

Sleep and Pain



What is a good night's sleep?

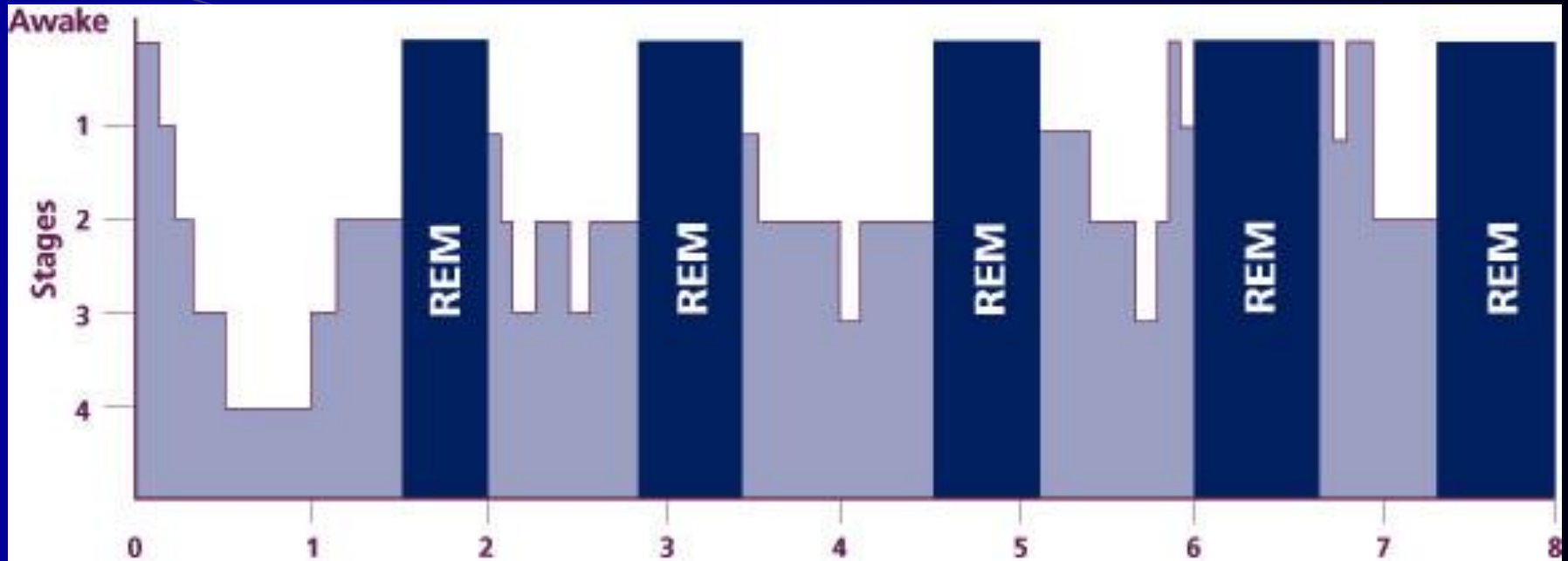


Normal Sleep

- Quantity – 7-8 hours for most people
- Quality – restful, awoken refreshed



Sleep Architecture



TYPE OF SLEEP	STAGE OF SLEEP
<p>NREM:</p> <p>NREM sleep contributes to physical rest and may bolster the immune system.</p> <p>Researchers often group NREM stages 3 and 4 together, calling them delta sleep.</p>	<p>Stage 1 (Light Sleep):</p> <p>A transitional stage between waking and sleeping, usually lasting 5 or 10 minutes. Breathing becomes slow and regular, the heart rate decreases, and the eyes exhibit slow rolling movements.</p>
	<p>Stage 2 (True Sleep):</p> <p>A deeper stage of sleep where fragmented thoughts and images pass through the mind. Eye movements usually disappear, muscles relax, and there is very little body movement.</p>
	<p>Stage 3 (Deep Sleep):</p> <p>A further deepening of sleep with additional slowing of heart and breathing rates.</p>
	<p>Stage 4 (Deep Sleep):</p> <p>This is the deepest stage of sleep, in which arousal is the most difficult. Typically, sleep walking and bed-wetting occur in this stage.</p>



REM Sleep:

REM sleep contributes to psychological rest and long-term emotional well-being. It may also bolster memory.

