



SLEEP DISORDERS

Daniel F. Kripke, MD
UC, San Diego

revised from a collaboration with

Nicholas G Ward, MD
University of Washington

Andrea Fagiolini, M.D.
University of Pittsburgh

Pre-Lecture Exam

Question 1

- 1. The most common cause of insomnia is**
 - A. Use of sleeping pills
 - B. Poor sleeping habits
 - C. Depression
 - D. Alcoholism
 - E. Sleep apnea

Question 2

- 2. Hypnotic drugs are indicated**
- A.** for insomnia due to chronic medical conditions.
 - B.** for insomnia due to depression.
 - C.** for insomnia due to sleep breathing disorders
 - D.** for transient problems lasting less than 30 days
 - E.** All of the above

Question 3

- 3. A hypnotic which causes little daytime sedation is:**
- A. Lorazepam
 - B. Zolpidem
 - C. Temazepam
 - D. Flurazepam
 - E. Diphenhydramine

Question 4

4. The usual maximum dose of zolpidem for an elderly woman is
- A. 5 mg
 - B. 10 mg
 - C. 15 mg
 - D. 20 mg
 - E. 25 mg

Question 5

- 5.** A hypnotic which helps people fall asleep when taken at bedtime is:
- A. Zaleplon
 - B. Temazepam
 - C. Lorazepam
 - D. Oxazepam
 - E. Ethchlorvynol

Question 6

- 6. The most popular drug for sleep complaints accompanying depression is:**
- A. Zolpidem
 - B. Zaleplon
 - C. Trazodone
 - D. Melatonin
 - E. Temazepam

Question 7

- 7. Effective treatment for chronic insomnia may include:**
- A. Zaleplon
 - B. Sleep restriction therapy
 - C. Zolpidem
 - D. Quazepam
 - E. Triazolam

Question 8

- 8. The most common cause of excessive sleep is:**
- a. Primary hypersomnia
 - b. Depression
 - c. Tricyclic antidepressants
 - d. Sleep apnea
 - e. Irregular habits

Question 9

- 9. Useful treatments for sleep apnea include:**
- A.** Mandible and tongue appliances
 - B.** Dieting
 - C.** Sleep position training
 - D.** Continuous positive airway pressure
 - E.** All of the above

Question 10

10. To treat delayed sleep phase, use:

- A. Vitamin B6
- B. Bright light in the morning
- C. Relaxation and sleep hygiene
- D. Methylphenidate
- E. Bright light just before bedtime



OUTLINE

- **Sleep disorders: definitions**
- **Insomnia**
- **Hypnotics choice: risks**
- **Cognitive Behavioral Therapy**
- **Sleep apnea**
- **Narcolepsy**
- **PLMDI (periodic limb movements)**
- **Circadian rhythm sleep disorders**



KEY POINTS

- **Hypnotics risks usually outweigh benefits**
- **Cognitive-behavioral therapy is best for chronic insomnia**
- **Sleep apnea is the most common cause of excess sleepiness**
- **Circadian rhythm disorders can be treated using the phase response curve**

Sleep Disorders

- **Primary**
- **Related to Another Mental Disorder**
- **Due to a General Medical Condition**
- **Substance-Related**

Sleep Disorders

- Insomnia
- Breathing
- Hypersomnia
- Circadian
- Parasomnia
- Movement



INSOMNIA: 1) Sleep Difficulty

- Complaints of disturbed sleep in the presence of adequate opportunity and circumstance for sleep
 - (1) difficulty in initiating sleep
 - (2) difficulty in maintaining sleep or
 - (3) waking up too early
 - ? nonrestorative or poor-quality sleep
- NIH conference on chronic insomnia
<http://consensus.nih.gov/2005/2005InsomniaSOS026html.htm>



INSOMNIA: 2) Daytime Hyperarousal

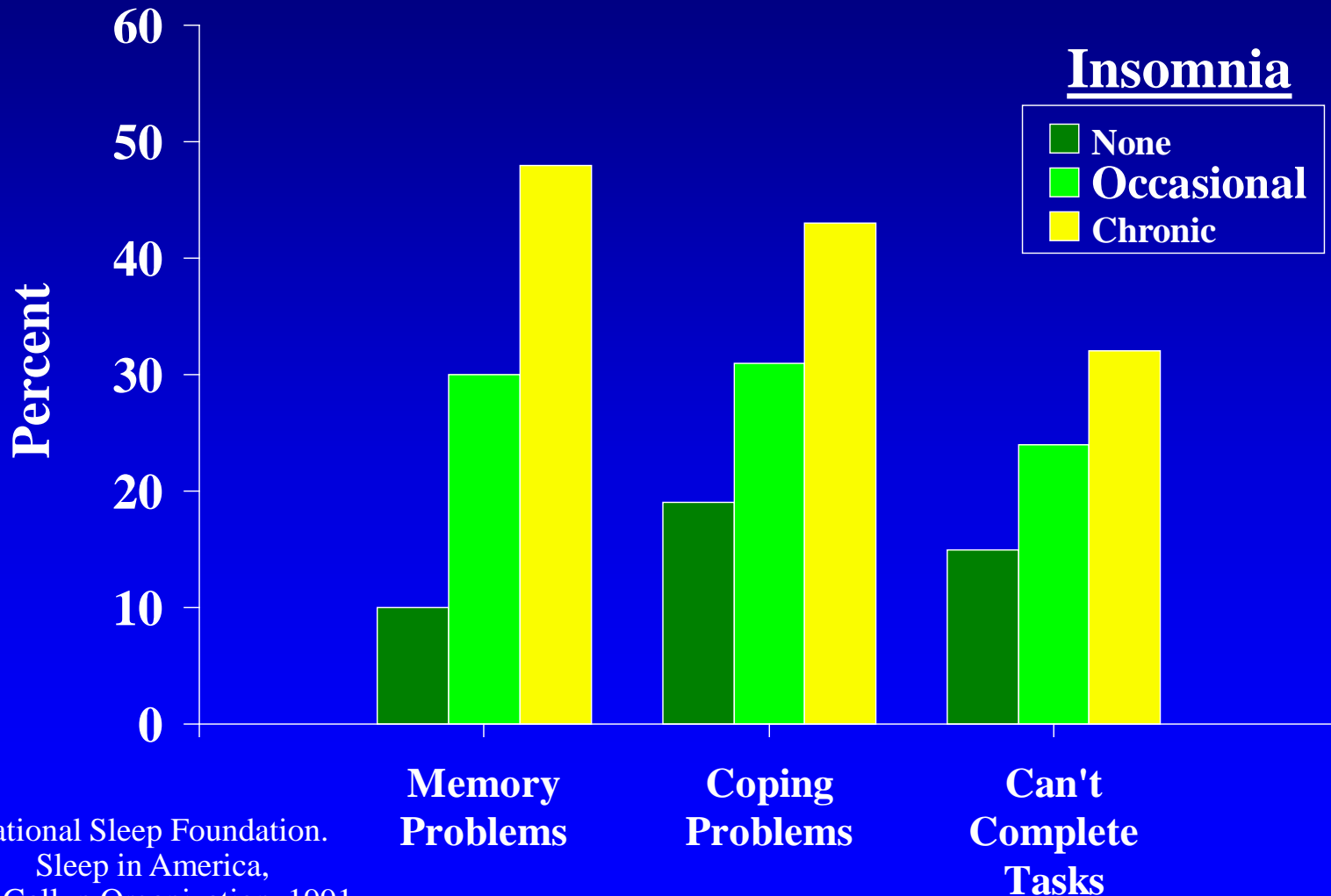
**Neurochemical or structural disorder
involving neural networks governing
sleep-wake states**



DISORDER OF HYPERAROUSAL



INSOMNIA: 3) Functional Impairment (might be related to comorbidities)

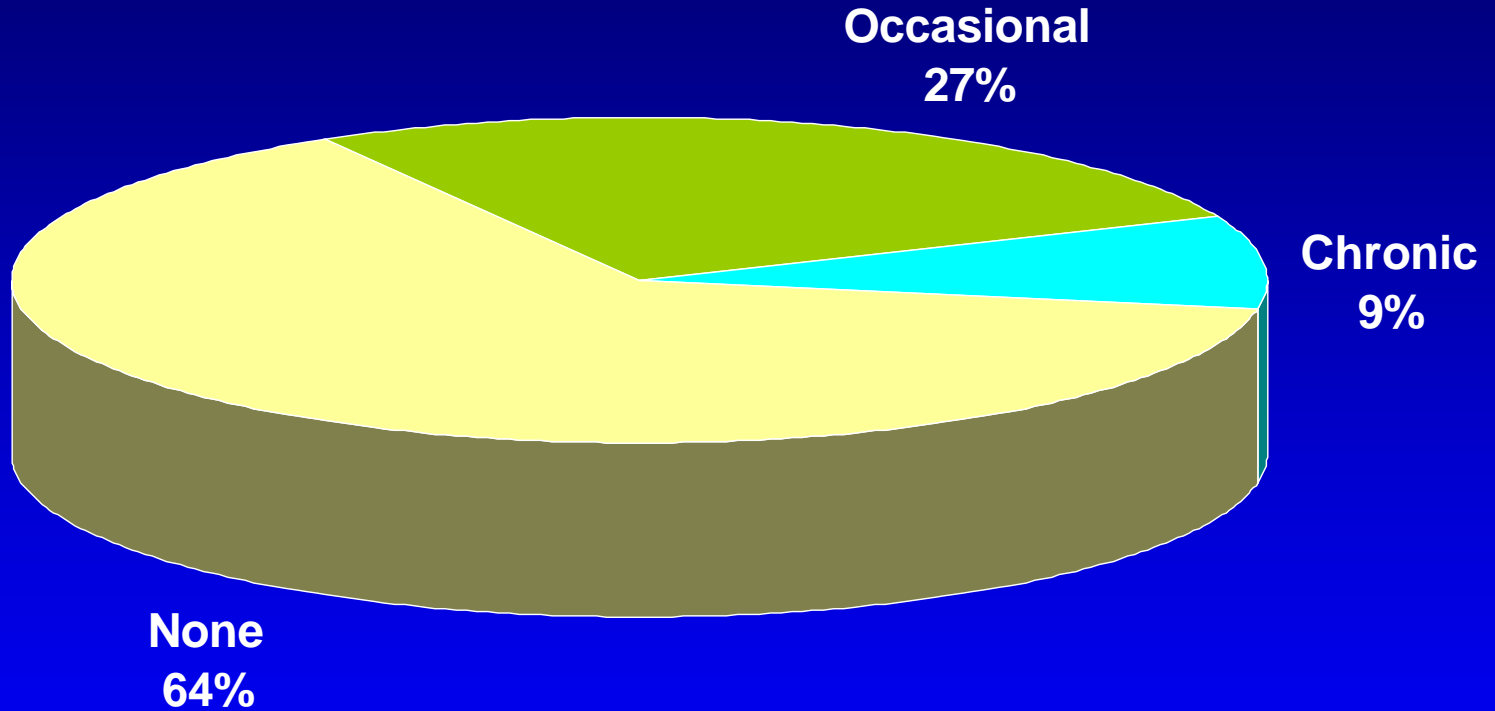


National Sleep Foundation.
Sleep in America,
The Gallup Organization, 1991



- Most insomnia is comorbid with other disorders, especially depression, substance abuse and anxiety.
- In **comorbid insomnia**, it is unclear when treatment focus should be on comorbidities.
- **Primary insomnia** is insomnia without comorbidities.

