important areas of functioning.

C. The sleep difficulty occurs at least 3 nights per week.

D. The sleep difficulty is present for at least 3 months.

E. The sleep difficulty occurs despite adequate opportunity for sleep.

F. The insomnia is not better explained by and does not occur exclusively during the course of another sleep-wake disorder.

G. The insomnia is not attributable to the physiological effects of a substance.

H. Coexisting mental disorders and medical conditions do not adequately explain the predominant complaint of insomnia.

Behavioral Approach to Insomnia Treatment

- *Lifestyle changes*, such as decreasing caffeine and alcohol intake, adjusting exercise, regulating not only diet but the amount and time we eat, and stopping smoking.

- *Good sleep hygiene.*
- *Stimulus-control therapy.*
- *Relaxation therapy.*
- *Sleep-restriction therapy.*
- *CBT.*

At the physiological level, behavioral treatments work in the same way as medications—by decreasing the activity of the arousal systems in the brain producing wakefulness.

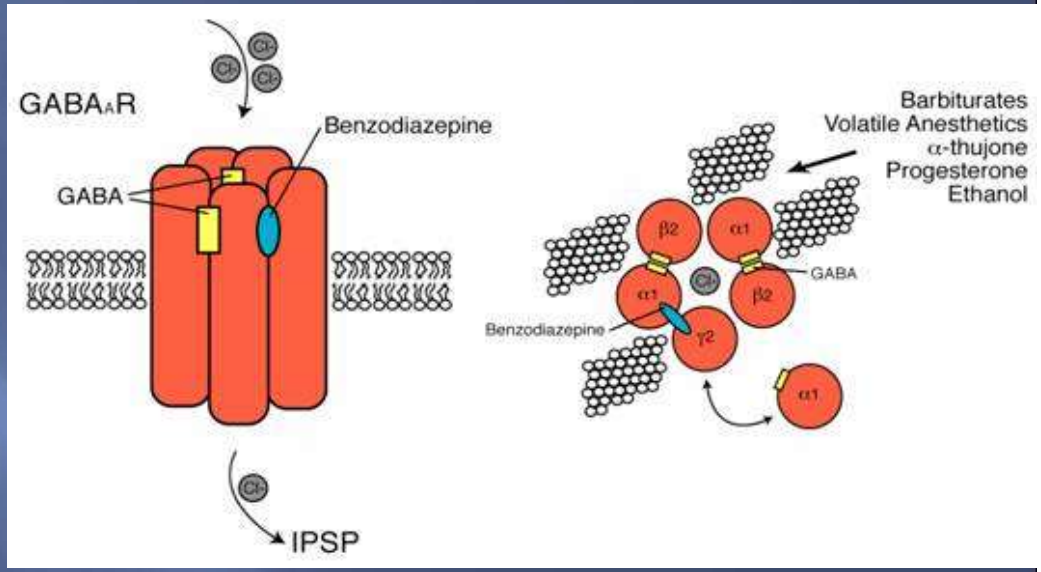
Pharmacologic Approach to Insomnia Treatment

- OTC products (e.g. antihistamines such as diphenhydramine and doxylamine or nutritional supplement melatonin).

- Prescription Sleep Medications:
  1) Until the 1960s, barbiturates, such as phenobarbital, were widely used as sedatives.
  2) In 1964, benzodiazepines (benzodiazepine receptor agonists) were introduced and soon became the mainstay of pharmacologic treatment.
  3) In the early 1990s, a new generation of nonbenzodiazepines (or nonbenzodiazepine receptor agonists) was introduced that target only certain receptor subtypes of the GABA complex.
  4) Ramelteon.
  5) Sedating antidepressants
  6) Sedating antipsychotics.

Hypnotic benzodiazepines

- Triazolam – short; 0.125-0.25 mg
- Estazolam – intermediate; 1-2mg
- Temazepam – intermediate; 15-30mg
- Flurazepam - long
- Quazepam – long



ADDICTION!

This class of drugs suppresses REM sleep and reduces stages 3 and 4 sleep while increasing stage 2 sleep.

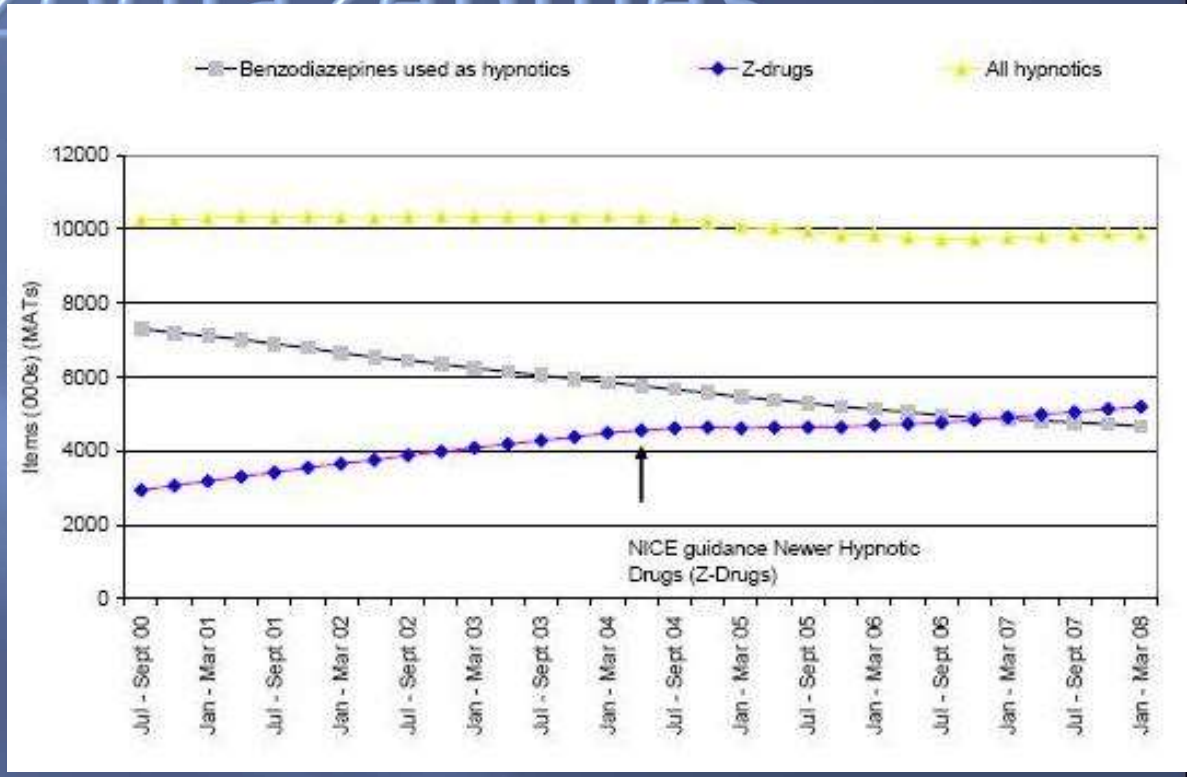
Side effects: somnolence, dizziness, drowsiness, light-headedness, incoordination.

Contraindicated in pregnancy.

Hypnotic nonbenzodiazepines

- Zolpidem – 5-20 mg
- Zaleplon – 10 mg
- Zopiclone – 7,5 mg
- Eszopiclone – 1-3 mg

ADDICTION!



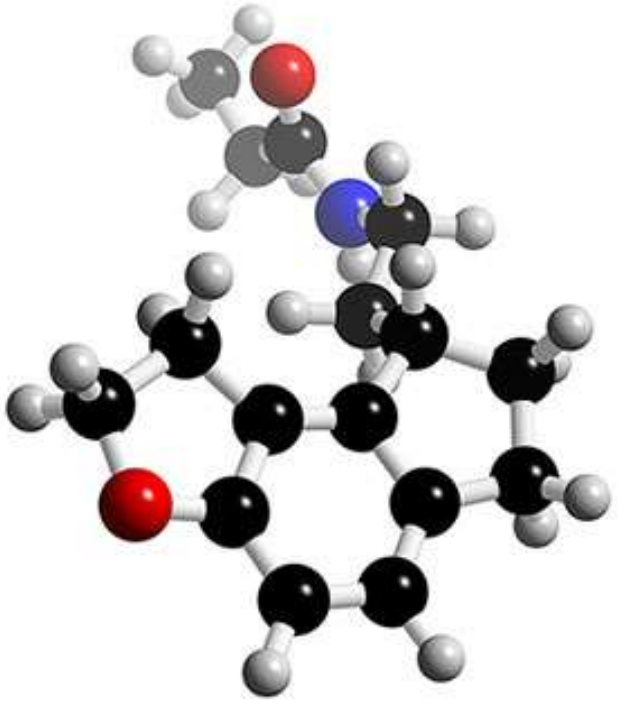
Unlike benzodiazepines, normal sleep architecture not suppressed.

Side effects: nausea, dizziness, headache, drowsiness, unpleasant taste, dry mouth.

Contraindicated in hypersensitivity.

Ramelteon

- Work by selectively affecting melatonin receptors (neurons) in the suprachiasmatic nucleus (SCN).
- Ramelteon has been found to be effective in helping those who have difficulty falling asleep. Because there has been no evidence that ramelteon has a potential for abuse or dependence, it can be prescribed for long-term use in adults (?).
- 8 mg taken within 30 minutes of going to bed
- Side effects: somnolence, dizziness, fatigue.



Hypersomnolence disorder

- A. Self-reported excessive sleepiness (hypersomnolence) despite a main sleep period of at least 7 hours, with at least one of the following symptoms:
  1) Recurrent periods of sleep or lapses into sleep within the same day;
  2) A prolonged main sleep episode of more than 9 hours per day that is nonrestorative;
  3) Difficulty being fully awake after abrupt awakening.
- The hypersomnolence occurs at least three times per week for at least 3 months.
- The hypersomnolence causes significant distress or impairment in social, occupational, or other areas of functioning.
- The hypersomnolence cannot be explained by the effects drug abuse or medication.
- The hypersomnolence cannot be attributed to another sleep disorder (i.e., narcolelpsy, breathing-related sleep disorder, circadian rhythm sleep-wake disorder, or parasomnia).
- A coexisting mental disorder or medical condition does not adequately explain the hypersomnolence.

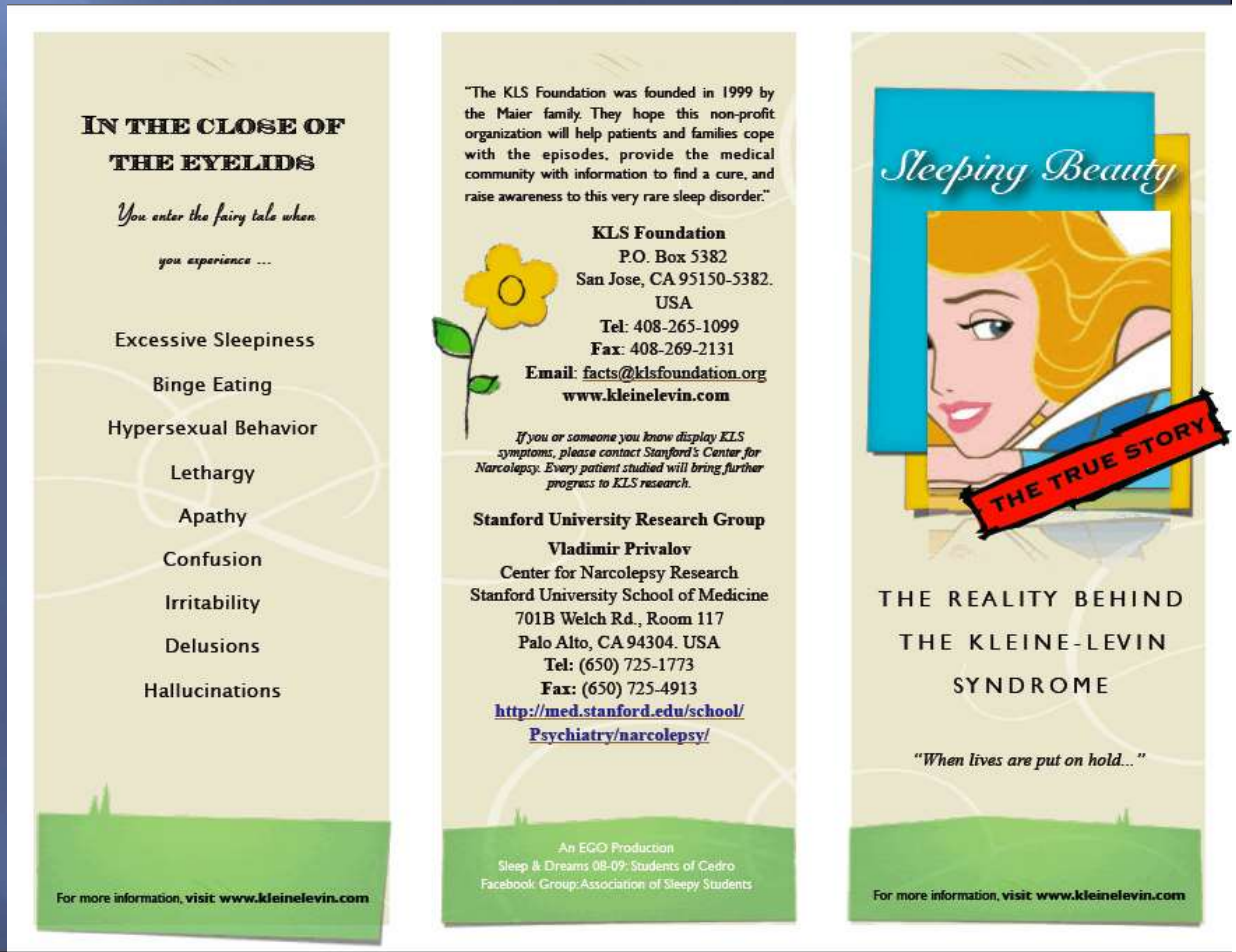
Hypersomnolence disorder

Idiopathic hypersomnia:

- **in most cases unknown;**
- familial cases associated with HLA-Cw2 and HLA-DR11 genotypes;
- viral illnesses such as Guillain-Barré syndrome, hepatitis, mononucleosis, and atypical viral pneumonia.

