

Insomnia

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INSOMNIA - perceived **inability to obtain sufficient restorative sleep** (i.e. **subjective*** sense that sleep is inadequate, insufficient, or interrupted) despite adequate opportunity for sleep.

***subjective** - sleep requirements vary among individuals; restorative aspect of sleep is difficult to measure!

N.B. to be considered disorder, complaint of insomnia should be accompanied by **distress** and/or **impairment in daytime functioning**.

- **10%** USA adults have *chronic insomnia*, and another **15%** have *short-term insomnia*.
- PREVALENCE is higher in **women** and in **older persons**.

TRANSIENT insomnia - lasts up to 1 week.

SHORT-TERM insomnia - lasts from few days to 3 weeks.

LONG-TERM (s. CHRONIC) insomnia - lasts for months or years.

ETIOPATHOPHYSIOLOGY

Insomnia can occur with *virtually any sleep disorder* as well as with host of medical and psychiatric disorders.

Long-term use of hypnotic drugs is major cause of persistent insomnia!

A. Difficulty falling asleep (SLEEP-ONSET INSOMNIA):

N.B. differentiate from PHASE-DELAYED SLEEP SYNDROME!

- 1) **acute situational stress** (e.g. new job, upcoming deadline, exam) - *adjustment sleep disorder*.
- 2) **circadian rhythm disorders** (incl. shift workers, international travelers).
- 3) **somatized anxiety** (in *psychophysiologic insomnia*).
- 4) **bodily dysfunctions** - pain, decreased mobility, disturbing sensations or movements (e.g. parkinsonics unable to roll over in bed; unusual sensations in RLS; pain from arthritis or cluster headaches).
- 5) various **primary sleep disorders** - alterations in CNS systems that initiate sleep.
- 6) insomnia **secondary to neurological / psychological disorders** (e.g. *dementia* may cause reversal of normal day-night sleep cycle; *major depression* or *bipolar disorder in acute manic phase* may cause insomnia).
- 7) **external stimuli** (noise, excessive heat or cold, bright light).
- 8) **drugs**; esp. discontinuation of chronic *hypnosedative* treatment → severe rebound insomnia.
 - *stimulants* and *antiparkinson drugs* are directly associated with insomnia.

- B. **Difficulty maintaining consolidated sleep** (SLEEP FRAGMENTATION, s. SLEEP MAINTENANCE INSOMNIA):
- 1) *alcohol* intake before bed.
 - 2) various *primary sleep disorders* - alterations in CNS systems that maintain sleep (e.g. PLMD, sleep apnea).
 - 3) various *medical conditions* (e.g. nocturia, cardiac disease, RA).
- C. **Early morning awakening** before adequate sleep is obtained (SLEEP OFFSET INSOMNIA):
- N.B. differentiate from PHASE-ADVANCED SLEEP!
- 1) major *depression* or *obsessive-compulsive disorder* - early morning awakening with excessive rumination
 - 2) frequent complaint of *elderly*.
- D. **Normal duration but non-refreshing sleep** (NONRESTORATIVE SLEEP)
- *mental activity* (ruminative thoughts) during sleep and awakenings may contribute to impression that sleep is not restorative.
 - some have impression that they sleep very little (often report no sleep at all), even when laboratory recordings reveal near-normal sleep (*sleep state misperception*).
H: education; behavioral treatment and hypnotics are helpful for some (amnesic effects interrupt subjective impression that consciousness has been maintained during sleep).

Differentiate between PREDISPOSING, PRECIPITATING, and PERPETUATING factors

PREDISPOSING factors:

- 1) **personality** (tense, nervous, worried persons who internalize problems and have somatic responses to stress)
- 2) increasing **age**
- 3) medical **illnesses**, deterioration of CNS functions responsible for sleep initiation and maintenance.

