

# Sleep, Sleep Loss, and Sleep Problems

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# Overview

- The Need for Sleep
- Sleep in a Nutshell
- Obstructive Sleep Apnea
- Insomnia/Shift Work

FEBRUARY 10, 1986

\$1.95

# TIME

SPACE SHUTTLE  
CHALLENGER  
JANUARY 28, 1986



# Challenger Disaster

Why did the Space Shuttle Challenger explode?

Sleep Deprived NASA Managers made an erroneous decision to launch.

# Nighttime Catastrophes Attributed to Human Error

- Bhopal Chemical Plant
- Chernobyl Atomic Power Station
- Three Mile Island Atomic Power Station
- Peach Bottom Atomic Power Station
- Rancho Seco Atomic Power Station
- Davis-Besse Atomic Power Station

# Daytime Sleepiness

- 70% of a group of train drivers reported they dozed off while driving a train.
- 82% of oil refinery shift workers stated they suffered from lack of sleep.
- Physicians during “on-call” nights slept an average of 2.8 hours.

# Societal Costs of Sleepiness

Sleepiness accounts for approximately 10% of fatal car accidents, however, it interacts with the other two major causes of accidents: **alcohol** (18%) and **inattention** (15%)

# Boy dies in head-on collision when man falls asleep driving

By **DANI DODGE**  
of the Mail Tribune

ASHLAND — Adam Jasper Burnson, 11, strapped on his bike helmet and headed home a half-hour early from a friend's house Thursday. A responsible boy, he wanted to make sure he'd get to his martial-arts class on time.

He never made it.

As Adam pedaled his lime-green mountain bike toward his Spring Creek Drive home at about 3:20 p.m., he was struck head-on by a red Chevrolet pickup truck on Highway 66 near Crowson Road. His helmet shattered in the accident. Adam — a gifted student who just graduated fifth grade at Walker Elementary School — was pronounced dead four hours later at Rogue Valley Medical Center.

The truck's driver, Lewis William Baker, 70, of Medford, said he fell asleep at the wheel, according to Oregon State Police. Three teenagers riding in the back of the pickup were unharmed.

One of those teens was Baker's grandson.

"We just heard a big thud," said a shaken Jason Allen Baker, 16, shortly after the accident. "We looked in back of us — there was a

wheel sticking out of the ditch."

The accident occurred as Adam was westbound on the shoulder of Highway 66. The pickup was eastbound on Highway 66, its occupants headed for Emigrant Lake. When the driver fell asleep, the truck crossed the highway and struck Adam, according to OSP Sgt. Michael Buckman.

Witnesses told police the pickup was traveling no more than 35 mph.

Buckman said the case will be turned over to the Jackson County district attorney on Tuesday at the earliest. Immediately after the accident, the driver was taken to a hospital for blood tests to determine if he was impaired by drugs or alcohol.

The first person on the scene was a local nurse, who immediately started cardiopulmonary resuscitation, according to the OSP. An emergency-room doctor, from out of the area on vacation, also stopped and assisted.

But their resuscitation efforts failed. Adam suffered massive head and chest injuries and a broken leg in the accident.

At about 4 p.m., Adam's mother, Katrina Burnson, became worried and called the

see **BIKE**, Page 5A



# Prevalence of Sleepiness

It is estimated that at least 36% of the population suffers from sleep loss, including:

- One-third of young adults secondary to chronic partial sleep deprivation
- 7% of adults secondary to sleep disorders
- 2% of adults secondary to shift work

# Daytime Sleepiness

- One-third of adults sleep  $< 6.5$  hours during the workweek<sup>1</sup>
- Approximately one-third of normal adults fall asleep in  $\leq 5$  minutes<sup>2</sup>

# Daytime Sleepiness

When total sleep times in normal young adults are reduced **1 - 1.5 hours** for one night, decreases of up to one-third are found in objective alertness.<sup>1</sup>