REM Stage (Dream Sleep):

A dramatic decrease in muscle tone and an essential paralysis characterize this stage of sleep. Other characteristics are irregular breathing, increased heart rate, and rapid eye movements. The brain's oxygen consumption increases, and temperature regulatory mechanisms are absent. In this stage, people experience vivid, active dreams with complex symbols.



How is Sleep Related to Pain?



1. Poor tissue repair

2. Poor filtering

Poor
Sleep

Increased
Pain

Alpha Intrusion



Pain Interferes with Normal Sleep

- Alpha wave intrusion on sleep – deep, delta wave sleep is disrupted
Sleep. 1997 Aug;20(8):632-40. The effect of cutaneous and deep pain on the electroencephalogram during sleep--an experimental study.
- The alpha-EEG anomaly is. . . [seen] for patients with FM and it has been described in patients with RA, osteoarthritis and primary Sjogren's syndrome. The anomaly has also been described in patients without rheumatic disorders, such as in various psychiatric diseases, post-infectious and post-traumatic patients with fatigue and pain, and patients suffering from the chronic fatigue syndrome.
- Drewes AM. Pain and sleep disturbances. Clinical, experimental, and methodological aspects with special reference to the fibromyalgia syndrome and rheumatoid arthritis (Thesis). Aalborg: Aalborg University, Denmark, ISBN 87-90562-00-3.



Poor Sleep Increases Pain

- Pain severity was related to fewer hours slept and delayed sleep onset.
- J Pain Symptom Manage. 1991 Feb;6(2):65-72.
- Low levels of somatomedin C in patients with the fibromyalgia syndrome. A possible link between sleep and muscle pain.
- Arthritis Rheum. 1992 Oct;35(10):1113-6.

○ Sleep deprivation lowers the pain threshold –
bypasses the “Caller ID”



Sleep in Fibromyalgia

- Poorer sleepers tended to report significantly more pain. A night of poorer sleep was followed by a significantly more painful day, and a more painful day was followed by a night of poorer sleep.
 - Sequential daily relations of sleep, pain intensity, and attention to pain among women with fibromyalgia *Pain*. 1996 Dec;68(2-3):363-8.
- Lower concentrations of tryptophan and metabolites have been found in the cerebrospinal fluid of patients with FM
- Lower levels of IGF-1 have been found in people with FM (related to low growth hormone), which depends on stage 3 + 4 sleep for its production



Epidemiology

- Within a year: 30% of people
- At any one time:
 - 10% chronic insomnia
 - 15% short-term insomnia
- 50% is psychological



- People buy more over-the-counter and prescription sleeping medications than any other drug.
 - CBS Healthwatch



How Can you Improve Sleep?



Remove the peas





The Rules of Tacks

- o If you are sitting on a tack, it takes a lot of aspirin to make the pain go away.
- o If you are sitting on 2 tacks, removing one does not lead to a 50% improvement in symptoms.

-Sid Baker, M.D.



Causes

- Exogenous – Outside World
- Physical – Your Body
- CNS – Your nervous system
- Psychological
 - Sleep state Misperception



Causes - Exogenous

- o External stimuli:
 - o Noise
 - o Excessive heat or cold
 - o Bright light
 - o Partner with snoring or restless legs
 - o Pets

Stimulants

- o Coffee
- o Chocolate
- o Tea

- o Marijuana, alcohol
- o Medications:
 - o Sleeping pills and Tranquilizers (“rebound”)
 - o Thyroid preparations
 - o Oral contraceptives
 - o Beta-blockers
 - o SSRI’s



Alcohol and Sleep



- o Alcohol is more disruptive to sleep than caffeine
 - o The body will produce adrenaline to compensate for the alcohol in the system
 - o Alcohol makes people thirsty



Causes - Physical

- Bodily dysfunctions:
 - Pain.
 - Decreased mobility.
 - Disturbing sensations or movements
 - Periodic limb movements – see next slide
 - Cardiac or respiratory problems
 - Asthma
 - Heart failure
 - Sleep apnea
 - GI – reflux, IBD
- Age.



Periodic Limb Movements, “Restless Legs”

- o Familial – consider megadoses of folic acid
 - o 10-30 mg per day
- o Check iron – iron deficiency may also provoke
- o For nocturnal myoclonus:
 - o Magnesium
 - o Vitamin E
 - o Parkinson’s Drugs



Sleep Apnea

- Snoring
- Daytime Sleepiness
- Hypertension
- Car accidents
- Heart Failure
- Stroke
- Arrhythmia
- Etc.



Causes - CNS

- Alterations in the central nervous system (CNS) that initiate and maintain sleep.
 - Brain: stroke, head injury, dementia.
 - Metabolic: liver disease, blood sugar, etc.
 - For repetitive 3 am awakening, try a protein snack before bed.
 - Hormonal: thyroid, menopause.

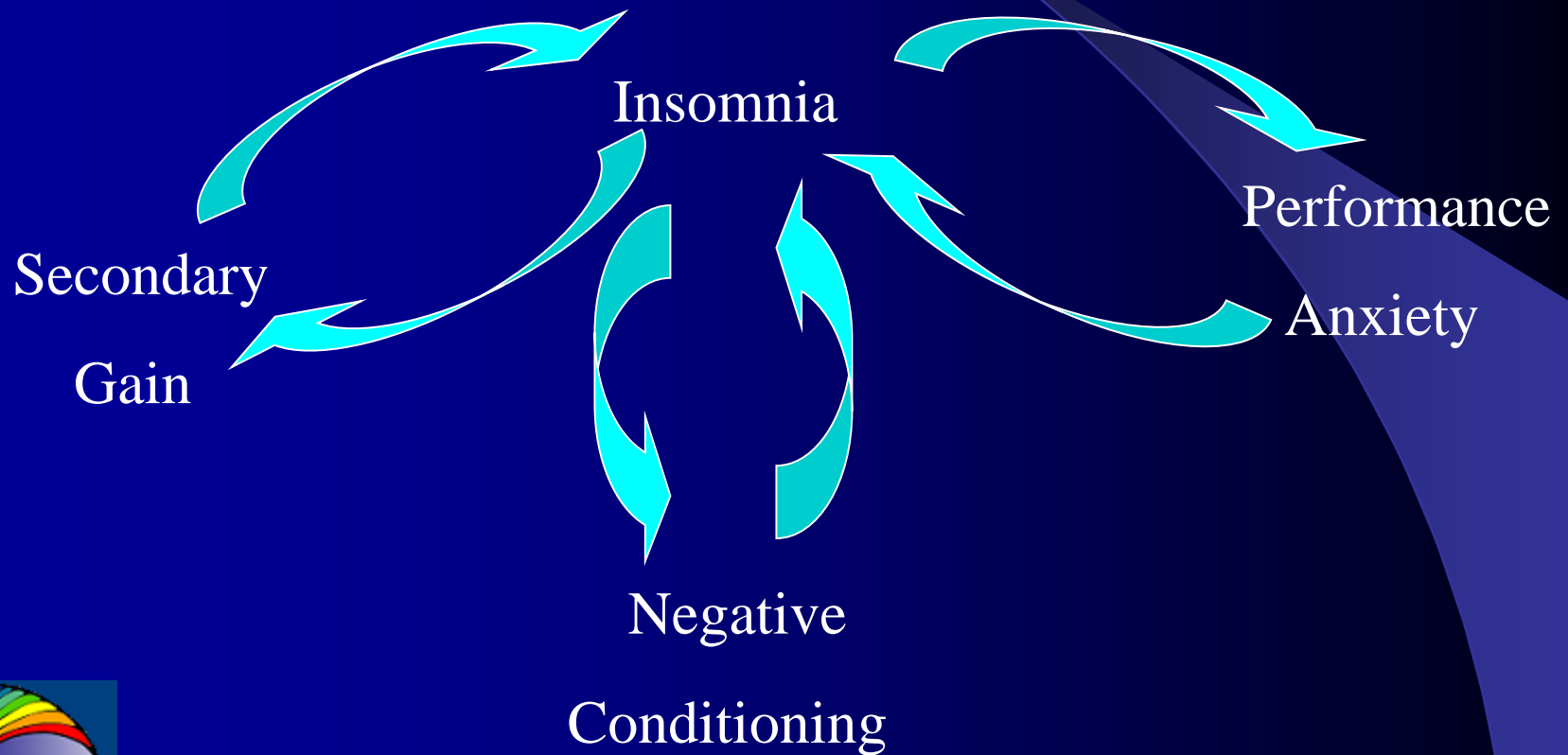


Causes - Psychological

- o Personality:
 - o Anxious, tense, somatic vs.
 - o Relaxed, phlegmatic.
- o Stress.
 - o Life changes (birth, death, divorce, move, etc.).
- o Depression
- o Circadian rhythm sleep disorder
- o Poor Sleep Hygiene



The Vicious Cycles



Differentiating Causes

- Difficulty falling asleep
 - Poor sleep hygiene
 - Conditioned insomnia (behavioral conditioning)
 - Restless legs syndrome
 - Circadian rhythm disorder
 - Advanced sleep-phase syndrome
 - Delayed sleep-phase syndrome
- Difficulty staying asleep
 - Medications
 - Drug or alcohol use
 - Psychiatric disorders (e.g. Depression, anxiety)
 - Medical disorders
 - Sleep-disordered breathing (e.g., Sleep apnea)
 - Nocturnal myoclonus



Solutions

- o Remove causal factors
- o Behavioral changes –
 - o Sleep hygiene
 - o Sleep restriction therapy
 - o Stimulus control therapy
 - o Relaxation techniques
- o Herbs and Medications



Remove Causal Factors

- Stop alcohol, stimulants, etc
- Treat pain
- Treat heart failure, sleep apnea, etc
- Earplugs/ heavy curtains, etc
- Treat partner



Solutions

- Remove causal factors
- Behavioral changes –
 - **Sleep hygiene**
 - Sleep restriction therapy
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 - Relaxation techniques
