

Sleep disorders in Geriatrics



Dr. Laleh Mahmoudi
PharmD, iBCPS
Associate Professor
Department of Clinical Pharmacy
Shiraz University of Medical Science



Introduction

- Approximately **one-third** of the adult life is expended on sleep.
- Sleep deficiency associates with **increased disease risk**, including **cardiovascular and metabolic disease**, **psychiatric illness**, **substance abuse**, **pregnancy complications**, and **impaired neurobehavioral and cognitive impairment**.

Introduction

- **At least 10%** of the **American population** is reported to suffer from a **sleep disorder** that is clinically significant and of public health concern.

-
- An epidemiological survey performed in **Japan** reported an insomnia prevalence of **21.4%**
 - Insomnia was defined to include at least one instance of difficulty initiating sleep (8.3%), maintaining sleep (15.0%), or early morning awakening (8.0%).
 - **> 50% of older adults** suffer from insomnia, and these subjects are often undertreated.

-
- Sleep disturbances are **common symptoms** in adults and are related to various **factors**:
 - Use of caffeine, tobacco, and alcohol
 - Sleep habits
 - Comorbid diseases

- **Modern life** is characterized by:

- Reduced sleep times
- **Worsened sleep quality**
 - Changes in modern lifestyles (working late and using the computer and internet and watching TV late at night)

-
- At any age, managing insomnia is a challenging issue that may **require lifestyle changes**.
 - The recognition of insomnia is **especially important** in the **elderly** due to age- related increases in **comorbid medical conditions** and **medication use** as well as age- related changes in **sleep structure**, which shorten sleep time and impair sleep quality

-
- The consequences of **inadequate** and **inappropriate sleep** in determining the quality of life of the elderly.
 - Social participation is the key to healthy ageing.
 - However, data from the **US National Social Life, Health, and Aging Project** has shown that older adults with greater social participation slept better, but increasing social participation did not improve sleep

-
- The percentage of the **elderly population** is growing due to increased life expectancy and improved socioeconomic development.
 - By 2025, the elderly population would **be >25%** of the population in developed nations.
 - It already **exceeded 30%** in Japan in **2012**.
 - The increase in the aged population will bring with it a huge burden of sleep-related health problems.
 - Although ageing is a global phenomenon, little data are available on regional trends in sleep-related problems.

Sleep Stages, Time, and Architecture of Different Age Groups

- **Behaviorally**, sleep is characterized by reduced motor activity, decreased response to stimulation, stereotyped posture, and relatively easy reversibility.
- **Scientifically**, sleep is defined on the basis of **electro-physiological signals** like EEG, electromyogram, and electrooculogram.
- The modern definition and classification of sleep :
 - Human sleep was classically divided into REM sleep and non-REM sleep, which consisted of four stages: S1, S2, S3, and S4.
 - However, the American Academy of Sleep Medicine slightly modified the staging rules and terminologies in 2007: S3 and S4 were grouped together as **N3**, and S1 and S2 were renamed N1 and N2

Polysomnography

- Each sleep stage serves a **physiologic function** and can be monitored in **sleep laboratories** by **polysomnography**.
- Polysomnography is the term used to describe three electrophysiologic measures: the **electroencephalogram (EEG)**, the **electromyogram**, and the **electrooculogram** of each eye.

Non-rapid Eye Movement Sleep

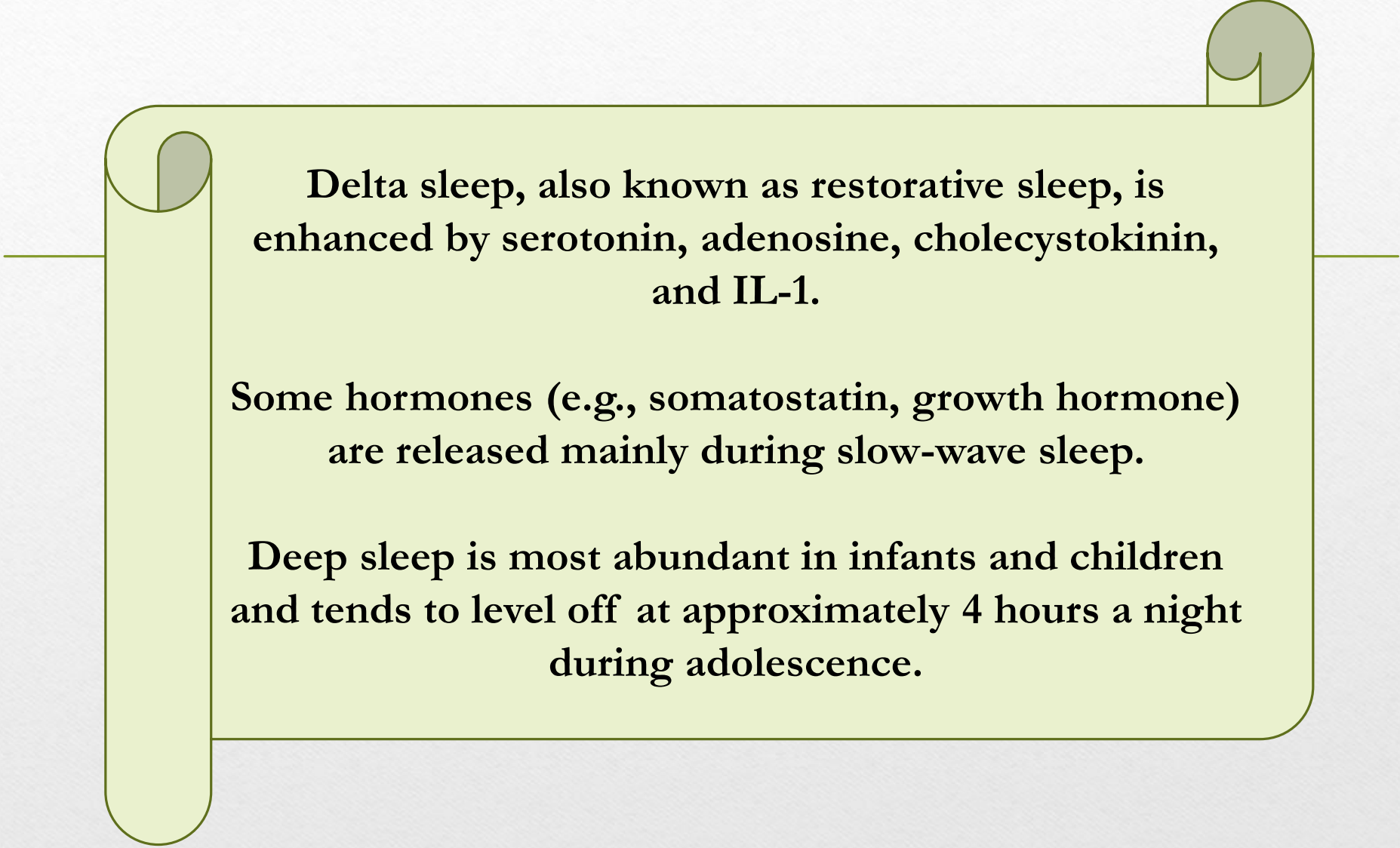
- It is divided into **four stages**, with different **quantities of time** and **functions** in each stage.
- **Stage 1** is a transition between **sleep** and **wakefulness** known as **relaxed wakefulness**, which generally makes up approximately **2%-5%** of **sleep**.

Non-rapid Eye Movement Sleep

- Approximately **50% of total sleep time** is spent in **stage 2**, which is **lighter sleep**.
- Stage 2 provides **rest** for the **muscles and brain** through **muscle atonia** and **low-voltage brain wave activity**.
- **Arousability** from sleep is **highest** during **stages 1 and 2**.

Non-rapid Eye Movement Sleep

- Stages 3 and 4 are slow-wave (delta) or **deep sleep**.
- Stage 3 occupies an average of 5% of sleep time, whereas stage 4 constitutes 10% to 15% of sleep time in young, healthy adults.
- In contrast to stages 1 and 2, it is difficult to awaken someone during stages 3 and 4, or delta sleep.



Delta sleep, also known as restorative sleep, is enhanced by serotonin, adenosine, cholecystokinin, and IL-1.

Some hormones (e.g., somatostatin, growth hormone) are released mainly during slow-wave sleep.

Deep sleep is most abundant in infants and children and tends to level off at approximately 4 hours a night during adolescence.