PRECIPITATING factors cause **acute insomnia:**

- 1) stress (e.g. death or illness of loved one, divorce or separation, change in occupational status, examinations)
- 2) medical / psychiatric illness
- 3) medications
- 4) move to new location, change in sleeping environment
- 5) change in sleep-wake schedule

PERPETUATING factors cause **chronic insomnia:**

- patients become apprehensive as they lie down to sleep, fearing that struggle to obtain sleep will commence again - *greater effort expended in trying to sleep, more elusive sleep becomes!*
 - pattern may become established over time → recurrent, persistent insomnia.
- 1) *anxiety* about sleep, fear of insomnia, conditioned negative associations
 - 2) *poor sleep hygiene*. see S40 p.
 - 3) *secondary gain* (nighttime snacks and alcohol use, TV use, time off from work, role of sickly child or dependent adult)
 - 4) *performance anxiety* (belief that good sleep is requirement for effective functioning next day); insomnia may be less severe on weekends and during vacations, when concerns about effects on daytime function are less.
- *watching clock* as each minute and hour passes only increases sense of urgency, further confounding efforts to sleep.

Chronic insomnia primarily occurs in patients with PREDISPOSING factors. These factors may cause occasional night of poor sleep but not chronic insomnia. PRECIPITATING factor causes acute insomnia. If poor sleep habits or other PERPETUATING factors occur in following weeks to months, chronic insomnia develops despite removal of precipitating factor.

CLINICAL FEATURES

Nocturnal symptoms:

- a) toss and turn in bed.
N.B. *increased time spent in bed* (with hope to obtain enough sleep) usually results in increased time awake in bed rather than increased time asleep → negative conditioning.
- b) watch TV, read, eat, drink, use bathroom.
- c) do housework / homework (persons who do not like to waste time).

Daytime symptoms - poor concentration, fatigue, irritability, mood changes, anxiety, muscle aching.

- if patient is having no daytime effects, he probably is getting adequate sleep and complaint of insomnia is truly subjective!
- fatigue is sometimes accompanied by sleepiness, but most insomniacs are unable to nap even if they lie down.
N.B. excessive daytime sleepiness is rare in insomnia!
- *substance abuse* (alcohol, sedative medications) is common.
- psychiatric disturbance (esp. *depression, anxiety disorders*) is present in 40% insomniacs!
N.B. *dysphoria* is common feature of all types of insomnia (but may mask primary depression as cause of insomnia).
N.B. most insomniacs are *anxious*, anxiety is usually *focused on sleep* (vs. *generalized anxiety* suggests anxiety disorder as cause of insomnia).

COURSE OF INSOMNIA is variable:

- a) many patients have lifetime of sleep problems
- b) others have episodic bouts of poor sleep separated by years of tranquil nights.

COMPLICATIONS

- insomnia > 12 months → increased risk for *depression, anxiety disorders, alcohol abuse*.
- *drug* treatment complications. see below
- decreased *job performance* and *self-esteem*.
- increased risk of *motor vehicle accidents*.

PHYSIOLOGY OF SLEEP DEPRIVATION

- after 24 hours of sustained wakefulness:
 - 1) *metabolic activity* of brain↓↓ (up to 6% for whole brain and up to 11% for specific cortical* and basal ganglionic areas). * esp. in prefrontal and parietal associational areas
 - 2) *core body temperature* ↓
 - 3) *immune system function* ↓ (WBC count and activity ↓)
 - 4) *growth hormone* release ↓
 - 5) increased *heart rate* variability.
- **higher-order cognitive tasks** are affected early and disproportionately.
 - in tests requiring both speed and accuracy, *speed* fails before *accuracy* begins to fail.
 - in tasks requiring judgment, increasingly *risky behaviors* emerge (high cost of action seemingly is ignored as sleep-deprived individual focuses on limited benefit).
 - impairment of cognitive work requiring *simultaneous focus on several tasks*.

- loss of ability to simultaneously appreciate peripheral and centrally presented visual stimuli (*visual simultanagnosia* and *peripheral visual neglect*).
- small amounts of sleep loss (e.g. 1 hour per night over many nights) have subtle cognitive costs, which appear to go unrecognized by individual!!!
N.B. severe sleep restriction for week leads to *profound cognitive deficits* similar to those seen in some stroke patients, which appear to go unrecognized by individual.
- explanation for decreasing performance:
 - 1) occurrence of **microsleep** - brief (several seconds) runs of theta or delta activities that break through otherwise beta or alpha EEG of waking.
 - 2) **sensory perceptual impairments** (such as visual neglect phenomena).

