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Polysomnography and Sleep Disorders

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Summary

The classification of sleep disorders is based both on clinical and neurophysiological criteria and is undergoing constant refinement. Sleep disorders can be caused by either a primary disorder of a mechanism controlling sleep or inadequate function of an end organ, such as the upper airways and lungs. Understanding the physiology and pattern of normal sleep is an important foundation for interpreting the clinical symptoms, signs, and neurophysiological abnormalities observed in patients with sleep disorders. The term polysomnography refers to the simultaneous recording of multiple sleep parameters, including a limited electroencephalogram, respiratory parameters, chest excursion, limb movements, and the electrocardiogram. Polysomnography is important for assessing a variety of sleep disturbances, including disorders such as sleep-related breathing disorders (including obstructive sleep apnea), rapid eye movement behavior disorder, and periodic movements of sleep. The multiple sleep latency test and maintenance of wakefulness test are studies that are especially useful in the evaluation of narcolepsy and other hypersomnias.

Key Words: Multiple sleep latency test; narcolepsy; obstructive sleep apnea; periodic movements of sleep; polysomnography; sleep.

1. INTRODUCTION

The understanding of sleep disorders and the development of sleep disorders medicine as a discipline has depended on the ability to simultaneously measure and record multiple physiological parameters during sleep. The term "polysomnography" was introduced in the early 1970s to describe both the recording and the interpretation of these variables. The technique of polysomnographic recording evolved from EEG with critical modifications that allowed researchers to correlate changes in EEG with changes in other physiological systems. In the late 1930s, Alfred L. Loomis, E. Newton Harvey, and Garret Hobart *(1)* introduced the concept of recording electroencephalographic activity continuously through the night and, in doing so, identified five sleep stages. In 1953, Eugene Aserinsky, working in Nathaniel Kleitman's laboratory at the University of Chicago, added electrodes to record the eye movements he had observed through the lids of sleeping subjects. By waking subjects during intense periods of rapid eye movement (REM), these researchers discovered that the REMs were associated with dreaming and, thus, discovered REM sleep *(2)*. Soon thereafter, William Dement, working in the same laboratory, established that REM alternated with non-REM (NREM) sleep in cycles of approx 90 min *(3)*. Later, after research showed that REM was associated with loss of muscle tone (REM sleep atonia), surface EMG electrodes on the chin

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were added to the EEG and the electro-oculogram (EOG) recordings to better define the REM sleep state. A committee of early sleep researchers refined the rules for recording and scoring sleep stages in 1968. The product of that effort, known as the "Rechtschaffen and Kales criteria" (R and K criteria) remains the international "gold-standard" in the field *(4)*. In the progression of the development of the polysomnogram (PSG), the pivotal discovery of sleep apnea in the 1960s resulted in the addition of simultaneous respiratory and cardiac monitoring. Both REMs and apneas are evident with direct observation but were not appreciated as important until studied with neurophysiological techniques. It is now difficult to understand how these obvious human behaviors could have been ignored for so long; there are perhaps no better examples of clinical neurophysiology amplifying human observation.

This chapter will focus on the standardized techniques used to measure sleep-related physiological parameters and their practical application to the diagnosis of specific sleep disorders.

2. CLINICAL ASSESSMENT OF SLEEP DISORDERS

A sleep disorder generally occurs for one of two reasons. It may represent a primary disorder of a mechanism controlling sleep or failure of a specific end organ, such as the upper airways and lungs. As in all of clinical medicine, testing must be ordered and interpreted within the context of the patient's clinical presentation, with a clear understanding of the questions to be answered and the inherent limitations of the study proposed. Most patients present with complaints of excessive daytime sleepiness, difficulty initiating or maintaining sleep, or some sort of unpleasant event that occurs during sleep. Detailed medical and sleep histories with careful attention to underlying medical and psychiatric illness, daytime schedules, lifestyle issues, medications, and drug use are prerequisites for the intelligent analysis of the problem and planning of the appropriate testing. A complete physical examination should always be obtained before referral for study. Sleep logs, which document daily sleep–wake behaviors, may be valuable tools that complement both the office history and the interpretation of the objective data acquired in the sleep laboratory.

2.1. Classification of Sleep Disorders

The American Academy of Sleep Medicine (AASM) has established a classification of sleep disorders, the "International Classification of Sleep Disorders," 2nd ed. (ICSD-2) *(5)*. A summary of this classification is given in Table 1.

A detailed discussion of these disorders is outside the scope of this chapter. Later subheadings will discuss the sleep disorders that are best suited to analysis by neurophysiological testing.

3. OVERVIEW OF SLEEP

REM sleep, sometimes called paradoxical sleep or dreaming sleep, and NREM sleep are the two sleep states. NREM and REM sleep alternate in recurring cycles of approx 90 min.

NREM sleep is divided into four stages (stages 1–4), which represent progressive deepening of sleep. Stage 1 sleep is characterized by the gradual disappearance of the alpha rhythm of quiet wakefulness, which is replaced by theta activity and some fast activity. The emergence of sleep spindles and K-complexes establishes the onset of stage 2 sleep. Stage 3 and stage 4 sleep are defined by the presence of high-voltage slow activity. Stage 3 and stage 4 sleep are often described together as slow-wave sleep or delta sleep.

The normal young adult descends in an orderly progression through the four NREM stages. Slow-wave sleep appears approx 30 to 40 min after sleep onset. The first REM period

Table 1
International Classification of Sleep Disorders-2: Diagnostic Categories

I	Insomnias
II	Sleep-related breathing disorders
III	Hypersomnias of central origin not due to a circadian rhythm sleep disorder, sleep-related breathing disorder, or other cause of disturbed nocturnal sleep
IV	Circadian rhythm sleep disorders
V	Parasomnias
VI	Sleep-related movement disorders
VII	Isolated symptoms, apparently normal variants, and unresolved issues
VIII	Other sleep disorders

follows this slow-wave sleep, approx 70 to 90 min after sleep onset. The PSG during REM sleep shows dramatic changes. A sudden loss of EMG activity occurs in the chin muscles, which is indicative of generalized skeletal muscle atonia. REMs occur in phasic bursts and the EEG shows mixed frequencies similar to waking and stage 1 sleep, sometimes with a characteristic sawtooth pattern.

The first REM period is short, lasting approx 10 min. The end of the first REM period completes the first sleep cycle. Thereafter, NREM sleep continues to alternate with REM sleep; the healthy adult goes through 4 to 6 cycles. Slow-wave sleep is concentrated in the first third of the night, whereas REM sleep episodes become progressively longer later in the night. Slow-wave sleep is prominent in adolescence and decreases significantly with age, whereas REM sleep duration tends to remain stable throughout adulthood. Newborns, however, demonstrate up to 50% REM sleep.

REM and NREM sleep differ physiologically. REM sleep is characterized by both phasic and tonic changes in physiology. The drop in baseline EMG correlates with a tonic change. REMs correlate with phasic changes. Tonic physiological changes also include impaired thermoregulation, reduction in ventilatory chemosensitivity, hypotension, bradycardia, increased cerebral blood flow, and intracranial pressure, increased respiratory rate, and penile erection. Phasic changes include vasoconstriction, increased blood pressure, tachycardia, and further increases in cerebral blood flow and respiratory rate. During NREM sleep, the physiological state is more stable, with an overall reduction in blood pressure, heart rate, cardiac output, and respiratory rate. One characteristic feature of NREM, slow-wave sleep is the secretion of growth hormone.

The control of sleep onset, duration, and stage changes is poorly understood. It is thought that there are two sleep drives, one homeostatic and the other circadian. The homeostatic drive increases with the duration of wakefulness, whereas the circadian signals are controlled by the suprachiasmatic nucleus of the hypothalamus. Recent evidence has shown that neurons of the ventrolateral preoptic nucleus of the hypothalamus are sleep active and sleep promoting, confirming old observations that lesions in this area induce insomnia. These neurons express the inhibitory transmitters, galanin and GABA, and innervate wake-promoting areas, including the hypocretin (also known as orexin) containing neurons of the posterolateral hypothalamus, histaminergic neurons of the tuberomammillary nucleus, the serotonergic dorsal raphe, norepinephrine containing neurons of the locus ceruleus, and the cholinergic neurons of the dorsal midbrain and pons. In turn, monoaminergic wake-promoting areas inhibit the ventrolateral preoptic nucleus, thereby resulting in reciprocal inhibition that self-reinforces

stable periods of sleep and wake. In this model, homeostatic and circadian drives are hypothesized to shift the balance between states by still unknown mechanisms. Adenosine that accumulates during wakefulness, the effect of which is antagonized by caffeine, may be one of the factors that signals the homeostatic drive to sleep. Neurons critical for generating REM sleep are found in the lateral pons and adjacent midbrain, including the cholinergic cells of the pedunculopontine and lateral dorsal tegmental nuclei. These neurons are inhibited by norepinephrine, serotonin, and histamine. Hypocretin-1 cells in the posterolateral hypothalamus stimulate aminergic cells and, thus, also contribute to the inhibition of REM sleep while simultaneously promoting wakefulness. Loss of hypocretin-1-containing cells is now known to underlie the pathophysiology of narcolepsy (*see* Section 6.2.1.) (*see* Espana and Scammell for a recent review of sleep neurobiology; ref. *6*).

Some disorders are exacerbated by or occur only during certain sleep stages. Sleepwalking, for example, occurs with arousal from slow-wave sleep. Epileptic seizures tend to be facilitated by NREM sleep but inhibited by REM sleep. Obstructive sleep apnea (OSA) is typically worse in REM sleep because of REM atonia and alteration of respiratory chemosensitivity.

Because of this changing physiological template, a careful neurophysiological study of sleep is useful in understanding a wide variety of disease processes.

4. POLYSOMNOGRAPHY

Polysomnography is the term applied to the simultaneous and continuous measurement of multiple physiological parameters during sleep. In practice, the term PSG has come to mean a specific type of polysomnographic study in which measurements allow for:

1. The identification of sleep stage.
2. Monitoring of cardiopulmonary function.
3. Monitoring of body movements during sleep.

This study is typically obtained at night in a sleep laboratory for the purpose of identifying, as best as possible given the novel environment, the patient's typical sleep and its associated pathologies. The AASM has developed guidelines for the indication for polysomnography *(7)*. These indications include:

1. Suspicion of sleep-related breathing disorders.
2. Treatment and followup of sleep-related breathing disorders.
3. In combination with the MSLT for suspected narcolepsy.
4. Evaluation of sleep-related behaviors that are violent, potentially injurious, or do not respond to conventional therapy.
5. To assist in the diagnosis of paroxysmal arousals that are suggestive of seizure disorder (with additional video and EEG).
6. Evaluation of sleep-related movement disorders.

Many experienced clinicians also obtain PSGs in the evaluation of insomnia, circadian rhythm disorders, nocturnal angina, arrhythmia, hypertension, gastroesophageal reflux, and headache, because these entities are commonly exacerbated by coexisting sleep disorders that may not be evident on clinical grounds.

Standard PSG measurements in current clinical practice include (*see* Table 2):

1. EEG (C4–A1 and/or C3–A2).
2. Eye movement recording (EOG).
3. EMG of chin (surface).

Table 2
Parameters Recorded in Standard PSG, MSLT, and MWT

	Parameters recorded
PSG	EEG (C4–A1, C3–A2)
	Additional EEG if indicated
	EOG
	EMG (chin)
	Airflow
	Respiratory effort
	O_2 saturation est. (S_pO_2)
	EKG
	EMG limb, anterior tibialis muscles; extensor digitorum muscles when indicated
	Body position
	Esophageal pH (rarely)
MSLT and MWT	EEG (C4–A1, C3–A2)
	EEG (O1–A1, O2–A2)
	EOG
	EMG (chin)
	EKG
	Optional: respiratory monitoring

EOG, electro-oculogram; MWT, maintenance of wakefulness test; MSLT, multiple sleep latency test; PSG, polysomnogram; S_pO_2, pulse oximetry.

4. Respiratory effort (chest and abdomen).
5. Airflow (nasal/oral).
6. Oxygen saturation (pulse oximetry).
7. EKG (one lead).
8. EMG (surface) of anterior tibialis muscles.
9. Body position.

Other measurements may be performed as dictated by the clinical question. Video monitoring and additional EEG electrodes are commonly added for the question of nocturnal seizure disorder (Video EEG–PSG), whereas continuous blood pressure monitoring, penile tumescence recordings, and gastroesophageal pH measurements are only rarely performed in clinical situations. PSGs performed in the sleep laboratory are termed "attended" PSGs, which indicates that a technician is available throughout the study who may intervene to assure quality or to initiate therapies, such as the application of positive pressure for the treatment of sleep apnea. Full polysomnography is available at the bedside or for at-home testing, and although of high quality, is not generally accepted as equal in reliability to attended studies.

Four-channel studies geared for screening of respiratory cardiorespiratory abnormalities but lacking reliable methods of identifying whether the patient is awake or asleep, are poorly validated against formal polysomnography. However, these may have some usefulness when full polysomnographic study is not available.

Polysomnographic techniques with fewer recording channels are also applied to two other sleep laboratory tests: the multiple sleep latency test (MSLT) and the maintenance of wakefulness test (MWT). The MSLT measures the tendency to fall asleep during the day and screens for the occurrence of inappropriate daytime episodes of REM sleep. The MWT measures the ability to stay awake in multiple daytime naps.

4.1. The PSG

4.1.1. Sleep Stage Scoring/Sleep Architecture

Sleep stage "scoring" or "staging" refers to the lengthy process of identifying sleep stages recorded on the PSG. Identification of sleep stages requires the simultaneous assessment of three channels of the PSG: EEG, EOG, and chin EMG. The continuously recorded EEG is, by convention, analyzed in 30-s intervals, known as epochs. Sleep stages are identified or "scored" using the R and K criteria outlined in Section 4.1.1.1. (*see* Table 3). Because one epoch can show features of more than one sleep stage, the sleep stage that occupies more than 50% of the 30-s interval is assigned to that epoch. Although stage scoring can be performed in a limited fashion by computer, the accuracy is poor and most laboratories rely on visual scoring by trained sleep technicians.

Sleep architecture refers to the distribution and temporal sequence of sleep stages (Table 4), which contribute to a quantitative understanding of the night's sleep. Most analyses also include a hypnogram, a graphic display of sleep stages on a time line throughout the night that assists in the qualitative assessment of sleep. Hypnograms and sleep architecture parameters are produced by computer analysis of the visually derived data. Figure 1 shows representative hypnograms across ages. Table 5 shows ranges of normative values for sleep stages in adults. Architecture and stage distribution are influenced by commonly used medications. A summary of some of these medication effects is given in Table 6.

4.1.1.1. Sleep Stages: Technique and Scoring Rules

"A Manual of Standardized Terminology, Techniques and Scoring System for Sleep Stages of Human Subjects," edited by Rechtschaffen and Kales, is the internationally accepted standard for sleep staging (R and K criteria) *(4)*. Although those who intend to master sleep scoring need to study the manual directly, the following text and Table 3 provide useful summaries abstracted directly from the R and K manual.

4.1.1.1.1. Technical Requirements for Scoring

4.1.1.1.1.1. EEG A single EEG channel is used for the purposes of scoring sleep stages. The acceptable derivations are C4 or C3 (International 10–20 System) referred to the opposite ear or mastoid; two channels are recorded with one used as a backup for technical problems during the night. This sleep derivation tends to confuse electroencephalographers who do not typically record using an opposite side reference. The opposite side derivation was chosen to maximize inter-electrode distance. Because the amplitude of the EEG waveform is dependent on inter-electrode distance, and because amplitude is included in the criteria for stages 3 and 4 sleep (*see* below), the convention has remained. Filtering also influences the amplitude of the waveform. Traditional EEG recording uses a low filter frequency of 1 Hz, but the EEG of sleep studies is filtered at a low-frequency setting of 0.3 Hz to maximize amplitude of lower-frequency waves. A 1-Hz low-frequency filter reduces the amplitude of a 1-Hz signal by 20%. Using an incorrect low-frequency filter will, therefore, result in underscoring of stages 3 and 4 sleep. The high-frequency settings are typically the same for traditional EEG and

Table 3
Outline of Scoring Criteria According to "R and K" Manual

Stage/state	*Electroencephalogram (EEG)*	*Electrooculogram (EOG)*	*Electromyogram (EMG)*
Relaxed wakefulness	Eyes closed: rhythmic alpha (8–13 cps); prominent in occipital; attenuates with attention Eyes open: relatively low voltage mixed frequency	Voluntary control; REMs or none; blinks; slow eye movements when drowsy (SEMs) when drowsy	Tonic activity, relatively high; voluntary movement
Non-rapid eye movement sleep (NREM)			
Stage 1	Relatively low voltage, mixed frequency May be theta (3–7cps) activity with greater amplitude Vertex sharp waves Synchronous high voltage theta bursts in children	SEMs	Tonic activity, may be a slight decrease from waking
Stage 2	Background: relatively low voltage, mixed frequency Sleep spindles: waxing, waning, 12–14 cps ($\geq$0.5 s) K-complex: negative sharp wave followed by slower positive component (0.5 s); spindles may ride on Ks; Ks maximal in vertex; spontaneous or in response to sound	Occasionally SEMs near sleep onset	Tonic activity, low level

(Continued)

Table 3 ***(Continued)***

Stage/state	*Electroencephalogram (EEG)*	*Electrooculogram (EOG)*	*Electromyogram (EMG)*
Stage 3	≥20%, ≤50% high amplitude (>75 μV), slow frequency (≤2 cps); maximal in frontal	None, picks up EEG	Tonic activity, low level
Stage 4	>50% high amplitude, slow frequency	None, picks up EEG	Tonic activity, low level
Rapid eye movement sleep (REM)	Relatively low voltage mixed frequency Saw tooth waves Theta activity Slow alpha	Phasic REMs	Tonic suppression; phasic twitches
Movement time	Obscured	Obscured	Very high activity

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Table 4
Sleep Variables

Variable	*Abbreviation*	*Definition*
Time in bed	TIB	The time from lights out until the subject chooses to end the study
Sleep period time	SPT	TIB minus time awake after lights out before sleep onset, and minus time in bed after awakening in the morning
Total sleep time	TST	Total time the subject actually slept. This is SPT minus any time awake during the night
Sleep efficiency index	SE	TST/TIB. Often reported as a percentage. This is an important measure of sleep quality
Percentage of each stage		This may be reported as either a percentage of the SPT or the TST. The usual convention is to report percentage of SPT with stage W included as a sleep stage
Sleep-onset latency	SL	Time from lights out until the onset of sleep. Sleep onset is usually defined as the onset to the first epoch of any sleep stage. Sometimes reported as latency to stage 2
Number of awakenings		Records the number of times the subject returns to stage W after sleep onset
Number of arousals		Records the number of EEG arousals

polysomnography and are set at 70 Hz. Central lead placements are used because sleep-specific EEG waveforms (K-complexes, spindles, vertex waves, high-voltage slow activity, and sawtooth waves, *see* Section 4.1.1.1.2.) tend to be maximal in these areas. The posterior predominant alpha rhythm of the relaxed wakeful state is adequately, but not ideally, observed in the central leads. To better visualize the alpha rhythm, many laboratories add occipital channels, but R and K scoring rules are nonetheless based on the central derivations.