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Principles of Sleep Hygiene

- Go to bed and get up at the same time each day
- Avoid daytime naps or limit them to one midafternoon nap
- Avoid evening alcohol use
- Avoid caffeinated drinks (late in the day)



Sleep Hygiene Continued

- Reduce or eliminate tobacco use, especially at night or in the evening
- Exercise in moderation; avoid evening exercise
- Use the bed only for sleep and sexual activity



Sleep Hygiene Continued

- Keep the bedroom dark, quiet, and cool
- Avoid stress and worrisome thoughts in the evening before sleep
- Avoid screen time or bright light for an hour before bed



Light Therapy

- Bright light in the morning
- Avoidance of bright light in the evening

- This works even in alcohol withdrawal



Stimulus Control Therapy

- o Associate bed, sleep environment only with sleep, intimacy
 - o No reading, eating, or watching TV in bed.
 - o Get out of bed and to do something relaxing if unable to sleep after 15 to 20 minutes.
(Not TV – light and content are arousing)



Solutions

- Remove causal factors
- Behavioral changes –
 - Sleep hygiene
 - **Sleep restriction therapy**
 - Stimulus control therapy
 - Relaxation techniques
- Herbs and Medications



Sleep Restriction Therapy

- o No Naps
- o Rise at same time regardless of how little sleep
- o Limit sleep to 1-2 hours less than reported amount of sleep
 - Makes sleep more continuous
- o Then gradually increase sleep time



Solutions

- Remove causal factors
- Behavioral changes –
 - Sleep hygiene
 - Sleep restriction therapy
 - Stimulus control therapy
 - **Relaxation techniques**
- Herbs and Medications



Relaxation techniques

- o Mental
 - o Prayer
 - o Journal
 - o Imagery
 - o Biofeedback
 - o Delta wave inducing sleep CD
 - o Music – postoperative study in CABG patients
- o Physical
 - o Breathing
 - o Progressive Relaxation
 - o Sounder Sleep System



Non-Drug Therapies Really Do Work!

- o Behavioral management of sleep disturbances secondary to chronic pain.

J Behav Ther Exp Psychiatry. 1989 Dec;20(4):295-302.

Documented effectiveness of a behavioral program on EEG and sleep architecture in patients with chronic pain.



The Sounder Sleep Solution

Based on a program developed by Michael
Krugman

www.soundersleep.com

Solutions

- Remove causal factors
- Behavioral changes –
 - Sleep hygiene
 - Sleep restriction therapy
 - Stimulus control therapy
 - Relaxation techniques
- Herbs and Medications



Pills and Potions

Herbs and Medications to Aid Sleep

Medications – Pros and Cons

Pros

- Work quickly
- Covered by insurance

Cons

- Stop working (Tolerance)
- Dependence – Rebound
- Sedation
 - Fall Risk
 - Confusion
- Amnesia



Natural Substances

- Minerals
 - Calcium and Magnesium
- Amino Acids: Tryptophan, 5HTP
- Hormones: Melatonin
- Herbs
- Aromatherapy



Serotonin

- Neurotransmitter in the brain that triggers sleep
- Made from tryptophan – amino acid found in foods such as milk, turkey



5HTP

- Increase REM sleep (typically by about 25%)
- Increase deep sleep stages 3 and 4
- No increase in total sleep time

- 100–300 mg 30–45 minutes before retiring



Melatonin

- Hormone produced by the pineal gland – part of the system that aligns our body with light and dark
 - Dosage: 3 mg at bedtime is more than enough
 - Dosages as low as 0.1 and 0.3 mg have been shown to produce a sedative effect when melatonin levels are low
- Caution: Could disrupt the normal circadian rhythm. In one study, a daily dosage of 8 mg/day for only 4 days resulted in significant alterations in hormone secretions



Passionflower



- o The herbal “specific” for staying asleep
- o Studied vs. serax (benzodiazepine) for anxiety:
 - o Equally effective for anxiety
 - o No cognitive or motor impairment



Valerian

- Takes 2 – 3 weeks to start working
- Shown to significantly
 - reduce sleep latency
 - improve sleep quality
 - reduce night-time awakenings
- Usually reduces morning sleepiness.



Valerian

- Studies:
 - Compared with placebo, valerian showed a significant effect
 - 44% reporting perfect sleep
 - 89% reporting improved sleep.



Valerian

- Studies:

- Double-blind study of insomniacs:

- Valerian root extract (160 mg) and Melissa officinalis extract (80 mg)
 - Benzodiazepine (triazolam 0.125 mg)
 - Placebo.

- Results:

- Valerian effect comparable to drug
 - Able to increase deep sleep stages 3 and 4.
 - Did not cause daytime sedation
 - No evidence of diminished concentration based on the Concentration Performance Test
 - No impairment of physical performance



Other Herbs Used Traditionally

- o Lemon Balm
- o Hops
- o Chamomile
- o Skullcap
- o Kava – cautions for the liver
- o End Fatigue Revitalizing Sleep Formula



Aromatherapy

- o Essential oil – scent or in hydrotherapy
 - o Lavender – nursing home study
 - o Rose
 - o Ylang-ylang
 - o Neroli



Drugs

The background is a dark blue gradient. A curved line starts from the top left and curves towards the bottom right. A dark blue triangular shape is positioned in the bottom right corner, pointing towards the center.

The Ideal Sleeping Pill

- Shorten latency to sleep
- Maintain normal physiological sleep all night without blocking normal behavioral responses to the crying baby or the alarm clock
- Leave neither hangover nor withdrawal effects the next day
- No tolerance or side effects, such as impairment of breathing, cognition, ambulation, and coordination
- Not habit-forming or addicting.

