Circadian Rhythm Sleep Disorders
(s. Chronobiological Disorders)

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TIME ZONE CHANGE (JET LAG) SYNDROME

SHIFT WORK SLEEP DISORDER

DELAYED SLEEP PHASE SYNDROME (DSPS)

ADVANCED SLEEP PHASE SYNDROME

NON-24-HOUR SLEEP-WAKE DISORDER

IRREGULAR SLEEP-WAKE PATTERN

CHRONOBIOLOGICAL DISORDERS - disruption of inherent circadian pattern of wakefulness and sleep → shift in phase relation between internal biological clock and desired sleep-wake schedule (i.e. disorders of sleep TIMING rather than sleep GENERATION):

a) sleep at wrong time of day
b) cannot sleep at right time of night (N.B. this is not true insomnia!)

• diagnosed by proper clinical history (sleep logs).
• management – aim is to entrain biological clock to appropriate phase:
  1) appropriate sleep scheduling
  2) exposure to bright light.

TIME ZONE CHANGE (JET LAG) SYNDROME

• arises from transmeridian flights of long duration (usually at least three time zones).
• reflects adaptation necessary to reset internal rhythm to day-night cycle of destination.
• symptoms are proportional to number of time lines crossed; do not occur even with long flights north to south!
• enhanced by sleep deprivation (before prolonged trip, altered conditions during flight) + alcohol use during flight.
• internal clock adaptation speed:
  1 hour / per day after phase advance (eastbound flight);
  1.5 hours / per day after phase delay (westbound flight).
  N.B. recovery may take as long as 7-10 days (esp. for eastward travel).

• treatment & prophylaxis:
  1) pretravel sleep schedule should be shifted 1-2 hours closer to destination schedule.
  2) hypnotic use (e.g. ZOLPIDEM) during trip (to minimize in-flight sleep loss) and in new time zone.
  3) correctly timed bright light exposure and immediate adoption of new time zone schedule.
  4) early evening ingestion of 0.5-5.0 mg MELATONIN (as health food supplement).

SHIFT WORK SLEEP DISORDER

• sleep problems are similar to jet lag (8-hour shift = flight across eight time zones).
• main differences from jet lag:
  1) no reinforcement of external light-dark cycles
  2) absence of social patterns that conform to new sleep schedule.
CIRCADIAN RHYTHM SLEEP DISORDERS

- after single change in shift, 2 weeks may be needed for readjustment; shift workers often are required to change their schedules every 2-4 weeks + nighttime sleep on weekends → chronic desynchronization with their circadian clock.

- remission during vacations!

- treatment: MODAFINIL (Provigil®), ARMODAFINIL (Nuvigil™) - both FDA approved!

- prophylaxis:
  - *bright light* at night and *dark bedrooms* in daytime.
  - best is to sleep during day, but most persons are unwilling to spend days off asleep (H: 2-3 hour nap in afternoon and 4-6 hours of sleep in morning after work).
  - *forward rotations* - shift rotations days→ evenings→ nights are better tolerated than rotations in opposite direction.
  - *less frequent rotations* - shift rotations no more than once every 2-3 weeks.

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**DELAYED SLEEP PHASE SYNDROME (DSPS)**

- difficulty falling asleep at night and difficulty waking up on time in morning; normal sleep length and internal sleep organization.

- phase shift occurs during weekends if bedtimes and rise times are delayed; such phase delays (induced by sleeping later) are not corrected during week.

- adolescence (usual time of DSPS appearance): increased sleep needs + social factors and greater independence prevent earlier bedtimes → many adolescents sleep later on weekends → DSPS → patients tend to "choose" late-night activities because they are unable to sleep at that time (circulus vitiosus).

- DSPS may affects ≈ 7% urban adolescents.

  N.B. DSPS may be initial manifestation of depression in adolescents.

- treatment (condition is usually very refractory to treatment) - *schedule is most critical element*:
  - advance times of going to bed and arising from bed by 15 min each day or two beginning with usual weekend sleep times.
  - N.B. it is easier to achieve phase delay than phase advance!
  - alternative quicker approaches (with more rapid phase shifts) are more socially disruptive and require strong motivation.
  - once desired schedule is achieved, it must be rigorously maintained 7 days per week.
  - *bright-light phototherapy* during morning hours is also helpful.

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**ADVANCED SLEEP PHASE SYNDROME**

- evening sleepiness and early morning awakening (sleep onset at 6-9 PM and awakening 1-3 AM are typical).

- more likely to occur in elderly persons.

- treatment - *schedule is most critical element* (reverse to DSPS); *bright-light phototherapy* during evening hours.

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**NON-24-HOUR SLEEP-WAKE DISORDER**

- caused by *destruction of retinohypothalamic tract* - major cause of sleep-wake complaints in blind persons!

  N.B. chiasmal lesions that interrupt retinohypothalamic tract may cause syndrome even when visual loss is incomplete.

- without retinal input, internal clock moves in and out of phase with environmental clock (i.e. completely out of touch with 24-hour cycle) - *cyclical fluctuation* is typical (cycles may be of
several weeks duration) - individuals maintain 25- to 27-hour biologic day despite all attempts to entrain themselves to 24-hour cycle.

- when phase difference is large, *sleep times become highly irregular* (prolonged wakefulness lasting up to 40-50 hours may be followed by sleep periods of 12-20 hours and then resumption for few days of relatively normal schedule).

- treatment (for patients who retain some retinal input to suprachiasmatic nucleus) - appropriately timed exposure to high-intensity bright light.

**TASIMELTEON** (HETLIOZ®) – FDA approved melatonin receptor agonist, to treat non-24-hour sleep-wake disorder (“non-24”) in totally blind individuals.

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**IRREGULAR SLEEP-WAKE PATTERN**

- sleep episodes of varying length at irregular intervals (vs. Non-24-Hour Sleep-Wake Disorder – has cyclical fluctuation).

- caused by destruction of suprachiasmatic nucleus (or its effector pathways).

- occurs mainly in institutionalized persons with severe static or progressive encephalopathies.

- picture is often complicated by nocturnal agitation and use of sedatives or antipsychotic medications to control agitation.

- treatment - morning exposure to bright light, increased daytime activity, prohibition of morning and evening naps.

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**BIBLIOGRAPHY** see p. S40 >>