Most laboratories now use digital recording techniques that allow for manipulation of montages, time base, filter settings, and channel sensitivity. The EEG sampling rate should be at least 200 Hz and the monitor display should also allow appropriate resolution of the waveforms.

4.1.1.1.1.2. Eye Movement Recording Eye movement recording is necessary for the identification of REM sleep. Slow eye movements are characteristic of the onset of stage 1 sleep and aid in the identification of that sleep stage. Two channels are devoted to the EOG. Standard EEG electrodes are applied 1 cm above and lateral to the outer canthus of one eye and 1 cm below and lateral to the outer canthus of the other eye (E1 and E2, also called ROC and LOC).

The R and K manual recommends using the same ear or mastoid as a reference electrode for both channels, but, in usual practice, the eye electrodes are referred to the opposite ear or mastoid. As a result of the eye's natural dipole (cornea positive), vertical or lateral eye movements are identified as out-of-phase deflections on the two channels. This arrangement makes eye movements easily distinguishable from frontal EEG activity inadvertently picked up by the EOG electrodes. Frontal EEG activity will appear as in- phase activity. Typical filter settings are 0.3 Hz and 15 Hz, which allow for good resolution of both slow and fast eye movements.

4.1.1.1.1.3. Chin EMG EMG activity can be easily recorded from surface EEG-type electrodes applied to muscles on and under the chin. The EMG activity so measured is an indication of muscle activity, which is called "muscle tone" in the sleep literature. Analysis of chin muscle

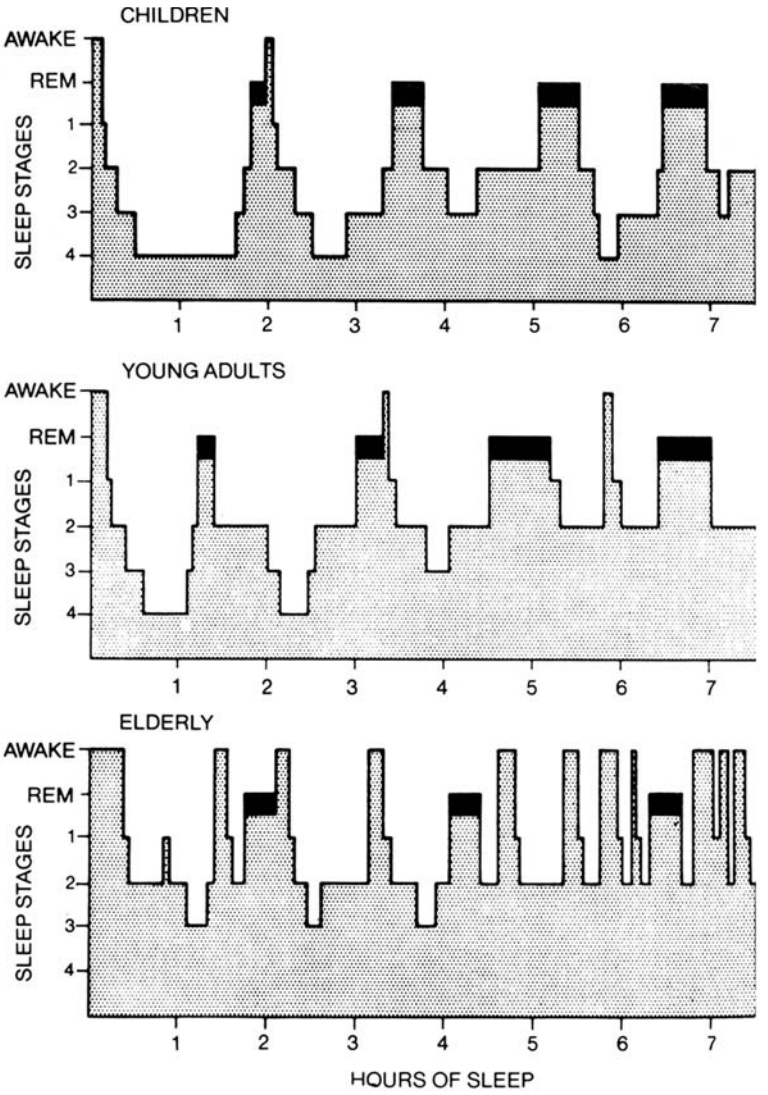

Fig. 1. Normal sleep cycles. Rapid eye movement (REM) sleep (darkened area) occurs cyclically throughout the night at intervals of approximately 90 min in all age groups. REM sleep shows little variation in the different age groups, whereas stage 4 sleep decreases with age. In addition, the elderly have frequent awakenings and a marked increase in total wake time. From ref. *17* with permission.

tone is necessary to identify normal and abnormal REM sleep. In the normal condition, REM sleep is characterized by a well-sustained, typically sudden, drop in tone with some intermittent phasic activity. The activity in the chin electrode is used in the formal staging of REM sleep discussed in Section 4.1.1.1.2.8. Three electrodes are placed, one on the chin and two on the muscles under the chin, one on each side. Only two electrodes are used, referred to each other, but if one fails because of movement, the third is available without waking the patient. Surface EMG electrodes are filtered to remove slow artifacts and allow the high-frequency muscle activity to be observed. A low-frequency setting of 10 Hz and a high-frequency setting of 70 Hz are commonly used.

Table 5
Normative Values for Sleep Stages in Adults

Sleep stages	*20–29 yr*		*30–39 yr*		*40–49 yr*		*50–59 yr*		*60–69 yr*	
%SPT	*Males*	*Females*	*Males*	*Females*	*Males*	*Females*	*Males*	*Females*	*Males*	*Females*
Wake	1.26 ± 1.08	0.53 ± 0.49	1.47 ± 1.94	1.84 ± 3.97	6.29 ± 5.56	1.63 ± 1.30	4.33 ± 2.33	4.95 ± 6.48	7.73 ± 6.02	8.93 ± 8.47
1	4.44 ± 1.62	4.18 ± 2.39	5.71 ± 3.43	4.17 ± 1.65	7.56 ± 3.03	5.64 ± 2.00	7.56 ± 3.94	4.85 ± 2.20	9.73 ± 3.97	7.69 ± 4.12
2	45.54 ± 5.17	52.37 ± 5.89	56.89 ± 7.36	53.77 ± 7.73	54.75 ± 11.14	54.01 ± 8.55	61.71 ± 10.30	57.80 ± 6.50	56.79 ± 8.76	54.78 ± 8.59
3 and 4	20.76 ± 4.78	17.69 ± 6.73	12.46 ± 5.58	14.00 ± 7.26	8.54 ± 6.84	12.05 ± 8.31	4.92 ± 7.70	10.63 ± 6.07	2.66 ± 5.05	7.17 ± 6.81
REM	28.00 ± 5.66	25.23 ± 3.63	23.47 ± 3.86	26.22 ± 5.27	22.85 ± 4.00	26.67 ± 4.10	21.48 ± 4.01	21.77 ± 3.26	23.09 ± 3.59	21.43 ± 4.04

REM, rapid eye movement sleep.
Abstracted from ref. *16*.

Table 6
Medication Effects on the Polysomnogram

Medication	*SWS*	*REM*	*Miscellaneous*
TCAs	⇔	⇓	
SSRIs/SNRIs	⇔	⇓	Venlafaxine is a 5HT and NE uptake inhibitor SSRIs and SNRIs ⇑ Non-REM slow eye movements
Trazodone	⇔	⇓	
Nefazadone	⇔	⇑	
Bupropion	⇔	⇑	NE and DA uptake inhibitor
Mirtazapine	⇔	⇔	
MAOIs	⇔	⇓	
Lithium	?	⇓	
BZDs	⇓	⇔	⇑ Spindle activity and stage 2
Zolpidem	⇔	⇔	
Dopaminergic drugs	?	?	Mixed results
Anticonvulsants			Minimal data
Phenytoin	⇑	?	
Barbiturates	⇓	⇓	⇑ Spindle activity
Carbamazepine	⇑	⇓	
Tiagabine	⇑	⇔	
Gabapentin	⇑	⇔	
Lipophilic beta-blockers	⇓	⇓	
Clonidine	?	⇓	
Opioids	⇓	⇓	Can ⇓ respiratory drive
Amphetamines	⇔	⇓	
Caffeine	⇓	?	Adenosine antagonist; adenosine ⇑ SWS
Alcohol (acute)	?	⇓	After ETOH metabolism there is a REM rebound
Alcohol (chronic)	⇓	⇓	
Sodium oxybate	⇑	⇑⇓	Approved for cataplexy and excessive sleepiness

4.1.1.1.2. Sleep Stage Scoring Rules

A summary of sleep stage scoring rules abstracted from the R and K manual is abstracted below and in Table 3.

4.1.1.1.2.1. Stage W Stage W (Fig. 2) refers to the waking state. Wakefulness is characterized by a low-voltage mixed-frequency EEG and/or the alpha rhythm. A posteriorly predominant rhythm in the alpha frequency (8–13 Hz), which attenuates with eye opening, is characteristic of the relaxed wakeful state with the eyes closed. This rhythm is generally referred to as the alpha rhythm, but is sometimes referred to as the Berger rhythm by electroencephalographers. In disease states (e.g., encephalopathy or hypothyroidism), the alpha rhythm may not reach the alpha frequency, an example of why it is important to not confuse the term "alpha rhythm" with the term "alpha frequency." When the eyes are open, low-voltage mixed-frequency rhythms are observed. Wake is usually also accompanied by the REMs of normal exploratory visual behavior, associated with high chin tone.

4.1.1.1.2.2. Movement Time Movement time is a scoring term applied to epochs that are obscured by movement artifact for more than 50% of the 30-s epoch, and occur before or

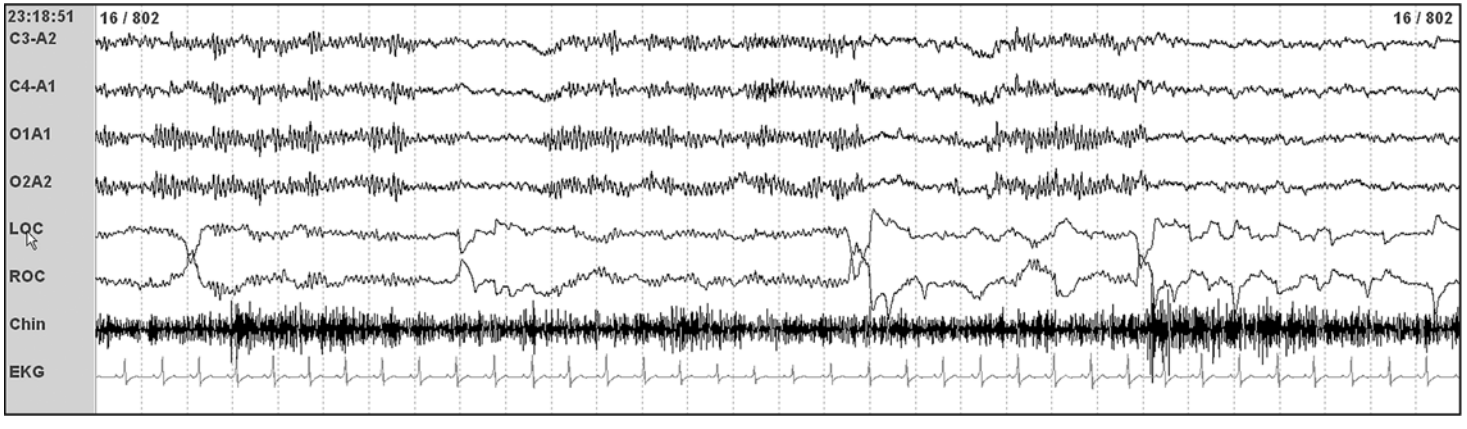

Fig. 2. Wake. The posterior dominant alpha rhythm block with eye opening. Fast eye movements typical of wakefulness are noted as rapid out-of-phase deflections. (30-s epoch)

after scorable sleep epochs. Movement time is not quantitated as either sleep or wake, but scored as a separate category.

4.1.1.1.2.3. Movement Arousal Movement arousal is a term used in the R and K manual that applies primarily to sleep stage scoring criteria. A movement arousal is defined as "any increase in EMG on any channel, which is accompanied by a change in pattern on any additional channel."

4.1.1.1.2.4. EEG Arousal Intrusions during sleep that seem to cause a disturbance with lightening of sleep, but without full awakening are termed "EEG arousals." A formal definition of EEG arousal has been generated by The Atlas Taskforce of the American Sleep Disorders Association *(8)* and is not in the R and K manual. An EEG arousal is defined as: "An abrupt shift in EEG frequency which may include theta, alpha, and/or frequencies greater than 16 Hz, but not spindles, subject to the following rules and conditions:

1. The subject must be asleep for at least 10 s before an arousal can be scored.
2. Minimum interval of sleep between two arousals is 10 s.
3. The EEG frequency shift must be 3 s or greater in duration.
4. Arousals do not require increases in chin EMG in NREM sleep.
5. Arousals require increased chin EMG in REM sleep.
6. EMG changes alone are not sufficient for scoring an arousal.
7. K-complexes and delta waves are not scored as arousals unless they occur within a frequency shift as described above.
8. Blocking artifact is not an arousal unless accompanied by the EEG frequency shift.
9. Three seconds of alpha frequency activity during sleep is not scored as an arousal unless there has been a 10-s period free of alpha
10. Transitions from one sleep stage to another are not in themselves arousals." *(8)*

4.1.1.1.2.5. Stage 1 Subjects typically descend from stage W to stage 1 sleep (Fig. 3). This stage is defined by the presence of a relatively low-voltage mixed-frequency EEG with a predominance of slower activity in the 3- to 7-Hz range. Sharp negative centrally predominant waves called vertex waves may be observed. Faster-frequency activity of 12 to 14 Hz may occur. At sleep onset, stage one is identified by the drop out of the alpha rhythm that predominates in the relaxed state before sleep. When greater than 50% of a 30-s epoch shows the slower activity of stage 1 sleep, the epoch is scored as stage 1. Slow, rolling eye movements that help the scorer identify the transition to sleep frequently accompany this stage. Stage 1 sleep may also appear intermittently throughout the night, often in response to a disturbance and is, thus, considered a "light" sleep stage. An increase in stage 1 sleep is, thus, one important measure of sleep disruption. This stage is frequently not perceived by the subject as sleep, particularly early in the night.