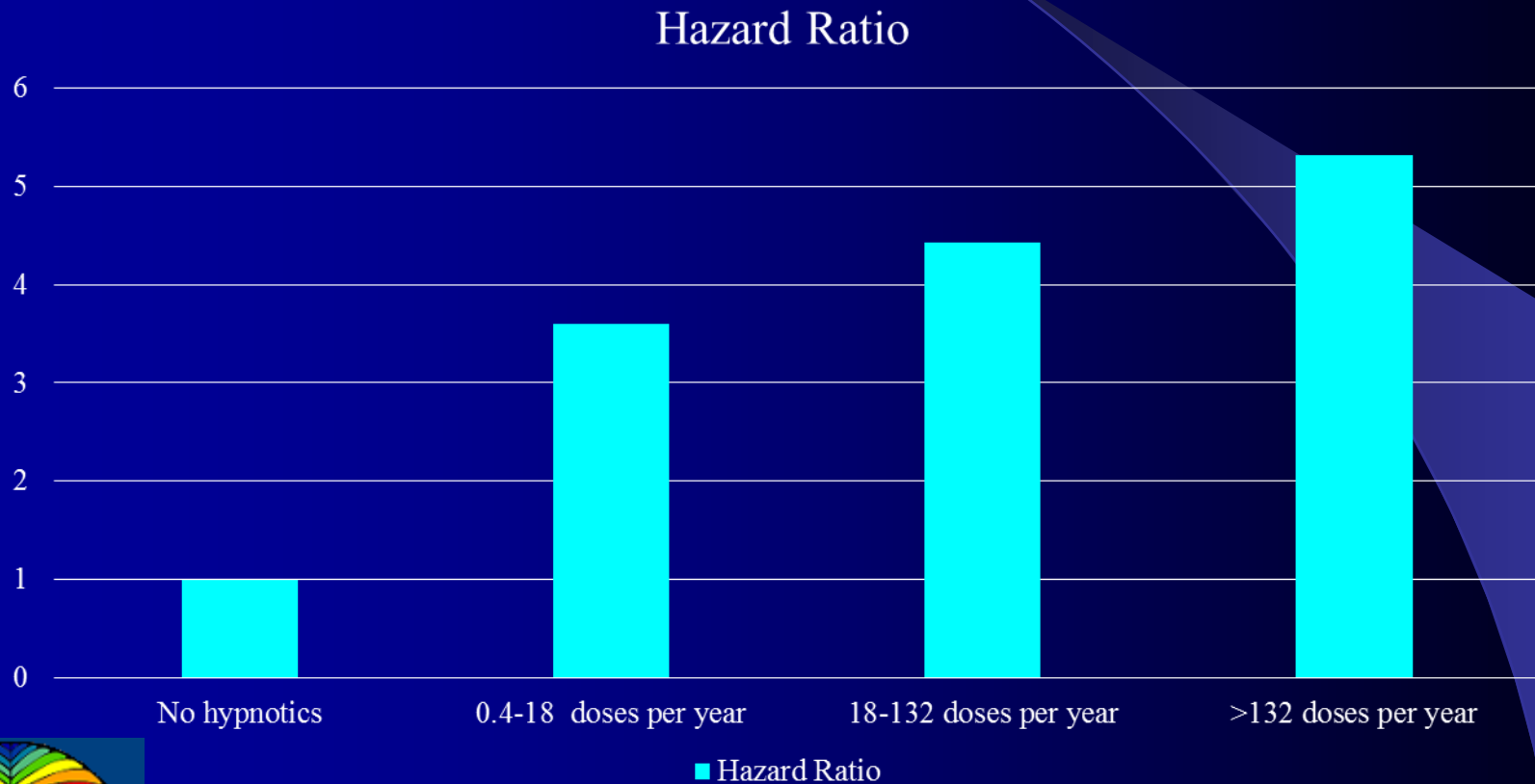


The Ideal Sleeping Pill

- o Has not been developed



Mortality according to Hypnotic Prescriptions



Confirmed for zolpidem, temazepam, lunesta,
sedative antihistamines BMJ Open 2012;2: e000850.



