

# Sleep Disorders

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# Sleep Disorders 1

- Introduction
- Insomnia Disorder
- Hypersomnolence Disorder
- Narcolepsy

## ***Breathing-Related Sleep Disorders***

- Obstructive Sleep Apnea Hypopnea
- Central Sleep Apnea
- Sleep-Related Hypoventilation

# Sleep Disorders 2

## *Circadian Rhythm Sleep-Wake Disorders*

- Delayed Sleep Phase Type
- Advanced Sleep Phase Type
- Irregular Sleep-Wake Type
- Non-24-Hour Sleep-Wake Type
- Shift Work Type

## *Parasomnias*

- Non-REM Sleep Arousal Disorders
- Nightmare Disorder
- REM Sleep Behavior Disorder
- Restless Legs Syndrome
- Substance/Medication-Induced Sleep Disorder

# Sleep-Wake Disorders – Introduction

- To clarify when referral to a sleep specialist is appropriate
- Persistent sleep disturbances
  - Often accompanied by depression, anxiety, cognitive changes
  - **Established risk factor** for mental illness, SUDs
  - May be **prodromal expression** of a mental illness
    - Possible opportunity for early intervention or to attenuate full episode
- Coexisting conditions are **the rule**
  - Breathing-related sleep disorders
  - Disorders of heart/lung (CHF, COPD)
  - Neurodegenerative disorders (Alzheimer's disease)
  - MSK disorders (osteoarthritis)
  - May not only disturb sleep, but may be worsened during sleep
- REM sleep behavior disorder
  - Early neurodegenerative ( $\alpha$ -synucleinopathy, Parkinson's disease)

# Insomnia Disorder

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# Insomnia Disorder – Diagnostic Criteria

- A. Dissatisfaction with sleep quality/quantity (1+/3):
  - 1. Difficulty **initiating** sleep
  - 2. Difficulty **maintaining** sleep
  - 3. **Early-morning awakening + inability to return to sleep**
- B. Significant distress or impairment
- C. Occurs **3+ nights per week**
- D. Present for **3+ months**
- E. Occurs despite **adequate opportunity** for sleep
- F. Not better explained by another sleep-wake disorder
- G. Not due to substance
- H. Not better explained by coexisting AMD or AMC

# Insomnia Disorder – Diagnostic Specifiers

- *Specify if:*
  - **With non-sleep disorder mental comorbidity** (incl SUD)
  - **With other medical comorbidity**
  - **With other sleep disorder**
- *Specify if:*
  - **Episodic:** Symptoms for 1-3 months
  - **Persistent:** Symptoms for 3+ months
  - **Recurrent:** 2+ episodes within 1 year

# Insomnia Disorder – Diagnostic Features

- Different manifestations of insomnia at different sleep periods
  - **Sleep-onset insomnia** (initial insomnia)
    - Difficulty initiating sleep
  - **Sleep-maintenance insomnia** (middle insomnia)
    - Frequent or prolonged awakenings throughout night
  - **Late insomnia**
    - Early-morning awakenings + inability to return to sleep
  - Specific type often varies over time
- Most common SINGLE sx of insomnia → **difficulty maintaining**
  - 2<sup>nd</sup> most common = **difficulty falling asleep**
  - Most common OVERALL presentation = **combination**
- Quantification
  - Self-report, sleep diaries, other methods (actigraphy, PSG)



# Insomnia Disorder – Diagnostic Features

- Non-restorative sleep → common complaint
  - Does not feel rested upon awakening, despite **adequate duration**
  - Usually assoc with **initial or middle insomnia**
  - Can occur in **isolation** → other/unspecified insomnia disorder
- Quantify insomnia severity (illustrative purposes only)
  - Difficulty initiating → subjective **sleep latency >30 minutes**
  - Difficulty maintaining → subjective time awake **after onset >30 minutes**
  - No standard definition of early morning awakening
    - Awakening **>30 mins before scheduled time**
    - Before **total sleep time reaches 6.5 hours**
- Age-dependent changes
  - Decr ability to sustain sleep
  - Shift in timing of main sleep period

# Insomnia Disorder – Diagnostic Features

- May involve daytime impairments
  - **Fatigue**
  - **Daytime sleepiness** → less common generally
    - More common if **elderly** or if **comorbid AMC/sleep disorder**
  - Cognitive impairments
    - **Attention, concentration, memory**
    - Performing simple manual skills
  - Mood disturbances
    - Typically **irritability, mood lability**
    - Less commonly **depressive, anxiety sx**
- Not everyone has distress or impairment
  - **Healthy older adults** → sleep continuity often interrupted
    - May still identify as good sleepers

# Insomnia Disorder – Associated Features

- Often assoc with physiological, cognitive arousal/conditioning
  - Preoccupation with sleep/inability to sleep → may become **vicious cycle**
    - Can **override normal sleep-onset** mechanisms
  - Persistent insomnia → may acquire **maladaptive sleep habits/cognitions**
    - Excessive time in bed, erratic sleep schedule, napping
    - Fear of sleeplessness/daytime impairment, clock monitoring
  - May fall asleep **more easily when NOT trying to do so**
    - Away from own bedroom, usually routines
- Daytime complaints/symptoms
  - **Fatigue, decr energy, mood disturbances** (anxiety, depression)
  - Excessive focus on **perceived effects** of sleep loss

# Insomnia Disorder – Associated Features

- High scores on self-report psychological/personality inventories
  - Mild **depression/anxiety**, **worrisome cognitive style**
  - **Somatic focus**
  - Emotion-focused/**internalizing style** of conflict resolution
- Cognitive impairment patterns → inconsistent
  - Tasks of **higher complexity**
  - Tasks requiring **frequent changes in performance strategy**
  - Require **more effort to maintain cognitive performance**

# Insomnia Disorder – Prevalence

- Adults
  - **33% → report insomnia sx** (10-20% of primary care)
    - More common among **FEMALES (1.44x)**
    - Can be symptom or independent disorder
    - Often comorbid with AMC or **AMD (40-50%)**
  - **10-15% → daytime impairments**
  - **6-10% → insomnia disorder** (MOST PREVALENT of all sleep disorders)

# Insomnia Disorder – Development & Course

- Onset → any time during life
  - First episode most common during **young adulthood**
    - Less commonly begins in childhood or adolescence
  - Women → may onset during **menopause + persist** (after other sx resolve)
  - Late-life → often assoc with other health-related conditions
- Situational (acute) → usually **few days to weeks**
  - Assoc with life events, rapid changes in sleep schedule/environment
    - Acute psychological stress or mental disorder e.g. MDD)
  - May be **insidious** without identifiable precipitating factor
  - **May persist longer** after triggering event (due to **conditioned arousal**)

# Insomnia Disorder – Development & Course

- Episodic/recurrent (assoc with stressful events)
  - Chronicity → 45-75% (after 1-7 years)
  - May still have night-to-night variability (occasional restful nights)
  - May have history of “light sleeping”
- Insomnia sx change with age
  - More prevalent among middle-age + older adults
    - Young adults → more commonly **difficulties initiating sleep**
    - Older adults → more commonly **maintaining sleep**
  - Less data in children + adolescents
    - Conditioning factors, inconsistent sleep schedules/bedtime routines
    - Psychological + medical factors

# Insomnia Disorder – Risk & Prognostic Factors

- More likely when predisposed exposed to precipitating events
  - Major life events, chronic daily stress
  - More likely to have persistent insomnia after initial trigger gone
  - Perpetuating factors → sleep habits, sleep schedule, fear of not sleeping
- Temperamental
  - **Anxiety, worry-prone** personality/cognitive styles
  - **Incr arousal** predisposition, tendency to **repress emotions**
- Environmental
  - Noise, light, temperature, high altitude



# Insomnia Disorder – Risk & Prognostic Factors

- Genetic & physiological
  - **FEMALE gender**, advanced age
  - **Familial disposition**
    - Higher prevalence among monozygotic twins
    - Higher in 1<sup>o</sup> family members (vs gen pop)
    - Unclear mechanism
- Course modifiers
  - **Poor sleep hygiene** (caffeine, irregular sleep schedules)

# Insomnia Disorder – Gender-Related Issues

- More prevalent among → **FEMALES**
  - First onset often with **birth of new child**, or with **menopause**
  - Higher prevalence among **older females**
    - But better preservation of sleep continuity + slow-wave sleep (vs males)

# Insomnia Disorder – Diagnostic Markers

- Polysomnography → usually impaired sleep continuity
  - Incr **sleep latency**, **time awake** after sleep onset
  - **Decr sleep efficiency** (% time in bed asleep)
  - **Incr stage 1 sleep**
  - **Decr stage 3 + 4 sleep**
  - PSG does not always match clinical presentation
    - Individuals misestimate sleep duration, wakefulness
- Quantitative EEG
  - More high-frequency during sleep-onset period, non-REM sleep
    - Suggestive of incr cortical arousal
- Insomnia (on objective sleep measures)
  - **Lower sleep propensity**
  - Typically **do NOT show incr daytime sleepiness**

# Insomnia Disorder – Diagnostic Markers

- Generalized activation of HPA axis (not consistent)
  - Incr **cortisol** levels, **HR variability**, **reactivity to stress**, **metabolic rate**
- No consistent or characteristic abnormalities on physical exam
  - May appear **fatigued or haggard**
  - May appear **over-aroused or wired**
  - May have more **stress-related psychophysiological sx**
    - Tension headache, muscle tension/pain, GI sx

# Insomnia Disorder – Functional Consequences

- Interpersonal, social, occupation problems
  - Insomnia, excessive concern, daytime irritability, poor concentrations
- Decr attention/concentration → COMMON
  - May be related to higher rates of **accidents**
- Persistent insomnia
  - **MDD, hypertension, MI**
  - Work **absenteeism, decr productivity**
  - Decr **quality of life**
  - Incr **economic burden**

# Insomnia Disorder – Differential Diagnosis (1)

- Normal sleep variations

- “**Short sleepers**” → no difficulty falling/staying asleep
  - No characteristic daytime sx (fatigue, concentration, irritability)
  - May attempt to sleep longer → may create insomnia-like pattern
- **Inadequate sleep opportunity**
  - Emergency situations, professional/family obligations

- Situational/acute insomnia

- Lasts few days to weeks (<3 mos) → may cause sig distress/impairment

- Delayed sleep phase and shift work types (CRSW disorder)

- Difficulties only when trying to sleep at **social normal times**
- No difficulty at delayed times, or with **endogenous circadian rhythm**
- History of shift work

# Insomnia Disorder – Differential Diagnosis (2)

- Restless legs syndrome
  - **Urge to move legs, unpleasant leg sensation**
  - Often produces difficulties initiating/maintaining sleep
- Breathing-related sleep disorders
  - Loud snoring, breathing pauses, excessive daytime sleepiness
  - 50% of sleep apnea → also report insomnia sx (females, older adults)
- Narcolepsy
  - Predominant daytime sleepiness, cataplexy, sleep paralysis, hallucinations
- Parasomnias
  - Unusual behaviors/events during sleep → predominate clinical picture
- Substance/medication-induced sleep disorder, insomnia type

# Insomnia Disorder – Comorbidity

- Bidirectional risk relationship with many medical conditions
  - **Diabetes, CAD, COPD, arthritis, fibromyalgia, chronic pain**
  - Insomnia incr risk of medical conditions
  - Medical conditions incr risk of insomnia
  - Direction of relationship not always clear, may change
- Comorbid mental disorder common
  - May be risk factor or early symptom
  - Esp Bipolar, depressive, anxiety disorders
  - May progress to SUD
    - Medications/alcohol to help sleep
    - Anxiolytics for tension/anxiety
    - Caffeine/stimulants for excessive fatigues



# Hypersomnolence Disorder

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# Hypersomnolence Disorder – Diagnostic Criteria

- A. **Excessive sleepiness, despite >7 hours main sleep (1/3):**
  - 1. **Recurrent periods/lapses of sleep**, within same day
  - 2. **Non-restorative, prolonged main sleep episode** (>9 hours) per day
  - 3. **Difficulty being fully awake**, after abrupt awakening
- B. **Occurs 3+ times per week, for 3+ months**
- C. **Significant distress or impairment**
- D. **Not better explained by another sleep disorder**
- E. **Not due to substance**
- F. **Not better explained by AMD or AMC**

# Hypersomnolence Disorder – Diagnostic Specifiers

- *Specify if:*
  - **With mental disorder** (incl SUDs)
  - **With medical condition**
  - **With another sleep disorder**
- *Specify if:*
  - **Acute:** duration <1 month
  - **Subacute:** duration 1-3 months
  - **Persistent:** duration >3 months
- *Specify current severity (frequency):*
  - **Mild:** 1-2 days/week
  - **Moderate:** 3-4 days/week
  - **Severe:** 5-7 days/week

# Hypersomnolence Disorder – Diagnostic Features

- Hypersomnolence
  - **Excessive sleep quantity** → nocturnal or daytime
  - **Decr wakefulness** → sleep propensity, difficulty waking, staying awake
  - **Sleep inertia** → impaired performance, vigilance after waking
- Able to **fall asleep quickly + good sleep efficiency (>90%)**
- Sleep inertia (“sleep drunkenness”)
  - Difficulty waking/transition → minutes to hours
  - May appear **confused, disoriented, combative, ataxic**
  - Affects motor dexterity, inappropriate behavior, memory deficits, groggy
  - May have **automatic behaviors** (without recall)

