Normal Sleep and Insomnia

Normal sleep is dependent on the following:
1) the appropriate timing of sleep within the 24-hour circadian rhythm
2) physical comfort
3) an appropriate environment
4) intact central nervous system function
5) and relative absence of psychological distress

The restorative functions of sleep are dependent on an intact “sleep architecture.” More than 50% of patients with advanced cancer experience disturbed sleep, especially when pain is a symptom. The most common sleep complaints are insomnia or the subjective complaint of poor sleep, and excessive daytime sleepiness.

The complaint of insomnia includes:
1) insufficient sleep
2) problems falling asleep or staying asleep
3) frequent awakenings
4) poor quality of sleep
5) or sleeping at the wrong time of the day

Patients with cancer are more likely to sleep less at night because of frequent nighttime disruptions and increased inactivity during the day that leads to napping. This has implications for caregiver burden, as well.

Causes of Insomnia

Physiological causes of insomnia include:
1) Pain - very closely linked to impaired sleep - both cause and effect
2) Metabolic abnormalities
3) Medications, including chemotherapeutic agents and AIDS treatments, esp. AZT. Withdrawal from sedative-hypnotics is an important cause of insomnia.
4) Sleep apnea - may be worsened by opioid analgesics
5) Nausea, vomiting, peptic ulcer and reflux disease
6) Delirium
7) Hypoxia/ Dyspnea

Psychological causes of insomnia include:
1) Depression - moderate to severe depression is seen in 25-50% of cancer patients - insomnia is an important diagnostic marker for depression.
2) Anxiety - in one study, 63% of cancer patients with anxiety had insomnia - causes of anxiety are multi-factorial, but include the inability to sleep - anxiety may manifest as nightmares - anxiety may be an early sign of delirium

Environmental causes of insomnia include:
1) change in environment
2) Frequent interruptions - (such as come with hospitalization)
3) Noise

Problems attributable to sleep deprivation:
1) Fatigue
2) Sleepiness - affects social interactions, treatment participation.
3) Impaired concentration
4) Irritability
5) Depression
6) ? Altered immune response
7) ? Delirium

The causes of excessive daytime sleepiness include:
1) Not enough sleep or disturbed sleep at night
2) Medications including:
   - analgesics
   - sedatives
   - antidepressants
   - and chemotherapy
3) Metabolic disorders, tumor effects (e.g. cytokines)
4) Psychological withdrawal
5) Depression
6) Disruption of sleep-wake schedule
7) Sleep apnea

N.B. Excessive daytime sleepiness should not be dismissed as inevitable in terminal illness. Radiotherapy is associated with both insomnia and excessive daytime sleepiness. Other causes of poor sleep include nutritional deficiency, alcohol and caffeine.
Drug accumulation is an issue with the elderly with long-term use. Withdrawal is common even after short-term use.
- May precipitate confusion in patients with cognitive dysfunction.
- Can cause carry-over sedation into the next day. This may be beneficial in highly anxious patients.
- Temazepam (15-30 mg po qhs), oxazepam (10 mg po qhs) and lorazepam (0.5 mg po qhs) are safest in the elderly due to little change in clearance.
- Zolpidem (5-10 mg po qhs) is not chemically related but similar in action and with rapid clearance (a good alternative in the elderly).
- Benzos may exacerbate respiratory disturbances in sleep, but may be used cautiously in patients with no major blood gas abnormalities.
- May affect daytime functional abilities and performance.

2) Sedating anti-depressants
- May be safer over long periods.
- No concerns with addiction, but delirium from central anti-cholinergic activity a potential concern, as well as other anti-cholinergic side-effects.
- Trazadone (25-100 mg po qhs) is a sedating non-tricyclic anti-depressant with fewer anti-cholinergic side-effects; orthostatic hypotension should be monitored.
- Amitriptyline (10-50 mg po qhs) is more effective, but with many anticholinergic side-effects; NOT recommended in the elderly.
- Doxepin (10-25 mg po qhs) may be a better alternative for the elderly if Trazadone is ineffective. Also has significant anticholinergic side-effects.
- May try SSRIs if a patient cannot tolerate side-effects or above anti-depressants ineffective.
- Tricyclics also have adjuvant analgesic effects and may be useful when pain, insomnia, and depression coexist.
- Anti-depressants may also be useful when complaint is “non-restorative” sleep.

3) Sedating anti-histamines can be useful if pruritus or oral secretions interfere with sleep. These include diphenhydramine, hydroxyzine, cyproheptadine, etc. These can also potentiate anti-cholinergic effects (e.g., confusion, delirium, and urinary retention) and potentiate CNS depression with alcohol.

4) For delirious patients with insomnia, the more sedating neuroleptics are the treatment of choice.

5) Miscellaneous
- In idiopathic periodic limb movement and restless leg syndrome, clonazepam, L-dopa, and opioids may help.

Reference: