Medical Education Systems, Inc.

Course

REM SLEEP 917

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REM Behavior Disorder

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Learning Objectives

Upon successful completion of this continuing education course, you will be able to:

- Define what is meant by “REM Behavior Disorder” (RBD) and discuss the causes
- Identify and discuss the potential consequences of having RBD
- Explain how RBD is diagnosed
- Identify and explain the treatments available for RBD

REM Sleep Behavior Disorder

As the name suggests, REM sleep behavior disorder occurs during REM [Rapid Eye Movement] sleep. Patients with this disorder experience episodes of acting out some or all of their dreams. This disorder is more common in middle-aged or elderly men.

The patient may walk, talk, jump, hit, or perform any other action during their dreaming. Most people (the "normal") are partially paralyzed during REM sleep, which prevents them from moving at all. They are unaware of the environment outside of their dream during the disorder's occurrences. When patients have been awakened during REM sleep disorder events, they usually describe dreams involving the same actions they had just made. These episodes do not occur every night, and can range in frequency and severity.

This disorder was first described in 1986. Little is known about this disorder. Clonazebam, or klonopin, a type of benzodiazepine drug, can sometimes prevent these episodes from happening. Other treatment consists of taking careful measures to ensure the safest sleeping environment as possible. Often it is best for the person to sleep alone, so that the bed partner won't be injured. There have been instances in which a sleeper with this or a similar disorder has committed a violent crime while sleeping.

> Basically: "The brain activity during REM, begins in the pons, a structure in the brainstem and neighboring midbrain regions. The pons sends signals to the thalamus and to the cerebral cortex, which is responsible for most thought processes. It also sends signals to turn off motor neurons in the spinal cord, causing a temporary paralysis that prevents movement."
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> Technically: "In normal REM sleep the pons strongly activates the inhibitory center in the medulla. The midline inhibitory zone in the pons inhibits the lateral locomotor strip. The result is complete paralysis. In REM sleep without paralysis, the lesions break the connections from the pons to the locomotor strip and to the medullary center. In REM sleep the pons is activated, exciting the medullary inbibitory area by projections (tegmento-reticular tract) which connects the pons to the inhibitory center. The medullary center inhibits the motor neurons and gives rise to atonia. A lateral locomotor strip, down the outside of the brain stem, plays an important role in the reduction of motor drive. It is connected to structures in the spinal cord. In REM sleep the pons stimulates the inhibitory zone, turning off the locomotor strip and shutting down motor drive." Dr. Silvia Cardoso, a neuroscientist at a Brazilian university who edits Brain & Mind, an electronic journal on neuroscience, explains that the basis for this REM disorder seems to be a disruption of the brain stem systems that normally mediate REM atonia."

What is REM Behavior Disorder?

For most people, dreams are purely a "mental" activity: they occur in the mind while the body is at rest. But people who suffer from REM behavior disorder (RBD) act out their dreams. They physically

move limbs or even get up and engage in activities associated with waking. Some talk, shout, scream, hit, punch, or fly out of bed while sleeping! RBD is usually noticed when it causes danger to the sleeping person, their bed partner, or others they encounter. Sometimes ill effects such as injury to self or bed partner sustained while asleep trigger a diagnosis of RBD. The good news is that RBD can usually be treated successfully.

Why Does RBD Occur?

What we call "sleep" involves transitions between three different states: wakefulness, rapid eye movement (REM) sleep, which is associated with dreaming, and non rapid eye movement (N-REM) sleep. There are a variety of characteristics that define each state, but to understand REM Behavior Disorder it is important to know that it occurs during REM sleep. During this state, the electrical activity of the brain, as recorded by an electroencephalogram, looks similar to the electrical activity that occurs during waking. Although neurons in the brain during REM sleep are functioning much as they do during waking, REM sleep is also characterized by temporary muscle paralysis.

In some sleep disorders such as narcolepsy and parasomnias, like REM behavior disorder, the distinctions between these different states breaks down; characteristics of one state carry over or "invade" the others. Sleep researchers believe that neurological "barriers" that separate the states don't function properly, though the cause of such occurrences is not entirely understood.

Thus, for most people, even when they are having vivid dreams in which they imagine they are active, their bodies are still. But, persons with RBD lack this muscle paralysis, which permits them to act out dramatic and/or violent dreams during the REM stage of sleep. Sometimes they begin by talking, twitching and jerking during dreaming for years before they fully act out their REM dreams.

In the course of "acting out their dreams," people with RBD move their arms and legs in bed or talk in their sleep, or they might get out of bed and move around without waking or realizing they're dreaming. The only sensations the sleeper experiences are what is occurring in their dream. And many of these dreams can be violent or frightening, causing injury to the sleeper and his bed partner.

Who discovered RBD?

The first series of cases of RBD was described in 1985 by Mark Mahowald, MD, and Carlos Schenck, MD, of the University of Minnesota. In *Principles and Practice of Sleep Medicine* (W.B. Saunders Company, 2000), they outlined several case histories of people with RBD:

- A 77-year old minister had been behaving violently in his sleep for 20 years, sometimes even injuring his wife.
- A 60-year old surgeon would jump out of bed during nightmares of being attacked by "criminals, terrorists and monsters."
- A 62-year old industrial plant manager who was a war veteran dreamt of being attacked by enemy soldiers and fights back in his sleep, sometimes injuring himself.
- A 57-year old retired school principal was inadvertently punching and kicking his wife for two years during vivid nightmares of protecting himself and family from aggressive people and snakes.

"Past history and current neurological and psychiatric evaluations were unremarkable, apart from the findings reported," the authors noted. "All four men were known by day to be calm and friendly individuals."

Who has RBD?

Drs. Mahowald and Schenck and others have found that more than 90% of RBD patients are male, and that the disorder usually strikes after the age of 50, although some patients are as young as nine years old. Most RBD patients are placid and good-natured when awake; however, many of them display rhythmic movements in their legs during non-REM and slow-wave sleep.

A telephone survey of more than 4,900 individuals between the ages of 15 and 100 indicated that about two percent of those surveyed experience violent behaviors during sleep; Mahowald and Schenck estimate that one-quarter of them were probably due to RBD, which means it may be experienced by 0.5% of the population.

What causes RBD?

Studies of animals may explain REM behavior disorder. Animals who have suffered lesions in the brain stem have exhibited symptoms similar to RBD. Cats with lesions affecting the part of the brain stem that involves the inhibition of locomotor activity will have motor activity during REM sleep: they will arch their backs, hiss and bare their teeth for no reason, while their brain waves register normal REM sleep.

"REM behavior disorder underscores the importance of basic science research in animals," says Mahowald, "because without the information obtained in basic science animal research, the disorder could never have been identified. Sleep is such a young field that we have the opportunity to take advantage of the fact that there is a close collaboration between basic science and clinicians."

How is RBD diagnosed?

Because a number of parasomnias may be confused with RBD, it is necessary to conduct formal sleep studies performed at sleep centers that are experienced in evaluating parasomnias in order to establish a diagnosis. In RBD, a single night of extensive monitoring of sleep, brain, and muscle activity will almost always reveal the lack of muscle paralysis during REM sleep, and it will also eliminate other causes of parasomnias.

How is RBD treated?

Clonazepam, a benzodiazapine, curtails or eliminates the disorder about 90% of the time. The advantage of the medication is that people don't usually develop a tolerance for the drug, even over a period of years. When clonazepam doesn't work, some antidepressants or melatonin may reduce the violent behavior. However, it's a good idea to make the bedroom a safe environment, removing all sharp and breakable objects.

What other disorders are associated with RBD?

Drs. Schneck and Mahowald have conducted research indicating that 38% of 29 otherwise healthy patients with REM behavior disorder went on to develop a parkinsonian disorder, presumably

Parkinson's disease (PD), a degenerative neurological disease characterized by tremors, rigidity, lack of movement or loss of spontaneous movement, and problems with walking or posture. Other studies have found associations between RBD and other neurodegenerative diseases related to Parkinson's. "We don't know why RBD and PD are linked," says Dr. Mahowald, "but there is an obvious relationship, as about 40% of individuals who present with RBD without any signs or symptoms of PD will eventually go on to develop PD."

Should patients with RBD be concerned about developing Parkinson's?

"People with RBD will understandably be concerned about the possibility of the later development of PD, given the statistics," says Mahowald. "We are not aware of anything that can be done to prevent or delay the development of PD in those destined to do so. We recommend an annual evaluation by a neurologist, so if PD is going to develop, it can be detected and treated at the earliest possible time.

"Given the fact that the majority of patients with RBD who went on to develop PD were already taking clonazepam, it is unlikely that clonazepam will reduce the likelihood of developing PD in those so predisposed."

And now for a look at RBD from different perspectives:

RBD Overview

Patients with rapid eye movement behavior disorder (RBD) act out dramatic and/or violent dreams during rapid eye movement (REM) stage sleep. Another feature of RBD is shouting and grunting. RBD seems similar to other sleep disorders that involve motor activity, like sleepwalking or periodic limb movement disorder. Unlike these conditions, RBD movements occur during REM sleep, which is usually characterized by a state of atonia, or sleep paralysis. Diagnosis and treatment involves polysomnography, drug therapy, and the exclusion of potentially serious neurological disorders.

RBD is usually seen in men 60 years old or older, but also occurs in younger people and in women. Incidents of REM behavior disorder are often described anecdotally to family members and not to physicians, so statistics of incidence are inexact.

Physiology and Causes

Rapid eye movement behavior disorder is an uncommon sleep disorder first described in 1986. There is no known cause for RBD. It is, however, known to occur during rapid eye movement sleep, which is characterized by brain activity patterns that resemble wakefulness and which has been documented with polysomnography and other sleep tests. Most dreaming occurs during REM sleep. Another characteristic of REM sleep is a general state of atonia, or muscle paralysis. So, while the brain is very active during REM sleep, the body is usually still.

Sleep Paralysis

The basic mechanism for REM sleep paralysis is found in the brainstem, the part of the brain that connects the spinal chord to the cerebral hemispheres and that consists of the pons, midbrain, and the medulla oblongata. Though physicians do not thoroughly understand the complex processes, it is known that the brainstem undergoes changes in REM sleep that result in paralysis of the body’s voluntary muscles. Certain neurotransmitters, like acetylcholine (Ach), become dormant and do not communicate motor activity. The absence of muscular contraction during REM can be seen with polysomnography. The electroencephalogram (EEG) shows elevated brain activity during REM.

Physicians and sleep technicians hypothesize that the brain naturally and purposely prevents motor activity during REM sleep to ensure restful, inactive sleep during the most electrically active stage of sleep. In this context, sleep paralysis describes a normal state of sleep, unlike sleep paralysis experienced in narcolepsy, which affects people while they are trying to stay awake.

Motor Activity and REM Sleep

In RBD, neurotransmitters are not blocked, and the voluntary muscles become tonic, or tensely contracted, allowing a sleeping person to move his or her muscles during REM. Rapid eye movement behavior disorder is characterized by significant submental (under the chin) and limb muscle tone. The combination of heightened cerebral activity and muscular tonicity results in physically acting out dreams that involve excited and sometimes violent movement.

The body can be rigid and extremely tense during episodes of RBD. For example, a person might straighten his or her leg, flexing it intensely for several seconds or a minute. Often, sleepers curl up slightly, while flexing their limbs and chin.

People with RBD typically remember little nothing of this activity, unless they fall out of bed, bump into the furniture, or injure themselves and wake up. But they can usually remember and tell the dreams they were having during an episode.

Dreams that involve physical or violent activity—such as fighting, dancing, running, chasing, attacking, being attacked, running from an assailant—are more likely to trigger RBD activity. Sleepers with RBD sometimes injure their bed partners. Some people have been known to leave the bed, run into a wall, run through a window, or run down the stairs. But RBD activity is usually confined to the bed and the surrounding area.

Diagnosis

In addition to polysomnography, which records activity levels during REM sleep, diagnosis of RBD is based on sleep history, testimony of sleep partners, and one or several overnight video recordings of REM sleep activity. Video recordings present patients with an impressive and surprising revelation of their disorder.

Most cases of RBD are not associated with other disorders. It is, however, necessary to rule out myoclonic seizures, which are the product of neurological dysfunction and which may compromise health if not treated. Also, RBD symptoms have been described in cases of degenerative neurological disorder, like brainstem lesions. In cases of severe RBD and perhaps those that do not respond to treatment, diagnosis with magnetic resonance imaging (MRI scan) may help physicians exclude or detect other conditions, such as those listed below.

- Narcolepsy
- Dementia
- Subarachnoid hemorrhage (of the region where the spinal chord meets the brain)
- Stroke
- Parkinson’s Disease

- Olivopontocerebellar degeneration (of the pons, cerebellum, and olivary nucleus)
- Multiple Sclerosis
- Guillain-Barre' syndrome (destruction of peripheral nerves)
- Antidepressant use (including Fluoxetine and tricyclics)
- Treated obstructive sleep apnea

RBD and Parkinson's Disease
There is some evidence to suggest that RBD precipitates Parkinson's disease. Parkinson's disease is caused by the continual death of dopamine-producing brain cells. Dopamine inhibits and regulates muscle control. Parkinson's disease and RBD have been known to happen concurrently, but the relationship has not been proven. In one study, nearly 40% of men in their late 60s, who demonstrated RBD, later developed Parkinson's disease. Parkinson's disease affects as many women as it does men, but this isn't true of RBD.

Treatment

Clonazepam - Patients with RBD usually respond to treatment with clonazepam when taken nightly. Clonazepam is an antidepressant with anticonvulsant effects that has been shown to block neurotransmission in people with RBD, allowing them to achieve atonia and a state closer to REM paralysis. People with renal complications, pregnant women, and people who are taking other medications may not be good candidates for treatment with clonazepam.

Safety - People with RBD risk injuring themselves and their sleep partners. The frequency and intensity of RBD episodes are sometimes too much for a sleep partner to endure. This is often hard for those who suffer from RBD to understand, because they usually don't remember the episode because they sleep through it. Sleeping in a big bed can minimize the chance a sleep partner will be injured, but sleep partners often end up sleeping in different beds or even in different rooms.

A ground floor bedroom is recommended, especially for people who actually leave the bed during an episode. Placing heavy drapes over the windows to make going through them difficult, removing sharp objects from the room, padding the bed and nearby furniture, and clearing the floor around of furniture are all steps that can be taken to prevent injury.

Withdrawal from certain medications (e.g., tricyclics, monoamine oxidase inhibitors), alcohol, caffeine, and illicit drugs can cause acute episodes of RBD. Sudden discontinuation of controlled medication should be avoided under all circumstances.

REM Sleep Behavior Disorder

ABM Salah Uddin, MD, **Consulting Staff, Department of Internal Medicine, Carraway Methodist Medical Center** Tambi Jarmi, MD, **Staff Physician, Department of Internal Medicine, Carraway Methodist Medical Center**

Background: Rapid eye movement (REM) sleep behavior disorder (RBD) is a newly described disorder, recognized as a distinct clinical entity following a series of reports in 1986 of adults with

RBD. RBD is the best studied REM sleep parasomnia. Clinically, RBD is characterized by loss of normal voluntary muscle atonia during REM sleep associated with complex behavior while dreaming. According to the International Classification of Sleep Disorders, the minimal diagnostic criteria include movements of the body or limbs associated with dreaming and at least one of the following criteria: potentially harmful sleep behavior, dreams that appear to be acted out, and sleep behavior that disrupts sleep continuity (American Sleep Disorders Association, 1997). In 1965, experimental models showed that cats with bilateral pontine lesions adjacent to the locus ceruleus act out their dreams.

Pathophysiology: Normally, generalized atonia of muscles occurs during REM sleep. This atonia results from active inhibition of motor activity by pontine centers (i.e., perilocus ceruleus) that exert an excitatory influence on the medulla (i.e., magnocellularis neurons) via the lateral tegmentoreticular tract. These neuronal groups, in turn, hyperpolarize the spinal motor neuron postsynaptic membranes via the ventrolateral reticulospinal tract. In RBD, the brainstem mechanisms generating the muscle atonia normally seen in REM sleep may be interfered with.

Studies by Eisensehr et al using iodine 123 (^{123}I) immunoperoxidase technique (IPT) single photon-emission computed tomography (SPECT) demonstrated that striatal presynaptic dopamine transporters are reduced in idiopathic RBD. Recent studies by Fantini et al demonstrated impairment of cortical activity in idiopathic RBD, particularly in the occipital region during both wakefulness and REM sleep compared with controls. Results were similar to the functional studies such as perfusion and metabolic impairment pattern observed in diffuse Lewy body (DLB) disease and to some extent in Parkinson disease. Similar cortical activity in the frontal and temporal regions was impaired only during wakefulness. The subcortical structures involved in the pathophysiology of RBD provide dopaminergic (nigrostriatal neurons), noradrenergic (locus coeruleus), and cholinergic innervation (pedunculopontine tegmental nucleus) of the cerebral cortex and play a role in cortical activation during wakefulness and REM sleep.

In essence, RBD may be the prodrome of neurodegenerative disease, such as DLB or Parkinson disease. In experimental studies in cats, bilateral pontine lesions resulted in a persistent absence of REM atonia associated with prominent motor activity during REM sleep similar to that observed in RBD in humans.

Frequency:

- In the US: The exact incidence and prevalence of RBD are unknown because of inadequate reporting and misdiagnosis. However, a recent telephone survey indicated a 2% overall prevalence of violent behaviors during sleep, 25% of which were likely to be due to RBD. This gives a prevalence of 0.5% of RBD in the general population.
- Internationally: No difference in the frequency of RBD exists internationally.

Mortality/Morbidity: The morbidity and mortality rates of RBD depend on the etiology.

- No death has been reported in idiopathic cases; however, patients and bed partners may experience serious injury. In the reported cases, 32% of patients had injured themselves and 64% had assaulted their spouses. Subdural hematomas occurred in 2 patients.
- In secondary cases, the morbidity and mortality rates depend on the specific underlying disease itself.

Race: Racial differences in incidence and prevalence of RBD have not been reported.

Sex: RBD occurs predominantly in males. In a recent report by Olson et al, of 93 patients with RBD, only 12 (13%) were females.

Age: Typically, RBD is a disease of elderly persons. The risk increases after the sixth decade, although the disease may occur at all ages, including childhood.

Clinical

History:

- The presenting complaint is violent dream-enacting behaviors during REM sleep, often causing self-injury or injury to the bed partner. The dream-enacting behaviors are usually nondirected and may include punching, kicking, leaping, or running from bed while still in REM sleep.
- Directed behavior, such as homicide, has not been reported.
- The patient may be wakened or may wake spontaneously during the attack and recall vividly the dream that corresponds to the physical action.
- In some cases, an extended prodrome of prominent limb and body movements occurs before the development of RBD.

Physical: The neurologic examination findings are unremarkable in idiopathic cases; in secondary cases, the physical findings depend on the underlying disorder.

Causes: In a recent study, Nightingale et al suggested that 36% of persons with narcolepsy experience symptoms of RBD. This link has lead to the identification of a strong association of RBD with HLA class II genes.

- RBD may be idiopathic, or it may occur in association with various neurological conditions, such as brainstem neoplasm, multiple sclerosis affecting the brainstem, olivopontocerebellar atrophy (OPCA), DLB disease, Alzheimer dementia, progressive supranuclear palsy (PSP), or Shy-Drager syndrome.
- The incidence of RBD is increased in Parkinson disease, and RBD may precede the development of parkinsonism by several years. The relationship between RBD and Parkinson disease is complex, however, as not all patients with RBD develop parkinsonism.
- Additional degeneration of brainstem neurons is postulated to play a significant role in the control of this condition.
- Various neuroimaging and pharmacologic studies suggest involvement of dopaminergic systems in both restless legs syndrome (RLS) and RBD.

  Differentials

Absence Seizures
Benign Childhood Epilepsy
Benign Neonatal Convulsions
Complex Partial Seizures
Confusional States and Acute Memory Disorders
Dizziness, Vertigo, and Imbalance
Epilepsia Partialis Continua

Epilepsy in Adults with Mental Retardation
Epilepsy in Children with Mental Retardation
Epilepsy, Juvenile Myoclonic
Epileptic and Epileptiform Encephalopathies
Frontal Lobe Epilepsy
[Psychogenic Seizures]

Other Problems to be Considered:

Primary disorders of arousal
Sleep terrors
Sleep walking
Confusional arousals

Secondary disorders of arousal
Obstructive sleep apnea (OSA)
Periodic limb movements in sleep (PLMS)
Gastroesophageal reflux (GERD)
Nocturnal seizure (e.g., frontal lobe epilepsy)

Other possibilities
Posttraumatic stress disorder (PTSD)
Psychogenic dissociative disease
Malingering
Frightening hypnagogic or hypnopompic hallucinations

Workup

Lab Studies:

- Routine medical history should include questions that screen for abnormal sleep movements and altered dreams. Routine laboratory tests are usually not helpful.

Imaging Studies:

- Imaging studies are not indicated in idiopathic cases. They are indicated if neurological dysfunction is suggested by history and neurologic examination. However, a recent study demonstrated that IPT-SPECT might be a useful tool in the diagnosis of RBD.

Other Tests:

- The most important diagnostic studies include the following:
    - Polysomnographic (PSG) video recording: This is the most important diagnostic test in RBD. On PSG, at least some tonic or phasic abnormalities of muscle tone are observed during REM sleep accompanying the attack, though usually patients have both.
    - Monitoring electro-oculogram (EOG)
    - EEG
    - ECG

- Nasal flow
- Multiple electromyography (EMG) channels utilizing chin, bilateral extensor digitorum, and tibialis anterior muscles

Treatment

Medical Care:

- RBD is treated symptomatically by various medications; however, the response varies in individual cases. Therefore, all available medications should be tried before considering the patient's RBD as intractable.
- The other important aspect of management of patients with RBD is environmental safety. Potentially dangerous objects should be removed from the bedroom, and the mattress should be placed on the floor or a cushion should be put around the bed.

Consultations: The neurologist may consult a sleep specialist for proper diagnosis and treatment of RBD.

Diet: No special recommendations or restrictions of diet exist for RBD.

Medication

The treatment of RBD can be challenging in some patients with underlying neurodegenerative conditions. Clonazepam is highly effective in the treatment of RBD. It is effective in nearly 90% of patients with little evidence of tolerance or abuse. The response usually begins within the first week, often on the first night. The initial dose is 0.5 mg at bedtime, with some patients warranting a rapid increase to 1 mg. With continued treatment for years, moderate limb twitching with sleep talking and more complex behaviors reemerge. Nevertheless, control of the violent behaviors persists. The treatment should be continued indefinitely, as violent behaviors and nightmares relapse promptly with discontinuation of medications in almost all patients. The specific mechanism of action of clonazepam in RBD is unknown but may reflect its serotonergic properties.

Treatment without significant affect on daytime cognition and alertness is highly desirable. In a small recent study by Boeve et al, a persistent benefit was shown with melatonin with and without low dose of clonazepam beyond 1 year of therapy in 57%. The effective dose of melatonin was 3-6 mg PO qhs; only 36% experienced side effects, which resolved with decreased dosing. The dosage may be increased q5-7d up to 12 mg/d in some cases if tolerated. The mechanism of melatonin is unclear; Kunz and Bes suggested that melatonin restored RBD-related desynchronization of the circadian rhythms.

Other medications, such as tricyclic antidepressants, may be effective in some patients. However, tricyclics are known to precipitate RBD. Levodopa may be very effective in patients in whom RBD is the harbinger of Parkinson disease. In addition, anecdotal reports exist of responses to carbamazepine, clonidine, and L-tryptophan.

Drug Category: *Benzodiazepines* -- By binding to specific receptor sites, these agents appear to potentiate the effects of GABA and facilitate inhibitory GABA neurotransmission and other inhibitory transmitters.

Drug Name	Clonazepam (Klonopin) -- Very effective in treatment of RBD in small doses. Exact mechanism of action unknown. Little evidence of tolerance or abuse with such small doses.
Adult Dose	Initial dose: 0.5 mg PO qhs; may be increased rapidly to 1 mg/d in some cases
Pediatric Dose	Not established
Contraindications	Documented hypersensitivity; severe liver disease; acute narrow-angle glaucoma
Interactions	Phenytoin and barbiturates may reduce effects; CNS depressants increase toxicity
Pregnancy	C - Safety for use during pregnancy has not been established.
Precautions	Caution in chronic respiratory disease or impaired renal function; withdrawal symptoms can result from abrupt discontinuation of medication

Drug Category: *Tricyclic antidepressants* -- This is a complex group of drugs that have central and peripheral anticholinergic effects, as well as sedative effects.

Drug Name	Amitriptyline (Elavil) -- Although known to precipitate RBD, effective in individual cases.
Adult Dose	10 mg PO qhs initially; may be increased gradually to 75 mg/d
Pediatric Dose	Not established
Contraindications	Documented hypersensitivity; MAOIs in past 14 d; history of seizures, cardiac arrhythmias, glaucoma, or urinary retention
Interactions	Phenobarbital may decrease effects; CYP2D6 enzyme system inhibitors (e.g., cimetidine, quinidine) may increase levels; inhibits hypotensive effects of guanethidine; may interact with thyroid medications, alcohol, CNS depressants, barbiturates, and disulfiram
Pregnancy	D - Unsafe in pregnancy
Precautions	Caution in cardiac conduction disturbances and history of hyperthyroidism, renal or hepatic impairment; avoid using in elderly

Drug Category: *Antiparkinsonian agents* -- These agents often are indicated for patients with Parkinson disease.

Drug Name	Levodopa/carbidopa (Sinemet) -- May be very effective in patients in whom RBD is harbinger of Parkinson disease. Comes in different strengths of 25/100 mg, 25/250 mg, and 10/100 mg.
Adult Dose	10/100 mg PO qhs initially; may be increased slowly to 25/100-250 mg in some cases
Pediatric Dose	Not established
Contraindications	Documented hypersensitivity; narrow-angle glaucoma; malignant melanoma; undiagnosed skin lesions
Interactions	Hydantoins, pyridoxine, phenothiazine, and hypotensive agents may decrease effects; antacids and MAOIs increase toxicity
Pregnancy	C - Safety for use during pregnancy has not been established.
Precautions	Certain adverse CNS effects (e.g., dyskinesias) may occur at lower dosages and earlier in therapy with SR form; caution in patients with history of myocardial infarction, arrhythmias, asthma, or peptic ulcer disease; sudden discontinuation may cause worsening of Parkinson disease; high-protein foods should be distributed throughout day to avoid fluctuations in levodopa absorption

Follow-Up-Further Outpatient Care:

- As RBD has strong relationships with many neurodegenerative disorders, such as Parkinson disease, multiple system atrophy, and dementia, the neurologist always should explore the possibility of RBD in these conditions. RBD symptoms may be the first manifestations of these disorders; therefore, careful follow-up is needed.

In/Out Patient Meds:

- Symptoms relapse promptly on discontinuation of medications in almost all patients; therefore, the drug should be continued indefinitely.

Prognosis:

- The prognosis of RBD depends on etiology. In idiopathic cases, the symptoms are controlled with medications. In secondary cases, the prognosis depends on the primary disease.

Patient Education:

- Educate the patient and the bed partner for environmental safety.
- Potentially dangerous objects should be removed from the bedroom, and the mattress should be placed on the floor or a cushion placed around the bed.

- For excellent patient education resources, visit eMedicine's Sleep Disorders Center. Also, see eMedicine's patient education articles REM Sleep Behavior Disorder, Disorders That Disrupt Sleep (Parasomnias), and Sleep Disorders and Aging.

Medical/Legal Pitfalls:

- RBD is a treatable condition. However, misdiagnosis and treatment may result in potential medico-legal problems. Commonly, violent behaviors of RBD involve patients' responses to some form of perceived threat. For example, the patient may dream that he is rescuing his wife from attacks, though at that time he actually is striking his wife. Some patients may strangle their bed partners. Appropriate recognition and treatment can avoid these dangerous injuries and their medico-legal

REM Sleep Behavior Disorder Is An Early Marker Of Neurodegenerative Diseases

The front page of the July 2006 issue of The Lancet Neurology, the journal with the highest international impact, contains a work that shows the relationship between disorders during REM sleep and future neurodegenerative pathologies. This study has been conducted by a Hospital Clinic group led by Dr. Alex Iranzo. This study is a good example of the fact that a correct diagnosis of sleep disorders by a specialist group can achieve a high relevancy. This diagnosis is possible in the Hospital Clinic thanks to the Multidisciplinary Unit of Sleep Disorders, which is in operation since May 2003, and which consists in 17 specialists from five areas, namely, neurology, psychiatry, psychology, otorhinolaryngology, and pulmonology. This organization permits a multidisciplinary approach with high-resolution tests, department clinical protocols and sessions, with a clear optimization of resources. The most frequent pathologies treated in this unit are sleep apnea, snoring, REM sleep behavior disorders, narcolepsy, night epilepsy or hypersomnia. Only last year, 3,809 visits, 1,819 sleep tests and 40 surgical interventions were made in the unit.

As well as clinical and teaching areas, this unit has high research activity as shown by the study explained below. This work has been led by Dr. Alex Iranzo, member of the Unit of Neurology of Hospital Clinic and of the Functional Studies of the Nervous System Group of the Institut dInvestigacions Biomediques August Pi i Sunyer (IDIBAPS). Not only The Lancet Neurology published the work, but also it dedicates the front page to the article, and a reflection by Canadian neurologists Dr. Ronald Postuma (Department of Neurology of the Montreal General Hospital de Quebec) and Dr. Jacques Montplaisir (Centre DEtude du Sommeil in the Hospital du Sacre-Coeur de Montreal).

This article is based in a descriptive study conducted since 1991 in which 44 patients from the Unit of Sleep Disorder of the Hospital Clinic were assessed. Given the low incidence of this disorder, the sample of patients studied by this Catalan group is the highest until today. All these patients presented idiopathic REM sleep behavior disorder. These patients, usually over 60 years, suffer from unpleasant dreams and express uneasiness by screaming, crying, kicking, punching and even falling from their beds.

According to the results of this study, 20 of these patients (45%), after being correctly diagnosed in the

center and followed up during five years, developed a neurodegenerative disease. This incidence is much higher than what is expected in the general population of the same age and gender. Therefore, scientists drew the conclusion that this disorder permits the early detection of neurodegenerative diseases such as Parkinson's disease, Lewy body dementia, multiple system atrophy or mild cognitive impairment. Furthermore, the fact that the twenty patients who developed a neurodegenerative disease were those who had suffered from REM sleep behavior disorder for the longest time, suggests that this incidence could be superior in the future.

The importance of these results lie firstly in the future possibility of administrating neuroprotective drugs to patients with the REM sleep behavior disorder who have still not developed a degenerative disease. Furthermore, the monitoring of these patients will permit an early administration of palliative drugs, which are already available. Toward this end, the Ministry of Health has awarded this group with a FIS award named "Prognostic markers of the development of a neurodegenerative disease in patients affected with REM sleep behavior disorder".

REM Sleep Behavior Disorder Found To Be Precursor Of Brain-degenerating Diseases Later In Life

Mayo Clinic sleep medicine specialists have found that almost two-thirds of patients with REM sleep behavior disorder (RBD) develop degenerative brain diseases by approximately 11 years after diagnosis of RBD. Findings will be presented in June at the Associated Professional Sleep Societies' SLEEP 2006 meeting in Salt Lake City.

"This study found RBD most frequently led to neurodegenerative diseases called the synucleinopathies: Parkinson's disease or dementia with Lewy bodies," says Maja Tippmann-Peikert, M.D., Mayo Clinic sleep medicine specialist, neurologist and the study's lead researcher. "From our findings, I would consider those with RBD at increased risk for these diseases."

RBD is a sleep disorder in which patients act out their dreams, which are often unpleasant and violent, according to Dr. Tippmann-Peikert. This acting out results from a loss of normal muscle paralysis in REM (rapid eye movement) sleep, the dream stage, which ordinarily prevents enacting one's dreams.

"The danger with RBD is that patients can hurt themselves or their spouses during the acting out behaviors -- bruises, lacerations, bone fractures and even subdural hematomas (brain hemorrhages) have been reported," says Dr. Tippmann-Peikert.

In this study, the investigators mailed questionnaires to 39 patients diagnosed with RBD at the Mayo Clinic Sleep Disorders Center between 1988 and 1995. If a patient had died, the questionnaire was mailed to surviving relatives. Of the 23 patients who agreed to participate, five had developed dementia or Parkinson's disease, and 10 reported neurological symptoms highly suggestive of dementia or Parkinson's disease. The patients in this study were an average of 11.2 years beyond their diagnoses of RBD.

This study is the second long-term follow-up study following patients with idiopathic, or inexplicable, RBD, confirming previous findings by Carlos Schenck, M.D., and Mark Mahowald, M.D., of Minnesota Regional Sleep Disorders Center at Hennepin County Medical Center in Minneapolis.

Other studies are under way to determine whether RBD is a state of pre-Parkinson's, pre-dementia or pre-multiple system atrophy (another type of synucleinopathy), according to the Mayo Clinic researchers.

Researchers have reported that as the brain-degenerating disease progresses, RBD may decrease in frequency and intensity or resolve completely, says Dr. Tippmann-Peikert.

There is no intervention to prevent those with RBD from progressing to Parkinson's disease, dementia or multiple system atrophy, says Dr. Tippmann-Peikert, as the origin of RBD is not clear enough to develop an appropriate therapy. Even though no preventive treatment exists yet, she says RBD patients can:

* Use safety precautions in their bedrooms to prevent injury (e.g., move nightstands away from the bed, use extra pillows or pillows on the floor next to the bed for extra padding, remove dangerous objects such as weapons from the bedroom, lock all windows and doors to walk-out decks)
* See a sleep specialist and, if prescribed, take medications to suppress RBD symptoms
* Become familiar with the signs and symptoms of Parkinson's disease, dementia or multiple system atrophy
* Follow up regularly with a sleep specialist to monitor for signs of brain-degenerating illnesses, and consider a referral to a neurologist if any signs appear

Dr. Tippmann-Peikert also stresses the importance of diagnosing RBD as early as possible.

"Awareness of excessive nocturnal behaviors and dream enactment and bringing it to the attention of a physician could lead to an early diagnosis of Parkinson's disease, dementia or multiple system atrophy," she says. "Hopefully, early identification of patients with idiopathic RBD will lead to close monitoring and early treatment of any developing neurological disorders."

Novel chromosomal aberration in a patient with a unique sleep disorder

Abstract

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A 45 year old woman presenting with periodic hypersomnia for 17 years is reported on. She would sleep for three weeks followed by the same period awake. Polysomnography in the somnolent period disclosed an excess of total sleeping time with remarkably increased stage 1, 3/4, and REM sleep, without cataplexy or sleep paralysis. HLA typing was incompatible with narcolepsy or REM sleep behavioral disorder. Her chromosomes showed premature centromere division with chromatid puffing in areas of constitutive heterochromatin, which is exclusively found in the syndrome of infants termed Roberts' syndrome/SC phocomelia. Other laboratory findings were not normal. It is suggested that the present case is a novel sleep disorder related to a unique chromosomal aberration.
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Introduction

Premature centromere division with chromatid puffing is a rare chromosomal aberration which is exclusively found in Roberts' syndrome.[1] This is a report of the first adult case with the above chromosome aberration presenting a unique sleep disorder as the main manifestation, but without malformations seen in Roberts' syndrome. Polysomnography disclosed an excess of total sleeping time with 43% of REM sleep, which differs from the patterns of any known hypersomnia such as narcolepsy or periodic hypersomnia.[2]

Case History

A 45 year old woman was admitted to our hospital for the evaluation of her episodes of periodic hypersomnia which began at the age of 28. She was born mildly asphyxiated and weighed 1700 g at 36 weeks of gestation. Her physical and mental development were slow; she first walked at the age of 3. She had graduated from a special junior high school for physically and mentally disabled children, and had worked in a sewing factory for 13 years. She had never been married or pregnant. Her menarche was at 16 and menopause was at 43 years of age. She had a cerebellar hemorrhage when she was 37 years old. Bilateral visual disturbance due to optic nerve atrophy developed after 40 years of age. Her parents were first cousins. There was no family history of neurological or psychiatric disorders.

When she was 28 years old, she began to fall asleep for two to five days without any prodrome. After finishing the somnolent period, she could work in the factory at the beginning of the illness. However, the duration of the hypersomnia became longer within two years. She slept for almost three weeks and this was followed by the same duration of wakefulness. During the somnolent period, she slept continuously unless her mother woke her to eat light meals and for urination. When she awoke in remission, she ate much and stayed awake until midnight and this was followed by three to five hours of listlessness to a drowsy state. The remission periods also lasted three weeks and then another somnolent period would begin. The cycle continues until now, even after admission. Menstruation did not affect this cycle. She had not received any medication.

On admission, she was a thin, short women; 138 cm in height and 29 kg in weight. She had a relatively small face and head with a maximum head circumference of 47 cm and looked older than her actual age. She had no obvious physical anomalies of her body or limbs except for a mild high arched palate. The physical examination was not informative, including secondary sex characteristics (fig 1). Although her responses were slightly slow, she was alert and cooperative. Her intelligence score was 67 on the Wechsler adult intelligence scale.

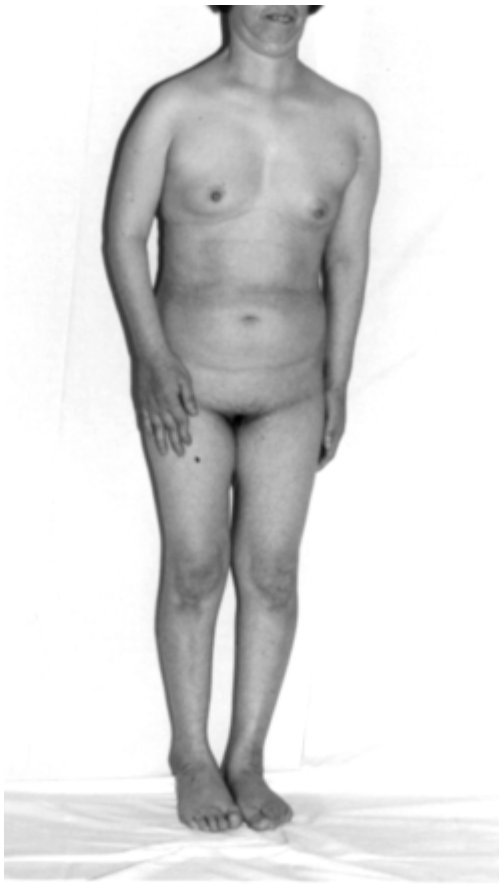

Figure 1 Patient at 45 years of age. She had no obvious physical anomalies of her body or limbs.

Neurological examination disclosed bilateral optic nerve atrophy and mild bilateral facial palsy of central type. Her visual acuity was 5/20 in the left eye and she was almost blind in the right eye. The remaining cranial nerves were intact. Muscle tone, strength, and tendon reflexes were normal and planter reflexes were flexor. There was no evidence of cataplexy or sleep paralysis. Other neurological examinations, including tests for cerebellar function, were also normal.

Urinalysis, routine blood tests, ECG, and chest radiography were normal. Endocrinological studies showed normal urinary 17-ketosteroid and 17-hydroxycorticosteroid concentrations and normal blood growth hormone, thyroid stimulating hormone, follicle stimulating hormone, prolactin, aldosterone, and adrenocorticotrophic hormone in the somnolent and alert periods. Her CSF was acellular and the content of protein, sugar, homovanillic acid, vanillylmandelic acid, 5-hydroxyindolacetic acid, serotonin, and γ-aminobutyric acid concentrations were normal in both the somnolent and alert periods. Serum and CSF concentrations of amino acids were normal. HLA typing of DQB1 was 0601/0601 and DR2 was positive. Cranial CAT/CT disclosed periventricular lucencies in the vicinity of the anterior horns of the lateral ventricle and slight cerebral atrophy. Brain MRI showed high signal intensity areas in the bilateral thalamus, putamen, and white matter in T 2 weighed images and low signal intensity in the corpus callosum in T 1 weighed images. Single photon emission CT (SPECT) was considered to be normal in both somnolent and alert periods. EEG in the somnolent period showed a slower and more irregular basic rhythm than that in the alert period, which was accompanied by occasional slow waves of moderate amplitude.

The pattern of her sleep was analyzed in the somnolent period by polysomnography, using an ambulatory EEG monitoring system and standard techniques.[3] Total sleeping time was 924 minutes in a total 1200 minutes. recording time. Total sleeping time was composed of 16.3% of stage 1, 14.6% of stage 2, 26.1% of stages 3-4, and 43% of REM sleep. Non-REM and REM sleep cycles were irregular and the REM stage appeared at random.

Cytogenetic analysis was performed on her peripheral blood lymphocytes cultured with phytohaemagglutinin. We analyzed 50 cells which showed 10 cells of 45X and 40 cells of 46XX. Metaphase chromosomes showed a mosaicism of 45X/46XX and showed premature centromere division and chromatid puffing which were designated as a "typical Roberts' syndrome effect"[1] in all areas of constitutive heterochromatin (fig 3).

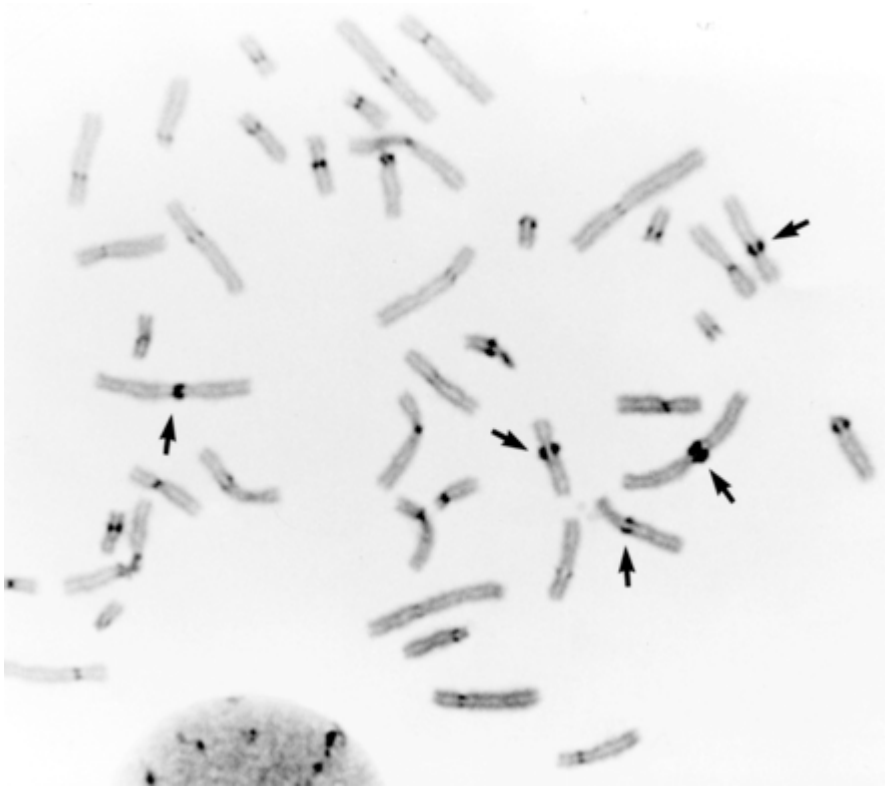

Figure 3 C banded metaphase from the patient. All the chromosomes show the typical Roberts' syndrome effect, with centromere division and chromatid puffing (repulsion) in areas of constitutive heterochromatin (arrows indicate typical ones).

Discussion

Periodic hypersomnia, first reported by Kleine in 1925, is a syndrome characterized by hypersomnia persisting for two days to three weeks. Levin reported a syndrome associated with morbid hunger in the hypersomnia stage. The syndrome is now called Kleine-Levin syndrome, and classified as a specific type of periodic hypersomnia. As periodic hypersomnia rarely shows strict periodicity, it is now called recurrent hypersomnia (the International Classification of Sleep Disorders issued in 1990). The hypersomnia seen in the present case is unique. The exact alternative cycle of hypersomnia and wakefulness is different from that seen in periodic hypersomnia. The long lasting course in this patient is also different from the course of periodic hypersomnia or intermittent repetitive pseudocoma

reported by some researchers. Clinical features and HLA typing are not compatible with narcolepsy and the REM sleep behavior disorder.

Analysis with polysomnography showed another unique point of her hypersomnia. Total sleeping time of normal subjects was composed of 5-10% of stage 1, 50% of stage 2, 20% of stage 3-4, and 20%-25% of REM sleep. Sleep pattern of periodic hypersomnia was reported as follows; total sleeping time and the percentage of REM sleep are identical to normal controls, whereas the percentage of stage 2 is decreased and that of stage 3/4 is increased. Her actual sleep time was 77% of total recording time, which was obviously prolonged compared with periodic hypersomnia and healthy subjects. The percentage of stage 1, stage 3/4, and REM sleep in total sleeping time were also remarkably increased compared with periodic hypersomnia. The REM-non-REM sleeping cycle was irregular. This indicates that her sleep was different from those of either normal subjects or the patients with periodic hypersomnia and was characterized by a pattern of increased deep sleep and REM sleep, and decreased light sleep. Although we could not detect any anatomical or chemical abnormalities which induced the sleep cycle, some mediators such as cytokines or other soluble factors may regulate these unusual sleep-remission cycles and REM-non-REM cycles. It has been shown recently that interleukin-1, tumor necrosis factor (TNF), or hormones such as growth hormone releasing hormone induce sleep and regulate the cycle of REM and non-REM sleep. (TNFα was undetectable in her CSF).

Her chromosomes displayed very rare abnormalities reported exclusively in Roberts' syndrome. Petrinelli *et al* reported similar chromosomal abnormalities in the sibling of Roberts' syndrome, who had no physical or neurological abnormality. However, sleep disorder accompanied by the similar chromosomal aberration has not been reported. Roberts' syndrome is a rare autosomal recessive condition characterized by pronounced tetraphocomelia, midfacial clefts, severe mental and physical retardation, and death at a very early age, none of which was found in the present case. Although her chromosomes showed a mosaicism in 45X/46XX, she did not have characteristics of Turner's syndrome except for short stature and late menarche.

It remains to be elucidated whether or not the chromosomal aberration was causally related to the sleep disorder. Because she had cerebellar hemorrhage and MRI disclosed abnormal lesions in the thalami, it is possible that the sleep disorder may be secondary to the vascular lesions. It is also unknown whether the chromosomal aberration induces vascular abnormalities. Bassetti *et al* reported hypersomnia after a paramedian thalamic stroke. However, paramedian thalamic stroke has an acute onset and has not been reported to show periodic hypersomnia. Polysomnography in paramedian thalamic stroke has shown an increased stage 1 and normal REM sleep. Thus we suggest that the present case is a novel sleep disorder related to a unique chromosome aberration.

Another issue:

ASP vs. REM Behavior Disorder

The body is supposed to be paralyzed during REM sleep. The brain is very active during REM sleep and paralyzes the body to prevent a dreamer from harming self and others by acting out dreams.

If the neural mechanism that is supposed to carry out this paralysis fails, the patient is said to have REM Behavior Disorder, RBD.

It seems possible that the Awareness possible during an episode of REM Behavior Disorder may parallel the Awareness possible during Sleep Paralysis - with the exception that awareness ***of*** the body's sleep paralyzed condition would not occur.

What is ASP?

> Awareness during Sleep Paralysis, or ASP, is any Awareness during the Paralysis that ***naturally*** occurs in Rapid Eye Movement (REM) Sleep to prevents us from harming ourselves or others by acting out our dreams.

Does it matter what the experiencer is or is not ***aware of?***

> No. There are no exclusions based on the content of the experience --- what the experiencer is aware ***of***.
>
> Themes expressed in the content of the experiencer's report define the *genre* of the ASP experience.

Surely the perception of paralysis is necessary!

> Someone experiencing Awareness during Sleep Paralysis may or may not be *aware of* the body's sleep paralyzed state. Awareness ***of*** Sleep Paralysis is a subset of Awareness ***during*** Sleep Paralysis.

How can you have Awareness ***during*** Sleep Paralysis without ***of*** Sleep Paralysis?

> When there is some indication *other than perception of the body's sleep paralyzed condition* that the body is in a REM sleep state.

Can you give an example of that?

> Lucid Dream Experiences.
>
> Stephen LaBerge and other researchers have found that Lucid Dreams occur almost exclusively during REM sleep. In addition, it has been learned that the body is paralyzed more strongly during lucid dreams than during ordinary REM sleep dreams, probably because the brain is more active.
>
> So every lucid dream is an example of Awareness ***during*** Sleep Paralysis. But lucid dreamers are only sometimes Aware ***of*** the Sleep Paralysis.
>
> More often the lucid dreamer focuses on manipulating the dreamscape or pays attention to something much more interesting than bodily immobility.

Consequently, if Awareness during Sleep Paralysis can explain the bulk of those Alien Abduction reports that start out with the experiencer lying down or resting, it is possible that the very small number of cases where there is evidence that the experiencer walked around during the experience would be explained as cases of RBD.

REM sleep behavior disorder is a parasomnia that occurs later in the night than NREM disorders. It differs from the parasomnias discussed previously because it usually affects middle-aged or elderly individuals. Frequently, sufferers will also have a neurological disorder. The temporary muscle paralysis that normally occurs during REM sleep does not occur in this disorder. Because the muscles are not paralyzed, individuals may act out potentially violent behaviors during sleep and cause injuries to themselves or their bed partners.

First evidence of neurochemical basis for obstructive sleep apnea and REM behavior disorder found

The first tantalizing clues that chemical imbalances in the brain may be partly to blame for certain life-disrupting sleep disorders are being reported in two new studies by University of Michigan Health System researchers.

In two papers in the July 8 issue of the journal Neurology, the team reports apparent links between deficits in brain chemistry and obstructive sleep apnea (OSA) and REM sleep behavior disorder (RBD). Both are relatively common sleep problems that disturb the slumber -- and daytime behavior -- of millions of Americans.

The new findings were made using two types of neurochemical brain scans and detailed sleep studies in 13 patients with multiple system atrophy (MSA), a rare and fatal degenerative neurological disease almost always accompanied by severe sleep disorders. Their results from the MSA patients, who all had both sleep apnea and REM behavior disorder, were very different from those of 27 healthy control subjects.

Specifically, the researchers found that MSA patients had a far lower density of certain brain cells, or neurons, that produce the key chemicals dopamine and acetylcholine. The greater their lack, the worse their sleep problems were.

The patients with the fewest dopamine-producing neurons in the striatum of their brains had the worst RBD symptoms of thrashing, talking and violent flailing while they slept. And patients with the lowest levels of acetylcholine-producing neurons in the brainstem had the most interruptions in their breathing during sleep.

And while the researchers are careful to note that their findings to date can only show a correlation, not causation, between brain chemistry and sleep disorders, they plan further research to explore the relationship.

"It’s exciting to be able to show this major neurochemical deficit for the first time, and confirm what others have suspected," says lead author Sid Gilman, M.D., F.R.C.P., the William J. Herdman Professor and chair of the Department of Neurology at the U-M Medical School. "We don’t yet know if we will find this same effect in patients with other neurological diseases or in people who are otherwise neurologically well, but these findings are already suggesting further research opportunities."

For instance, the U-M team is recruiting patients with Parkinson’s disease for a similar study, to see if

brain chemistry disruptions from their disorder may also be linked to sleep problems. Gilman says he and other specialists suspect that sleep disorders may be an early symptom in many cases of Parkinson's disease.

Gilman and his colleagues chose MSA patients as their first subjects for studying sleep disorders and brain chemistry because of their extremely high incidence of OSA, RBD and other sleep problems; their disease's tendency to cause degeneration of certain nerve cells in their brains and spinal cords; and clinical evidence that some of their sleep problems can be successfully treated with medications that replace lost dopamine.

MSA is a complex, debilitating and life-shortening disease that affects only about 75,000 people nationwide, though many others are thought to be misdiagnosed. Also known as Shy-Drager Syndrome, MSA usually strikes people in their 40s, 50s or 60s, and affects blood pressure, muscle tone and movement, balance, bladder control and sleep. Patients experience debilitating and rapidly progressing symptoms, usually dying within seven to 10 years of diagnosis.

In addition to plaguing MSA patients, sleep disorders are also a fact of life for millions of others.

Obstructive sleep apnea, in which breathing temporarily stops or diminishes dozens or even hundreds of times during a person's sleep, may affect 3 percent of adults but goes undiagnosed in most of them. Its most notable symptoms are snoring and excessive daytime sleepiness, though it can also affect blood pressure, memory and even reaction time while driving.

REM sleep behavior disorder, meanwhile, occurs less often but is outwardly more dramatic. Patients literally act out their dreams during the rapid-eye movement, or REM, phase of sleep, moving their arms and legs, getting out of bed, talking and shouting, and even hitting or punching. RBD can endanger the sleeping person, or his or her bed partner,

"Usually, while we sleep, our brains keep our hearts and lungs going automatically -- while disabling the muscles that might otherwise let us unconsciously act out our dreams," Gilman explains. "But many people, including most MSA patients, have sleep disorders that close off their airway and interrupt their nighttime breathing, as in obstructive sleep apnea, or cause them to thrash, talk and walk about, as in REM sleep behavior disorder."

The precise causes of these problems are unknown, although obesity is known to be involved in OSA. None of the participants in the newly published studies were obese, and the control subjects were matched with the MSA patients by age and gender.

UMHS researchers have been studying sleep disorders for years at the Michael S. Aldrich Sleep Disorders Laboratory. The newly published studies, funded by the National Institute of Neurological Diseases and Stroke, were possible because of the unique blend of clinical and research resources available at UMHS.

Gilman and his colleagues run one of the nation's most comprehensive and busiest clinics for patients with MSA, receiving patients via referrals from physicians around the country. In 1998, Gilman chaired a national panel that established diagnostic criteria for MSA.

In addition to having a ready source of MSA patients willing to take part in research studies, UMHS

has a dedicated facility and staff for inpatient sleep research in its General Clinical Research Center, and the expertise and facilities needed to study brain chemistry through the imaging techniques known as positron emission tomography (PET) and single-photon emission computed tomography (SPECT).

The new studies used radioactive PET and SPECT tracers that attach specifically to proteins on cells that release dopamine and acetylcholine, thereby revealing the density of such cells in various brain areas. Gilman and his colleagues matched each MSA patient's PET and SPECT results with his or her results from two successive nights of polysomnography, a detailed sleep study that records everything from brain activity and breathing to muscle movement and pulse.

In addition to correlating brain chemistry with the overall severity of sleep disorder symptoms, the new studies even give hints as to how the brain chemistry changes may affect the specific muscles involved in those symptoms.

For instance, the specific brainstem areas where the largest deficits in acetylcholine neurons were seen -- know as the PPT/LDT nuclei -- are connected to the part of the brain that controls the muscles of the upper airway and tongue. Those muscles are crucial to maintaining uninterrupted breathing during sleep.

Gilman notes that the correlation between brain chemistry and sleep symptom severity suggested by the new results is bolstered by recent evidence showing the MSA patients experience nerve loss in some of the same specific brain areas pinpointed in the current study.

Sleep Disorders

Overview

Sleep disturbances occur in about 12% to 25% of the general population and are often associated with situational stress, illness, aging, and drug treatment. It is estimated that 45% of people with cancer have sleep disturbance. Physical illness, pain, hospitalization, drugs and other treatments for cancer, and the psychological impact of a malignant disease may disrupt the sleeping patterns of persons with cancer. Poor sleep adversely affects daytime mood and performance. In the general population, persistent insomnia has been associated with a higher risk of developing clinical anxiety or depression. Sleep disturbances and, ultimately, sleep-wake cycle reversals, can be early signs of a developing delirium. (Refer to the PDQ summary Cognitive Disorders and Delirium for more information.) Adequate sleep may increase the cancer patient's pain tolerance.

Sleep consists of two phases: rapid eye movement (REM) and non-REM (NREM) sleep. [5] REM sleep, also known as dream sleep, is the active or paradoxic phase of sleep in which the brain is active. NREM is the quiet or restful phase of sleep. NREM, also referred to as slow wave sleep, is divided into 4 stages of progressively deepening sleep based on electroencephalogram findings.

The stages of sleep occur in a repeated pattern or cycle of NREM followed by REM, with each cycle lasting approximately 90 minutes. The sleep cycle is repeated 4 to 6 times during a 7- to 8-hour sleep period. [6] The sleep-wake cycle is dictated by an inherent biological clock or circadian rhythm. Disruptions in individual sleep patterns can disrupt the circadian rhythm and impair the sleep cycle.

Four major categories of sleep disorders have been defined by the Sleep Disorders Classification Committee:

1. **Disorders of initiating and maintaining sleep (insomnias).**
2. **Disorders of the sleep-wake cycle.**
3. **Dysfunctions associated with sleep, sleep stages, or partial arousals (parasomnias).**
4. **Disorders of excessive somnolence.**

Sleep Disturbance in Cancer Patients

Cancer patients are at great risk for developing insomnia and disorders of the sleep-wake cycle. Insomnia is the most common sleep disturbance in this population and is most often secondary to physical and/or psychological factors related to cancer and/or cancer treatment. Anxiety and depression, common psychological responses to the diagnosis of cancer, cancer treatment, and hospitalization, are highly correlated with insomnia.

Sleep disturbances may be exacerbated by paraneoplastic syndromes associated with steroid production and by symptoms associated with tumor invasion, such as draining lesions, gastrointestinal (GI) and genitourinary (GU) alterations, pain, fever, cough, dyspnea, pruritus, and fatigue. Medications, including vitamins, administration of corticosteroids, neuroleptics for nausea and vomiting, and sympathomimetics for the treatment of dyspnea, as well as other treatment factors can negatively impact sleep patterns.

Side effects of treatment that may affect the sleep-wake cycle include the following:

- Pain.
- Anxiety.
- Night sweats/hot flashes.
- GI disturbances (i.e., incontinence, diarrhea, constipation, nausea).
- GU disturbances (i.e., incontinence, retention, GU irritation).
- Respiratory disturbances.

Medications commonly used in the treatment of cancer can cause insomnia. Sustained use of central nervous system (CNS) stimulants (e.g., amphetamines, caffeine, diet pills including some dietary supplements that promote weight loss and appetite suppression), sedatives and hypnotics (e.g., glutethimide, benzodiazepines, pentobarbital, chloral hydrate, secobarbital sodium, amobarbital sodium), cancer chemotherapeutic agents (especially antimetabolites), anticonvulsants (e.g., phenytoin), adrenocorticotropin, oral contraceptives, monoamine oxidase inhibitors, methyldopa, propranolol, atenolol, alcohol, and thyroid preparations can cause insomnia. In addition, withdrawal from CNS depressants (e.g., barbiturates, opioids, glutethimide, chloral hydrate, methaqualone, ethchlorvynol, alcohol, and over-the-counter and prescription antihistamine sedatives),

benzodiazepines, major tranquilizers, tricyclic and monamine oxidase inhibitor antidepressants, illicit drugs (e.g., marijuana, cocaine, phencyclidine, opioids) may cause insomnia.

The most commonly prescribed hypnotics can interfere with REM sleep, resulting in increased irritability, apathy, and diminished mental alertness. Abrupt withdrawal of hypnotics and sedatives may lead to many symptoms including nervousness, jitteriness, seizures, and REM rebound. Berlin defined REM rebound as a “marked increase in REM sleep with increased frequency and intensity of dreaming, including nightmares.” The increased physiologic arousal that occurs during REM rebound may be dangerous for patients with peptic ulcers or a history of cardiovascular problems.

Hospitalized patients are likely to experience frequent interruptions of sleep due to treatment schedules, hospital routines, and roommates, which singularly or collectively alter the sleep-wake schedule. Other factors influencing sleep-wake schedules in the hospital setting include age, noise, temperature, comfort, pain, and anxiety.

Consequences of sleep disturbances can influence outcomes of therapeutic and supportive care measures. The patient with mild-to-moderate sleep disturbances may experience irritability and inability to concentrate, which may in turn affect the patient's compliance with treatment protocols, ability to make decisions, and relationships with significant others. Depression and anxiety can also be end results of sleep disturbances. Supportive care measures are directed toward promoting quality of life and adequate rest.

Assessment

Assessment is the initial step in management strategies. Assessment data should include documentation of predisposing factors, sleep patterns, emotional status, exercise and activity level, diet, symptoms, medications, and caregiver routines. The sections below outline recommendations for a sleep history and physical examination. Data can be retrieved from multiple sources: the patient's subjective report of sleep difficulty, objective observations of behavioral and physiologic manifestations of sleep disturbances, and reports from the patient's significant others regarding the patient's quality of sleep.

The diagnosis of insomnia is primarily based on a careful, detailed medical and psychiatric history. The American Sleep Disorders Association has produced guidelines for the use of polysomnography as an objective tool in evaluating insomnia. The routine polysomnogram includes the monitoring of electroencephalography, electro-oculography, electromyography, effort of breathing and air flow, oxygen saturation, electrocardiography, and body position. Polysomnography is the major diagnostic tool in sleep disorders and is indicated in the evaluation of suspected sleep-related breathing disorders and periodic limb movement disorder, and when the cause of insomnia is uncertain or when behavioral or pharmacologic therapy is unsuccessful.

Risk Factors for Sleep Disorders

- Disease factors including paraneoplastic syndromes with increased steroid production; symptoms associated with tumor invasion (e.g., obstruction, pain, fever, shortness of breath, pruritus, fatigue).
- Treatment factors including symptoms related to surgery (e.g., pain, frequent monitoring, opioids); chemotherapy (e.g., exogenous corticosteroids); symptoms related to chemotherapy.

- Medications such as opioids, sedatives/hypnotics, steroids, caffeine/nicotine, some antidepressants, dietary supplements including some vitamins, diet pills, and other products promoting weight loss and appetite suppression.
- Environmental factors.
- Physical and/or psychological stressors.
- Depression (refer to the PDQ summary Depression for more information).
- Anxiety (refer to the PDQ summary Anxiety for more information).
- Delirium (refer to the PDQ summary Cognitive Disorders and Delirium for more information).
- Daytime seizures; snoring; headaches.

Characterization of Sleep

- Usual patterns of sleep, including usual bedtime, routine prior to retiring (e.g., food, bath, medications), length of time before onset of sleep, and duration of sleep (awaking episodes during night, ability to resume sleep, and usual time of awakening).
- Characteristics of disturbed sleep (changes following diagnosis, treatment, and/or hospitalization).
- Perception of significant others as to quantity and quality of patient's sleep.
- Family history of sleep disorders.

Management

Management of sleep disturbances should focus on treatment of symptoms related to the cancer and its treatment, and identification and management of environmental and psychological factors. Treatment of the malignancy may resolve the sleep disturbance. When sleep disturbances are caused by symptoms of cancer or treatment, measures that control or alleviate symptoms are often the key to resolving sleep disturbances. Management of sleep disturbances combines nonpharmacologic and pharmacologic approaches individualized for the patient.

Nonpharmacologic Management of Sleep Disturbances

The environment can be modified to decrease sleep disruption. Minimizing noise, dimming or turning off lights, adjusting room temperature, and consolidating patient care tasks to decrease interruptions can increase the amount of uninterrupted sleep.

Other actions or interventions that may promote rest include the following:

- Keeping the patient's skin clean and dry.
- Giving backrubs and/or massaging areas of the body to bring comfort to the patient (e.g., bony prominences, head and scalp, shoulders, hands, feet).
- Keeping bedding and/or surfaces of support devices (chairs, pillows) clean, dry, and wrinkle-free.

- Ensuring adequate bedcovers for warmth.
- Regulating fluid intake to avoid frequent awakening for elimination.
- Encouraging bowel and bladder elimination before sleep.
- Promoting optimal bowel function (increased fluids, dietary fiber, use of stool softeners and laxatives).
- Using a condom catheter for nocturnal incontinence.
- Providing a high-protein snack 2 hours before bedtime (e.g., milk, turkey, or other foods high in tryptophan).
- Avoiding beverages with caffeine and other stimulants including dietary supplements that promote metabolism changes and appetite suppression.
- Encouraging the patient to dress in loose, soft clothing.
- Facilitating comfort through repositioning and support with pillows as needed.
- Encouraging exercise or activity no less than 2 hours before bedtime.
- Encouraging the patient to keep regular bedtime and awakening hours.
- Minimizing and coordinating necessary bedside contacts for inpatients.

Psychological interventions are directed toward facilitating the patient's coping processes through education, support, and reassurance. As the patient learns to cope with the stresses of illness, hospitalization, and treatment, sleep may improve. Relaxation exercises and self-hypnosis performed at bedtime can be helpful in promoting calm and sleep. Cognitive-behavioral interventions that diminish the distress associated with early insomnia and change the goal from “need to sleep” to “just relax” can diminish anxiety and promote sleep. Communication, verbalization of concerns, and openness between the patient, family, and health care team should be encouraged.

Many people who experience insomnia have been found to practice poor sleep hygiene (such as smoking and drinking alcohol just before bedtime), which can exacerbate or perpetuate insomnia. Therefore, a complete assessment of sleep hygiene (i.e., time in bed; napping during the day; intake of caffeine, alcohol, or heavy/spicy/sugary foods; exercise; sleep environment) and use of behavioral management strategies (i.e., fixed bedtime; smoking, dietary, and alcohol restrictions 4–6 hours before bedtime; increased exercise) may prove effective in reducing sleep disturbance.

Pharmacologic Management of Sleep Disturbances

When sleep disturbances are not resolved with other supportive care measures, the use of sleep medications on a short-term or intermittent basis may be helpful. Prolonged use of sleep medications for persistent insomnia, however, can impair natural sleep patterns (i.e., rapid eye movement [REM] deprivation) and alter physiologic functions. Prolonged use (>1-2 weeks) of these medications may result in tolerance, psychological and physical dependence, drug intoxication, and drug hangover.

A newer agent, zolpidem, has reportedly not been associated with tolerance, dependence, sleep cycle alterations, or rebound insomnia. Zolpidem tartrate (Ambien) is administered in doses of 5 to 10 mg, 30 minutes before bedtime. To date, it has not been widely used or studied in cancer patients.

Benzodiazepines have been widely used in the management of sleep disturbances. Used as an adjunct to other treatment for short periods of time, these agents are safe and effective in producing natural sleep because they are less disruptive of REM sleep than are other hypnotic agents. Benzodiazepines have an antianxiety effect in low doses and a hypnotic effect in high doses. Commonly used sleep aids are not well studied in cancer patients. A randomized double-blind, placebo-controlled trial of triazolam was carried out in a major cancer center in women undergoing initial breast cancer surgery. The drug was superior to placebo with regard to improved sleep and restfulness. The remaining literature is sparse with regard to empirical studies and randomized controlled trials of sleep aids and is mostly anecdotal.

Benzodiazepines differ from each other in duration of action and pharmacokinetics. Liver disease has less effect on the metabolism of lorazepam, oxazepam, and temazepam than on the metabolism of other benzodiazepines. Whereas long-acting agents may produce daytime hangover, short-acting agents are more often associated with dependence, rebound insomnia, early morning insomnia, daytime anxiety, and serious withdrawal effects, such as seizures. The following general characterizations can be made:

- Intermediate- and short-acting benzodiazepines are characterized by half-lives of 4 to 24 hours.
- Short-acting benzodiazepines are characterized by the following:
    - Few active metabolites.
    - Rarely, accumulation with multiple doses.
    - Minimal effect on drug clearance by age and liver disease.
- Long-acting benzodiazepines are characterized by the following:
    - Half-lives of longer than 24 hours.
    - Pharmacologically active metabolites.
    - Accumulation with multiple dosages.
    - Impaired clearance in older patients and those with liver disease.

Nonbenzodiazepine sleep aids include antidepressants, antihistamines, and antipsychotics. Antihistamines have been popular drugs for the management of sleep disturbances among cancer patients. The anticholinergic properties of antihistamines relieve nausea and vomiting as well as insomnia. These agents must be used with caution since daytime sedation and delirium can occur, especially in the elderly. Tricyclic antidepressants, such as amitriptyline or doxepin (Sinequan), may be effective in patients who are not depressed as well as those who are depressed. When given at bedtime, these sedating agents can eliminate the need for an additional hypnotic.

Low doses of tricyclic antidepressants can be effective sleep agents and may be the treatment of choice for insomnia in patients who have neuropathic pain and appetite loss (e.g., doxepin 50-100 mg at

bedtime; amitriptyline 25-100 mg at bedtime). In low doses, trazodone (50-150 mg) can promote sleep and is often combined with other antidepressants (e.g., fluoxetine 20 mg in the morning) in depressed patients with insomnia. A unique antidepressant, mirtazapine (Remeron), has been used clinically to treat depression and also induces sleep, stimulates appetite, and can decrease nausea in low bedtime doses. The hypnotic effects of marijuana (tetrahydrocannabinol or THC) are similar to conventional hypnotics in reducing REM sleep; however, side effects prior to sleep induction and hangover make the use of THC less acceptable than benzodiazepines.

Low-potency neuroleptics (e.g., thioridazine 10-25 mg) are useful in promoting sleep in patients with insomnia associated with organic mental syndromes and delirium. (Refer to the PDQ summary Cognitive Disorders and Delirium for more information.)

Barbiturates are generally not recommended for the management of sleep disturbances in cancer patients. Barbiturates have a number of adverse effects, including the development of tolerance, and they also have a narrow margin of safety.

Most hypnotics are effective initially but lose efficacy when used regularly, and they can become a primary cause of sleep disturbances.

Medications Commonly Used To Promote Sleep

Drug category	Medication	Hypnotic dose (route)	Onset (duration of action)
Benzodiazepines	diazepam (Valium)	5-10 mg (capsule, tablet)	30-60 min (6-8 h)
	temazepam (Restoril)	15-30 mg (capsule)	60 min, minimum (6-8 h)
	triazolam (Halcion)	0.125-0.5 mg (tablet)	30 min (peaks 1-1.5 h)
	clonazepam (Klonopin)	0.5-2.0 mg (tablet)	30-60 min (8-12 h)
Tricyclic antidepressants	doxepin (Sinequan)	10-150 mg	30 min
	amitriptyline (Elavil)	10-15 mg	30 min
	nortriptyline (Pamelor)	10-50 mg	30 min
Chloral derivatives	chloral hydrate	0.5-1.0 g (capsule, syrup, suppository)	30-60 min (4-8 h)
Second generation antidepressants	trazodone (Desyrel)	25-150 mg	30 min
	nefazodone (Serzone)	50-100 mg	30 min

Drug category	Medication	Hypnotic dose (route)	Onset (duration of action)
mirtazapine (Remeron)	15-60 mg	30 min	
Antihistamines	diphenhydramine (Benadryl)	25-100 mg (tablet, capsule, syrup)	10-30 min (4-6 h)
hydroxyzine (Vistaril, Atarax)	10-100 mg (tablet, capsule, syrup)	15-30 min (4-6 h)	
Neuroleptics	thioridazine (Mellaril)	10-50 mg	30-60 min
chlorpromazine (Thorazine)	10-50 mg	30-60 min	
Other	zolpidem tartrate (Ambien)	5-20 mg	30 min (4-6 h)
zaleplon (Sonata)	10-20 mg	30 min (4-6 h)	

Melatonin, a hormone produced by the pineal gland during the hours of darkness, plays a major role in the sleep/wake cycle. Although further study is indicated, melatonin may play an important role in the treatment of certain types of chronic sleep disorders. It is suggested that melatonin exerts a hypnotic effect through thermoregulatory mechanisms. By lowering the core body temperature, melatonin reduces arousal and increases sleep propensity. Melatonin is likely to be an effective hypnotic agent for sleep disruption associated with elevated temperature due to low circulating melatonin levels. The combined circadian and hypnotic effects of melatonin suggest a synergistic action in the treatment of sleep disorders related to the inappropriate timing of sleep and wakefulness. Adjuvant melatonin may also improve sleep disruption caused by drugs known to alter normal melatonin production (e.g., beta-blockers and benzodiazepines).

Melatonin replacement has been shown to improve sleep in children with endocrine tumors that diminish the natural production of the hormone.

This efficacy has not been shown beyond this particular study. Melatonin may affect the way tumor cells respond to chemotherapy and radiation therapy. Some studies in colon and brain cancer suggest the effect of melatonin on chemotherapy and on radiation therapy may be beneficial. Not enough is known, however, to assure patients on these therapies that melatonin treatment for insomnia is safe. The use of melatonin to treat insomnia in cancer patients is under evaluation. Because the effect of melatonin on chemotherapy can vary, it is important for patients taking chemotherapy to consult with their health care professionals before using melatonin.

Changes in sleep/wake patterns are among the hallmarks of biologic aging. Evidence suggests that circulating melatonin levels may be significantly lower in physically healthy elderly people and in insomniacs than in age-matched control subjects. In view of these findings, melatonin replacement therapy may be beneficial in the initiation and maintenance of sleep in the elderly. Melatonin replacement, however, has not been studied in elderly people with cancer as a treatment for insomnia.

Special Considerations

The Patient With Pain

Since enhanced pain control improves sleep, appropriate analgesics or nonpharmacologic pain management should be administered before introducing sleep medications. Tricyclic antidepressants can be particularly useful for the treatment of insomnia in patients with neuropathic pain and depression. Patients on high-dose opioids for pain may be at increased risk for the development of delirium and organic mental disorders. Such patients may benefit from the use of low-dose neuroleptics as sleep agents (e.g., thioridazine 25-50 mg or haloperidol 0.5-1.0 mg).

The Older Patient

Older patients frequently have insomnia due to age-related changes in sleep. The sleep cycle in this population is characterized by lighter sleep, more frequent awakenings, and less total sleep time. Anxiety, depression, loss of social support, and a diagnosis of cancer are contributory factors in sleep disturbances in older patients.

Sleep problems in older adults are so common that nearly half of all hypnotic prescriptions written are for persons older than 65 years. Although normal aging affects sleep, the clinician should evaluate the many factors that cause insomnia, such as medical illness, psychiatric illness, dementia, alcohol and/or polypharmacy, restless legs syndrome, periodic leg movements, and sleep apnea syndrome. Nonpharmacologic treatment of sleep disorders is the preferred initial management, with the use of medication when indicated and referral to a sleep disorder center when specialized care is necessary.

Providing a regular schedule of meals, discouraging daytime naps, and encouraging physical activity may improve sleep. Hypnotic prescriptions for older patients must be adjusted for variations in metabolism, increased fat stores, and increased sensitivity. Dosages should be reduced by 30% to 50%. Problems associated with drug accumulation (especially flurazepam) must be weighed against the risks of more severe withdrawal or rebound effects associated with short-acting benzodiazepines. An alternate drug for older patients is chloral hydrate.

Somnolence Syndrome in Children

Cranial irradiation and intrathecal methotrexate are used to prevent the development of central nervous system leukemia in children with acute lymphocytic leukemia. Somnolence syndrome (SS) is a complication of cranial irradiation occurring in 30% to 50% of patients who receive over 1,800 cGy at daily dose fractions of 150 to 200 cGy. The syndrome may appear 4 to 6 weeks following completion of therapy. SS is characterized by mild drowsiness to moderate lethargy and, occasionally, low-grade fever. The pathophysiology is unknown, but electroencephalogram and cerebral spinal fluid abnormalities are detectable in affected children. Although supportive care measures cannot prevent the occurrence of SS, acknowledgment of the existence of this problem may prevent or minimize anxieties for children and parents when symptoms of SS appear.

Sleep Apnea Following Mandibulectomy

Anterior mandibulectomy can result in the development of sleep apnea. All patients with head and neck tumors who have had extensive anterior oral cavity resection should be evaluated prior to decannulation of the tracheostomy tube. Subsequent flap and/or reconstruction of the lower jaw seems to prevent the development of sleep apnea. In contrast, facial sling suspension of the lower lip does not

prevent the development of sleep apnea. Assessment for symptoms and preparation for the appearance of symptoms in this population provide indications for interventions related to sleep apnea.

On a more philosophical note:

Sleep, Dreams and REM Sleep Behavior Disorder

Mahalia Cohen

The discovery of rapid eye movement (REM) sleep suggested that sleep was not, as it was thought to be, a dormant state but rather a mentally dynamic one. Your brain is, in fact, very active in this state, almost to the level at which it is when a person is awake. Yet during this active stage in which most dreams occur, the movements of the rest of the body are completely stilled. To imagine this paralysis during dreams not occurring is a frightful image, since in many cases dreams are violent and active. When the neurotransmitters that control the movement of the body do not work properly the person develops REM sleep behavioral disorder (RBD).

While we are sleeping the sensory world is essentially revolving around us without our knowledge. Our senses of hearing, touch, taste, sight, and smell no longer function as they do when we are awake. Except for the threshold for each of these senses that each of us has while we sleep, our inner systems are working essentially free of input from the outside world. And yet people are able to have vivid dreams. The cortex can only pass into sleep mode with the help of the area of the brain called the thalamus. The thalamus is one of the two structures that make up the diencephalon, the lower part of the fore brain. Its main function in mammals is as the relay station of sensory information its way to the cortical center. Specific regions of the thalamus, as well as different nuclei process different sensory information on its way to the cortex.

In normal sleeping patterns a person usually passes through five phases of sleep, the fifth being REM. The sleeping human passes cyclically through these five phases throughout a night's rest. These phases can be defined in electrical activity of the brain; much like the activity of the heart is often defined. The technique of measuring the electrical activity of the brain is call Electro-encephalogram, or EEG.

When the electrical events of a person's brain are graphed on a electrical magnitude versus time axis the graph of a person who is in different stages of being asleep or awake appear to have different levels of electrical activity occurring in the brain.

During the cycle of the phases each lasts for a different period of time during the time we are sleeping. The first stage is the lightest stage of sleep and is characterized by drifting in and out of sleep and slow muscle and eye activity. When people are awakened during this phase they usually have fragmented visual memory of what they were experiencing while asleep. The second stage is the one in which the most time is spent, close to fifty percent, during this stage three electrical activity, measured by electrodes, slows down except for infrequent bouts of rapid waves called sleep spindles. Stage three and four are considered stages of deep sleep, delta wave appear during phase three and are produced almost exclusively during phase four. Delta waves are extremely slow brain waves. Though there is no consistent eye movement or muscle activity during these two periods, they are the phases of sleep when some children experience bedwetting, night terrors, or sleepwalking.

The next phase is REM sleep, after reaching stage four the pattern of progressively slower, larger brain wave and deeper sleep, reverses and sleep becomes lighter until the REM sleep state is reached. REM is the most active part of sleep, in which the rain waves, when viewed using EEG have a pattern the most similar to those of person who is awake. REM sleep and dreaming, which occurs mainly during REM, are triggered by the pons, a bridge that connects the brainstem with the cerebellum, and

neighboring structures of the brainstem. A pathway originates in a group of acetylcholinergic neurons located in these rostral pons. These neurons project to the sensory areas of the thalamus and to the reticular nucleus. In the sensory areas of the thalamus control whether the gate that allows information from the outside world pass into the brain is open or closed. The acetylcholine produced by the pons' neurons sensitizes these neurons of the thalamus to sensory input by slightly depolarizing, and hence changing the level of potassium. By contrast the reticular nucleus is inhibited by the acetylcholine, as a result the thalamus lets sensory information through , and the cortex is highly active. This process is very similar to what occurs when a person is awake. In the other stage of sleep in which the brain is less active the system works in the opposite manner. The acetylcholine system is inactive, the reticular nucleus is uninhibited and can thus inhibit the thalamus, as a result the cortical neurons move in a slow rhythm , very different from the active state they are in while the creature is awake, or in REM sleep.

The majority of the Dreaming that occurs during a sleep cycle occurs during the REM or paradoxical sleep state. As described above the brain literally awakens internally during REM sleep. In a person with normal sleep behavior the REM sleep stage is one of near paralysis for the entire body other than the muscles of the eye and the middle ear. This occurs because of descending inhibition, in which a group of cells in the medulla that descend down the spinal cord and inhibit motor activity. RBD, rapid eye movement sleep behavior disorder, is characterized by the afflicted person acting out their dreams, which are usually violent in nature. The violent nature of these dream enactments is very distinct from the person's normal waking personality. This suggests that RBD is not only a motor control disorder, but a dream disorder as well. When the person awakens they can remember their dream vividly but cannot recall their physical actions during the dreams. Most of the incidents that occur within the dream are similar in affect to those that the individual was enacting, in one instance an adult male nearly strangled his wife while dreaming that he was saving her from drowning.

The majority of patients afflicted with RBD though there are cases of females and children having this disorder. About 25% of diagnosed patients tested reported limb twitching, talking, yelling, jerking and a progressive decline in motor control during sleep.

These symptoms starkly contrast to the typical atonia, lack of normal muscle tension, which is associated with the REM phase of sleep. In very few isolated cases have any family history of RBD been found. In approximately half of the cases chronic RBD is associated with several different neuropathologies including: vascular insult, tumors, degenerative disorders, etc. In instances where RBD is not a consequence of some other affliction it may be a warning sign of Parkinson's disease.

RBD and other similar dissociative disorders bring up interesting questions about the self. In one respect an individual self is more active during these phases of sleep since there actions and functions are more similar to those that occur when that individual is awake, and supposedly has full use of the self. Yet during these sleep stages the individual loses awareness and control of there physical and mental self. The dreams that they experience, as seen in cases studies, are rarely attributed to what occur in their daily life, and thus are the vivid images are not provided for by their memory bank. Furthermore they have little control over their physical presence, which is controlled by the dream sequence and have no recollections of the actions that took place after they are awakened. These two opposing standpoints leave the question: is the self retained when awareness of the individual’s own actions is lost?

A case study:

An 84-year-old man presents with shouting and strange behaviors at night. His wife describes him suddenly yelling and punching at the air during the night. This seems to arise from sleep and he does not awaken. He has knocked over the bedside lamp and twice struck his wife, so she decided to sleep in a nearby twin bed. She is hesitant to sleep in another room in case, as a result of his agitation, he falls out of bed.

Patients with REM behavior disorder (RBD) appear to "act out their dreams" by yelling or gesturing during REM sleep (dream enactment). They lack the muscle atonia normally found in REM sleep, leading to frequent muscle twitches as well as more complex movements during REM sleep. Polysomnography has also revealed an increase in slow wave sleep and increased limb movements during non-REM sleep. The clinical significance of these non-REM changes is unclear. The differential diagnosis of these events includes nocturnal seizures, non-REM parasomnias, and voluntary behaviors occurring during wakefulness. Polysomnography is not necessarily required to establish the diagnosis of RBD in the case of a patient with a classic presentation. However, sleep studies with careful attention to electromyographic tone during REM sleep can be helpful to exclude other disorders or to identify coexisting OSA.

The prevalence of RBD has not been established. Risk factors include male gender (90% of patients described in the literature) and aging (most aged 50 years or older). Selective serotonin reuptake inhibitors and venlafaxine have been suggested as possible triggers. Patients and their bed partners can be seriously injured by hitting, kicking, rolling, and other more complex behaviors. REM behavior disorder is associated with several neurologic disorders, including Parkinson's disease (15 to 33% of patients), multiple system atrophy (69 to 90%), and dementia with Lewy bodies (prevalence of RBD is unknown). These neurodegenerative disorders all share the pathologic finding of cerebral intracellular inclusion bodies containing α-synuclein.

The primary treatment of RBD symptoms is clonazepam. It suppresses both electromyographic activity during REM sleep and the associated motor behaviors. Dream enactment returns when clonazepam is discontinued. One review of long-term clonazepam use (mean 3.5 years) demonstrated that it was generally well tolerated and dose escalation did not occur. Because the patients with RBD tend to be elderly and most have other neurologic disease, it is optimal to use the lowest possible dose of the benzodiazepine to reduce the risk of falls and impaired cognition. When the long half-life of clonazepam presents a problem, temazepam is a possible alternative. Benzodiazepines should be used by patients with OSA only if their obstructive symptoms are concurrently and successfully treated, usually with nasal CPAP.

And finally, a researcher's overview of RBD:

When the Brain Disrupts the Night

By ERICA GOODE

> The original title I chose for my book Prozac: Panacea or Pandora? was Our Serotonin Sleepwalk Nightmare. At the time of the first edition (1994) everyone argued that no one would know enough about serotonin to understand that the book was about antidepressants so we went ahead with the name of the most popular of the SSRIs - Prozac.

Now for those of you who have read my book or heard me lecture you are aware of the reason for the title I chose - my focus on the most serious of the side effects of SSRIs - the REM Sleep Behavior Disorder (RBD). The largest chapter of my book is devoted to this disorder which I consider the most dangerous of all the reactions to an SSRI. I firmly believe that RBD is the reason for much of the violence we see with the serotonergic antidepressants and the serotonergic antipsychotics as well as Fen-Phen and Redux which are also serotonergic.

To help those who have not read my book and are not familiar with RBD let me quote one statement from an article (below) that ran in the New York Times last month: "REM behavior disorder [RBD] is the only parasomnia routinely associated with violence. But sleepwalkers have also been known to stab their relatives, molest children or confidently stride out of third-story windows, in states varying from confused wakefulness to partial arousal to the deepest stages of non-REM or slow-wave sleep."

Even though no one else has focused on this disorder as I have for so long and worked so hard to get the public to see that these drugs are causing the REM Sleep Behavior Disorder, the following information shocked even me! In fact I am still trying to catch my breath because the original medical article is even more shocking than this NY Times *article.*

Let me first give you a little background before you read the article. In 1991 I made a call to Dr. Carlos Schenk, the author of this study. I told him that I was concerned at how much evidence there was that Prozac (the only SSRI on the American market at the time) was causing the REM Sleep Behavior Disorder. I told him what patients on these drugs were reporting that would show they were experiencing this as a side effect.

He listened intently and then told me that there was not any research to back up my conclusion.

I told him that was okay, but that I had ABSOLUTELY NO DOUBT that Prozac was triggering this most dangerous sleepwalk state and that someone had better do the research because this was something that had the potential of affecting many people worldwide.

Dr. Schenk never called me back to let me know that he immediately began doing that research. He went back through the records at the Minnesota Regional Sleep Disorders Center in Minneapolis where he and his research partner Dr. Mark Mahowold are known as the leading researchers in America on this disorder. Amazingly he found in going through the records for the past 41 months that an astounding 48.8% of all those who had come through the clinic and been diagnosed as suffering from RBD were on Prozac!

If that information was not shocking enough as the information reached the doctors, who then began to watch for this connection, rather than having to go back through old records to see if there might be someone on Prozac who had this disorder, found that 80% of those with the signs of RBD were on Prozac!!! And on top of that the symptoms of this disorder continued in one patient for 19 months AFTER coming off only short term use of Prozac!! Severe sleep disturbance continued for months after coming off the drug. Which is why I mention the importance of using so many natural alternatives to rebuild after being on these drugs.

Of the significance of this information the author of the NY Times article states, "No one yet

knows how common such side effect are, or their implications — if any."

I would gladly tell them how common this side effect is and how far reaching the implications are!!!! That is what I have been trying to tell them for over a decade! Phil and Brynn Hartman would LOVE to explain to them the implications of SSRI induced RBD if they only could, as would thousands of others who have lost their lives to this side effect.

As I say in nearly every lecture I give, "What could be more terrible than to chemically induce first of all someone's most horrifying nightmare and then sleepwalk? In this way the individual acts out the one thing that is the most terrifying thing to them." This is clearly why we have cases of such loving and caring mothers, like Andrea Yates, killing their children - that was her worst nightmare. And no one loved Phil Hartman more than his wife Brynn who even went to a friend's home after shooting him to the friend to come home with her to tell her if she had shot Phil or if she was having a nightmare because she could not tell which was real.

In my opinion the fact that SSRIs are producing the majority of RBD is possibly the most significant piece of research we have ever seen on SSRI antidepressants.

Dr. Ann Blake Tracy, Executive Director, International Coalition For Drug Awarenesswww.drugawareness.org & author of Prozac: Panacea or Pandora? - Our Serotonin Nightmare (800-280-0730) Awake, Jim Smith was an amiable and popular man.

As the director of public works in the small town of Osseo, Minn., he could be counted on to make house calls day or night, attending to burst pipes or broken water mains.

In fall, he hunted deer with buddies, who affectionately called him Smitty. In summer, he took his family pan fishing for crappie.

It was only when Mr. Smith fell asleep that something changed.

Wrapped in slumber, he would shout obscenities, kick the walls, punch the pillows. Sometimes, he hit his wife, Dee, in the back or grabbed her by the hair. One night, dreaming that he was putting a wounded deer out of its misery, he came close to breaking his wife's wrist.

"I just didn't sleep real sound," Mrs. Smith recalled. "Once he started talking or swearing, I would be afraid that the next thing, he would be swinging his fists."

In an earlier century, Mr. Smith might have undergone exorcism to expel the demons that possessed him when his eyes closed. In the 1960's, psychiatrists might have traced his problem to repressed aggression and prescribed a sojourn on the analytic couch.

But in the last two decades, researchers have begun to systematically investigate a variety of disorders — called parasomnias — involving odd or dangerous behavior during sleep. One is called REM behavior disorder, in which people act out their dreams.

This was the diagnosis Mr. Smith received in 1987 when he sought treatment at the Minnesota Regional Sleep Disorders Center in Minneapolis.

Parasomnias are more common than was once thought, researchers are finding. They can be successfully treated, and most have nothing to do with mental illness.

At the same time, research on such sleep problems is challenging basic assumptions about sleep and wakefulness, showing that the borders between the two states are far from clearly demarcated. And in the case of REM behavior disorder, one of the most studied parasomnias, investigators are finding surprising links to physical illness.

For example, at the annual meetings of the Associated Professional Sleep Societies in June, Dr. Carlos H. Schenck, a psychiatrist and senior scientist at the Minnesota sleep center, and Dr. Mark W. Mahowald, a neurologist and the director of the clinic, will present findings indicating that of 26 otherwise healthy patients in whom REM behavior disorder was diagnosed in the 1980's, 17 went on to develop Parkinson's disease.

Other studies, at the Mayo Clinic and elsewhere, have found associations between the sleep disorder and other neurodegenerative diseases related to Parkinson's, including a form of dementia known as Lewy body disease and an illness called multiple system atrophy.

Mr. Smith, now 72 and retired, learned in May 2001 that he had Parkinson's.

The connection between REM behavior disorder and Parkinson's is the latest twist in a story that began 20 years ago, when a retired grocer named Donald Dorff came to Dr. Schenck complaining of what he called "violent moving nightmares." In one such dream, Mr. Dorff, believing he was a quarterback heading for a touchdown, ran forcefully into his bedroom dresser.

Wiring his new patient up in the sleep laboratory, Dr. Schenck discovered that Mr. Dorff's violent behavior occurred during periods of rapid eye movement, or REM, sleep, a stage that accounts for 20 to 25 percent of nighttime repose in humans and that shows up on electroencephalogram recordings as a pattern of electrical activity similar to that seen during waking. Most dreaming takes place in REM sleep.

During REM, the brain dispatches signals to the muscles, telling them to perform the movements that would be appropriate if the person were awake.

In most sleepers, however, another brain circuit also kicks into action during REM to prevent the dreamer from carrying out those instructions. Nerve cells transmit chemical messages that paralyze all muscles in the body except the diaphragm, one small muscle in the ear and the muscles that move the eyes.

Mr. Dorff's problem appeared to be that the normal paralysis of REM was missing. The same was true for four other elderly patients, described by Dr. Schenck and his colleagues in a 1986 report documenting the first human cases of the disorder. In fact, the researchers realized, the patients were acting a lot like a group of laboratory cats studied in the mid-1960's by a French sleep expert, Dr. Michel Jouvet.

Trying to locate the regions of the brain responsible for REM sleep, Dr. Jouvet and his colleagues destroyed cells in an area of the brainstem called the pons. Even with this damage, the cats still entered REM sleep, the scientists found. But instead of lying still, they stood up, looked around and sometimes stalked imaginary prey.

Subsequent studies, by Dr. Adrian R. Morrison at the University of Pennsylvania School of Veterinary Medicine, showed that the extent of the behavior exhibited by the animals during REM depended on where in the pons the lesions were made. For example, when the cell damage encompassed nerve pathways extending from the amygdala, a brain structure involved with emotion, the cats would attack humans or other cats.

As with Mr. Dorff, who died in 1999, and Mr. Smith, studies show that more than 80 percent of patients who show up at sleep disorder clinics with REM behavior disorder are men, middle-aged or older, and most, Dr. Schenck said, are noticeably placid and good-natured in their waking life. Many display rhythmic movements of their legs even during non-REM or slow-wave sleep.

Most patients also report unusually vivid dreams (sometimes beginning long before they start acting them out) in which they are being threatened or attacked or engaging in active sports.

One man dreamed that his boss was chasing him with a hatchet; another that he was being pursued by a lion, said Dr. Bradley F. Boeve, a neurologist at the Mayo Clinic who studies REM behavior disorder and Parkinsonian illnesses.

Sometimes, Dr. Schenck said, a husband will awake from a dream in which he is protecting his wife from danger, only to find that in fact he has been pummeling her.

“She wants to know why he’s beating up on her and he says, `I’m not, I’m beating up this man,’ “Dr. Schenck said, how the sleep problem is connected to neurodegenerative illnesses later in life.

But recent work by Dr. Jerome Siegel at the University of California at Los Angeles offers another piece of the in other cases, patients have no memory of what stirred them to action. On a hunting trip, for example, Mr. Smith leaped abruptly from bed and began singing “God Bless America,” to the amusement of his bunkmates. But he could not recall the dream that inspired this burst of patriotism.

An increasing number of studies link REM behavior disorder to neurological disease. The damage to the pons that in animals suspends paralysis during REM sleep is not regularly found in humans with the disorder. And it is not yet entirely clear puzzle and may help explain a possible connection to Parkinsonian diseases.

Neurons in particular areas of the midbrain, just above the pons, have a potent effect in suppressing muscle tone, Dr. Siegel has found. In rats, damage to those areas produces muscle movements during REM similar to those seen in human patients with the sleep disorder. And the nerve cells in those regions are very close to, and interconnected with, neurons in a midbrain center known to suffer cell damage in Parkinson’s.

“Given the connection between REM behavior disorder and Parkinson’s,” Dr. Siegel said, “the hypothesis that we’re pursuing is that the degenerative process that causes Parkinson’s may spread to the region responsible for inhibiting muscle tone” or vice versa.

Brain scans of patients have added to the suspicion that the sleep disorder in some way signals the beginning of Parkinsonian disease. In 2000, Dr. Ilonka Eisensehr of the University of Munich reported finding a kind of “Parkinsonian fingerprint” — a reduction in the enzyme that transports the messenger chemical dopamine in the striatum, the region of the midbrain where Parkinson’s originates — in the brain scans of patients with REM behavior disorder who did not yet have any other signs of neurological disease.

In a development that experts call troubling, sleep clinics are also seeing a number of patients who develop some symptoms associated with REM sleep disorder while taking Prozac, Zoloft or others of the newer generation of antidepressant drugs called selective serotonin reuptake inhibitors or S.S.R.I.’s

A 1992 study by scientists at the Minnesota sleep clinic found that 20 of 41 patients taking Prozac for depression or obsessive-compulsive disorder exhibited “extensive, prominent eye movements” during light non-REM stages of sleep, a phenomenon the researchers have called “Prozac eyes.” In one patient, the eye movements were still present 19 months after the man stopped taking the antidepressant.

Other reports suggest that some people taking the drugs experience muscle jerks or other movements during sleep or waking Dr. John Winkelman, the medical director of the sleep health center at Brigham and Women’s Hospital in Boston, said he had seen a number of patients who developed REM behavior disorder while taking S.S.R.I.’s.

“A couple of people threw themselves out of bed,” Dr. Winkelman said.

No one yet knows how common such side effects are, or their implications — if any. And other drugs — barbiturates and stimulants, for example — can also contribute to REM behavior disorder. But the findings, the experts say, should encourage doctors to prescribe responsibly.

“The drugs are very effective,” Dr. Mahowald said. “But it’s the physician’s responsibility to make sure the patient’s condition is severe enough to warrant prescribing a neuroactive agent.”

On the other hand, some psychiatric drugs are effective in treating the sleep disorder. Dr. Boeve said he found the drug Seroquel helpful for some patients.

What eventually kept Mr. Smith from inflicting further damage on his wife was clonazepam, a tranquilizer that Dr. Schenck and other experts have shown almost always calms patients’ turbulent nights.

“It helped right away,” Mrs. Smith said.

REM behavior disorder is the only parasomnia routinely associated with violence. But sleepwalkers have also been known to stab their relatives, molest children or confidently stride out of third-story windows, in states varying from confused wakefulness to partial arousal to the deepest stages of non-REM or slow-wave sleep. Other sleep disorder patients, who suffer from a

condition called nocturnal dissociative disorder, awaken and leave their beds to re-enact scenes of physical or sexual abuse, sometimes cutting themselves with razors or banging their heads against the wall. Afterward, they remember nothing about their nighttime behavior.

Reports of violence during slumber date back to the ancient Greeks.

In Homer's "Odyssey," Elpenor, the youngest of Odysseus' crew, wakes suddenly from a drunken nap and runs off the roof of a house, breaking his neck.

Simon Fraser, a 19th-century Scot who killed his 18-month-old son by dashing him against the wall, said he did so while dreaming that a wild beast had jumped on the bed and was attacking the boy. "I am guilty in my sleep, but not guilty in my senses," he insisted.

More recently, the defendants in several murder cases have used sleep as a defense, in one instance successfully: a Canadian, Kenneth Parks, was acquitted after experts testified that he was in a somnambulistic state when, in May 1987, he drove 14 miles to the house of his in-laws, where he stabbed his mother-in-law to death and nearly killed his father-in-law.

Such cases, Dr. Mahowald said, make it clear that sleep and waking are hardly distinct states.

In many normal people, he said, detailed neurophysiological studies of the brain show that the signs of sleep persist for an hour after awakening, though an EEG indicates that the person is already fully awake.

"Most people's concept is that the entire brain is in one state of being, and that's just not true," Dr. Mahowald said. "You can have parts of the brain that are awake while others are asleep."

Glossary of Sleep Terms

Abdominal Movement - In diagnostic sleep studies, abdominal movement is recorded. This is one of the measures of respiratory effort, reflecting movement of the diaphragm.

Advanced Sleep Phase Syndrome (ASPS) - Phases of the daily sleep/wake cycle are advanced with respect to clock time. This is classified as a circadian rhythm disorder. The sleep phase occurs well ahead of the conventional bedtime and the tendency is to wake up too early.

Alpha rhythm - EEG oscillations, prominent over the occipital cortex, with a frequency of 8-13 Hz in adults; indicative of the awake state; present in most, but not all, normal individuals; most consistent and predominant during relaxed wakefulness.

Alpha intrusion - brief occurrence of alpha activity during a stage of sleep.

Ambulatory Monitor - Portable system used to record (continuously) multiple physiological variables during sleep.

Apnea - Literally means "no breath"; the cessation of airflow at the nostrils and mouth for at least 10 seconds.

Apnea index (AI) - A measure of the severity of sleep apnea; the number of apnea events per hour.

Apnea/Hypopnea index (AHI) - the number of apneas and hypopneas per hour. 5-20=mild, 21-50=moderate, above 51 severe

Arousal - abrupt change from sleep to wakefulness, or from a "deeper" stage of non-REM sleep to a "lighter" stage

Arousal Disorder - parasomnia disorder presumed to be due to an abnormal arousal function. Classical arousal disorders: sleepwalking, sleep terrors and confusional arousals.

Arousal Threshold - ease that a sleeping person is awakened.

Arrhythmia - irregularity or absence of the heart rhythm caused by disturbances in transmission of electrical impulses through cardiac tissue.

Auto Adjusting Continuous Positive Airway Pressure Device (SmartPAP) (Auto-PAP) - A type of CPAP machine monitoring changes in breathing and compensates automatically by making appropriate adjustments in pressure.

Automatism - automatic action--especially any action performed apparently without intention or awareness.

Basic Sleep Cycle - progression through orderly succession of sleep states and stages. For the healthy adult, the first cycle is begins by going from wakefulness to non-REM sleep. The first REM period follows the first period of non-REM sleep, and the two sleep states continue to alternate throughout the night with an average period of about 90 minutes. A night of normal human sleep usually consists of 4-6 non-REM/REM sleep cycles.

Benzodiazepines - developed in the 1950's, this class of compounds tranquilize and sedates.

Beta Activity - brain waves with a frequency of greater than 13 Hz (Hertz).

Bi-Level - Bi-level pressure device used to treat sleep apnea. The "bi" refers to two pressures: a lower pressure for exhalation and a higher pressure for inhalation. Bi-Level machines are more expensive than a standard CPAP, but some patients tolerate it better because they can exhale comfortably against the constant inhalation pressure. (Sometimes called **Bi-PAP,** but that is a trademark name of one system)

Biological Clock - term for the brain process causing us to have 24-hour fluctuations in body temperature, hormone secretion, and other bodily activities. The most important function fosters the daily alternation of sleep and wakefulness. The biological clock is found in a pair of tiny bilateral brain areas called the suprachiasmatic nuclei.

Body Position - four positions are identified which a patient may be sleeping; back, left side, right side or abdomen. The time spent sleeping in each position and the number of respiratory events in a particular position are tabulated.

Bradycardia - heart rhythm with a rate lower than 60 beats per minute in an adult.

Brain Waves – the brain's spontaneous electrical activity studied by electroencephalography (EEG).

Bruxism – teeth grinding during sleep

Cardiac Arrest - sudden cessation of the heart beat.

Cardiovascular - Pertaining to blood vessels and the heart

Cataplexy - sudden, dramatic decrement in muscle tone and loss of deep reflexes that leads to muscle weakness, paralysis, or postural collapse. Usually caused by outburst of emotion: laughter, startle, or sudden physical exercise; one of the tetrad of symptoms of narcolepsy.

Central apnea - absence of airflow and inspiratory effort; apnea caused by irregularity in the brain's control of breathing.

Central Nervous System (CNS) - brain and spinal cord.

Cheyne-Stokes respiration - breathing pattern typified by regular "crescendo-decrescendo" or waxing and waning fluctuations in respiratory rate and tidal volume.

Chronotherapy - treatment for circadian rhythm sleep disorder by systemically changing sleeping and waking times to reset the biological clock.

Circadian rhythm - innate, daily, fluctuation of behavioral and physiological functions, including sleep waking, generally tied to the 24 hour day-night cycle but sometimes to a different (e.g., 23 or 25 hour) periodicity when light/dark and other time cues are removed.

Compliance - adhering to or conforming with a regimen of treatment such as CPAP

CPAP - Continuous Positive Airway Pressure; the device used to treat sleep apnea by sending positive airway pressure at a constant, continuous pressure to help keep an open airway, allowing the patient to breathe normally through his/her nose and airway

CPAP Pressure - pressure needed to maintain an open airway in a sleep apnea patient treated with CPAP, expressed in centimeters of water (cm H20). The positive pressure can range from 5 - 20 cm H20. Different patients require different pressures. The value is determined in a CPAP titration study.

Deep Sleep - refers to combined non-REM sleep stages 3 and 4 in sleep studies

Delayed sleep phase - A condition occurring when the clock hour at which sleep normally occurs is moved back in time in a given, 24 hour sleep-wake cycle. The result is a temporarily displaced (delayed) occurrence of sleep within the 24 hour cycle.

Delta sleep - stage(s) of sleep in which EEG delta waves are prevalent or predominant (sleep stages 3 and 4, respectively).

Delta waves - EEG activity with a frequency less than 4 Hz. In human sleep stage scoring, conventionally the minimum criteria for scoring delta waves is 75 UV (peak-to-peak) amplitude, and 0.5 second duration (2 Hz).

Diagnostic Sleep Study - monitoring of several physiological activities in a sleeping individual. Usually performed to determine the absence or presence of a specific sleep disorder. The sleep study can occur in a sleep disorders center or in a patient's home with portable recording equipment.

Diaphragm - large, concave muscle attached to the rib cage at bottom of the chest (top of the abdomen). Inhalation occurs when diaphragm contracts. Exhalation is passive as the muscle relaxes.

Diurnal - active and wakeful in the daytime versus active in the nighttime

DME - Durable Medical Equipment. Equipment such as wheelchairs and walkers which are prescribed for use by or on the order of a physician, also includes CPAP and BI-Level machines.

Drowsiness, Drowsy - quiet wakefulness occurring prior to sleep onset.

Dyssomnia - a disorder of sleep or wakefulness; not a parasomnia

Electrocardiography (EKG) – a method of measuring the electrical activity of the heart.

Electrodes - small devices transmitting biological electrical activity from subject to polygraph

Electroencephalogram (EEG) - recording through the scalp of electrical potentials from the brain and the changes in these potentials. The EEG is one of the three basic variables (along with the EOG & EMG) used to score sleep stages and waking. Surface electrodes are used to record sleep in humans, recording potential differences between brain regions and a neutral reference point, or between brain regions.

Electromyogram (EMG) - recording of electrical activity from the muscular system; in sleep recording, synonymous with resting muscle activity or potential. The chin EMG, along with EEG and EOG, is one of the three basic variables used to score sleep stages and waking. Surface electrodes are used to record sleep in humans, measuring activity from the submental or masseter muscles. These reflect the changes in resting muscle activity. During REM sleep the chin/cheek EMG is tonically inhibited.

Electro-oculogram (EOG) - recording of voltage changes resulting from shifts in position of the eyeball-possible because each globe is a positive (anterior) and negative (posterior) dipole; along with the EEG and the EMG, one of the three basic variables used to score sleep stages and waking. Human sleep recordings utilize surface electrodes placed near the eyes to record the movement of the eyeballs. Rapid eye movements in sleep indicate a certain stage of sleep (usually REM sleep).

ENT - Ear, Nose and Throat. A doctor specializing in diseases of the Ear, Nose and Throat. These specialists often do surgery as well, and may be referred to as an ENT surgeon.

EPAP - Expiratory Positive Airway Pressure. Pressure prescribed for the expiratory (breathing out) phase of an individual on Bi-level CPAP therapy for OSA (obstructive sleep apnea).

Epidemiology - Scientific discipline studying the incidence, distribution, and control of disease in a population. Includes the study of factors affecting the progress of an illness, and, in the case of many chronic diseases, their natural history.

Epoch - A standard 30 second duration of the sleep recording that is assigned a sleep stage designation; for special purposes, occasionally longer or shorter epochs are scored.

Epworth Sleepiness Scale - index of sleep propensity during the day as perceived by patients, and derived from the answers to 8 questions.

Esophageal Pressure - measurement used to determine respiratory effort and by inference, airway resistance. Considered an invasive measure, generally used only in polysomnographic testing, conducted in sleep disorders centers.

Excessive daytime sleepiness or somnolence (EDS) - subjective report of difficulty in staying awake, accompanied by a ready entrance into sleep when the individual is sedentary

Expiratory Phase - air is expelled during this phase of the breathing cycle

Fatigue - feeling of tiredness or weariness usually associated with performance decrements

Fiberoptic Nasopharyngoscope - flexible fiberoptic scope used in the examination of nasal passages, pharynx, hypopharynx and larynx.

Fibromyalgia - a disease syndrome whose primary symptoms are muscle pain and fatigue.

Flattening Index - number indicating the amount of airflow limitation caused by partial closure of the upper airway. 0.3 indicates an open airway, 0.15 is mildly obstructed, 0.1 is severely limited airflow, and 0.0 reflects a totally closed airway. Flattening Index is used to identify the condition known as Upper Airway Resistance Syndrome (UARS), and is continuously recorded in both diagnostic sleep studies and CPAP titrations.

Flow Limitation – the partial closure of the upper airway impeding the flow of air into the lungs.

Forbidden Zone – the period of strongest clock-dependent alerting, usually in the evening. Prevents falling asleep.

Fragmentation (pertaining to Sleep Architecture) - interruption of a sleep stage as a result of the appearance of a lighter stage, or to the occurrence of wakefulness, which leads to disrupted non-REM-REM sleep cycles.

GABA (Gamma-Amniobutyric Acid) - major neurotransmitter in the brain, which is considered to be involved in muscle relaxation, sleep, diminished emotional reaction and sedation.

Gastroesphageal Reflux Disease (GERD) - flow of stomach acid upwards into the esophagus that can cause arousals and disrupt sleep.

Genioglossus tongue advancement – a possible surgical treatment used for sleep apnea and/or snoring, improving the airway behind the base of the tongue. The genioglossus, the main tongue muscle, relaxes during sleep, often allowing the tongue to fall into the airway. The muscle attaches to the middle of the lower jaw. A segment of bone containing this muscle is pulled forward and stabilized, opening the airway space behind the tongue.

Habitual Snorers - those who snore nearly every night

Heart Rate or beats per minute (bpm) – pace/speed of the heart measured in beats per minute. 60-80 is considered normal in adults.

Hertz (Hz) - unit of frequency; equal to cycles per second (cps).

Histogram (sleep) - graph indicating sleep stages thoughout the night.

Humidification - moisture is added to the airflow as an adjunct to CPAP (Continuous Positive Airway Pressure) therapy in treating obstructive sleep apnea (OSA). Humidification can be added to the CPAP by diverting the airflow over or through a cool or heated water reservoir (humidifier) to prevent the upper airway from drying out.

Hyoid Suspension – a possible surgical procedure sometimes used in the treatment of sleep apnea and/or snoring, designed to improve the airway behind the base of the tongue. The hyoid bone is located in the neck where some tongue muscles attach. The hyoid bone is pulled forward in front of the voice box and can open the airway space behind the tongue.

Hyperactivity – typical behavior in a child with a sleep disorder which is causing lack of quality sleep

Hypercapnia – excessive or elevated carbon dioxide in the blood

Hyperirritability - Extreme irritability; seen in sleep deprived subjects.

Hypersomnia – excessive, prolonged sleep

Hypertension -High blood pressure.

Hypnagogic imagery (-hallucinations) - Vivid sensory images occurring at sleep onset but particularly vivid with sleep-onset REM periods; feature of narcoleptic REM naps.

Hypnagogic startle - "sleep start" or sudden body jerk, observed normally just at sleep onset, resulting in at least momentary awakening

Hypnophobia - Morbid fear of falling asleep.

Hypnotics - Sleep-inducing drugs.

Hypopharynx - lowermost portion of the pharynx leading to the larynx and esophagus.

Hypopnea - shallow breathing in which the air flow in and out of the airway is less than half of normal--usually associated with oxygen desaturation.

Hypoventilation - reduced rate and depth of breathing.

Hypoxemia - abnormal lack of oxygen in the blood in the arteries.

Hypoxia - deficiency of oxygen reaching the tissues of the body.

Imidazopyridines - New class of compounds inducing sleepiness. (Zolpidem, trade name Ambien, is in this class).

Inappropriate Sleep Episodes – unplanned sleep periods often occuring in an unsafe situation (i.e., while driving). These episodes are always due to sleep deprivation.

Insomnia – complaint describing difficulty in sleeping

Inspiratory Phase - part of the breathing cycle in which air is inhaled.

Invasive – referring to a medical procedure in which a bodily orifice or the skin must be penetrated for the purpose of collecting data, or for diagnosing or treating a disorder

IPAP - Inspiratory Positive Airway Pressure. Physician prescribed pressure for the inspiratory phase on a Bi-level CPAP device, used in the treatment of OSA.

Jet Lag - disturbance induced by a major rapid shift in environmental time during travel to a new time zone

K-Alpha - type of micro arousal; K complex followed by several seconds of alpha rhythm.

K complex - sharp, negative, high-voltage EEG wave, followed by a slower, positive component. K complex, occurring spontaneously during NREM sleep, beginning in (and defining) stage 2. K complexes can be elicited during sleep by external (particularly auditory) stimuli as well.

Laser assisted uvulopalatoplasty (LAUP) - can eliminate or decrease snoring but has not been shown to be effective in the treatment of sleep apnea.

Leg Movement - Leg movements are recorded in both diagnostic sleep studies and titration studies.

Letter of Medical Necessity (LMN) - certification by a physician that the prescribed item(s) is/are medically indicated, reasonable and necessary with reference to the standards of medical practice and treatment of a patient's condition

Light-Dark Cycle - periodic pattern of light (artificial or natural) alternating with darkness

Light Sleep - term used to describe non-REM sleep stage 1, and sometimes, stage 2.

Light Therapy - used in the treatment of SAD (Seasonal Affective Disorder) and other conditions. Exposes the eyes to light of appropriate intensity and duration and at the appropriate time of day to effect the timing, duration and quality of sleep.

Limit-Setting Sleep Disorder – disorder due to child's difficulty in falling asleep by delaying and refusing to go to bed

Linear Sleepiness Rating Scale - measure of subjective sleepiness. The scale contains a horizontal line, 100 mm in length --the right extreme is labeled "Very Sleepy" and the left extreme is labeled "Very Wide Awake."

Macroglossia - large tongue; usually a congenital disorder (present at birth)

Maxillofacial - pertaining to the jaws and face.

Mandibular Maxillary Osteotomy and Advancement (MMOA) - procedure developed for patients with retrolingual obstruction, patients with retropalatal and retrolingual obstruction who have not responded to CPAP and uvulopalatopharyngoplasty (UPPP).

Melatonin - hormone secreted by the brain's pineal gland

Micro-arousal - partial awakening from sleep

Micro-sleep - period lasting up to a few seconds during which the polysomnogram suddenly shifts from waking characteristics to sleep.

Mixed (sleep) apnea - interruption in breathing during sleep beginning as a central apnea then becoming an obstructive apnea.

Monocyclic - a single major sleep period and a single major wake period in a 24-hour day.

Motor Activity in Sleep - any muscular movement during sleep

Motor Atonia – the absence of muscle activity during sleep

Movement arousal - body movement associated with arousal or awakening; a sleep scoring variable.

Movement time - term used in sleep record scoring to denote when EEG and EOG tracings are obscured for more than 15 seconds due to movement.

Multiple sleep latency test (MSLT) - a series "nap tests" utilized in the assessment of excessive daytime sleepiness.

Muscle Tone – amount of tension in a muscle.

Myoclonus - muscle contractions in the form of "jerks" or twitches.

Nap - short period of planned sleep generally obtained at a time separate from the major sleep period.

Narcolepsy - sleep disorder characterized by excessive sleepiness, cataplexy, sleep paralysis, hypnogogic hallucinations, and an abnormal tendency to pass directly from wakefulness into REM sleep

Nasal Airflow/Nasal Ventilation - recording of the complete respiratory cycle by measuring inspiratory and expiratory airflow

National Commission on Sleep Disorders Research (NCSDR) - the commission (created by the U.S. Congress in 1990) conducted a comprehensive study of the social and economic impact of sleep disorders in America and made recommendations based on its findings to the Congress in January 1993

Neurology - branch of medicine that referring to the nervous system and its diseases

Neurotransmitters - endogenuous chemical components that are released from axon terminals of one neuron and transmit the signal to the next neuron by combining with its receptor molecules. Neurotransmitters important in the control of sleep and wakefulness include: norepinephrine, serotonin, acetylcholine, dopamine, adrenaline and histamine.

Nightmare - unpleasant and/or frightening dream occurring in REM sleep (different from a night terror)

Night Terrors - also known as sleep terrors, or pavor nocturnus. Night terrors are characterized by an incomplete arousal from slow wave sleep. If, the individual is awakened during a night terror, he/she is usually confused and does not remember details of the event. Night terrors are different from nightmares; if an individual is awakened during a nightmare, he/she functions well and may have some recall of the nightmare.

Nocturia - excessive, often frequent, urination during the night

Nocturnal - "Of the night;" pertaining to events happening during sleep or the hours of darkness.

Nocturnal Confusion - episodes of delirium and/or disorientation near or during nighttime sleep; often seen in victims of Alzheimers Disease and more common in the elderly

Nocturnal sleep-related eating disorder (NS-RED)- Getting up during the night and eating while sleepwalking. No recall in the morning.

Nocturnal Enuresis (Bedwetting) - urinating while asleep

Non-Invasive - Medical procedure not penetrating the skin or a body cavity.

NREM or non-REM sleep - characterized by slower and larger brain waves and little or no dream behavior; quiet sleep, slow-wave sleep; approximately 80% of sleep

NREM Sleep Intrusion - brief period of NREM sleep patterns appearing in REM sleep; a portion of NREM sleep not appearing in its usual sleep cycle position

Obesity-Hypoventilation Syndrome - term applied to obese individual's hypo ventilating during wakefulness.

Obstructive apnea - cessation of airflow (at least 10 seconds) in the presence of continued inspiratory effort; cessation of breathing during sleep, due to a mechanical obstruction, such as a semi-collapsed trachea, tongue relaxed to back of the throat, or a large among of tissue in the uvula area.

Obstructive Hypopnea - periodic and partial closure of the throat during sleep resulting in reduced air exchange at the level of the mouth and/or nostril.

Ondine's Curse - the respiratory center in the brain is unable to stimulate breathing in response to an increased amount of carbon dioxide in the blood. Ondine's Curse or central alveolar hypoventilation typically worsens during sleep.

Optimum Sleep - average amount of sleep needed every night by an individual.

Oxygen Desaturation - less than normal amount of oxygen carried by hemoglobin in the blood; values below 90% are considered abnormal

Oxygen Saturation - measure of oxygen carried by hemoglobin in the blood. Normal values 90% - 100%.

Oximeter (Pulse) - gives estimates of arterial oxyhemoglobin saturation (SaO2) by utilizing selected wavelengths of light to none invasively determine the saturation of oxyhemoglobin (SpO2)

Oximetry (Pulse) - continuous monitoring of oxygen saturation of arterial blood from a pulse oximeter; the sensor is usually attached to the finger.

O2 - Chemical symbol for oxygen. Criterion lowest percent O2 saturation: Greater than 85%=mild, 80% to 85%=moderate, less than 80%=severe

Parasomnia - an event happening during sleep, or induced or exacerbated by sleep, such as sleepwalking or asthma; not a dyssomnia.

Paroxysmal nocturnal dyspnea (PND) - respiratory distress and shortness of breath due to pulmonary edema, appearing suddenly and often awakening the sleeping individual.

Pathological Sleep - abnormal sleep patterns.

Pavor Nocturnus (Night Terrors) - See Night Terrors.

Perceptual Disengagement - change in consciousness at the onset of sleep when environmental stimuli are no longer perceived, and there is no longer any conscious, meaningful interaction with the environment.

Periodic Breathing - repetitive apneic pauses, common in premature infants.

Periodic Limb Movement Disorder - also known as periodic leg movements and nocturnal myoclonus. Characterized by periodic episodes of repetitive and highly stereotyped limb movements occuring during sleep. The movements are often associated with a partial arousal or awakening; however, the patient is usually unaware of the limb movements or frequent sleep disruption. Between the episodes, the legs are still. There can be marked night-to-night variability in the number of movements or in the existence of movements.

Persistent Insomnia - continuing insomnia responding poorly to treatment.

Pharynx - area posterior to the nares and the oral cavity; passageway for air from the nasal cavity and/or the mouth to the lungs via the larynx and the trachea, for food and liquids from the mouth to the esophagus

Phase advance - movement to a position earlier in the 24 hour sleep - wake cycle of a period of sleep or wake; for example, a shift of the sleep phase from 11 p.m. - 7 a.m. to 8 p.m. - 4 a.m.

Phase delay - Phase delay is exactly the opposite of phase advance, i.e., a shift later in time.

Phasic (Event/Activity) - brain, muscle, or autonomic related event of a brief and episodic nature occurring in sleep. Usually occur during REM sleep, such as eye movements and/or muscle twitches

Photoperiod - duration of light in a light/dark cycle.

Pickwickian Syndrome - obesity accompanied by somnolence, lethargy, chronic hypoventilation, hypoxia, and secondary polycythemia (a condition marked by an abnormal increase in the number of circulating red blood cells); usually has severe obstructive sleep apnea

Pineal Gland - gland in the brain secreting the hormone melatonin.

PLMD-Arousal Index - number of sleep-related periodic leg movements per hour of sleep that are associated with an EEG arousal

Polycyclic - multiple sleep periods and wake periods in a 24-hour day.

PO2 - partial pressure of oxygen (O2) in the blood. A value above 60 is usually considered a safe level: lower than 60 indicated hypoxemia and potential danger for the patient.

Polysomnogram (PSG) - continuous and simultaneous recording of physiological variables during sleep, i.e., EEG, EOG, EMG (the three basic stage scoring parameters), EKG, respiratory air flow, respiratory excursion, lower limb movement, and other electrophysiological variables.

Polysomnograph - biomedical instrument for the measurement of multiple physiological variables of sleep

Polysomnographic Technologist - health care professional trained in performing diagnostic sleep studies

Post-Prandial Drowsiness - sleepiness that occurs after a meal, usually lunch

Post-Traumatic Stress Disorder - re-experiencing of a traumatic event in the form of repetitive dreams, recurrent and intrusive daytime recollections, and/or dissociative flashback episodes.

Premature morning awakening - early termination of the sleep period in a sleep maintenance DIMS due to inability to return to sleep after the last of several awakenings

Prescribed CPAP Pressure - pressure(s) or settings determined by a CPAP titration sleep study, which a physician prescribes for a patient's CPAP therapy machine

Pulse Oximetry - non-invasive measure of oxygen saturation; that is the amount of oxygen saturated in the hemoglobin in terms of percentage; not as accurate as the values obtained from an arterial blood gases (ABG) test and should only be used as a gauge of oxygenation. Normal ranges are between 95-100%.

Quiet Sleep - The term frequently used instead of NREM sleep to describe the sleep of infants.

Radiofrequency (RF) - Electromagnetic radiation in the frequency range 3 kilohertz (kHz) to 300 gigahertz (GHz); considered to include microwaves and radio waves. Microwaves occupy the spectral region between 300 GHz and 300 MHz, while RF or radio waves include 300 MHz to 3 kHz.

Radiofrequency (RF) Procedure (also known as Somnoplasty) - procedure for treating nasal obstruction, snoring and in some cases, sleep apnea. The procedure uses radiowave energy to reduce snoring and the size of the soft palate.

RDI - Respiratory Disturbance Index, includes all respiratory events per hour.

REM sleep, rapid eye movement sleep - sleep characterized by the active brain waves, flitting motions of the eyes, and weakness of the muscles; most dreaming occurs in this stage, which accounts for about 20% of sleep in adults.

REM Density - A function that expresses the frequency of eye movements per unit of time during REM sleep.

REM-Associated Disorders - Sleep disturbances that occur in REM sleep.

REMS latency - The period of time in the sleep period from sleep onset to the first appearance of stage REMS.

REM Motor Atonia - The active suppression of activity in the antigravity and voluntary muscles during REM sleep. The muscles are completely flaccid and limp.

REM onset - designation for commencement of a REM period; used also as a shorthand term for a sleep-onset REM period

REM period - REM portion of a NREM-REM cycle; early in the night it may be as short as a half-minute, whereas in later cycles longer than an hour.

REM rebound or recovery - lengthening and increase in frequency and density of REM periods, which results in an increase in REM percent above base line. REM rebound follows REM deprivation once the inhibitory influence is removed

REM Sleep Behavior Disorder (RBD) - disorder in which REM motor atonia is partially or completely absent and the individual acts out the ongoing dream. The behavior in REM behavior disorder is often correlates with the ongoing, hallucinatory REM dream episode.

REM Sleep Episode - REM sleep portion of a NREM-REM sleep cycle. Early in the first sleep period, episodes may be only several minutes in duration. Later REM episodes almost are always longer, 20 to 30 minutes up to an hour.

REM Sleep Intrusion - brief interval of REM sleep appearing out of its usual positioning in the NREM-REM sleep cycle.

REM Sleep Latency - interval from sleep onset to the first appearance of REM sleep

REM Sleep Onset - designation for the first epoch of a REM sleep episode

REM Sleep Percent - proportion of total sleep time occupied by REM sleep

REM Sleep Rebound - compensatory increase in REM sleep following experimental reduction. Extension of time in, and an increase in frequency and density of REM sleep episodes; usually an increase in REM sleep percent of total sleep time above baseline values

Respiratory Care Practitioner (RCP) - licensed health care professional specifically trained in cardiopulmonary assessment, diagnostics, therapy administration, and patient education, including the identification and treatment of sleep disorders

Restless Legs Syndrome (RLS) - sleep disorder characterized by a deep creeping, or crawling sensation in the legs that tends to occur when an individual is not moving. There is an almost irresistible urge to move the legs; the sensations are relieved by movement.

Restlessness (Referring to Quality of Sleep) - Persistent or recurrent body movements, arousals, and/or brief awakenings in the course of sleep

Sedatives - compounds tending to calm, and reduce nervousness or excitement and foster sleep

Sedentary Situation - not requiring physical activity, e.g. working at a desk, sitting in a meeting or in a theater, watching television.

Septoplasty - surgery on the nasal septum (dividing the nasal passage)

Serotonin - neurotransmitter in the brain that modulates mood, appetite, sexual activity, aggression, body temperature and sleep

Shiftwork - working hours outside of the conventional daytime hours of 9:00 a.m. to 5:00 p.m.

Sleep - a state marked by lessened consciousness, lessened movement of the skeletal muscles, and slowed-down metabolism

Sleep Apnea - cessation of breathing for 10 or more seconds during sleep

Sleep architecture - NREM/REM stage and cycle infrastructure of sleep understood from the vantage point of the quantitative relationship of these components to each other

Sleep cycle - synonymous with NREM-REM cycle

Sleep Debt - result of recurrent sleep deprivation which occurs over time when an individual does not experience a sufficient amount of the restorative daily sleep that is required to maintain a sense of feeling rested and refreshed. .

Sleep Deprivation - acute or chronic lack of sufficient sleep.

Sleep Disorders - broad range of illnesses arising from many causes, including, dysfunctional sleep mechanisms, and abnormalities in physiological functions during sleep, abnormalities of the biological clock, and sleep disturbances that are induced by factors extrinsic to the sleep process

Sleep efficiency (SE) - proportion of sleep in the period potentially filled by sleep--ratio of total sleep time to time in bed

Sleep Episode - interval of sleep that may be voluntary or involuntary

Sleep Extension - extending sleep time by increasing the time in bed

Sleep Fragmentation - brief arousals occurring throughout the night, reducing the total amount of time spent in the deeper levels of sleep.

Sleep hygiene - conditions and practices that promote continuous and effective sleep, including regularity of bedtime and arise time; conforming time spent in bed to the time necessary for sustained and individually adequate sleep (i.e., the total sleep time sufficient to avoid sleepiness when awake); restriction of alcohol and caffeine beverages in the period prior to bedtime; employment of exercise, nutrition, and environmental factors so that they enhance, not disturb, restful sleep

Sleep Hyperhydrosis - excessive sweating during sleep.

Sleep Inertia - feelings of grogginess and/or sleepiness that persist longer than 10 to 20 minutes after waking up

Sleep interruption - breaks in the sleep architecture resulting in arousal and wakefulness

Sleep latency - time period measured from "lights out," or bedtime, to the beginning of sleep

Sleep log (-diary) - daily, written record of an individual's sleep-wake pattern containing such information as time of retiring and arising, time in bed, estimated total sleep period, number and duration of sleep interruptions, quality of sleep, daytime naps, use of medications or caffeine beverages, nature of waking activities, and other data

Sleep-maintenance DIMS or insomnia - disturbance in maintaining sleep once achieved; persistently interrupted sleep without difficulty falling asleep

Sleep Mentation - thoughts, feelings, images, perceptions, hallucinations, and active dreams taking place during sleep

Sleep onset - transition from wake to sleep, normally into NREM stage 1 (but in certain conditions, such as infancy and narcolepsy, into stage REMS)

Sleep Onset Imagery - images and experiences during the moments following the transition from wake to sleep

Sleep-onset REM period - atypical beginning of sleep by entrance directly into stage REM

Sleep paralysis - waking and not being able to move for a short period of time, usually occurs out of REM (dream) sleep.

Sleep pattern (24 hour sleep-wake pattern) - individual's clock hour schedule of bedtimes and rise times as well as nap behavior: may also include time and duration of sleep interruptions

Sleeping Pills - compounds that have a sedative effect, used to produce sleepiness

Sleep Related Accidents - accidents caused by individuals who were sleep deprived and who, as a result, had impaired judgment

Sleep Restriction - limitation of the number of hours in bed

Sleep spindle - episodically appearing, spindle-shaped aggregate of 12-14 Hz waves with a duration of 0.5-1.5 seconds, one of the identifying EEG phenomena of NREM stage 2 sleep

Sleep Stage Demarcation - significant polysomnographic characteristics that distinguish the boundaries of the sleep stages.

Sleep stage NREM - major sleep state apart from REMS; comprises sleep stages 1-4

Sleep stage 1 - a stage of NREM sleep occurring after wake. Its criteria consist of a low-voltage EEG with slowing to theta frequencies, alpha activity less than 50%, EEG vertex spikes, and slow rolling eye movements; no sleep spindles, K-complexes, or REMS. Stage 1 normally assumes 4-5% of total sleep.

Sleep stage 2 - a stage of NREM sleep characterized by sleep spindles and K complexes against a relatively low-voltage, mixed-frequency EEG background; high-voltage delta waves may comprise up to 20% of stage 2 epochs; usually accounts for 45-55% of total sleep time.

Sleep stage 3 - a stage of NREM sleep defined by at least 20 and not more than 50% of the period (30 second epoch) consisting of EEG waves less than 2 Hz and more than 75 uV (high -amplitude delta waves); a "delta" sleep stage; with stage 4, it constitutes "deep "NREM sleep; appears usually only in the first third of the sleep period; usually comprises 4-6% of total sleep time.

Sleep stage 4 - all statements concerning NREM stage 3 apply to stage 4 except that high-voltage, slow EEG waves, cover 50% or more of the record; NREM stage 4 usually takes up 12-15% of total sleep time. Somnambulism, sleep terror, and sleep-related enuresis episodes generally start in stage 4 or during arousals from this stage

Sleep stage REM - the stage of sleep found in all mammal studies, including man, in which brain activity is extensive, brain metabolism is increased, and vivid hallucinatory imagery, or dreaming occurs (in humans). Also called "paradoxical sleep" because, in the face of this intense excitation of the CNS and presence of spontaneous rapid eye movements, resting muscle activity is suppressed. The

EEG is a low-voltage, fast-frequency, non alpha record. Stage REMS is usually 20-25% of total sleep time.

Sleep structure - similar to sleep architecture. Sleep structure, in addition to encompassing sleep stage and cycle relationships, assesses the within-stage qualities of the EEG and other physiological attributes.

Sleepiness (somnolence, drowsiness) - difficulty in maintaining the wakeful state so that the individual falls asleep if not actively kept aroused; not simply a feeling of physical tiredness or listlessness

Sleep talking - talking in sleep takes place during stage REMS, representing a motor breakthrough of dream speech, or in the course of transitory arousals from NREMS and other stages. Full consciousness is not achieved and no memory of the event remains.

Sleepwalker or Sleepwalking - individual subject to somnambulism (one who walks while sleeping). Sleepwalking typically occurs in the first third of the night during deep NREM sleep (stages 3 and 4).

Sleep-wake, 24 hour cycle - the clock hour relationships of the major sleep and wake phases in the 24 hour cycle: similar to sleep pattern.

Sleep-wake shift (-change, -reversal) – sleep wholly or partially moved to a time of customary waking activity, and the latter is moved to the habitual sleep period; common in jet lag and shift work.

Sleep-Wake Transition Disorder - disorder occuring during the transition from wakefulness to sleep or from one sleep stage to another; a form of parasomnia

Slow wave sleep (SWS) - sleep stages 3 and 4

SmartPAP (Smart CPAP) - (Smart [Continuous] Positive Airway Pressure) Medical device used in the treatment of obstructive sleep apnea providing preset levels of continuous airflow, and automatically adjusting to keep the breathing passages open by sensing changes in airway integrity. The air flows from the device through a tube that connects to a nose or face mask.

Snoring - noise produced primarily with inspiratory respiration during sleep owing to vibration of the soft palate and the pillars of the oropharyngeal inlet. Many snorers have incomplete obstruction of the upper airway, and may develop obstructive sleep apnea.

Soft Palate - membranous and muscular fold suspended from the posterior margin of the hard palate and partially separating the oral cavity from the pharynx

Somatic Complaints - awareness of pain or problems in the body

Somnambulism - walking while asleep

Somnifacient - inducing sleep; hypnotic, as in a drug

Somnolence - prolonged drowsiness or sleepiness.

Somnoplasty - commercial name for radiofrequency treatment of certain sleep disorders

Soporific - causing or tending to cause sleep

Spindle REMS - condition in which sleep spindles persist atypically in REMS; seen in chronic DIMS conditions

Stanford Sleepiness Scale (SSS) - 7-point rating scale consisting of seven numbered statements describing subjective levels of sleepiness/alertness

Subjective Sleepiness - feelings of sleepiness

Substance Abuse - excessive use of alcohol or drug; substances can cause sleep disturbances

Subwakefulness syndrome - syndrome defined as a defect in the CNS support system for waking. The few individuals reported with subwakefulness syndrome have daytime drowsiness and daytime sleep episodes that are always composed of NREMS stages 1 or 2. The naps occur repetitively

Sudden Infant Death Syndrome (SIDS) - sudden and unexpected death of an apparently healthy infant, whose death remains unexplained after the performance of an adequate postmortem investigation. Death usually occurs during sleep. SIDS is a classification that is used to describe a deceased infant. It is not a disease, nor can it be a diagnosis for a living baby.

Synchronization - chronobiological term used to indicate that two or more rhythms recur with the same phase relationship. In an EEG tracing, the term is used to indicate an increased amplitude with an occasional decreased frequency of the dominant activities.

Synchrony - scheduling sleep to synchronize with the biological clock

Tachycardia - rapid heart rate, usually defined by a pulse rate of over 100 beats per minute (bpm).

Thermocouples - small devices placed near the nostrils or mouth to measure air flow by sensing temperature changes; expired air is warmer than inspired air.

Thermoregulation - regulation of body temperature in mammals.

Theta waves - EEG activity with a frequency of 4-8 Hz

Thoracic Excursion - thoracic (chest) movement, indicating respiratory effort. Usually measured by the placement of a sensor band, which includes a strain gauge around the chest. The sensor band records chest wall movement associated with respirations...

Tidal Volume - amount of air that passes in and out of the lungs in an ordinary breath; usually expressed in liters

Titration - progressive, stepwise increase in CPAP pressure applied during a polysomnogram to establish the optimal treatment pressure

Tolerance - in pharmacology, refers to the reduced responsiveness to a drug's action as the result of previous continued and/or multiple exposure

Tonic (Event/Activity) - brain, muscle, or autonomic events, which are continuous. Usually refers to continuous activity (e.g. muscle atonia) during REM sleep.

Tonsils - pair of prominent masses of lymphoid tissue that are located opposite each other in the throat between the anterior and posterior pillars of the fauces (the narrow passage from the mouth to the

pharynx situated between the soft palate and the base of the tongue). Composed of lymph follicles grouped around one or more deep crypts.

Tonsillectomy - surgical removal of the tonsils

Total Recording Time - duration of time from sleep onset to final awakening. I n addition to total sleep time, it is comprised of the time taken up by wake periods and movement time until wake-up.

Total sleep period - period of time measured from sleep onset to final awakening. In addition to total sleep time, it is comprised of the time taken up by arousals and movement time until wake-up

Total sleep time (TST) - amount of actual sleep time in a sleep period; equal to total sleep period less movement and awake time. Total sleep time is the total of all REMS and NREMS in a sleep period.

Tracheotomy - surgical procedure to create an opening in the trachea (windpipe) so that one can breathe

Tracheostomy - refers to the opening in the trachea. As a treatment for severe obstructive sleep apnea, a tube to assist oxygenation and ventilation and/or to overcome an obstruction in the airway located superiorly.

Transducer - device designed to convert energy from one form to another

Transient Arousals - brief awakenings from sleep

Transient Insomnia - difficulty sleeping for only a few nights

Tricyclic Antidepressants - medication for depression. Most tricyclic antidepressants also reduce REM sleep; also used to control cataplectic attacks, hypnogogic hallucinations, and sleep paralysis.

Tumescence (penile) - hardening and expansion of the penis: penile erection. Commonly referred to as nocturnal penile tumescence (NPT) in sleep recordings.

Turbinate - small, shelf-like, cartilaginous structures covered by mucous membranes, which protrude into the nasal airway to help warm, humidify, and cleanse inhaled air on its way to the lungs.

Twilight Zone - slang popular term to describe the waking state of individuals whose MSLT scores are 5 minutes or less. Such individuals are usually sleep deprived or suffer from a sleep disorder.

Twitch (Body Twitch) - very small body movement such as a local foot or finger jerk which is not usually associated with an arousal.

Unattended CPAP Titration Study - sleep study that is usually performed in the home, after determining that a patient has a sleep related breathing disorder such as OSA or Upper Airway Resistance Syndrome, and is likely to benefit from CPAP therapy.

Unintended Sleep Episode - sleep episode that is not planned and may happen during an activity in which such an episode is hazardous, such as when driving a car or working with machinery

Upper Airway - part of the respiratory anatomy that includes the nose, nostrils, sinus passages, septum, turbinates; the tongue, jaws, hard and soft palate, muscles of the tongue and throat, etc.

Upper Airway Resistance Syndrome (UARS) - part of the spectrum of obstructive sleep-related breathing disorders in which repetitive increases in resistance to airflow in the upper airway lead to brief arousals and daytime fatigue. Apneas and hypopneas (see RDI) may be totally absent. Blood oxygen levels can be in the normal range.

Uvula - small soft structure hanging from the bottom of the soft palate in the midline above the back of the tongue.

Uvulopalatopharyngoplasty (UPPP) - also abbreviated as UPP or UP3 this operation is performed on the throat to treat snoring and sleep apnea. UPPP is an accepted means of surgical treatment has a curative rate of less than 50%. Scientific evidence suggests that UPPP works best in retropalatal and combination retropalatal and retrolingual obstruction

Wake time - total time that is scored awake in a polysomnogram occurring between sleep onset and final wake-up

White Noise - mixture of sound waves extending over a wide frequency range that may be used to mask unwanted noise that may interfere with sleep

Wilkinson Addition Test **- performance test; numbers added for one hour. Often included in a battery of tests to measure the impact of acute or chronic sleep loss.**

Withdrawal - effects experienced when a patient stops taking sleeping pills

Zeitgeber - environmental time cue that entrains biological rhythms to a specific periodicity. Known Zeitgebers are light, melatonin and physical activity. To be effective, these signals must occur when the biological clock is in a responsive phase.

Post-Test

Select the best answer to each of the following items. Mark your responses on the Answer Form.

1. For most people, dreams are purely a "mental" activity: they occur in the mind while the body is at rest. But people who suffer from act out their dreams.

a. Insomnia
b. Restless leg syndrome
c. REM behavior disorder (RBD)
d. Parasomnia

2. In essence, RBD may be the prodrome of neurodegenerative disease, such as DLB or Parkinson disease.

a. True
b. False

3. RBD is usually seen in _____.

a. men aged 35-50
b. women aged 35-50
c. women 60 years or older
d. men 60 years old or older

4. For most people, even when they are having vivid dreams in which they imagine they are active, their bodies are still. But, persons with RBD lack _____, which permits them to act out dramatic and/or violent dreams during the REM stage of sleep.

a. electrical activity
b. muscle paralysis
c. normal synapse activity
d. None of the above

5. Rapid eye movement behavior disorder is an uncommon sleep disorder first described in _____.

a. 1948
b. 1966
c. 1986
d. 1996

6. People with RBD typically remember little nothing of this activity, unless they fall out of bed, bump into the furniture, or injure themselves and wake up. But they can usually remember and tell the dreams they were having during an episode.

a. True
b. False

7. Patients with RBD usually respond to treatment with clonazepam when taken nightly.

a. True
b. False

8. According to the International Classification of Sleep Disorders, the minimal diagnostic criteria include movements of the body or limbs associated with dreaming and at least one of the following criteria: _____.

a. potentially harmful sleep behavior
b. dreams that appear to be acted out
c. sleep behavior that disrupts sleep continuity
d. All of the above

9. In RBD, the brainstem mechanisms generating the muscle atonia normally seen in REM sleep may be interfered with.

a. True
b. False

10. Regarding the diagnosis of RBD, the most important diagnostic studies include the following: _____.

a. Polysomnographic (PSG) video recording
b. Monitoring electro-oculogram (EOG)
c. ECG
d. All of the above

11. Clonazepam, a benzodiazapine, curtails or eliminates the disorder (RBD) about _____% of the time.

a. 40
b. 55
c. 75
d. 90

12. RBD movements occur during REM sleep, which is usually characterized by a state of atonia, or sleep paralysis. Diagnosis and treatment involves _____..

a. polysomnography
b. drug therapy
c. the exclusion of potentially serious neurological disorders
d. All of the above

13. In RBD, neurotransmitters are not blocked, and the voluntary muscles become tonic, or tensely contracted, allowing a sleeping person to move his or her muscles during REM.

a. True
b. False

14. Most cases of RBD are not associated with other disorders.

a. True
b. False

15. There is some evidence to suggest that RBD precipitates _____.

a. Guillain-Barre' syndrome
b. Parkinson's disease
c. Alzheimer's disease
d. None of the above

16. Patients with RBD usually respond to treatment with clonazepam when taken nightly.

a. True
b. False

17. People with RBD risk injuring themselves and their sleep partners. The frequency and intensity of RBD episodes are sometimes too much for a sleep partner to endure.

a. True
b. False

18. Normally, generalized atonia of muscles occurs during REM sleep. This atonia results from active inhibition of motor activity by pontine centers (i.e., perilocus ceruleus) that exert an excitatory influence on the medulla (i.e., magnocellularis neurons) via the lateral tegmentoreticular tract.

a. True
b. False

19. Typically, RBD is a disease of elderly persons. The risk increases after the sixth decade, although the disease may occur at all ages, including childhood.

a. True
b. False

20. RBD is treated symptomatically by various medications; however, the response varies in individual cases. Therefore, all available medications should be tried before considering the patient's RBD as intractable.

a. True
b. False

21. Special recommendations or restrictions of diet exist for RBD.

a. True
b. False

22. As RBD has strong relationships with many neurodegenerative disorders, such as _____, the neurologist always should explore the possibility of RBD in these conditions. RBD symptoms may be the first manifestations of these disorders; therefore, careful follow-up is needed.

a. Parkinson disease
b. dementia
c. multiple system atrophy
d. All of the above

23. The prognosis of RBD depends on etiology. In idiopathic cases, the symptoms are controlled with medications. In secondary cases, the prognosis depends on the primary disease.

a. True
b. False

24. RBD is a treatable condition. However, misdiagnosis and treatment may result in potential medico-legal problems. Commonly, violent behaviors of RBD involve patients' responses to some form of perceived threat.

a. True
b. False

25. RBD most frequently led to neurodegenerative diseases called the synucleinopathies: Parkinson's disease or dementia with Lewy bodies

a. True
b. False

26. There are interventions to prevent those with RBD from progressing to Parkinson's disease, dementia or multiple system atrophy

a. True
b. False

27. Clinical features and HLA typing are not compatible with narcolepsy and the REM sleep behavior disorder.

a. True
b. False

28. It has been shown recently that interleukin-1, tumor necrosis factor (TNF), or hormones such as growth hormone releasing hormone induce sleep and regulate the cycle of REM and non-REM sleep. (TNFα was undetectable in her CSF).

a. True
b. False

29. The body is supposed to be paralyzed during REM sleep. The brain is very active during REM sleep and paralyzes the body to prevent a dreamer from harming self and others by acting out dreams. If the neural mechanism that is supposed to carry out this paralysis fails, the patient is said to have REM Behavior Disorder, RBD.

a. True
b. False

30. Awareness during Sleep Paralysis, or ASP, is any Awareness during the Paralysis that naturally occurs in Rapid Eye Movement (REM) Sleep to prevent us from harming ourselves or others by acting out our dreams.

a. True
b. False

31. If Awareness during Sleep Paralysis can explain the bulk of those Alien Abduction reports that start out with the experiencer lying down or resting, it is possible that the very small number of cases where there is evidence that the experiencer walked around during the experience would be explained as cases of RBD.

a. True
b. False

32. REM sleep behavior disorder is a parasomnia that occurs later in the night than NREM disorders.

a. True
b. False

33. In two papers in an issue of the journal Neurology, a research team reports apparent links between deficits in brain chemistry and obstructive sleep apnea (OSA) and REM sleep behavior disorder (RBD). Both are relatively common sleep problems that disturb the slumber -- and daytime behavior -- of millions of Americans.

a. True
b. False

34. The patients with the most dopamine-producing neurons in the striatum of their brains had the worst RBD symptoms of thrashing, talking and violent flailing while they slept. And patients with the lowest levels of acetylcholine-producing neurons in the brainstem had the most interruptions in their breathing during sleep.

a. True
b. False

35. REM sleep behavior disorder occurs infrequently but is outwardly very dramatic. Patients literally act out their dreams during the REM, phase of sleep, moving their arms and legs, getting out of bed, talking and shouting, and even hitting or punching. RBD can endanger the sleeping person, or his or her bed partner.

a. True
b. False

36. Melatonin, a hormone produced by the _____ during the hours of darkness, plays a major role in the sleep/wake cycle.

a. pituitary gland
b. adrenal gland
c. pineal gland
d. None of the above

37. When the neurotransmitters that control the movement of the body do not work properly the person develops REM sleep behavioral disorder (RBD).

a. True
b. False

38. RBD is not only a motor control disorder, but a dream disorder as well.

a. True
b. False

39. The majority of patients afflicted with RBD though there are cases of females and children having this disorder. About _____% of diagnosed patients tested reported limb twitching, talking, yelling, jerking and a progressive decline in motor control during sleep.

a. 10
b. 25
c. 45
d. 70

40. The primary treatment of RBD symptoms is clonazepam. It suppresses both electromyographic activity during REM sleep and the associated motor behaviors.

a. True
b. False

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