

Circadian Rhythm Sleep Disorders (s. *Chronobiological Disorders*)

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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.

- 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.

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 affect ≈ 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.

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.

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.

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.

BIBLIOGRAPHY see p. S40 >>