Prevalence of Insomnia in U.S.



National Sleep Foundation. Sleep in America, The Gallup Organization, 1991



INSOMNIA TREATMENT

- **Most hypnotics are only FDA-approved and indicated for short-term use, e.g., < 1 month.**
- **Most hypnotics are not recommended for chronic treatment.**
- **However, acute treatment of chronic insomnia often leads to long-term use.**

Hypnotics for Short-Term Use

Short Half - Life

Zolpidem: receptor specificity, low rebound, favorable kinetics, expensive

Triazolam: favorable kinetics, high rebound, strange behavioral and memory problems

Zaleplon: receptor specificity, half life too short

Medium Half - Life

Temazepam: Medium absorption, daytime sedation

Estazolam

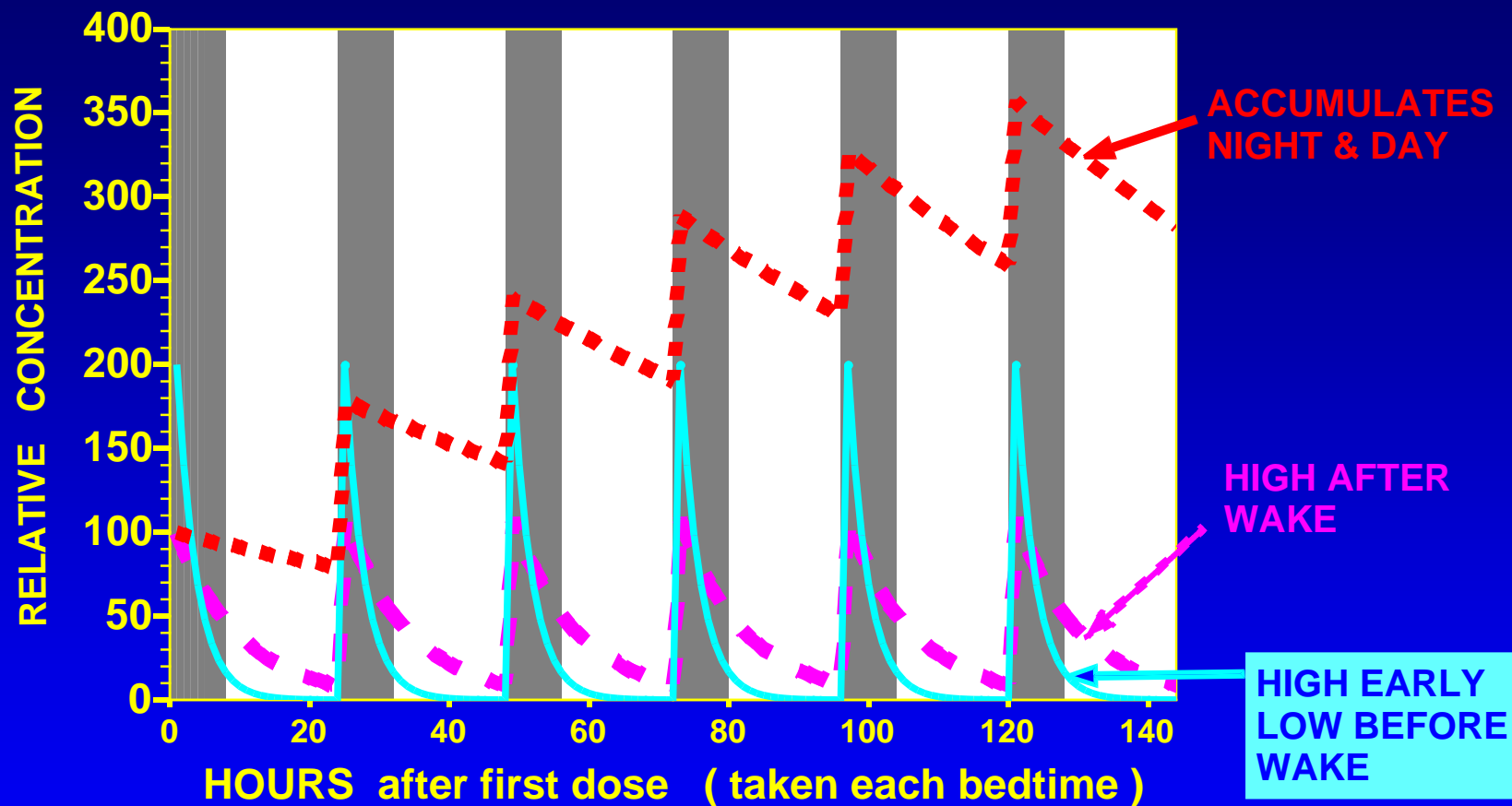
Lorazepam: Medium absorption

Alprazolam?

Medium absorption = onset of action ~ 1 hour



HALF-LIFE EFFECTS ON PLASMA LEVELS



HALF LIVES OF HYPNOTICS

■ ■ ~ 8 HOURS

— ~ 2 HOURS

■ ■ ■ ~ 48 HOURS +

■ SLEEP TIME

EXAMPLES:

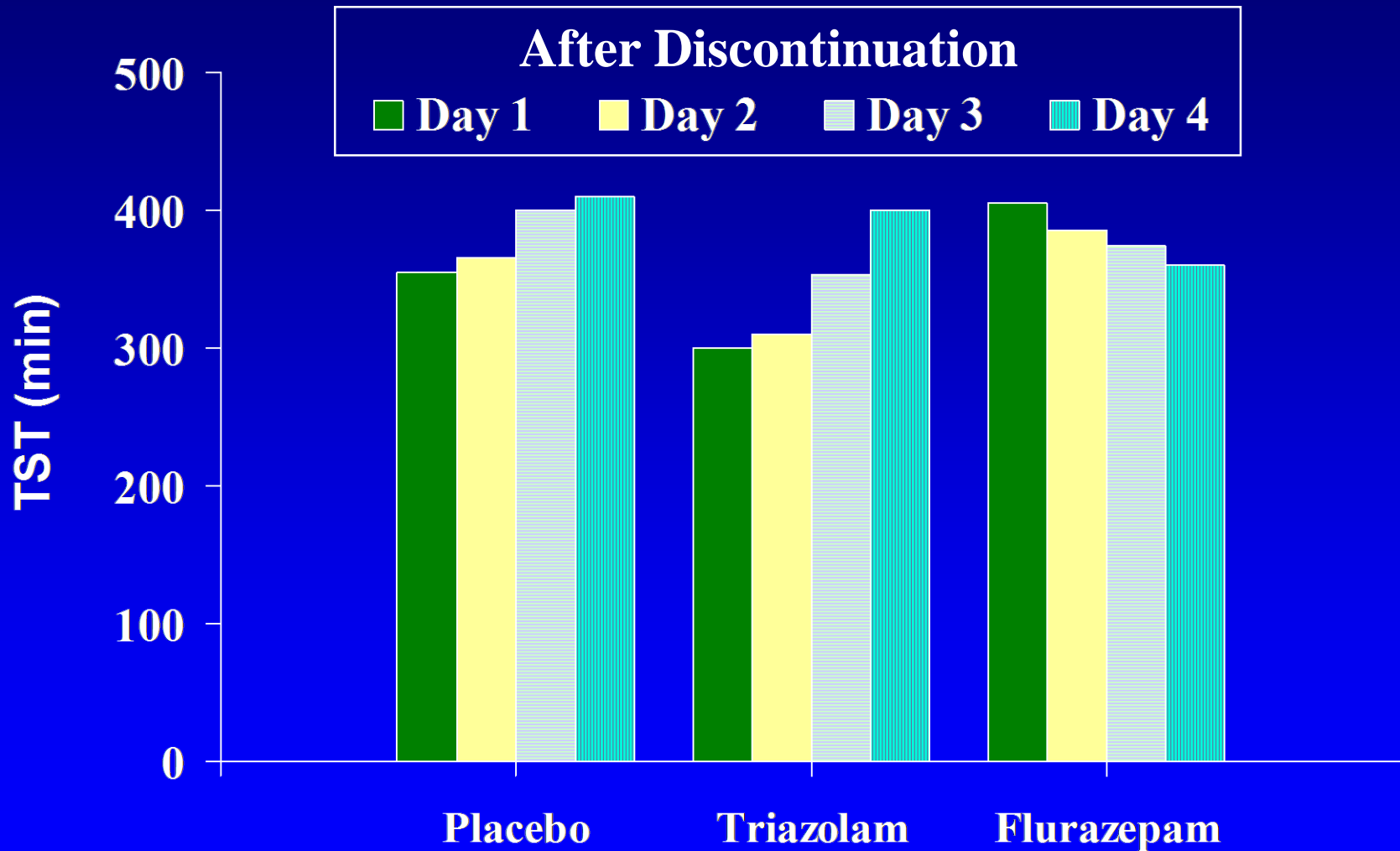
TEMAZEPAM
LORAZEPAM
OXAZEPAM

TRIAZOLAM
ZOLPIDEM
ZALEPLON

DIAZEPAM
FLURAZEPAM
QUAZEPAM

Rebound Insomnia

Half-Life Effects on Total Sleep Time





DAYTIME IMPAIRMENT

- Preponderance of evidence that all hypnotics result in daytime **impairment**, NOT improved function.
- Daytime impairment is much worse from hypnotics with half-life $\gg 4$ hours.
- Risks include increased automobile accidents, falls, memory loss, and confusion.



Hypnotics for Short-Term Use: Long Half-Life

All risk higher daytime sedation and falls in the elderly

- Flurazepam
- Diazepam: rapid absorption, first-pass short half life, but metabolites accumulate
- Quazepam: little rebound
- Because delayed accumulation and elimination risks daytime sedation, increased falls, and confusion risk, **long half-life hypnotics are not generally indicated**

Overdose

- **Benzodiazepine agonists alone rarely cause death.**
- **Benzodiazepines combined with alcohol or other sedating drugs may be lethal.**
- **Barbiturates, ethchlorvynol, glutethimide, etc. may be much more lethal.**



OVER AGE 60, RISKS > BENEFITS

Results of meta-analysis: not recommended

- Number needed to treat for improved sleep quality was 13.
- Number needed to harm for any adverse event was **6!**

Glass J, Lanctot KL, Herrmann N, Sproule BA, Busto UE.

Sedative hypnotics in older people with insomnia:

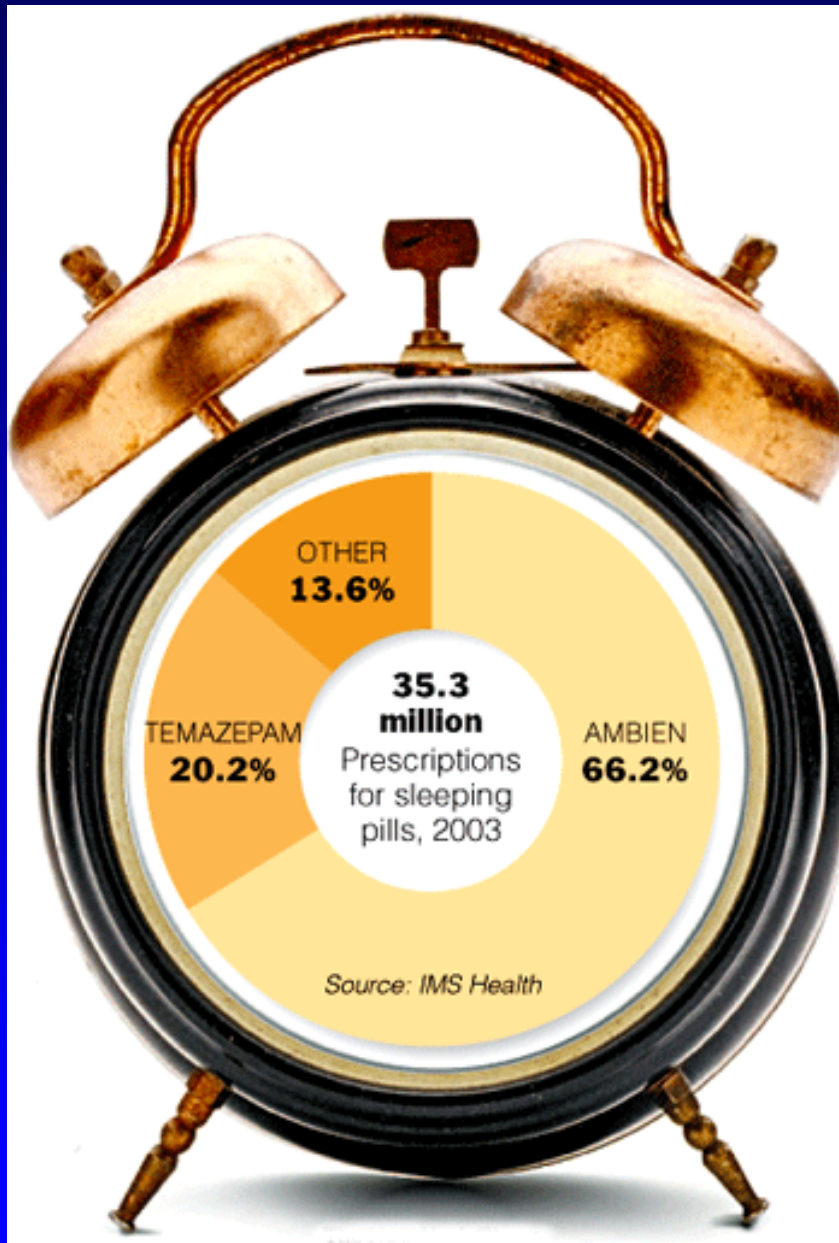
meta-analysis of risks and benefits. *BMJ* 2005 November 11.



TEN STUDIES SHOW INCREASED MORTALITY ASSOCIATED WITH HYPNOTICS USE*

Kripke et al 1979
Allgulander et al 1987
Allgulander et al 1990
Rumble and Morgan 1992
Thorogood et al 1992
Merlo et al 1996
Sundquist et al 1996
Kojima et al 2000
Kripke et al 2002
Mallon et al 2002

* Causality unproven. Unknown if applies to the most modern
hypnotics.



--NY Times, 2005

- Zolpidem dominated hypnotics market in 2003
- Eszopiclone & ramelteon introduced in 2005
- Some evidence that trazodone is prescribed for sleep ~ as often as zolpidem
- Alcohol and over-the-counter antihistamines used ? more widely than hypnotics for sleep

Zolpidem Pharmacokinetics

- Rapidly absorbed from GI tract (T_{\max} 1.6 h)
- Short half - life (2.5 h)
- Usual dose is 10 mg
- Increased C_{\max} and T_{\max} in elderly, but no accumulation
- Recommended dose in elderly is 5 mg
- No dosage adjustment in patients with renal dysfunction
- Reduce dosage in patients with hepatic dysfunction

Zolpidem (Ambien)

Doses \leq 20 mg

- **Selectively binds to ω_1 (AKA BZ₁ or α_1) receptor of GABA complex**
 - Does not effectively bind to ω_2 and ω_3 receptor
- **Has little respiratory depressant, myorelaxant, or anticonvulsant effects**
- **Behaves more like a benzodiazepine in doses over 20 mg**
 - Also over 20mg, risks of nausea and diarrhea increase
- **Not usually recommended in doses above 10mg**

Zolpidem Pharmacokinetics

Most Commonly Observed Adverse Events Seen at Statistically Significant Differences from Placebo

Short -term

— Drowsiness	2%
— Dizziness	1%
— Diarrhea	1%

Long-term

— Dizziness	5%
— Drugged feelings	3%

Zolpidem (Ambien) Clinical Effects

- **Rapid onset of action**
 - Often under 30 minutes
 - Take just prior to going to bed
- **Hypnotic effect precedes myorelaxant effect**
 - Most patients don't feel sleepy first, so they can fall asleep anywhere without warning
- **Prolongs total sleep only average of 20 - 45 min.**
 - May not treat early AM insomnia
- **Better quality of sleep and feeling of refreshment reported more often than increased sleep time**



Zolpidem (Ambien) Clinical Effects

- **No daytime sedation in young adults**
- **Mild first-night rebound insomnia**
- **Preserves stages 3/4 sleep**



Potential Problems with Zolpidem (Ambien)

- Higher doses (≥ 20 mg) may look like Halcion: REM \downarrow , rebound, etc.
- Acute effects
 - Increased postural sway
 - perhaps more falls
 - Memory and task difficulty
 - could be problem in dementia
 - Will not cover benzo hypnotic withdrawal
- Occasionally produces dependence or tolerance



UNCOMMON ADVERSE EFFECTS OF “Z” DRUGS

- **Hallucinations**
- **Somnambulistic night eating**
- **Confusion**

TRAZODONE

- **No studies of hypnotic efficacy beyond 2 weeks**
- **May have more adverse effects than benzodiazepine agonists**
- **Probably does not cause dependency**

TRAZODONE for INSOMNIA

- **Sleep lab studies report efficacy**
- **Dose: 25 - 50mg; low-adipose patients usually require less**
- **Onset of action: 20-60 minutes**
 - **Average peak level in 23 minutes**
- **Effect on sleep stages:**
 - **Increases stage 4**
 - **Slight decrease in REM**



TRAZODONE for INSOMNIA

- **Advantages**
 - Rapid onset of action
 - Usually minimal or no tolerance develops
 - May augment other antidepressants
- **Disadvantages**
 - Hypotension, dizziness
 - Daytime sedation ~20% of patients
 - GI disturbance
 - Priapism in men (1:800 to 1:10,000)

Pharmacological Treatment of Insomnia

Sedating TCA Antidepressants: Side Effects

- Not generally recommended for insomnia
- Orthostatic hypotension
- Daytime sedation
- Anticholinergic effects
 - Dry mouth
 - Blurred near vision
 - Urinary retention
 - Constipation
 - Confusion

Nonbenzodiazepine Hypnotics

- **Chloral hydrate**
 - Onset - 1 hour
 - Half-life 4 - 10 hours
- **EEG - Little effect**
- **Side effects**
 - Gastric irritation - use milk or antacid
 - Organ toxicity - avoid in hepatic, renal or cardiac disease
- **Decreased hepatic metabolism**
- **LD₅₀ - 10gm**
- **Habituation and dependence - > 1 week**

Antihistamines for Insomnia

- **Both OTC and prescription agents used to treat insomnia**
- **Most contain hydroxyzine, diphenhydramine, or doxylamine**
- **May cause insomnia or worsen existing insomnia**
- **All risk negative effects on next-day functioning**