Rapid Eye Movement Sleep

- Whereas **NREM sleep** is necessary for **rest and rejuvenation**, the purpose of REM sleep remains a **mystery**.
- REM sleep is **greatest in infants**, accounting for **about 50%** of total sleep time.
- As aging occurs **before 2 years** and throughout adulthood, REM sleep is usually **20% to 25% of sleep**.
- REM sleep is also called **paradoxical sleep** because it has aspects of both **deep sleep** and **light sleep**.

Rapid Eye Movement Sleep characteristics

Muscle and
sympathetic tone
drop

Neurochemical
processes and
higher cortical
brain function

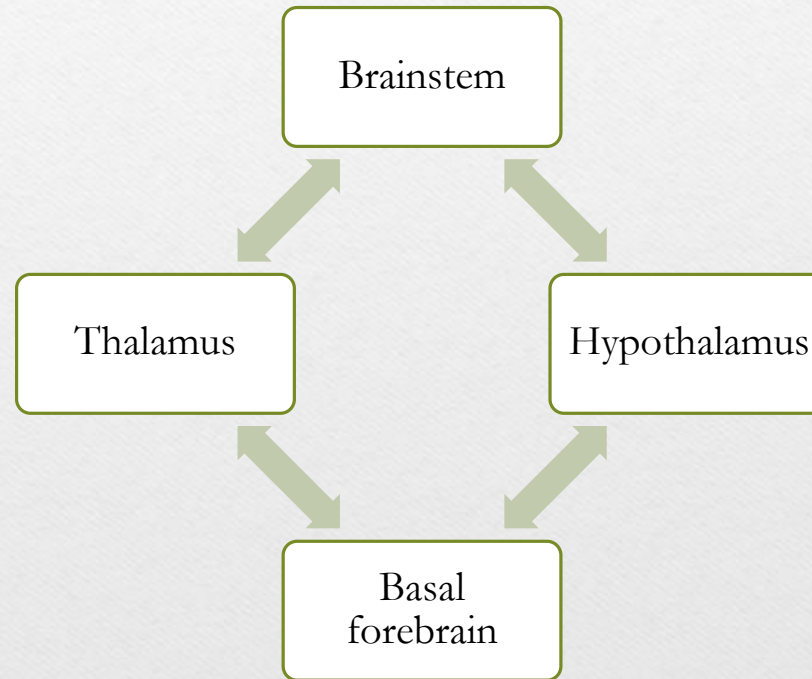
Dreaming

Irregular breathing

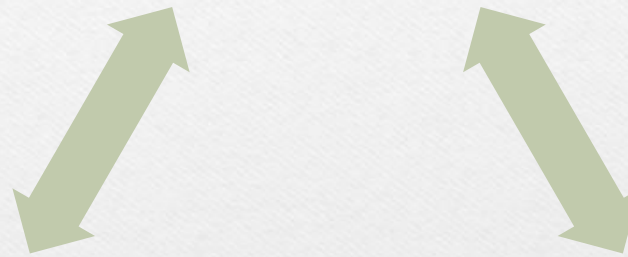
Body temperature
typically lowers

Decrease in
cardiac output and
urine volume

Brain neurochemistry of sleep



Noradrenergic,
histaminergic, and
acetylcholine-containing
neurons promote wakefulness.

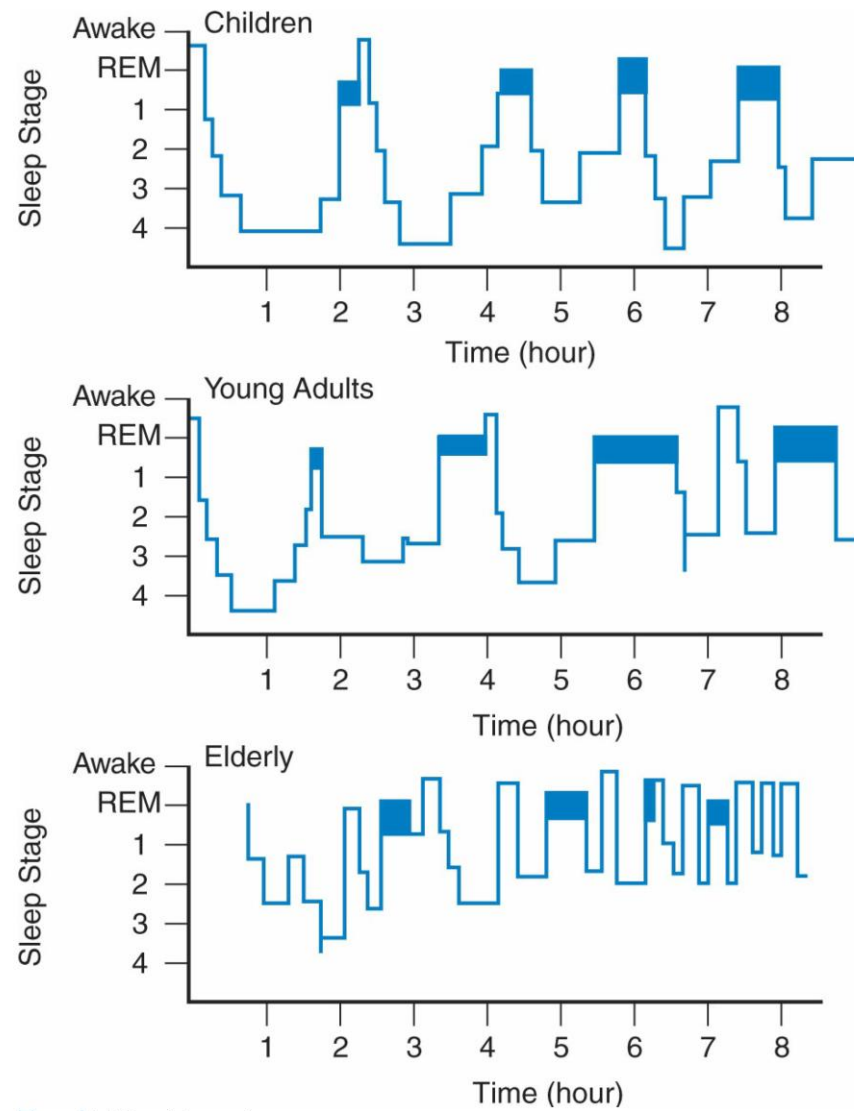


Hypocretin 1 and 2, also known as **orexin A and B**, are neuropeptides that modulate the sleep-wake cycle.

Excitatory amino acids, such as **glutamate** and stimulating neuropeptides (e.g., **substance P**, **thyrotropin-releasing factor**, **corticotropin-releasing factor**) also promote wakefulness.

-
- Sleep starts with a period of **NREM sleep** (slow wave sleep) in healthy young adults
 - REM sleep takes place after **a short period of NREM** sleep.
 - This alteration between NREM and REM occurs about **4-5 times** during a normal night's sleep.
 - During NREM sleep, the HR and BP decline, but GI motility and parasympathetic activity increase.
 - In contrast, REM sleep is characterized by a profound loss of muscle tone, but the eyeballs show bursts of rapid eye movements.

Normal sleep cycles



-
- The **quantity** and **quality** of sleep change profoundly across the lifespan.
 - In **newborns**, the total duration of sleep in a day can be **14–16 h**.
 - Circadian sleep–wake rhythm with periodicity in physiological, biochemical, and psychological processes is modulated by the suprachiasmatic nucleus of the hypothalamus as well as the pineal gland.
 - These brain areas set the **body clock**