<sup>1</sup>Rosenthal et al., 1993; Bonnet et al., 1995

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# Sleep Staging

NREM Sleep

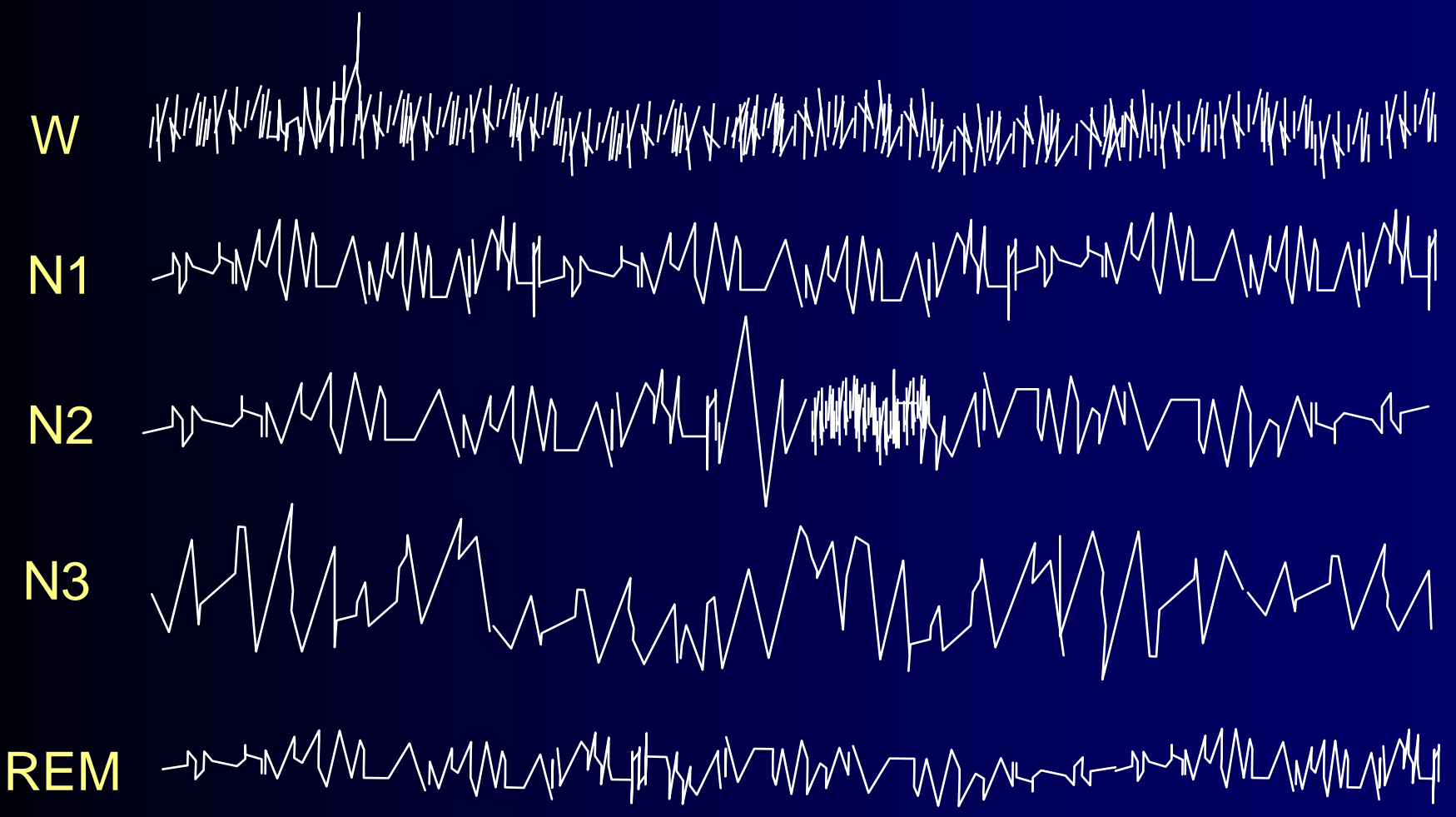
Stage N1

Stage N2

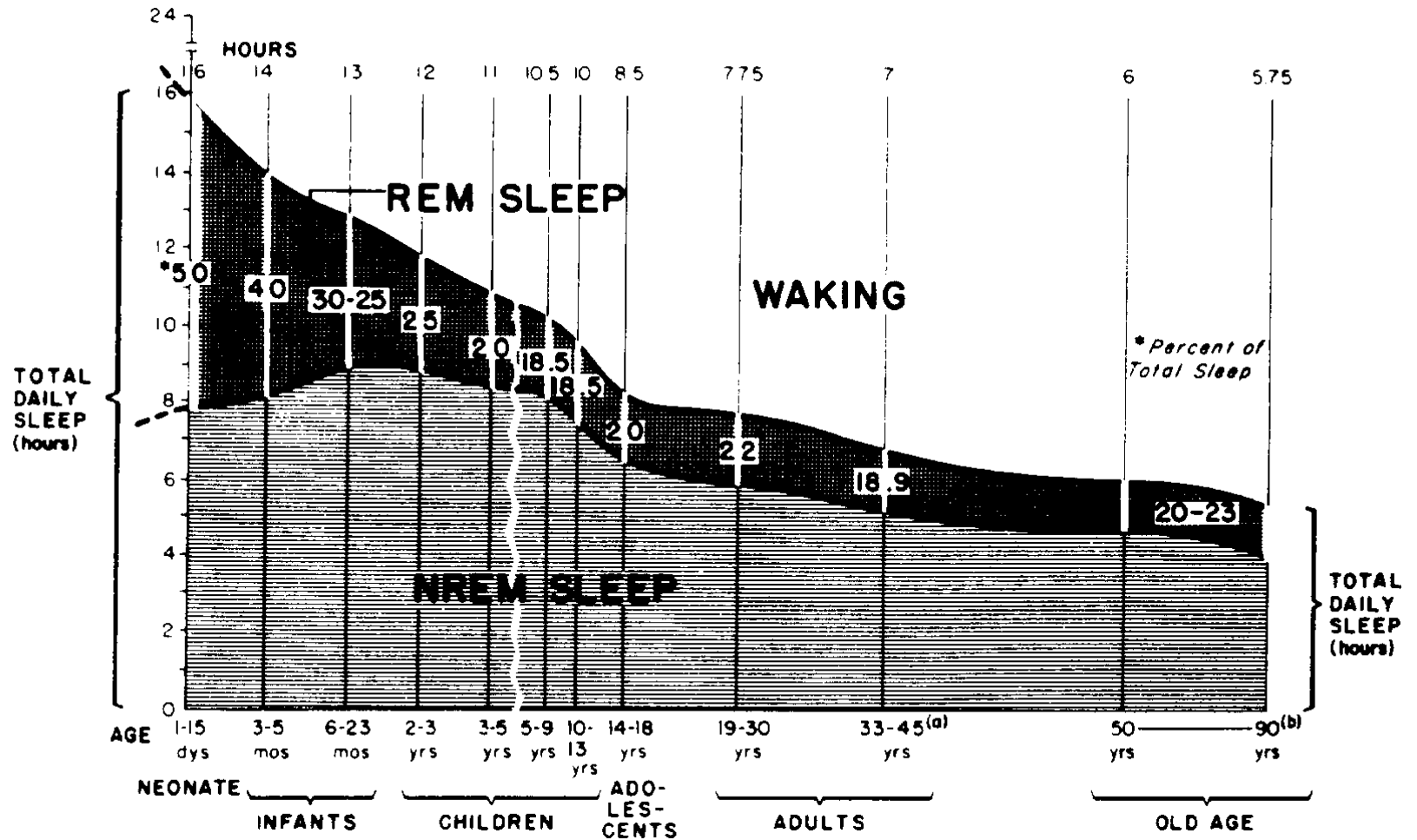
Stage N3

REM Sleep

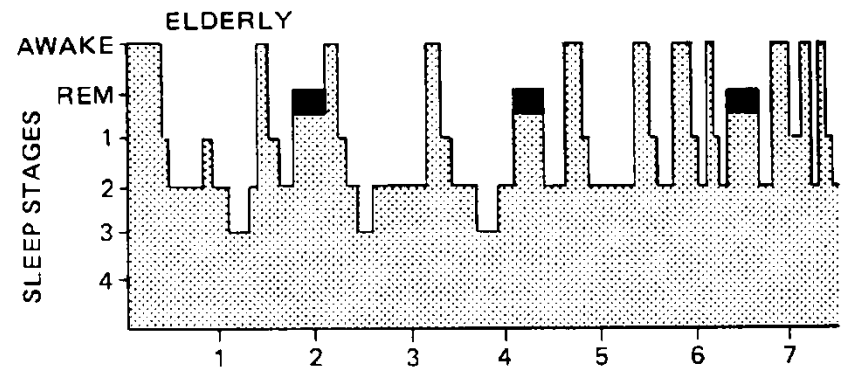
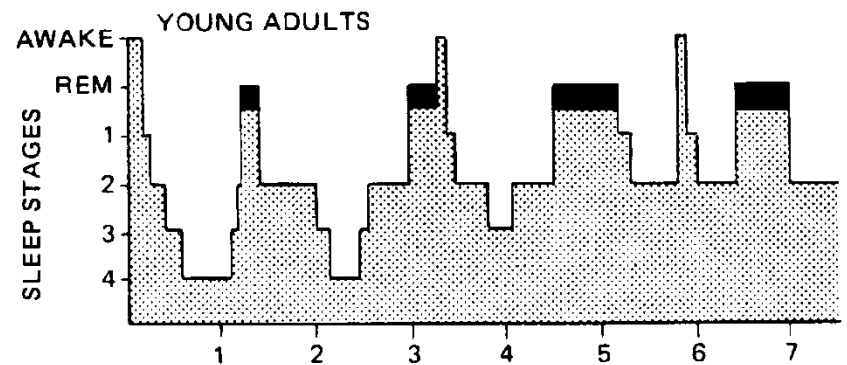
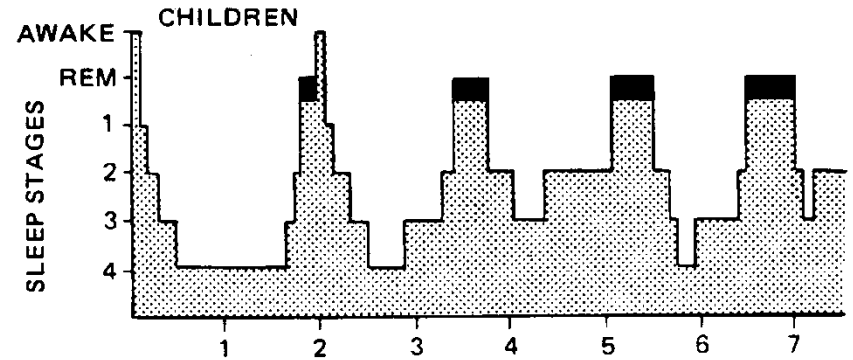
# EEG Patterns of Wakefulness and Sleep