# Hypersomnolence Disorder – Diagnostic Features

- Major sleep episode → 9+ hours, NON-restorative
  - Difficulty waking in morning
  - Some **may have normal** nocturnal sleep duration (6-9 hours)
- Unintentional daytime naps
  - **Long** (1+ hour), **non-restorative**, does **not improve alertness**
  - **Nearly everyday** (regardless of nocturnal sleep duration)
  - Sleepiness develops over time (not sudden sleep attack)
  - Typically in **low-stimulation situations** (lectures, reading, TV, driving)
    - May occur in high-attention situations (work, meetings, social)

# Hypersomnolence Disorder – Associated Features

- Symptoms shared with other sleep disorders (e.g. narcolepsy)
  - **Non-restorative sleep** → 80% of hypersomnolence disorder
  - **Difficulty waking** → 80% of hypersomnolence disorder
  - **Sleep inertia** → 36-56% of hypersomnolence disorder, HIGHLY SPECIFIC
  - Automatic behaviors
  - Short naps unrefreshing, appear sleepy, falling asleep
- Subset with family history hypersomnolence
- Subset with sx of autonomic dysfunction
  - Recurrent **vascular-type headaches**
  - Reactivity of peripheral vascular system (**Raynaud's phenomenon**)
  - **Fainting**

# Hypersomnolence Disorder – Prevalence

- In sleep disorders clinics, among pts c/o daytime sleepiness
  - 5 – 10% dx with hypersomnolence disorder
- In US/EU gen pop
  - 1% with episodes of sleep inertia
- Gender ratio → EQUAL (M=F)

# Hypersomnolence Disorder – Development & Course

- Onset

- Mean age at onset = **age 17-24**
- Fully manifest in **late adolescence or early adulthood**
- Pediatric cases RARE
- Dx usually made 10-15 years after first symptoms

- Course → **persistent, progressive**

- Average nighttime sleep duration → **9.5 hours** (up to 20 hours)
- May be able to reduce sleep time during working days
  - Increased on weekends/holidays (+3 hours)
- Difficulty waking, sleep inebriate (40%)
- Sleepiness may be worsened by **development of other sleep disorders**
- Hyperactivity → may be sign of daytime sleepiness in children
- Voluntary napping increases with age (NORMAL)



# Hypersomnolence Disorder – Risk & Prognostic Factors

- Environmental

- Hypersomnolence may be incr by **psychological stress, alcohol use**
- **Viral infection** → precede/accompany in 10% of cases
  - HIV pneumonia, infectious mononucleosis, GBS
- **Head trauma** → hypersomnolence may appear 6-18 months after

- Genetic & physiological

- May be familial (? autosomal dominant inheritance)

# Hypersomnolence Disorder – Diagnostic Markers

- Nocturnal polysomnography
  - Normal-prolonged sleep duration
  - **Short sleep latency**
  - Normal-increased sleep continuity
  - Normal REM sleep distribution
  - **Sleep efficiency >90%**
  - May have **incr slow-wave sleep**
- Multiple sleep latency test
  - (Sleep tendency = mean sleep latency <8 minutes)
  - In hypersomnolence disorder → **high sleep tendency**
    - Mean sleep latency → typically <10 minutes, frequently <8 minutes
  - **Sleep-onset REM periods** (within 20 minutes of sleep onset)
    - May be present (less than 40-50% of nap opportunities)

# Hypersomnolence Disorder – Functional Consequences

- Low alertness while fighting need for sleep
  - Decr **efficiency, concentration, memory**
- Work + social relationships
  - **Morning obligations**
  - **Daytime sleep episodes** → embarrassing
    - Dangerous if driving, operating machinery

# Hypersomnolence Disorder – Differential Diagnosis (1)

- Normal variation in sleep
  - “**Long sleepers**” → no excessive sleepiness, sleep inertia
    - No automatic behaviors, **sleep is refreshing**
    - If shorter nocturnal sleep (due to social/work demands) → daytime sx
  - “**Behaviorally induced insufficient sleep syndrome**”
    - Inadequate nocturnal sleep (<7 hours), may have daytime sleepiness
    - Typically **catch up** with longer sleep when free
    - Unlikely to **persist** for decades
    - Do not dx hypersomnolence disorder if unsure of sleep duration
      - May trial **sleep extension** for 10-14 days
- Poor sleep quality + fatigue
  - **Not necessarily relieved by increased sleep**
  - May be difficult to differentiate fatigue (vs excessive sleepiness)

# Hypersomnolence Disorder – Differential Diagnosis (2)

- Breathing-related sleep disorders
  - May have similar patterns of excessive sleepiness
  - **Loud snoring, pauses in breathing, brain injury**
  - **Cardiovascular disease, hypertension, heart failure**
  - **Obesity, oropharyngeal anatomical abnormalities**
  - PSG → can confirm **apneic events** (not in hypersomnolence disorder)
- Circadian rhythm sleep-wake disorders
  - Often daytime sleepiness
  - Hx **abnormal sleep-wake schedule** (shifted/irregular hours)
- Parasomnias
  - Rarely prolonged, undisturbed nocturnal sleep or daytime sleepiness
- Other mental disorders
  - Hypersomnolence may be essential/associated feature
    - **MDE with atypical features, depressed phase of bipolar**

# Hypersomnolence Disorder – Comorbidity

- Mood disorders
  - Depressive disorders, MDD with seasonal pattern
  - Depressive episodes in bipolar disorder
  - May have depression sx → may be related to psychosocial consequences of persistent incr sleep need
- Risk of SUD → esp self-medication with **stimulants**
- Neurodegenerative conditions assoc with hypersomnolence
  - **Alzheimer's disease, Parkinson's disease**
  - **Multiple system atrophy**

# Narcolepsy

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# Narcolepsy – Diagnostic Criteria

- A. Recurrent **irrepressible need to sleep**, lapsing into sleep, or **napping within same day** → **3x per week, for 3 months**
- B. 1/3 symptoms:
1. **Cataplexy episodes**, few times per month, either:
    - **Brief episodes** (seconds-minutes), sudden **bilateral loss of muscle tone**, maintained **consciousness**, precipitated by **laughter/joking**
    - **In children** or within 6 months onset, **spontaneous grimaces** or **jaw-opening episodes with tongue thrusting** or **global hypotonia**, without any obvious emotional triggers
  2. **Hypocretin deficiency** → low CSF levels of hypocretin-1
  3. **Short REM sleep latency**
    - **Nocturnal PSG** → REM sleep latency <15 mins
    - **Multiple sleep latency test** → mean sleep latency <8 mins + 2+ sleep-onset REM periods



# Narcolepsy – Diagnostic Specifiers

- *Specify subtype:*
  - **Narcolepsy without cataplexy, but with hypocretin deficiency**
    - May have “cataplexy-like” symptoms
  - **Narcolepsy with cataplexy, but without hypocretin deficiency**
    - Rare subtype (<5%)
  - **Autosomal dominant cerebellar ataxia, deafness, narcolepsy**
    - Exon 21 DNA (cytosine-5)-methyltransferase-1 mutation
    - Late-onset (age 30-40)
  - **Autosomal dominant narcolepsy, obesity, type 2 diabetes**
    - Rare, assoc with mutation in myelin oligodendrocyte glycoprotein gene
  - **Narcolepsy secondary to AMC**
    - Destruction of hypocretin neurons
      - Infectious (Whipple’s disease, sarcoidosis), trauma, tumors

# Narcolepsy – Diagnostic Specifiers

- *Specify current severity:*
  - **Mild:** infrequent cataplexy (less than once per week), naps 1-2x per day, less disturbed nocturnal sleep
  - **Moderate:** cataplexy every 1-2 days, multiple naps per day, disturbed nocturnal sleep
  - **Severe:** drug-resistant cataplexy, multiple attacks daily, nearly constant sleepiness, disturbed nocturnal sleep

# Narcolepsy – Subtypes

- Extremely rare to have low CSF + negative PSG/MSLT
  - Repeat testing advised
- Exclude → seizures, other causes of falls, conversion disorder
- HLA DQB1\*06:02
  - May be negative in narcolepsy with cataplexy, but without hypocretin deficiency
  - May be positive in narcolepsy secondary to AMC (?autoimmune)
- Head trauma/infections
  - Can cause **transient decr in CSF hypocretin-1 levels**
    - Without hypocretin cell loss

# Narcolepsy – Diagnostic Features (1)

- Recurrent daytime naps or lapses into sleep
  - Typically occurs daily (minimum 3x per week, for 3 months)
- Generally produces cataplexy
  - Most commonly → brief episodes of sudden bilateral **loss of muscle tone**
    - Precipitated by emotions (typically laughing/joking)
    - May affect neck, jaw, arms, legs, whole body
    - May result in head bobbing, jaw dropping, complete falls
  - **Awake + aware during cataplexy**
  - For criterion B1a → must be triggered by laughing/joking, few times/month
  - NOT weakness (after exercise or unusual emotional triggers)
  - UNLIKELY if lasting hours-days, or not triggered by emotions (NOT ROFL)
- In children, close to onset → may be **atypical cataplexy**
  - Primarily affecting face → **grimaces, jaw opening + tongue thrusting**
  - May present as low-grade continuous **hypotonia, wobbling gait**

## Narcolepsy – Diagnostic Features (2)

- Loss of hypothalamic hypocretin (orexin)-producing cells
  - **Hypocretin deficiency** (<1/3 control values, >100 pg/mL)
    - **CSF-hypocretin-1 = GOLD STANDARD**
    - **Rarely without cataplexy** (still low CSF levels of hypocretin-1)
      - In youths who may develop cataplexy later
  - Likely **autoimmune** → **99% carry HLA-DQB1\*06:02** (12-39% in controls)
    - May be helpful to check before LP for CSF hypocretin-1
- Nocturnal PSG, then MSLT → to confirm dx
  - Must stop all psychotropic medications, 2 weeks of adequate sleep
    - PSG → **short REM latency (<15 mins)**
    - MSLT → mean sleep latency <8 mins
      - Sleep-onset REM periods in 4-5 naps

# Narcolepsy – Associated Features (1)

- Autonomic behaviors → if severe sleepiness
  - Semi-automatic, haze-like fashion, without memory/consciousness
- Hypnagogic/hypnopompic hallucinations → **20-60%**
  - Hypnagogic → falling asleep, Hypnopompic → waking up
  - More vivid (than dreamlike mentation at sleep onset in normal sleepers)
- Nightmares, vivid dreams → common
  - Also in REM sleep behavior disorder
- Sleep paralysis (upon falling asleep/waking) → **20-60%**
  - Occurs in many normal sleepers, esp with stress/sleep deprivation

## Narcolepsy – Associated Features (2)

- Nocturnal eating may occur → obesity common
- Nocturnal sleep disruption → COMMON, may be disabling
  - Freq long or short awakenings
- Daytime sleepiness
  - May fall asleep in waiting area or during clinical exam
- During cataplexy (attacks usually <10 seconds)
  - May **slump in chair**, have **slurred speech**, **drooping eyelids**
  - **ABSENT REFLEXES** during cataplexy (vs conversion disorder)

# Narcolepsy – Prevalence

- Narcolepsy-cataplexy attacks → **0.02-0.04% of gen pop**
  - May have **slight male** preponderance



# Narcolepsy – Development & Course (1)

- Onset

- Typically in **children, adolescents, young adults** (rarely older adults)
  - 2 PEAKS of onset → **age 15-25 + age 30-35**
- Onset may be **abrupt or progressive**
  - If **abrupt onset in children** → HIGHEST severity
    - Severity then decr with age/tx → cataplexy may disappear
    - May be assoc with **obesity, premature puberty** (if prepubescent)
  - Onset in adults often less clear → some report lifetime sleepiness

- Course → PERSISTENT, lifelong

- Most common first sx (90%) = **SLEEPINESS**, incr need for sleep
- 2nd most common first sx = **cataplexy** (50% within 1 yr, 85% within 3 yrs)
- Other early sx → **hypnagogic hallucs, vivid dreaming, REM SBD**
- RAPID progression to **inability to stay awake during day**
  - Also inability to **maintain good sleep at night** (no incr in sleep needs)

## Narcolepsy – Development & Course (2)

- Atypical cataplexy → may be in first 3 months, esp in children
- Sleep paralysis → around puberty (if prepubertal onset)
- Exacerbation of sx
  - Non-adherence to medications
  - Development of concurrent sleep disorder (esp **sleep apnea**)
- In children & adolescents
  - Often develop **aggression or behavioral problems**
    - (secondary to sleepiness/nighttime sleep disruption)
    - Increasing workload, social pressure → less available sleep time
- Pregnancy → does NOT consistently modify sx
- After retirement → more opportunity for naps, less stimulants
- Maintaining **REGULAR SCHEDULE** → benefits all ages

# Narcolepsy – Risk & Prognostic Factors

- Temperamental

- **Parasomnias** more common (sleepwalking, bruxism, REM SBD, enuresis)
- Report need more sleep (than other family members)

- Environmental

- **Infections** likely triggers of autoimmune process
  - **Group A strep throat infection**, influenza, winter infections
- **Head trauma, abrupt changes in sleep-wake pattern** (job, stress)