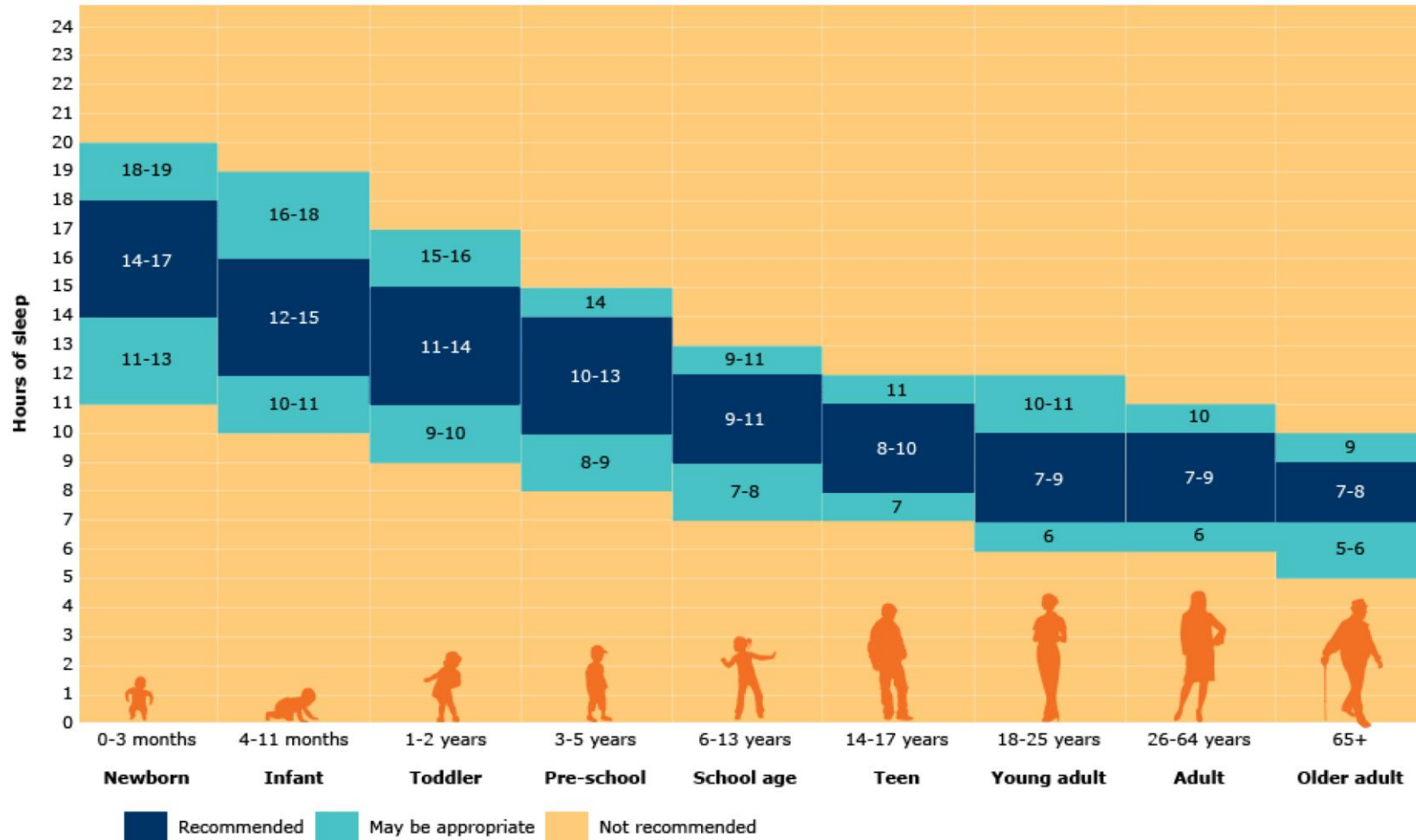
Sleep Changes in Old Age

- In **young adults**, sleep of **7.0–8.5 h** is considered fully restorative.
- The amount of sleep needed by each person is usually constant, although there is a wide variation among individuals.
- During **old age**, overnight sleep is often fragmented and lasts for **less than 6.0–7.5 h**.
- The reason for these changes in sleep and circadian rhythms with ageing is not fully understood.

Sleep Changes in Old Age

- Changes in the sleep patterns are a part of the **normal ageing process**.
- Older people have **difficulty falling asleep** and in **staying asleep**, due to frequent arousals.
 - In fact, the required total sleep time **remains nearly constant** throughout adulthood.
 - It is only the **sleep architecture** and **depth** that changes with ageing
- Older people spend more time in the lighter stages of sleep than in deep sleep.
- This results in their **waking up several times** during the night.
 - This phenomenon is described as **sleep fragmentation** with ageing.

Sleep duration recommendations by age from the National Sleep Foundation



Reasons for Altered Sleep Architecture in Old Age

- The circadian oscillations that alter body functions including sleep become less pronounced during old age.
- This is reflected in the **decreased melatonin peak** in the elderly.
- Older people commonly exhibit **advanced sleep phase syndrome**, as they tend to go to sleep earlier and wake up earlier than young adults.
 - This could be due to reduced light exposure.
 - As such, bright light therapy is suggested as a treatment option for them.

Two interacting regulatory systems

- The timing of sleep–wake cycles is regulated by **two interacting regulatory systems**: the sleep–wake homeostatic drive and the internal circadian clock.
- The interaction of these two systems keeps young adults alert during the day and enables them to sleep without interruption at night.
- As people age, the internal clock becomes less efficient, and this results in interrupted sleep, falling asleep earlier, and waking up earlier in the morning.
- Ageing reduces the amplitude of circadian oscillation in all the physiological parameters, including the **melatonin level**.

Hormonal regulators

- Melatonin is important to regulate normal sleep cycles.
- Melatonin is produced during "dark hours" of sleep and is released in response to changes in light and inhibits the neurotransmitters involved in arousal, such as histamine, norepinephrine, dopamine, and serotonin.
- Melatonin has also been noted to induce sedation and lower core body temperature.

Two interacting regulatory systems

- Decline in the efficiency of the central clock affects day/night synchronization in the metabolic pathways and endocrine mechanism.
- Circadian rhythms govern not only the physiological variables such as energy metabolism, sleep–wake cycles, body temperature, and locomotor activity, but they also influence the **behavioral systems**.
- Age-associated **brain atrophy** and **cortical thinning** are likely to contribute to these changes.

Ageing Process at Cellular Level Affects Sleep

- **Ageing** in general is a complex process with changes at the molecular, cellular, and genetic levels.
- A **progressive loss** of physiological integrity as well as **impaired and deteriorated** body functioning increase the risk for **metabolic disorders, cardiovascular diseases, neurodegenerative diseases, and even cancer.**
- **Telomeres** are the chromosomal regions that are particularly **susceptible to age-related deterioration.**
- Insomnia in older adults (aged 70–88 years) is associated with shorter telomere length in peripheral blood mononuclear cells.
- Moreover, sleep disturbances may also enhance cellular ageing in the later years of life.

Insomnia in The Elderly

- Insomnia is one of the most common sleep disorders in the elderly.
- According to American Academy of Sleep Medicine, 'Insomnia is defined as a **persistent difficulty** with sleep initiation, duration, consolidation, or quality that occurs **despite adequate opportunity** and circumstances for sleep, and results in some form of **daytime impairment**'.
- But according to the DSM-5th edition, 'insomnia is defined as reported **dissatisfaction** with sleep quantity or quality and associated with difficulty with sleep initiation, maintenance, or early-morning awakening and that causes clinically **significant distress or impairment**, occurs **at least 3 nights** per week for 3 months, occurs despite adequate opportunity for sleep, and is not better explained by another disorder or substance abuse

Insomnia in The Elderly

- According to some reports, there is a **higher prevalence of insomnia** in the aged in nursing homes and rural areas.
 - However, other studies have found no differences in the insomnia patterns of elders in nursing homes and in other homes.
- The 2004 National Health Interview Survey in the USA showed that the percentage of elderly men and women sleeping less than 6 h is as high as **20–25%**.
- Although insomnia increases with age, comorbid health conditions largely influence the clinical severity.

Gender differences in insomnia

- Gender differences in insomnia in the aged population cannot be ignored as insomnia is generally **higher in women**.
- In older women, with or without symptoms of depression, sleep disturbances increase with age.
- **Elevated anxiety** is another culprit that lowers sleep quality.
- It was reported that the female US veterans (i.e. those who had served in the armed forces on active duty for a period of 180 days or more) had a higher risk for insomnia and sleep-disordered breathing than non-veteran participants, making them more prone to cardiovascular diseases and diabetes.
- Issues related to sleep disturbances in postmenopausal women, especially those coping with osteoarthritis, have yet to be fully examined

Sleep, Depression, and Anxiety

- Good quality sleep is considered a blueprint for maintaining mental health.
- It is well documented that anxiety and depression are common in the aged population.
- Depression in aged subjects can lead to adverse outcomes, including impairment in executive functions, medical illnesses, disability, increased mortality, and increased health services utilization.
- Accelerated age-related changes in sleep architecture may be linked to depressed mood in older adults.
- Sleep of short and long durations are also associated with increased risk of depression in adults

-
- Sleep disturbances are regarded as secondary to depression due to depression's comorbidity with sleep disorders.
 - However, recent evidence has indicated that sleep disturbances not only precede the occurrence of depression, but are also associated with increased risk for depression crosssectionally and longitudinally

SLEEP AND PAIN

- Chronic pain is a common debilitating condition among the elderly population.
- A national study of Medicare beneficiaries in the USA showed that bothersome pain afflicts half of the older adults, and it increases significantly with greater disease burden.
- This leads to emotional distress, thereby reducing sleep quality, which in turn can reduce pain thresholds and increase feelings of fatigue.
- In addition, symptoms of depression, fatigue, and insomnia were more severe in subjects with moderate-to-extreme pain interference than in those who reported less pain.
- Prevalence of pain and the number of pain locations are higher in older women than in men.