# Sleep Stage - Ontogeny



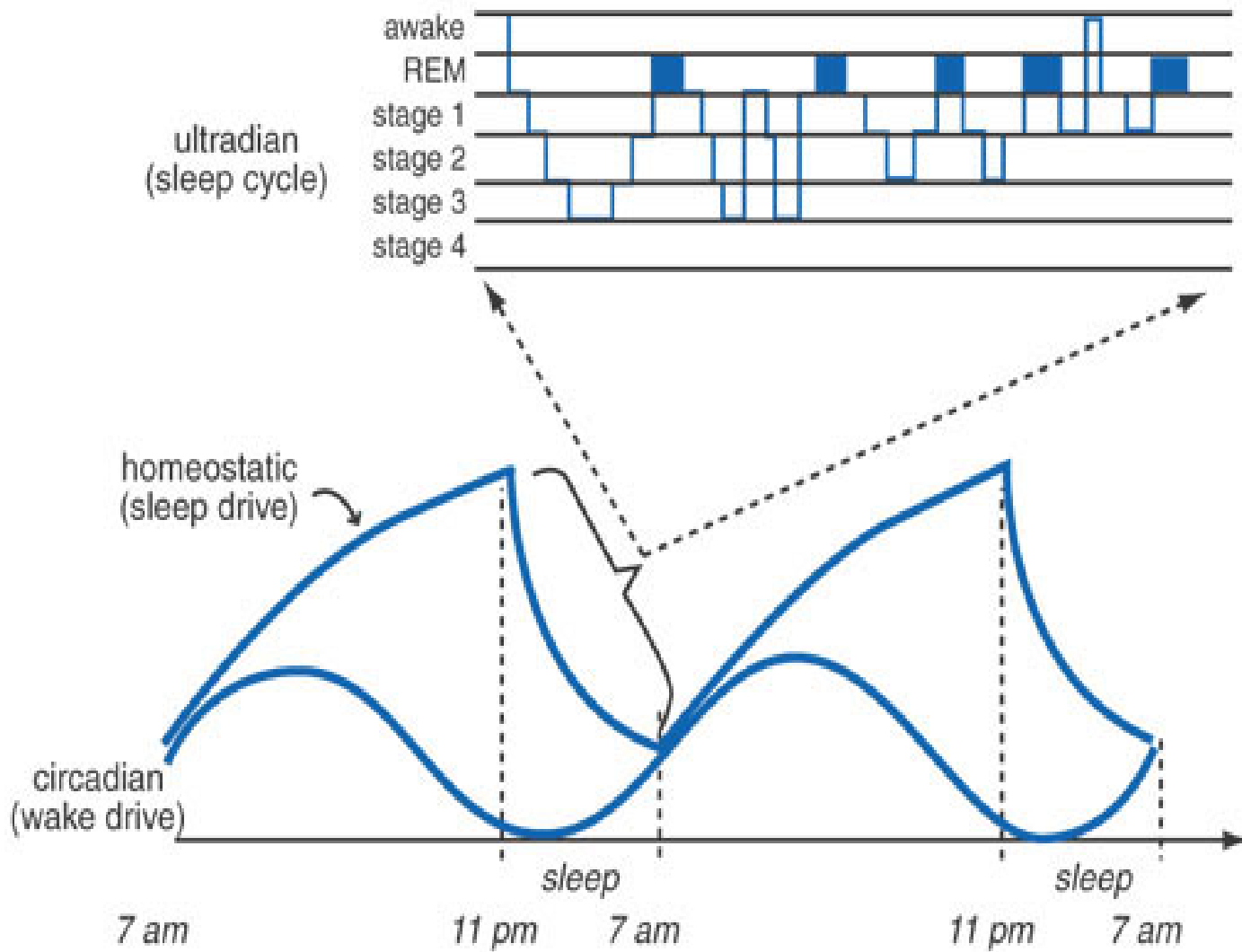
# Sleep histogram - Ontogeny



HOURS OF SLEEP



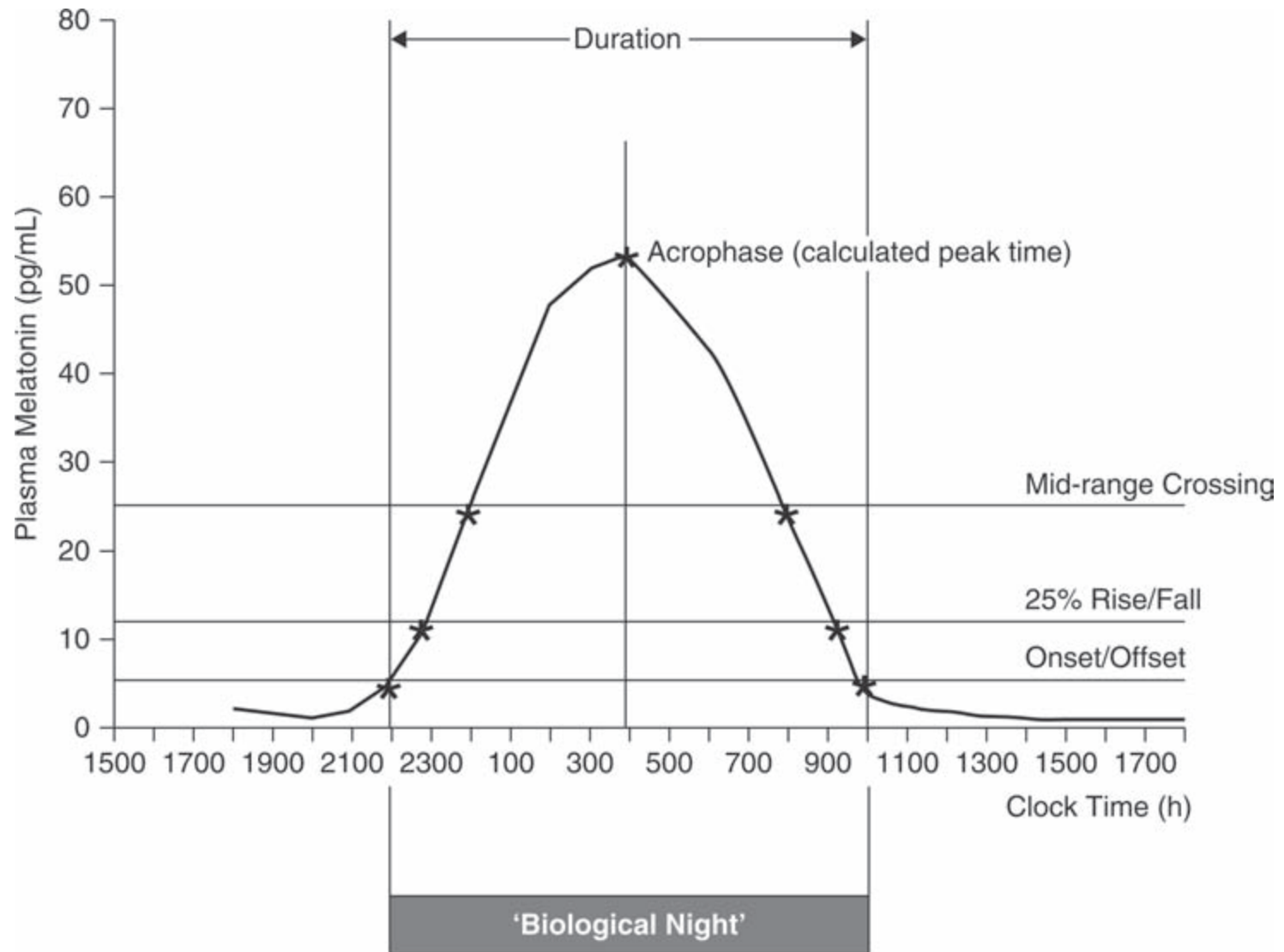
# Processes Regulating Sleep



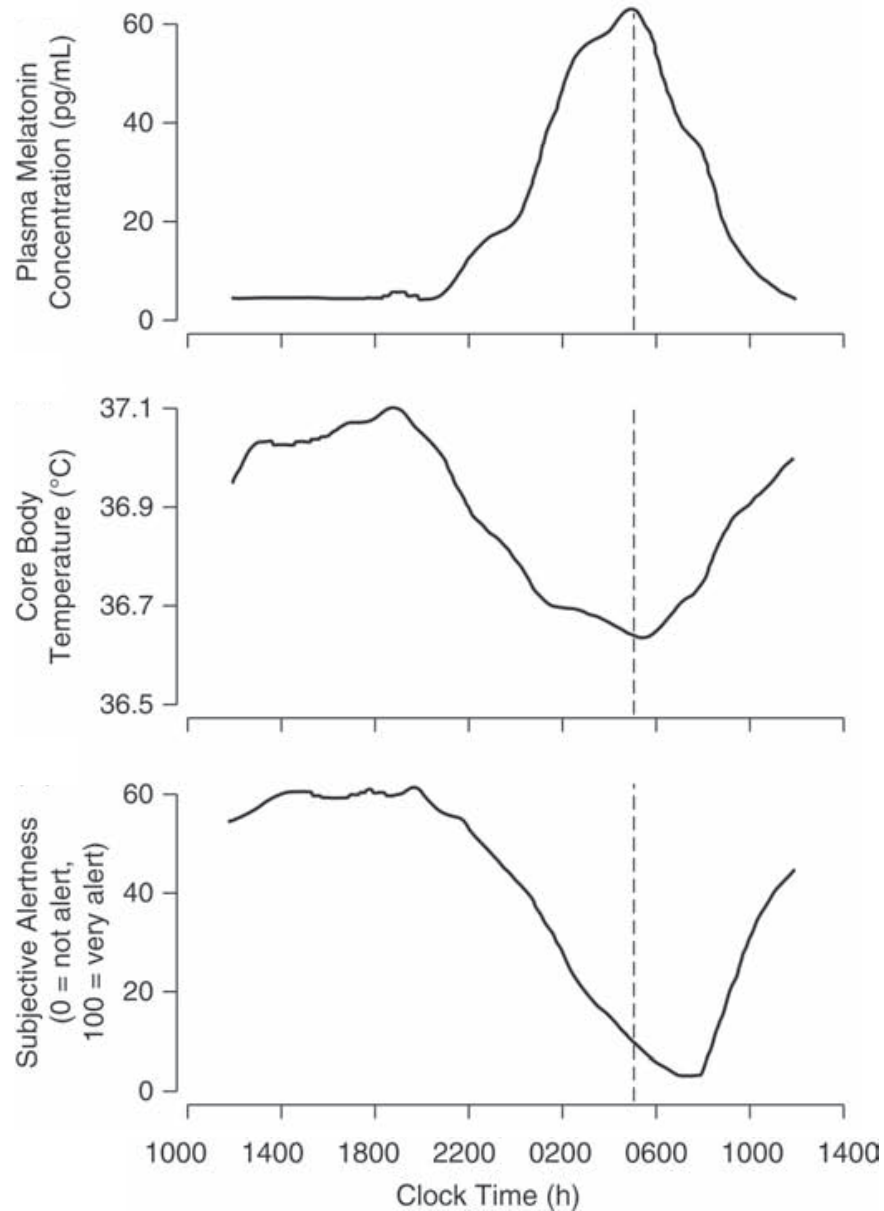
# Melatonin

- Endogenous hormone involved in circadian rhythm regulation
- The pineal gland secretes melatonin
  - Tryptophan → serotonin → melatonin
- Secretion is inhibited by light exposure and maximum secretion is at night