4.1.1.1.2.6. Stage 2 Stage 2 sleep (Fig. 4) is defined by the appearance of K-complexes and or sleep spindles, each lasting at least 0.5 s, in the absence of slow activity sufficient to meet the scoring requirements of stage 3 or 4 sleep (*see* Section 4.1.1.1.2.7.). A sleep spindle is a series of 12- to 14-Hz waves with a fusiform morphology. The K-complex in the R and K criteria is defined differently than that definition accepted by the EEG community. The K-complex in R and K is defined as "EEG wave form having a well-delineated negative sharp wave which is immediately followed by a positive component. Waves of 12 to 14 cps may or may not constitute a part of the complex" *(4)*. In the EEG literature, a K-complex refers to a vertex sharp wave accompanied by a sleep spindle. There is no amplitude criterion for a K-complex. As soon as either a spindle or K-complex of 0.5-s duration appears, stage 2 is

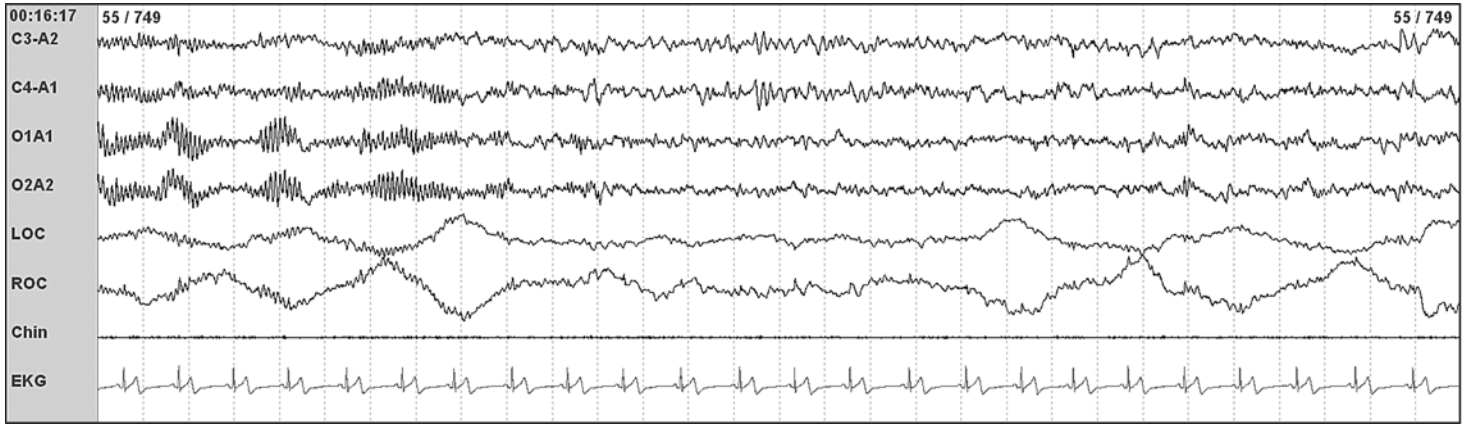

Fig. 3. Stage 1. Slow roving eye movements occur and the posterior dominant alpha rhythm comprises less than 50% of the epoch. (30-s epoch)

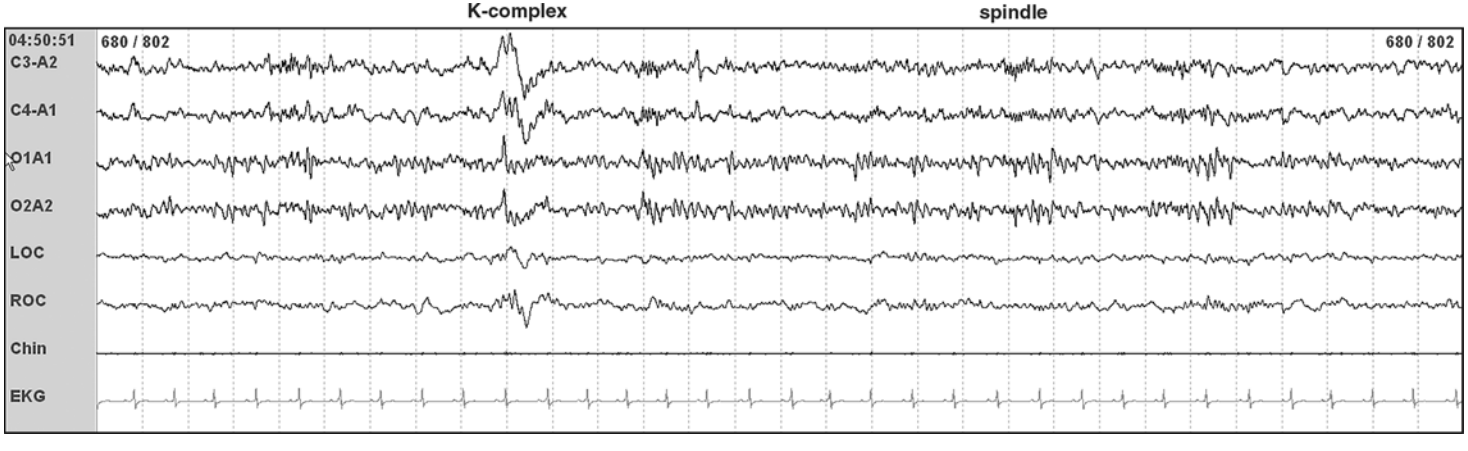

Fig. 4. Stage 2. This is a typical epoch of stage 2 demonstrating sleep spindles and a K-complex. This stage is defined by the presence of either K-complexes or spindles, each lasting at least 0.5 s in duration. (30-s epoch)

established. K-complexes and spindles appear intermittently. To score uneventful intervals between the appearance of these transients, the "3-min rule" is applied: "If less than 3 min of record which would ordinarily meet the requirements for stage 1 intervene between sleep spindles and/or K-complexes, these intervening epochs are to be scored stage 2, if there is no indication of movement arousal or pronounced increase in muscle tone during the interval in question" *(4)*. Stage 2 is the most abundant and easily identified sleep stage.

4.1.1.1.2.7. Stages 3 and 4 Stages 3 and 4 are characterized by the presence of high-voltage slow activity. The slow waves that define these stages must be 2 Hz or less and >75 μV in amplitude. If slow waves meeting these criteria are observed for at least 20% but not more than 50% of the epoch, that epoch is scored as stage 3 (Fig. 5). Stage 4 sleep (Fig. 6) is characterized by the same high-voltage slow waves for more than 50% of the epoch. Stages 3 and 4 sleep are commonly referred to as "delta sleep" or "slow-wave sleep." The terminology differences between the EEG and the sleep literature are again notable. A delta wave in sleep terminology is high-amplitude and 2 Hz or less, whereas a delta wave in EEG terminology is 3 Hz or less. It is worth pointing out, again, that slow-wave filters can distort the amplitude of the waveform. If a standard EEG filtering of 1 Hz is applied, the amplitude of waves of 1 Hz will be reduced by 20%.

4.1.1.1.2.8. Stage REM Scoring of REM sleep (Fig. 7) is more complicated than the other sleep stages. In REM, tonic and phasic physiological changes are reflected in EEG, EOG, and EMG; characteristic changes in all three leads are required to identify the stage. REM sleep is defined by a low-voltage mixed-frequency EEG, episodic REMs, and chin EMG activity that is at the lowest level recorded during the study. The drop in EMG activity is a hallmark of normal REM sleep and correlates with generalized skeletal muscle atonia (REM atonia). Sawtooth waves, a notched theta-frequency waveform evident in frontal and vertex areas, are often observed in association with eye movements. Although saw-tooth waves are unique to REM and aid identification of the stage, they are neither sufficient nor necessary for REM stage scoring.

Alpha activity in REM is usually faster than in stage 1 but slower than in wakefulness. Spindles occasionally appear in REM sleep, but any period less than 3 min between two spindles is scored as stage 2 sleep if no eye movements or movement arousals are observed in that interval (if movement arousals occur the stage reverts to stage 1, assuming other criteria for that stage are met). Difficulties in determining the precise beginning and end of the REM stage arise because:

1. EEG, EOG, and EMG do not typically change simultaneously.
2. REMs are episodic events.

Epochs are scored as REM from the point of EMG amplitude decrease, providing that REMs occur in subsequent epochs before the reappearance of spindles, K-complexes or a movement arousal. If one of these events occurs in the interval between the drop in tone and the first eye movement, REM is scored from that event forward, assuming that EMG is still at the REM stage level (i.e., the lowest level of the record). Epochs that are contiguous with stage REM epochs with low-voltage mixed-frequency EEG activity are scored as REM, if the EMG remains at the REM stage level and there is no movement arousal, regardless of whether REMs are present on the EOG in that epoch. A detailed explanation of REM rules is available in the R and K manual.

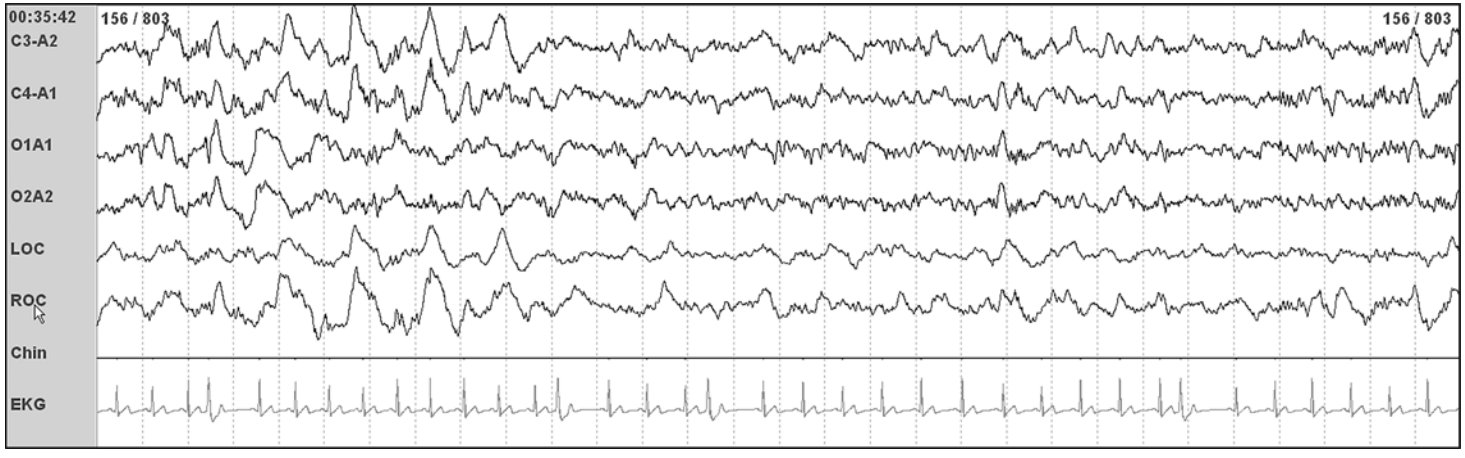

Fig. 5. Stage 3. This stage requires at least 20% and not more than 50% of the epoch to demonstrate activity ≤2 Hz with an amplitude >75 mV.

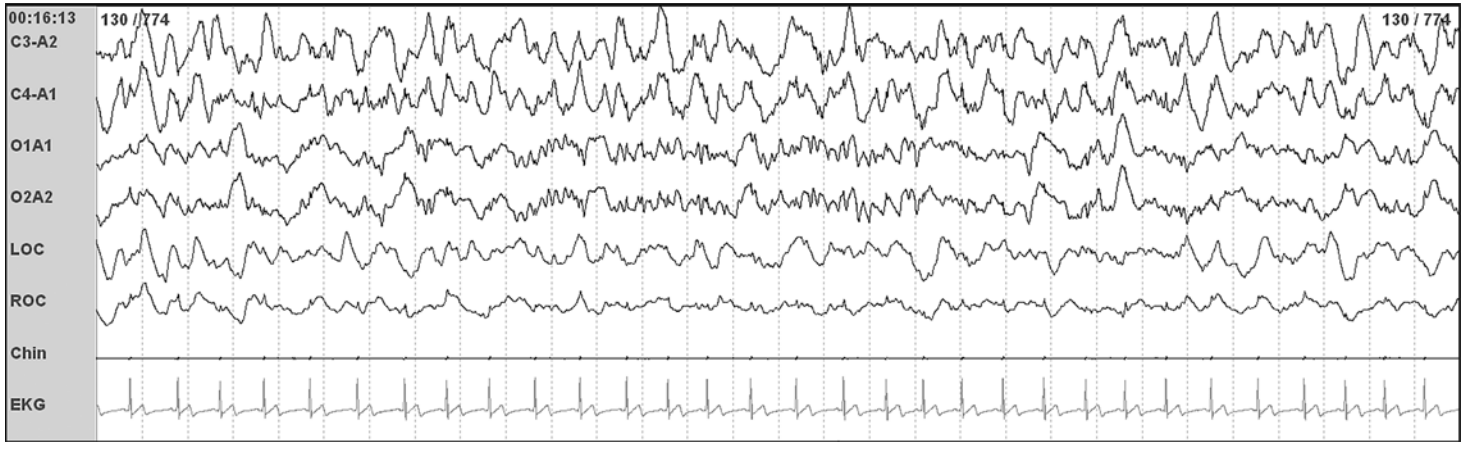

Fig. 6. Stage 4. This stage requires more than 50% of the epoch to demonstrate activity ≤2 Hz with an amplitude >75 mV.

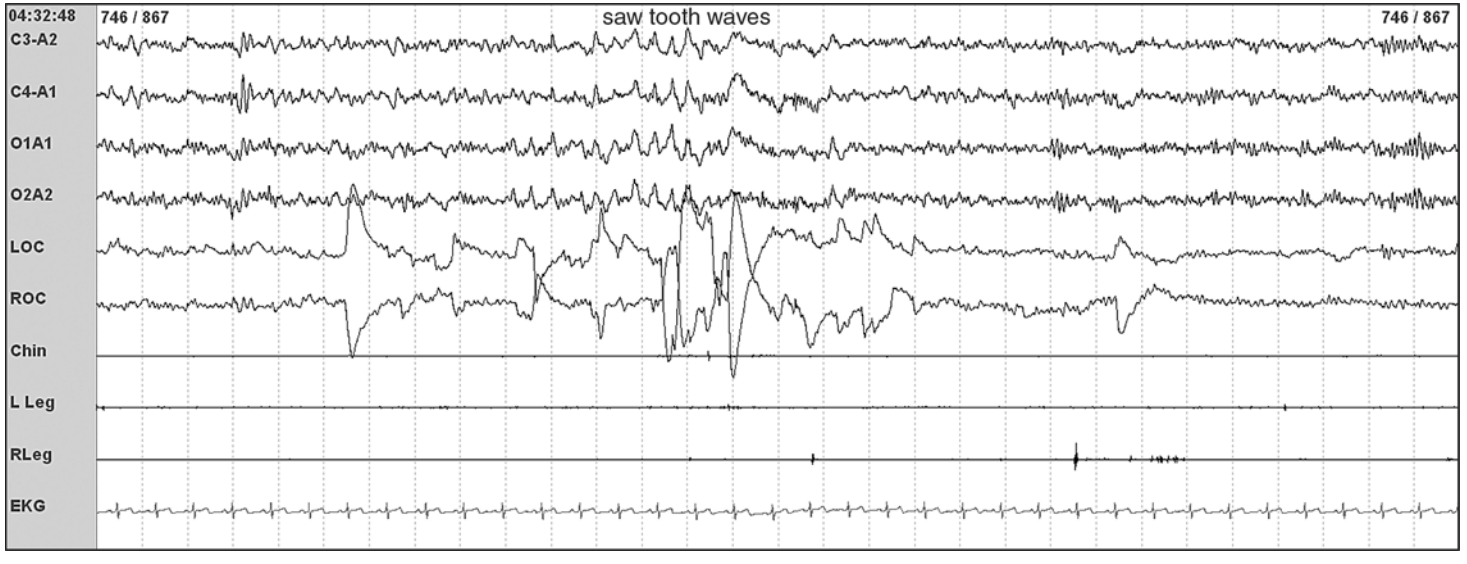

Fig. 7. Rapid eye movements. Rapid eye movements are observed with the tonic EMG level recorded at the lowest level during the study. Occasionally, sawtooth waves and phasic increases in EMG activity occur. (30-s epoch)

4.1.2. Respiratory Measures

The recording of airflow, respiratory effort, and oxygen saturation allows for the determination of abnormal breathing patterns during sleep. These abnormalities underlie the sleep-related breathing disorders. A variety of abnormal breathing events exist, including: apnea, a complete cessation of airflow; hypopnea, a reduction in airflow; and respiratory effort-related arousal (RERA), an EEG arousal induced by respiratory effort but not meeting criteria for an apnea or hypopnea. Surprisingly, there has been a lack of uniform definition of these events, based in large part on differing recording methodologies. Current definitions that have the most widespread clinical use are based on guidelines provided by the Medicare Administration and endorsed by position statements by the AASM; these will be detailed in Sections 4.1.2.2.2. and 4.1.2.2.1. The definition and interpretation of abnormal respiratory events varies widely in practice and in publications. When interpreting the summary report of a PSG, it is essential that the clinician is aware of the laboratory's working definitions.

4.1.2.1. Methodology of Recording Respiratory Measures

4.1.2.1.1. Airflow

Pneumotachographs are the gold-standard for the measure of airflow. Flow is measured across a resistor by a differential manometer. Pneumotachographs generally require a cumbersome mask that is leak-free and seals both mouth and nose. This technique is used in research laboratories but not in routine diagnostic clinical studies. Positive-pressure machines may have built in pneumotachographs, however, that assist in determining flow during the application of pressure in therapeutic studies.

Thermistors or thermocouples placed at both the nose and the mouth are the most commonly used devices for measuring airflow during PSGs. These devices identify the differences in temperature of inspired and expired air, resulting in an easily measured signal. Because change in temperature is not dependent on the volume of air moved, thermistors and thermocouples are sensitive to any airflow, but cannot measure airflow volumes. They have the advantage of measuring airflow at mouth and nose simultaneously, but have the disadvantage of overestimating airflow and underestimating abnormalities.

Nasal pressure transducers are used in many laboratories to assess airflow. These devices are more sensitive than thermistors or thermocouples to subtle changes in flow consistent with obstruction. The pressure transducer is inserted into a nasal cannula. The pressure tracing obtained is a direct function of flow. The shape of the signal reflects the airflow limitation that is observed in partial or complete obstruction of the airway and is an indirect measure of airway resistance. Flattening of the inspiratory signal and/or amplitude reduction indicates limitation of airflow (Fig. 8). The device overestimates decreased airflow when the patient breathes through the mouth. As a result, it is generally recommended that nasal pressure transducers are used with a thermistor or thermocouple.

Respiratory inductance plethysmography (RIP) is a technique used to measure changes in volume of the chest and abdomen. These volume changes can provide a measure of tidal volume. Bands around the chest and abdomen incorporate coils that expand and contract during breathing. Changes in length of the bands induce changes in the oscillating frequency of the circuit. An output signal can be calibrated for volumes in the abdominal and chest compartments. To accurately measure airflow, the system must be carefully calibrated in supine and upright positions. Calibration in obese patients is difficult. Most often, the system is not calibrated and is used as a qualitative measure of chest and abdominal effort.

