Sleep is a naturally recurring state characterized by reduced or absent consciousness, relatively suspended sensory activity and inactivity of nearly all voluntary muscles. It is distinguished from wakefulness by a decreased ability to react to stimuli and is more easily reversible than being in coma. Sleep is a heightened anabolic state accentuating the growth and rejuvenation of the immune, nervous, skeletal and muscular systems [1].

The purposes and mechanisms of sleep are only partially clear and the subject of many studies. Sleep is sometimes thought to help to conserve energy, though this theory is not fully adequate as sleep only decreases metabolism by about 5–10% [2].

Physiology of sleep

Sleep is divided into two broad types: rapid eye movement (REM) and non-rapid eye movement (NREM or non-REM) sleep. NREM is further subdivided into three stages as follows [3]:

- **NREM stage 1**: This is a stage between sleep and wakefulness. The muscles are active and the eyes roll slowly, opening and closing moderately;
- **NREM stage 2**: In this stage, it gradually becomes harder to awaken the sleeper;
- **NREM stage 3**: The sleeper is less responsive to the environment. Many environmental stimuli no longer produce any reactions.

**REM sleep**

The sleeper enters REM where most muscles are paralyzed. REM sleep is turned on by acetylcholine secretion and is inhibited by neurons that secrete serotonin. This level is also referred to as paradoxical sleep because the sleeper, although exhibiting EEG waves similar to waking state, is harder to arouse than at any other sleep stage. Vital signs indicate arousal and oxygen consumption by the brain is higher than when the sleeper is awake [2, 4].

Sleep proceeds in cycles of REM and NREM, usually four or five of them per night. There is a greater amount of deep sleep earlier in the night, while the proportion of REM sleep increases in the two cycles just before natural awakening [5].

**Functions of REM sleep**

Most dreams occur during REM sleep. Deprivation of REM may lead to psychological disturbances and dramatic shift in subsequent sleep patterns when the subject is allowed to sleep without interruption. The longer the deprivation, the larger and longer the REM rebound, suggesting that REM sleep is physiologically necessary. However, the purpose of REM sleep or dreaming remains largely unexplained [4].

There is activation of sensory systems during REM sleep. The visual system is intensely activated and all dreams have visual experiences. Neuroimaging studies have indicated activation of the limbic system, suggesting a biologic basis of activation of memories and emotions in REM sleep. Studies in animals indicated that those neurons that had been active during the day fired at a significantly higher rate in REM sleep than inactive neurons, suggesting that a general function of REM sleep is processing of the information acquired during the day [6].

**Neural mechanisms involved in the sleep-wake cycle**

The body’s sleep-wake cycle is usually under the control of circadian rhythm which is regulated by the suprachiasmatic nucleus of the hypothalamus. Incoming light transduced by retinal ganglion cells is believed to be the primary factor synchronizing circadian rhythm. Serotonin acts as a modulatory neurotransmitter which inhibits the effects of light on the system and is associated with different aspects of the sleep-wake cycle. There is minimal serotonergic input during REM sleep and maximal input directly following REM. Thus, these neurons may normally inhibit phasic REM events and their silence during REM sleep indicates a termination of this inhibition [7].

On the other hand, many sleep-promoting factors have been identified, including muramyl peptides, lipopolysaccharides, prostaglandins, interleukin-1, interferon-alpha 2, tumor necrosis factor, sleep-inducing peptide and vasoactive intestinal peptide. Besides enhancing sleep, they exert effects on the body temperature and on the immune response [8].

In the past few years, it has been established that the cholinergic activating system is important in waking and REM sleep. REM-on neurons (selective activity during REM sleep) in the brainstem use acetylcholine as a neurotransmitter. Most of the physiologic events of REM sleep have effector neurons located in the brainstem reticular...
formation. These neurons are important for the rapid eye movements and the muscle atonia of REM sleep [9].