# Normal Profile of Plasma Melatonin Secretion

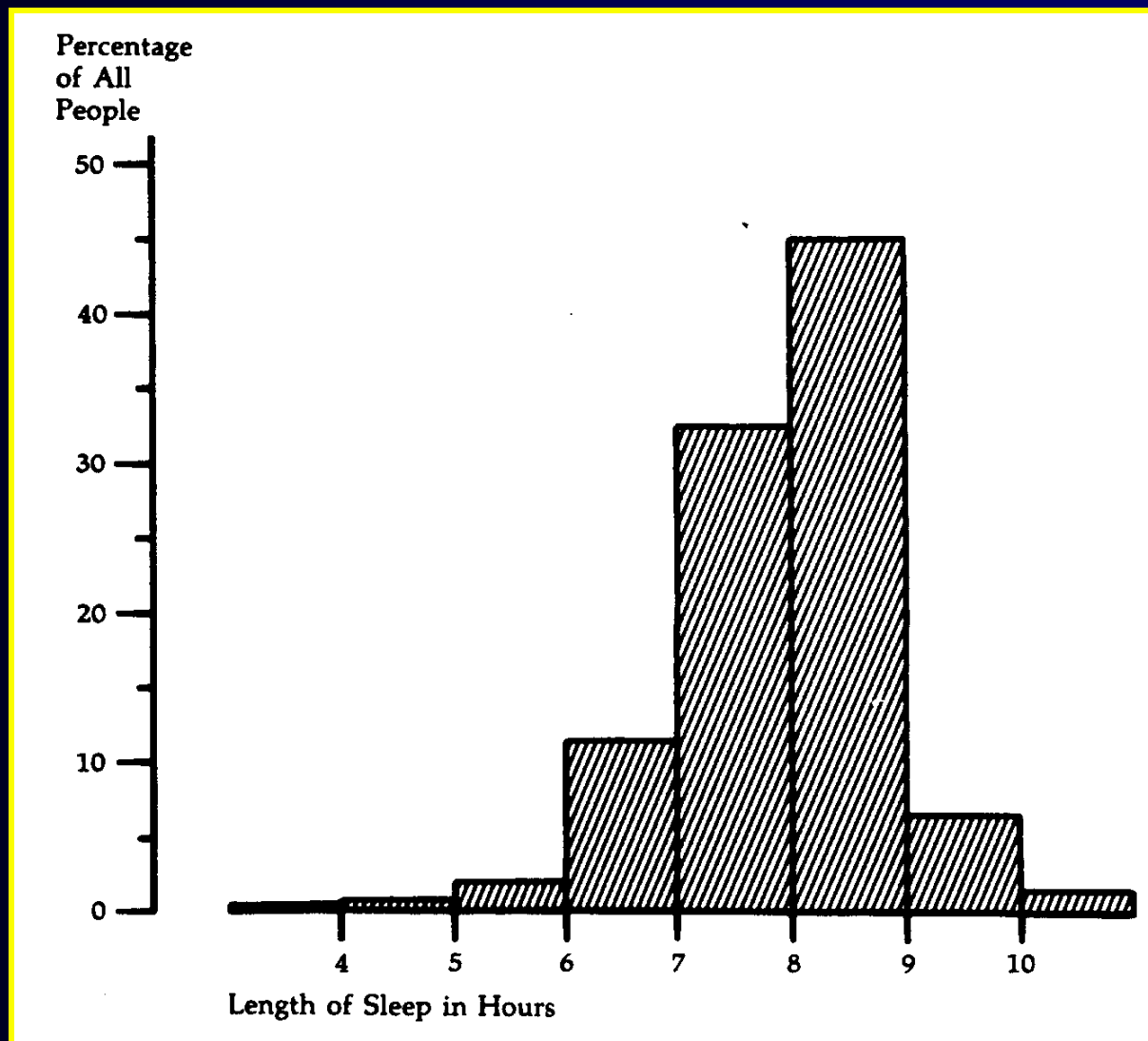


Arendt J, Skene DJ. Special considerations for treatment of circadian rhythm sleep disorders. In: Kushida CA (ed.), Handbook of Sleep Disorders, 2<sup>nd</sup> ed., New York: Informa Healthcare, 2009.



Arendt J, Skene DJ. Special considerations for treatment of circadian rhythm sleep disorders. In: Kushida CA (ed.), Handbook of Sleep Disorders, 2<sup>nd</sup> ed., New York: Informa Healthcare, 2009.

# Total Sleep Requirement



## Daily Sleep Diary

**Please complete each morning when you wake up:**

Date>>	/ /	/ /	/ /	/ /	/ /	/ /	/ /
1. Yesterday, when did you take a nap, from what time to what time?							
2. What medications did you take last Night? (Include dosage)							
3. Last night, what time did you turn off the light intending to go to sleep?							
4. How long did it take you to fall asleep?							
5. What time did you wake up for your final awakening this morning?							
6. What time did you get out of bed?							
7. How many times did you wake up during the night?							
8. Estimate the total amount of time you spent awake during the night after you fell asleep.							
9. How much time elapsed between the time you turned out the light and the time you finally got up?							
10. How much total sleep did you get? (the amount in #8 minus the amounts in # 3 and #7)							
11. Rate how rested/refreshed you feel now: 1 = not rested....10 = very rested							
12. Rate the quality of your sleep last night? 1 = very poor...10 = excellent							
13. Rate overall how sleepy you felt yesterday, during the day: 1 = not sleepy....10 = very sleepy							
<b>Other Comments:</b> If you forgot to press the watch button or forgot to wear the watch, please note so here. Note here also when the watch was not worn.							

# The Epworth Sleepiness Scale

How likely are you to doze off or fall asleep in the following situations, in contrast to feeling just tired? 0 = would *never* doze, 1= *slight* chance of dozing, 2 = *moderate* chance of dozing, 3 = *high* chance of dozing

Chance of Dozing

Sitting and Reading	_____
Watching TV	_____
Sitting inactive in a public place (meeting, theater, etc.)	_____
As a passenger in a car for 1 hour without a break	_____
Lying down in the afternoon when circumstances permit	_____
Sitting and talking to someone	_____
Sitting quietly after lunch without alcohol	_____
In a car, while stopped for a few minutes in traffic	_____

**Total**

- The Need for Sleep
- Sleep in a Nutshell
- Obstructive Sleep Apnea
- Insomnia/Shift Work





“...and on the box sat a fat and red-faced boy, in the state of somnolency.” C. Dickens

# Symptoms of OSA

- Loud, disruptive snoring
- Witnessed breathing pauses during sleep
- Excessive daytime sleepiness  
(i.e., fatigue, tiredness, exhaustion)



# Prevalence of OSA

24% of Adult Men

9% of Adult Women

40% of All Patients in a Primary Care Setting

# OSA Predisposing Factors

- Age (40 - 60 years)
- Obesity
- Male Gender (8 : 1 male : female)
- Anatomic Abnormalities
- Hypothyroidism
- Medications, Alcohol