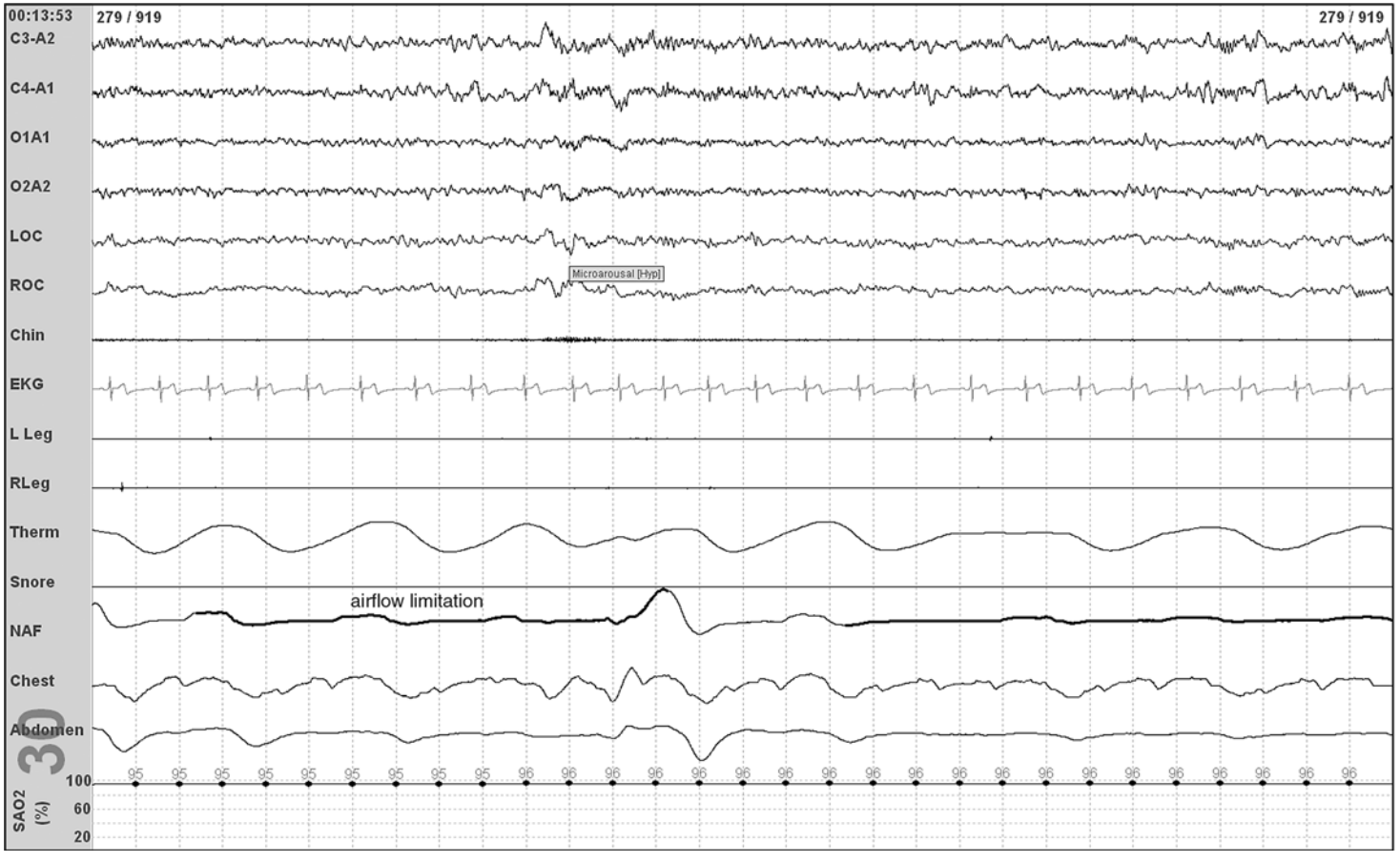

Fig. 8. RERA. Airflow limitation on the nasal air pressure transducer (NAF) is associated with an EEG arousal and steady oximetry readings. This epoch also demonstrates an arousal. (30-s epoch)

4.1.2.1.2. Respiratory Effort

Intra-esophageal pressure measurement, which reflects pressure changes in the intrathoracic compartment, is the gold-standard for measurement of chest effort. Increased airway resistance results in increased negative pressures. A manometer is inserted in the esophagus through a pediatric feeding tube that remains in place for the duration of the study. The discomfort and inconvenience of inserting the manometer make this a technique that is used in only a few centers.

RIP, when uncalibrated, provides a qualitative measurement of movement of the chest and abdomen with respiration.

Stain gauges and piezoelectric bands both also provide qualitative measure of the movement of chest and abdomen. One band is placed around the chest and the other around the abdomen. Piezoelectric bands are the most commonly used instruments for these measurements because of ease of use and low cost, but reliability is less than with RIP.

Intercostal EMG is a simple technique in which standard EEG electrodes are applied to an intercostal space close to the diaphragm. Respiratory effort is evident with a surface EMG recording, similar to the chin EMG. These recordings are a useful second measure of respiratory effort, but are prone to failure in obese patients.

4.1.2.1.3. Oxygen Saturation

Pulse oximetry is a noninvasive method of monitoring the percentage of hemoglobin that is saturated with oxygen. The pulse oximeter consists of a probe attached to the patient's finger or ear lobe. A source of light originates from the probe at two wavelengths. By calculating the absorption at the two wavelengths, the processor can estimate the proportion of hemoglobin that is oxygenated.

4.1.2.2. Types of Respiratory Events

4.1.2.2.1. Apnea

An apnea is defined as the absence of airflow for at least 10 s. There are three types:

1. Obstructive apnea (Fig. 9): absence of airflow for at least 10 s with evidence of persistent respiratory effort.
2. Central apnea (Fig. 10): absence of airflow for 10 s without evidence of any of respiratory effort.
3. Mixed apnea (Fig. 11): absence of airflow for 10 s with initial absence of effort followed by a return of respiratory effort before resumption of airflow.

4.1.2.2.2. Hypopnea

The term hypopnea refers to a decrease in airflow (Fig. 12). There have been many definitions of this event proposed. The current clinical definition that is recognized by Medicare and endorsed by the AASM is as follows: "Hypopnea in adult patients is defined as an abnormal respiratory event lasting at least 10 s with at least a 30% reduction in thoracoabdominal movement or airflow as compared to baseline, and with at least a 4% oxygen desaturation." Hypopneas can be associated with airway obstruction or a centrally mediated reduction in respiratory effort. In clinical practice, it is difficult to distinguish obstructive hypopneas from central hypopneas unless an esophageal pressure monitor is used. Because most effort and airflow monitors are not quantitative, there is debate regarding whether the criterion of 30% reduction in these measures is practical.

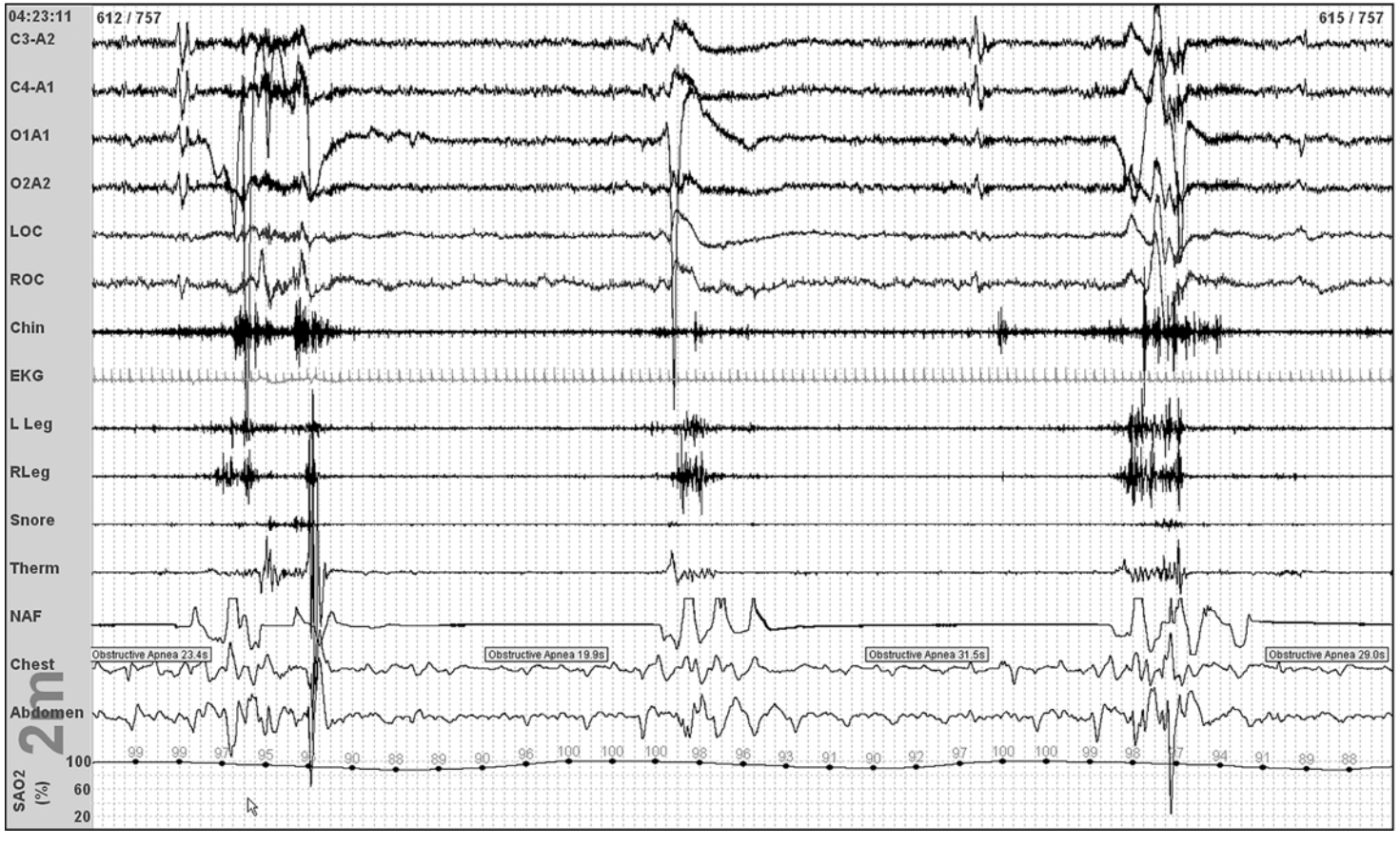

Fig. 9. Obstructive sleep apnea. Each apnea demonstrates persistent thoracoabdominal effort and is associated with airflow obstruction lasting at least 10 s. The epoch also reveals cyclic drops in oxygen saturation and respiratory-induced limb movements, which are not required for scoring apneas. (2-min window)

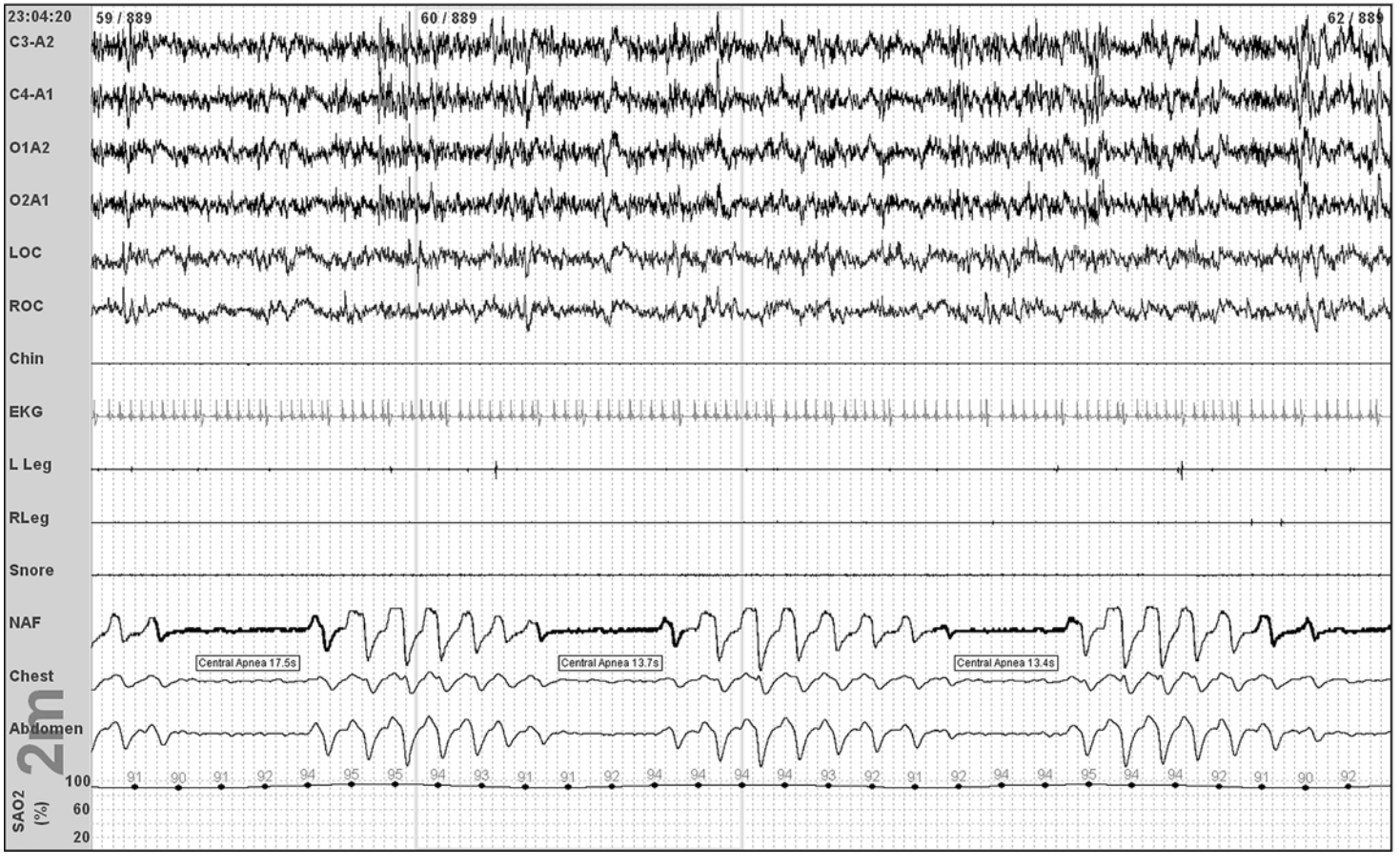

Fig. 10. Central sleep apnea. Each apnea is characterized by an absence of airflow and thoracoabdominal effort for at least 10 s. Desaturations are seen with the events but are not required. (2-min window)

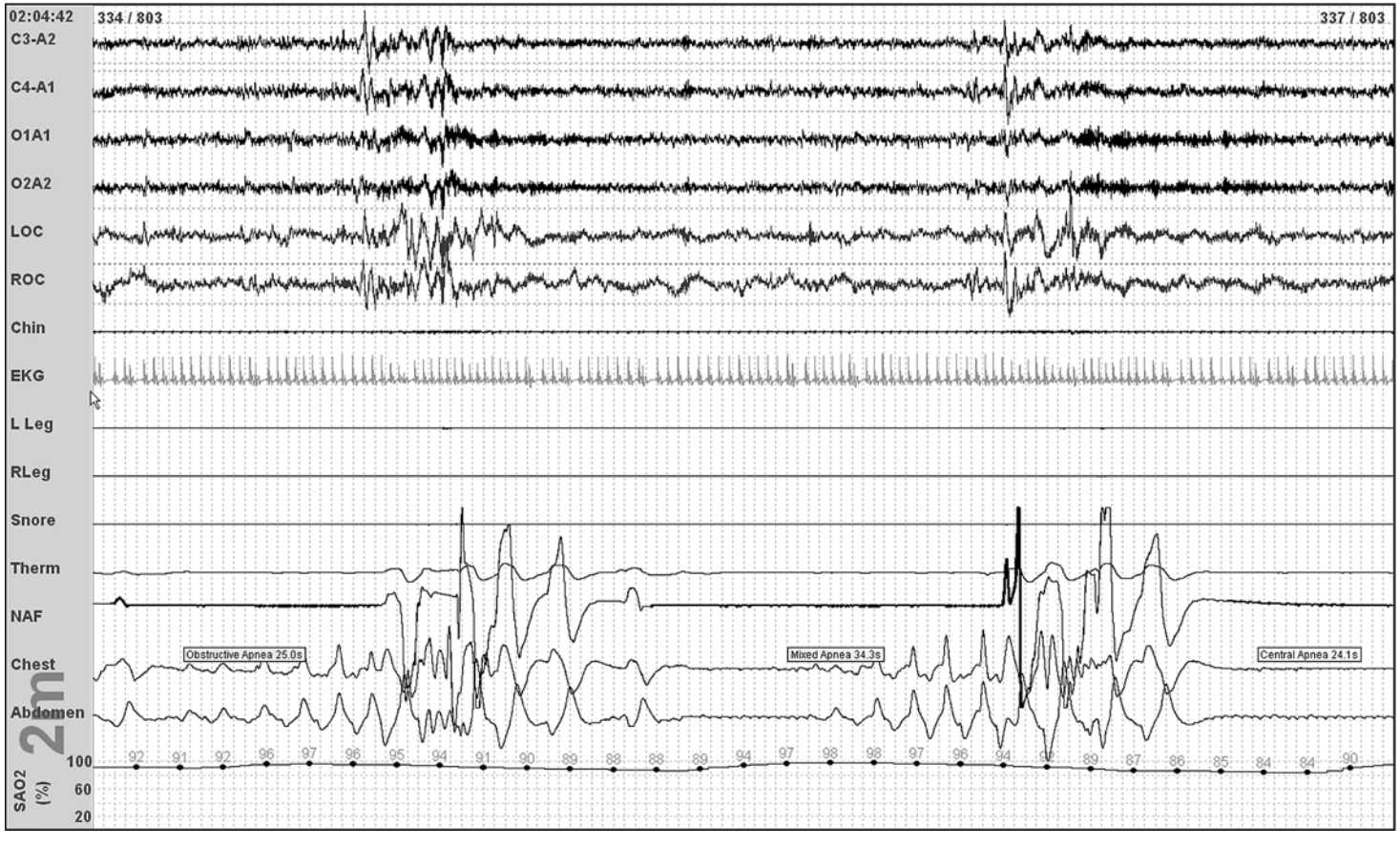

Fig. 11. Mixed apnea. This recording exhibits three apneas. The second is termed a mixed apnea because the event starts as a central event and evolves into an obstructive apnea. Mixed apneas often occur in association with obstructive and central apneas. In this case, an obstructive apnea precedes the event and a central apnea follows it. (2-min window)