SLEEP AND CARDIOVASCULAR DISEASES

- Sleeping less than 4–5 h or more than 10 h per night is linked to increased mortality.
- A recent report on a middle-aged Chinese population found increased coronary artery disease in those sleeping less than 6 h per night.
- In a Japanese population, long sleep duration among the elderly with poor sleep quality is associated with a higher risk of mortality linked to cardiovascular disease.
- A similar trend was also observed in aged American Indians.
- According to this report, cardiovascular diseases were least prevalent among the subjects who slept for 7–8 h per night

SLEEP AND DEMENTIA

- Dementia is one the major problematic conditions in the elderly.
- A recent meta-analysis and detailed review indicated that sleep disturbances may predict the risk of incident dementia.
- Sleep-disordere was a risk factor for all-cause dementia, Alzheimer's disease (AD), and vascular dementia.
- Sleep disturbances are common (25–40%) in AD patients.
- Sleep problems in these patients are a serious concern as they further adversely affect the behavioural and psychological symptoms of dementia and also increase the risk factors associated with patients' day-to-day activities

SLEEP AND PHYSICAL DISABILITY

- Physical disability is yet another issue in the elderly that marks the loss of independence, as difficulty in performing activities necessary for independent living increases.
- This affects sleep regardless of whether a person has assistance at home or is in a hospital intensive care unit.
- For those who have assistance at home, there are genuine concerns that their caregiver's sleep is also affected.

Other Medical Conditions Contributing to Sleep Problems of Old Age

- The majority of older adults have significant sleep disturbances, which are related to a variety of causes.
- Physical and psychiatric illnesses, and the medications used to treat them, also contribute towards sleep problems in old age.
- The prevalence of insomnia is higher among older adults and is frequently related to an underlying medical or psychiatric condition

Sleep disorders in aging: Insomnia

- Insomnia is the number one sleep disorder complaint in older adults.
- Insomnia is defined as difficulty falling asleep, staying asleep, or sleep that is nonrestorative.
- The causes of insomnia can range from medical, psychological, and psychiatric issues to environmental and behavioral issues.
- Insomnia can also stem from using drugs that may increase physiologic processes, alcohol, medications, or other substances.
- Often, elders encounter insomnia due to chronic pain and discomfort that may be caused by arthritis, esophageal reflux, and nocturia

-
- People with insomnia often experience excessive daytime sleepiness, difficulty in concentrating, and significantly reduced quality of life.
 - Both behavioral therapies and prescription medications are considered effective means to treat insomnia.
 - Reports have suggested that addressing the conditions of depression and cognitive impairment in the elderly population may help improve not only their quality of life but also reduce insomnia.

Sleep disordered breathing (SDB) and sleep apnea

- Older people also experience other sleep disorders that disturb normal sleep patterns and affect quality of life.
- SDB, or sleep apnea, affects approximately 25% of elders.
- The most common form of SDB in older adults is OSA
- Risk factors for OSA, which affects more men than women, include:
 - obesity, age, and diabetes.

OSA

- Since normal ventilation does not occur in elders with OSA and there is a cessation of airflow for more than 10 seconds, sleep is interrupted and the person may be aroused from slumber.
- This cycle causes fragmented, nonrestorative sleep.
- After years of living with this untreated problem, patients may experience right-sided heart failure, cardiac dysrhythmias, stroke, or even death.
- Snoring, which is most commonly associated with being overweight and having anatomical alterations in the upper airway, worsens with age.
- Loud snoring can be a symptom of obstructive sleep apnea, a condition in which breathing stops for as long as 10–60 s.
- A drop in oxygen in the blood during this period alerts the brain, causing a brief arousal and breathing resumes.
- Repeated stoppages of breathing cause multiple sleep disruptions at night and can result in daytime sleepiness.

Restless legs syndrome (RLS).

- Another cause of sleep disruption in older adults is RLS.
- This condition affects more than 20% of adults over age 80.
- To be diagnosed with RLS, a person must meet the following criteria: a strong urge to move the legs and feelings described as creeping, itching, tugging or gnawing; symptoms start or become worse at rest; symptoms improve with leg movement and may offer complete or partial relief; and symptoms are worse at night.

RLS

- Restless legs syndrome is a neurological disorder that can be caused or precipitated by drugs or medicines, such as SSRIs, lithium, CCBs, or withdrawal from sedatives or opioids.
- Due to the increasing problem of polypharmacy in older people, RLS is becoming more common.
- Diagnosing RLS is a lengthy process because diabetes and anemia must be ruled out with lab tests.

-
- Other medical problems can also produce sleep disorders in old age.
 - Common medical problems such as hypertension, diabetes mellitus, renal failure, respiratory diseases (e.g. asthma), immune disorders, and gastroesophageal reflux disease are all associated with sleep problems.

-
- Hypersomnia disorders such as **narcolepsy** and **idiopathic hypersomnia**, which are conditions characterized by the impairment of arousal systems, typically emerge in younger subjects and are **rare** in older subjects.

Sleep assessment in elders

- Assessing sleep disorders is critical when providing care for this population.
- The Epworth Sleepiness Scale (ESS) is a reliable, well-known sleep scale and is considered the best practice in nursing care to assess sleepiness in older adults
- The ESS distinguishes between the average amount of sleep and problems with sleep deprivation that require intervention.

Epworth Sleepiness Scale (ESS)

What is your total score from the Epworth Sleepiness Scale?

Choose

1 if score is 0-6

3 if score is 11-13

2 if score is 7-10

4 if score is > 14

Situation	Chance of dozing (0-3)			
Sitting and reading	0	1	2	3
Watching television	0	1	2	3
Sitting inactive in a public place - for example, a theater or meeting	0	1	2	3
As a passenger in a car for an hour without a break	0	1	2	3
Lying down to rest in the afternoon	0	1	2	3
Sitting and talking to someone	0	1	2	3
Sitting quietly after lunch (when you've had no alcohol)	0	1	2	3
In a car, while stopped in traffic	0	1	2	3
Total Score				13