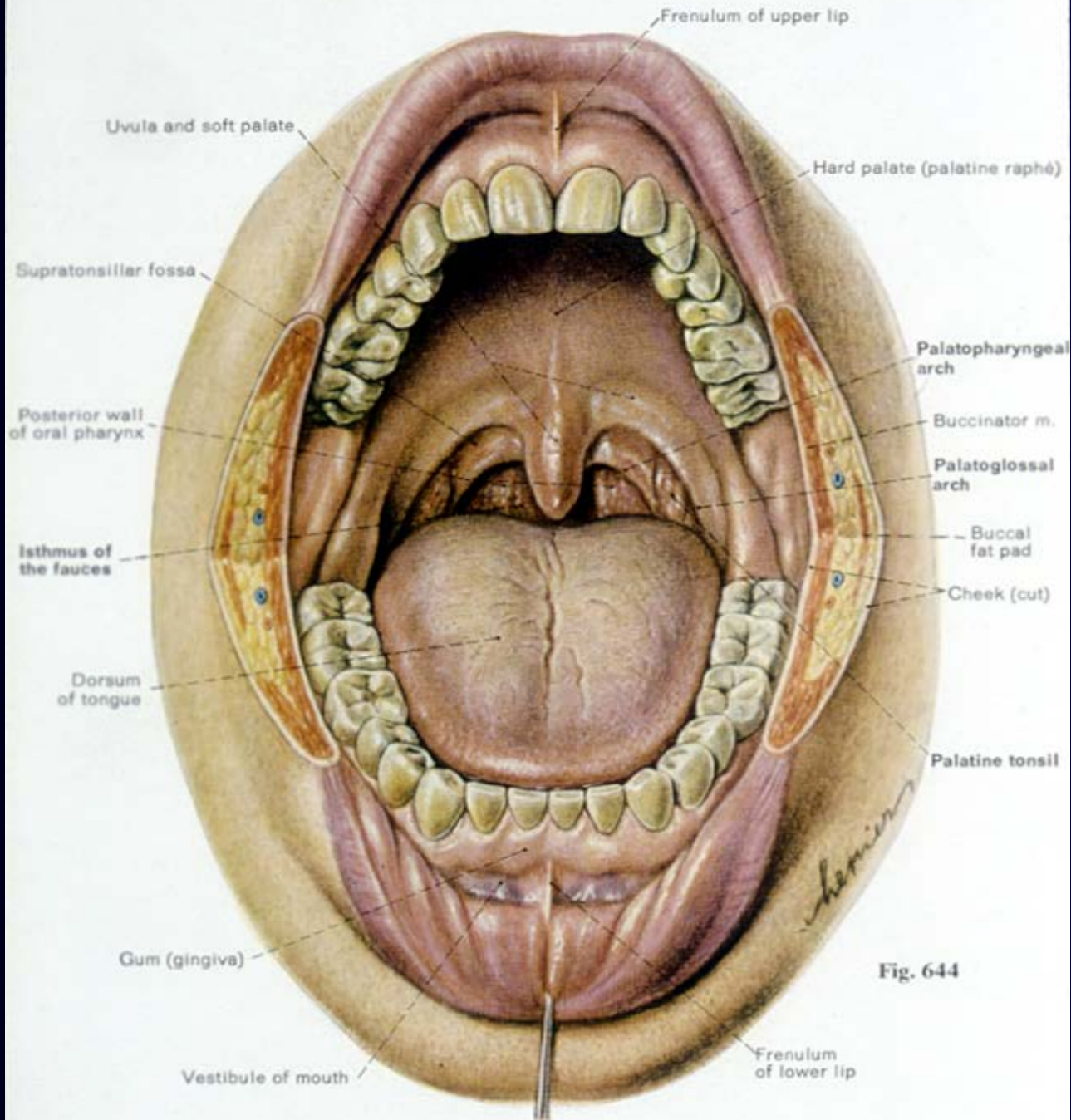


Fig. 644

W 1075  
C 353

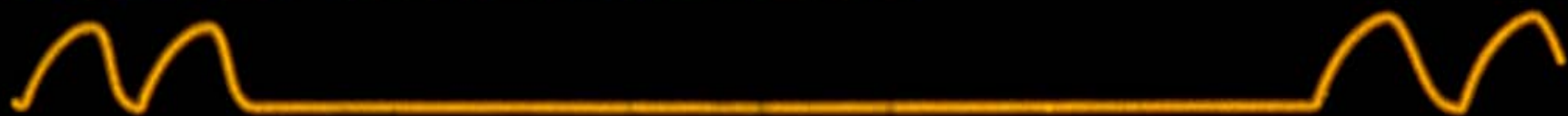
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# OBSTRUCTIVE APNEA

## NASAL/ORAL AIRFLOW



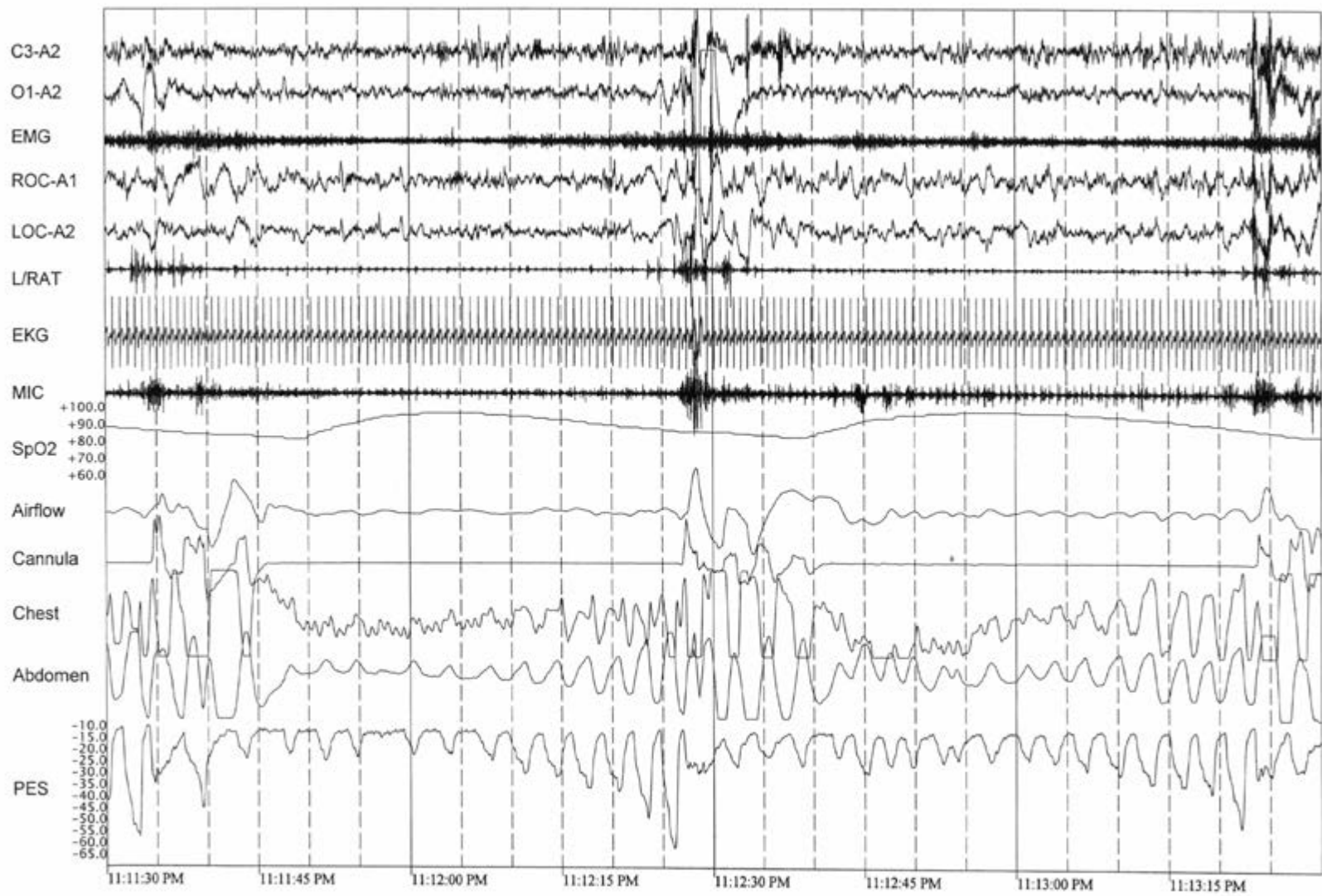
## THORACIC RESPIRATION



## O<sub>2</sub> SATURATION







## OSA

### Symptoms

Habitual, Loud Snoring  
Nocturnal Breathing Pauses,  
Choking, Gasping  
Excessive Daytime Sleepiness



## Outcomes and/or Comorbid Conditions\*

### Problems With Daytime Functioning

Daytime Sleepiness  
Motor Vehicle Crashes  
Psychosocial Problems  
Decreased Cognitive Function  
Reduced Quality of Life

### Cardiovascular and Cerebrovascular Disease

Hypertension  
Coronary Artery Disease  
Myocardial Infarction  
Congestive Heart Failure  
Stroke