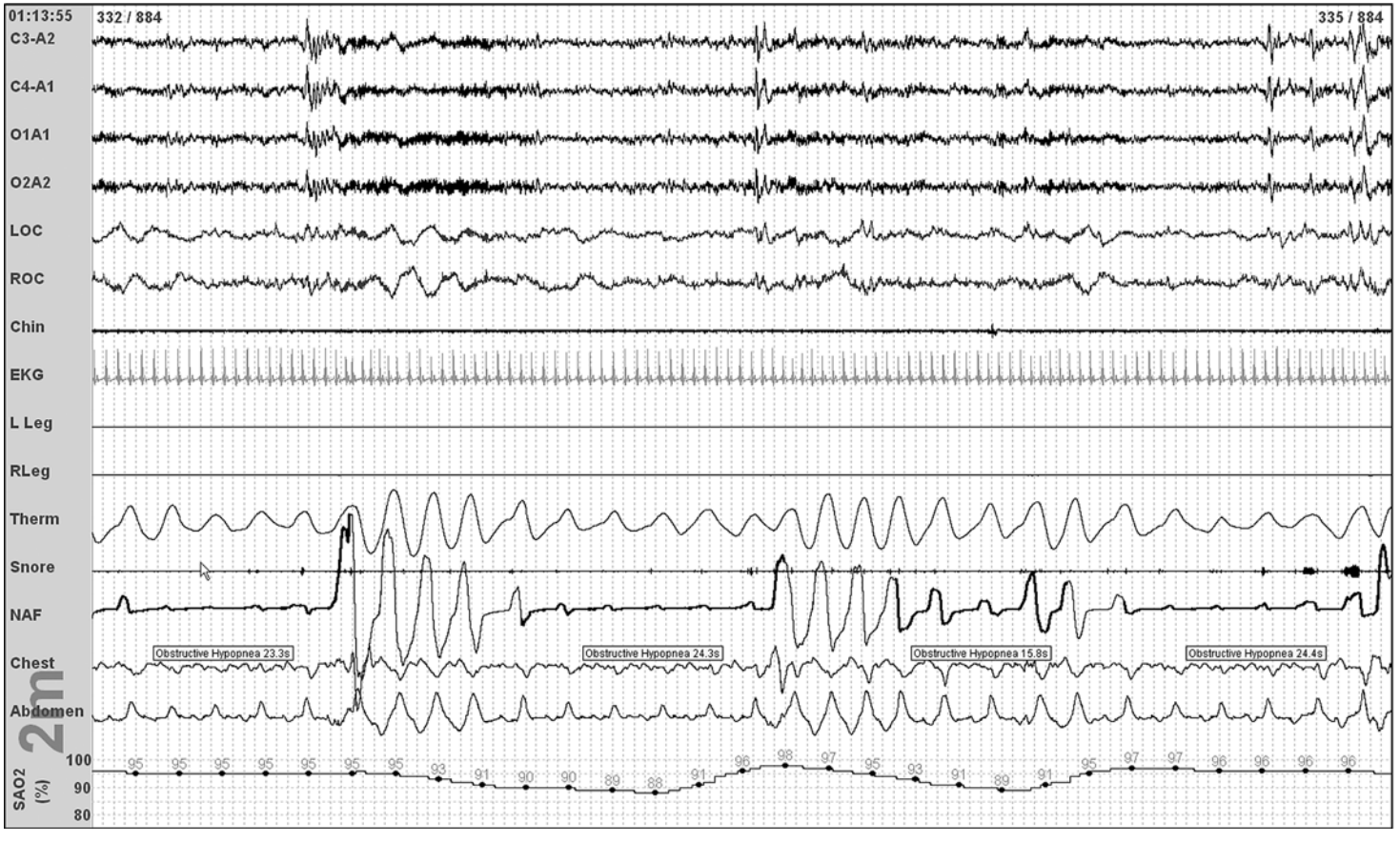

Fig. 12. Hypopnea. This is an example of recurrent "Medicare hypopneas." Medicare requires at least a 30% reduction in airflow or thoracoabdominal movement, lasting at least 10 s, with a drop in oxygen saturation of at least 4%. (2-min window)

4.1.2.2.3. Respiratory Effort-Related Arousal

When airway resistance increases, oxygen saturation and tidal volume may stay the same as respiratory effort increases to overcome the obstruction. The result of increased respiratory effort may be an arousal that disturbs sleep. These abnormalities are termed RERAs (Fig. 8) *(7)*. Evidence of increased respiratory effort in association with arousal is best evidenced by an esophageal manometer, but that technique is rarely available. Pressure transducers can show evidence of flow limitation before arousal. Changes in breathing patterns before arousal may also be correlated with increased airway resistance. The event should last 10 s. RERAs are not scored in all laboratories; some laboratories refer to these events as hypopneas or "hypopneas not meeting Medicare criteria."

4.1.2.3. Quantification of Respiratory Abnormality

1. Apnea hypopnea index (AHI): the apnea hypopnea index is calculated by adding the total number of apneas and hypopneas and dividing by the number of hours of sleep. When used with the definitions above, the index is useful as a standardized measure that reflects severity of sleep-disordered breathing.
2. Respiratory disturbance index (RDI): all respiratory events scored are added together and divided by the number of hours of sleep to generate the RDI. The RDI is not a standard measure because different laboratories measure respiratory events differently. If a laboratory measures RERAs, for example, they will be reflected in the RDI.
3. Oxygen saturation: laboratories typically report several measure of oxygen saturation, including lowest saturation, baseline saturation, and percent time at various levels of saturation.

4.1.2.3.1. EKG

A single channel EKG is recorded. There is no standard lead placement. Some laboratories use a modified Lead II (right shoulder, left leg), most use a precordial lead.

Recording EKG allows for continuous review of cardiac rhythm during the night. Cardiac abnormalities often correlate with respiratory abnormalities and sleep stages. Respiratory obstruction may result in periods of vagally mediated cardiac slowing followed by sympathetically induced increased rates with arousal. Hypoxia and increased sympathetic drive during arousal can exacerbate arrhythmia. REM sleep may be associated with prominent autonomic changes reflected in the rhythm strip.

4.1.3. Limb EMG

Surface EMG recording of the limbs allows for analysis of movement disorders and movement arousals during sleep. Usually only the anterior tibialis muscles of both legs are studied, but recordings may also be obtained from the arms (extensor digitorum muscles). The anterior tibialis muscles are studied because they have a good correlation with the movements observed in periodic limb movement disorder (PLMD; Subheading 6.4.1.), a disorder that exists with and without the complaint of restless legs (Subheading 6.4.2.). Leg movements may also accompany respiratory events or other sources of arousal. Periodic leg movements, by definition, occur in periodic sequences, whereas other leg movements may not be periodic.

4.1.3.1. Techniques for Recording Limb Movements

Two surface electrodes are placed on the bellies of the anterior tibialis muscles of both legs and each recorded in a bipolar fashion. A high-frequency filter of at least 128 Hz is recommended. The surface EMG obtained is calibrated while the patient is awake with a 30° dorsiflexion and plantar flexion of the great toe without resistance. Activity during sleep is compared with this biological calibration.

4.1.3.2. Techniques for Scoring and Reporting Limb Movements

The AASM has established the following scoring guidelines *(10)*:

1. Leg movement: a burst of anterior tibialis activity with a duration of 0.5 to 5 s and with an amplitude of at least 25% of the calibration movements.
2. Periodic leg movement sequence is defined as four or more leg movements separated by between 5 s and 90 s. These should be scored during both sleep and wake. Periodic leg movements during wakefulness are suggestive of restless legs syndrome (RLS) and correlate with periodic limb movements during sleep (PLMS) (Fig. 13).
3. Leg movement with arousal: to assess the impact of the events on sleep, leg movements that cause arousal are counted. The arousal must not follow leg movement onset by more than 3 s.

Leg movements associated with respiratory events are counted and classified as respiratory related.

Leg movements are reported in terms of both an absolute number as well as indices of events per hour of sleep with and without arousal. Leg movements within sequences (and therefore periodic) should be distinguished from leg movements not within sequences.

4.1.4. Body Position

Body position sensors allow correlation of respiratory abnormalities with position. Severity of sleep-disordered breathing may vary significantly with position.

4.1.5. Video EEG–PSG

Because only a limited EEG montage is used for the analysis of sleep stage in a standard PSG, extended EEG montages are necessary to attempt to identify epileptic activity during sleep. These studies are usually obtained in patients who complain of unusual nocturnal events that could represent seizure activity. Video monitoring helps characterize the behavioral components of the disorder in relationship to the neurophysiological findings. Respiratory monitoring may identify respiratory precipitants to seizure activity that would have been overlooked in routine or extended EEG analysis. The number of channels recorded is dependent on the capability of the recording equipment; a full EEG is optimal. A common eight-channel EEG recording added to the routine PSG includes includes: F7–T3, T3–T5, T5–O1, F8–T4, T4–T6, T6–O2, F3–C3, and F4–C4.

4.1.6. Interpretation of the PSG

Polysomnographic interpretation requires both an independent analysis of the component measurements and an overall synthesis of how these variables interact with each other.

Most reports include a quantitative report of sleep architecture, respiratory measures, EKG, limb movements, and a limited description of EEG. Diagnostic requirements for specific disorders using these measures are described in Tables 7 to 11.

Qualitative interpretation of the PSG is also important, and relies on the polysomnographer's ability to identify patterns of interaction between variables that vary from the norm and may be disease specific. A summary of statistics does not replace an epoch-by-epoch review of the record. Interpretation is dependent on the clinical context, making it important that the clinician approaches the process of reading a sleep study with an understanding of the patient's medical background and the specific questions posed. For example, an arousal from slow-wave sleep may be an insignificant polysomnographic finding, and subtle periods of decreased airflow are also common. In the context of a patient who presents with episodes of sudden fear and panic during sleep, however, the presence of a sudden arousal from slow-wave

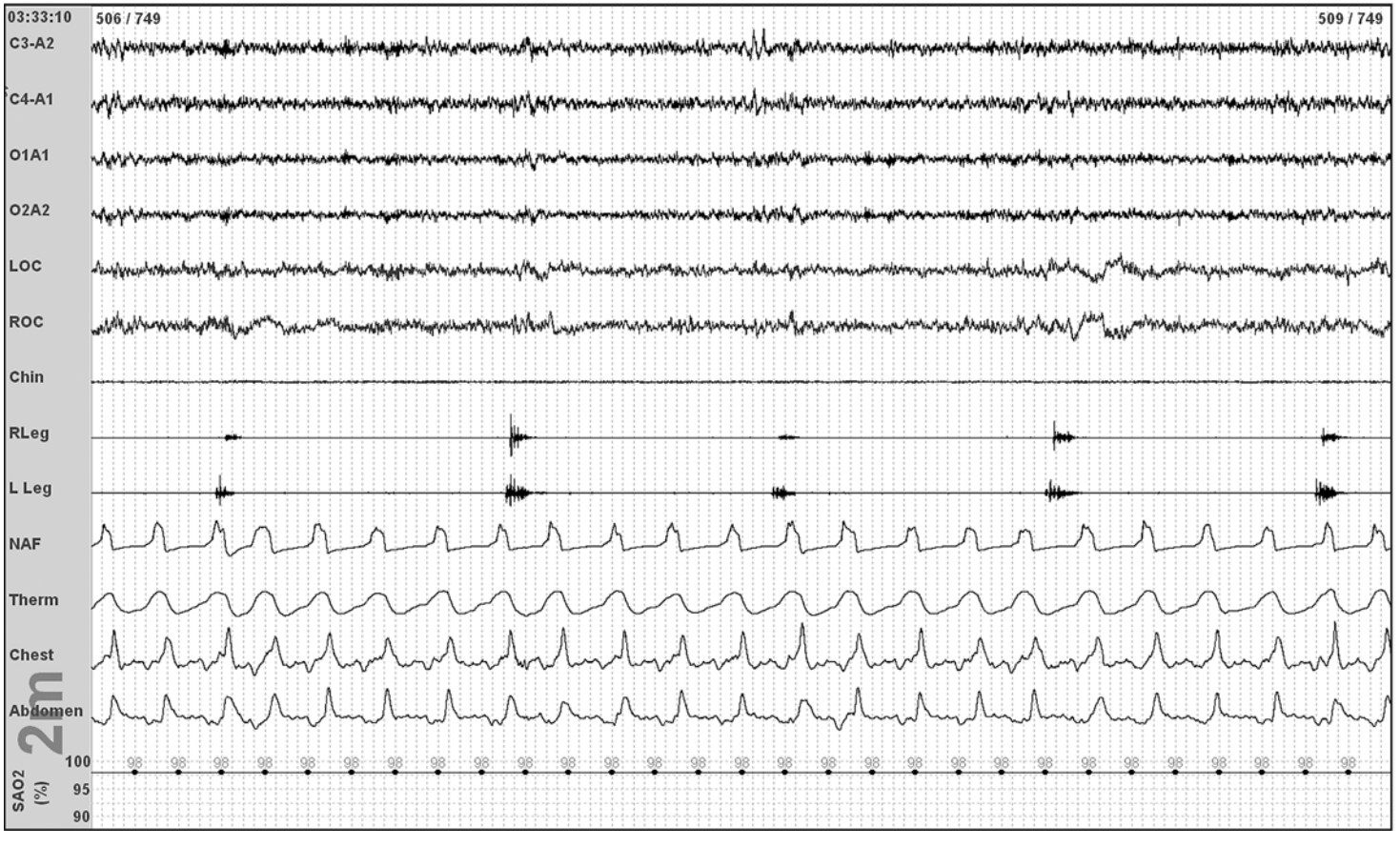

Fig. 13. Periodic limb movements during sleep. The limb movements in this case occur bilaterally and are independent of respiratory instability. The morphology is easily identified by its periodicity. (2-min window)

Table 7
Central Sleep Apnea

Disorder	*Clinical criteria*	*Polysomnographic criteria*	*Other requirements*	*Other features*
Primary central sleep apnea	At least one of the following: • Excessive daytime sleepiness • Frequent arousals and awakenings during sleep or insomnia complaints • Awakening short of breath	Five or more central apneas per hour of sleep	The disorder is not better explained by another current sleep disorder, another medical or neurological disorder, medication use, or substance use disorder.	$PaCO_2$ low normal <40 during wakefulness O_2 desaturation is usually mild Sleep is fragmented by respiratory events
Cheynes Stokes breathing pattern	No symptoms are required Patients often report symptoms of sleep disruption, insomnia, excessive daytime sleepiness, or awakening short of breath.	At least 10 central apneas and hypopneas per hour of sleep in which the hypopnea has a crescendo–decrescendo pattern of tidal volume accompanied by frequent arousals from sleep and derangement of sleep architecture	The disorder occurs in association with a serious medical illness, such as heart failure, stroke, or renal failure. The disorder is not better explained by another current sleep disorder, another medical or neurological disorder, medication use, or substance use disorder.	Oxygen desaturations usually not less than 80%. Distinguished from hypoventilation syndromes by $PaCO_2$ <45 Sleep is fragmented. Arousals are frequently associated with crescendo breathing. Attenuated by REM sleep

(Continued)

Table 7 ***(Continued)***

Disorder	*Clinical criteria*	*Polysomnographic criteria*	*Other requirements*	*Other features*
High-altitude periodic breathing	Recent ascent to altitude of at least 4000 m	Recurrent central apneas, >5/hr, with cycle length 12–34 s, primarily in NREM	None	Sleep is fragmented. Attenuated by REM
Central sleep apnea due to drug or substance	The patient has been taking a long-acting opioid for at least 2 mo.	Five or more central apneas or periodic breathing (10 or more central apneas or hypopneas per hour of sleep with crescendo–descrescendo pattern and arousals)	The disorder is not better explained by another current sleep disorder or medical or neurological disorder.	May complicate other sleep-related breathing disorders
Primary sleep apnea of infancy (apnea of prematurity, <37 wk; apnea of infancy >37 wk)	No requirements	Prolonged central respiratory pauses of 20 s or more in duration, or shorter episodes with obstructive or mixed features with clinical compromise (e.g., bradycardia, hypoxemia, cyanosis, or hypotonia)	The disorder is not better explained by another current sleep disorder, medical or neurological disorder, or medication.	Exacerbated by REM sleep Findings may not occur nightly; polysomnographic study may be normal. Additional EEG and esophageal pH employed frequently.

Abstracted from ref. *5*, with permission.

Table 8
Obstructive Sleep Apnea

Disorder	*Clinical criteria*	*Polysomnographic criteria*	*Other requirements*	*Other features*
Obstructive sleep apnea	At least one of the following: • The patient complains of unintentional sleep episodes during wakefulness, daytime sleepiness, unrefreshing sleep, fatigue, or insomnia • The patient wakes with breath holding, gasping, or choking • The bed partner reports loud snoring, breathing interruptions, or both during the patient's sleep	With clinical criteria noted: Five or more apneas, hypopneas or RERAs per hour of sleep with evidence of respiratory effort during all or a portion of each respiratory event Without clinical criteria noted: Fifteen or more apneas, hypopneas, or RERAs per hour of sleep with evidence of respiratory effort during all or a portion of each respiratory event	The disorder is not better explained by another current sleep disorder, another medical or neurological medication use, or substance use disorder.	In this definition of sleep apnea there is no requirement that respiratory events are associated with oxygen desaturation. The Medicare-approved criteria for obstructive sleep apnea justifying treatment with positive pressure are different than the diagnostic criteria established by the International Classification of Sleep Disorders-2. Medicare does not recognize RERAs. Hypopneas by Medicare criteria require ≥4% desaturation and ≥30% decrease in respiratory effort or airflow. Using these criteria, positive pressure will be covered under Medicare in adult patients if (1) the AHI is ≥15 or (2) the AHI is ≥5 and ≤14 with documented symptoms of excessive daytime sleepiness, impaired cognition, mood disorders, or insomnia; or documented hypertension, ischemic heart disease or history of stroke.

Abstracted from ref. *5* with permission.