- Genetic & Physiological

- Monozygotic twin concordance = **25-32%**
- **10-40x risk in 1° degree relatives** (prevalence 1-2%)
- Strong assoc with **HLA DQB1\*06:02 (99%)**
  - Slight modification from other polymorphisms

# Narcolepsy – Culture-Related Issues

- Described in ALL ethnic groups, many cultures
- Among African Americans
  - More cases **without cataplexy**, or with **atypical cataplexy**
  - May complicated dx (esp if obesity, OSA)

# Narcolepsy – Diagnostic Markers (1)

- Functional imaging
  - **Impaired hypothalamic responses** to humorous stimuli
- Nocturnal PSG followed by MSLT → confirms dx
  - Esp if initial dx, before dx, hypocretin not documented yet
  - Should stop all psychotropic drugs, normalize sleep-wake patterns
- PSG → **short REM sleep latency** (<15 mins)
  - **HIGHLY specific** (only 1% in control), moderately sensitive (50%)
  - May also see freq arousals, decr sleep efficiency, incr stage 1 sleep
    - Periodic limb movements (40%), sleep apnea
- MSLT → **short mean sleep latency** (<8 mins)
  - **AND sleep-onset REM periods** (in 2 of 4-5 nap test)
  - Positive in 90-95% narcolepsy (2-4% controls)

## Narcolepsy – Diagnostic Markers (2)

- Hypocretin deficiency → **CSF hypocretin-1 immunoreactivity**
  - Useful if suspected conversion disorder, atypical cataplexy, tx-refractory
  - CANNOT interpret if **severely ill (infection, head trauma, comatose)**
    - NOT affected by medications, sleep deprivation, circadian time
  - Other CSF results normal (cytology, protein, glucose)

# Narcolepsy – Functional Consequences

- Impaired DRIVING + WORKING
  - Should avoid **working with machinery, bus driver, pilot**
  - If untreated → risk of **social isolation, accident injury**
  - If controlled with tx, may drive (but not long distances alone)

# Narcolepsy – Differential Diagnosis (1)

Narcolepsy	Hypersomnolence Disorder
<ul style="list-style-type: none"> <li>• More discrete “<b>sleep attacks</b>”</li> <li>• <b>Cataplexy</b></li> <li>• <b>Intrusion elements of REM sleep</b> during transitions between sleep + awake (sleep-related hallucs, sleep paralysis)</li> <li>• MSLT → <b>shorter sleep latency, multiple SOREMPs</b></li> </ul>	<ul style="list-style-type: none"> <li>• Longer, less disrupted nocturnal sleep</li> <li>• <b>Greater difficulty waking</b></li> <li>• More persistent <b>daytime sleepiness</b></li> <li>• Longer, less refreshing daytime naps</li> <li>• <b>Minimal dreaming</b> during daytime naps</li> </ul>
<ul style="list-style-type: none"> <li>• BOTH have <b>daytime sleepiness, similar age at onset, stable course</b></li> </ul>	



# Narcolepsy – Differential Diagnosis (2)

- Sleep deprivation, insufficient nocturnal sleep
  - Common in **adolescents, shift workers**
  - May have positive MSLT if sleep deprived or delayed sleep phase
- Sleep apnea syndromes
  - **Obstructive sleep apnea** more common (esp if obesity)
    - Cataplexy may be overlooked, assumed to be unresponsive OSA
- Major depressive disorder
  - **NO cataplexy, MSLT normal** (different subjective vs objective sleepiness)
- Conversion disorder
  - Atypical features (long-lasting cataplexy, unusual triggers)
  - MSLT normal (no SOREMPs)
  - Reflexes NORMAL

# Narcolepsy – Differential Diagnosis (3)

- ADHD
  - Sleepiness can cause behavioral problems (aggression, inattention)
- Seizures → may be confused with cataplexy in young children
  - Not usually triggered by emotions or laughing/joking
  - More likely to hurt themselves when falling
  - Rarely isolated atonia, positive EEG findings
- Chorea, movement disorders
  - May be confused with cataplexy in young children
    - **PANDAS** → strep throat infection, high antistreptolysin O antibodies
  - Overlapping movement disorder around onset of cataplexy
- Schizophrenia
  - Sleep-related hallucinations, delusions from stimulant tx
    - If also cataplexy, should assume due to narcolepsy first

# Narcolepsy – Comorbidity

- May co-occur with → bipolar, depressive, anxiety disorders
  - More rare with schizophrenia
- Assoc with incr BMI/obesity (esp if untreated narcolepsy)
  - Rapid weight gain common in **sudden onset in young children**
- If sudden aggravation of pre-existing narcolepsy
  - Consider OSA

# Breathing-Related Sleep Disorders

*OSA Hypopnea*

*Central Sleep Apnea*

*Sleep-Related Hypoventilation*

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# Obstructive Sleep Apnea Hypopnea

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# OSA Hypopnea – Diagnostic Criteria

## A. Either:

1. 5+ obstructive apneas/hypopneas PER HOUR (on PSG) + either:
  - **Nocturnal breathing disturbance** (snoring, snorting, gasping, pauses)
  - **Daytime sleepiness, fatigue, unrefreshing sleep**
    - Despite adequate sleep opportunities
    - Not better explained by AMD or AMC
2. 15+ obstructive apneas/hypopneas PER HOUR (regardless of other sx)

# OSA Hypopnea – Diagnostic Specifiers

- *Specify current severity:*
  - **Mild:** apnea hypopnea index  $<15$
  - **Moderate:** apnea hypopnea index 15-30
  - **Severe:** apnea hypopnea index  $>30$
- Apnea hypopnea index → count per hour
- Overall disease severity
  - Level of nocturnal desaturation (sig if  $>10\%$  sleep time at  $\text{SaO}_2 < 90\%$ )
  - Sleep fragmentation (arousal index  $>30$ , or stage N3 sleep  $<5\%$ )
  - Associated symptoms
  - Day time impairment

# OSA Hypopnea – Diagnostic Features

- MOST COMMON breathing-related sleep disorder
  - Repeated **upper airway (pharyngeal) obstructions**
    - Apnea = total absence of airflow
    - Hypopnea = reduction in airflow
  - In adults → reduction in breathing for **>10 seconds**
    - In children → 2 missed breaths
    - Typically assoc with **drops in SaO<sub>2</sub> >3% ± EEG arousal**
  - Cardinal symptoms → **SNORING + DAYTIME SLEEPINESS**
- Diagnosis based on → **PSG + symptoms**
  - Assoc findings → **central obesity, crowded pharyngeal airway, incr BP**



# OSA Hypopnea – Associated Features

- Freq nocturnal awakenings → may report **INSOMNIA sx**
- Other common sx (non-specific)
  - Heartburn, nocturia, morning headaches, dry mouth
  - Erectile dysfunction, decr libido
  - More rare → difficulty breathing lying supine/sleeping
- Hypertension COMMON → >60%

# OSA Hypopnea – Prevalence

- Very common disorder
  - Children → **1-2%**
  - Middle-age adults → **2-15%**
  - Older adults → **>20%** (may have high rates of undiagnosed)
- Higher prevalence groups
  - **Obesity**, older adults, certain racial/ethnic groups
  - **MALES (2-4x)**
    - Gender difference declines in older age (higher in menopause)
    - NO gender difference in prepubertal children

# OSA Hypopnea – Development & Course (1)

- “J-shaped distribution”
  - **Peak age 3-8** → compromised nasopharynx by large tonsillar tissue
    - Declines with growth of airway, regression of lymphoid tissue
  - **Increases in midlife + menopause**
  - Course in older age unclear → may level off or increase with age
- Insidious onset, gradual progression, persistent course
  - **Loud snoring** often present for **many years** (since childhood)
    - **Weight gain** → may exacerbate sx
  - Most commonly manifests **age 40-60** (but can occur any age)
    - In adults, apneas/hypopneas incr by 2 over 4-5 years
    - Higher apnea/hypopnea index if **older, male, incr BMI**
- May spontaneously improve
  - With **weight loss** (esp after bariatric surgery)
  - In children → **seasonal variation, overall growth**

## OSA Hypopnea – Development & Course (2)

- Young children → more subtle sx, difficult dx
  - **PSG useful** to confirm dx → sleep fragmentation not as apparent
  - Reports of snoring less sensitive (parent-reported)
  - **Agitated arousals, unusual sleep postures** (on hands, knees)
  - **Nocturnal enuresis** → suspicion if previous dry at night
  - **Daytime sleepiness** (not as common/pronounced as adults)
    - Daytime mouth breathing, swallowing difficulty, poor speech articulation
  - May present with **failure to thrive, developmental/growth delays**
    - Obesity less common risk factor
- Younger than age 5 → more often present with **nighttime sx**
  - Observed apneas, labored breathing (vs behavioral)
- Older than age 5 → more often **daytime sx**
  - Sleepiness, impulsivity, hyperactivity, learning difficulties, morning H/A

# OSA Hypopnea – Risk & Prognostic Factors

- Genetic & Physiological

- MAJOR risk factors → **obesity, male gender** (vs premenopausal females)
  - Gender differences in airway structure
- Maxillary-mandibular **retrognathia or micrognathia**
- **Family history** of sleep apnea
- Genetic syndrome reducing upper airway patency
  - **Down's syndrome, Treacher Collin's syndrome**
- **Adenotonsillar hypertrophy** (esp young children)
- **Menopause** (influence of sex hormones on ventilatory control, body fat)
- Certain endocrine syndromes (**acromegaly**)
- **Sedating medications** → may worsen course

- Strong genetic basis

- **2x risk among 1<sup>o</sup> relatives**

# OSA Hypopnea – Culture-Related Issues

- Potential for sleepiness/fatigue → reported differently by culture
  - Snoring may be considered sign of health, not concerning
- Asian ancestry
  - May be at incr risk of OSA → despite low BMI
  - May be due to craniofacial risk factors, narrowing nasopharynx

# OSA Hypopnea – Gender-Related Issues

- Females
  - May more commonly report **fatigue** (vs sleepiness)
  - May **underreport snoring**

# OSA Hypopnea – Diagnostic Markers

- Polysomnography
  - Sleep-related respiratory disturbances, sleep continuity
    - Associated changes in oxygen saturation
  - PSG in children
    - Labored breathing, paradoxical movements, hypercapnia
    - Partial obstructive hypoventilation with cyclical desaturations
    - Apnea hypopnea index threshold as low as 2
- Validated sleep measures (MSLT, maintenance of wakefulness)
  - May identify sleepiness
- Other investigations
  - Arterial blood gas
    - May have **waking hypoxemia/hypercapnia** → otherwise normal awake
      - Possible co-existing lung disease or hypoventilation
  - Imaging → may show narrowing of upper airway
  - Cardiac testing → may show impaired ventricular function
  - Bloodwork → incr Hb or Hct (severe nocturnal O2 desaturation)



# OSA Hypopnea – Functional Consequences

- If mod-severe OSAH → **50% report daytime sleepiness**
- If snoring/sleepiness → 2x risk of **occupational accidents**
- Incr AH index → 7x risk of **MVA**
  - Government reporting requirements
- Measures of health-related quality of life → **REDUCED**
  - Esp **physical + vitality subscales**

# OSA Hypopnea – Differential Diagnosis (1)

- Primary snoring → otherwise asymptomatic, no abn PSG
  - OSAH → may also report nocturnal gasping, choking
- Other sleep disorders → ddx requires PSG
  - Hypersomnia, central sleep apnea, sleep-related hypoventilation
- Narcolepsy → can dx both
  - Daytime naps → shorter, more refreshing, more dreams
  - PSG, MSLT → shorter REM sleep latency
  - **Both assoc with obesity**
- Insomnia disorder → can dx both
  - Difficulty initiating/maintaining sleep, early-morning awakenings
  - No snoring

# OSA Hypopnea – Differential Diagnosis (2)

- Panic attacks
  - Nocturnal panic attacks → may have gasping, choking
    - But lower freq, intense autonomic arousal, no excessive sleepiness
    - PSG → no apneas, no O2 desaturation
  - OSAH → no daytime panic attacks
- ADHD → **can co-occur** (watch for OSAH risk factors)
  - Both have inattention, hyperactivity, internalizing, academic impairment
- Substance/medication-induced insomnia/hypersomnia
  - Certain substances exacerbate OSAH
    - Alcohol, barbiturates, benzos, tobacco

# OSA Hypopnea – Comorbidity

- Associated medical conditions
  - **Systemic hypertension, CAD, heart failure, stroke, DM, incr mortality**
    - If mod-severe OSAH → 30-300% risk
  - Rarely → pulmonary HTN, right heart failure
    - Very severe disease, hypoventilation, cardiopulmonary disease
  - May co-occur with **cerebrovascular disease, Parkinson's disease**
- Depressive symptoms → 1/3 of those referred for OSAH
  - 10% → severe depression scores
  - **AH index correlated** with severity of depression sx
    - May be stronger assoc in **males**

# Central Sleep Apnea

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# Central Sleep Apnea – Diagnostic Specifiers

- A. PSG → **5+ central apneas** per hour of sleep
- B. Not better explained by another current sleep disorder