Many peptides such as substance P are co-localized with acetylcholine in brainstem neurons. They may modify responsiveness to acetylcholine and may have independent actions. In addition, histamine-containing neurons are located in the posterior hypothalamus and are REM-off. The histamine system has been considered as one of the wakefulness promoting systems, in agreement with drowsiness as a common side effect of antihistamines [10].

Orexin is a hypocretin that has been associated with feeding behaviors and also has been found to have a role in the sleep behavior. Many areas of the brain associated with the sleep-wake cycle, specifically the lateral and dorsal hypothalamus, have orexin neurons and receptors. Orexin has been found to activate norepinephrine neurons in the locus ceruleus which are believed to play a role in promoting wakefulness [11].

Sleep timing
Sleep timing is controlled by the circadian clock, sleep-wake homeostasis and, within certain limits, willed behavior. The circadian clock works with adenosine, a neurotransmitter that inhibits many processes associated with wakefulness. Adenosine is created over the course of the day and high levels of adenosine lead to sleepiness. The timing is affected by one’s chronotype. It is the circadian rhythm that determines the ideal timing of a correctly structured and restorative sleep episode [12].

Homeostatic sleep propensity (the need for sleep as a function of the amount of time elapsed since the last adequate sleep episode) must be balanced against the circadian element for satisfactory sleep. Along with corresponding messages from the circadian clock, this tells the body it needs to sleep. Sleep duration is affected by the gene DEC2. Some people who have a mutation of this gene sleep two hours less than normal [13].

Optimal amount of sleep
Human sleep needs vary by age and among individuals, and sleep is considered to be adequate when there is no daytime sleepiness or dysfunction. One of the most significant determinants of a person’s normal sleep pattern is age. REM sleep occupies about 20-25% of the sleep time in normal young adults. The daily total sleep requirement declines steadily throughout childhood and adolescence and then often declines further with old age [14].

Sleep disorders
A sleep disorder is a medical disorder of the sleep patterns of a person. Some sleep disorders are serious enough to interfere with normal physical, mental and emotional functioning. Disruptions in sleep can be caused by a variety of causes. When a person suffers from difficulty falling asleep and staying asleep with no obvious cause, it is referred to as insomnia [15]. Dysomnia refers to a group of sleep disorders with the symptoms of trouble falling asleep or maintaining sleep, which may cause an elevated sense of sleepiness during the day.

Insomnia is characterized by many symptoms including trouble with retaining sleep, fatigue, decreased attention and dysphoria. Individuals with insomnia often worry about the negative health consequences, which can lead to development of anxiety and depression [16]. In addition, sleep disorders may also cause the patient to sleep excessively, a condition known as hypersomnia. Management of sleep disturbances that are secondary to mental, medical, or substance abuse disorders should focus on treatment of the underlying conditions [17].

Insomnia can be classified as transient, acute or chronic [16, 18]:

- Transient insomnia lasts for less than a week. It can be caused by another disorder, by changes in the sleep environment, by the timing of sleep, severe depression or by stress. Its consequences – sleepiness and impaired psychomotor performance – are similar to those of sleep deprivation [5].
- Acute insomnia is the inability to consistently sleep well for a period of less than a month. This occurs despite adequate opportunity and circumstances for sleep and often results in problems with daytime function. Acute insomnia is also known as short term insomnia or stress related insomnia [19].
- Chronic insomnia lasts for longer than a month. It can be caused by another disorder or it can be a primary disorder. People with high levels of stress hormones or shifts in the levels of cytokines are more likely to have chronic insomnia. Its effects vary according to its causes including muscular fatigue, hallucinations and/or mental fatigue. Chronic insomnia can cause double vision [18].

Hypersomnia
Hypersomnia is trouble staying awake and excessive daytime sleepiness. Patients usually complain of fatigue, headache, decreased energy and difficulty in concentration [20]. The most common causes of hypersomnia are insufficient sleep, medications, sleep apnea and narcolepsy:

Insufficient sleep: Many people do not schedule sufficient time for sleep at night and sleepiness is to be expected due to sleep deprivation. This is managed by education the patient about healthy sleep habits [21].