Table 9
Sleep-Related Hypoventilation/Hypoxemic Syndromes

Disorder	*Clinical criteria*	*Polysomnographic criteria*	*Other requirements*	*Other features*
Sleep-related nonobstructive alveolar hypoventilation syndrome	Symptoms not required Patients often report symptoms of sleep disruption, insomnia, or excessive daytime sleepiness	Episodes of shallow breathing longer than 10 s in duration associated with arterial oxygen desaturation and either frequent arousals from sleep or brady-tachycardia	No primary lung diseases, skeletal malformations, or peripheral neuromuscular disorders that affect ventilation are present The disorder is not better explained by another current sleep disorder, another medical or neurological disorder, medication use, or substance use disorder.	Carbon dioxide levels show an increase during episodes of hypoventilation. Daytime blood gases may be normal or abnormal.
Congenital central alveolar hypoventilation syndrome	Patient exhibits shallow breathing or cyanosis and apnea of perinatal onset during sleep	Polysomnographic monitoring during sleep demonstrates severe hypercapnia and hypoxia, predominantly without apnea	Hypoventilation is worse during sleep than during wakefulness. Rebreathing ventilatory response to hypoxia or hypercapnia is absent or diminished. The disorder is not better explained by another current sleep disorder, another medical or neurological medication use, or substance use disorder.	Rare disorder, recently associated with mutations of *PHOX2B* gene
Sleep-related hypoventilation/ hypoxemia due to pulmonary parenchymal or vascular pathology	Lung parenchymal disease or pulmonary vascular disease is present and believed to be the primary cause of hypoxemia	Polysomnography or sleeping arterial blood gas shows at least one of the following: • Sp O_2 during sleep <90% for more than 5 min with a nadir of at least 85% • More than 30% of total sleep time at an SpO_2 <90%	The disorder is not better explained by another current sleep disorder, another medical or neurological disorder, medication use, or substance use disorder.	$PaCO_2$ is not routinely measured during PSG. End tidal CO_2 is measured in some laboratories.

		• Sleeping $PaCO_2$ that is abnormally high or disproportionately increased relative to levels during wakefulness		
Sleep-related hypoventilation/ hypoxemia due to lower airways obstruction	Lower airways obstructive disease is present and is believed to be the primary cause of the hypoxemia.	Polysomnography or sleeping arterial blood gas shows at least one of the following: • SpO_2 during sleep of <90% for >5 min with a nadir of at least 85% • More than 30% of total sleep time at an SpO_2 <90% • Sleeping $PaCO_2$ that is abnormally high or disproportionately increased relative to levels during wakefulness.	The disorder is not better explained by another current sleep disorder, another medical or neurological disorder, medication use, or substance use disorder.	$PaCO_2$ is not routinely measured during PSG. End tidal CO_2 is sometimes measured in some laboratories.
Sleep-related hypoventilation/ hypoxemia due to neuromuscular and chest wall disorders	A neuromuscular or chest wall disorder is present and believed to be the primary cause of hypoxemia.	Polysomnography or sleeping arterial blood gas shows at least one of the following: • SpO_2 during sleep of <90% for more than 5 min with a nadir of at least 85% • More than 30% of total sleep time at an SpO_2 <90% • Sleeping $PaCO_2$ that is abnormally high or disproportionately increased relative to levels during wakefulness.	The disorder is not better explained by another current sleep disorder, another medical or neurological disorder, medication use, or substance use disorder.	Exacerbated by REM sleep because of muscle atonia Present in a wide variety of disorders that impair chest wall function including obesity, kyphoscoliosis, and any disorder causing muscular weakness, such as the muscular dystrophies, ALS, and myasthenia Exacerbated by disorders that also reduce chemosensitivity, such as myotonic dystrophy

SpO_2, saturation by pulse oximetry; PSG, polysomnogram; REM, rapid eye movement sleep; ALS, amyotrophic lateral sclerosis.
Abstracted from ref. *5*, with permission.

Table 10
Narcolepsy and Idiopathic Hypersomnia

Disorder	*Clinical criteria*	*Polysomnographic criteria*	*Other requirements*	*Other features*
Narcolepsy with cataplexy	Complaint of excessive daytime sleepiness occurring almost daily for at least 3 mo A definite history of cataplexy, defined as sudden and transient episodes of loss of muscle tone triggered by strong emotions, most reliably, laughing	If cataplexy is clinically unequivocal, or CSF hypocretin fulfills criteria noted, polysomnographic study with PSG and MSLT are recommended but not required as confirmatory evidence. Full night PSG with minimum of 6 h sleep on night preceding MSLT Confirmatory MSLT must demonstrate: mean sleep latency ≤8 min with minimum of 2 SOREMPs.	CSF hypocretin-1 levels less than 110 pg/mL or 1/3 normal mean control can replace PSG and MSLT. At the time of PSG/MSLT, patients must be free of medications that influence sleep ×5 half-lives of longest acting metabolite. Prior to PSG/MSLT sleep–wake cycle should be standardized for at least 7 d, confirmed by sleep logs or actigraphy. The disorder is not better explained by another current sleep disorder, another medical or neurological disorder, medication use, or substance use disorder.	CSF hypocretin may be considered as alternative to PSG/MSLT if clinical situation warrants. PSG often shows other abnormalities including some sleep-disordered breathing, leg movements, fragmented sleep and REM behavior disorder Clinical correlation is required to determine whether these abnormalities are primary or secondary. Many patients cannot undergo a valid MSLT because sleep-influencing medications, especially antidepressants, cannot be discontinued. MSLT in this situation may be misleading.

Narcolepsy without cataplexy	Complaint of excessive daytime sleepiness occurring almost daily for at least three months Typical cataplexy is not present, atypical cataplexy-like episodes may be reported	Full-night PSG with minimum of 6 h sleep on night preceding MSLT required MSLT must demonstrate: mean sleep latency ≤8 min with minimum of 2 SOREMPs.	CSF hypocretin-1 levels usually not abnormal At the time of PSG/MSLT, patients must be free of medications that influence sleep ×5 half-lives of longest acting metabolite. Prior to PSG/MSLT, sleep wake cycle should be standardized for at least 7 d, confirmed by sleep logs or actigraphy. The disorder is not better explained by another current sleep disorder, another medical or neurological disorder, mental disorder, medication use, or substance use disorder.	CSF hypocretin unlikely to be helpful as alternative to PSG/ MSLT PSG often shows other abnormalities, including some sleep-disordered breathing, leg movements, fragmented sleep, and REM behavior disorder. Clinical correlation is required to determine whether these abnormalities are primary or secondary. Many patients cannot undergo a valid MSLT because sleep-influencing medications, especially antidepressants, cannot be discontinued. MSLT in this situation may be misleading.
Narcolepsy due to medical condition	Complaint of excessive daytime sleepiness occurring almost daily for at least three months A definite history of cataplexy, defined as sudden and transient episodes of loss of muscle tone triggered by strong emotions, most reliably, laughing, OR	If cataplexy is unequivocal or CSF orexin fulfills criteria noted, polysomnographic study with PSG and MSLT are recommended but not required as confirmatory evidence. Full-night PSG with minimum of 6 h sleep on night preceding MSLT Confirmatory MSLT must demonstrate: mean sleep latency ≤8 min with minimum of 2 SOREMPs.	A significant underlying medical or neurological disorder accounts for the symptoms. The disorder is not better explained by another current sleep disorder, another medical or neurological disorder, medication use, or substance use disorder.	CSF hypocretin may be considered as alternative to PSG/MSLT if clinical situation warrants.

(Continued)

Table 10 ***(Continued)***

Disorder	*Clinical criteria*	*Polysomnographic criteria*	*Other requirements*	*Other features*
	hypocretin-1 levels in CSF ≤110 pg/mL or 1/3 of normal mean control values			
Idiopathic hypersomnia with long sleep time	The patient has a complaint of excessive daytime sleepiness occurring almost daily for at least 3 mo. Prolonged nocturnal sleep, >10 h documented by interviews, actigraphy or, sleep logs Waking patient is difficult in the morning or at the end of naps.	PSG demonstrates no other sleep disorder. PSG sleep latency is short and sleep duration is ≥10 h. If MSLT performed, sleep latency is <8 min with fewer than 2 SOREMPs.	The disorder is not better explained by another current sleep disorder, another medical or neurological disorder, mental disorder, medication use, or substance use disorder.	Waking patient is typically difficult. MSLT not always performed because of difficulty both waking patient at the end of naps and keeping patient awake between naps PSG analysis of subtle respiratory events often identifies patients with sleep-disordered breathing as alternative diagnosis.
Idiopathic hypersomnia without long sleep time	The patient has a complaint of excessive daytime sleepiness occurring almost daily for at least 3 mo. The patient has normal nocturnal sleep (>6 h but <10 h), documented by interviews, actigraphy, or sleep logs.	Nocturnal PSG demonstrates a major sleep period that is normal in duration (>6 h but <10 h). PSG has excluded other causes of daytime sleepiness. MSLT after overnight PSG demonstrates a mean sleep latency of <8 min and fewer than 2 SOREMPs.	The disorder is not better explained by another current sleep disorder, another medical or neurological disorder, mental disorder, medication use, or substance use disorder.	PSG analysis of subtle respiratory events often identifies patients with sleep-disordered breathing as an alternative diagnosis.

CSF, cerebrospinal fluid, MSLT, multiple sleep latency test; PSG, polysomnogram; SREMPs, sleep-onset REM periods; REM, rapid eye movement sleep.
Abstracted from ref. *5*, with permission.

Table 11
REM Behavior Disorder and Disorders of Arousal From NREM

Disorder	*Clinical criteria*	*Polysomnographic criteria*	*Other requirements*	*Other features*
REM behavior disorder (RBD)	At least one of the following: • Sleep-related injurious, potentially injurious, or disruptive behaviors by history • Abnormal REM behaviors documented during polysomnographic monitoring	Presence of REM sleep without atonia: the EMG finding of excessive amounts of sustained intermittent elevation of submental EMG tone or excessive phasic submental or limb EMG twitching	Absence of EEG epileptiform activity during REM sleep unless RBD can be distinguished from concurrent REM sleep related seizure disorder. The disorder is not better explained by another current sleep disorder, another medical or neurological disorder, mental disorder, medication use, or substance use disorder.	Video recording and additional EMG limb leads (arms) are helpful. Often associated with and may precede parkinsonian syndromes Patients often report that behaviors were consistent with complex dream mentation.
Disorders of arousal from NREM	Characterized by confused behaviors emerging from NREM (typically slow-wave sleep) sleep including ambulation, routine, or inappropriate behaviors, or manifestations of terror, typically associated with partial or complete amnesia for the episode	None required Sudden spontaneous arousals from slow wave sleep may be noted with or without behavioral correlate. Polysomnogram useful to identify contributing causes of arousal	The disorder is not better explained by another current sleep disorder, another medical or neurological disorder, mental disorder, medication use, or substance use disorder.	Typically emerge in the first third of the night when slow-wave sleep is prominent Familial tendency, may be precipitated by another cause of arousal such as sleep-disordered breathing or leg movements Differential diagnosis includes seizure disorder and REM behavior disorder.

REM, rapid eye movement sleep; NREM, non-REM sleep.
Abstracted from ref. *5*, with permission.

sleep with evidence of preceding subtle airflow limitation, would suggest that sleep-disordered breathing was contributing to the manifestation of a disorder of arousal from NREM sleep. Ultimately, the interpretation of these qualitative features is dependent on the experience of the interpreting clinician.

4.2. The MSLT

The MSLT is a limited-montage polysomnographic study that evaluates subjects in a series of opportunities to nap during the day. It is a validated objective measure of the ability or tendency to fall asleep, and allows an opportunity to assess the presence of abnormal sleep-onset REM periods. The AASM published new practice guidelines for the clinical use of the MSLT in 2005 *(11)*.

4.2.1. Indications for the MSLT

As described in the current practice parameters, the MSLT is indicated for:

"1. The evaluation of patients with suspected narcolepsy to confirm the diagnosis.
2. The MSLT may be indicated as part of the evaluation of patients with suspected idiopathic hypersomnia to help differentiate idiopathic hypersomnia from narcolepsy."

The study is always preceded by a full-night PSG during the subject's usual sleep period. Total sleep time on this study must be at least 6 h.

4.2.2. Techniques of the MSLT

The montage for the MSLT includes scoring channels (EEG, chin EMG, and EOG) and EKG. Occipital leads (O1–A1, O2–A2) are added to better identify the drop out of alpha activity characteristic of sleep onset (Table 2). Occasionally, limited respiratory channels are added.

The standard MSLT provides five opportunities to nap at 2-h intervals. The study starts 1.5 to 3 h after termination of nocturnal PSG. The patient is studied in a dark quiet room; the instruction is to close the eyes and attempt to sleep.

Sleep logs or actigraphy should be obtained for at least 1 wk before the study to ascertain sleep–wake cycles to assure that naps are obtained during the patient's usual wake times.

For diagnostic purposes, the study is not valid if sleep-influencing drugs are either present or recently withdrawn (an exception would be to evaluate the effect of a drug on sleep latency, but this is typically a research application). A wide variety of medications are stimulants, depressants, or REM inhibitors. These medications need to be discontinued before the study by an interval of at least five half-lives of the longest active metabolite. When planning drug discontinuation before study, it is important to recognize that withdrawal effects on sleep architecture may persist after washout of the drug. Adequate time should be allowed for return of the patient's sleep to a baseline condition. Drug screening is usually obtained in the morning. Smoking is not allowed 30 min before the naps. Caffeine is also prohibited during the study.

4.2.3. Scoring of the MSLT

During each nap, the patient is given a 20-min opportunity to fall asleep. If no sleep occurs, the sleep latency is recorded as 20 min and the nap is ended.

Sleep onset is defined as the latency to the first epoch of any stage of sleep. An epoch of sleep is defined as greater than 15 s cumulative sleep in a 30-s epoch. If sleep occurs, the study is ended 15 min after the onset of sleep, by "clock time" not sleep time. Thus, if a patient fell asleep at minute 19, the study would end at minute 34, whether the patient were asleep or awake. If the patient fell asleep at minute 2, the study would end at minute 17.

REM latency is defined as the time from the first epoch of sleep to the first epoch of REM including any wake epochs that may occur. A REM epoch requires greater than 15 s of REM in a 30-s epoch.

Reporting should include start and end times of naps, mean sleep latency averaged over the five naps, number of sleep-onset REM periods, and latency to each REM period.

4.2.4. Interpretation of the MSLT

The primary measures of importance in the MSLT are:

1. The presence or absence of sleep-onset REM.
2. The mean sleep latency.

The occurrence of REM sleep at any time during a nap is defined as sleep-onset REM. Because REM sleep typically occurs 90 min after sleep onset, REM onset within 15 min of sleep onset during a nap is an abnormal finding; most narcoleptics have two sleep-onset REM periods in five naps, as will be discussed later, in Subheading 6. *(11)*. However, sleep-onset REM is not a specific finding. Previous sleep deprivation, medication (especially medication withdrawal), and circadian rhythm disturbances may result in sleep-onset REM. This fact underscores the fact that the study can only be interpreted when there is a careful analysis of the patient's clinical history and the conditions of the test. A recent extensive review of the MSLT by a Task Force of the Standards of Practice of the AASM concluded that the mean sleep latency on the MSLT does not discriminate well between populations of patients with sleep disorders and normal patients because of a large standard deviation of the mean *(12)*. The mean latency to sleep in normal subjects is approx 10 min, with a two standard deviation of 1.8 to 19 min. However, in the clinical context of the evaluation of a sleepy patient who, on clinical grounds, may have narcolepsy, the combination of assessment of sleep latency and the presence of sleep-onset REM is of use and is included in formal diagnostic criteria (Subheading 6.2.1.). In narcolepsy, the mean sleep latency is usually less than 8 min. In a meta-analysis of 255 patients with narcolepsy, the mean latency was reported as 3.1 min, with a standard deviation of 2.9 min.

4.3. The MWT

The MWT is another limited-montage laboratory polysomnographic study. It is a validated objective measure of the ability to stay awake for a defined time. Subjects are studied in a manner similar to the MSLT in daytime nap opportunities, but are instructed to stay awake rather than fall asleep. Protocols exist for both 20-min and 40-min trials, but the 20-min protocol is of limited use. New guidelines for the MWT were also recently published by the AASM *(8)*.

4.3.1. Indications for the MWT per AASM Practice Parameters are as Follows:

"1. The MWT 40-min protocol may be used to assess an individual's ability to remain awake when his or her inability to remain awake constitutes a public or personal safety issue.
2. The MWT may be indicated in patients with excessive sleepiness to assess response to treatment." *(11)*

4.3.2. Techniques of the MWT

The MWT uses the same montage as the MSLT. A previous-night PSG is not necessary but may be performed depending on the question to be answered by study. A four-trial protocol with each trial 40 min in duration is preferred. Four trials are performed at 2-h intervals, with

the first starting 1.5 to 3 h after the patient's usual wake time. The room should be lit by low light, 0.1 to 0.13 lux, equivalent to a 7.5-watt night light behind the patient's head. The patient is seated in bed. The subject is instructed to sit still and try to stay awake. Alerting measures such as singing or clapping are not allowed. Prescription medications, including stimulants, caffeine, and tobacco are allowed if the study is designed to assess ability to stay awake with these substances in place; these should be documented.

4.3.3. Scoring of the MWT

Trials are ended at 40 min if no sleep occurs. In contrast, if the subject experiences the occurrence of three continuous epochs of stage 1 sleep or one epoch or any other sleep stage (termed "unequivocal sleep"), the patient is awoken and trial ended.

Sleep onset is defined as the first epoch of greater than 15 s of cumulative sleep in a 30-s epoch.

Reporting should include start and stop times for each trial, sleep latency, total sleep time, stages of sleep achieved, and mean sleep latency for the four trials. Absence of sleep is recorded as a latency of 40 min.