# Central Sleep Apnea – Diagnostic Specifiers

- *Specify whether:*
  - **Idiopathic central sleep apnea:** caused by variability in respiratory effort, without evidence of airway obstruction
  - **Cheyne-Stoke breathing:** periodic crescendo-decrescendo variation in tidal volume → results in 5+ apneas/hypopneas per hour, frequent arousal
    - May also be observed during resting wakefulness → poor prognosis for mortality
  - **Central sleep apnea comorbid with opioid use:** effect of opioids on respiratory rhythm generators in the medulla, differential effects on hypoxic vs hypercapnic respiratory drive
- *Specify current severity:*
  - Based on frequency of breathing disturbances
  - Associated O<sub>2</sub> desaturations, sleep fragmentation
  - Sleep continuity + quality may be markedly impaired
    - Reductions in restorative stages of non-REM sleep (i.e. stage N3)

# Central Sleep Apnea – Subtypes

- Idiopathic central sleep apnea, Cheyne-Stoke breathing
  - Increased gain of **ventilatory control system** → “high loop gain”
    - Leads to instability of ventilation + PaCO<sub>2</sub> levels
    - **Periodic breathing** → hyperventilation alternating with hypoventilation
    - Typically slightly hypocapneic or normocapneic
- May manifest during initiation of treatment of OSAH
  - May occur in assoc with OSAH (*complex sleep apnea*)
    - Ratio of central to obstructive → predominant condition
  - Due to “high loop gain”
- CSA comorbid with opioid use
  - Effects on respiratory rhythm generators in medulla
  - Differential effects on hypoxic vs hypercapnic respiratory drive
  - May have **elevated pCO<sub>2</sub> levels** while awake
  - Chronic MMT → incr somnolence, depression



# Central Sleep Apnea – Diagnostic Features (1)

- Repeated episodes of apneas/hypopneas during sleep
  - Cause by **variability in respiratory effort**
  - Periodic or intermittent pattern
- Idiopathic central sleep apnea
  - **Sleepiness, insomnia, awakenings due to dyspnea**
  - 5+ central apneas per hour of sleep
- Cheyne-Stokes breathing
  - Occurs in heart failure, stroke, renal failure
  - **Periodic crescendo-decrescendo variation in tidal volume**
  - 5+ central apneas per hour → with **frequent arousals**

## Central Sleep Apnea – Diagnostic Features (2)

- Medications/substances used in mental health conditions
  - Can alter neuromuscular control of breathing
    - May exacerbate impairments of respiratory rhythm + ventilation
  - May contribute to sleepiness, confusion, depression
- Chronic use of long-acting opioids
  - Often assoc with impairment of respiratory control
  - May lead to central sleep apnea

# Central Sleep Apnea – Associated Features

- Symptoms can vary
  - **Sleepiness, insomnia**
  - **Sleep fragmentation**, awakening with dyspnea
  - Some are asymptomatic
- OSAH can co-exist with Cheyne-Stokes breathing
  - **Snoring + abruptly terminating apneas** may be observed

# Central Sleep Apnea – Prevalence

- Idiopathic CSA
  - Prevalence = UNKNOWN (thought to be rare)
- Cheyne-Stokes breathing
  - High if **depressed ventricular ejection fraction**
    - If EF <45% → **20% or higher**
    - If acute stroke → **20%**
  - Even more skewed to MALES (vs OSAH)
- Opioid CSA
  - Prevalence = **30%** if on chronic opioids for non-malignant pain or MMT

# Central Sleep Apnea – Development & Course

- Cheyne-Stokes breathing
  - Onset assoc with development of **heart failure**
    - Assoc with **oscillations in HR, BP, SaO2**
    - Incr SNS activity → may promote progression of heart failure
  - Significance in acute stroke not known (may be transient finding)
- Opioid CSA
  - Assoc with **chronic use** (several months)

# Central Sleep Apnea – Risk & Prognostic Factors

- Genetic & Physiological

- Cheyne-Stokes frequently presents in HEART FAILURE
  - Incr ventilatory chemosensitivity, hyperventilation
    - Due to pulmonary vascular congestion, circulatory delay
  - Further risk with **atrial fibrillation, older age, male gender**
  - Also seen in acute stroke, possibly renal failure

# Central Sleep Apnea – Diagnostic Markers

- Cheyne-Stokes → heart failure findings
  - JVP distension, S3 heart sound, lung crackles, lower extremity edema
- Polysomnography
  - Central sleep apneas → breathing cessation >10 seconds
  - Cheyne-stokes → crescendo-decrescendo variation in tidal volume
    - Result in central apneas/hypopneas → 5+ per hour
    - Cycle length = **60 seconds** (between end of apneas)

# Central Sleep Apnea – Functional Consequences

- Idiopathic CSA
  - Disrupted sleep, sleepiness, insomnia
- Cheyne-Stokes breathing
  - If comorbid heart failure → sleepiness, fatigue, insomnia
    - May be asymptomatic
    - Increased **cardiac arrhythmias, mortality, cardiac transplantation**
- Opioid CSA
  - Sleepiness, insomnia



# Central Sleep Apnea – Differential Diagnosis

- Other breathing-related sleep disorders, other sleep disorders
  - Differentiate with **polysomnography**
  - Predominant CSA vs OSAH → >50% central sleep apneas
  - Cheyne-Stokes → predisposing condition + PSG evidence
    - (vs insomnia due to other medical conditions)
    - High-altitude periodic breathing similar pattern
      - But shorter cycle time, only at high altitude, not assoc with HF
  - Opioid CSA → PSG evidence (vs insomnia)

# Central Sleep Apnea – Comorbidity

- Use of long-acting opioids (methadone)
  - May observe central apneas, periodic apneas, ataxic breathing
- Cheyne-Stokes
  - Heart failure, stroke, renal failure
  - More frequent if atrial fibrillation
  - More likely if **older, male, lower weight** (vs OSAH)

# Sleep-Related Hypoventilation

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# Sleep-Related Hypoventilation – Diagnostic Criteria

- A. PSG → **decr respiration + elevated CO2 levels**
  - 1. If no CO2 measurement → low Hb O2 saturation without apneic events
- B. Not better explained by another current sleep disorder

# Sleep-Related Hypoventilation – Diagnostic Specifiers

- *Specify whether*
  - **Idiopathic hypoventilation**
  - **Congenital central alveolar hypoventilation:** rare congenital disorder, present in perinatal period with shallow breathing, cyanosis or apnea
  - **Comorbid sleep-related hypoventilation:** due to medication condition
    - Pulmonary → ILD, COPD
    - Neuromuscular/chest wall → muscular dystrophies, post-polio, cervical spinal cord injury, kyphoscoliosis
    - Medications → benzos, opiates
    - Obesity → decr chest wall compliance, ventilation-perfusion mismatch, decr ventilatory drive (BMI >30, hypercapnia during wakefulness)
- *Specify current severity*
  - Based on degree of hypoxemia/hypercarbia during sleep
  - Evidence of end organ impairment (right heart failure)
  - Blood gas abnormalities during wakefulness → greater severity

# Sleep-Related Hypoventilation – Diagnostic Features

- More frequently occurs secondary (can be independent)
  - Medical + neurological disorders, medications, substances
- Often report (but not necessary for dx)
  - Excessive daytime sleepiness
  - Frequent arousals + awakenings during sleep
  - Morning headaches
  - Insomnia complaints

# Sleep-Related Hypoventilation – Associated Features

- Sleep-related complaints
  - Insomnia, sleepiness, morning headaches
  - Orthopnea (if diaphragm weakness)
- During sleep → may have **shallow breathing**
  - May have **co-existing OSAH or CSA**
  - May be assoc with **frequent arousals, bradycardia**
- Consequences of ventilatory insufficiency
  - **Pulmonary hypertension**
  - **Cor pulmonale** (right heart failure)
  - **Polycythemia**
  - **Neurocognitive dysfunction**
  - If severe → **blood gas abnormalities** during wakefulness

# Sleep-Related Hypoventilation – Prevalence

- Idiopathic → very uncommon
- Congenital central alveolar hypoventilation → rare
- Comorbid sleep-related hypoventilation → more common



# Sleep-Related Hypoventilation – Development & Course

- Idiopathic

- Thought to be slowly progressive disorder of respiratory impairment

- Congenital central alveolar hypoventilation

- Usually manifests at birth → **shallow, erratic or absent breathing**
- Can manifest during infancy, childhood, adulthood
  - Due to variable penetrance of *PHOX2B* mutation
- Children → more likely to have **ANS disorders, Hirschsprung's disease, neural crest tumors, characteristic box-shaped face**

- Comorbid sleep-related hypoventilation

- Severity reflects underlying condition → progresses with condition
- Complications → pulmonary hypertension, cor pulmonale, cardiac dysrhythmias, polycythemia, neurocognitive dysfunction, worsening respiratory failure

# Sleep-Related Hypoventilation – Risk & Prognostic Factors

- Environmental → CNS depressants (benzos, opiates, alcohol)
- Genetic & Physiological
  - **Idiopathic** → blunted chemoresponsiveness to CO<sub>2</sub>
    - Reflects underlying neurological deficits in ventilation centers
  - **Comorbid** → pulmonary, neuromuscular, chest wall, hypothyroidism, meds
    - May be consequence of **incr WOB**, impaired **respiratory muscles**, or decr **respiratory drive**
    - Neuromuscular disorders → impaired innervation or muscle function
      - Amyotrophic lateral sclerosis, spinal cord injury, diaphragmatic paralysis, myasthenia gravis, Lambert-Eaton syndrome, toxic/metabolic myopathies, post-polio syndrome, Charcot-Marie-Tooth syndrome
  - **Congenital** → *PHOX2B* gene, crucial for development of **embryonic ANS + neural crest derivatives**
    - Blunted response to hypercapnia (esp during non-REM sleep)

# Sleep-Related Hypoventilation – Gender-Related Issues

- Reflects gender distribution of underlying condition
  - E.g. COPD more common in males, incr age

# Sleep-Related Hypoventilation – Diagnostic Markers

- Polysomnography

- Sleep-related **hypoxemia + hypercapnia** (not better explained)
- **High  $\text{paCO}_2$  (>55) or increase in  $\text{pCO}_2$  (>10 to >50)** during sleep
  - Arterial blood gas during sleep may be impractical
- **O<sub>2</sub> desaturations** (<90% for 5 mins to at least 85%, or <90% for 30 mins)
  - No evidence of upper airway obstruction
  - Not as specific (other causes of hypoxemia)

# Sleep-Related Hypoventilation – Functional Consequences

- Effects of chronic exposure to hypercapnia + hypoxemia
  - Vasoconstriction of pulmonary vasculature → **pulmonary hypertension**
    - If severe → right heart failure (**cor pulmonale**)
  - Dysfunction of organs (brain, blood heart)
    - **Cognitive dysfunction, polycythemia, cardiac arrhythmias**
  - Hypercapnia → can **depress respiratory drive** (progressive resp failure)

# Sleep-Related Hypoventilation – Differential Diagnosis

- Other medical conditions affecting ventilation
  - Idiopathic sleep-related hypoventilation → very uncommon
    - Excludes lung, MSK, neuromuscular, other medical causes
  - Differentiate from sleep-related **hypoxemia** (lung disease)
- Other breathing-related sleep disorders
  - Ddx with polysomnography
  - SRH → **longer periods of O2 desaturation** (vs OSAH/CSA)
    - No discrete episodes or airflow decreases

# Sleep-Related Hypoventilation – Comorbidity

- Often occurs with medical condition/medication
  - Pulmonary (**ILD, COPD**)
  - Neuromuscular (**muscular dystrophies, post-polio, cervical SCI**)
  - Chest wall (**obesity, kyphoscoliosis**)
  - Medications (**benzos, opiates**)
- Congenital central alveolar hypoventilation
  - Often with autonomic dysfunction → **Hirschsprung's disease**
  - ?late-onset congenital central alveolar hypoventilation → ?idiopathic
- Co-existing OSAH → may exacerbate hypoxemia/hypercapnia

# Circadian Rhythm Sleep-Wake Disorders

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# CRSW Disorders – Diagnostic Criteria

- A. Sleep disruption due to **alteration/misalignment of circadian system**
- B. **Excessive sleepiness or insomnia**
- C. Significant distress or impairment

# CRSW Disorders – Diagnostic Specifiers

- *Specify whether:*
  - Delayed sleep phase type
    - Familial
    - Overlapping with non-24-hour sleep-wake type
  - Advanced sleep phase type
    - Familial
  - Irregular sleep-wake type
  - Non-24-hour sleep-wake type
  - Shift work type
  - Unspecified type
- *Specify if:*
  - **Episodic:** symptoms for 1-3 months
  - **Persistent:** symptoms for >3 months
  - **Recurrent:** 2+ episodes within 1 year

# Delayed Sleep Phase Type

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# Delayed Sleep Phase Type – Diagnostic Features

- Delayed timing of major sleep period
  - Usually **>2 hours** → in relation to **desired sleep/wake time**
  - Prominent **initial insomnia, difficult AM waking, excessive sleepiness**
  - Normalizes if able to **set own schedule** (sleep quality + duration)

# Delayed Sleep Phase Type – Associated Features

- Common associated features
  - **Mental disorder** (previous/concurrent)
  - Extreme/prolonged **difficult waking**
  - **Morning confusion**
- Psychophysiological insomnia
  - May develop as result of **maladaptive behaviors**
    - Repeated attempts to fall asleep earlier
    - Impair sleep + increase arousal