### Diabetes and the Metabolic Syndrome

# Treatment for Snoring\* and OSA

CPAP

Surgery\*

Dental Appliances\*

Weight Loss\*

Behavior Modification\*

Medications

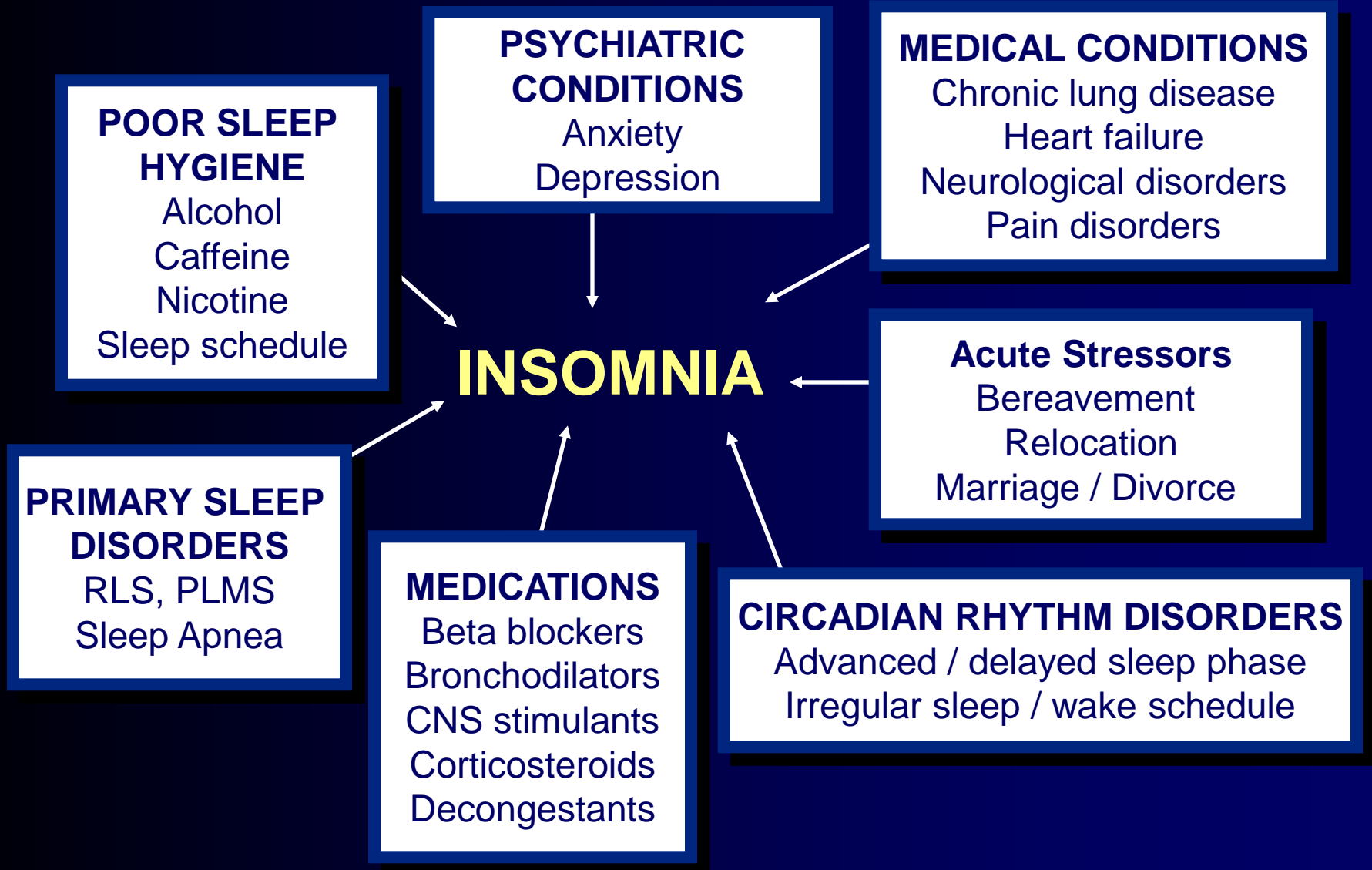


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# Demographic Features of Insomnia

- Up to 47% of American adults may suffer from insomnia
- 12% of all adults experience difficulty sleeping on a frequent basis

# Causes of Insomnia



# Insomnia Symptoms

- Inability to fall asleep when desired
- Conditioned arousal to the bedroom environment or sleep-related activities
- Increased somatized tension at bedtime

# General Insomnia Criteria

- Difficulty initiating or maintaining sleep
- or
- Waking up too early or sleep that is chronically nonrestorative or poor in quality
- Above sleep difficulty occurs despite adequate opportunity and circumstances for sleep



# Common Types of Insomnia

## Psychophysiological Insomnia

A disorder of somatized tension and learned sleep-preventing associations that result in a complaint of insomnia and associated decreased functioning during wakefulness

## Idiopathic Insomnia

A lifelong inability to obtain adequate sleep that is presumably due to an abnormality of the neurological control of the sleep-wake system

# Shift Work

- Insomnia, EDS, impaired performance when works hours are scheduled during usual sleep period
- ~ 20% of workforce in industrialized countries are shiftworkers; 40-80% of nightworkers complain of sleep problems; ~ 5-10% meet criteria for CRSD SW Type
- Complaints in relation to sleep schedule

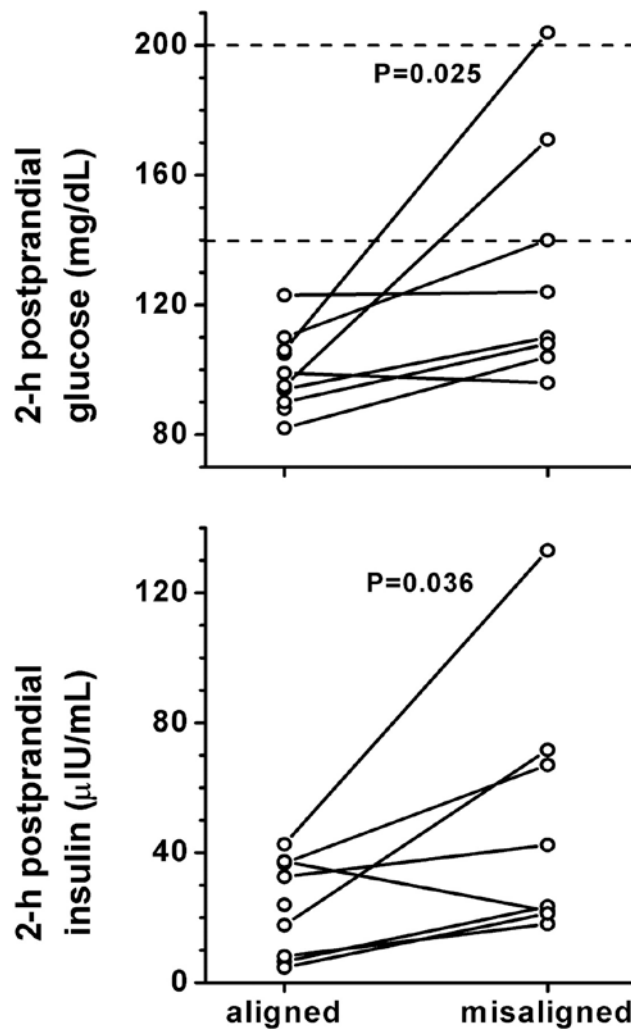
# Diagnosis of CRSD Shift Work Type

- There is a complaint of insomnia or excessive sleepiness that is temporally associated with a recurring work schedule that overlaps the usual time for sleep.
- The symptoms are associated with the shift-work schedule over the course of at least one month.
- Sleep logs or actigraphy monitoring (with sleep diaries) for at least 7 days demonstrates disturbed circadian and sleep-time misalignment.
- The sleep disturbance is not better explained by another current sleep disorder, medical or neurological disorder, mental disorder, medication use, or substance use disorder.