4.3.4. Interpretation of the MWT

Similar to the MSLT, the MWT has a wide range of normal values that makes it a poor discriminator between normal and abnormal populations. However, staying awake for four 40-min trials is considered strong objective evidence of the ability to stay awake in similar nonstimulating environments. It is understood that the test may not reliably predict sleepiness in another environment in which conditions, such as previous sleep, may be different. On the other hand, a mean latency of less than 8 min is abnormal. Latencies between 8 and 40 min are of unknown significance.

5. ACTIGRAPHY

Actigraphy is an ambulatory study that uses a small portable digital device, the actigraph, to record body movements of a subject during long periods of time, typically days, and, thus, enabling the assessment, by inference, of the subject's rest–activity cycle. The device is usually worn on the wrist, but may be worn on the trunk or ankle. The actigraph uses accelerometers to detect movement, which is sampled multiple times per second, averaged in epochs of 30 s or 1 min, and stored on the device for downloading at the end of the interval studied. A computer analysis of the data produces a histogram that demonstrates the activity level over successive 24-h periods. Other indices, such as sleep latency may be derived from this data. Actigraphy is best used with a sleep diary. Recording of sleep–wake behaviors with either a careful sleep log, or actigraphy is now required in the diagnostic criteria of the circadian rhythm disorders. Actigraphy is useful before the MSLT to document the preceding sleep–wake patterns. This avoids studying the patient under conditions of sleep deprivation or disturbed circadian phase. The technique is deemed a reliable method for detecting sleep in normal populations. However, using movement as a measure of wakefulness may not be reliable in patients with movement disorders. Nonetheless, the technique has been modified for use in detecting periodic leg movements in research applications.

6. CLINICAL APPLICATION OF TESTING

The sleep disorders described next are those that are particularly well-suited for polysomnographic analysis. The revised ICSD, Diagnostic and Coding Manual *(5)* establishes both clinical and

polysomnographic criteria for the diagnosis of sleep disorders, which are abstracted in Tables 7 to 11. As noted in Subheading 4., the AASM approved indications for polysomnography include:

1. Suspicion of sleep-related breathing disorders.
2. Treatment and follow up of sleep-related breathing disorders.
3. In combination with the MSLT for suspected narcolepsy.
4. Evaluation of sleep-related behaviors that are violent, potentially injurious, or do not respond to conventional therapy.
5. To assist in the diagnosis of paroxysmal arousals that are suggestive of seizure disorder (with additional video and EEG).
6. Evaluation of sleep-related movement disorders.

Even if polysomnographic analysis is not specifically required in the assessment of a sleep complaint, clinicians often find that the judicious use of polysomnography may be remarkably revealing. For example, although the diagnoses of the various insomnias do not include the requirement of a PSG, polysomnographic study may reveal subtle sleep-disordered breathing, leg movements inducing arousal, or show that no objective impairment of sleep correlates with the patient's subjective report.

6.1. Sleep-Related Breathing Disorders

Sleep-related breathing disorders are disorders in which respiration is abnormal during sleep. The PSG is a necessary test in the diagnosis and management of these disorders.

Disorders in this classification include central sleep apnea, OSA, and sleep-related hypoventilation syndromes.

Patients with sleep-related breathing disorders may present with a wide variety of complaints, including daytime sleepiness, insomnia, inattentiveness, cognitive decline, loud snoring, nocturnal gasping, witnessed apneas, nocturnal chest pain, nonrestorative sleep, and morning headaches. Nocturnal hypoxia exacerbates ischemic heart disease and promotes the development of pulmonary hypertension. OSA is known to be associated with excessive daytime sleepiness and the development of hypertension. Associations with insulin resistance, nocturnal arrhythmia, stroke, myocardial infarction, insomnia, and mood disorders are likely.

Central sleep apnea syndromes (Table 7) are characterized by episodes of decreased respiratory effort that are either cyclic or intermittent (Fig. 10). OSA syndromes (Table 8) are characterized by airway obstruction with persistent respiratory effort (Fig. 9). Lastly, sleep-related hypoventilation syndromes (Table 9) include a variety of disorders, either primary idiopathic or secondary to other medical conditions, that result in sleep-induced or sleep-exacerbated hypercapnia and hypoxia. These abnormalities are quantified using the respiratory monitoring techniques described in Subheading 4.1.

The PSG in each of these disorders is distinctive (Tables 7–9), but some abnormalities are common to this group of disorders. Abnormal respiratory events of any type tend to fragment sleep. Polysomnographic evidence of sleep fragmentation includes increased stage 1 sleep, delayed REM latency, decreased REM and stages 3 and 4 sleep, increased arousals, increased awakenings, and decreased sleep efficiency. Sleep latency may be prolonged.

Polysomnography is also an important tool in treatment of sleep-related breathing disorders. Positive pressure applied as either constant positive airway pressure or bi-level positive airway pressure is the mainstay of treatment for obstructive and some central apneas. The appropriate at-home pressures are determined through the process of "titration" in the sleep laboratory, in which pressures are gradually adjusted during the course of the night to eliminate apneas, hypopneas,

desaturations, and arousals. Supplemental oxygen is also frequently applied, and the effects monitored, during therapeutic PSGs with and without positive pressure, especially in patients with central sleep apnea or hypoventilation syndromes. Automatic titrating machines for at home use are available but have generally not replaced in-laboratory positive pressure titration.

6.2. Hypersomnias of Central Origin

Hypersomnias of central origin refer to a group of disorders that result in excessive daytime sleepiness but are not caused by disturbed nocturnal sleep or disorders of circadian rhythms. Excessive daytime sleepiness is defined as "the inability to stay awake and alert during the major waking episodes of the day, resulting in unintended lapses into drowsiness or sleep." Patients with these disorders may or may not demonstrate excessive sleep during a 24-h period. Diagnostic and Clinical Criteria of the ICSD for narcolepsy and idiopathic hypersomnia are outlined in Table 10. For the rarer disorders in this category, the reader is referred to the ICSD-2 *(2)*.

6.2.1. Narcolepsy

The most important and common disorder in this category is narcolepsy, with a prevalence of 0.02 to 0.18% in the United States. Narcolepsy is now classified as narcolepsy with cataplexy, narcolepsy without cataplexy, and narcolepsy secondary to medical condition. The last is extremely rare. Cataplexy refers to episodes of muscle weakness associated with strong emotion, often laughter. These episodes are typically brief, often involve the knees and/or face, and are unassociated with a change of consciousness, although sleep sometimes follows immediately. Cataplexy is pathognomonic of narcolepsy, but need not be present. Other common features of narcolepsy include hallucinations at sleep onset (hypnagogic hallucinations), sleep paralysis, inattentive "automatic behavior," and poorly maintained nocturnal sleep. Most of the characteristic symptoms of the disorder seem to reflect a disorder of the control mechanisms that regulate REM sleep. Episodes of REM occur at the wrong time, intruding on wakefulness, and the physiological components of REM sleep dissociate and appear independently. Cataplexy and sleep paralysis, for example, are manifestations of the muscle atonia of REM sleep appearing during wakefulness. Recent discoveries suggest that narcolepsy is caused by the loss of hypothalamic neurons containing the neuropeptide, hypocretin-1. In the past, neurophysiological testing with both the PSG and MSLT provided the only confirmatory evidence for the diagnosis of narcolepsy with and without cataplexy. New diagnostic guidelines include the option of obtaining cerebrospinal fluid levels of hypocretin-1, an assay that can be obtained by sending the sample to specialized centers. Approximately 90% of patients who demonstrate cataplexy have low hypocretin levels, whereas only 10 to 20% of patients classified as having narcolepsy without cataplexy show low hypocretin levels. Narcolepsy with cataplexy is highly associated with HLA subtype DQB1*0602, but because 12 to 38% of controls are positive for this antigen, HLA typing is not used as a diagnostic criterion. Narcolepsy without cataplexy has a less strong association with DQB1*0602. Many patients who carry the diagnosis of narcolepsy without cataplexy are likely to have been misdiagnosed and have another sleep disorder. The MSLT is a study that requires close attention to procedural detail and patient preparation, as described in Subheading 4.2. Improper administration of the MSLT results in both false-positive and false-negative results. The highest specificity (99.2%) and positive predictive value (87%) for MSLT findings are with the criteria of three or more sleep-onset REM periods combined with a mean sleep latency of less than 5 min *(13)*. Narcolepsy caused by medical condition, also referred to as symptomatic narcolepsy or secondary narcolepsy, is usually

associated with pathology of the hypothalamus and may also result in low hypocretin levels. Although this presentation is rare, a variety of disease processes have been identified in these patients, including tumors, cerebral infarct, sarcoidosis, Niemann-Pick type C, multiple sclerosis, disseminated encephalomyelitis, and paraneoplastic syndromes.

6.2.2. Idiopathic Hypersomnia

If no other condition can be identified that explains excessive daytime sleepiness, the diagnosis "idiopathic hypersomnia" is applied. Polysomnographic studies as well as a careful medical neurological and psychiatric assessment are particularly important in these disorders to exclude subtle or occult abnormalities. Brain MRI is appropriate. The ICSD-2 now classifies these patients as idiopathic hypersomnia with prolonged sleep time, and idiopathic hypersomnia without prolonged sleep time. When subjected to detailed study using the more-sensitive measures of respiratory effort noted in Subheading 4.1.2., many patients who carry this diagnosis are identified as having RERAs, indicative of a sleep-related breathing disorder.

6.3. Parasomnias

The term parasomnia refers to undesirable events that occur during sleep, sleep onset, or on arousal from sleep. Parasomnias often include complex behaviors. Although the behaviors may seem to be goal directed, they are not under conscious control. These disorders typically are sleep-stage specific. The classification includes:

1. Disorders of arousal (from NREM sleep).
2. Parasomnias usually associated with REM sleep.
3. Other parasomnias.

By ICSD-2 standards, polysomnographic analysis is required only for the diagnosis of REM behavior disorder. In practice, however, polysomnographic analysis is extremely useful both to document the disorders and, more importantly, to identify other sleep disorders that may act as precipitants to arousal and subsequent behavioral manifestations.

6.3.1. REM Behavior Disorder

REM behavior disorder (Table 11) is characterized by abnormal behaviors that emerge during REM sleep. The typical complaints are violent thrashing, hitting, or yelling, accompanied by nightmares. The disorder is more common in men older than 50 yr. Polysomnographic study shows that the behavioral outbursts are associated with the intermittent loss of the muscle atonia that normally characterizes the REM sleep state (Fig. 14). If awoken spontaneously or by others during the episode, patients are often, but not always, able to correlate the actions to dream mentation. The disorder is highly correlated with parkinsonian states, including Parkinson disease, dementia with Lewy bodies, and multisystem atrophy. The disorder can emerge years before these diagnoses are clinically apparent, but idiopathic and drug-induced REM behavior disorder presentations are also recognized.

6.3.2. Disorders of Arousal (From NREM Sleep)

Disorders of arousal from NREM sleep (Table 11) include sleep terrors, sleepwalking, and confusional arousals. These disorders are characterized by confusion and automatic behavior after sudden arousal from NREM, usually stages 3 or 4 sleep (slow-wave sleep) (Fig. 15). As a result, symptoms tend to occur early in the night, when slow-wave sleep is prominent. Patients may sit bolt upright with a blood-curdling scream and autonomic activation (sleep terror),

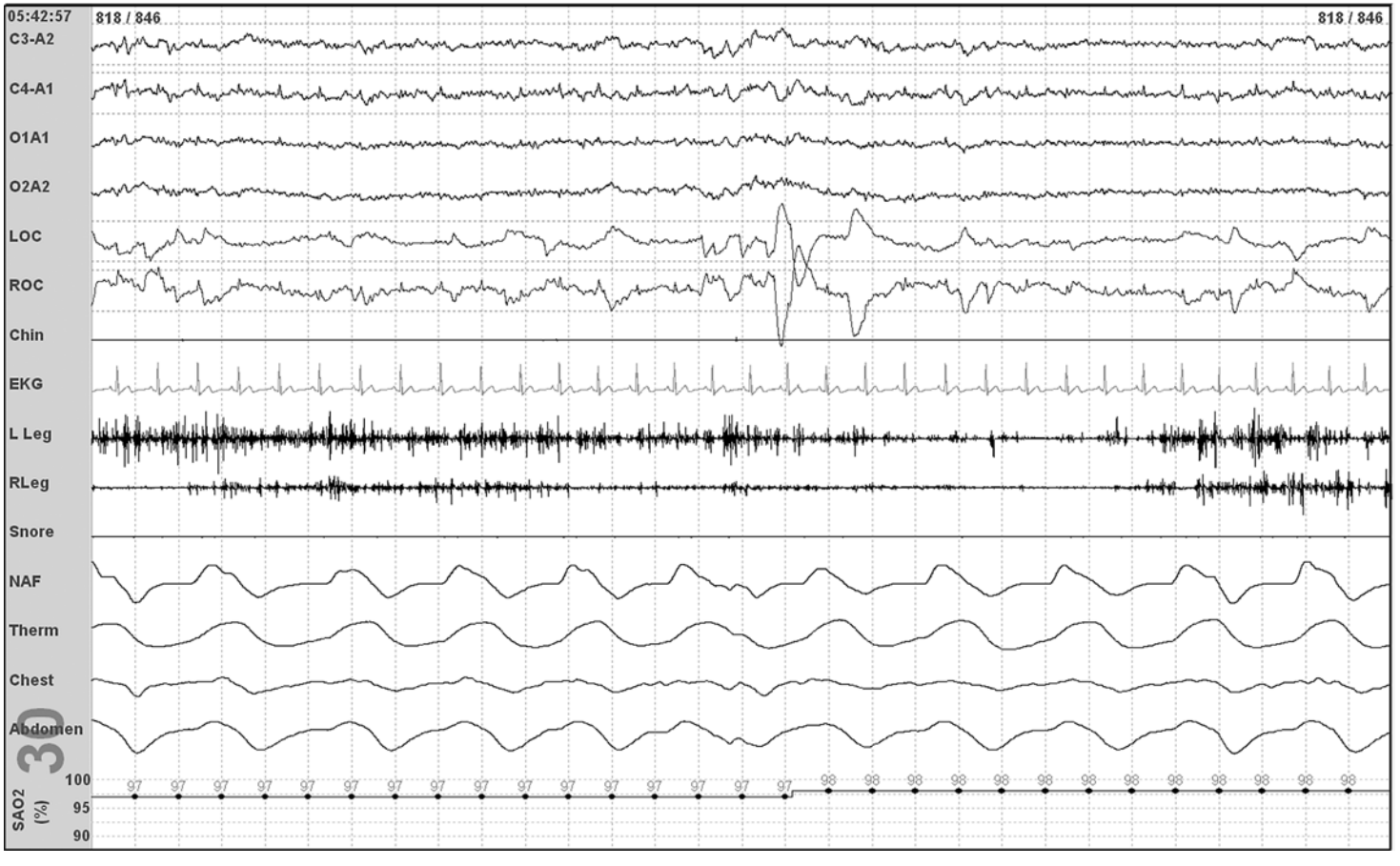

Fig. 14. Rapid eye movement (REM) behavior disorder. In this epoch, during REM there is a loss of the usual REM atonia. Excessive motor activity is captured in the leg EMG leads. The chin EMG tone remains atonic, as expected in REM. The elevation in motor tone associated with this disorder is rarely generalized. (30-s epoch)

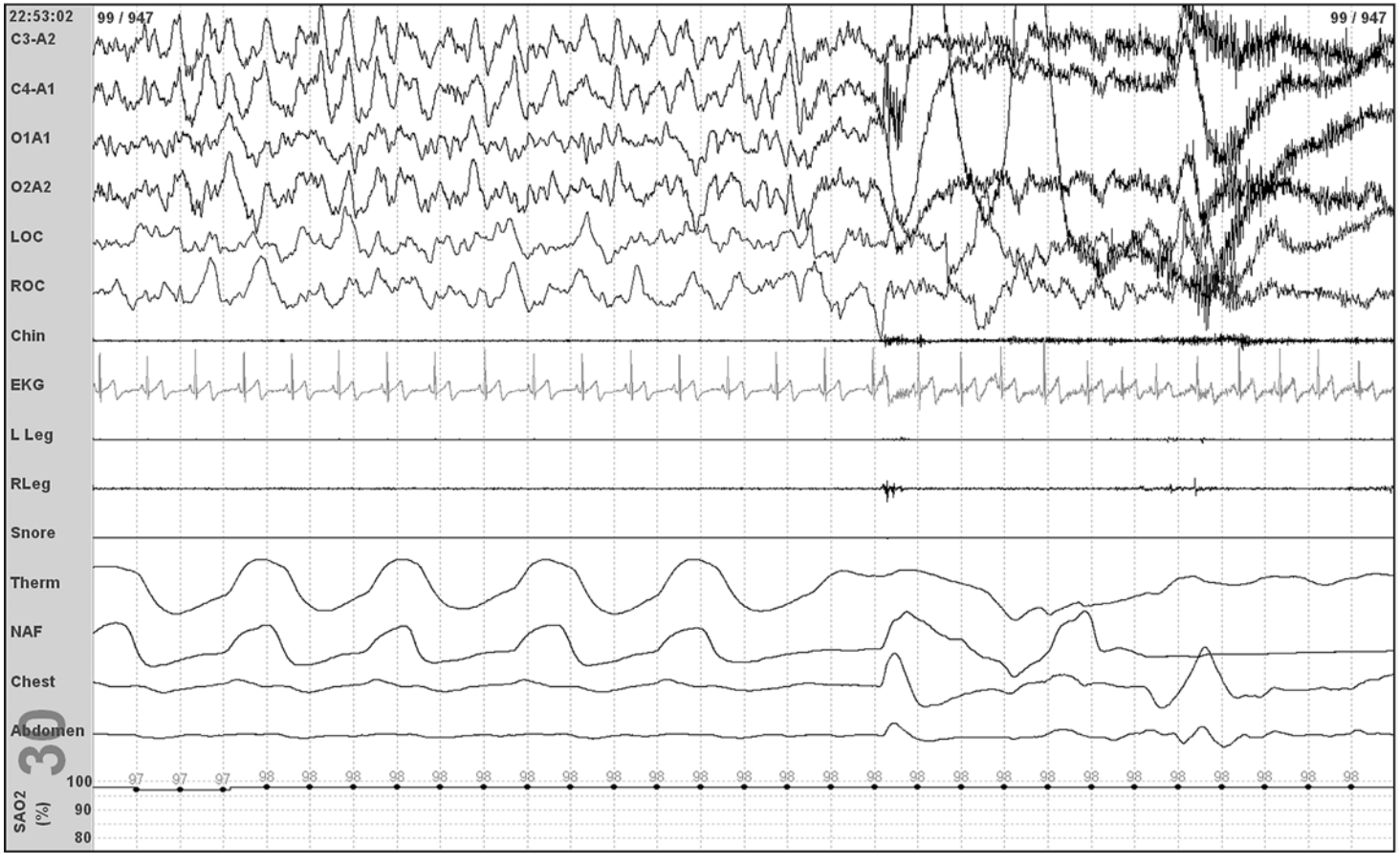

Fig. 15. Arousal from delta sleep. A sudden unprovoked arousal occurs from hypersynchronous delta sleep.

engage in complex acts (sleep walking), or arouse in a confused state (confusional arousal). Patients are difficult to fully awaken and are mostly amnestic for the episode. The tendency to arouse spontaneously from delta sleep tends to be a familial trait, with first presentation in childhood and resolution by adolescence. Stress, sleep deprivation, or any factors that contribute to sleep disruption, such as sleep-disordered breathing, are exacerbants that may result in the re-emergence of the behavioral syndrome in adulthood. Polysomnographic study may demonstrate the typical behaviors emerging from slow-wave sleep, sudden unexplained arousals from slow-wave sleep, or an underlying cause of arousal, such as sleep-disordered breathing or leg movements.