0 = would never doze

2 = moderate chance of dozing

1 = slight chance of dozing

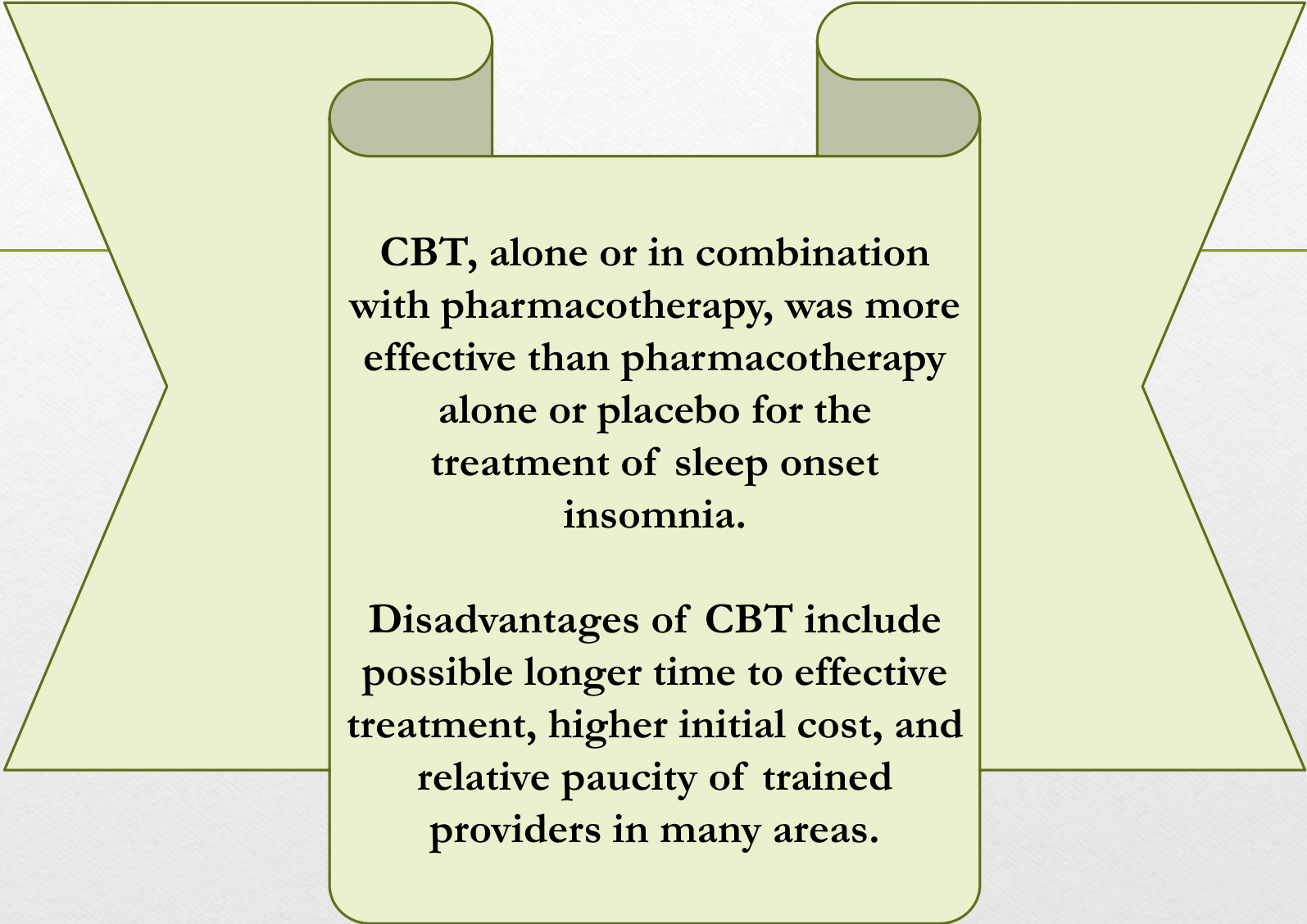
3 = high chance of dozing

-
- When conducting a history, if an older patient reports difficulty falling asleep or being able to stay asleep, frequent nighttime awakenings, or wakes up tired and groggy, further assessment and referral is warranted.
 - During a sleep assessment, the elder may report changes in behavior or mood or display physical signs of sleep deprivation that can signify an underlying sleep disorder.
 - Should ask about existing health problems and related medication use, including OTC products and alcohol.
 - Elders may self-medicate with OTC products that contain antihistamines or use alcohol as a sleep-inducing agent.

-
- Non-pharmacologic management of insomnia maybe advisable for many elderly patients.
 - Regular physical exercise is a simple strategy suggested for dealingwith sleep problems in elders because it may promoterelaxation and raise core body temperature, whichcould help in initiating and maintaining sleep.

Non-pharmacologic Treatment

- Cognitive-behavioral therapies (CBTs) are **effective, long-lasting interventions** for insomnia and considered the standard of care.
- They may be **more effective** than **pharmacotherapy** for **sleep onset latency** and **sleep efficiency**.
- The sleep benefits of these interventions are **not immediate** and can take **several weeks** to successfully implement.



CBT, alone or in combination with pharmacotherapy, was more effective than pharmacotherapy alone or placebo for the treatment of sleep onset insomnia.

Disadvantages of CBT include possible longer time to effective treatment, higher initial cost, and relative paucity of trained providers in many areas.

Sleep hygiene

- Seek out healthy social interaction to promote emotional stability and sense of wellbeing.
 - Take a warm shower and empty the bladder prior to sleep.
 - Exercise regularly, but not within four hours of sleep time.
- Avoid greasy fatty foods close to bedtime. Do not skip meals, as hunger may influence sleep quality.
 - Avoid alcohol, caffeine, and nicotine close to bedtime.
 - Keep a consistent schedule for sleep and daytime function.
- Sleep in a comfortable environment that is conducive to good sleep (appropriate bedding, temperature, noise levels, etc).
 - Establish a healthy, relaxing bedtime routine.
- Avoid television, computers, and screens (such as smart phones or tablets) for at least an hour before bedtime.
 - Use bed only for sleep and intimacy (stimulus control).

-
- Behavioral management in the older adult population must begin by eliminating common causes of insomnia.
 - For instance, teach elders to avoid caffeine and alcohol, and limit fluids before bedtime.
 - They should also avoid stimulating activities before bedtime, such as exercise, watching TV, or reading.
 - Good sleep habits can decrease problems with insomnia as well.
 - Developing a sleep ritual to ensure that the bedroom environment is soothing and relaxing helps reduce sleeplessness.
 - The bed should be used only for sleeping.
 - Elders should set an alarm clock and get up the same time each morning, and eliminate afternoon naps

-
- Proper nutrition, exercise, and healthy relationships improve mood, relieve depression, and allow for a better night's sleep.
 - Patients with medical diagnoses such as acid reflux are encouraged to eat an evening meal at least 3 to 4 hours before bedtime, with a nighttime light snack if necessary.
 - It is useful to note that sleeping with the head elevated may also help acid reflux symptoms.
 - If anxiety is present before bedtime, a warm bath may help calm nerves.
 - Often non-pharmacologic methods alone are **not effective** to treat sleep disorders.

New Approaches to remedial measures

- It should be noted that classes on drugs that are commonly used to manage insomnia, such as benzodiazepines and non-benzodiazepines, can lead to several residual side-effects like drug dependence, tolerance, rebound insomnia, muscle relaxation, hallucinations, depression, and amnesia on prolonged use.
- Consequently, there is a persistent need to find a safer hypnotics for the treatment of insomnia.
- Moreover, because of the numerous challenges associated with treating the elderly, there is an increased need to avoid potentially harmful medications

-
- Treatment with melatonin agonists has gained popularity because they have a better safety profile than sedative hypnotics that target γ -aminobutyric acid receptors.
 - Traditional medicines offer a wide range of herbs and herbal products with sedative properties, some of which can be used for prolonged periods without ill effects.
 - However, because of a lack of scientific validation, these herbs and herbal products have still not found a place in the mainstream clinical practice in sleep medicine.
 - So it is necessary to evaluate scientifically the hypnotic potential of the active principles of many of these herbs.

Pharmacologic interventions.

- Due to problems with polypharmacy in the older population, pharmacologic treatment for sleep disorders must be managed with caution.
- Pharmacologic interventions for insomnia include OTC and prescription medications.
- Major OTC sleep remedies contain antihistamines, such as diphenhydramine or doxylamine.
- Tolerance to OTC antihistamine remedies may only take 3 days and can leave older adults feeling drowsy and unproductive when they get up in the morning.
- Anticholinergic adverse reactions are often an unwanted result of treatment.

Pharmacologic interventions.

- OTC melatonin has been recommended by some practitioners to assist sleep.
- Melatonin helps patients fall asleep when taken 1 to 2 hours before bedtime and hastens time to REM sleep; however, it does not increase time spent in REM sleep.
- A newer prescription drug for insomnia, ramelteon (Rozerem), is a melatonin agonist that can help patients who experience problems with sleep onset.
- Ramelteon induces sleep within 30 minutes, but it is not effective maintaining sleep. Because ramelteon is not a controlled substance, long-term use is considered safe