Sleep apnea: It is a condition in which patients periodically stop breathing while asleep. There are two types of sleep apnea - central and obstructive. The most common cause of sleep apnea is due to temporary obstruction of the upper airway. The extreme changes in the concentrations of oxygen and carbon dioxide in the blood that develop after 1 minute or more without air rouse the sleeper, and a
few noisy choking gasps refill the lungs [22]. Obstructive sleep apnea is the most common medical cause of excessive daytime sleepiness. Usually, the patients are not aware of the episodes because they are brief and arousal is only partial. So, the history must be obtained indirectly from a spouse or roommate.

Manifestations include loud snoring, pauses in breathing, gasping for breath during sleep, dull headache and automatic behaviors. Polysomnography is used to confirm the diagnosis and to quantify the severity [23]. The most effective treatment of obstructive sleep apnea is nasal continuous positive airway pressure which raises the pressure in the oropharynx and thus in the upper airway, reversing the pressure gradient across the wall of the airway and keeping it open [24].

Narcolepsy: Narcolepsy is a syndrome consisting of excessive daytime sleepiness and disordered regulation of REM sleep resulting in intrusion of components of REM sleep into NREM sleep and the waking state. It has 2 types which include narcolepsy-cataplexy subtype and narcolepsy without cataplexy [25, 26].

Idiopathic hypersomnia
They are poorly defined conditions characterized by excessive daytime sleepiness and not diagnosed as narcolepsy (No REM abnormalities during polysomnography) [27].

Parasomnias
It means abnormal behavior during sleep. The most undesirable movements or behaviors that occur during sleep are associated with NREM sleep, probably because the atonia of REM sleep prevents most movements of any kind [28].

NREM sleep parasomnias
These are relatively common in children but they rarely lead to medical attention unless they are frequent and intense. In most cases, they resolve by late adolescence. They may represent a disorder of arousal from slow wave sleep resulting in episodes of only partial awakening [29]. They include night terrors, sleepwalking and restless leg syndrome:

Night terrors: These are sudden, partial arousal from sleep associated with screaming and motor activity. These episodes occur during the first third of the major sleep episode and begin with a terrifying scream followed by intense anxiety and signs of autonomic hyperactivity. Persons with night terrors may not fully awaken after an episode and usually have no detailed recall of the event the following morning. There is believed to be a genetic component to this phenomenon [30].

Sleepwalking (Somnambulism): It is considered as a disorder of impaired arousal. Sleepwalking is defined as repeated episodes of arising from sleep and walking about. It usually occurs during the first third of the sleep episode. Upon awakening, the person has amnesia for the episode. Episodes typically last less than 10 minutes [31].

Restless legs syndrome (RLS): It is a sensorimotor disorder that may severely affect sleep. It is characterized by a strong urge to move the legs accompanied by a strange feeling in the leg. The attacks are precipitated by rest with inactivity and they become worse in the evening or night than in the morning. The periodic leg movements may occur during sleep and/or while lying or sitting up awake. RLS involves a disorder of the transition states between wake and sleep. Although RLS produces chronic loss of sleep, there is no profound frank sleepiness in the daytime. RLS patients report fatigue and trouble concentrating during the day but do not fall asleep and appear to be overstimulated in the daytime [32].

Early-onset RLS (starting before age 45) appears to result mostly from iron metabolism abnormality producing brain iron insufficiency. The impaired iron status produces a hyperdopaminergic state with an exaggerated circadian pattern of dopamine release. The iron deficiency probably also disrupts other neurotransmitter systems, such as hypocretin (orexin) and histamine [33]. Late-onset RLS (starting after age 45) has more diverse causes, but patients appear to have dopamine abnormalities similar to those in early-onset RLS cases.

RLS etiology appears to have both a genetic and a strong environmental component, with the genetic component more important for early- than for late-onset RLS. Dopaminergic agonists and levodopa provide effective treatment for RLS because the pathophysiology may involve brain dopamine abnormalities. Also there is evidence for involvement of hypocretin-1 (orexin-A) and histamine [32, 34].

REM sleep parasomnias

REM sleep behavior disorder (RBD): In this condition, the atonia that normally accompanies REM sleep breaks down and patients act out parts of dreams. This is a motor and behavioral disorder typically affecting middle-aged or older males. The vigorous and violent behaviors of RBD commonly result in injury. It includes intermittent loss of the usual skeletal muscle atonia of REM sleep, with increased muscle tone and/or excessive muscle twitching.

RBD can be an acute or chronic disorder. Acute RBD, found in drug withdrawal or intoxication states, is generally a reversible condition. Chronic RBD requires pharmacotherapy and is commonly associated with many other conditions, especially synucleinopathies (Parkinson disease, dementia with Lewy bodies and multiple system atrophy) [29].

A close association of RBD with narcolepsy-cataplexy has been described, and there are patients with overlapping parasomnias, demonstrating motor-behavioral dyscontrol extending across NREM and REM sleep. The probable cause of RBD is pontine tegmental lesions, involving serotoninergic and cholinergic neurotransmission. It is thought that RBD results from lesions related to any underlying neurological disorder [35].

Nightmare disorder (dream anxiety): This condition consists of repeated awakenings with detailed recall of extended and very frightening dreams. The awakenings are more frequent in the second half of the sleep period. On awakening, the person rapidly becomes alert and oriented [36].

Diagnosis of sleep disorders
The following tests are used to diagnose insomnia [23]:

• Sleep diary: Tracking sleep patterns may help a doctor reach a diagnosis;
• Epworth Sleepiness Scale: a validated questionnaire that is used to assess daytime sleepiness;
• Polysomnogram: a test measuring brain and muscle activity including breathing during sleep.
• Multiple sleep latency test: a test for daytime sleepiness, usually administered the day after overnight polysomnography.
• Actigraphy: a test used to assess sleep-wake patterns, usually for a week or more. Actigraphs are wrist-worn devices, about the size of a wristwatch, that measure movement.
• Mental health examination: Because insomnia may be a symptom of depression, anxiety or another mental health disorder, examination of the mental status, mental health history and basic mental evaluations may be important parts of the assessment for a person complaining of insomnia.

Treatment of sleep disorders

Treatments for sleep disorders generally can be grouped into four categories including behavioral and psychotherapeutic treatment, rehabilitation and management, medication and other somatic treatment [17].

None of these general approaches is sufficient alone for all patients with sleep disorders. The choice of a specific treatment depends on the patient’s diagnosis, medical and psychiatric history as well as the experience of the treating clinician. Often, behavioral/psychotherapeutic and pharmacological approaches can be combined to maximize therapeutic benefits. Management of sleep disturbances that are secondary to medical, mental, or substance abuse disorders should focus on treatment of the underlying conditions [23].

Medications and somatic treatments may provide the most rapid symptomatic relief from some sleep disturbances. Certain disorders like narcolepsy, are best treated with drugs such as Modafinil. Others, such as chronic and primary insomnia, may be more responsive to behavioral interventions. Special equipment may be required for treatment of several disorders such as obstructive apnea, the circadian rhythm disorders and bruxism. In these cases, when severe, an acceptance of living with the disorder, however well managed, is often necessary [23, 25].

A number of studies suggests that hypnosis may be helpful in alleviating some types and manifestations of sleep disorders in some patients. Acute and chronic insomnia often respond to relaxation and hypnotherapy, along with sleep hygiene instructions. Hypnotherapy also helps with nightmares and sleep terrors. There are several reports of successful use of hypnotherapy for parasomnias specifically for head and body rocking, bedwetting and sleepwalking. Hypnotherapy can be carried out with benzodiazepines such as temazepam which is a commonly prescribed drug for insomnia and other sleep disorders [37, 38].

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