DIAGNOSIS

- 1) **history with sleep diary** - most crucial part of evaluation!
- 2) **psychiatric evaluation** - if psychiatric etiology is consideration.
- 3) **POLYSOMNOGRAPHY** - indicated in:
 - a) apnea
 - b) periodic leg movements
 - c) failure to respond to treatment
 - d) sleep state misperception.

MANAGEMENT

- treatment is based on **underlying causes** (secondary insomnia → treat underlying psychiatric or medical disorder).

From therapeutic perspective, **PERPETUATING factors** are often most important (most amenable to change).

- improved **sleep hygiene** can lead to marked improvement. see S40 p.
N.B. *poor sleep hygiene may be result of other* (esp. psychiatric) *problems*.

BEHAVIORAL THERAPY

- considered most appropriate treatment for **PRIMARY INSOMNIA!**
 - behavioral therapy is based on fact that “primary insomnia is associated with physiologic, emotional, and cognitive arousal and conditioning to arousal in bed”.
- 1. **Relaxation therapy**: patient is taught to recognize and control tension through series of exercises (tensing and then relaxing each muscle group in systematic way).
- 2. **Stimulus control therapy** - reassociates bed with sleepiness instead of arousal.
- 3. **Sleep-restriction therapy** is based upon fact that excessive time in bed often perpetuates insomnia; limiting time in bed → more efficient sleep.

MEDICATIONS (HYPNOTICS)

for pharmacologic data - see Rx1-3 p.

- most helpful in **TRANSIENT SITUATIONAL INSOMNIA**.
- may also be used as adjunctive therapy in some patients with **CHRONIC INSOMNIA** (but specific cause of insomnia must be actively sought!).

- some chronic insomniacs do well using hypnotics **1-2 nights per week** when they feel they simply must have good night's sleep.
- some find it **reassuring to have hypnotic available** in medicine cabinet; knowledge reduces anxiety, and actual use may be minimal.
- some use hypnotic **nightly for years** with good response and no dose escalation.
- some obtain **no benefit** from hypnotics or become **dependent**, or both.
- principles of hypnotic therapy:
 - 1) use low doses for max. 2-4 weeks.
 - 2) avoid continued nightly use (i.e. use only when truly necessary).
 - 3) hypnotics never should be used with alcohol.
 - 4) pregnancy is contraindication.
 - 5) for elderly patients start with ½ dose!
 - 6) **depressed patients** should be given limited amounts to reduce risk of attempting suicide with hypnotic!
- problems with hypnotics:
 - 1) sleep architecture destruction (esp. REM sleep suppression).
 - 2) nocturnal confusion
 - 3) next-day memory impairment and sedation, drug hangover (esp. barbiturates).
 - 4) rebound insomnia (H: drug dosage should be tapered prior to withdrawal).
 - 5) tolerance, addiction & dependence with severe withdrawal (esp. barbiturates).
 - 6) potentiation of other CNS depressants, risk of lethal overdose.

Medications currently approved in the U.S. fall into 2 broad classes:

- 1) benzodiazepine receptor agonists (BzRAs)
 - 2) melatonin receptor agonists (MRAs)
1. **BENZODIAZEPINES** - preferred drugs - not general neuronal depressants, very safe; avoid in sleep apnea patients.

Any benzodiazepine can be used to treat insomnia!

SHORT-acting benzodiazepines (e.g. **TRIAZOLAM***) – useful for **sleep induction**.

INTERMEDIATE-acting benzodiazepines (e.g. **TEMAZEPAM***, **ESTAZOLAM***) – useful for frequent **awakenings**.

LONG-acting benzodiazepines (e.g. **FLURAZEPAM***, **QUAZEPAM***) – useful for **sleep induction** and frequent **awakenings**; also increase **sleep duration**; may result in daytime sedation.
 2. **SELECTIVE BENZODIAZEPINE RECEPTOR AGONISTS** (but NONBENZODIAZEPINES) – **ZOLPIDEM***, **ZALEPLON***, **ZOPICLONE**, **ESZOPICLONE*** – advantageous over benzodiazepines – likely to become first choice agent for treatment of insomnia!
 3. **MELATONIN AGONISTS**: **RAMELTEON*** (nonsedating medication indicated for difficulty with sleep onset), **MELATONIN** (much less effective than conventional hypnotics; currently not recommended).
 4. **OREXIN ANTAGONISTS**: **SUVOREXANT** (Belsomra®)*, **LEMBOREXANT** (Dayvigo®)*
 - orexins, 2 similar neuropeptides originating in lateral hypothalamus, have been shown to be important in consolidation of wakefulness.
 - patients with narcolepsy are excessively sleepy and have deficiency in orexin activity.
 - pharmacologic reduction of nighttime orexin activity might promote sleep consolidation.
 5. **CHLORAL HYDRATE** - induces sleep in 30 min and lasts 6 hrs; mostly used for 1-3 nights to treat transient insomnia.
 6. **ANTI-HISTAMINES** (e.g. **DIPHENHYDRAMINE**) - effective only in *mild forms of situational insomnia*; numerous side effects (esp. anticholinergic).

7. Sedating **ANTIDEPRESSANTS** (**AMITRIPTYLINE, DOXEPIN, TRAZODONE, NEFAZODONE, IMIPRAMINE**) - low doses are sometimes useful as alternatives to standard hypnotics (esp. if depression is present); tolerance to hypnotic effect does not develop.
8. Short-acting **BARBITURATES** (**PENTOBARBITAL**, etc) – should not be used (except in rare case of patient who has been taking them for years and cannot be withdrawn).
9. **GLUTETHIMIDE** – not recommended (very narrow therapeutic index – overdose likely!!!).

* FDA approved for insomnia treatment

EXPERIMENTAL HYPNOTICS

5-HT_{2A} Receptor Antagonists (e.g. EPLIVANSERIN, PIMAVANSERIN, PRUVANSERIN, VOLINANSERIN), aka ASTAR (Antagonist of Serotonin Two A Receptors).

Histamine Receptor Modulators

- OTC sleep aids are all antihistamines (DIPHENHYDRAMINE, DOXYLAMINE), but they often cause residual sedation + anticholinergic effects.

PSYCHOPHYSIOLOGICAL INSOMNIA

- insomnia caused by **somatized anxiety** (learned sleep-preventing associations) that is manifest as restlessness, apprehension, ruminative thoughts, and hypervigilance, all of which interfere with sleep.

Behavioral disorder in which patient is preoccupied with perceived inability to sleep

- most common form of primary insomnia!
- usually follows situational insomnia (triggered by emotionally stressful event) → poor sleep habits acquired during stressful period persist long after initial incident (conditioned response).
- patients prefer regular routines and view good sleep as necessity.
- **awakening** (that would ordinarily be just long enough for change in body position) **is followed by anxiety** (that sleep will not return + consequences of not sleeping) → **hyperalertness**; rapid return to sleep becomes impossible.

Vicious cycle: more patient tries to sleep, less successful attempts become!

- patients fall asleep more easily at **unscheduled times** (when not trying) or **outside home environment** (e.g. at lecture or while driving).
- **polysomnography** - objective sleep disturbance with abnormally long sleep latency, frequent nocturnal awakenings, and increased stage 1 amount.
- **treatment** - BEHAVIORAL THERAPY is mainstay;
 - **sleep restriction therapy** - mild sleep deprivation (eliminating naps and temporarily restricting time in bed to 1-2 hours less than nightly reported amount of sleep) makes sleep more continuous; once sleep is consolidated, time in bed can be gradually increased.
 - **sleep hygiene!!!**
 - patients are encouraged to **get out of bed and to do something relaxing if unable to sleep after 15-20 minutes.**

Viktor's NotesSM for the Neurosurgery Resident
Please visit website at www.NeurosurgeryResident.net