Pharmacologic Treatment



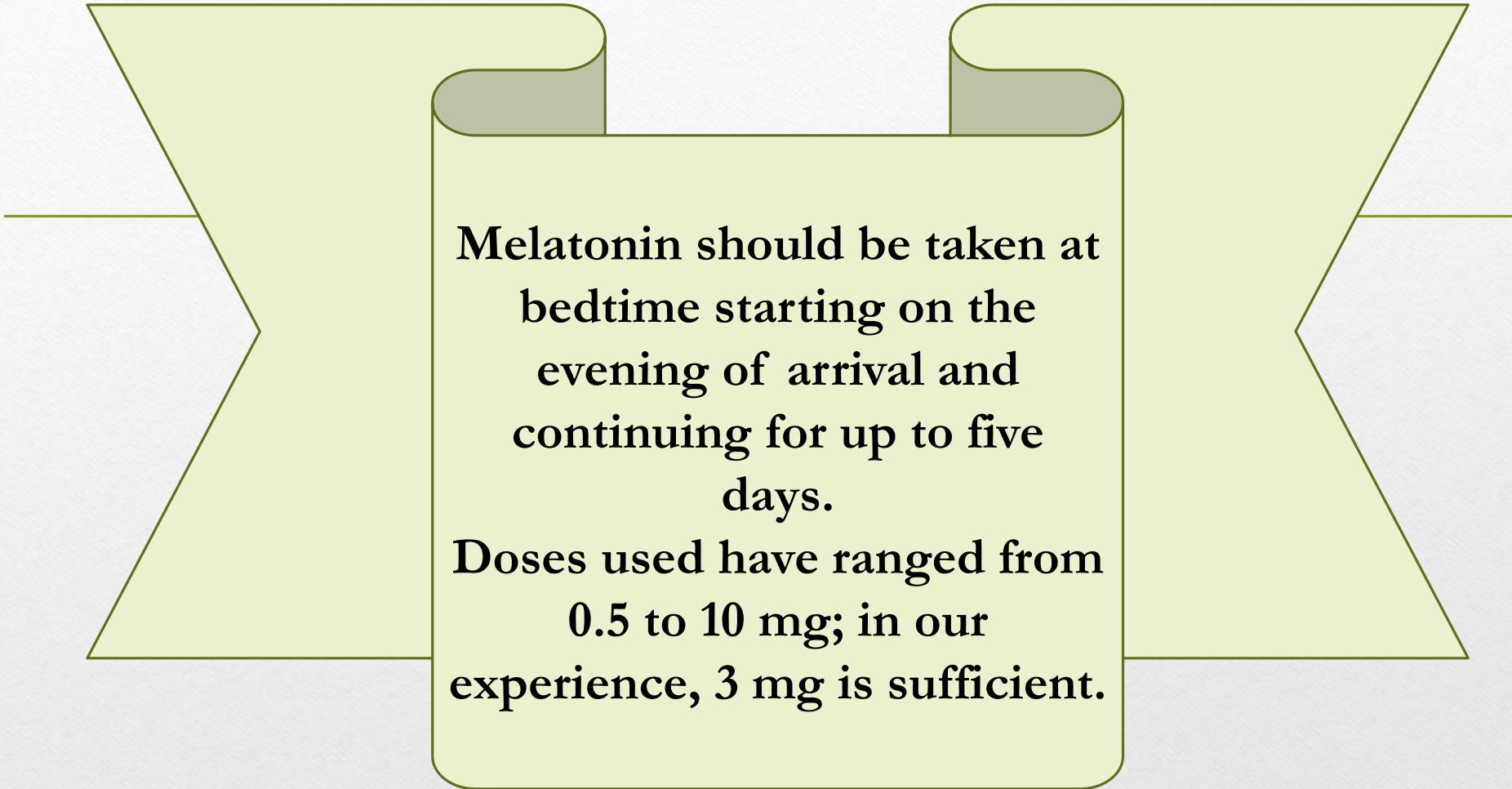
- Melatonin
 - Doses between **0.5 and 5 mg** taken close to the **target bedtime** in the **new time zone** can decrease sleep disturbances.
 - Melatonin **0.5 to 10 mg** has been found effective for entraining the circadian rhythms in **blind people**, alleviating insomnia in developmentally **disabled, handicapped, or autistic spectrum children and adults**, and treating short-term, initial insomnia in children with **attention deficit hyperactivity disorder (ADHD)**.

Although doses of **0.5 to 5 mg melatonin** are well tolerated when used for short-term period (**three months or less**).

Melatonin side effects include **sleepiness, headache, and nausea**.

Melatonin use has been associated with reports of **depression, liver disease** and **vasoconstrictive, immunologic, and contraceptive effects**.





**Melatonin should be taken at
bedtime starting on the
evening of arrival and
continuing for up to five
days.**

**Doses used have ranged from
0.5 to 10 mg; in our
experience, 3 mg is sufficient.**

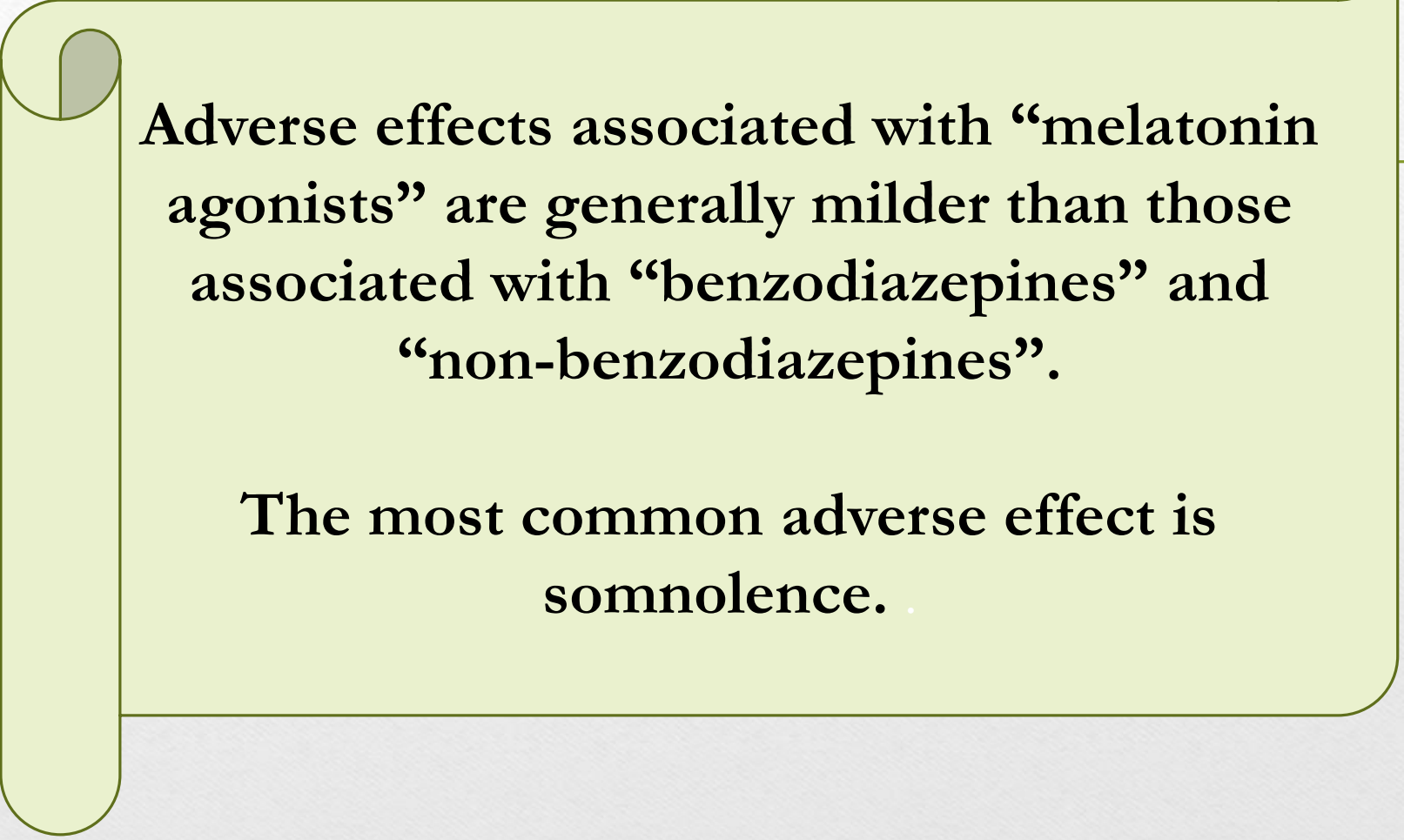
Pharmacologic Treatment

- **Ramelteon**
 - It binds to **melatonin receptors** expressed in the **suprachiasmatic nucleus** with much higher affinity than **melatonin itself** and has a half-life of **1.5 to 5 hours**.
 - It is more effective in treating **sleep onset insomnia** compared with **sleep maintenance insomnia**.
 - It is contraindicated in patients taking **fluvoxamine**, since fluvoxamine may decrease the **metabolism of ramelteon**.