# Shift Work/Circadian Misalignment

- Limited epidemiological evidence of increased risk of obesity, diabetes, and cardiovascular disease in shift workers / sleep deprived individuals
- Hypothesis: circadian maladaptation to chronically sleeping at abnormal circadian times
- PNAS 2009: Experimental circadian misalignment, “forced desynchrony” by 12 hours in 10 healthy adults demonstrated abnormal postprandial glucose in prediabetic range; suppressed leptin; increased blood pressure

# Circadian Misalignment Reduces Glucose Tolerance and Insulin Sensitivity



Scheer F A J L et al. PNAS 2009;106:4453-4458

# General Treatment

- Behavioral techniques are used first
- Relaxation, stress management, and stimulus control techniques may be beneficial
- An occasional mild hypnotic may be used on an infrequent basis
- Psychologic or psychiatric counseling may be useful

# Relaxation therapy

Sleep efficiency improved 64-72% for non-medicated patients with insomnia

- Progressive muscle relaxation – decreased wake time by 20-30 min<sup>1</sup>
- Meditation
- Self hypnosis
- Electromyographic biofeedback

1. Morin CM. *Sleep*. 1999;22:1-23.

# Sleep Restriction Technique

Wake after sleep onset reduced by 54%;  
sleep efficiency increased by 24%<sup>1</sup>

- Accumulate “sleep debt”
- Standardize awakening time
- Start with mean sleep estimate
- Add 15 minutes per week to time in bed, as long as sleep efficiency is at least 90%
- Time in bed decreased by same amount when sleep efficiency decreases below 80%

1. Morin CM. *Sleep*. 1999;22:1-23.



# Temporal and Stimulus Control Techniques

Expected 52% improvement after one year

- Standardize awakening time
- Avoid daytime naps
- Turn off the light immediately upon retiring
- Avoid reading, watching television, eating or working in bed
- 20 - minute rule

# Circadian Sleep Disorders

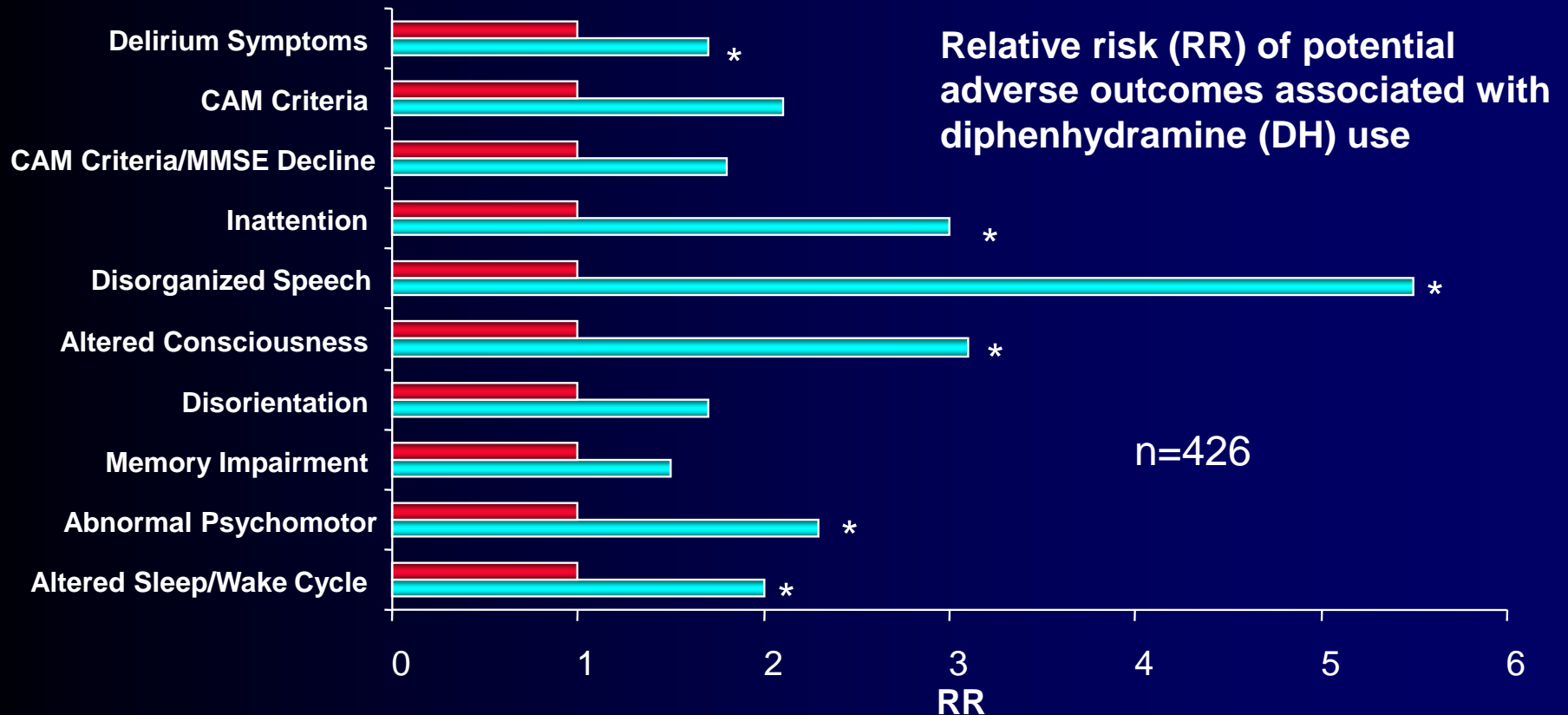
## Phototherapy

- Bright light in the morning can phase advance sleep onset
- Bright light in the evening can phase delay sleep onset
- Light intensity recommended at 2,000 lux for 30-45 minutes
- Morning light should be administered immediately after waking up

# Key Points

- Diagnosis, not complaint, should determine treatment and medication use.
- Hypnotic drugs do little to directly enhance sleep. The major benefit is to reduce arousal, therefore allowing sleep to occur.

# Cognitive Effects of Diphenhydramine in Older Hospitalized Patients



CAM=Confusion Assessment Method.  
MMSE=Mini-Mental State Examination.

■ DH-exposed

■ DH-nonexposed

\* $P < 0.05$ .

# Antidepressants

- Trazodone is the most commonly prescribed medication for the treatment of insomnia in the US<sup>1</sup>
  - In the short-term, trazodone is sedating and can improve some sleep parameters.<sup>2</sup>
- Doxepin has beneficial effects on sleep for up to 4 weeks for individuals with insomnia<sup>3</sup>
- Data on other antidepressants in individuals with chronic insomnia are lacking<sup>4</sup>

1. Walsh JK. *Sleep*. 2004;27:1441-1442.

2. Saletu-Zyhlarz GM, et al. *Neuropsychobiology*. 2001;44:139-149.

3. Hajak G, et al. *J Clin Psychiatry*. 2001;62:453-663.

4. NIH State of the Science Conference Statement. *Sleep*. 2005;28:1049-1057.

# Benzodiazepines

- Effective in short-term insomnia management
- Adverse events
  - Rebound insomnia
  - Residual daytime sedation
  - Impaired cognitive function
  - Motor incoordination
  - Dependence

# Benzodiazepine Receptor Agonists

- Frequency and severity of adverse effects are much lower in the newer benzodiazepine receptor agonists
- In the short term, tolerance and abuse of the benzodiazepine receptor agonists are not major problems in the general population with chronic insomnia
- Long-term use needs further study

# Benzodiazepine Receptor Agonists

Agonist	Usual Dose (mg)	Time to Peak Plasma Concentration (hours)	Half-life (hours)	Active Metabolite
Eszopiclone	2-3	1	6	No
Zaleplon	5-20	1	1	No
Zolpidem	5-10	1.6	2.6	No
Zolpidem Extended Release	6.25-12.5	1.5	2.8	No



# Potential Adverse Events

- Anterograde amnesia
- Masking of untreated problem
- Daytime sedation
- Rebound insomnia & anxiety
- Disinhibition
- Tolerance and dependence
- Distortion of normal sleep
- Cognitive and psychomotor impairment

# Shift Work Type Management

- Behavioral techniques
- Circadian adaptation enhanced by bright light
  - Start early in night shift, end 2 hrs before end of shift
  - Wear dark glasses during morning commute home
- Short-acting hypnotics and melatonin have been found to be effective in some studies
- Management of excessive sleepiness
  - Scheduled naps
  - Wake-Promoting Agents: Modafinil has been shown to improve sleepiness and performance, but both remain in the pathologic range

# Ramelteon

- Activates melatonin (MT) receptors
  - MT<sub>1</sub> (acts to inhibit firing of SCN)
  - MT<sub>2</sub> (phase-shifting action)

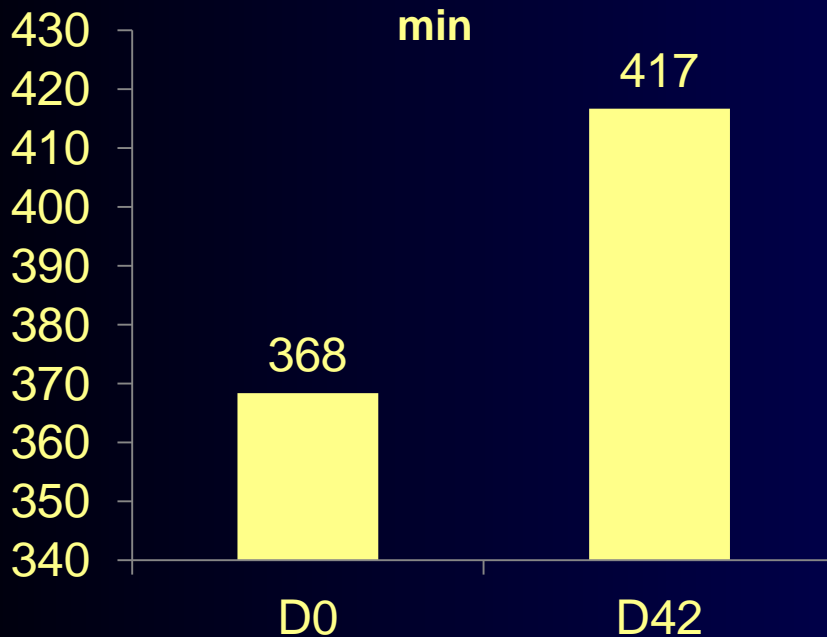
No measurable affinity for other receptors including  $\omega$ , opiate, and dopamine receptors; ion channels; or transporters

# Agomelatine

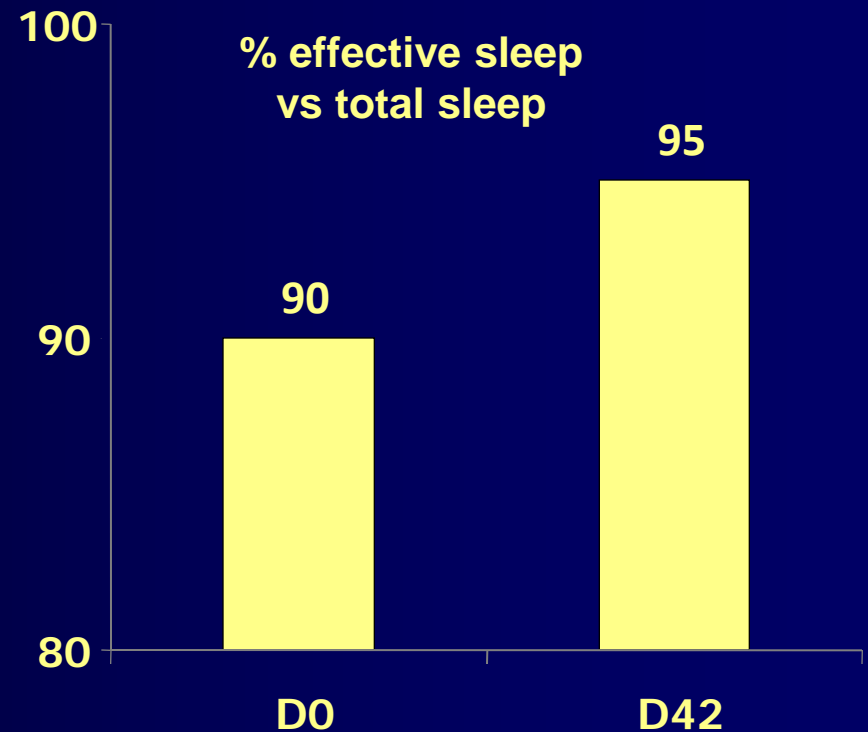
- Antidepressant approved in EU, novel mechanisms of action – MT1, MT2 agonist, 5HT2C antagonist; MDD doses of 25-50mg are effective
- Studies have shown positive influence of agomelatine on sleep continuity and quality as well as shortened sleep latency
- Also shown to alleviate disrupted circadian rhythms associated with seasonal affective disorder
- Animal models of disrupted circadian systems show restoration of circadian rhythms with agomelatine

# Agomelatine Effects on Sleep

## TOTAL SLEEP TIME



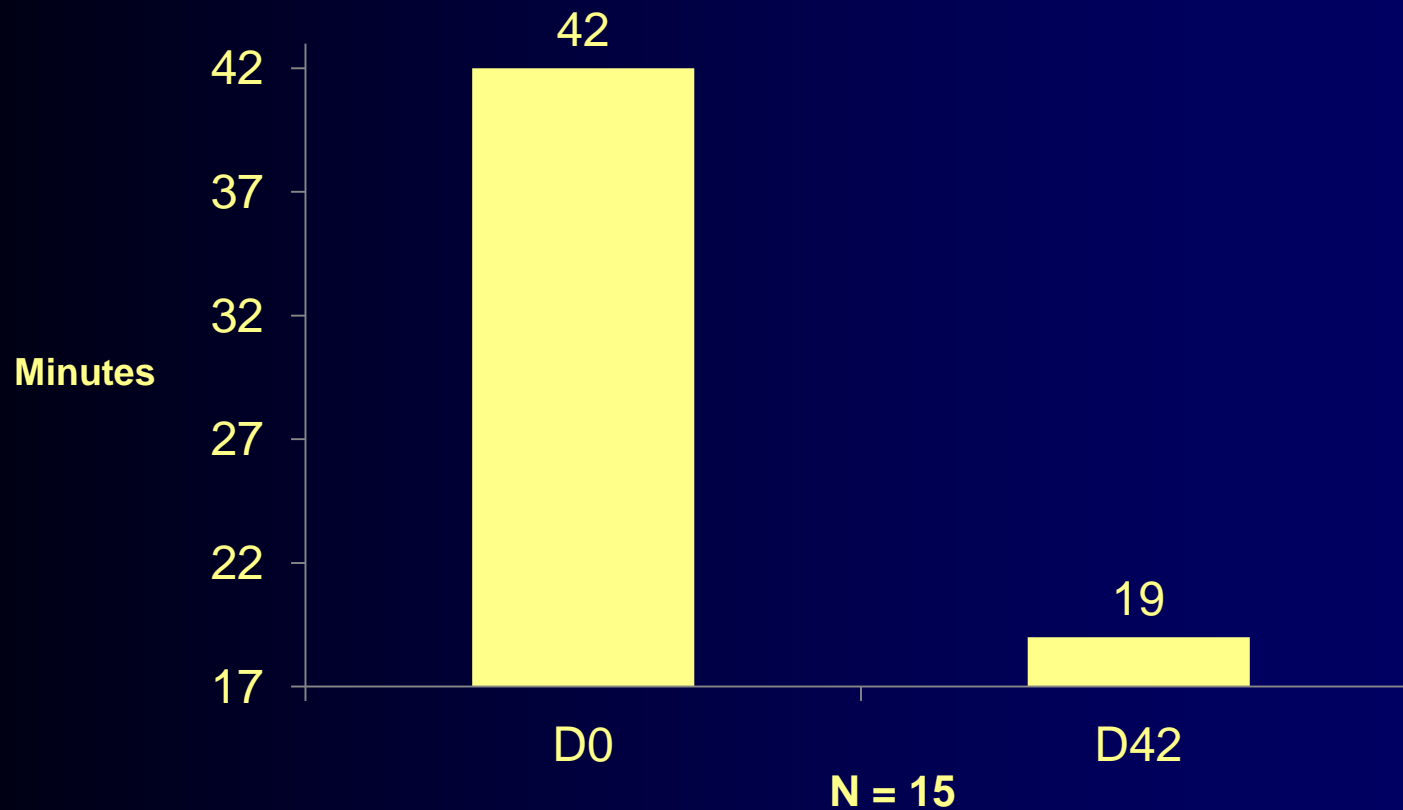
## SLEEP EFFICIENCY



N= 12

# Agomelatine Effects on Sleep

## INTRA-SLEEP AWAKENING



# DO

- Maintain regular bedtimes and awakenings
- Optimize your sleep amounts
- Use bright light in the morning
- Create a comfortable, quiet, dark, and temp-controlled bedroom environment
- Establish a regular pattern of relaxing behaviors within an hour before bedtime
- Exercise on a regular basis

# DON'T

- Take a nap
- Eat or drink heavily before bedtime
- Lie awake for long periods of time
- Allow disturbances (e.g., phones, pets, family)
- Read or watch television in bed (unless these activities definitely make you drowsy)
- Use alcohol, caffeine, or nicotine



# Stanford Sleep Medicine Center

- Multidisciplinary expertise in all sleep disorders (children and adults)
- Treatment options include medications, Cognitive Behavioral Therapy (CBT) for Insomnia, positive airway pressure devices (e.g., CPAP), oral appliances, and upper airway surgery for Sleep Apnea
- Specialized clinics in Narcolepsy, Restless Legs Syndrome, Parasomnias, Behavioral Sleep Medicine, Sleep Surgery
- 18-bed capacity at SHC (14 for patient overnight study and 4 for research)
- 10 full-time attending faculty from multiple disciplines and 8 full-time clinical fellows