Kleine-Levin syndrome (KLS)

is a rare disorder that starts during adolescence and has a male gender preference. The patients have recurrent episodes of hypersomnia, which are often associated with compulsive overeating, hypersexuality and disinhibition..



Narcolepsy

A. Recurrent periods of an irrepressible need to sleep, lapsing into sleep, or napping occuring within the same day. These must have been occuring at least 3 times per week over at leat 3 months.

B. The presence of at least 1 of the following:

(1) Cataplexy (i.e., brief episodes of sudden bilateral loss of muscle tone, most often in association with intense emotion).

(2) Hypocretin deficiency in CSF.

(3) Nocturnal sleep polysomnography showing REM sleep latency =< 15 min., or a MSLT showing a mean sleep latency =< 8 min. and 2 or more sleep onset REM period.

Narcolepsy

- Narcolepsy is estimated to occur in 0.03% to 0.18% of the general population. Israeli studies suggest a much lower frequency in Israeli Jews.
- Narcolepsy most commonly begins in the second decade, with a peak incidence around 14 years of age.
- First-degree relatives of a narcoleptic proband are at about a 20-40 times greater risk of developing narcolepsy-cataplexy than are individuals in the general population.
  Narcolepsy-cataplexy is associated strongly with HLA DR2.
- Hypnopompic hallucination, sleep paralysis.

Narcolepsy and hypersomnia treatment

- Methylphenidate
  - helps reduce excessive daytime sleepiness, improving the symptoms of narcolepsy in 65%-85% of patients.

- Modafinil
  - was discovered as a novel drug that promotes long-lasting wakefulness. It has been shown in several trials to reduce excessive daytime sleepiness.

- Cataplectic attacks are usually treated by clomipramine, imipramine, fluoxetine, or sodium oxybate (gamma-hydroxybutyrate).

Breathing-related sleep disorders

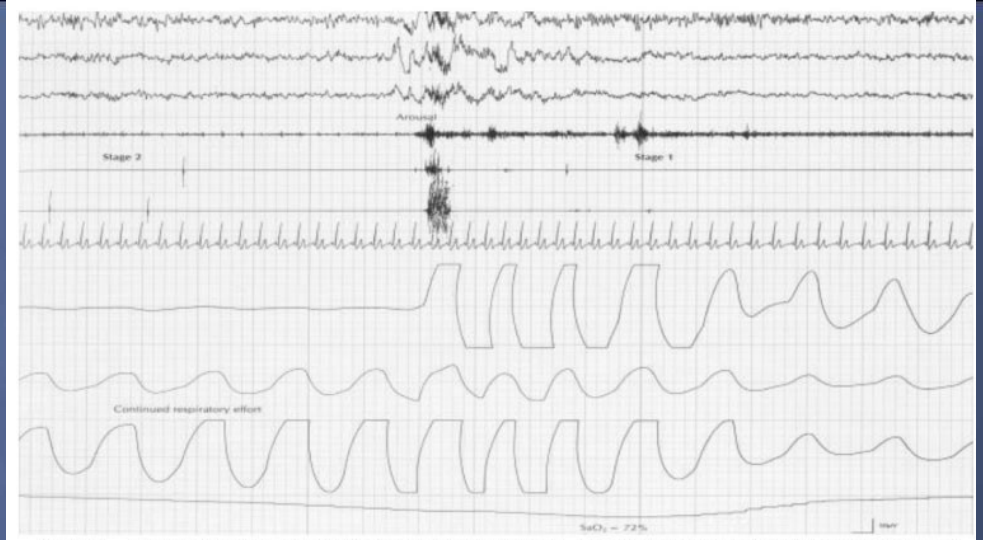
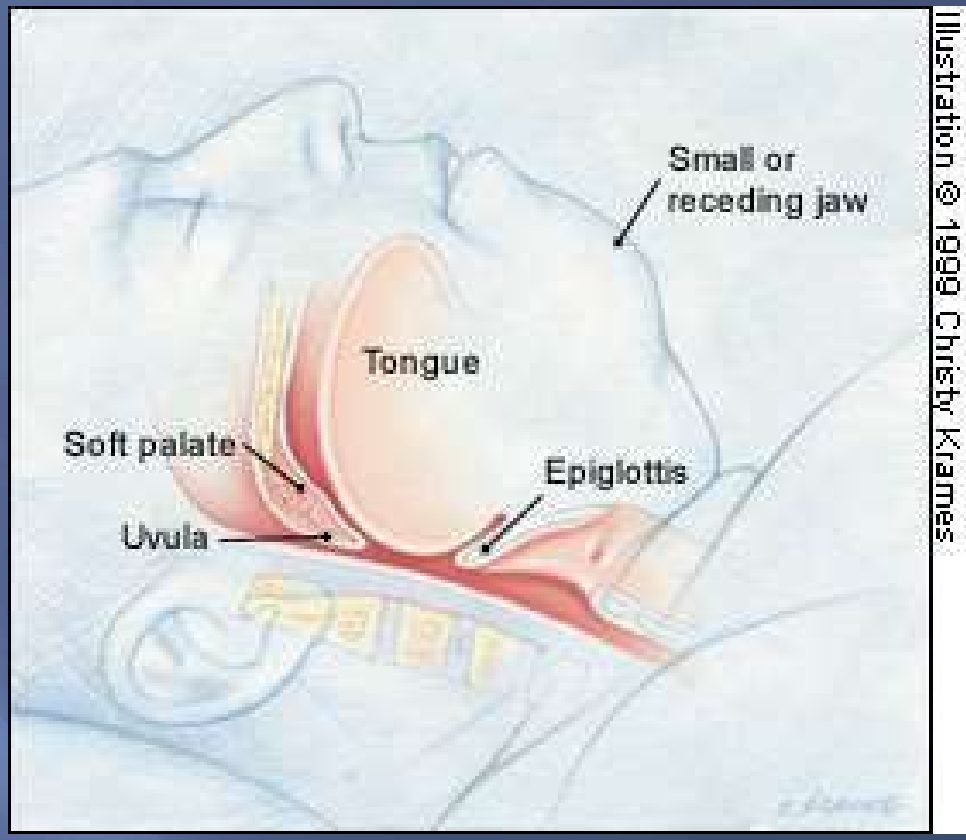


Figure 2 - Polysomnographic recording of obstructive sleep apnea. The recording channels correspond to, from top to bottom: 3 electroencephalogram channels, 1 submental electromyogram channel, 2 electro-oculogram channels, 1 electrocardiogram channel, 1 nasal flow channel, 1 thoracic belt channel, 1 abdominal belt channel, and 1 pulse oximetry channel.

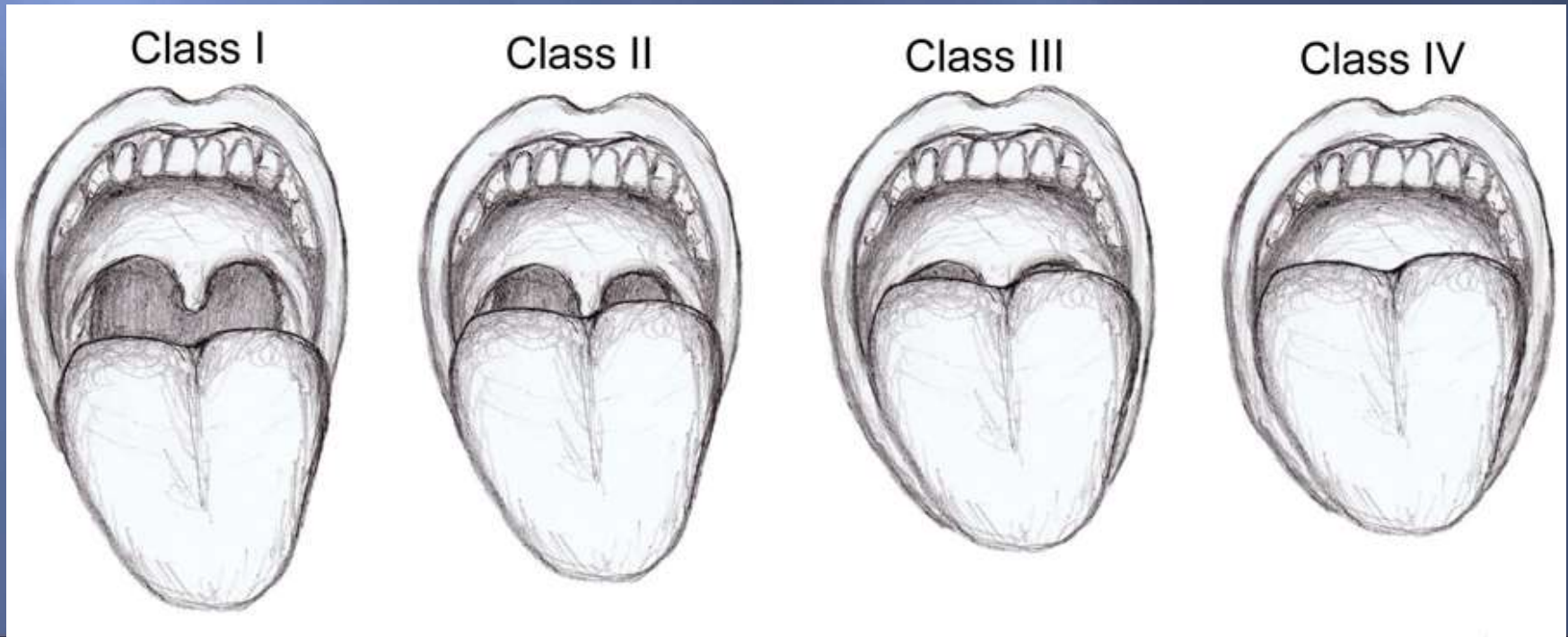
A. Sleep disruption, leading to excessive sleepiness or insomnia, that is judged to be due to a sleep-related breathing condition (e.g., obstructive or central sleep apnea syndrome or sleep-related hypoventilation).

B. The disturbance is not better accounted for by another mental disorder and is not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or another general medical condition (other than a breathing-related disorder).

Obstructive Sleep Apnea Syndrome - etiopathogenesis



Mallampati score



Obstructive Sleep Apnea Syndrome - associated features

It is a potentially life-threatening condition that requires immediate medical attention.

The risks of undiagnosed obstructive sleep apnea include:

- heart attacks,
- strokes,
- impotence,
- irregular heartbeat,
- high blood pressure,
- other heart diseases,
- increased insulin resistance.

In addition, obstructive sleep apnea causes daytime sleepiness that can result in accidents, lost productivity and interpersonal relationship problems.

Obstructive Sleep Apnea Syndrome - treatment

- Mild Sleep Apnea is usually treated by some *behavioral changes*. Losing weight, sleeping on your side are often recommended.

- There are *oral mouth devices* (that help keep the airway open) on the market that may help to reduce snoring in three different ways. Some devices:
  (1) bring the jaw forward or
  (2) elevate the soft palate or
  (3) retain the tongue
  (from falling back in the airway and blocking breathing).

- Moderate to severe sleep apnea is usually treated with a **C-PAP (continous positive airway pressure)**.
  C-PAP is a machine that blows air into your nose via a nose mask, keeping the airway open and unobstructed.
  For more severe apnea, there is a **Bi-level (Bi-PAP) machine**. The Bi-level machine is different in that it blows air at two different pressures. When a person inhales, the pressure is higher and in exhaling, the pressure is lower.

Obstructive Sleep Apnea Syndrome - surgery

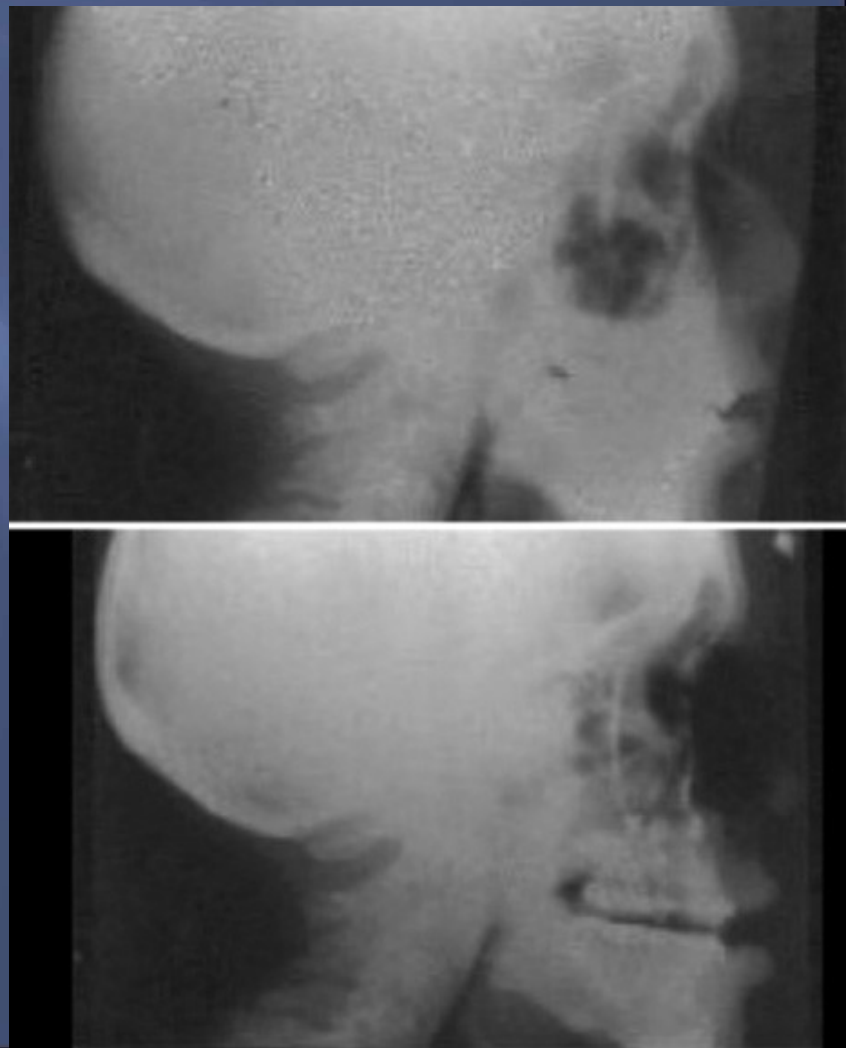
- Fixing a deviated septum;
  Removing the tonsils and adenoids or polyps.

- UVULOPALATOPHARYNGOPLASTY (UPPP): The uvula is removed along with excess tissue.

- MANDIBULAR MYOTOMY: cutting a rectangular piece of bone in the anterior (front part) portion of the mandible (jaw) to which the tongue muscles are attached. At that point, the rectangular piece is pulled outward, rotated 90 degrees and attached so it overrides the defect produced by the osteotomy (cutting of bone), where it is reattached. This pulls the tongue forward six to ten millimeters and almost always eliminates the sleep-related obstruction.

- LASER ASSISTED UVULOPLASTY (LAUP)

- SOMNOPLASTY: uses radio waves to shrink tissue in air passages .



Circadian Rhythm Sleep Disorders

The major feature of these disorders is a mismatch between the patient's sleep pattern and the sleep pattern that is desired or regarded as the societal norm.

- ***Shift work type***
  consists of symptoms of insomnia or excessive sleepiness that occur as transient phenomena in relation to work schedules.

- ***Delayed sleep-phase type*** is a disorder in which the major sleep episode is delayed in relation to the desired clock time, resulting in symptoms of sleep-onset insomnia or difficulty in awakening at the desired time.

- ***Advanced sleep-phase type*** is a disorder in which the major sleep episode is advanced in relation to the desired clock time, resulting in symptoms of compelling evening sleepiness, an early sleep onset, and an awakening that is earlier than desired.

Time zone change (jet lag) syndrome

- Varying degrees of difficulties in initiating or maintaining sleep, excessive sleepiness, decrements in subjective daytime alertness and performance, and somatic symptoms (largely related to gastrointestinal function) following rapid travel across multiple time zones.
  - Because the adjustment process of the circadian system is slow, averaging 60 minutes of phase adjustment per day after a phase-advance shift (eastbound flight) and 90 minutes per day after a phase-delay shift (westbound flight), symptoms can last for several days after the flight.
  - Decreased daytime performance.
  - Altered appetite or gastrointestinal function.
  - An increase in the frequency of nocturnal awakenings to urinate.
  - General malaise.

Circadian Rhythm Sleep Disorders

- Treatment
  - Bright light therapy (>600 lux); a higher intensity of light (>6000 lux over 30-60 min) is often necessary to accomplish acute phase shifts; the timing of light therapy is also important because it affects the degree and direction of the rhythm shift;
  - Chronotherapy: a gradual shift in sleep time in accordance with the patient's tendency;
  - Enhancing environmental cues;
  - Medications: benzodiazepines, nonbenzodiazepine hypnotics, melatonin 0,5-5 mg, melatonin agonists.

Restless Legs Syndrome

The criteria for diagnosis of RLS are based on those developed by the International RLS Study Group; 4 basic elements must be present to make the diagnosis:

- A compelling urge to move the limbs, usually associated with paresthesias/dysesthesias;
- Motor restlessness, as seen in activities such as floor pacing, tossing and turning in bed, and rubbing the legs;
- Symptoms worse or exclusively present at rest (ie, lying, sitting) with variable and temporary relief on activity;
- Circadian variation of symptoms that are present in the evening and at night (Often, symptoms are relieved after 5:00 am. In more severe cases, symptoms can be present throughout the day without circadian variation.)

A positive response to dopaminergic therapy supports the diagnosis of RLS.

Restless Legs Syndrome

- The disorder can be associated with pregnancy, anemia, rheumatoid arthritis and uremia. When associated with pregnancy, restless legs syndrome usually appears after the 20th week of the pregnancy.
- Symptoms of restless legs syndrome have been identified in 5% of normal subjects, 11% of pregnant women, 15% to 20% of uremic patients, and up to 30% of patients with rheumatoid arthritis.
- The peak onset is usually in middle age.
- Appears to be more common in females (female-to-male ratio of 2:1).

Restless Legs Syndrome - treatment

- Sleep hygiene measures and lifestyle changes should be recommended to all patients.

- Treatment of restless leg syndrome is first directed toward any underlying illness, if known (for example, a search for iron deficiency by blood testing to reveal underlying iron deficiency anemia).

- Medications used to treat restless leg syndrome include:

  carbidopa-levodopa, rotigotine, pergolide, bakclofen, bromocriptine, clonidine, gabapentin, ropinirol and pramipexole, carbamazepine, benzodiazepines (clonazepam, diazepam, triazolam, temazpam); opioids or tramadol for intermittent symptoms.

Periodic limb movement disorder

- periodic episodes of repetitive and highly stereotyped limb movements that occur during sleep;
- the periodicity ranges from 20-40 seconds with a variable duration. The movements are said to occur mainly in non–rapid eye movement (NREM) sleep
- a link between restless legs syndrome and periodic limb movement (comorbidity, underlying causes, treatment)

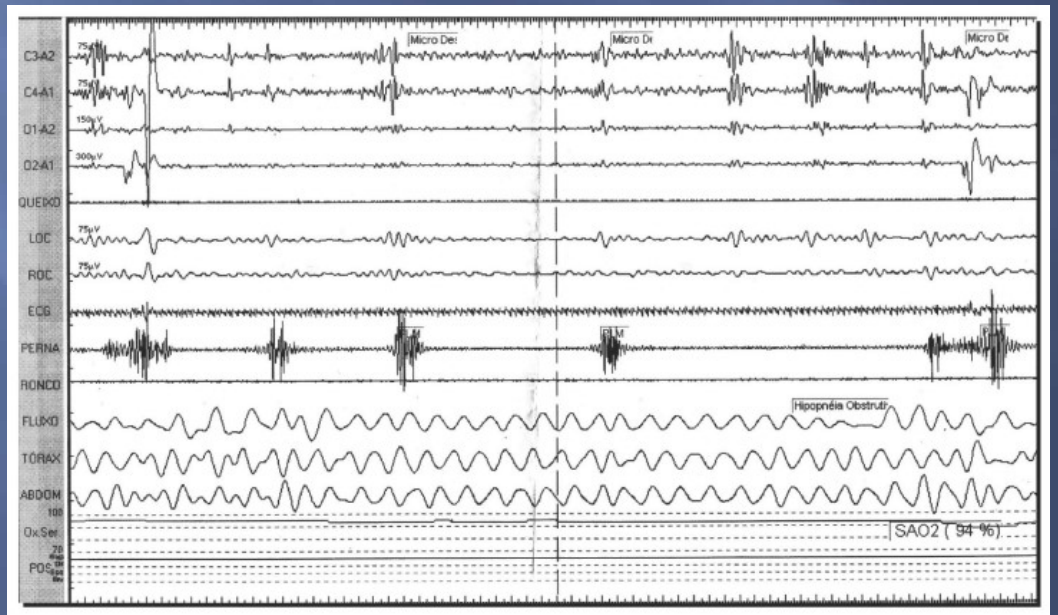


Figure 5 - Periodic Lower Limb Movements

Parasomnias: NREM sleep arousal disorders

- Impaired arousal from sleep has been postulated as a cause for these disorders.
- The onset of these disorders in slow-wave sleep is a typical feature.

- ***Sleepwalking*** consists of a series of complex behaviors that are initiated during slow-wave sleep and result in walking during sleep (between 1% and 15% of the general population).
  - sleep-related eating
  - sexsomnia

- ***Sleep terrors*** are characterized by a sudden arousal from slow-wave sleep with a piercing scream or cry, accompanied by autonomic and behavioral manifestations of intense fear. People do not recall a dream after a night terror and typically do not remember the episode the next morning.

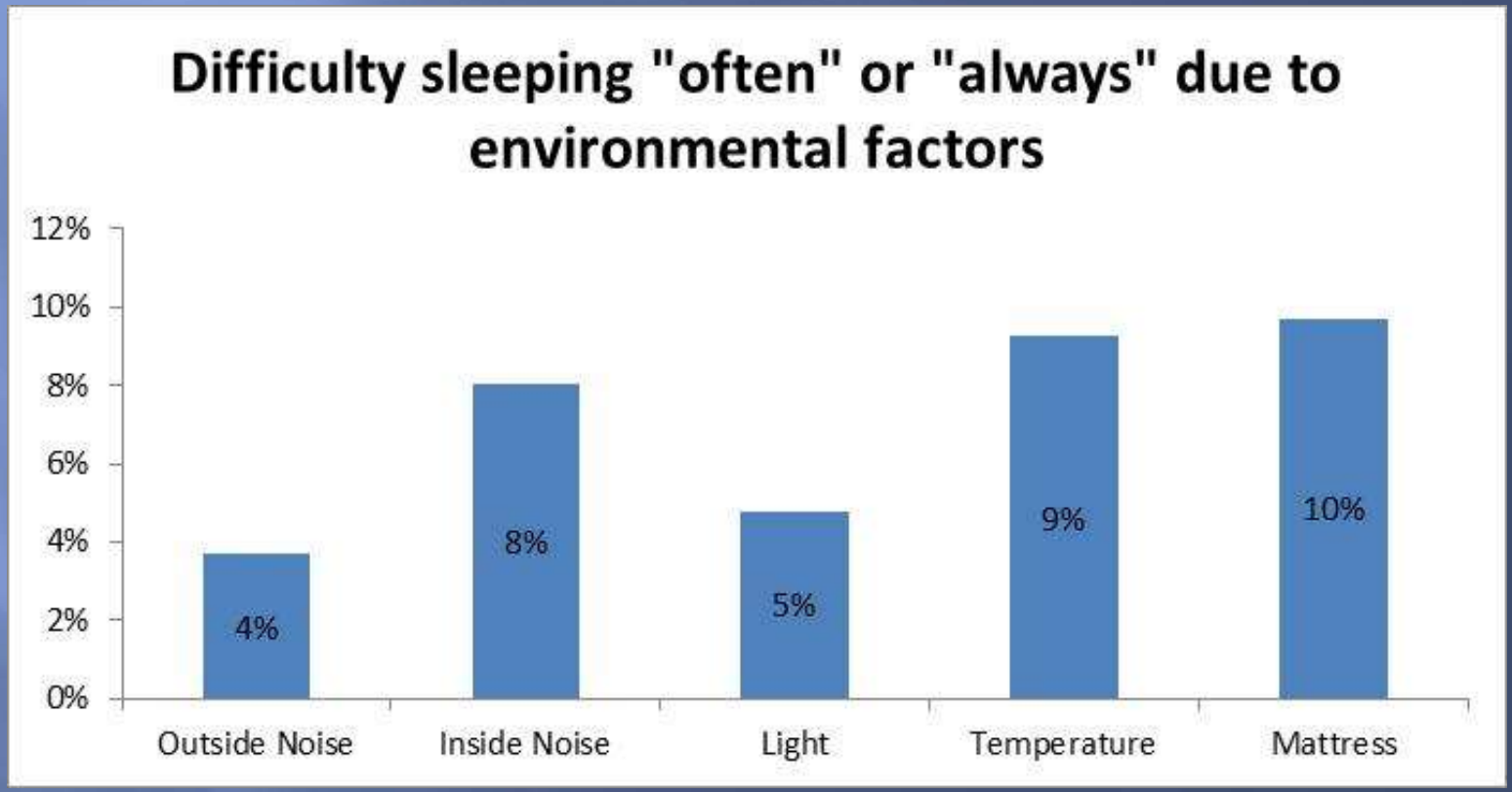
Parasomnias Usually Associated with REM Sleep

- ***REM sleep behavior disorder –*** a failure of the patient to have atonia during the REM stage sleep.
- ***Nightmare disorder*** - frightening dreams that usually awaken the sleeper from REM sleep.
  - A large number of children (10% to 50% of the population) will suffer from nightmares between ages three and six years.
  - Approximately 50% of adults admit to having at least an occasional nightmare.
  - A sizable proportion (20%-40%) of these patients have a diagnosis of schizotypal personality (most frequent), borderline personality disorder, schizoid personality disorder, or schizophrenia.
  - Nightmares that follow trauma can sometimes occur in non-REM sleep, especially stage 2.