Ramelteon

Fluvoxamine or
Ciprofloxacin

It may increase the risk of ramelteon toxicity.



Adverse effects associated with “melatonin agonists” are generally milder than those associated with “benzodiazepines” and “non-benzodiazepines”.

The most common adverse effect is somnolence.

Other prescription treatments for insomnia

- Drugs such as benzodiazepines, nonbenzodiazepines, and antidepressant medications.
- These medications are acceptable for short-term usage to "reset" the circadian clock and allow a good night's sleep.

Other prescription treatments for insomnia

- Benzodiazepines indicated for insomnia include: triazolam (Halcion); flurazepam (Dalmane); quazepam (Doral); estazolam (ProSom); and temazepam (Restoril).
- Therapy with these drugs, when kept **to 2 to 3 weeks**, is associated with a relatively low addiction risk.
- If longer-term therapy is warranted, they are indicated for use only **2 to 3 nights per week** because tolerance and dependence may occur.
- After discontinuing the benzodiazepine, **rebound insomnia and withdrawal symptoms** can be minimized by weaning patients off the medication.
- If possible, avoid the longer-acting benzodiazepines, as they are associated with prolonged sedation and an increased risk of falls

GABA-facilitating hypnotics, such as benzodiazepines, induce sleep and decrease arousals between stages, providing more continuous stage 2 sleep.

Benzodiazepines, however, also may decrease stage 4 slow-wave sleep and suppress REM, leading to REM sleep rebound on abrupt discontinuation.

Pharmacologic Treatment

- **Benzodiazepines**
 - The most common adverse effects associated with the benzodiazepines are **residual daytime sedation, drowsiness, dizziness, lightheadedness, cognitive impairment, motor incoordination, and dependence.**
 - **Physiologic dependence** on benzodiazepines, resulting in a withdrawal and **abstinence syndrome**, develops usually after **2 to 4 months of daily** use of the **longer half-life benzodiazepines.**
 - **Shorter half-life benzodiazepine** use can result in **physiologic dependence** earlier (**days to weeks**) and may be associated with **more withdrawal problems.**

-
- Three drugs, eszopiclone (Lunesta), zolpidem (Ambien), and zaleplon (Sonata), are considered benzodiazepine-like in their action; they induce sleep easily and leave the patient feeling refreshed.
 - These drugs may be safer to use long term, as they are less addicting and vary in their time to onset and duration of action.
 - Zaleplon (Sonata) has a duration of action of only 4 hours, which helps the patient fall asleep, even in the middle of the night, and still awake refreshed.
 - Zolpidem (Ambien) has a short duration of action. However, avoid using the extended-release formulation because of slowed elimination and metabolism in the elderly population.
 - Additionally, zolpidem has been associated with **hazardous, sleep-related activities such as driving, cooking, and eating while sleeping.**
 - The drug must be discontinued in patients who experience a sleep-driving episode.

Antidepressants

- Certain antidepressants may be used to treat insomnia in geriatric patients.
- If the patient has coexisting depression, that disorder should be addressed with the appropriate antidepressant drug.
- Antidepressants as hypnotics are not typically a first-choice treatment regimen, as these drugs may cause significant daytime sleepiness and postural hypotension, among other adverse reactions.
- For sleep disorders, this category of drugs may be helpful in older adults who have not had success with other measures, have a history of substance abuse, or have insomnia resulting from antidepressants that cause CNS stimulation.

-
- In this class, atypical antidepressants include trazodone (Desyrel) and nefazodone (Serzone), as well as tricyclic antidepressants such as amitriptyline and nortriptyline (Aventyl).
 - These drugs may be prescribed as adjunctive agents to the other "daytime" antidepressant the individual is already taking.
 - As a result, adverse reactions and drug interactions can be numerous, and it is necessary to take a careful health and drug history prior to prescribing any sleep agents for elderly patients.

Pharmacologic Treatment

- **Antidepressants**
 - **Doxepine** has been **approved by the FDA** at doses of **3 and 6 mg** primarily for the treatment of insomnia.
 - Other antidepressants (e.g., **amitriptyline [25-100 mg]**, **trazodone [50-100 mg]**) may be useful in the management of patients who have **insomnia associated with depression**.

Pharmacologic Treatment

- **Orexin receptor antagonists**
 - **Suvorexant** is an **orexin receptor antagonist**, FDA-approved in 2014 for treatment of insomnia characterized by **difficulty falling asleep** and/or **maintaining sleep**.
 - The initial recommended daily dose is **10 mg within 30 minutes of bedtime** and with at least **7 hours of sleep time** available.
 - **Suvorexant** should be taken on **an empty stomach** as time to sleep onset may be delayed by **1.5 hours** if taken **with or soon after a meal**.

Pharmacologic Treatment

- **Orexin receptor antagonists**
 - If needed, the dose can be increased in 5 mg increments to the maximum recommended daily dose of **20 mg at bedtime**.
 - No **rebound insomnia** or **withdrawal symptoms** have been observed following **abrupt discontinuation**.
 - When compared to **zolpidem**, **suvorexant** is associated with **less abuse potential**.
 - The **most commonly reported adverse effect** in clinical trials evaluating suvorexant was **daytime somnolence**.

NDC 0006-0033-30 This package contains 30 Tablets in 3 Blister Cards.
Each Blister Card contains 10 Tablets.

Belsomra®
(suvorexant) tablets 

10 mg

Dispense the accompanying Medication Guide to each patient.
Each tablet contains 10 mg suvorexant.
USUAL DOSAGE: See Package Insert.
Store at 20°C to 25°C (68°F to 77°F); excursions permitted to 15°C to 30°C (59°F to 86°F) [see USP Controlled Room Temperature]. Store in the original package until use, to protect from light and moisture.
Selling or giving away Belsomra® may harm others and is against the law.
Rx only



NDC 0006-0335-30 This package contains 30 Tablets in 3 Blister Cards.
Each Blister Card contains 10 Tablets.

Belsomra®
(suvorexant) tablets 

20 mg

Dispense the accompanying Medication Guide to each patient.
Each tablet contains 20 mg suvorexant.
USUAL DOSAGE: See Package Insert.
Store at 20°C to 25°C (68°F to 77°F); excursions permitted to 15°C to 30°C (59°F to 86°F) [see USP Controlled Room Temperature]. Store in the original package until use, to protect from light and moisture.
Selling or giving away Belsomra® may harm others and is against the law.
Rx only



Usual dose: 10 mg once daily within 30 minutes of bedtime; may increase to a maximum of 20 mg once daily if the 10 mg dose is well tolerated but not effective. Maximum daily dose: 20 mg

OSA

- Treating insomnia in older adults secondary to sleep apnea may include continuous positive airway pressure (CPAP).
- This treatment remains the most effective therapy for patients suffering from sleep apnea.
- Treatment with a CPAP machine eliminates upper-airway flow limitations in most patients, and it is associated with improved daytime symptoms and objective measures of sleepiness in patients with mild or severe abnormalities in the apnea-hypopnea index.
- Using CPAP can help reverse the detrimental effects of OSA, such as cardiac dysrhythmias, hypertension, and heart failure.

-
- **RLS**
 - Treating RLS can be difficult and may require different therapies and combinations of drugs before relief is found.
 - Little evidence-based nursing and treatment studies have been performed on patients with RLS.
 - Treatment for RLS includes a thorough assessment of patient signs and symptoms, and searching for underlying medical reasons, such as peripheral neuropathy or diabetes.
 - For older adults with mild to moderate symptoms of RLS, may suggest taking supplements to correct deficiencies in iron, folate, and magnesium.
 - Studies also have shown that maintaining a regular sleep pattern can reduce symptoms

قرص خواب آور طبیعی
بدون نسخه پزشکی (OTC)

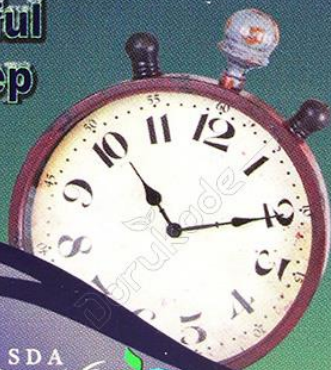
Simosleep®

30 Tablets

*** Super Snooze ***

*** Wake up Refreshed ***

Promotes
Restful
Sleep



Amount Per Serving

Calcium (as Calcium Carbonate)	50mg
Magnesium (as Magnesium Oxide)	25mg
Valerian (Valeriana Officialis) (Root)	100mg
Hops (Humulus lupulus) (Flower)	50mg
Chamomile (Matricaria recutita) (Flower)	50mg
Passion Flower (Passiflora incarnata) (aerial)	25mg
Taurine	50mg
Melatonin	5mg

SIMOSLEEP is useful in case of:

- occasional sleeplessness
- Jet lag
- Delayed sleep phase syndrome
- Major Depressive Disorder
- Antioxidant & Anticancer

Directions:

Take one (1) tablet one hour or thirty minutes before bedtime, or as directed by your healthcare provider.