Antihistamines for Insomnia Effects

- Onset 45 min - 1 hour
- Duration variable - frequently longer than 8 hours
- Decreases REM sleep

Antihistamines for Insomnia: Side Effects

- **Confusion - especially in elderly**
- **Anticholinergic - e.g., urinary retention**
- **AM sedation**
- **Habituation**
- **REM rebound on withdrawal**
 - **Causes and/or worsens insomnia**
 - **Can result in chronic use when acute treatment was planned**



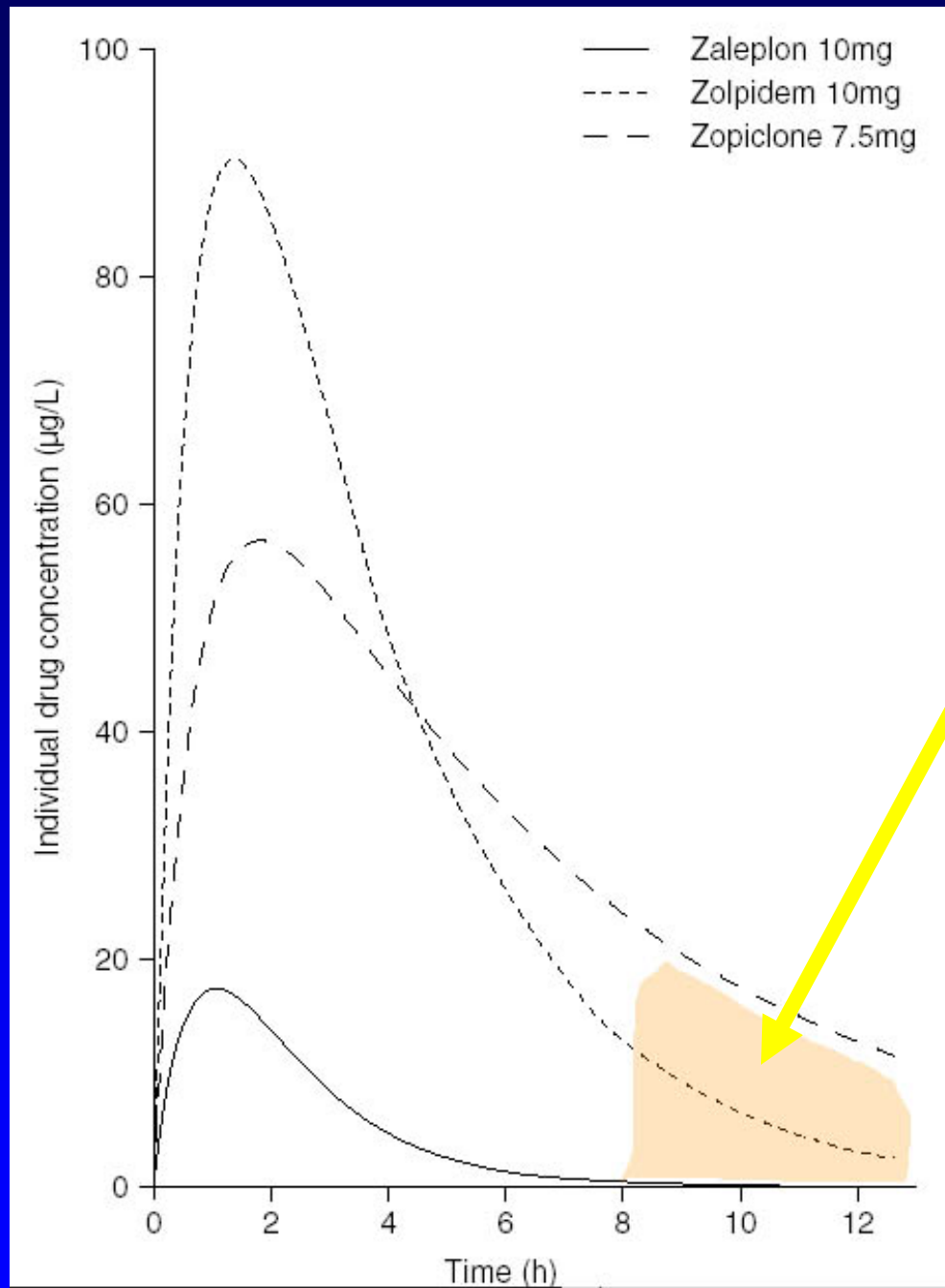
ESZOPICLONE

- FDA permitted an indication for long-term use, 2005
- Based on one study with only self-report evidence of effectiveness*
- The study did suggest improved daytime function compared to placebo.
- However, severe adverse effects were 3 times as common with eszopiclone as with placebo.

* Krystal AD, Walsh JK, Laska E et al. *Sleep* 2003;26(7):793-9.



	LUNESTA eszopiclone	AMBIEN zolpidem
HALF LIFE	6 hours (9 hours in elderly)	2.6 hours (? 3 hours in elderly)
RECEPTOR SPECIFICITY	Medium	High




**Predicted
Eszopiclone
HANGOVER.
Ambien CR
similar to
Lunesta**

Adapted from:
Drover, D.R.
Clin. Pharmacokinetics.
2004;43:227-238.



ESZOPICLONE

- **Likely to produce more hangover than zolpidem or zaleplon**
- **Impairs morning digit symbol substitution as compared to placebo**
- **Same active ingredient as zopiclone, which was associated with excess auto accidents in Europe**



“In the LUNESTA 2 mg group, compared with baseline, there was a significant increase in WASO and a decrease in sleep efficiency, both occurring only on the first night after discontinuation of treatment.” *--Lunesta Approved Labeling Text, December 15, 2004*

- (Also as compared to placebo)
- Eszopiclone **withdrawal insomnia** demonstrated

“Adverse events . . . that suggest a dose-response relationship in adults include viral infection, dry mouth, dizziness, hallucinations, infection, rash, and unpleasant taste, with this relationship clearest for unpleasant taste.” [The rate of unpleasant taste for LUNESTA 3 mg was 34%.]

---Lunesta Approved Labeling Text, December 15, 2004



RAMELTEON

- **FDA approved long-term use indication, 2005**
- **Melatonin agonist**
- **Does not bind to benzodiazepine-GABA receptor: no cross-tolerance**
- **Complex metabolism, active metabolites**

RAMELTEON

- **No published clinical trials for treatment of insomnia patients at time of introduction**
- **Appears to reduce sleep latency but has little value for maintaining sleep—like melatonin**



RAMELTEON

- **Little benefit:**
10-15 min. shorter sleep latency

- **Little risk.**



RAMELTEON

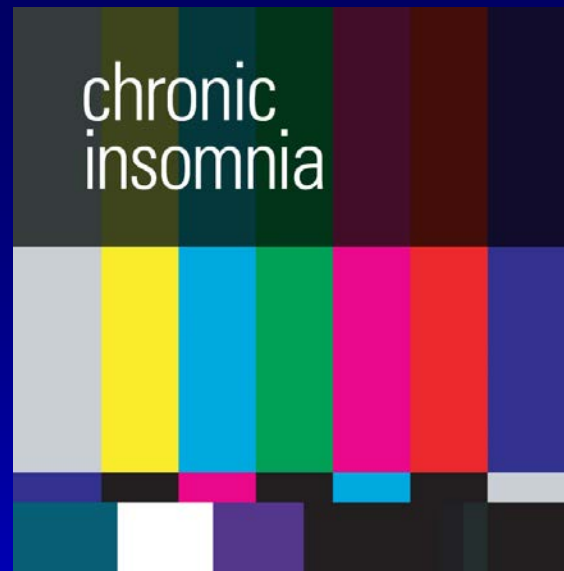
- **Likely to have no risk of dependency and less other risks than benzodiazepine agonists**
- **Possible affects on reproductive endocrinology, e.g., prolactin, testosterone**

Considerations for Pharmacologic Treatment

- Elderly
 - Altered pharmacokinetics / accumulation
 - Increased incidence of sleep apnea
 - Effects on daytime performance
- History of heavy snoring
- Renal, hepatic, or pulmonary disease
- Concomitant therapy/potential interactions
- Psychiatric illness
- Occupation -- driving

CHRONIC INSOMNIA

- Most insomnia is **chronic**
- Lasts for years
- Natural history not well studied



NIH conference on chronic insomnia found better evidence for cognitive-behavioral treatments than for long-term pharmacologic agents.

- <http://consensus.nih.gov/2005/2005InsomniaSOS026html.htm>



COGNITIVE-BEHAVIORAL TREATMENT OF INSOMNIA

- **Cognitive treatment: why “Don’t worry!”**
- **Sleep hygiene (education and counseling)**
- **Relaxation therapies (e.g., deep breathing, meditation, muscle relaxation)**
- **Sleep restriction therapy (limitation of time spent in bed)**