Over-the-counter Drugs

- o e.g. Nytol, Sleep-Eez, Sominex, Anacin PM, Excedrin PM, Tylenol PM, Unisom
- o antihistamines
 - not addictive
 - not effective in sustaining stage IV sleep
 - can affect the quality of sleep.

• **YOU SLEEP MORE, BUT IT IS WORSE SLEEP**



Implications of Half-Life

Blood
Level

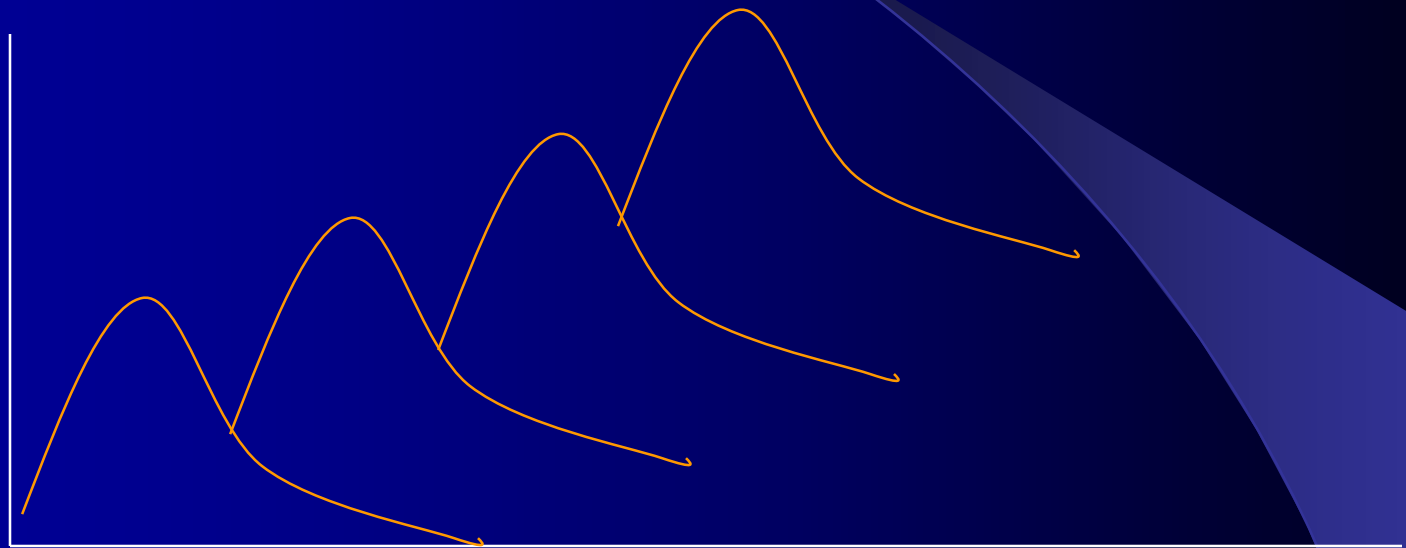


Half life

Time



Blood
Level



Time



Long vs. Short-Acting Hypnotics

	Short	Long
Hangover	+	++++
Accumulation	0	+++
Tolerance	+++	+
Withdrawal insomnia	+++	+
Decrease anxiety	0	+++
Amnesia	+++	++



Table 1 -- Drugs with a Food and Drug Administration indication for insomnia

Drug name	Mechanism of action	Dose range	Elimination half-life
Estazolam (ProSom)	BzRA	1–2 mg	10–24 h
Flurazepam (Dalmane)	BzRA	15–30 mg	48–120 h ^[a]
Temazepam (Restoril)	BzRA	15–30 mg	8–20 h
Triazolam (Halcion)	BzRA	0.125–0.25 mg	2.4 h
Quazepam (Doral)	BzRA	7.5–15 mg	48–120 h ^[a]
Zolpidem (Ambien)	BzRA	5–10 mg	1.4–3.8 h
Zolpidem ER	BzRA	6.25–12.5 mg	2.8 h
Zaleplon (Sonata)	BzRA	5–20 mg	1 h
Eszopiclone (Lunesta)	BzRA	1–3 mg	6 h
Ramelteon (Rozerem)	MtRA	8 mg	1–2.6 h