Sleep-wake transition disorders ?

- Occur in the transition from wakefulness to sleep, sleep to wakefulness, or, more rarely, in sleep-stage transitions.
- All of these disorders can occur commonly in otherwise healthy persons and, therefore, are regarded as altered physiology rather than pathophysiology.
  - ***Rhythmic movement disorder*** comprises a group of stereotyped, repetitive movements involving large muscles, usually of the head and neck; the movements typically occur immediately prior to sleep onset and are sustained into light sleep.
  - ***Sleep starts*** are sudden, brief contractions of the legs, sometimes also involving the arms and head, that occur at sleep onset.
  - ***Sleep talking*** is the utterance of speech or sounds during sleep without simultaneous subjective detailed awareness of the event.
  - ***Nocturnal leg cramps*** are painful sensations of muscular tightness or tension, usually in the calf but occasionally in the foot, that occur during the sleep episode.

Environmental Factors Disturbing Sleep



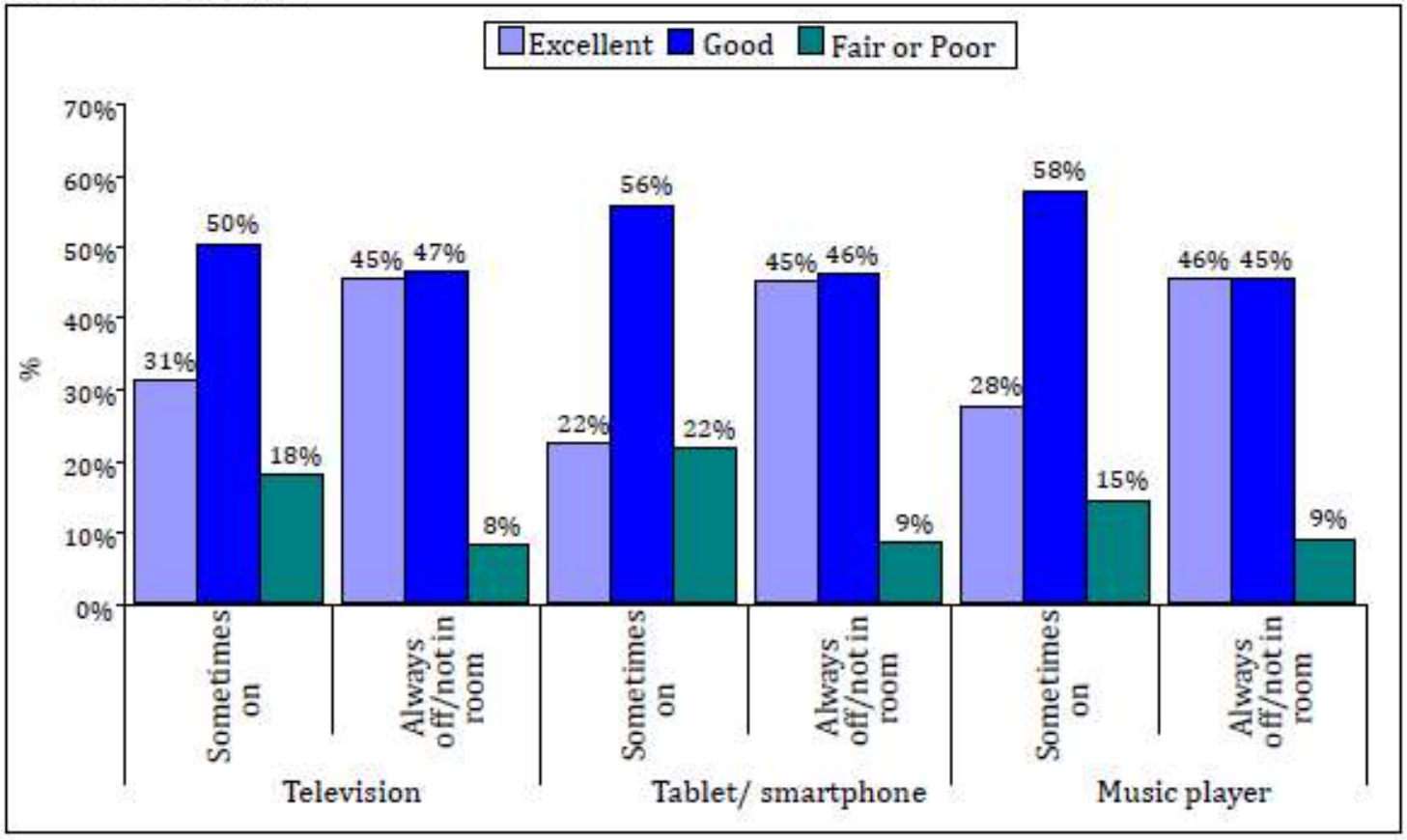
National Sleep Foundation, 2013

Key Findings: *Electronics and Sleep*

Impact of Electronics on Child Sleep (Continued)

Sleep quality was also associated with electronic devices left on at night. In unadjusted analyses, sleep quality was significantly worse for children who sometimes left the television, tablet/smartphone and music player on at night. After adjusting for age, sleep quality was significantly more likely to be only fair or poor for children who sometimes left the television on at night (p=.002) and who sometimes left a tablet or smartphone on at night (p=.04).

Exhibit 8. Sleep quality for children with specific electronic devices in the bedroom who do and do not always turn the device off at night.



Approach to the Patient with a Sleep Complaint

(Start with the Sleep History)

Chief Complaint

SNORING

Pauses in Breathing noted during sleep ?

- YES → **EDS ?** (Excessive Daytime Sleepiness)
- NO → **EDS ?** (Excessive Daytime Sleepiness)

EDS ? (Excessive Daytime Sleepiness)

- YES → **Insufficient Sleep Syndrome and Poor Sleep Hygiene ?**
- NO → **Nocturnal Respiratory Screening Test**

Nocturnal Respiratory Screening Test

- **Findings NOT c/w a Dx of OSA**
  - Tx Snoring with:
    - Weight Loss
    - Positional Therapy
    - Surgery (i.e. LAUP)
    - dental Appliance
    - Nasal Strips
- **Findings c/w a Dx of OSA**
  - Treat to decrease risk of cardiovascular or cerebrovascular disease

EDS

Excessive Daytime Sleepiness

Insufficient Sleep Syndrome and Poor Sleep Hygiene ?

- YES → **Improve Sleep Hygiene and Reevaluate**
- NO → **MLST** Multiple Sleep Latency Test with a NPSG (sleep study)

If NPSG Neg and MSLT is Pos for EDS, then Dx=Idiopathic Hypersomnulence or if Pos with 2 or more REM episodes then Dx=Narcolepsy

Treat Both with Stimulant Medications

INSOMNIA

Difficulty Staying Asleep (Sleep Maintenance Insomnia) OR **Difficulty Falling Asleep** (Sleep Initiation Insomnia)

Difficulty Staying Asleep (Sleep Maintenance Insomnia)

- YES → **Order a Routine Full NPSG** (Sleep Study)

Order a Routine Full NPSG (Sleep Study)

If pos for OSA or UARS then first line treatment is nasal CPAP

Difficulty Falling Asleep (Sleep Initiation Insomnia)

- **Symptoms of Restless Leg Syndrome?**
  - YES → Treat with Dopa Agonist medications such as Sinemet or Bromocriptine. Alternative medications include Benzodiazipines or Opiates
  - NO → **Other Medical or Psychiatric cause for Sleep Initiation Insomnia**
    - NO → **Psychophysiologic Insomnia** Treat with Behavioral approaches (good sleep hygiene) and occasional mild sedative hypnotic medications
    - YES → Treat Accordingly

Have a good sleep ☺

Case study 1

David is a 22-year-old senior in college who is referred by his primary care physician for evaluation of chronic tiredness and sleepiness. David reports that he has always been the type of person who likes to stay up late and, when given the choice, wake up late in the mornings. This didn't use to be a problem as he would generally manage to take care of his daily chores or school homework, but over the last 6 months or so his need for increased sleep started to interfere with his ability to complete his school assessments in time. He decided to seek help after his girlfriend told him that he's "sleeping his life away" and threatened to break up with him as he would most times prefer to sleep rather than doing things with her.

After a careful interview, David clarified that what he called tiredness was his need to take multiple naps, sometimes during the same day. He stated that he would suddenly feel that he "needed to sleep" which would be quickly followed by a sudden nap. He reported that he frequently fell asleep in the middle of his classes or at times he needed to find a place to lie down and take a nap while having lunch or dinner with his friends. More times than not he would have difficulties getting up in the morning regardless of the time he went to bed and his daytime sleepiness did not correlate with the amount of sleep he got the night before.

David denied experiencing cataplexy or a having a history of automatic behaviors during the day or at night. He states that he sleeps soundly, falls asleep easily, and does not usually remember his dreams (meaning he does not have frequent vivid dreams or nightmares). He appears appropriately concerned about his difficulties but denies feeling down, depressed or overanxious. Other than the times when he needs to fall asleep "pronto" he states that his level of energy is "pretty good." He enjoys college, spending times with his girlfriend and friends, and looks forward to graduation and getting a "real job."

Case study 2

Jason was a good student throughout grade school and middle school. However, when he began high school, he started to have odd symptoms that made his academic performance plummet. He was unable to stay awake during class, even when he had gotten plenty of sleep the night before. Even worse were the periods of paralysis called ……. If he was startled by a slamming locker door, he might collapse and be unable to move for a few minutes. In his freshman year he broke three pairs of glasses as a result of these bouts of …….

The diagnosis finally came when Jason was a junior in high school. Along with about 200,000 other Americans, Jason suffers from a disorder of the central nervous system called …….

Learning the name of his disease didn't cure Jason, but it has helped him to manage the symptoms. For example, he now takes …… to keep himself awake during his normal daily activities. Even with these ……., he still needs to nap throughout the day, which he can manage by carefully organizing his schedule.

Case study 3

Mr S, a 53-year-old man, is referred to a sleep disorders clinic for evaluation of insomnia and daytime somnolence. He has been struggling with depression and anxiety, for which he is being treated.

Mr S reports that he has had insomnia for many years and that it had gotten worse in the past 10 years. He has trouble with sleep initiation—it often takes him more than an hour to get to sleep. Once he is asleep, he wakes up multiple times then struggles to get back to sleep. He tosses and turns in bed until morning and gets up feeling tired and exhausted.

His primary care physician prescribed ……., but this caused sleepwalking episodes, so Mr S discontinued it. …….. was tried, but it caused weight gain and was also discontinued. He takes …….. for insomnia and fluoxetine for depression. This combination has been helpful, but he still has persistent symptoms of insomnia and depression. His wife reports that he snores and there have been occasions when he stopped breathing while sleeping. He has comorbid type 2 diabetes mellitus, hypertension, and gastroesophageal reflux disease.

The primary diagnosis is DSM-5 ……... Given the comorbid symptoms of depression and ……., it would be difficult to evaluate whether Mr S has DSM-IV primary insomnia; DSM-5 allows the clinician to make a causal attribution between insomnia and comorbid depression and …….

Comorbid …….. is diagnosed on the basis of clinical and polysomnographic evaluations. Mr S is treated with continuous positive airway pressure. He reports improvement in his energy level during daytime, but he continues to struggle with insomnia. His nighttime awakenings decreased to 2 or 3 times and nocturia is diminished as well. Despite these improvements, he still struggles with insomnia. An increase in the dose of ……. by 75 mg and initiation of …… for insomnia helped him significantly. Mr S is sleeping better and continues ……..; treatment with …… continues, with a slow and gradual taper.

CASE 4

A 30-year old woman is referred for evaluation of excessive daytime sleepiness for the past 10-12 years. She has become more concerned because of several "near miss" motor vehicle incidents. She is a college graduate with a degree in early childhood education. She is the director of a day care facility and works 8 AM to 6 PM five days per week. She has been in this job for the past 4 years. Her responsibilities include supervision of the teaching staff and a variety of administrative tasks. She also fills in for teachers during their breaks or vacations.