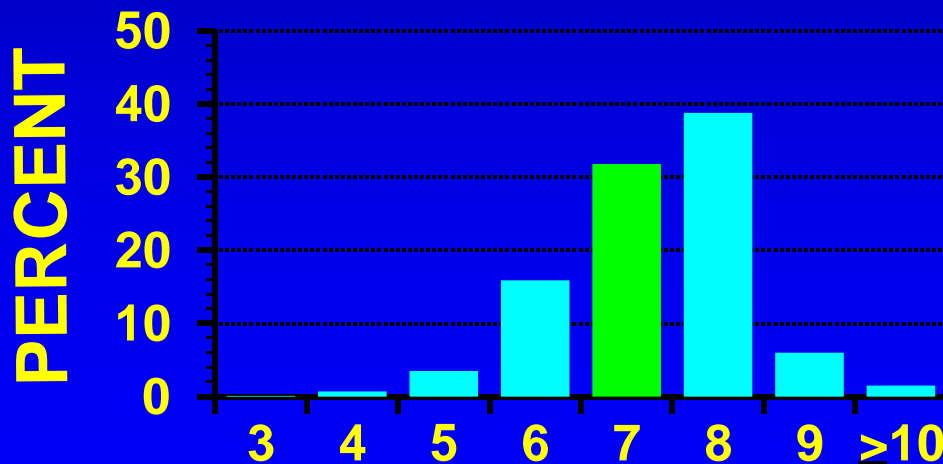
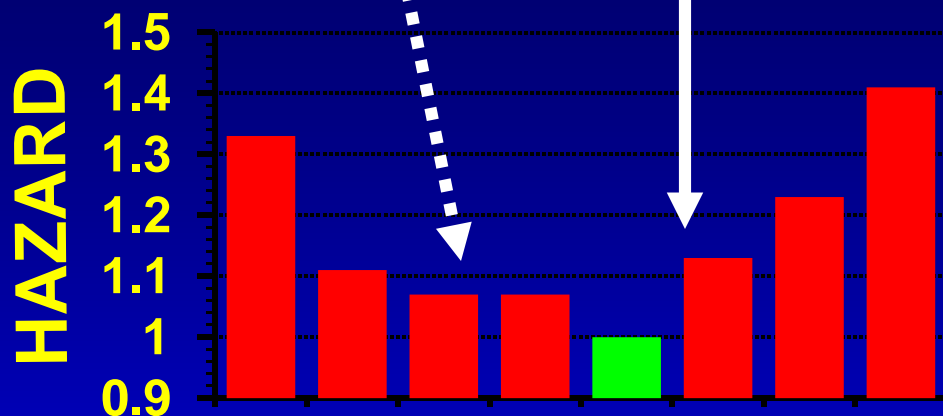


COGNITIVE TREATMENT: TEACH

- **The healthiest people sleep 6.5 – 7.5 hours**
- **The average adult in the U.S. sleeps 6.5 hours: you don't need 8 hours**
- **Do not spend longer in bed than you need to feel rested**
- **Spend more time in bed if you are sleepy in the day – IF more time in bed gives more sleep**

NOT MUCH RISK TO SLEEPING 5-6 HOURS

8 HOURS SLEEP HIGHER MORTALITY



It is safe not to sleep 8 hours, as long as patient is not too sleepy:

Kripke et al., *Arch. Gen. Psychiatry* 2002;59:131-136

HOURS of SLEEP



Good Sleep Hygiene

- Sleep hygiene
 - consistent bedtime and wake time
 - Do not spend extra hours in bed to make up for poor sleep
 - No long daytime naps (e.g. 90 min)
 - Can try 15 - 40 min naps and closely follow sleep logs to decide if naps are OK
 - Don't go to bed unless sleepy
- Avoid caffeine from mid afternoon on
- Limit alcohol in the evening
- Use bedroom only for sleeping and sex
 - No work
 - No TV, etc.



Avoid alerting in bed

- If patient needs to spend time worrying, do it outside of bed.
- No scary mystery books or TV in bed
- Avoid alerting activities in bed.



SLEEP RESTRICTION

- Reducing time-in-bed has powerful and lasting benefits for insomnia
- e.g., patient who says she only sleeps 6 hours should reduce time-in-bed to 6 hours
- Corrects negative conditioning to bedtime experience



SLEEP RESTRICTION

- **If patient is sleeping 85% of time in bed, may increase time in bed by 15 min. per week**
- **If patient reports sleeping <85% of time in bed, then time in bed should be reduced**
- **Maintain regular get-up time**

Measures That Can Decrease Sleep Latency

- **Decreased stimulation prior to bedtime (avoid “action” movies, arguments, etc.)**
- **Sexual intercourse (good sex, not bad sex)**
- **Light bedtime snack (perhaps milk or other tryptophan-increasing foods, e.g., carbohydrates, dairy products)**
- **Tension-release relaxation exercises: meditative, autogenic, Jacobsonian, etc.**



SLEEP APNEA

The most common cause of complaints of excessive sleepiness (falling asleep in the day)





SLEEP APNEA DETECTION

- Observed patient stops breathing 10 or more seconds
- Patient notices waking up unable to breathe or gasping for air
- All night finger oximetry shows saturation intermittently dipping



- Snoring, a common sign



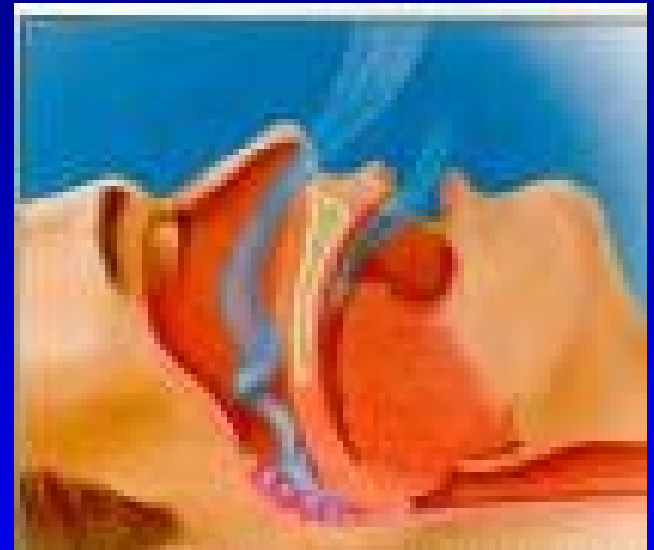
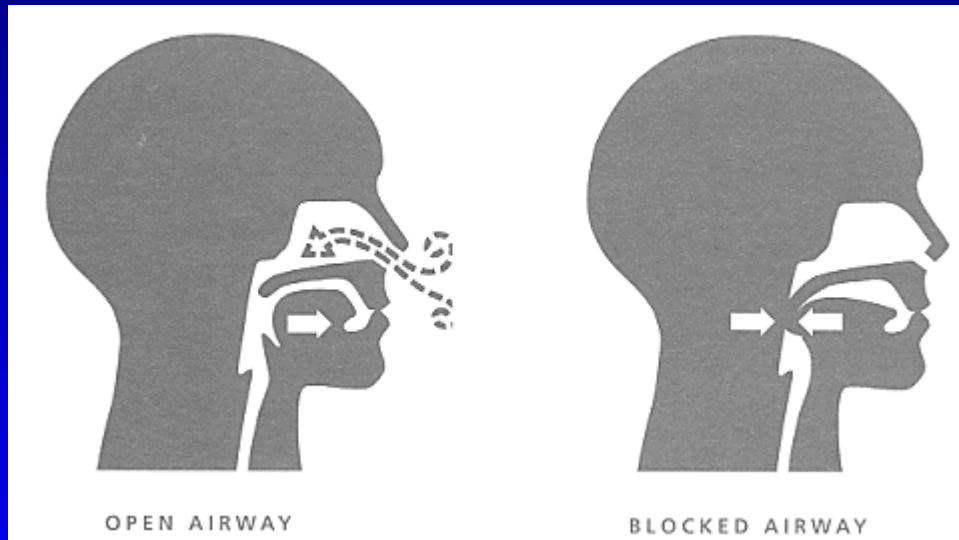
Pathophysiology:

- impairment in central respiratory drive: malfunctioning in neurologic regulation of the set of muscles that dilate the upper airway during inspiration
- anatomic factors that reduce lumen size (e.g., **obesity**)
- reduction of phasic muscle activity (e.g, sedative-hypnotics, alcohol)
- genetic factors



collapse of upper airway during respiration

APNEA





APNEA CONSEQUENCES

- **Insomnia (occasionally)**
- **Daytime somnolence**
- **Impaired intellectual functioning**
- **Impaired concentration**
- **Depression**

APNEA Diagnosis

- Electroencephalogram
- Electromyogram
- Respiratory Tracing
 - (e.g., measurements of oral and nasal airflow with thermistors)
- Oximetry
 - (oxygen saturation)
- Always Useful:
 - Electrocardiogram (possibly 24-hour-monitoring)

ASSOCIATED FEATURES

- **loud snoring**
- **obesity**
- **hypertension (systemic and pulmonary)**
- **cardiac arrhythmias**
- **nocturnal cardiac ischemia**
- **myocardial infarction**

Sleep Apnea Epidemiology

- **Almost all obstructive sleep apneics snore**
- **Pure central sleep apneics don't snore**
- **50 - 60% of hypersomniacs have mixed or obstructive types**
- **10% of persistent insomniacs have the central variety**

Sleep Apnea Epidemiology In Normal Populations

- **30 - 60% y.o. workers (hypersomnia with apnea)**
 - 2 - 4 % in women
 - 4 - 8 % in men Young et al. 1993
- **40 - 64 y.o. males**
 - Median had 10 events/hr
 - No significant correlation between apneas and daytime well being was seen in this representative sample Kripke et al. 1997

Sleep Apnea Epidemiology In At-Risk Populations

- **Mild apnea in > 50% of adults
< age 65**
- **Mild apnea in 80% > 65 years**



Treatment

- Behavioral
 - abstinence from sedative-hypnotics
 - sleep position training (avoid supine position)
 - weight loss
- Mechanical
 - mouth appliances
 - **CPAP**: continuous positive airway pressure
- Surgical
 - e.g. uvulopalatopharyngoplasty; laser palatoplasty, mandibular advancement, etc.