# Delayed Sleep Phase Type – Prevalence

- Prevalence
  - General population = **0.17%**
  - Adolescents = **>7%**
- Prevalence NOT established for familial type
  - But **family hx of delayed sleep phase is common**

# Delayed Sleep Phase Type – Development & Course

- Onset → variable
  - Typically in **adolescence + early adulthood**
    - May be due to both physiological (hormones) + behavioral factors
    - Delayed sleep phase assoc with **onset of puberty**
  - May persist for months to years → before dx established
- Course → **persistent (>3 months)**
  - **Intermittent exacerbations** throughout adulthood
    - Usually triggered by **work/school schedule changes** (earlier rise)
    - If able to alter work schedule → may have remission
  - **Relapse** of symptoms COMMON
  - **Severity may decrease** with age (may not in familial form)

# Delayed Sleep Phase Type – Risk & Prognostic Factors

- Physiological

- Predisposing factors
  - **Longer than average circadian period**
  - **Changes in light sensitivity**
  - **Impaired homeostatic sleep drive**
- Some may be **hypersensitive to evening light** (delays circadian clock)
- Some may be **hyposensitive to morning light** (prevents phase advance)

- Genetic

- May play role in **familial + sporadic forms**
  - Circadian gene mutations (*PER3*, *CK1e*)



# Delayed Sleep Phase Type – Diagnostic Markers

- Compete history + sleep diary/actigraphy
  - Should include **weekends** (less strict work/social obligations)
  - Ensure **consistently delayed sleep-wake pattern**
- Biomarkers
  - e.g. **salivary dim light melatonin**
  - Only use if dx unclear

# Delayed Sleep Phase Type – Functional Consequences

- Severity of insomnia + excessive sleepiness varies
  - Largely **depends on work/social demands**

# Delayed Sleep Phase Type – Differential Diagnosis

- Normal variations in sleep
  - Late schedule that does NOT cause distress
  - Common in adolescents + young adults
- Other sleep disorders
  - Ddx → insomnia disorder, other CRSW disorders
  - Excessive sleepiness → other sleep disturbances
    - Breathing-related sleep disorders, insomnia
    - Sleep-related movement disorders
    - Medical, neurological, mental disorders
  - Overnight PSG → ?sleep apnea
  - **Circadian nature!**

# Delayed Sleep Phase Type – Comorbidity

- Strong association with:
  - Depression, somatic symptom disorder, IAD, personality disorder
- Comorbid conditions may exacerbate insomnia + sleepiness
  - Comorbid sleep disorders (insomnia disorder, RLS, sleep apnea)
  - Depression, bipolar, anxiety disorders
- **Non-24-hour sleep-wake type** → may overlap
  - Commonly have hx of delayed circadian sleep phase

# Advanced Sleep Phase Type

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# Advanced Sleep Phase Type – Diagnostic Features

- Earlier (advanced) timing of major sleep period
  - Usually **>2 hours** → in relation to **desired sleep/wake time**
  - Prominent **early morning insomnia, excessive daytime sleepiness**
  - Normalizes if able to **set own schedule** (sleep quality + duration)
- “Familial” specifier
  - **Family hx often present** → but prevalence NOT established
  - Specific mutations → **autosomal dominant** inheritance
  - Onset of symptoms **EARLIER** (childhood, early adulthood)
  - Course **PERSISTENT** → severity may **INCREASE** with age

# Advanced Sleep Phase Type – Associated Features

- “Morning types” → earlier sleep-wake times
  - Circadian biomarkers (melatonin, core body temp) → **2-4 hours earlier**
- If delayed bedtime required → will continue early rise time
  - Leads to persistent **sleep deprivation + daytime sleepiness**
- May develop substance abuse
  - **Hypnotics/alcohol** → combat sleep-maintenance insomnia
  - **Stimulants** → reduce daytime sleepiness

# Advanced Sleep Phase Type – Prevalence

- Prevalence in middle-age adults = 1%
- Increased prevalence in OLDER individuals
  - Probably due to **sleep-wake time + circadian phase advance**



# Advanced Sleep Phase Type – Development & Course

- Onset
  - Usually in **LATE adulthood** → familial form may be earlier
- Course → persistent (>3 months)
  - Severity may INCREASE (depending on work/social schedules)
  - Clinical expression may vary (depending on obligations)
    - If able to alter work schedules → may have remission
  - **Increasing age** → tends to **advance sleep phase**
    - Unclear whether due to circadian timing or homeostatic sleep regulation
- Behavioral/environmental treatments
  - Designed to control **sleep-wake structure, light exposure**
  - Lack of adherence → relapse, incr severity

# Advanced Sleep Phase Type – Risk & Prognostic Factors

- Environmental

- **Altered timing of light exposure** → may advance circadian rhythm
  - Decreased in late afternoon/early afternoon
  - Increased in early morning (due to early waking)
  - May incr risk of advanced sleep phase type
    - Not exposed to light during phase-delay region of curve
    - Perpetuates advanced phase
- **Familial advanced sleep phase type**
  - Shortening of endogenous circadian rhythm → advanced sleep phase
  - (does not systematically shorten with age)

- Genetic

- **Autosomal dominant inheritance**
  - *PER2*, *CKI* gene mutations

# Advanced Sleep Phase Type – Culture-Related Issues

- African Americans
  - May have **shorter circadian period**
  - May have **larger phase advances to light** (vs Caucasians)
  - May incr risk of developing advanced sleep phase type

# Advanced Sleep Phase Type – Diagnostic Markers

- **Sleep diary + actigraphy** (similar to delayed sleep phase type)

# Advanced Sleep Phase Type – Functional Consequences

- Excessive sleepiness → negative effects
  - **Cognitive performance, social interaction, safety**
- May develop substance abuse
  - **Hypnotics/alcohol** → combat sleep-maintenance insomnia
  - **Stimulants** → reduce daytime sleepiness

# Advanced Sleep Phase Type – Differential Diagnosis

- Other sleep disorders
  - Consider **behavioral factors** (esp in older adults)
    - Irregular sleep schedules, voluntary early waking
    - Early morning light exposure
  - Rule out other sleep-wake disorders, AMD, AMC (that cause early waking)
- Depressive, bipolar disorders
  - **Early morning waking, fatigue, sleepiness** → prominent in MDD

# Advanced Sleep Phase Type – Comorbidity

- May co-occur with
  - Medical conditions, mental disorders assoc with early morning waking
  - (e.g. insomnia disorder)

# Irregular Sleep-Wake Type

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# Irregular Sleep-Wake Type – Diagnostic Features

- No discernable sleep-wake circadian rhythm
  - No major sleep period
  - Sleep fragmented into 3+ periods (during 24-hour day)

# Irregular Sleep-Wake Type – Associated Features

- Typical presenting symptoms
  - **Insomnia at night**
  - **Excessive daytime sleepiness** (+ napping)
- Fragmented sleep periods
  - Longest sleep period typically → between **2 – 6 AM** (usually **<4 hours**)
- May be assoc with → **isolation or reclusion**
  - May lead to **lack of external stimuli** (does not entrain normal pattern)
- Most COMMONLY assoc with **neurocognitive disorders**
  - Also many **neurodevelopmental disorders**

# Irregular Sleep-Wake Type – Prevalence

- UNKNOWN

# Irregular Sleep-Wake Type – Development & Course

- Onset → variable
  - More common in **OLDER** adults
- Course → persistent

# Irregular Sleep-Wake Type – Risk & Prognostic Factors

- Temperamental

- Neurodegenerative disorders
  - **Alzheimer's, Parkinson's, Huntington's**
- Neurodevelopmental disorders

- Environmental

- **Low-amplitude circadian rhythm**
  - Decr exposure to environmental light
  - Decr structured daytime activity
  - Esp hospitalized individuals → weak external entraining stimuli
- Individuals with **dementia exposed to sig less bright light**

# Irregular Sleep-Wake Type – Diagnostic Markers

- **Sleep history, sleep diary (by caregiver), actigraphy**

# Irregular Sleep-Wake Type – Functional Consequences

- Often results in **insomnia + excessive sleepiness**
  - May also disrupt **caregiver's sleep**

# Irregular Sleep-Wake Type – Differential Diagnosis

- Normal variations in sleep
  - **Voluntary irregular sleep-wake schedule, poor sleep hygiene**
    - May result in insomnia + excessive sleepiness
- Other medical conditions, mental disorders, medication



# Irregular Sleep-Wake Type – Comorbidity

- Often comorbid with:
  - **Neurodegenerative disorders** (major NCD)
  - **Neurodevelopmental disorders** (IDD)
  - **Traumatic brain injury**
- May be comorbid with:
  - AMC/AMD with **social isolation, lack of light + structured activities**

# Non-24-Hour Sleep-Wake Type

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# Non-24-Hour Sleep-Wake Type – Diagnostic Features

- Abnormal synchronization
  - Between **24-hour light-dark cycle** and **endogenous circadian rhythm**
- Typically presents with:
  - **Insomnia, excessive sleepiness, or both**
  - Alternates with **short asymptomatic periods**
- Symptoms depends
  - When **trying to sleep vs circadian rhythm** sleep propensity
  - Begins with aligned sleep phase (during asymptomatic period)
    - Gradual increase in sleep latency (initial insomnia)
    - **Continual drift of sleep phase**
    - Sleep time into daytime (sleepiness)

# Non-24-Hour Sleep-Wake Type – Associated Features

- Most common among → **blind or visually impaired**
  - Due to decreased light perception
- If not visually impaired
  - Often **delayed sleep phase**
  - **Decr light exposure**
  - **Decr structured social/physical activity**
  - **Increased sleep duration**

# Non-24-Hour Sleep-Wake Type – Prevalence

- Prevalence
  - General population → unclear
  - Sighted individuals → RARE
  - **Blind individuals → 50%**

# Non-24-Hour Sleep-Wake Type – Development & Course

- Onset → variable
  - Blind → depends on **onset of visual impairment**
  - Sighted → may develop in **adolescence/early adulthood**
    - (overlap with delayed sleep phase type)
- Course → persistent
  - Clinical expression may vary across lifespan → due to schedule changes
    - Intermittent **remission + exacerbations**
  - Relapses due to non-adherence to treatments
  - Exacerbating factors → **sleep loss, circadian entrainment disruption**
    - Irregular sleep-wake schedules
    - Degree of light exposure at critical times of day
    - Insomnia, daytime sleepiness, function worsen

# Non-24-Hour Sleep-Wake Type – Risk & Prognostic Factors

- Environmental

- If sighted → behavioral factors + physiological tendency
  - Decr exposure/sensitivity to **light, activity cues**
  - **Social isolation** (often in mental disorder)
  - **Change in sleep habits** (night shift work, job loss)
- Hospitalized individuals (with neurological/psychiatric disorders)
  - Become **insensitive to social cues** (predisposing)

- Genetic & Physiological

- **Blindness** = risk factor
- Associated with **traumatic brain injury**

# Non-24-Hour Sleep-Wake Type – Diagnostic Markers

- **History, sleep diary, actigraphy**
- Phase markers (e.g. melatonin)
  - Can help determine circadian phase in sighted/blind individuals



# Non-24-Hour Sleep-Wake Type – Functional Consequences

- Prominent complaints
  - Initial + middle insomnia
  - Excessive sleepiness
  - Both
- Unpredictability of sleep-wake times
  - Typically **daily delay drift**
  - May result in **inability to attend school, maintain steady job**
  - May increase potential for **social isolation**

# Non-24-Hour Sleep-Wake Type – Differential Diagnosis

- Circadian rhythm sleep-wake disorders
  - **Delayed sleep phase type** → may have similar progressive delay for days
- Depressive disorders
  - May result in **similar circadian dysregulation + symptoms**

# Non-24-Hour Sleep-Wake Type – Comorbidity

- Common comorbidities
  - **BLINDNESS**
  - **Depressive, bipolar disorders**

# Shift Work Type

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# Shift Work Type – Diagnostic Features

- Working outside of normal 8AM-6PM daytime window
  - Regularly scheduled basis (esp at night)
  - Persistent sleep symptoms → both required
    - **Excessive sleepiness at work**
    - **Impaired sleep at home**
  - Reversion to daytime work routine → **symptoms resolve**
- Frequent travel across time zones → similar effects

# Shift Work Type – Prevalence

- Prevalence = UNCLEAR
  - **Night worker population → 5-10%**
    - (16-20% of workforce)
  - Incr prevalence into **middle-age + beyond**

# Shift Work Type – Development & Course

- Onset

- Can appear at any age
- More prevalent if **age >50**
  - May show similar rates of circadian phase adjustment (vs younger)
  - But significant more **sleep disruption** as consequence

- Course

- Typically **worsens with time** (if disruptive work hours persists)

# Shift Work Type – Risk & Prognostic Factors

- Temperamental

- Predisposing factors
  - **Morning-type disposition**
  - **Need for longer sleep duration** (>8 hours)
  - **Strong competing social/domestic needs** (parents of young children)
- Protective (lowers risk)
  - Ability to commit to **nocturnal lifestyle**
  - Few competing day-oriented demands

- Genetic & Physiological

- Shift works more likely to be **obese**
  - Incr risk of **OSA** → may exacerbate symptoms



# Shift Work Type – Diagnostic Markers

- Sleep history, sleep diary, actigraphy

# Shift Work Type – Functional Consequences

- May perform poorly at work
  - Risk for **accidents** → at work, on drive home
- Risk for poor health
  - Mental health → **AUD, SUD, depression**
  - Physical health → **GI disorders, CV disease, diabetes, cancer**
- If hx bipolar disorder → risk of **manic episodes**
- Interpersonal problems

# Shift Work Type – Differential Diagnosis

- Normal variations in sleep with shift work
  - Depends on extent of **symptom severity, distress level**
- Other sleep disorders
  - Consider if **persistence of work-type symptoms** even when on day-oriented routine for several weeks

# Shift Work Type – Comorbidity

- Shift work type associated with
  - Incr **AUD, SUD, depression**
- Shift work associated with
  - **GI disorders, CV disease, diabetes, cancer**

# Parasomnias

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# Parasomnias - Introduction

- Abnormal, experiential, physiological events
  - Occur with **sleep, specific sleep stages, sleep-wake transitions**
- Most common parasomnias
  - **Non-REM sleep arousal disorders**
  - **REM sleep behavior disorders**
- Sleep + wakefulness NOT mutually exclusive
  - Sleep NOT necessarily global, whole-brain phenomenon

# Non-REM Sleep Arousal Disorders

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# Non-REM Sleep Arousal Disorders – Diagnostic Criteria

- A. Recurrent **incomplete awakenings from sleep**, usually during **first third of major sleep episode** and either:
  - 1. **Sleepwalking**: walking about, with blank/staring face, difficult to wake
    - Relatively unresponsive to efforts to communicate
  - 2. **Sleep terrors**: abrupt terror arousals from sleep
    - Often begin with panicky scream
    - Intense fear + autonomic arousal (mydriasis, tachycardia, rapid breathing, sweating)
    - Relatively unresponsive to comfort
- B. **Minimal dream imagery recalled**
- C. **Amnesia of episode**
- D. Significant distress or impairment
- E. Not due to substance
- F. Not better explained by co-existing AMD/AMC



# Non-REM Sleep Arousal Disorders – Diagnostic Specifiers

- *Specify whether:*
  - Sleepwalking type
    - With sleep-related eating
    - With sleep-related sexual behavior (sexsomnia)
  - Sleep terror type

# Non-REM Sleep Arousal Disorders – Diagnostic Features

- A) Recurrent incomplete arousals

- Usually beginning during **first third** of major sleep episode
  - Typically **brief (1-10 mins)** → up to 1 hour (max duration unknown)
  - **Eyes typically OPEN**
- Many exhibit BOTH arousal subtypes (**sleepwalking + sleep terrors**)
  - Unitary underlying pathophysiology → complex behaviors
  - Reflect varying degrees of **wakefulness + NREM sleep**
  - Conscious awareness, motor activity, autonomic activation

- A1) Sleepwalking

- May begin during ANY stage of NREM sleep
  - Most COMMONLY during **slow-wave sleep (first third of sleep)**
- **Reduced alertness + responsiveness** → if awakened:
  - **Limited recall** of episode (or next morning)
  - May be **brief period of confusion, difficulty orienting**
  - Followed by full recovery of cognitive function + appropriate behavior

# Non-REM Sleep Arousal Disorders – Diagnostic Features

- A2) Sleep terrors (“night terrors”, “pavor nocturnus”)
  - **Abrupt awakening**, usually with **panicky scream/cry**
    - Usually begin during **first third of major sleep episode**
    - Typically lasts **1-10 mins** (may be much longer, esp children)
  - Abruptly sits up → **intense autonomic arousal + fear behaviors**
    - Pupillary dilation, tachycardia, rapid breathing, sweating
  - **Difficult to wake/comfort**
    - If awakened → minimal/fragmented recall of dream
    - Inconsolable, unresponsive to efforts

# Non-REM Sleep Arousal Disorders – Associated Features

- Sleepwalking → wide variety of behaviors
  - May begin with **confusion, simple behaviors** (sitting up, looking around)
  - **Progressively complex (but still usually routine, low complexity)**
    - Walking about, out of room/building, running from apparent threat
    - May use bathroom, eat, talk, more complex behaviors
    - Reports of unlocking doors, operating machinery, driving car
  - May include **inappropriate behavior**
    - Most commonly → **urinating in closet/wastebasket**
  - May last **few to 30 minutes (or longer)**
  - State of **relative analgesia** → painful injuries not appreciated until awake
- Sleep-related eating → varying degrees of amnesia/awareness
  - **Inappropriate foods** may be ingested, only find evidence next morning
- Sleep-related sexual behavior → varying degrees of sexual activity
  - More common in **MALES**
  - May lead to **serious interpersonal relationship or medicolegal** problems

# Non-REM Sleep Arousal Disorders – Associated Features

- Sleep terrors
  - Overwhelming **sense of dread + compulsion to escape**
  - May have **fragmented dream images**
    - No story-like dream sequence (like nightmares)
  - Usually does NOT awaken fully → usually **returns to sleep**
    - Amnesia of episode next morning
  - Usually only **one episode per night**
  - Rarely during daytime naps

# NREM Sleep Arousal Disorders – Prevalence

- Isolated/infrequent NREM sleep arousal → VERY COMMON
- Sleepwalking episodes
  - Children → **10-30% with at least 1 episode, 2-3% sleepwalk often**
    - Prevalence of sleepwalking DISORDER much lower (1-5%)
  - Adults → **1-7%, 0.5-0.7% weekly to monthly episodes**
    - Lifetime prevalence = 29%
    - 12-month prevalence = 3.6%
- Sleep terrors
  - Prevalence in general population = UNKNOWN
  - Sleep terror episodes
    - Age 18 months = 37%
    - Age 30 months = 20%
    - Adults = 2.2%

# NREM Sleep Arousal Disorders – Development & Course

- Onset
  - Most commonly in **childhood**
  - **Decreasing frequency with age**
  - Onset in adults (with no prior history) → search for specific etiology
    - **OSA, nocturnal seizures, medication effects**

# NREM Sleep Arousal Disorders – Risk & Prognostic Factors

- Environmental

- Incr likelihood of EPISODES
  - **Sleep deprivation, sleep-wake schedule disruptions, fatigue**
  - **Physical/emotional stress, sedative use**
- Incr likelihood of DISORDERS
  - **Sleep deprivation, fever**

- Genetic & Physiological

- Sleepwalking → 80% have family hx of sleepwalking/sleep terrors
  - If both parents have hx → 60% of offspring
- Sleep terrors → freq positive family hx of sleepwalking/sleep terrors
  - **10x increase** prevalence among 1<sup>o</sup> relatives
  - Much more common in **monozygotic twins** (vs dizygotic)
- Exact mode of inheritance unknown



# NREM Sleep Arousal Disorders – Gender-Related Issues

	Sleepwalking	Sleep terrors
<b><i>Females</i></b>	<ul style="list-style-type: none"> <li>• CHILDHOOD more females</li> <li>• More eating during sleepwalking</li> </ul>	
<b><i>Males</i></b>	<ul style="list-style-type: none"> <li>• ADULTHOOD more males</li> </ul>	<ul style="list-style-type: none"> <li>• CHILDHOOD more males</li> </ul>
<b><i>Children</i></b>	<ul style="list-style-type: none"> <li>• More often FEMALE</li> </ul>	<ul style="list-style-type: none"> <li>• More often MALE</li> <li>• More likely complete amnesia or vague sense of fear</li> </ul>
<b><i>Adults</i></b>	<ul style="list-style-type: none"> <li>• More often MALE</li> <li>• More likely violent or sexual activity</li> </ul>	<ul style="list-style-type: none"> <li>• EQUAL gender ratio</li> <li>• More detailed recollection of fearful images</li> </ul>

# NREM Sleep Arousal Disorders – Diagnostic Markers

- Can arise from ANY stage of NREM sleep
  - Most commonly **deep NREM (slow-wave) sleep**
  - Most likely in **first third of night** → uncommon during daytime naps
  - PSG EEG → **theta/alpha frequencies** during episode (partial arousal)
    - May be obscured by motion artifact
- PSG + audiovisual monitoring → to document sleepwalking
  - **No PSG features specific for sleepwalking** (if episode not captured)
    - Sleep deprivation may incr likelihood of capturing event
    - Instability of deep NREM sleep → but not specific/diagnostic
  - **No PSG features specific for sleep terrors** (if episode not captured)
    - **No ANTICIPATORY autonomic changes** (vs nightmares: HR, RR)
    - Intense autonomic activity (2-3x HR) assoc with AROUSALS

# NREM Sleep Arousal Disorders – Functional Consequences

- Clinically significant distress or impairment → diagnosis
  - **Frequency** of events
  - Potential for **violence or injurious behavior** → uncommon
    - Those in close proximity, not “sought out”
    - Rarely forensic implications
  - **Embarrassment** → social relationships, isolation, occupation
  - **Disruption/distress of others** (household members)
- Typically NOT assoc with significant mental disorders
- Sleep-related eating behaviors
  - Poor diabetes control, weight gain
  - Accidental self-injury, dangerous/toxic inedibles

# NREM Sleep Arousal Disorders – Differential Diagnosis (1)

- Nightmare disorder → during **REM sleep**
  - **Awaken easily**, report **vivid + story-like dreams**, occur **LATER** in night
- REM sleep behavior disorder → during **REM sleep**
  - **Prominent, complex movements** → often **personal injury**
  - **Awaken easily**, report **vivid + detailed dreams**, “act out dreams”
- Parasomnia overlap syndrome
  - Features of BOTH **sleepwalking + REM sleep behavior disorder**
- Breathing-related sleep disorders
  - May also have **confusional arousal**, subsequent **amnesia**
  - Characteristic **snoring, breathing pauses, daytime sleepiness**

## NREM Sleep Arousal Disorders – Differential Diagnosis (2)

- Sleep-related seizures → can have both
  - Form of epilepsy → Predominantly/exclusively during sleep
    - More **stereotypic, multiple times** per night, during **daytime naps**
- Alcohol-induced blackouts → NO LOSS OF CONSCIOUSNESS
  - Reflect **isolated disruption of memory** during drinking episode
  - May have **extremely complex behaviors** → no other signs of intoxication
    - May be indistinguishable from NREM sleep arousal disorders
- Dissociative amnesia, with dissociative fugue (nocturnal)
  - Arises from **period of wakefulness during sleep**
    - (vs precipitously from sleep, without intervening wakefulness)
  - Often history of **childhood physical/sexual abuse**
  - May be very difficult to distinguish from sleep walking

# NREM Sleep Arousal Disorders – Differential Diagnosis (3)

- Malingering, other voluntary behavior during wakefulness
- Panic disorder
  - May also cause **abrupt waking from deep NREM sleep with fearfulness**
  - But produce **rapid + complete awakening**
  - WITHOUT confusion, amnesia, motor activity (of NREM sleep arousal)
- Substance/medication-induced complex behaviors
  - Benzos, sedative-hypnotics, opiates, cocaine, nicotine
    - Antipsychotics, TCAs, chloral hydrate
  - May arise from sleep period, maybe extremely complex
    - Underlying **isolated amnesia**
- Night eating syndrome
  - **Delay in circadian rhythm of food ingestion**
  - Assoc with insomnia, depression

# NREM Sleep Arousal Disorders – Comorbidity

- Sleepwalking

- In adults → assoc with **major depressive episodes, OCD**

- Sleep terrors

- In children/adults → may have elevated scores for **depression/anxiety** on personality inventories

# Nightmare Disorder

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# Nightmare Disorder – Diagnostic Criteria

## A. Extremely dysphoric + well-remembered dreams

1. Usually involving **efforts to avoid threats** (to survival/security/integrity)
2. Generally during **second half** of major sleep episode

## B. On waking → **rapid oriented + alert**

## C. Significant distress or impairment

## D. Not due to substance

## E. Not better explained by co-existing AMC/AMD

# Nightmare Disorder – Diagnostic Specifiers

- *Specify if:*
  - **During sleep onset**
- *Specify if:*
  - **With associated non-sleep disorder** (incl SUDs)
  - **With associated other sleep disorder**
  - **With associated other medical condition**
- *Specify if:*
  - **Acute:** duration <1 month
  - **Subacute:** duration 1-6 months
  - **Persistent:** duration >6 months
- *Specify current severity:*
  - **Mild:** <1 episode per week
  - **Moderate:** >1 episode per week, not nightly
  - **Severe:** nightly episodes

# Nightmare Disorder – Diagnostic Features (1)

- Nightmares

- **Length, elaborate, story-like sequences** of dream imagery
  - Seem real → incite **anxiety, fear, other dysphoric emotions**
- Arise almost exclusively during **REM sleep** → can throughout sleep
  - More likely in **second half** → when dreaming **longer + more intense**
  - Factors facilitating earlier nightmares (incl at sleep onset)
    - **Sleep fragmentation/deprivation, jet lag, REM-sensitive meds**

- Nightmare content

- Attempts to avoid/cope with **imminent danger, negative emotions**
- After traumatic experience → “**replicative nightmares**” (most do not)
- On awakening → **well-remembered, described in detail**