Sleepiness was first noted during her college years and was attributed to an erratic schedule and late night studying. For the past 8 years however despite a regular schedule, with a bedtime of 10:30 PM and wake time of 6:15 AM, the sleepiness persists. Although she wakes easily in the morning, by 9 AM she feels so sleepy that

she takes a brief nap in the office (with the door shut). She sleeps for 15 minutes and wakes refreshed. This urge to nap recurs an additional two times daily. It is particularly difficult when she is filling in for a teacher and can't nap. She is usually aware of dreams during the naps.

At night she falls asleep quickly (5 minutes) and briefly awakens once or twice during the night. She describes frequent sleep paralysis when going to sleep. This also happens during many of her naps. She has often noticed a shadowy figure or image in the room when falling asleep at night. She has also experienced transient weakness, usually when laughing vigorously, several times over the past 8 years.

The patient walks to work, so her driving is limited, though she has had a couple close calls when driving around town on weekends.

She drinks 4-5 cups of coffee throughout the day. She has 1-2 glasses of wine most evenings. She denies use of illicit drugs and is a non-smoker. She is otherwise healthy and is taking no medication other than oral contraceptives.

She is aware of similar sleepiness in her younger brother (age 24).

The physical examination is unremarkable.

1) Based on the history, what is the differential diagnosis?

2) What are the features that suggest ……?

3) What further diagnostic evaluation, if any, do you recommend?

The …… revealed at total sleep time of 425 minutes with a 90% sleep efficiency. The REM sleep latency was 12 minutes.

Sleep staging was normal and there were no other abnormalities.

The MSLT revealed a mean sleep latency of 3.4 minutes and there were 3 sleep-onset REM periods.

4) Are the sleep laboratory findings helpful?

5) How would you treat this patient?

6) What would you tell this patient about the general prognosis and treatment expectations?

Treatment for sleepiness was initiated with …….. and the patient was encouraged to maintain a regular schedule with adequate time in bed each night. Since the auxiliary symptoms were rather frequent and quite troubling, she was also prescribed

…….. Her sleepiness improved significantly with

methylphenidate, though she still elected to minimize driving.

She has had few episodes of cataplexy when she ran out of fluoxetine.

CASE 5

The patient is a 32 year-old man who presents with many years of disturbed sleep. He denies trouble falling asleep or usual awareness of waking in the night. However upon waking in the morning he feels unrefreshed. His schedule is very irregular due to work demands (frequent travel and early morning and late evening meetings). He has no current bed partner but is told, by family members, that he yells and calls out during the night. He has also broken a lamp that was on a bedside table during one of these episodes. The patient is unaware of these activities until the next morning (and then, only if some damage occurred).

The past medical history is notable for previous "heavy" drinking, and an episode of depression during his mid-twenties that was treated with fluoxetine. The family history is positive for depression in his father.

The physical examination is normal.

1) What is your differential diagnosis?

The patient is treated for …… with …… with good response. He is also counseled to improve his sleep habits specifically to maintain regular hours and get adequate sleep each night. His sleep was then reportedly quieter (by family members) and he felt more refreshed upon morning waking.

Eight months later he called the office because of resumed activity during sleep. Work has remained hectic; his schedule is "a mess". More and more he feels as if he is in a fog and "just swept along". He has continued the temazepam but wonders if it is affecting his ability to focus.

2) What factor(s) may be contributing to the current complaints?

3) How would you respond and treat?

The patient returns for an overnight sleep evaluation (……). The findings reveal a sleep efficiency of 96% with excess deep and REM sleep. There were 3 arousals from deep sleep during which the patient looked confused and agitated and was thrashing his arms.

4) Was the sleep study helpful?

5) What would you now recommend to the patient?

CASE 6

The patient is a 42 year old man with a 10 year history of worsening loud snoring which drives his wife out of the bedroom and is causing marital discord. He awakens with snoring and occasionally is aware of brief gasping upon awakening. Despite going to bed earlier and napping more, he is always tired. He falls asleep whenever sedentary including at work, and while driving and there have been near collisions. His employment requires frequent and sometimes long drives. His memory, concentration, libido and patience have all decreased. There has been a gradual weight gain of over 40 pounds over the past 12 years. He notices more nocturia, episodic acid reflux, and dry mouth at night.

The medical history includes hypertension treated with Hytrin because his doctor thought it might also help the nocturia. He also has allergic rhinitis treated as needed with and OTC antihistamine/decongestant. The family history includes a father who snored and was sleepy, treated for hypertension and died of an MI at age 60. His brothers are all overweight. His sister has hypothyroidism.

He has 3 children, all with seasonal allergies, and the youngest (age 4) snores. He is married for the past 15 years and notes some marital problems regarding finances and reduced interactions with his wife and children. He is under scrutiny at work for sleepiness on the job. He drinks 2 whiskeys per night and is a nonsmoker.

On physical examination he is mildly hypertensive. He is 240 pounds and 5'10". Nasal passages are mildly erythematous and congested. He has a long soft palate and large tongue. He is a Mallampati C (3) rating. His jaw is normal, and neck is thick and short, without thyromegaly. The balance of the examination is unremarkable.

1) What features are most consistent with the diagnosis of ……?

2) Identify the aggravating factors and precipitating events for this condition.

3) What additional health risks does this patient have?

4) What further diagnostic studies are recommended?

5) How else should you counsel this patient?

Anorexia Nervosa

- inability to maintain a minimally normal weight,
- a devastating fear of weight gain,
- relentless dietary habits that prevent weight gain,
- a disturbance in the way in which body weight and shape are perceived
- potentially life-threatening physiologic effects
- causing enduring psychological disturbance.

Signs and symptoms

- Vital sign changes found in patients with anorexia nervosa :

-hypotension,
-bradycardia,
-hypothermia
-dry skin
-hypercarotenemia
-lanugo body hair
-acrocyanosis
-atrophy of the breasts
-swelling of the parotid and submandibular glands
-peripheral edema
-thinning hair
-loss of muscle mass
-a flat affect
-psychomotor retardation (esp. in the later stages of the disease)

Neurologic disturbances:

- Peripheral neuropathy
- Ventricular enlargement

Integumentary findings include the following:

- Dry skin and hair
- Hair loss
- Lanugo body hair

Blood tests findings:

- Anemia
- Leukopenia
- Thrombocytopenia
- Low blood glucose (impaired insulin clearance)
- Low parathyroid hormone levels
- Elevated liver function tests

Reproductive disturbances:

- Infertility
- Low–birth-weight infant

Diagnosis

- Because an eating disorder is a clinical diagnosis, no definitive diagnostic tests are available for anorexia nervosa. However, given the multi-organ system effects of starvation, a thorough medical evaluation is warranted.

  - Physical and mental status evaluation
  - Complete blood count (CBC)
  - Metabolic panel
  - Urinalysis
  - Pregnancy test (in females of childbearing age)

Differential diagnosis

- Cancer
- Chronic, undiagnosed organic disease (infectious, congenital, or metabolic)
- *Clostridium difficile* colitis, clostridial cholecystitis
- Cytomegalovirus esophagitis, cytomegalovirus colitis
- Esophageal motility disorders, esophageal spasm, esophageal stricture
- Inflammatory bowel disease, including Crohn disease and ulcerative colitis
- Low vitamin D and calcium levels (hypocalcinosis)
- Myeloma
- Osteoporosis
- Osteopenia
- Celiac disease
- Chronic mesenteric ischemia
- Constipation
- Hypothyroidism
- Irritable bowel syndrome
- Malabsorption
- Panhypopituarism
- Hyperthyroidism
- Protein-losing entherpathy
- Pellagra
- Sheehan syndrome
- Systemic lupus erythematosus (SLE)

Anorexia nervosa in DSM-5

- Restriction of energy intake relative to requirements, leading to a **significantly low body weight** in the context of age, sex, developmental trajectory, and physical health; significantly low weight is defined as a weight that is **less than minimally normal or, for children and adolescents, less than that minimally expected**

- Intense fear of gaining weight or of becoming fat, or persistent behavior that interferes with weight gain, even though the patient's weight is already significantly low

- Disturbance in the way in which one's body weight or shape is experienced, undue influence of body weight or shape on self-evaluation, or persistent lack of recognition of the seriousness of the current low body weight

The DSM-5, which was published in May 2013, revised the definition of anorexia from the DSM-IV to focus more on behaviors , such as calorie restrictions and removed the qualification of low weight being less than 85% ideal body weight.

Additionally, the criterion of amenorrhea in postmenarchal females was completely removed from the definition.

2 subtypes of anorexia nervosa

- Restricting, in which severe limitation of food intake is the primary means to weight loss
- Binge-eating/purging type, in which there are periods of food intake that are compensated by self-induced vomiting, laxative or diuretic abuse, and/or excessive exercise

Predisposing factors

- Female sex
- White race
- Adolescent age
- the middle and upper socioeconomic classes,
- Gay and bisexual males are more likely to have an eating disorder than heterosexual males, but they are also more likely to have bulimia than anorexia.
- Family history of eating disorders
- Perfectionistic personality
- Difficulty communicating negative emotions
- Difficulty resolving conflict
- Low self-esteem
- Maternal psychopathology eg.negative expressed emotion, maternal encouragement of weight loss (especially for childhood-onset of this disorder)

Genetic factors

- the genetic contribution to the disease is as high as 50-80%,
- possible variations of the 5HTT (serotonin transporter gene) genome, that are associated with subtypes of eating disorders and that interact with life-history factors
- an area on band 1p at the DF1153721 locus may be related to a 7% increased incidence of anorexia nervosa in first-degree relatives.
- genetic risk factors may also be predictive of specific complications in anorexia nervosa, such as bone loss.

Epidemiology

- **all developed countries and in all socioeconomic classes**, is **also found in developing countries** such as China and Brazil;
- 0.3-1% in women, 0.1-0.3% in men;

- dancers, long-distance runners, skaters, models, actors, wrestlers, gymnasts, flight attendants, college sorority members, and others;

- 5% of young women exhibit symptoms of anorexia but do not meet the full diagnostic criteria, and some studies show disordered eating behavior in 13% of adolescent girls in the United States.

Poor prognosis

- Onset before 11 years or in adulthood
- **restricting subtype**
- Lower weight (less than 75% of mean body weight [MBW]) and longer duration (more than 19 months)
- single-parent families,
- families in which parents have been married before,
- families in which several generations live together, possibly owing to greater expression of negative emotions in the household.

Psychiatric comorbidities

-Depression (15-60%)

-Anxiety disorders (20-60%)

- OCD

  - Obsessionality and impulsivity in individuals with anorexia nervosa correlate with a lower lifetime BMI, reflecting poorer long-term outcomes

- Substance abuse (12-21%)

- ADHD

- Personality disorders (20-80%):

  - obsessive-compulsive personality disorder
  - narcisstic personality disorder
  - borderline personality disorder
  - histrionic personality disorder
  - avoidant personality disorder

Mortality

- Pneumonia
- Suicide
- Kidney and other organs failure
- Weakened immune system

Patients who had a higher likelihood of poor outcomes, including death

- misused alcohol,
-had a low BMI at presentation,
-were of older age at first presentation.

Comorbid disorders, which strongly predicted patient mortality

- affective disorder
- suicidal behavior or self-harm,
- a history of mental-health hospitalization

Endocrine and metabolic disturbances

- Delayed puberty
- Amenorrhea
- Anovulation
- Low estrogen states
- Increased growth hormone
- Decreased antidiuretic hormone
- Hypercarotenemia
- Hypothermia
- Hypokalemia
- Hyponatremia
- Hypoglycemia
- Euthyroid sick syndrome
- Hypercortisolism
- Arrested growth
- Osteoporosis

Cardiovascular effects

- Cardiomyopathy
- Mitral valve prolapse
- Supraventricular and ventricular dysrhythmias
- Long QT syndrome
- Bradycardia
- Orthostatic hypotension
- Shock due to congestive heart failure

Renal disturbances

- Decreased glomerular filtration rate (GFR)
- Elevated BUN
- Edema
- Acidosis with dehydration
- Hypokalemia
- Hypochloremic alkalosis with vomiting
- Hyperaldosteronism
- Renal calculi

Gastrointestinal findings

- Constipation
- Decreased intestinal mobility
- Delayed gastric emptying
- Gastric dilation and rupture: from binge eating and purging; gastric rupture can lead to pneumothorax and pneumoperitoneum
- Mesenteric artery syndrome (SMA)
- Patients who induce vomiting develop:

- dental enamel erosion,
- palatal trauma,
- enlarged parotids,
- esophagitis,
- Mallory-Weiss lesions,
- elevated transaminase levels,
- seizures (due to electrolyte disturbances).

Physical criteria for hospital admission- children and adolescents

Anamnestic

- Rapid weight loss: more than 2 kg/week
- Refusal to eat: total aphagia, refusal to drink
- Feeling faint or collapsing, with suggestion that this is orthostatic in origin
- Patient suggests he/she is easily tired or exhausted

Clinical

- BMI < 14 kg/m2 (over 17 years), or BMI < 13.2 kg/m2 (15-16), or BMI < 12.7 kg/m2 (13 and 14)
- Slowing of thought and speech, confusion
- Symptoms of bowel obstruction
- Extreme bradycardia: pulse < 40/minute regardless of time of day
- Tachycardia
- BP < 80/50 mmHg, orthostatic hypotension
- Hypothermia < 35.5˚C
- Hyperthermia

Paraclinical

- Acetonuria (on urine stick testing), hypoglycaemia < 0.6 g/L
- Severe electrolyte imbalance or metabolic disorders, particularly: hypokalaemia, hyponatraemia, hypophosphataemia, hypomagnesaemia
- Increased creatinine (> 100 µmol/L)
- Cytolysis (> 4 x ULN)
- Leukopenia & neutropenia (< 1,000/mm3)
- Thrombocytopenia (< 60,000/mm3)

Physical criteria for hospital admission- adults

Anamnestic

- Extent and speed of weight loss: loss of >=20% of body weight in 3 months
- Fainting and/or falls or loss of consciousness
- Uncontrollable vomiting
- Failure of outpatient-based refeeding

Clinical

- Clinical signs of dehydration
- BMI < 14 kg/m2
- Significant muscle wasting with axial hypotonia
- Hypothermia < 35˚C
- Blood pressure < 90/60 mmHg
- Sinus bradycardia HR < 40/minute
- Tachycardia at rest > 60/minute if BMI < 13 kg/m2

Paraclinical

- ECG abnormalities apart from heart rate
- Hypoglycaemia, < 0.6 g/L if symptomatic or < 0.3 gL if asymptomatic
- Liver cytolysis > 10 x ULN
- Hypokalaemia < 3 mEq/L
- Hypophosphataemia < 0.5 mmol/L
- Renal failure: creatinine clearance < 40 mL/min
- Sodium levels: < 125 mmol/L (compulsive drinking, risk of convulsions) or > 150 mmol/L (dehydration)
- Leukopaenia < 1,000/mm3 (or neutrophils < 500/mm3)

Psychiatric criteria for hospital admission

Risk of suicide

- Suicide attempt, whether carried out or failed
- Specific plan for suicide
- Repeated self-mutilation

Comorbidities

- Any associated psychiatric disorder severe enough to require hospital admission
- Depression
- Substance abuse
- Anxiety
- Psychotic symptoms
- Obsessive compulsive disorders

Anorexia nervosa

- Obsessive, intrusive and continuous ideation, inability to control obsessive thoughts
- Refeeding: need for refeeding via nasogastric tube, or another feeding method that cannot be used on an outpatient basis
- Excessive and compulsive physical exercise (in association with another indication for hospital admission)
- Inability to control intensive purge behaviour without help

Motivation,

- Cooperation
- Previous failure of a properly conducted outpatient care programme
- Patient uncooperative, or cooperative only in a highly structured care environment
- Motivation insufficient to ensure compliance with outpatient care

Environmental criteria for hospital admission

Availability of family

- Family problems or lack of family to support patient in outpatient care
- Exhaustion of family members

Environmental

- Stress
- Severe family conflict
- High level of parental criticism
- Severe social isolation

Availability of care

- No outpatient treatment possible because of a lack of facilities (such treatment not possible because of distance)

Previous treatment

- Failure of outpatient care (worsening disease, or disease becomes chronic)

Recommended nutrition Prescription

- Initiate at 1,200 kcal to 1,400 kcal
  - Energy gradually by 100 kcal to 200 kcal increments.
- Protein: 0.8-1.2 g/kg of recommended body weight.
- Goal: Weight gain of 1-2 lbs/week.
- Small, frequent meals. Vitamin, mineral supplements.
- Tube feeding may be necessary for severely malnourished patients (especially if refusing po intake).

Management- refeeding

- Must be undertaken slowly, with modest increases in metabolic demands, in order to avoid **a refeeding syndrome,** including:
  - cardiovascular collapse ,
  - starvation-induced hypophosphatemia,
  - dangerous fluctuations in potassium, sodium, and magnesium levels.
- Cardiac arythmias are the most common reason of deaths
- A nutritionist or dietitian should be an integral part of the refeeding plan.
- Electrolyte repletion is necessary in patients with profound malnutrition, dehydration, and purging behaviors. Repletion may be done orally or parenterally, depending on the patient's clinical state.

Hypokalemia

- Features are numerous:
  - Cardiac arrhythmias
  - Hypotension
  - Cardiac arrest
  - Weakness
  - Paralysis
  - Confusion
  - Respiratory Depression

Hypomagnesemia

- Most cases not clinically significant
- Severe cases:
  - Cardiac arrhythmias
  - Abdominal discomfort
  - Anorexia
  - Tremors, seizures, & confusion
  - Weakness

Hypophosphatemia

- Predominant feature of RFS
- Impaired cellular-energy pathways
  - Adenosine triphosphate
  - 2,3-diphosphoglycerate
- Impaired skeletal-muscle function
  - Including weakness & myopathy
- Seizures & perturbed mental state
- Impaired blood clotting processes & hemolysis also can occur

Thiamine Deficiency

- Can result in Wernicke's encephalopathy or Korsakov's syndrome, associated with:
  - Ocular disturbance
  - Confusion
  - Ataxia
    - loss of ability to coordinate muscular movement
  - Coma
  - Short-term memory loss
  - Confabulation
    - Confusion of imagination with memory

Psychological therapies of anorexia nervosa

- Individual therapy (insight-oriented)
- Cognitive analytic therapy
- Cognitive-behavioral therapy (CBT)
- Enhanced cognitive-behavioral therapy (CBT-E)
- Interpersonal therapy (IPT)
- Motivational enhancement therapy
- Dynamically informed therapies
- Group therapy
- Family-based therapy (FBT)
- Specialist supportive clinical management (SSCM)
- Conjoint family therapy
- Separated family therapy
- Multifamily groups
- Relatives and caregiver support groups

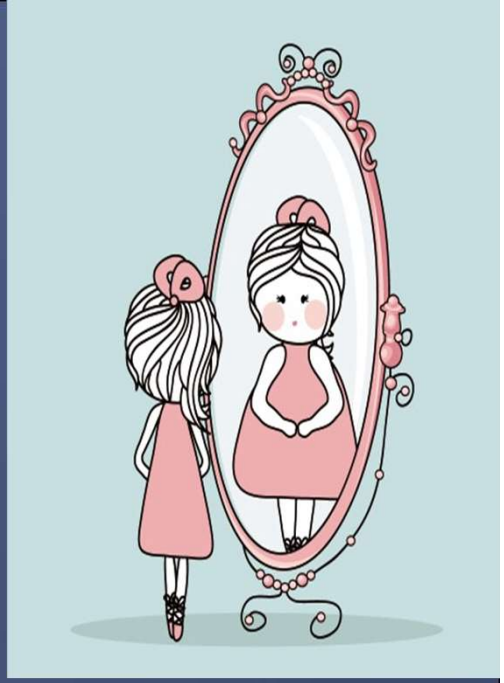
Psychopharmacologic therapy of anorexia nervosa

- Evidence regarding the efficacy of medication treatment for eating disorders is **weak or moderate**.
- Fluoxetine, due to effects on serotonin levels, has been found to be generally helpful in patients with anorexia nervosa stabilized with weight restoration.
- Psychotherapy with adjunctive low-dose olanzapine may be useful for anorexia nervosa during inpatient treatment, especially in the context of anxiety, obsessive eating-related ruminations, and treatment resistance due to failure to engage.

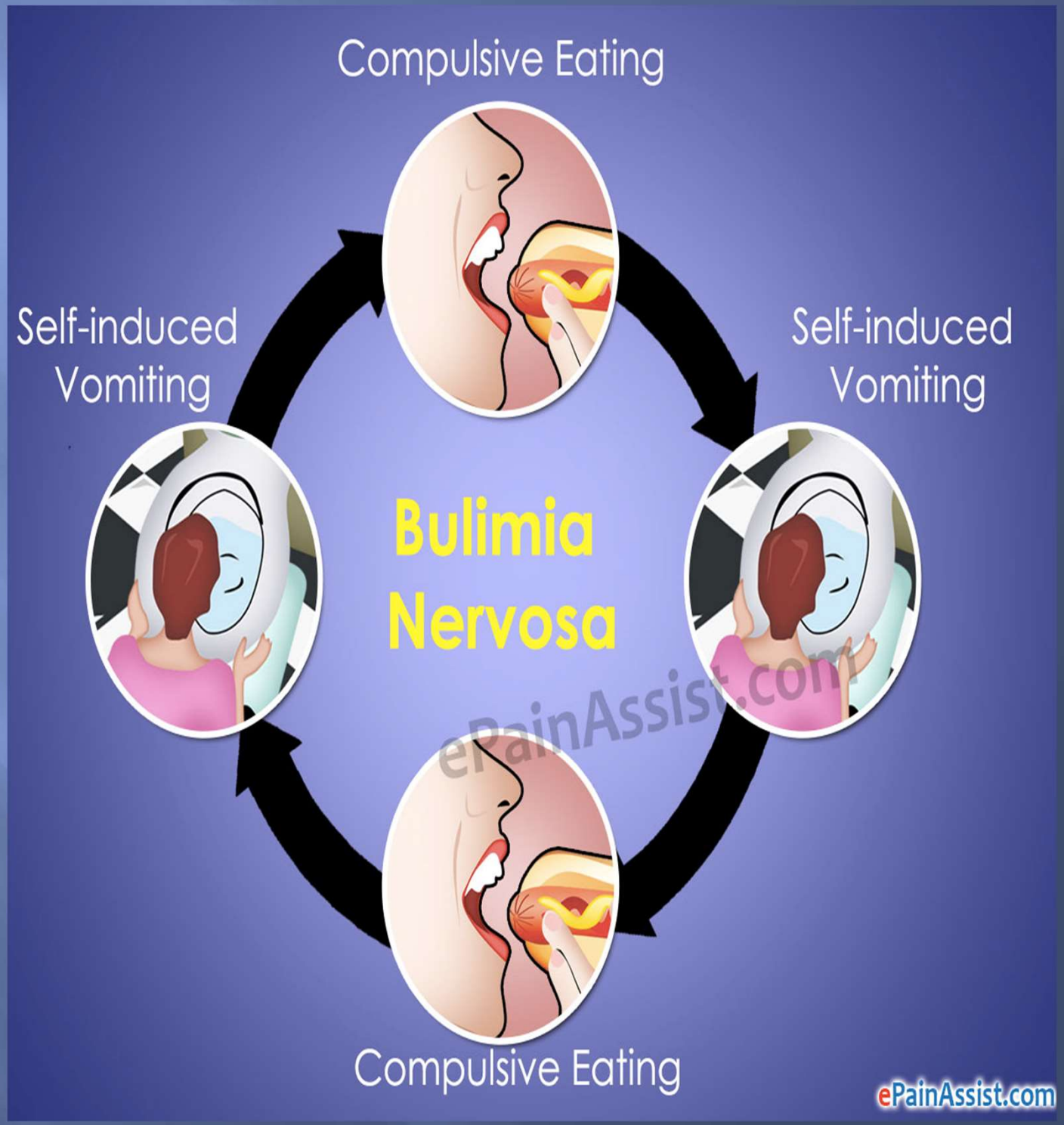
What is Pro Ana/Mia?

- A term many acknledge to mean the encouragement of anorexia nervosa as a way to live your life rather than an eating disorder.
- Pro Ana (anorexia) and Pro Mia (bulimia) websites are targeted towards people who believe that Anorexia is the only way to live and that anorexia/bulimia is the right lifestyle for them

Bulimia nervosa



- Includes regularly occurring compensatory behaviors that are intended to rid the body of the excess calories consumed during eating binges.
- Distinguished from the recently delineated syndrome of **binge-eating disorder**, in which no regular or consistent compensatory behavior accompanies the bingeing episodes.
- DSM-5 no longer maintains specific purging and nonpurging subtypes.
- Frequent association of cigarette smoking with bulimia nervosa may reflect compensatory behavior, in that nicotine use appears to suppress, whereas smoking cessation provokes, weight gain in some individuals.
- In up to 60% of cases, patients with bulimia nervosa report prior histories of anorexia nervosa.
- People with bulimia nervosa are typically of normal weight, although some degree of overlap between non-purging bulimia nervosa and binge-eating disorder is seen.
- The development of anorexia nervosa in individuals who initially present with bulimia nervosa is possible, although less common


Compulsive Eating
Self-induced Vomiting
Self-induced Vomiting
Bulimia Nervosa
Compulsive Eating
ePainAssist.com
ePainAssist.com

Bulimia -characteristics

- **Binge eating-** frequent episodes of binge eating associated with emotional distress and a sense of loss of control.

Eating, in a discrete period of time (eg, 2 hours) an amount of food that is significantly larger than is typical for most people during the same defined period. This behavior is associated with a perceived loss of control of eating during this time.

- **Compensatory behaviors:**

- self-induced vomiting,
- laxative abuse,
- excessive exercise generally experienced as being joyless and/or compulsive,
- episodes of fasting or strict dieting,
- diuretic abuse,
- use of appetite suppressants,
- failure to use insulin in those with type I diabetes
- use of medications intended to speed up metabolism (eg, thyroid hormone).

- **Self-evaluation:**

- a fear of weight gain
- usually some degree of body image distortion (believing one looks much fatter than is actually the case).
- abnormalities in mood and in perceptions of hunger and satiety (often)

Diagnostic criteria for bulimia nervosa- DSM5

- Recurrent episodes of binge eating: An episode of binge eating is characterized by both (1) eating, in a discrete period of time (eg, within any 2-hour period), an amount of food that is definitely larger than what most individuals would eat in a similar period of time under similar circumstances and (2) a sense of lack of control over eating during the episode (eg, a feeling that one cannot stop eating or control what or how much one is eating)
- Recurrent inappropriate compensatory behaviors in order to prevent weight gain, such as self-induced vomiting; misuse of laxatives, diuretics, or other medications; fasting; or excessive exercise
- The binge eating and inappropriate compensatory behaviors both occur, on average, at least once a week for 3 months
- Self-evaluation is unduly influenced by body shape and weight
- The disturbance does not occur exclusively during episodes of anorexia nervosa

Epidemiology

- Is thought to be significantly underrecognized.
- In the US the prevalence of bulimia nervosa is 1%.
- Lifetime prevalence is 0.5% for males and 1.5% for females.
- Those who are diagnosed with bulimia nervosa spend approximately 8.3 years with an episode.
- Appr. 65.3% of patients with bulimia have a body mass index (BMI) between 18.5-29.9 and only 3.5% have a BMI less than 18.5.
- Is more common among those whose occupation or hobbies require gaining and/or losing weight rapidly, such as wrestlers and competitive bodybuilders and in vocations such as: acting, modeling, and ballet dancing
- a progressive increase in the prevalence of anorexia nervosa and bulimia nervosa in the last several decades of the 20th century

Severity- bulimia

- Mild: An average of 1-3 episodes of inappropriate compensatory behaviors per week
- Moderate: An average of 4-7 episodes of inappropriate compensatory behaviors per week
- Severe: An average of 8–13 episodes of inappropriate compensatory behaviors per week
- Extreme: An average of 14 or more episodes of inappropriate compensatory behaviors per week

Race, sex and age

- Occurs predominantly in women. Most reports suggest a female-to-male ratio of 10:1, with reported ranges from 20:1 to 7:1.
- In some populations (eg, active duty military) body dissatisfaction and subclinical eating disorder rates among males have been reported to be in excess of 20%.
- The mean age of onset is 19.7, slightly older than the peak age of onset for AN, but lower than the age of onset for binge-eating disorder.
- The prevalence of bulimia nervosa in children younger than 14 years appears to be less than 5%.
- Bulimia nervosa has also been reported in the elderly.

Signs and symptoms

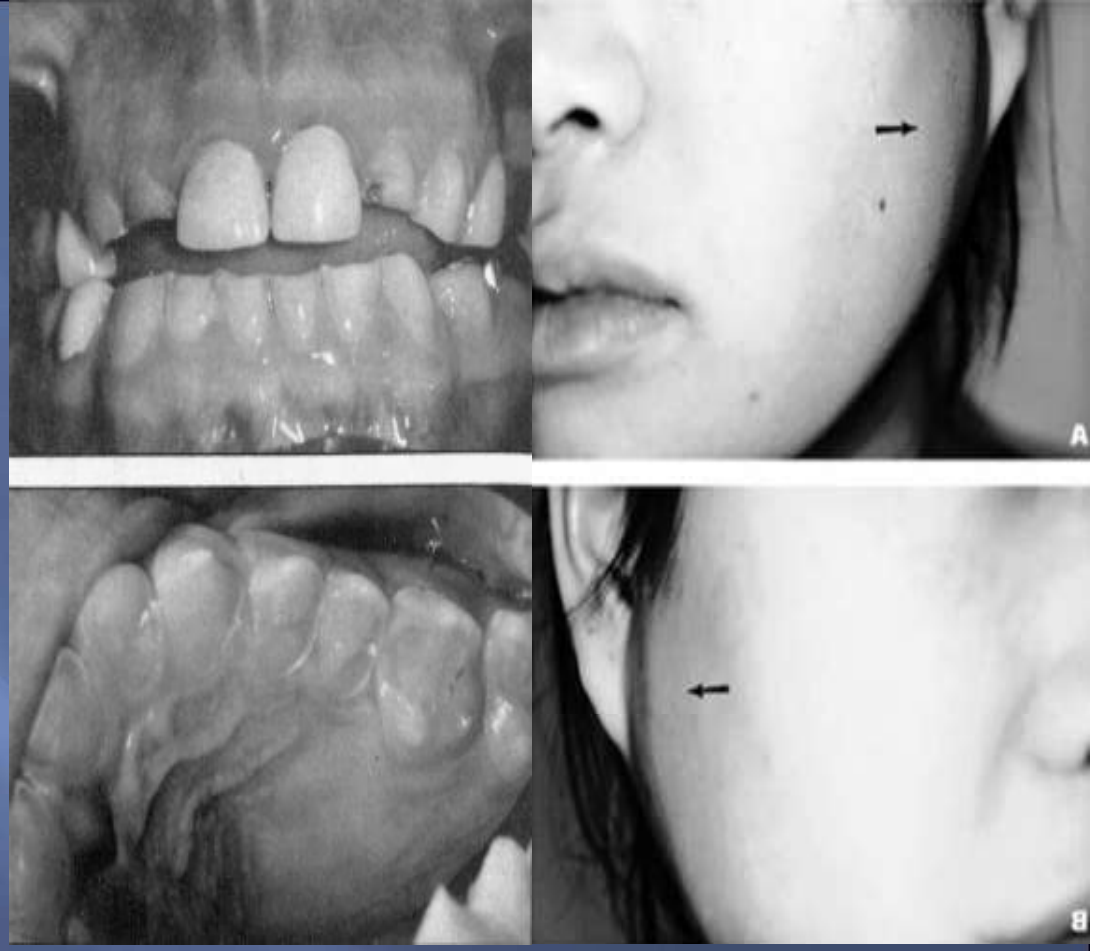
- General:
  - dizziness,
  - lightheadedness,
  - palpitations (due to dehydration, orthostatic hypotension, possibly hypokalemia)

- Gastrointestinal symptoms:
  - pharyngeal irritation,
  - abdominal pain (more common among persons who self-induce vomiting),
  - blood in vomitus (from esophageal irritation; more rarely, from actual tears, which may be fatal),
  - difficulty swallowing,
  - bloating,
  - flatulence,
  - constipation, and obstipation

- Pulmonary symptoms - Uncommonly, aspiration pneumonitis or, even more rarely, pneumomediastinum

- Amenorrhea - Occurs in up to 50% of women with bulimia nervosa; significant proportion of remaining patients have irregular periods; many more will have menstrual irregularity and scanty periods

Physical findings

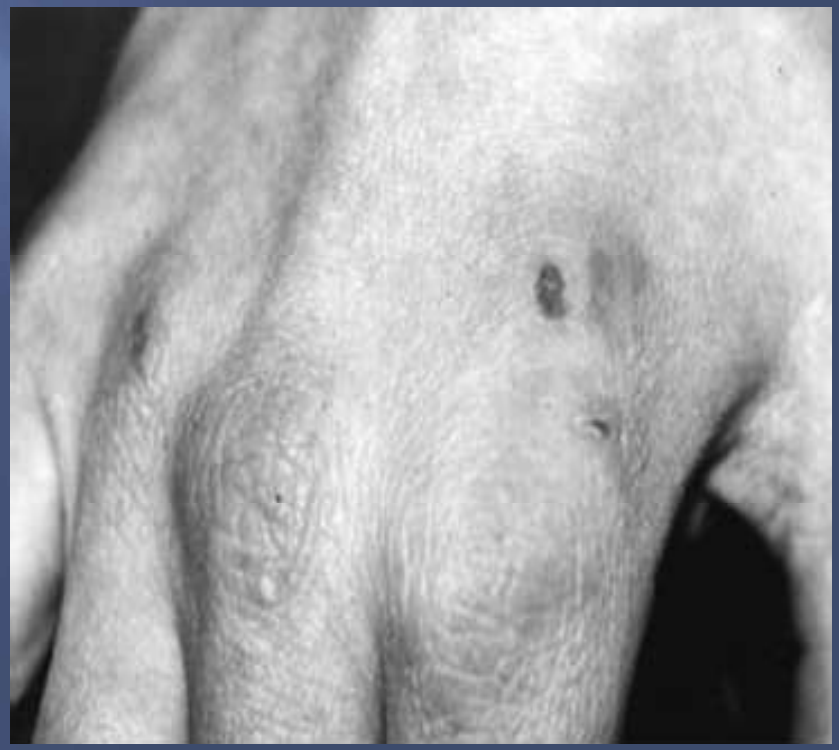


- Bilateral parotid enlargement
- Dental damage
- Bradycardia
- Tachycardia,
- Hypothermia,
- Hypotension
- Edema (mostly feet)
- In obese patients (minority)

- fat folds that favor humidity and maceration with bacterial and fungal overgrowth,
- striae due to skin overextension,
- stasis pigmentation related to peripheral vascular disease,
- plantar hyperkeratosis due to increased weight.

Skin manifestations

- Russell sign (callosities, scarring, and abrasions on the knuckles secondary to repeated self-induced vomiting).
- telogen effluvium (sudden, diffuse hair loss),
- acne,
- xerosis (dry skin),
- nail dystrophy (degeneration),
- scarring resulting from cutting, burning, and other self-induced trauma.



Screening tool- SCOFF questionaire

- Do you make yourself **S** ick because you feel uncomfortably full?
- Do you worry you have lost **C** ontrol over how much you eat?
- Have you recently lost more than **O** ne stone (about 14 lbs or 6.35 kg) in a 3-month period?
- Do you believe yourself to be **F** at when others say you are too thin?
- Would you say that **F** ood dominates your life?

A high index of suspicion is required in any depressed or anxious weight-conscious young woman.

Screening tool- The Eating Disorder Screen for Primary Care (ESP)

- Are you satisfied with your eating patterns?
- Do you ever eat in secret?
- Does your weight affect the way you feel about yourself?
- Have family members suffered from an eating disorder?
- Do you currently suffer with or have you in the past suffered with an eating disorder?

Mental state examination

- Appearance: Patients are typically neat, well dressed, and show attention to detail. Grooming is often meticulous and may further demonstrate a patient's concern about personal appearance.
- Behavior: Patients usually do not have kinetic abnormalities, but anxious feelings may heighten psychomotor agitation. Movements are spontaneous, and patients generally are cooperative and able to carry out requested tasks.
- Cooperation: Patients generally avoid eye contact due to shame and embarrassment.
- Mood and affect: Patients often demonstrate a depressed mood but may also have significant anxiety.
- Speech: Content and articulation are generally normal.
- Thought process: Patients likely have a linear thought process that is goal-directed.
- Thought content: Thoughts tend to revolve around food and concerns regarding body image and weight.
- Perceptual disturbances: Delusions and hallucinations are typically absent

Mental state examination

- Suicidal ideation:

-a significant consideration, especially in patients with depressed mood,

-often restricted to thoughts rather than concrete plans

- Cognition:

- patients are generally alert, and oriented to their surroundings.

- attention and concentration typically measured by serial sevens and digit span are normal.

- immediate memory is normal, as is recent and remote memory recall

- intellect is usually judged as normal (sometimes may surpass average)
- capacity to read and write is within normal limits.
- visuospatial functions are intact.

- Judgment:

- patients generally demonstrate poor judgment regarding self care and treatment.

- Insight:

- is variable (patients typically admit to episodes of binge eating, but do not appreciate their inappropriate fixation on eating or their distorted ideas of body image and weight)

Laboratory testings

- Comprehensive blood chemistry panel

- important in detecting possible occult metabolic complications of bulimia.
- with significant vomiting, **hypokalemic metabolic alkalosis** is possible.
- among patients with significant laxative abuse, **normokalemic metabolic acidosis may occur**.
- hyponatremia, hypocalcemia, hypophosphatemia, and hypomagnesemia should be ruled out.
- persons with significant intravascular depletion may have elevated blood urea nitrogen levels.

- Complete blood cell count:

- used to exclude anemia or other occult hematologic abnormalities.

- Urinalysis:

- Urine specific gravity may reflect the state of hydration.

Some patients may water load in an attempt to gain some weight before their health care visit.

- Urine toxicology: Comorbid substance abuse should be ruled out with a urine toxicology screen.

Aditional testings and studies

- Pregnancy test:

- to rule out pregnancy in female patients presenting with amenorrhea.

- Amylase:

-hyperamylasemia is found in up to 30% of persons with significant vomiting because of hypersecretion from the salivary glands. a rough measure of purging activity.

- ECG:

  Due to the potential for **arrhythmias** and **cardiomyopathy** as possible complications, ECG should be performed in patients who are very thin, complaining of palpitations, have other signs or symptoms suggestive of cardiovacular concern, ie **prolonged QTc,** especially in the setting of hypokalemia, heighten the risk for cardiac decompensation in this population.

- A dual energy absorptiometry (DEXA)

- Due to the potential for osteoporosis, scan may be useful, particularly for patients with irregular menses, mood disorders, and/or who smoke cigarettes.