Treatment of Sleep Apnea Mild Obstructive

- Weight loss
- Avoid sedative-hypnotics including alcohol
- Sleeping on side
 - To train, sleeping with a rubber or tennis ball sewn into back of patient's night-garment
 - Cost of this medical procedure < \$2



Treatment of Sleep Apnea Moderate to Severe Obstructive

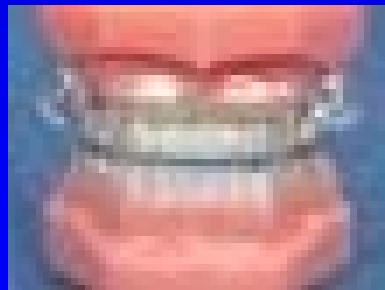
- **Continuous positive airway pressure**
- **Surgery (less proven)**
 - **Soft-palate surgery may decrease apneic episodes**
- **Mandibular and tongue advancement devices**

CONTINUOUS POSITIVE AIRWAY PRESSURE

CPAP TREATMENT



MOUTH APPLIANCES





Treatment of Central Apnea

- CPAP: ? risks/benefits
- Low-flow nasal oxygen
- Diaphragmatic pacing
- Medications
 - Estrogen
 - Stimulating antidepressants (protryptiline, desipramine)
 - Acetazolamide



SEDATIVE HYPNOTICS and SLEEP APNEA

- **Can push snorer into sleep apnea**
- **Can worsen sleep apnea**
- **Can worsen COPD**
- **Same risks with alcohol**



NARCOLEPSY

- **Irresistible attacks of refreshing sleep that occur almost daily over at least 3 months**
- **Cataplexy or recurrent intrusions of elements of rapid eye movement sleep into the transition between sleep and wakefulness, as manifested by either hypnopompic or hypnagogic hallucinations or sleep paralysis at the beginning or end of sleep episodes**
- **Not due to the direct physiological effects of a substance or a general medical condition**



NARCOLEPSY:

Disorder of hypocretin/orexin neurotransmission

HERITABLE TRANSMISSION



Chromosome 6: HLA DQB1*0602



NARCOLEPSY TREATMENT

- A. Modafinil: rarely associated with substance dependence
- B. Stimulants
 - Methylphenidate
 - Amphetamine: Tolerance more common; highest potential for illicit use
 - Pemoline
- C. Rem Suppressing Agents, e.g.:
 - Tricyclic antidepressant
 - γ -hydroxybutyrate

NARCOLEPSY TREATMENT₂

D. Other medications, ? e.g.:

- Codeine
- Propranolol
- Bromocriptine
- L-tyrosine
- Selegiline:
- Methysergide

E. Other approaches: scheduled naps throughout the wake period



Periodic Limb Movement Disorder Insomnia (PLMDI) and Restless Leg Syndrome

- RLS:
 - Legs squirm before sleep; not all-day like akathisia
 - Patient complains of onset insomnia
- PLMDI:
 - Periods of rhythmic kicking during sleep
 - Bed partner more likely to report it
 - Patient complains of hypersomnia or insomnia
- 50 - 80% of patients with RLS have PLMDI



Periodic Limb Movement Disorder Insomnia (PLMDI) and Restless Leg Syndrome

- Benzodiazepines or narcotics
 - Palliative, not curative
 - Soothes RLS discomfort
 - Increases sleep continuity in PLMDI
- Carbidopa-levopoda & related drugs
 - RLS - reduces discomfort
 - PLMDI - exacerbates and sometimes causes
 - Long term toxicity uncertain
- Iron supplementation for ferritin<50



Circadian Rhythm Sleep Disorders

- **Delayed Sleep Phase Type**
- **Advanced Sleep Phase Type**
- **Jet Lag Type**
- **Shift Work Type**

Pathophysiology:

MISALIGNMENT between sleep and biological rhythms



- due to external demands, e.g., night shift
- due to a diminished capacity to respond to external zeitgebers (e.g., blind subjects)
- genetic



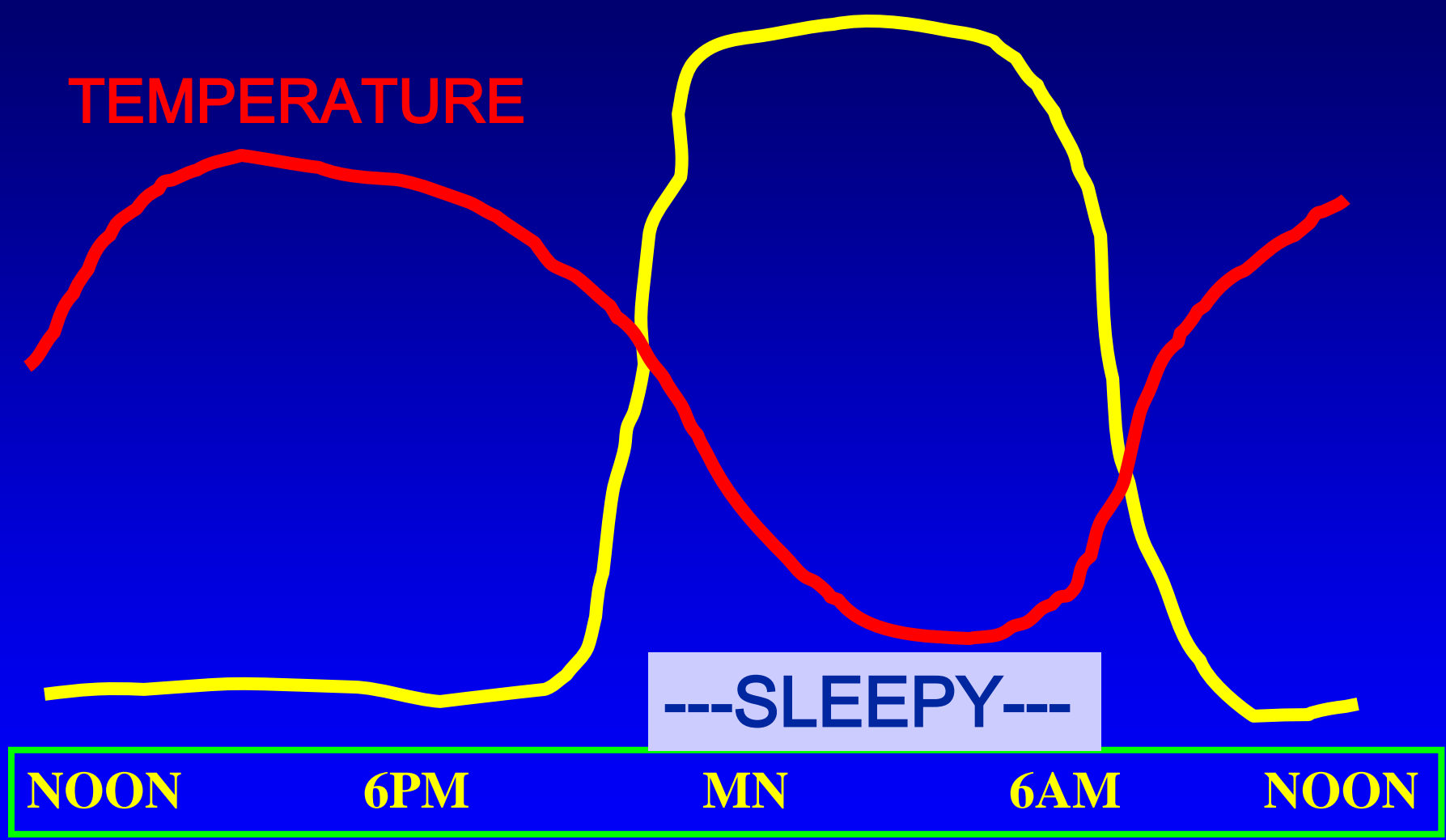
Symptoms of Delayed Sleep Phase

- **Can't get to sleep at night**
- **Can't get up in the morning**
- **Tired most of the day**
- **More alert in the evening**