## Nightmare Disorder – Diagnostic Features (2)

- Usually terminate with → **awakening + rapid full alertness**
  - **Dysphoric emotions may persist** into wakefulness
    - May cause difficulty **returning to sleep + lasting daytime distress**
- “Bad dreams” → may not induce awakening, only recalled later
- Hypnagogic nightmares → during **sleep-onset REM periods**
  - Often accompanied with **isolated sleep paralysis**
    - Sense of being both awake + unable to move voluntarily

# Nightmare Disorder – Associated Features

- Mild autonomic arousal
  - Sweating, tachycardia, tachypnea
- Not usually body movements or vocalizations
  - Due to REM-sleep related **loss of skeletal muscle tone**
  - May occur if **emotional stress, sleep fragmentation, PTSD**
  - If talking/emoting → typically **brief event terminating** nightmare
- Sig GREATER RISK for **suicidal ideation + suicide attempts**
  - Even if gender + mental illness taken into account

# Nightmare Disorder – Prevalence

- Prevalence INCREASES through childhood into adolescence
  - Preschool children (per parents) → **1.3 – 3.9%** (often or always)
  - Age 10-13 → increases for both males + females
  - Age 20-29 → increases for females (up to 2x males, males decrease)
  - After 30 → steady decreases for both (**gender difference remains**)
- Nightmares among adults
  - At least monthly → **6%**
  - Frequently → **1-2%**
  - (but idiopathic + PTSD nightmares combined indiscriminately)

# Nightmare Disorder – Development & Course

- Onset

- Often between **age 3-6**
- Peak prevalence/severity → **late adolescence/early adulthood**
- Most likely in children exposed to acute/chronic **psychosocial stressors**
  - May not resolve spontaneously

- Course

- **Minority persist** into adulthood → virtually lifelong
- Essential features same across age groups
  - Specific content may reflect individual's age

# Nightmare Disorder – Risk & Prognostic Factors

- Temperamental

- More frequent past **adverse events** (not necessarily trauma)
- Often **personality disturbances + psychiatric diagnosis**

- Environmental

- **Sleep deprivation/fragmentation, irregular sleep-wake schedules**
  - May alter timing, intensity, quantity of REM sleep → risk of nightmares

- Genetic & Physiological

- Genetic effects → disposition to nightmares, co-occurring parasomnias

- Course modifiers

- **Adaptive parental bedside behaviors** → may be PROTECTIVE
  - E.g. soothing child after nightmares



# Nightmare Disorder – Culture-Related Issues

- Significance of nightmares may vary by cultures
  - May affect disclosure

# Nightmare Disorder – Gender-Related Issues

- Nightmares more frequent in → **ADULT FEMALES**
- Content differs by sex
  - Adult females → **sexual harassment, loved ones disappearing/dying**
  - Adult males → **physical aggression, war/terror**

# Nightmare Disorder – Diagnostic Markers

- Polysomnography

- Abrupt awakenings from **REM sleep** → usually **second half** of night
  - May arise during NREM sleep (esp stage 2)
- Before waking → **HR, RR, eye movements** may quicken/incr variability

- Mildly impaired sleep

- **Decr efficiency, less slow-wave sleep, more awakenings**
- More freq **periodic leg movements**
- More **SNS activation** after REM sleep deprivation

# Nightmare Disorder – Functional Consequences

- More sig SUBJECTIVE distress
  - (vs demonstrable social/occupational impairment)
- If frequent awakenings or sleep avoidance
  - May have **excessive daytime sleepiness, poor concentration**
  - May have **depression, anxiety, irritability**
- Frequent childhood nightmares
  - May cause sig distress to parents/child

# Nightmare Disorder – Differential Diagnosis (1)

Nightmare Disorder	Sleep Terror Disorder
<ul style="list-style-type: none"> <li>• <b>Second half</b> in night</li> <li>• During <b>REM sleep</b></li> <li>• <b>Clear dream recall</b>, vivid, story-like</li> <li>• Mild autonomic arousal</li> <li>• <b>Complete awakenings</b> with full alertness</li> </ul>	<ul style="list-style-type: none"> <li>• <b>First third</b> of night</li> <li>• <b>NREM sleep</b> (stage 3 or 4)</li> <li>• <b>Limited dream recall</b>, not elaborate</li> <li>• Significant autonomic arousal</li> <li>• <b>Partial awakenings</b> with confusion, disorientation, partially responsive</li> </ul>

- REM sleep behavior disorder
  - **Complex motor activity + frightening dreams**
    - Often **violent dream enactments** + hx **nocturnal injuries**
  - More common among **late middle-age males**
  - Often described as nightmares → controlled with medications

# Nightmare Disorder – Differential Diagnosis (2)

- Bereavement
  - Dysphoric dreams, involving **loss + sadness**
  - With **self-reflection + insight** on awakening (vs distress)
- Narcolepsy
  - Nightmares common → but also **excessive sleepiness + cataplexy**
- Nocturnal seizures
  - Use **PSG + continuous video EEG**
  - Usually **stereotypical motor activity**
  - Nightmares often **repetitive**, reflect **epileptogenic features**
    - Diurnal auras (dread), phosphenes, ictal imagery
  - May also have **disorders of arousal** (esp confusional)
- Breathing-related sleep disorders
  - May have awakening with **autonomic arousal**
  - Usually NO recall of nightmares

# Nightmare Disorder – Differential Diagnosis (3)

- Panic disorder

- May produce **abrupt awakenings** with **autonomic arousal, fear**
- Nightmares NOT typically reported + daytime panic attack sx

- Sleep-related dissociative disorders

- May recall actual physical/emotional trauma as “dream” during EEG

- Medication/substance use

- Precipitating substances
  - Dopaminergics, beta-adrenergic antagonists, other antihypertensives
  - Amphetamine, cocaine, other stimulants
  - Antidepressants, smoking cessation aids, melatonin
- Withdrawal of REM-sleep suppressants (antidepressants, alcohol)
  - May produce **REM sleep rebound + nightmares**

# Nightmare Disorder – Comorbidity

- Comorbid medical conditions
  - Coronary heart disease, cancer, pain, parkinsonism
- Medical treatments
  - Hemodialysis, med/substance withdrawal
- Mental disorders
  - PTSD, insomnia disorder, schizophrenia, psychosis
  - Mood, anxiety, adjustment, personality disorders
  - Grief during bereavement
  - May dx both if independent clinical attention warranted
    - Or if nightmares not temporally related to AMD



# REM Sleep Behavior Disorder

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# REM Sleep Behavior Disorder – Diagnostic Criteria

- A. Arousal during sleep, **complex motor behavior ± vocalization**
- B. Arise **during REM sleep**
  - 1. 90 mins after sleep onset, more often later in sleep, uncommon in naps
- C. On waking → **complete awake + alert** (not confused)
- D. Either:
  - 1. **REM sleep without atonia** (on PSG)
  - 2. **Hix suggestive** of REM sleep behavior + **established synucleinopathy dx** (Parkinson's disease, MSA)
- E. Significant distress or impairment
- F. Not due to substance or AMC
- G. Not better explained by co-existing AMD or AMC

# REM Sleep Behavior Disorder – Diagnostic Features

- Repeated episodes arousal from REM sleep
  - Often with **complex motor behaviors ± vocalizations**
  - Reflect **motor response** to content → “dream **enacting behavior**”
    - Action-filled or violent dreams, being attacked or trying to escape
    - Vocalizations → loud, emotion-filled, profane
    - **Eyes remain closed**
  - May be very bothersome → individual, bed partner
  - May result in **significant injury** → falling, jumping, running, hitting, etc.
- Upon awakening → **immediately awake, alert, oriented**
  - Often able to **recall dream mentation** → closely correlated with behavior

# REM Sleep Behavior Disorder – Associated Features

- Behaviors typically → **prominent + violent**
  - Less behaviors may also occur
- Severity
  - Based on nature/consequences of behavior (vs just frequency)
    - Potential for harm, embarrassment, distress in others

# REM Sleep Behavior Disorder – Prevalence

- Prevalence = **0.4 – 0.5%** (gen pop)
  - May be higher in psychiatric disorders (? due to medications)
- Overwhelmingly affects → **MALES age >50**
  - Increasingly identified in females, younger pts

# REM Sleep Behavior Disorder – Development & Course

- Onset → may be **gradual or rapid**
- Course → usually **progressive**
- High assoc with underlying neurodegenerative disorder
  - Esp **synucleinopathies** (Parkinson's, Lewy body, MSA)
  - May appear LATER
  - REM sleep behavior disorder **may IMPROVE with progression**

# REM Sleep Behavior Disorder – Risk & Prognostic Factors

- Genetic & Physiological
  - Medications
    - **TCA, SSRIs, SNRIs, beta-blockers**
    - May result in **REM sleep without atonia**
    - Unclear if CAUSE or UNMASK

# REM Sleep Behavior Disorder – Diagnostic Markers

- Polysomnography → **REM sleep without atonia**
  - **EMG activity** during REM sleep (normally assoc with muscle atonia)
    - Tonic or phasic, affects different muscle groups
      - Submentalis, extensor digitorum, anterior tibialis
  - Requires more **extensive EMG + continuous video monitoring**
  - May also find EMG activity during NREM sleep
- REM sleep without atonia → in virtually **all cases of REM SBD**
  - Accompanying **dream-enacting behavior** necessary for dx
    - If no clinical history → simply asymptomatic REM sleep without atonia



# REM Sleep Behavior Disorder – Functional Consequences

- May occur on isolated occasions
- Embarrassment
  - May impair social relationships, occupation
  - Avoidance → friends over night, bed partners
- Risk of serious injury → to victim or bed partner

# REM Sleep Behavior Disorder – Differential Diagnosis

- NREM sleep arousal disorders → sleepwalking, sleep terrors
  - Generally occurs in **younger individuals**
  - Arise from **deep NREM sleep**, usually **early portion** of sleep period
  - On awakening → **confusion, disorientation, incomplete dream recall**
  - Differentiate with PSG
- Nocturnal seizures
  - Generally more **stereotyped** → but may **perfectly mimic**
  - Differentiate with PSG EEG → no REM sleep without atonia
- OSA
  - Behaviors may indistinguishable → resolve with effective OSA tx
  - Differentiate with PSG → no REM sleep without atonia

# REM Sleep Behavior Disorder – Differential Diagnosis

- Other specified dissociative disorder
  - “Sleep-related psychogenic dissociative disorder”
    - Arises from period of **well-defined wakefulness** during sleep period
    - More prevalent in **YOUNG FEMALES**
- Malingering
  - May perfectly mimic clinical features
  - Differentiate with PSG

# REM Sleep Behavior Disorder – Comorbidity

- Comorbid with 30% of narcolepsy patients
  - Affects younger range of narcolepsy
  - **Equal frequency** in males + females
- **>50% of idiopathic REM SBD** → eventually neurodegenerative
  - Often synucleinopathy (Parkinson's, LBD, MSA)
  - Often **predates any other sign by decades**

# Restless Legs Syndrome

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# Restless Legs Syndrome – Diagnostic Criteria

- A. Urge to move legs, related uncomfortable sensation (3/3):
  - 1. Begins or worsens during periods of **rest or inactivity**
  - 2. Partially or totally **relieved by movement**
  - 3. Worse or exclusively **in evening or night**
- B. Occurs **3+ per week**, for **3+ months**
- C. Significant distress or impairment
- D. Not better explained by AMD, AMC, behavioral condition
- E. Not due to substance or medication

# Restless Legs Syndrome – Diagnostic Features

- A) Sensorimotor, neurological sleep disorder
  - Desire to **move legs/arms**, assoc with **uncomfortable sensations**
    - Creeping, crawling, tingling, burning, itching
  - **Worse at rest** → movements of legs **to relieve discomfort**
  - **Worse in evening/night** → independent of activities
  - Mainly based on **self-report + history**
- Not due to **positional discomfort or leg cramps**
- Sleep symptoms
  - **Delay sleep onset, awaken from sleep, sleep fragmentation**
  - **Daytime sleepiness**
  - If severe → may no longer obtain relief from moving legs

# Restless Legs Syndrome – Associated Features

- Periodic leg movements in sleep (PLMS)
  - **90% of RLS** → demonstrate PLMS
  - **PLM during wakefulness** → supportive of RLS dx
- Other supportive features
  - Difficulty initiating + maintain sleep
  - Excessive daytime sleepiness
  - Reduction in sx with **dopaminergic treatment**
- Family hx of RLS among 1<sup>o</sup> relatives



# Restless Legs Syndrome – Prevalence

- Prevalence = **2 – 7%**
  - If 3x per week with mod-severe distress → **1.6%**
  - If minimum once per week → **4.5%**
- More likely in **FEMALES (1.5-2x)**
- Prevalence **increases with AGE** (until age 60)
- Prevalence lower in Asian populations

# Restless Legs Syndrome – Development & Course

- Onset
  - Typically occurs in **age 20-30s**
    - Many experience sx before dx (40% before age 20, 20% before age 10)
  - Prevalence **increases steadily** with age until age 60
    - Symptoms then stable or decreases slightly (sx similar across lifespan)
- Familial RLS (vs non-familial)
  - **Younger age at onset, slower progressive course**
- Course → differs by age at onset
  - Onset before age 45 → **slow progression of sx**
  - Late-onset → **rapid progression with aggravating factors**

# Restless Legs Syndrome – Development & Course

- RLS in children
  - Dx may be difficult due to self-report (can't be by parents)
    - “Urge to move” → “have to” or “got to” move
  - **66% of C&A** → report **daytime leg sensations**
    - Compare day vs night duration of sitting/lying down
  - Nocturnal worsening → tends to **persist**
  - Similar impairment → more in **behavioral + educational domains**

# Restless Legs Syndrome – Risk & Prognostic Factors

- Genetic & Physiological

- Predisposing: **female gender, advancing age, family hx of RLS**
  - **Genetic risk variants** → may be 2° to other disorders (**uremia**)
  - Those with genetic susceptibility develop RLS if further risk factors
- Precipitating: often time-limited → resolve after trigger disappeared
  - E.g. **iron deficiency**

- Defined pathophysiological pathways

- Common genetic variants → *MEIS1 (2p)*, *BTBD9 (6p)*, *MAP2K5 (15q)*
  - **BTBD9 (6q)** → very large excessive risk (80%), PAR 50%
  - *MEIS1 (2p)*, *BTBD9 (6p)* → less common in African/Asian, ?lower risk
- Disturbances in central **dopaminergic system, iron metabolism**
  - May also involve **endogenous opiate system**
  - **Dopaminergic drugs** (D2/D2 non-ergot agonists) effective
  - But **serotonergic antidepressants** → may induce/worsen RLS

# Restless Legs Syndrome – Gender-Related Issues

- More prevalent in FEMALES
  - But no diagnostic differences by gender
- Pregnancy → prevalence increased (**2-3x gen pop**)
  - Peaks during **third trimester**
  - Typically **improves/resolves soon after delivery**
  - Explains part of gender difference in prevalence
    - **Nulliparous females = same risk as age-matched males**

# Restless Legs Syndrome – Diagnostic Markers

- Polysomnography → significant abnormalities in RLS
  - Increased sleep latency
  - Higher arousal index
  - May have **periodic limb movements** (during sleep or quiet resting)

# Restless Legs Syndrome – Functional Consequences

- Severe RLS → **2-3%**
  - Significant impairment, assoc mental disorders (depression, anxiety)
- Milder RLS → less well characterized
  - Disruption of at least one activity of daily live
  - 50% negative impact on mood
  - 48% lack of energy
- Most common consequences
  - **Sleep disturbance** → decr sleep time, sleep fragmentation, overall
    - Daytime sleepiness, fatigue
  - Depression, GAD, panic disorder, PTSD
  - Quality of life impairments

# Restless Legs Syndrome – Differential Diagnosis

- Leg cramps, positional discomfort, habitual foot tapping
- Arthralgias, arthritis, myalgias
- Positional ischemia (numbness)
- Peripheral neuropathy, radiculopathy
- Uncharacteristic findings (unlikely RLS)
  - Knotting of muscle cramps, relief with single postural shift
  - Limitation to joints, soreness to palpitation
- Less common differential
  - Neuroleptic-induced akathisia, anxiety-induced restlessness, myelopathy,
  - Symptomatic venous insufficiency, peripheral artery disease, eczema
- These conditions could occur in RLS
  - Consider supportive features, family history, response to dopaminergics



# Restless Legs Syndrome – Comorbidity

- Common psychiatric comorbidities
  - Depressive, anxiety, attentional disorders
- Main medical comorbidity → **cardiovascular disease**
  - Common → iron deficiency, pregnancy, chronic renal failure
  - Other
    - Hypertension, diabetes, obesity, thyroid disease
    - Narcolepsy, OSA, migraine, fibromyalgia, peripheral neuropathy
    - Parkinson' disease, multiple sclerosis, osteoporosis, cancer

# Substance/Medication-Induced Sleep Disorder

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# Sub/Med-Induced Sleep Disorder – Diagnostic Criteria

- A. Prominent + severe **disturbance in sleep**
- B. History, physical exam, lab findings of:
  - 1. Symptom onset **during/soon after** → intoxication, withdrawal, exposure
  - 2. Substance/medication **capable** of producing symptoms
- C. Not non-substance/medication-induced
  - 1. Symptom onset preceding sub/med use
  - 2. Symptom persistence after cessation of sub/med use/intox/withdrawal
  - 3. Other evidence (previous non-sub/med-induced episodes)
- D. Not exclusively during **delirium**
- E. Significant distress or impairment

# Sub/Med-Induced Sleep Disorder – Diagnostic Specifiers

- *Specify whether:*
  - **Insomnia type:** difficulty falling/maintaining sleep, freq nocturnal awakenings, non-restorative sleep
  - **Daytime sleepiness type:** excessive sleepiness/fatigue during waking hours, or a long sleep period
  - **Parasomnia type:** abnormal behavioral events during sleep
  - **Mixed type:** multiple types, no clearly predominant symptom
- *Specify if:*
  - **With onset during intoxication**
  - **With onset during discontinuation/withdrawal**

# Sub/Med-Induced Sleep Disorder – Diagnostic Specifiers

- *Specify substance:*
  - Alcohol
  - Caffeine
  - Cannabis
  - Opioid
  - Sedative, hypnotic, or anxiolytic
  - Amphetamine (or other stimulant)
  - Cocaine
  - Tobacco
  - Other (or unknown) substance

# Sub/Med-Induced Sleep Disorder – Diagnostic Features

- Prominent sleep disturbance
  - Sufficiently severe to warrant **independent clinical attention**
  - Primarily assoc with **pharmacological effects** of a substance
- 4 types
  - Most common → **insomnia type, daytime sleepiness type**
  - Least common → **parasomnia type**
- Distinguish from another sleep disorder
  - Atypical age at onset or course

# Sub/Med-Induced Sleep Disorder – Associated Features

Intoxication	Withdrawal	Medications
<ul style="list-style-type: none"> <li>• Alcohol</li> <li>• Caffeine</li> <li>• Cannabis</li> <li>• Opioids</li> <li>• Sedatives</li> <li>• Hypnotics</li> <li>• Anxiolytics</li> <li>• Stimulants (cocaine)</li> <li>• Other</li> </ul>	<ul style="list-style-type: none"> <li>• Alcohol</li> <li>• Caffeine</li> <li>• Cannabis</li> <li>• Opioids</li> <li>• Sedatives</li> <li>• Hypnotics</li> <li>• Anxiolytics</li> <li>• Stimulants (cocaine)</li> <li>• Other</li> <li>• Tobacco</li> </ul>	<ul style="list-style-type: none"> <li>• Adrenergic ant/agonists</li> <li>• Dopamine ant/agonists</li> <li>• Cholinergic ant/agonists</li> <li>• Serotonergic ant/agonists</li> <li>• Antihistamines</li> <li>• Corticosteroids</li> </ul>

# Sub/Med-Induced Sleep Disorder – Associated Features

- Alcohol → typically **INSOMNIA** type
  - Acute intoxication → immediate sedative effect
    - Incr stage 3 + 4 NREM sleep, **decr REM sleep**
  - After initial effect → incr wakefulness, restless sleep, vivid/anxious dreams
    - Decr stage 3 + 4 sleep, **incr REM sleep**
  - May aggravate breathing-related sleep disorders
- Alcohol withdrawal
  - Extremely disrupted sleep continuity
  - **Incr REM sleep** (amount + intensity) → freq **vivid dreaming**
- Habitual alcohol use
  - 1<sup>st</sup> half of night → **short-lived sedative effect**
  - 2<sup>nd</sup> half of night → **disrupted sleep continuity**
  - Chronic users → **light, fragmented sleep** for weeks-years
    - Persistent **deficit in slow-wave sleep**



# Sub/Med-Induced Sleep Disorder – Associated Features

- Caffeine → **INSOMNIA** (dose-dependent)
  - May present with daytime sleepiness, related to withdrawal
- Cannabis
  - Acute → may **shorten sleep latency** (but may incr sleep latency too)
    - **Incr slow-wave sleep, decr REM sleep**
  - Chronic → tolerance to sleep effects develop
  - Withdrawal → sleep difficulties, unpleasant dreams for weeks
    - PSG → **decr slow-wave sleep, incr REM sleep**
- Opioids
  - Acute → may **incr sleepiness + subjective depth, decr REM sleep**
  - Chronic → tolerance to sedative effects develop, complaints of **insomnia**
    - **Exacerbate sleep apnea** (due to respiratory depressant effects)

# Sub/Med-Induced Sleep Disorder – Associated Features

- Sedative, hypnotic, or anxiolytic substances
  - Barbiturates, benzo receptor agonists (benzos, Z-drugs)
    - Meprobamate, glutethimide, methyprylon
  - Acute → incr sleepiness + decr wakefulness
  - Chronic → **tolerance** may develop + subsequent **return of insomnia**
    - **Daytime sleepiness** may occur
  - Exacerbate obstructive sleep apnea
  - Parasomnias → assoc with **benzo receptor agonists**
    - Esp if taken at higher doses or combined with other sedatives
  - Abrupt discontinuation → **exacerbation of insomnia**
    - Short-acting → most likely **rebound insomnia**
    - Long-acting → more often **daytime sleepiness**

# Sub/Med-Induced Sleep Disorder – Associated Features

- Stimulants

- Acute → decr total sleep, incr sleep latency, disturbed sleep continuity
  - **Decr REM sleep, decr slow-wave sleep**
  - MDMA → restless + disturbed sleep within 48 hours of intake
- Withdrawal → prolonged nocturnal sleep, excessive daytime sleepiness
  - **MSLT → incr daytime sleepiness**
  - Chronic → persisting anxiety, depression, sleep disturbances
    - (even if longer-term abstinence)

- Tobacco

- Chronic → **insomnia, decr sleep efficiency, incr daytime sleepiness**
  - **Decr slow-wave sleep**
- Withdrawal → **impaired sleep**
- If heavy smoker → may have nocturnal awakenings from tobacco craving

# Sub/Med-Induced Sleep Disorder – Development & Course

- In children → parents may observe with start of medication
- In adolescents + early adulthood → consider substances
  - Limited help-seeking, need collateral
- In older adults
  - **More medications**, higher risk of developing
  - May interpret sleep disturbance as part of normal aging
  - Higher risk in **major NCD**

# Sub/Med-Induced Sleep Disorder – Risk Factors

- Relevant to type of sleep disturbance
- Temperamental
  - Presence of insomnia in response to **stress or change in sleep**
  - Substance use generally precipitates/accompanies insomnia if vulnerable
  - Similar risk for other sleep disorders

# Sub/Med-Induced Sleep Disorder – Culture-Related Issues

- May depend on cultural background + local regulations

# Sub/Med-Induced Sleep Disorder – Gender-Related Issues

- More prevalent in **alcohol-consuming FEMALES (2x)**

# Sub/Med-Induced Sleep Disorder – Diagnostic Markers

- EEG patterns NOT diagnostic
  - Depends on stage of use, intake/intoxication, chronic, withdrawal
  - All-night PSG → severity of insomnia
  - MSLT → severity of daytime sleepiness
  - Monitor nocturnal respiration, periodic limb movements
- Sleep diaries + actigraphy (for 2 weeks)
- Drug screening



# Sub/Med-Induced Sleep Disorder – Functional Consequence

- Only unique consequence
  - **Increase risk for relapse (substance)**
  - Degree of sleep disturbance during alcohol withdrawal
    - **REM sleep rebound** predicts **risk of relapse of drinking**
    - Monitor sleep quality + daytime sleepiness around withdrawal

# Sub/Med-Induced Sleep Disorder – Differential Diagnosis

- Substance intoxication/withdrawal (whether predominant sleep)
- Delirium
- Other sleep disorders, sleep disorders due to AMC
  - Etiologically + temporally related
  - Can dx both

# Sub/Med-Induced Sleep Disorder – Comorbidity

- See other sections
  - Insomnia, hypersomnolence, central sleep apnea
  - Sleep-related hypoventilation
  - Circadian rhythm sleep-wake disorders, shift work type

# Other Specified Insomnia Disorder

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# Other Specified Insomnia Disorder

- Does not meet any full criteria
- Clinician chooses to specify
- Brief insomnia disorder
  - Duration <3 months
- Restricted to non-restorative sleep
  - Predominantly non-restorative sleep
  - No other sleep sx (initial or middle insomnia)

# Unspecified Insomnia Disorder

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# Unspecified Insomnia Disorder

- Does not meet any full criteria
- Clinician chooses NOT to specify

# Other Specified Hypersomnolence Disorder



# Other Specified Hypersomnolence Disorder

- Does not meet any full criteria
- Clinician chooses to specify
- Brief-duration hypersomnolence
  - Seen in Kleine-Levin syndrome

# Unspecified Hypersomnolence Disorder

# Unspecified Hypersomnolence Disorder

- Does not meet any full criteria
- Clinician chooses NOT to specify

# Other Specified Sleep-Wake Disorder

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## Other Specified Sleep-Wake Disorder

- Does not meet any full criteria
- Clinician chooses to specify
- Repeated arousals during REM sleep without polysomnography or history of Parkinson's disease or other synucleinopathy

# Unspecified Sleep-Wake Disorder

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# Unspecified Sleep-Wake Disorder

- Does not meet any full criteria
- Clinician chooses NOT to specify