- Routine neuropsychological testing is not indicated (neuropsychological testing may show decision-making abnormalities, as well as impairment in word recall, abstraction, attention, visuospatial functioning, and problem solving)

- Imaging studies are never routinely indicated or ordered for uncomplicated or typical cases of bulimia nervosa.

Physiological metabolic abnormalities

- low plasma insulin level,
- low C peptide level,
- low triiodothyronine level,
- low glucose level (both fasting and postbinge/postvomiting hypoglycemia are sometimes seen)
- increased beta-hydroxybutyrate
- Increased free fatty acid levels
- increased secretory diurnal amplitudes in cortisol and adrenocorticotropic hormone (ACTH)
- blunted responses to corticotrophin-releasing hormone (CRH)
- abnormal responses to dexamethasone suppression (like in in anorexia nervosa and MDD)
- higher growth hormone levels at night,
- nocturnal prolactin levels tend to be lower
- episodes of amenorrhea occuring in as up to 50% of women
- 50% of women have anovulatory cycles (impaired luteinizing hormone pulsatile secretion patterns and associated reduced estradiol and progesterone pulse amplitudes)
- about 20% of women have luteal phase defects.

Differential diagnosis

- Anorexia nervosa
- Binge-eating disorder (BED)
- Night eating syndrome *(NES)**
- Sleep-related eating disorder (SRED) *
- Kleine-Levin Syndrome
- Kluver-Bucy Syndrome
- Obsessive-Compulsive Disorder
- Obesity
- Depression
- Body dismorphic disorder

Biological factors

- **Neurotransmitters**
  - Serotonin: possibly related to weight regulation and eating behaviors, documented cases of **elevated serotonin** in the cerebral spinal fluid in patients with anorexia nervosa and bulimia nervosa.
  - Norepinephrine: lower levels of serum norepinephrine
  - Dopamine: dopamine activity is thought to be associated with distortion of body image,
- **Hormones**

Interactions between **orexigenic** (neuropeptide Y (NP-Y), peptide Y (PYY)), and **anorectic** factors (cholecystokinin (CCK), beta-endorphin).

- **Genetics**
  - Genetic links proposed at chromosomes 1, 3, and 10p related to bulimia nervosa.
  - Chromosome 10p may also be linked with obesity in addition to bulimia nervosa.

Developmental and psychological factors

- Childhood anxiety, (eg, difficulties separating from caretakers)
- History of childhood trauma and neglect, including subtle degrees of psychological abuse, teasing, and other interactions that generate self-doubt
- difficulties with self-esteem,
- impulsivity
- difficulties with affective self-regulation, impulsivity,
- perfectionism,
- body image distortion,
- susceptibility to triggers of a binge-purge cycle (which may occur around dieting and weight loss),
- poor coping skills.

Socio-cultural factors

- Precipitating events for a binge/purge cycle in people with bulimia nervosa are:

- anxiety states,
- emotional tension,
- boredom,
- environmental cues about food and eating,
- alcohol use,
- substance abuse,
- exhaustion

- Excessive concerns about physical appearance, body image and thinness seem central to both anorexia nervosa and bulimia nervosa.

Management - psychotherapy

1. Cognitive-behavioral therapy (CBT)

Behavioral approaches:,

- diary keeping;
- behavioral analyses of the antecedents,
- behaviors, and consequences (so-called ABCs) associated with binge eating and purging episodes;
- exposure to food paired with progressive response prevention regarding binge eating and purging.

Cognitive approach:

-distorted or maladaptive thoughts regarding weight and shape are identified, examined, and addressed,

- dysfunctional irrational beliefs are explored and confronted to allow better understanding, enhanced self-control, and improved body image.

2. Interpersonal psychotherapy (IPT)
3. Nutritional rehabilitation counseling
4. Family therapy

Pharmacological treatment

- Fluoxetine (Prozac) – the only SSRI approved by the FDA for the treatment of bulimia nervosa
- Other antidepressants - As a group, antidepressants are the mainstay of pharmacotherapy for bulimia nervosa; they may help patients with substantial concurrent symptoms of depression, anxiety, obsessions, or certain impulse disorder symptoms
- Mood stabilizers:

- topiramate, lithium, and valproic acid have been associated with adverse effects that can make these agents difficult to use in patients with bulimia nervosa; - lithium has not been demonstrated to be effective for bulimia nervosa per se

Surgical care

- Patients may develop an acute gastric obstruction and/or gastric dilatation(rarely resulting in gastric perforation leading to acute peritonitis), which presents with severe, continuous projectile vomiting that occurs soon after any oral intake.
- When the potential for

- gastric dilatation,

- outlet obstruction,

- esophageal tear (Mallory-Weiss syndrome) develop or in case of esophageal rupture, which can precipitate acute mediastinitis.

Need for hospitalization

- AAP Admission Criteria for Bulimia Nervosa
  - Syncope
  - Serum potassium concentration <3.2 mmol/L
  - Serum chloride concentration <88 mmol/L
  - Esophageal tears
  - Cardiac arrhythmias including prolonged QTc
  - Hypothermia
  - Suicide Risk
  - Intractable vomiting
  - Hematemesis
  - Failure to respond to outpatient treatment

Proposed DSM V Criteria

A. Recurrent episodes of binge eating. An episode of binge eating is characterized by both of the following:

1. eating, in a discrete period of time (for example, within any 2-hour period), an amount of food that is definitely larger than most people would eat in a similar period of time under similar circumstances
2. a sense of lack of control over eating during the episode (for example, a feeling that one cannot stop eating or control what or how much one is eating)

B. The binge-eating episodes are associated with three (or more) of the following:

1. eating much more rapidly than normal
2. eating until feeling uncomfortably full
3. eating large amounts of food when not feeling physically hungry
4. eating alone because of feeling embarrassed by how much one is eating
5. feeling disgusted with oneself, depressed, or very guilty afterwards

C. Marked distress regarding binge eating is present.

D. The binge eating occurs, on average, at least once a week for three months.

E. The binge eating is not associated with the recurrent use of inappropriate compensatory behavior (for example, purging) and does not occur exclusively during the course Anorexia Nervosa, Bulimia Nervosa, or Avoidant/Restrictive Food Intake Disorder.

Binge Eating: Lifetime Prevalence

	Women	Men
BED	3.5 %	2.0 %
BN	1.5 %	.5 %
Any binge eating (ED-NOS)	4.9 %	4.0 %

Hudson et al, 2007

BED: Prevalence in Obesity Tx

- Seeking treatment for obesity:
  - 30% with self-report
  - 4.2% - 18.8% with interview
- Undergoing bariatric surgery (Niego et al., 2007)
  - 2%-49% BED
  - 6% - 64% Any binge eating
- Surgical vs. non-surgical WLT
  - Higher levels of ED's in surgical group

Etiology

- Multiple influences
- Genetic
  - Aggregates in families (heritability 30-80%)
- Biological
  - Alterations in central and peripheral systems associated with regulation of appetite
- Environmental
  - Childhood obesity
  - Family overeating
  - Negative comments about weight/body/eating

BED: Characteristics

- Compared to controls
  - More frequent parental depression
  - Greater vulnerability to obesity
  - More exposure to negative comments about shape, weight, and eating
  - Greater perfectionism and negative self-evaluation
- Compared to other psychiatric disorders
  - More frequent childhood obesity
  - Greater awareness of negative comments about shape, weight, eating
- Compared to obesity
  - Greater weight and shape concerns
  - More personality disturbance
  - Greater likelihood of mood/anxiety disorders and lower QOL

BED: Subtyping

- Dietary
- Dietary – Negative Affect
  - Greater eating and weight obsessions
  - Greater social maladjustment
  - Higher lifetime rates of mood, anxiety, and personality disorders
  - Poorer response to treatment

Grilo et al., 2001; Stice et al., 2001

BED: Psychological Treatment

- Cognitive Behavioral Therapy (CBT)
  - Best established psychotherapy treatment
  - Grade of A in review of treatments *(NICE guidelines, 2005; strong empirical support from well-conducted, randomized trials)*
  - Self-help option (Guided Self-Help; GSH)
- Interpersonal Therapy (IPT)
- Dialectical Behavior Therapy (DBT)
- Psychopharmacology
  - Topiramate
  - Sibutramine

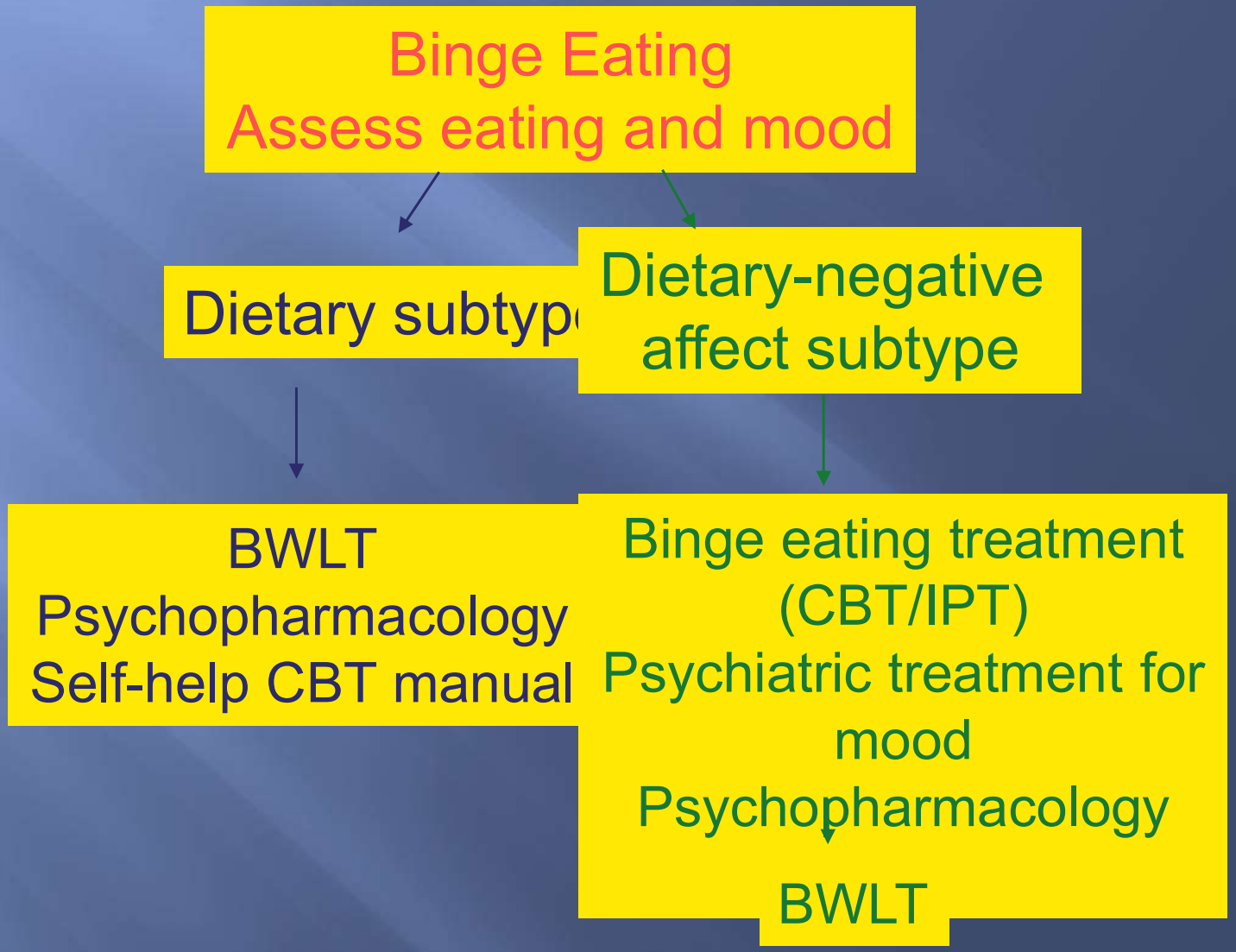
Behavioral Weight Loss Treatment

- CBT vs. BWLT (Munsch et al., 2007):
  - Posttreatment: CBT looks better
  - 12-months: Equally effective
  - Binge eating: faster decrease with CBT
  - Weight: faster decrease with BWLT
- CBT vs. BWLT (Grilo et al., 2011)
  - Both effective for BED but no substantial weight losses
  - Sequencing CBT then BWLT: no support
  - *BE remission associated with weight loss
  - Support for CBT, BWLT as alternative

BWLT and binge eating

- Binge eating is NOT a contraindication for BWLT
- But, BED *has* been associated with poorer weight loss outcomes (Pagot et al, 2007)
- And specialty treatments yield better outcomes on eating disorder psychopathology
- Recommendation depends on goals
- Subtyping of BED may help with decision
- Depression and distress associated with BED may warrant separate treatment

Binge Eating: Treatment Algorithm



Multidisciplinary Approach

- Behavioral health/mental health provider
  - CBT training
  - Experience with eating disorders
- Dietitian
- PCP
  - Rule out medical contributions, including medications
- Psychopharmacologist
- Exercise component
  - Trainer
  - Gym
  - Peer group