MELATONIN

TEMPERATURE



NOON 6PM MN 6AM NOON

---SLEEPY---

Preferred Sleep

DSPTS

TEMPERATURE

MELATONIN

---SLEEPY---

NOON

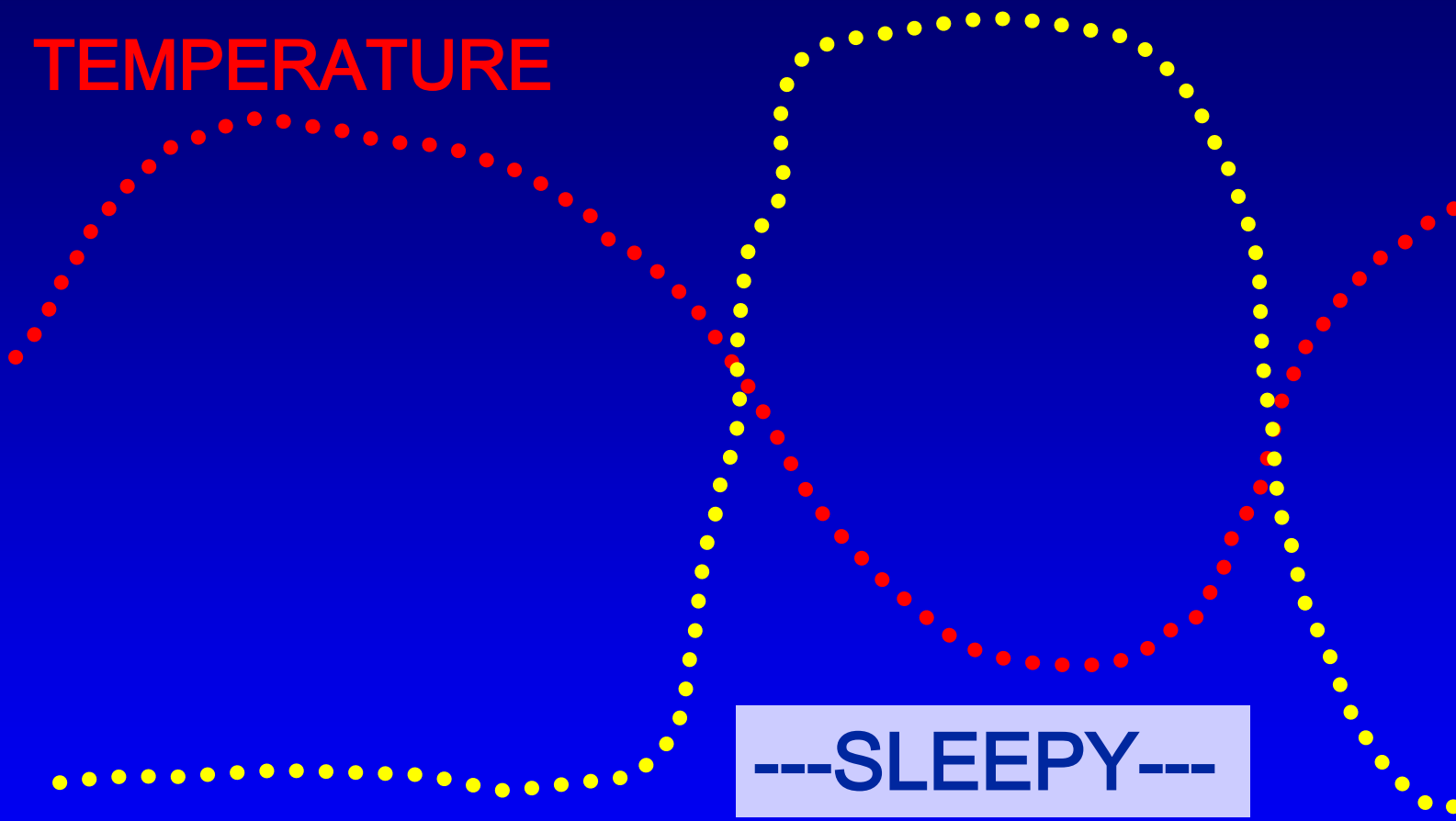
6PM

MN

6AM

NOON

Preferred Sleep





Treatment of Delayed Sleep Phase

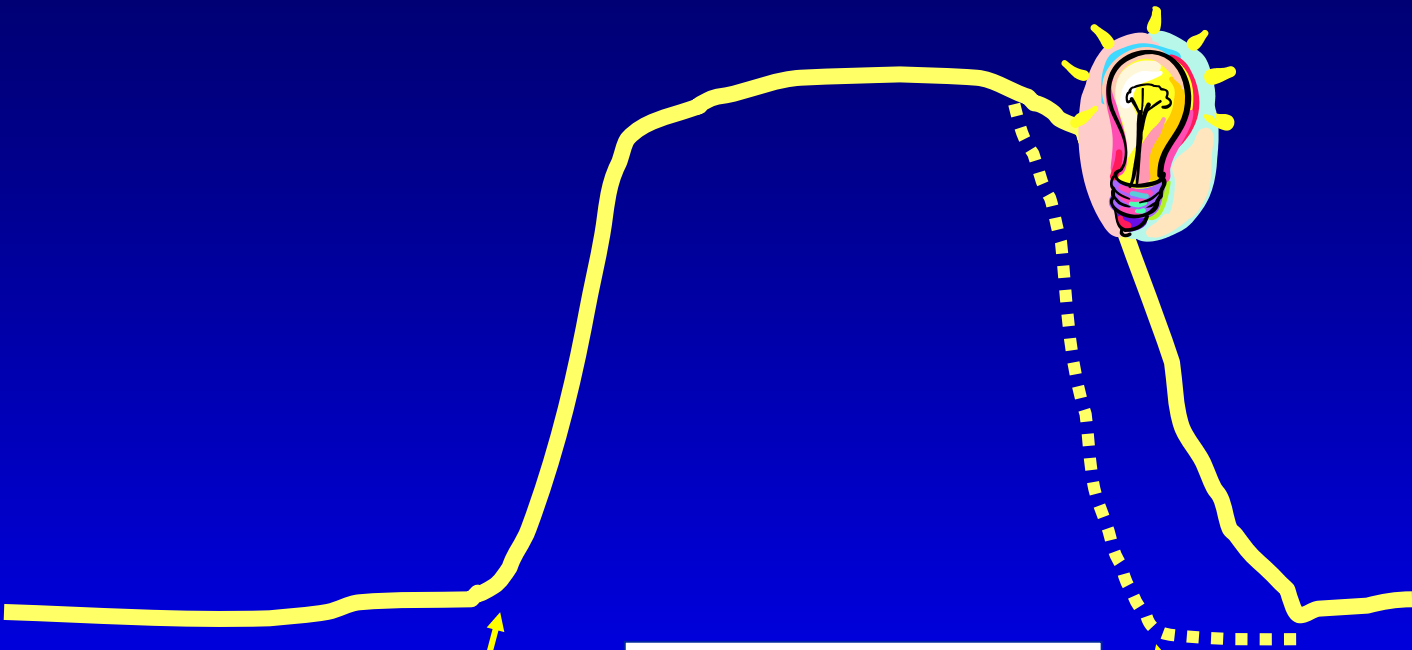
- Bright light in the morning: as soon after arising as possible
- Vitamin B12: 1-3mg orally daily
 - Some evidence that it phase advances
 - Might augment light treatment
- Melatonin 0.02-0.10 mg. ~10 hours after arising