TABLE 64-7 -- Clinical Characteristics of Benzodiazepines and Zolpidem

Name	Dose (mg)	Absorption	Active Metabolite	Half-Life
Chlordiazepoxide (Librium)	5-10	Intermediate	Yes	2-4 d
Diazepam (Valium)	2-10	Fast	Yes	2-4 d
Estazolam (ProSom) :	0.5-2.0	Intermediate	Yes	17 h
Flurazepam (Dalmane) :	7.5-30	Intermediate to fast	Yes	2-4 d
Clorazepate (Tranxene)	7.5-15	Fast	Yes	2-4 d
Clonazepam (Klonopin)	0.5-1.0	Intermediate	Yes	2-3 d
Quazepam (Doral) :	7.5-15	Intermediate	Yes	2-4 d
Oxazepam (Serax)	10-15	Slow	No	8-12 h
Lorazepam (Ativan)	0.5-4.0	Intermediate	No	10-20 h
Temazepam (Restoril) :	7.5-15	Slow	No	10-20 h
Alprazolam (Xanax)	0.25-2	Intermediate	No	14 h
Triazolam (Halcion) :	0.125-0.5	Intermediate	No	2-5 h
Midazolam (Versed)	7.5-15	Intermediate	No	2-3 h
Zolpidem (Ambien) :	5-10	Intermediate	No	2-5 h



Medications Used for Insomnia

Imidazopyridines Selective for alpha-1 GABA R	Zolpidem (Ambien) 5-10 mg Zaleplon (Sonata) 5-10 mg
Less selective GABA R agonist	Eszopiclone (Lunesta) 2-3 mg
Melatonin receptor agonist	Rozerem 8 mg
Antihistamines	Diphenhydramine (Benadryl) 25 – 50 mg
Sedating antidepressants	Amitriptyline (Elavil) 10–75mg
	Trazodone(Desyrel) 25–100mg
	Doxepin 10 – 75 mg
	Imipramine 25 – 100 mg
	Remeron 15 mg
Anticonvulsants	Neurontin 300 – 1500 mg Helps pain and PLM/Restless legs
	Gabitril 4 mg 1-3 at bedtime
Muscle relaxants	Soma 350 mg Addictive
	Flexeril 10 – 20 mg at bedtime
Other	GHB (Xyrem)



Effects on EEG Sleep Drug	Trade Name	Continuity	SWS	REM	Sedation Effects
TCA's					
Amitriptyline	Elavil	I (3)	I (1)	D (3)	4
Doxepin	Sinequan	I (3)	I (2)	D (2)	4
Imipramine	Tofranil	I (0-1)	I (1)	D (2)	2
Nortriptyline	Pamelor	I (1)	I (1)	D (2)	2
Desipramine	Norpramin	(0)	I (1)	D (2)	1
Clomipramine	Anafranil	I (0-1)	I (1)	D (4)	0
MAOIs					
Phenelzine	Nardil	D (1)	(0)	D (4)	0
Tranlycypromine	Parnate	D (2)	(0)	D (4)	0
SSRIs					
Fluoxetine	Prozac	D (1)	D (0-1)	D (0-1)	0
Paroxetine	Paxil	D (1)	D (0-1)	D (2)	0
Sertraline	Zoloft	(0)	(0)	D (2)	0
Citalopram	Celexa	D (1)	(0)	D (1)	ND
Fluvoxamine	Luvox	D (1)	(0)	D (1)	ND
Escitalopram	Lexapro	(0)	(0)	D (2)	0
Other					
Bupropion	Wellbutrin	D (0-1)	(0)	I (1)	0
Venlafaxine	Effexor	D (1)	D (1)	D (3)	2
Trazodone	Desyrel	I (3)	I (0-1)	D (1)	4
Mirtazapine	Remeron	I (3)	I (2)	(0)	3
Nefazodone	Serzone	I (1)	(0)	I (1)	1