Caution: Do not take if you are operating machinery or a vehicle.

Not intended for use by those under the age of 18. If you are pregnant or lactating, consult a physician prior to use.

قرص خواب آور طبیعی بدون نسخه پزشکی (OTC)
هر قرص حاوی ۵ میلی گرم ملاتونین همراه با گیاهان آرامبخش طبیعی میباشد.

نوار مصرف:

کمک به درمان بی خوابی
کمک به تنظیم خواب در مسافرت های هوایی

کمک به درمان افسردگی ناشی از کمبود ملاتونین
دارای خاصیت آنتی اکسیدانی و ضد سرطانی

میزان مصرف:

بناظر بر روزی ۱ عدد، نیم یا یک ساعت قبل از خواب

نوار هشدار:

مصرف بر اثر ماشین های باردار و شیرده و همچنین
سابق زیر ۱۸ سال توصیه نمی شود.

حتی که مصرف همزمان با داروهای دیگر با پزشک
معالج خود مشورت نمایید.

در صورت مصرف از رانندگی و کار کردن با ماشین
آلوده سنگین و خطرناک پرهیز کنید.

تذکره نگهداری:

فرآورده در دمای کمتر از ۳۰ درجه سانتی گراد،
دور از نور و رطوبت و دور از دسترس کودکان
نگهداری شود.

این دارو آورده ممکن راژیسی غذایی بوده و جهت
تشخیص، درمان و پیشگیری از بیماری نمی باشد.

Prescription:

IRC:4023421285655359



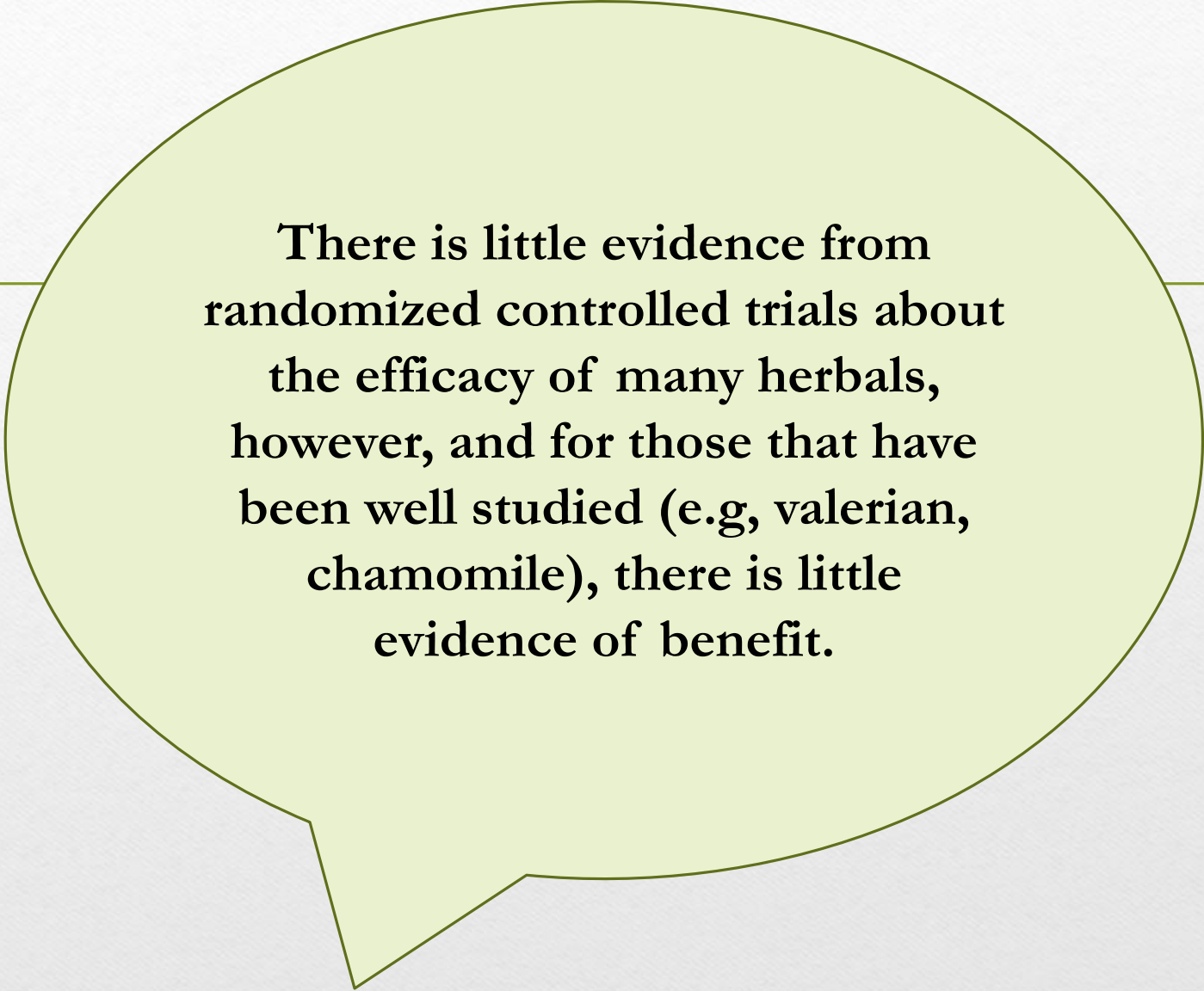
Batch No: GTN: 06263056100764
UID: 15076021907162038331
LOT: 9801
EXP: 10/07/2025

Nonpharmacologic therapies for RLS

- Encouraging moderate regular physical activity 3 days a week, or taking a hot bath before going to sleep.
- Although many patients report relief from these measures, rarely do these interventions completely eliminate RLS.
- Pharmacologic therapies for RLS include dopaminergics, benzodiazepines, opioids, and anticonvulsants.
- Dopaminergic agents, which are used to treat Parkinson disease, may reduce RLS symptoms and are, therefore, considered the treatment of choice.
- Dopaminergic agents include ropinirole (Requip), pramipexole (Mirapex), and levodopa and carbidopa (Sinemet) in an off-label use.
- Patients usually take these drugs in the evening several hours before bed, and sometimes tolerance to their effect is seen.

Pharmacologic therapies for RLS

- If patients experience tolerance to the dopaminergic agent, an increase in dosage, or a switch to a different classification of medication may be warranted.
- Benzodiazepines are known to reduce symptoms of RLS; however, they do not eliminate RLS altogether, and may lead to daytime sleepiness.
- Their use for RLS is considered off-label, and using geriatric dosage guidelines is important to prevent this adverse reaction.
- In severe cases of RLS, opioids may be prescribed to manage pain symptoms. Adverse reactions of opioids include dizziness, nausea, constipation, and vomiting



There is little evidence from randomized controlled trials about the efficacy of many herbals, however, and for those that have been well studied (e.g, valerian, chamomile), there is little evidence of benefit.

Safe prescribing practices for hypnotic medications in patients with insomnia

- Prescribe the lowest possible effective dose
- Avoid prescribing a dose greater than the maximum recommended dose
- Avoid combining with alcohol or other sedatives, including opioids
- Use increased caution in older adults and patients with renal and liver dysfunction
- In patients with comorbid depression, assess for suicidal ideation before prescribing and if present, monitor closely while considering other treatment options
- Instruct patients on proper timing of the drug in relation to desired sleep onset
- Instruct patients on drug half-life and expected duration of effect
- Advise against use if there is insufficient time for drug elimination between planned bedtime and rise time
- Discuss risk of next-day impairment in alertness, memory, coordination, and driving
- Discuss risk of complex sleep-related behaviors such as sleep walking, eating, and driving
- Schedule regular follow-up to review efficacy, side effects, non-pharmacologic options, and assess ongoing need for medication