Fluorescent Light Boxes





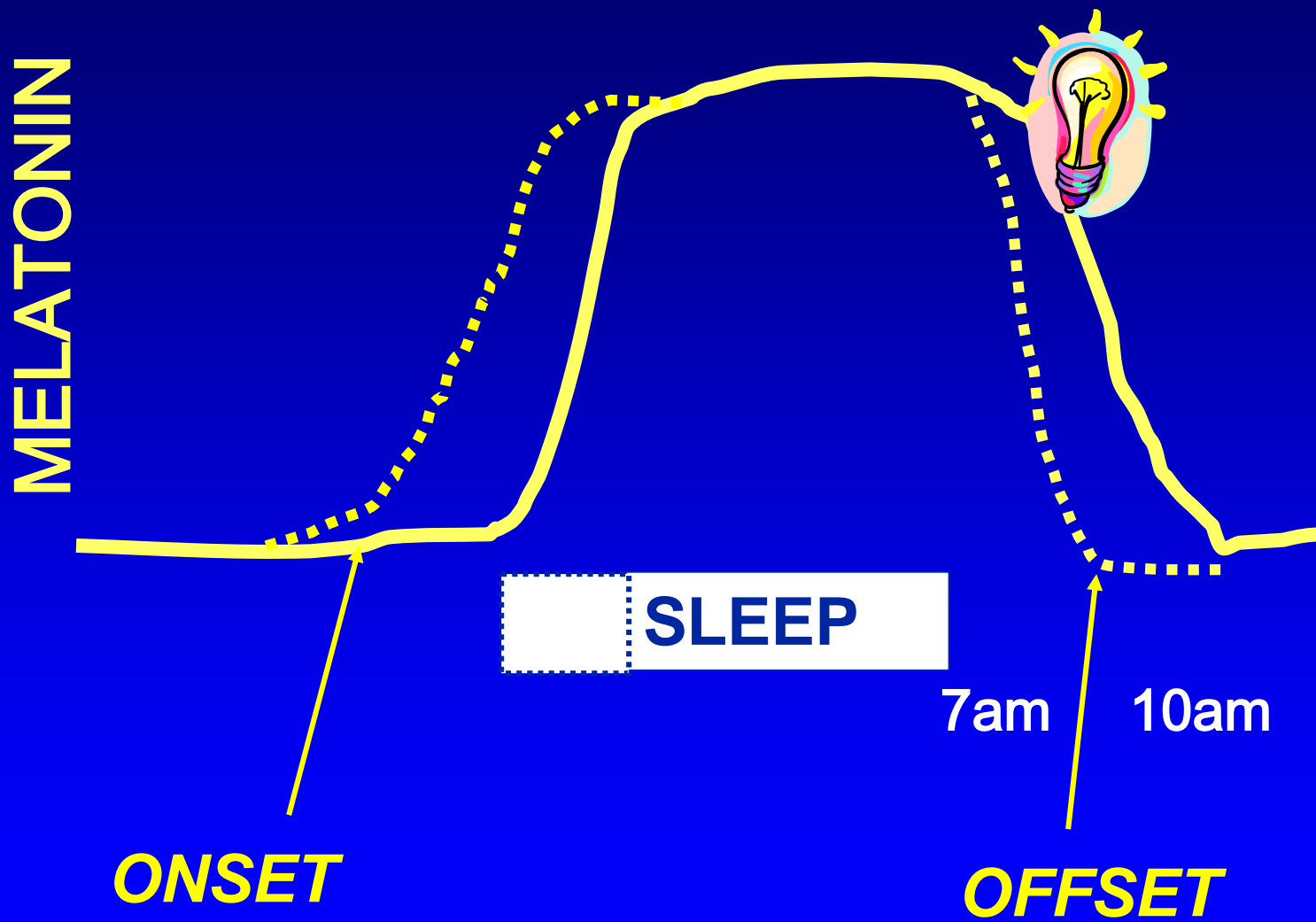
MELATONIN



ONSET

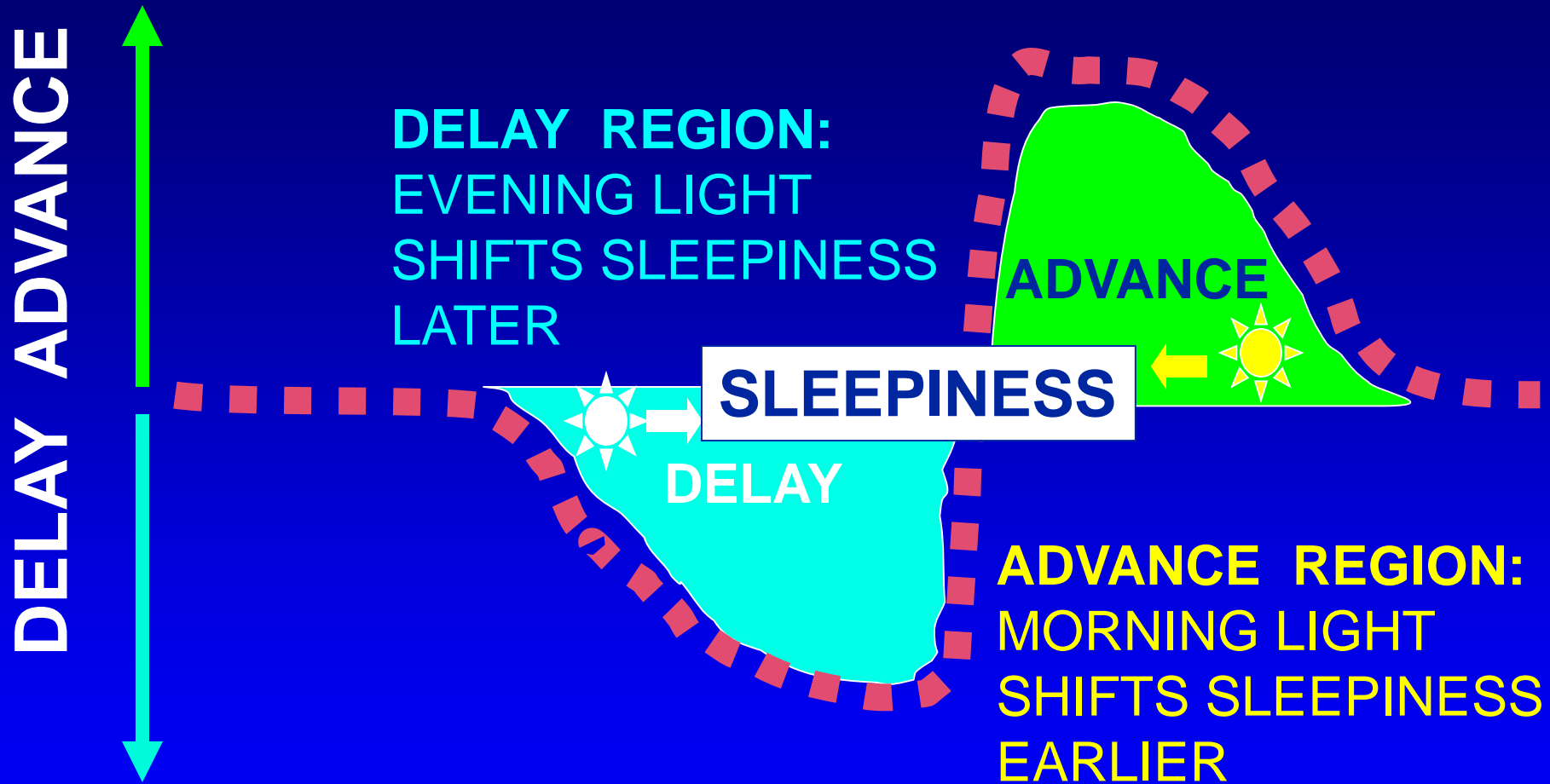
SLEEP

OFFSET





PHASE RESPONSE CURVE





Symptoms of Advanced Sleep Phase

- **Drowsy or falls asleep early in the evening**
- **Awakens too early in the morning**
- **Most energetic in the morning**



Treatment of Advanced Sleep Phase

- **Use brighter light in the evening**
 - just before bedtime
- **Often 50 - 100 watts fluorescent is sufficient**
 - Usually best near the television



MELATONIN

**A night hormone which makes
animal gonads atrophy
and can turn fur white**



MELATONIN RISKS

- **Long-term safety in humans not established:**
 - **Probably causes gonadal suppression in young men and women and may cause infertility**
 - **Suspected risks of seizure, myocardial infarction, or stroke**
 - **Purity and potency of over-the-counter preparations is variable**
 - **Might cause or protect against cancer**



MELATONIN for INSOMNIA

- **Effectiveness and safety not demonstrated for chronic insomnia**
- **Limited evidence of minor short-term benefits**
- **Some meta-analyses not favorable**

USES of MELATONIN

- **Jet lag:** weak efficacy (some, not all studies), but not without side effects
- **Shift work:** weak efficacy in some studies. No studies beyond a few days



SHIFT WORK

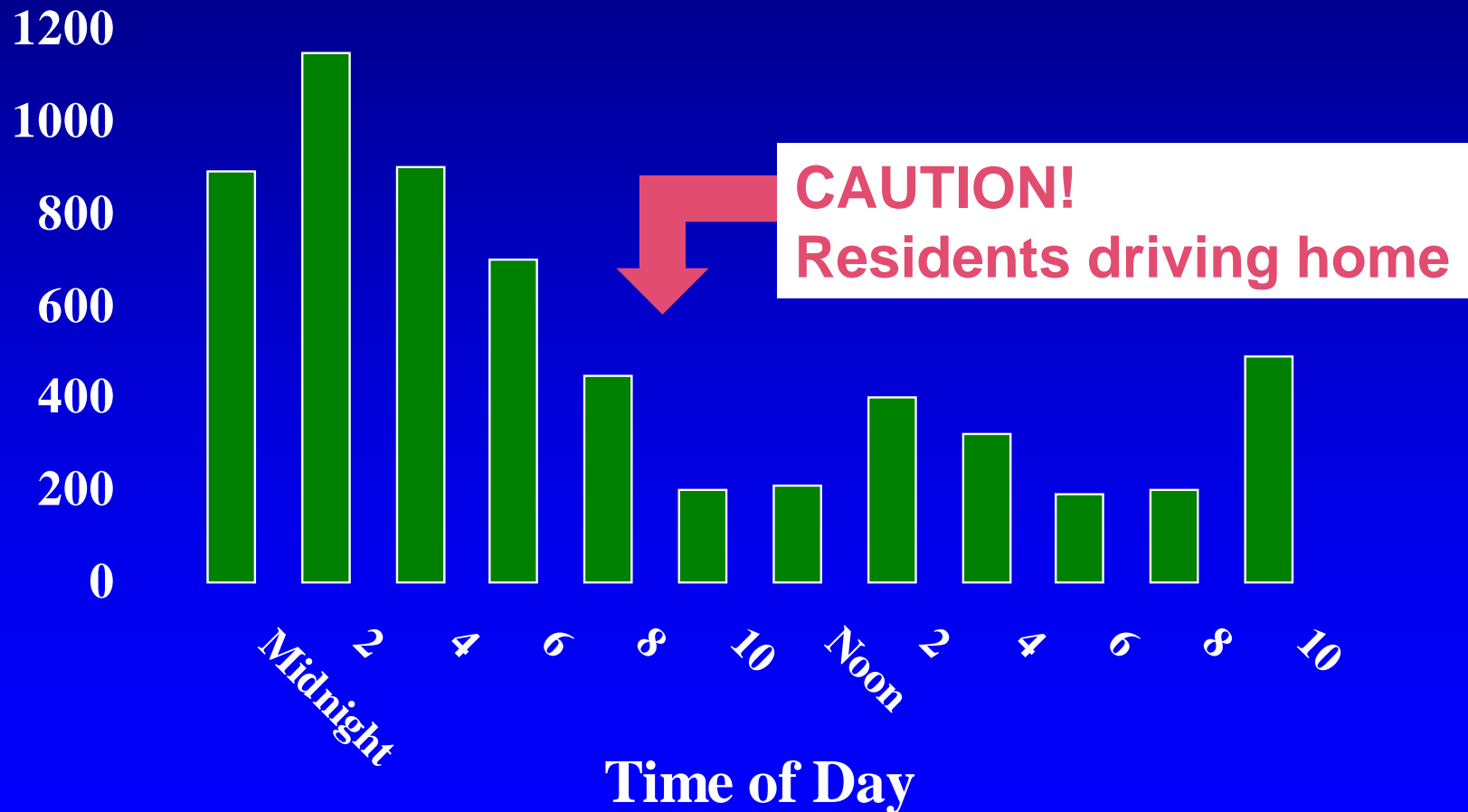
- **An increasing percentage of the population**
- **Impairs sleep and night performance**
- **Possibly associated with depression and shortened life**
- **Accidents**

SHIFT WORK TREATMENT

- **Melatonin is not as effective as bright light for treatment of shiftwork (<1 week studies)**
- **Long-term studies not available**

Fatigue-Related Auto Accidents

Compiled Data





RESIDENTS!

- **GET PLENTY OF SLEEP!**
- **BE CAREFUL DRIVING HOME!**

Post Lecture Exam

Question 1

1. The most common cause of insomnia is
 - A. Use of sleeping pills
 - B. Poor sleeping habits
 - C. Depression
 - D. Alcoholism
 - E. Sleep apnea

Question 2

- 2. Hypnotic drugs are indicated**
- A.** for insomnia due to chronic medical conditions.
 - B.** for insomnia due to depression.
 - C.** for insomnia due to sleep breathing disorders
 - D.** for transient problems lasting less than 30 days
 - E.** All of the above

Question 3

- 3. A hypnotic which causes little daytime sedation is:**
- A. Lorazepam
 - B. Zolpidem
 - C. Temazepam
 - D. Flurazepam
 - E. Diphenhydramine

Question 4

- 4.** The usual maximum dose of zolpidem for an elderly woman is
- A. 5 mg
 - B. 10 mg
 - C. 15 mg
 - D. 20 mg
 - E. 25 mg

Question 5

- 5.** A hypnotic which helps people fall asleep when taken at bedtime is:
- A. Zaleplon
 - B. Temazepam
 - C. Lorazepam
 - D. Oxazepam
 - E. Ethchlorvynol

Question 6

- 6. The most popular drug for sleep complaints accompanying depression is:**
- A. Zolpidem
 - B. Zaleplon
 - C. Trazodone
 - D. Melatonin
 - E. Temazepam

Question 7

- 7. Effective treatment for chronic insomnia may include:**
- A. Zaleplon
 - B. Sleep restriction therapy
 - C. Zolpidem
 - D. Quazepam
 - E. Triazolam

Question 8

- 8. The most common cause of excessive sleep is:**
- a. Primary hypersomnia
 - b. Depression
 - c. Tricyclic antidepressants
 - d. Sleep apnea
 - e. Irregular habits

Question 9

- 9. Useful treatments for sleep apnea include:**
- A.** Mandible and tongue appliances
 - B.** Dieting
 - C.** Sleep position training
 - D.** Continuous positive airway pressure
 - E.** All of the above

Question 10

10. To treat delayed sleep phase, use:

- A. Vitamin B6
- B. Bright light in the morning
- C. Relaxation and sleep hygiene
- D. Methylphenidate
- E. Bright light just before bedtime

Answers to Pre & Post Competency Exams

1. C

2. D

3. B

4. A

5. A

6. C

7. B

8. D

9. E

10. B