6.4. Sleep-Related Movement Disorders

Sleep-related movement disorders include conditions in which simple stereotyped movements are present during sleep and induce sleep disruption. Difficulty initiating and/or maintaining sleep are the typical complaints.

6.4.1. Periodic Limb Movement Disorder

The most prevalent of these disorders is PLMD. PLMD (Table 12) is characterized by periods of repetitive stereotyped leg movements that disturb sleep (PLMS) (Fig. 13). The leg movements are similar to the triple flexion response of the Babinski reflex, but arm movements may also occur. Other types of leg movements may be present without periodicity, or without sleep disruption, or may be secondary to other primary sleep disorders, in which case, the term PLMS is not appropriate. Leg movements, for example, frequently accompany arousals from sleep-disordered breathing. Many medications are implicated in the induction of periodic and aperiodic leg movements, most commonly selective serotonin reuptake inhibitors and tricyclic antidepressants.

6.4.2. Restless Legs Syndrome

RLS (Table 12) is a disorder characterized by an urge to move accompanied by uncomfortable sensations, predominantly in the legs, that are relieved by movement, occur when sedentary, and are worse in the evening *(14)*. This syndrome is closely associated with PLMD because 80 to 90% of patients with this disorder have PLMS. Some of these patients also demonstrate periodic limb movements while awake. RLS, however, is a syndrome based on clinical, not polysomnographic criteria. The disorder is familial in 50% of cases. Abnormalities of both dopamine and iron metabolism are implicated in the underlying pathophysiology. In patients with RLS, PET studies have shown decreased dopamine D2 binding and decreased dopamine storage in striatum. It has been postulated that brain iron deficiency underlies dopamine dysfunction in this disorder. Recent postmortem evidence suggests a deficiency of iron acquisition in the substantia nigra of patients with RLS. Iron deficiency is known to exacerbate or precipitate restless legs and periodic leg movements in familial and nonfamilial cases. Increasing iron stores by long-term iron supplementation is often therapeutic even in patients with low normal ferritin levels (less than 50). Dopaminergic agonists are highly successful treatments. Iron and dopamine may be functionally linked by the fact that tyrosine hydroxylase is a cofactor in dopamine metabolism. Secondary causes of RLS are subject to some debate because of limited data, and include uremia, neuropathy, medications (especially antidopaminergic drugs and selective serotonin reuptake inhibitors), and caffeine.

Table 12
Periodic Limb Movement Disorder and Restless Legs Syndrome

Disorder	*Clinical criteria*	*Polysomnographic criteria*	*Other requirements*	*Other features*
Periodic limb movement disorder	There is a clinical sleep disturbance or a complaint of daytime fatigue.	PSG: Stereotyped limb movements during sleep (PLMS) that are: • 0.5–5 s in duration • Of amplitude ≥25% of toe dorsiflexion during calibration • In a sequence of 4 or more movements • Separated by an interval of >5 s and <90 s PLMS index (events/hour of sleep) exceeds 15/h in adults, 5/h in children	PLMS are not better explained by another current sleep disorder, medical or neurological disorder, mental disorder, medication use, or substance use disorder.	If PLMS are present without sleep disturbance, the finding can be noted as a polysomnographic finding, but criteria are are not met for a diagnosis of PLMD PLMS are found in a variety of other sleep disorders, including narcolepsy, RBD and RLS. The term PLMD should not be used when diagnostic criteria for these disorders are fulfilled. Screen for low serum ferritin, neuropathy, and renal disease Leg movements decrease with low-dose dopaminergic agonists

(Continued)

Table 12 ***(Continued)***

Disorder	*Clinical criteria*	*Polysomnographic criteria*	*Other requirements*	*Other features*
Restless legs syndrome	The patient reports an urge to move the legs, usually accompanied or caused by uncomfortable and unpleasant sensations in the legs. The urge to move or the unpleasant sensations begin or worsen during periods of rest or inactivity, such as lying or sitting. The urge to move or the unpleasant sensations are partially or totally relieved by movement, such as walking or stretching. The urge to move or the unpleasant sensations are worse, or only occur, in the evening or night.	None PLMS occur in 80–90% of patients PLMW may be present	The disorder is not better explained by another current sleep disorder, another medical or neurological disorder, mental disorder, medication use, or substance use disorder.	Often familial Screen for low serum ferritin, neuropathy, and renal disease Symptoms improve with low-dose dopaminergic agonists.

PLMD, periodic limb movement disorder; RBD, REM behavior disorder; REM, rapid eye movement sleep; RLS, restless legs syndrome; PLMW, periodic leg movements during wakefulness.

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REVIEW QUESTIONS

1. Polysomnography:
   A. Is routinely performed in an ambulatory setting; only very sick, unstable patients require close monitoring in a laboratory.
   B. Is not required for the diagnosis of restless legs syndrome.
   C. Is essential for the diagnosis of insomnia.
   D. Is indicated only for the diagnosis of sleep apnea.
2. Stage 2 sleep is defined by the presence of:
   A. K-complexes or spindles of at least 0.5 s in duration in the absence of sufficient slow wave acitivity to define the presence of stages 3 and 4 sleep.
   B. Saw tooth waves.
   C. Absence of alpha activity for 50% of the epoch.
   D. K-complexes of at least 75 microvolts in amplitude.
3. Stage 1 sleep is characterized by all of the following except:
   A. Occasional vertex waves of less than 0.5 s.
   B. An epoch with less than 50% alpha activity.
   C. Slow rolling eye movements.
   D. Spindles lasting 0.5 s or more.
4. Stage 3 sleep is defined by epochs (30 s) with:
   A. Not more than 50%, but greater than or equal to 20% slow activity of 3 Hz or less with an amplitude of 75 μV.
   B. Not more than 50% but greater than or equal to 20% slow wave activity of 2 Hz or less with no amplitude criterion.
   C. Not more than 50% but greater than or equal to 20% slow wave activity of 2 Hz or less with an amplitude of >75 μV.
   D. At least 50% high-voltage slow activity of at least 2 Hz with an amplitude of 75 μV.
5. Scoring REM sleep requires:
   A. Saw tooth waves.
   B. EEG with an at least 8-channel montage.
   C. EMG of chin, eye movement recording (EOG), and EEG with central leads.
   D. EMG of both chin and anterior tibialis muscles.
   E. Phasic changes in respiration.
6. Current Center for Medicare and Medicaid Services (CMS) guidelines define hypopnea as:
   A. Any decrease in airflow.
   B. Any decrease in airflow or thoracoabdominal movement with an arousal or oxygen desaturation.
   C. 30% Decrease in airflow with 4% oxygen desaturation or an arousal.
   D. 30% Decrease in airflow or thoracoabdominal movement with at least 4% desaturation.
7. A mixed apnea is defined as:
   A. Absence of airflow for 10 s without any other criterion.
   B. Absence of airflow for 10 s with decreased but persistent respiratory effort on thoracoabdominal monitors throughout the event.
   C. Absence of airflow for less than 10 s with or without respiratory effort.
   D. Absence of airflow for 10 s with initial absence of respiratory effort followed by resumption of respiratory effort before airflow resumes.
8. Proper administration of a multiple sleep latency test (MSLT):
   A. Involves a patient sitting up in a minimally lit room to stay awake during the testing.
   B. Requires discontinuation of all drugs that affect sleep for a period of 15 days, or for a period of at least 5 times the half life of the drug and its longest acting metabolite.
   C. Consists of a neurophysiological recording during two 20-min long nap opportunities, typically scheduled on the afternoon preceding a whole-night PSG.
   D. Requires a minimum of 6 h of sleep deprivation on the night before testing.

9. A periodic leg movement sequence is scored when:
   A. There is any repetitive EMG activity in the anterior tibialis muscle of 0.5–5 s in duration, with an amplitude of at least 25% of the calibration EMG activity.
   B. There is a series of leg movements lasting at least 90 s, with an amplitude of 25% of the calibration EMG.
   C. Synchronous repetitive contractions of agonist and antagonist leg muscles are noted while awake or asleep.
   D. There is a series of 4 or more bursts of anterior tibialis EMG activity, each of 0.5–5 s in duration, with an amplitude of 25% of the calibration EMG, separated by more than 5 and less than 90 s.
10. Growth hormone secretion is associated with:
   A. The onset of REM.
   B. Stage one sleep.
   C. Arousal from slow-wave sleep.
   D. Slow wave sleep.
11. In a patient with excessive daytime sleepiness and equivocal cataplexy, a diagnosis of narcolepsy with cataplexy may be confirmed with which of the following:
   A. CSF fluid hypocretin measurements.
   B. MSLT alone.
   C. PSG showing no other sleep disorder accounting for sleepiness.
   D. PSG showing no other sleep disorder and MSLT showing sleep onset REM in any one of 5 naps and mean latency of at most 8 min.
12. Which of the following is not required for the diagnosis of restless legs syndrome:
   A. The patient reports the urge to move the legs accompanied by unpleasant sensations.
   B. Symptoms are precipitated by rest and relieved by activity.
   C. Symptoms are worse in the evening or night.
   D. Periodic limb movements are demonstrated on PSG.
13. By current guidelines, Medicare will approve treatment of obstructive sleep apnea with positive pressure in which of the following situations:
   A. Respiratory disturbance index of 15 or greater.
   B. Apnea hypopnea index of 15 or greater.
   C. Apnea hypopnea index of 15, only when there is an associated lowest oxygen desaturation to 88%.
   D. Apnea hypopnea index of 15, only if there are associated clinical symptoms.
14. The term "Disorder of Arousal" refers to:
   A. Any disorder that results in frequent arousals from sleep.
   B. A disorder characterized by abnormal tone during REM sleep.
   C. A disorder characterized by sudden arousal from NREM, usually slow wave sleep.
   D. A disorder characterized by marked difficulty waking after a normal sleep period.
15. REM behavior disorder is characterized by all of the following except:
   A. Often precedes the onset of parkinsonian disorders.
   B. Lack of the usual atonia during REM sleep.
   C. Violent and potentially self-injurious behaviors.
   D. Patients are typically amnestic for the behaviors.
16. Which of the following is not an effect of aging on sleep architecture:
   A. A reduction in slow wave sleep.
   B. A reduction in the percentage of REM sleep.
   C. A reduction in total sleep time.
   D. An increase in arousals.
17. What is the utility of the maintenance of wakefulness test (MWT)?
   A. It is used to diagnose narcolepsy.
   B. It measures both the ability to fall asleep and to stay awake in a controlled environment.
   C. It is a measure of the ability to stay awake in the provided testing conditions.
   D. It predicts the risk of an accident due to inappropriate episodes of sleep in the real world.

18. Restless leg syndrome responds to:
    A. Treatment with selective SSRIs.
    B. Treatment with dopaminergic antagonists.
    C. Treatment with dopaminergic agonists.
    D. No effective treatment is available.
19. The diagnosis of obstructive sleep apnea:
    A. Always requires the presence of obstructive apneas.
    B. Always is associated with significant oxygen desaturation.
    C. Requires that the patient demonstrate excessive daytime sleepiness.
    D. May be made in the absence of clinical criteria if the polysomnogram shows at least 15 obstructive events an hour including RERAs, hypopneas, and apneas.
20. A RERA (respiratory effort related arousal) is:
    A. Associated with increased negative intrathoracic pressure.
    B. Is obvious on chest and abdomen effort bands.
    C. Is typically associated with oxygen desaturation.
    D. Is never a major cause of sleep disruption.

REVIEW ANSWERS

1. B. Polysomnography is not required to establish a diagnosis of restless legs syndrome. The diagnosis of restless legs is made based on four essential criteria including: (1) an urge to move accompanied by uncomfortable sensations, predominantly in the legs that are (2) relieved by movement, (3) occur when sedentary and (4) are worse in the evening.
2. A. Stage 2 is defined by the presence of sleep spindles (≥0.5 sec) and/or K complexes (≥0.5sec) in the absence of sufficient slow activity to define stages 3 or 4 sleep.
3. B. The transition from drowsiness to stage 1 is characterized by slowing of the EEG. As this transition occurs, when less than 50% or a 30 second epoch demonstrates alpha activity, the epoch is scored stage 1. Slow rolling eye movements typically herald and occur during stage one sleep, but are not required for scoring.
4. C. The definition of Stage 3 is based on EEG frequency, amplitude, and epoch composition of delta activity. The delta activity required for stage 3 is <2 Hz, >75μV, and ≥20% but ≤50% of the epoch.
5. C. REM sleep is defined by low amplitude, asynchronous frequency EEG activity, REMs, in combination with the lowest tonic submental EMG level during sleep (usually atonia). Saw tooth waves are frequently present but are neither sufficient nor necessary for scoring REM.
6. D. Medicare (CMS) adopted the hypopnea definition used in the Sleep Heart Health Study an on-going large-scale epidemiologic study of sleep-disordered breathing. This definition does not include any measure of sleep disturbance.
7. D A mixed apnea is so called because of the presence of both central and obstructive features. The event begins with absence of respiratory effort and airflow. When respiratory effort resumes, airflow does not resume simultaneously because of obstruction of the airway. The total duration of absence of airflow is 10 s.
8. B. Medications that affect sleep architecture distort the findings on the MSLT by influencing both sleep latency and the presence of REM sleep. The current recommendation of the ICSD-2 is that prior to the administration of the MSLT the patient should be free of medications that influence sleep for 15 days, or at least five times the half- life of the drug and its longest metabolites. Rapid withdrawal of REM- influencing drugs may induce REM rebound and false positives. REM- inhibiting drugs produce false negative studies. Often, a meaningful MSLT cannot be obtained because the patient's underlying disorders do not allow for medication withdrawal.
9. D. Leg movements fulfilling the described requirements are necessary for the diagnosis of PLMD. Most adult patients demonstrate an index of greater than 15 leg movements per hour.
10. D. Maximal growth hormone release occurs within minutes of the onset of slow wave sleep.

11. A. Cerebrospinal hypocretin-1 <110 pg/ml or less than 1/3 normal control values is found in 90% of patients with narcolepsy with cataplexy and almost never in controls or other patients. The test may be useful when REM suppressant medications cannot be discontinued or when an MSLT is difficult to interpret. The test is not influenced by concurrent sleep disorders and psychotropic medications/substances.
12. D. Restless legs syndrome is a clinical diagnosis based on symptoms alone (*see* Question 1.) The disorder usually associated with PLMD, but periodic limb movements are not required to confirm the diagnosis of restless legs syndrome.
13. B. Medicare and other insurance carries adhering to Centers for Medicare and Medicaid Services (CMS) coverage criteria will approve treatment for obstructive sleep apnea if the AHI ≥15 in an asymptomatic patient or ≥5 with a history of any one or more of the following: excessive daytime sleepiness, impaired cognition, mood disorders or insomnia, or documented hypertension, ischemic heart disease, or history of stroke.
14. C. These non-REM parasomnias most often arise from slow wave sleep and are therefore occur more often during the first third of the night. A family history disorders of arousal is common and provocative factors include sleep deprivation, stress, medications, alcohol, caffeine and other sleep disorders that increase the probability of arousal such as sleep-related breathing disorders or PLMD.
15. D Patients with REM behavior disorder often report detailed dream activity consistent with observed dream-enacting behaviors. On the other hand, patients with non-REM parasomnias are typically amnestic for the demonstrated behaviors.
16. B. Under normal circumstances, the percentage of REM sleep in an older individual is similar to that of a younger adult. Slow wave sleep (stages 3 and 4 sleep) and total sleep time decrease with age. Arousals and sleep fragmentation increase with age.
17. C. The maintenance of wakefulness test (MWT) was designed to assess an individual's ability to resist sleep in a standardized, non-stimulating environment. The test has received criticism due to a lack of recreating realistic circumstances. Nonetheless, the MWT is often utilized to assess therapeutic response of a sleep disorder to treatment, and to evaluate an individual's ability to stay awake when impaired alertness poses a safety hazard.
18. C. Dopaminergic agonists are an effective treatment for RLS. Dopaminergic antagonists and SSRIs can exacerbate RLS.
19. D. Obstructive sleep apnea syndrome describes a spectrum of sleep related breathing disorders characterized by an absence or reduction in airflow despite continued respiratory effort. Some advocate that a response to CPAP aids in the diagnosis and others adhere to CMS guidelines as the definition. According to the AASM, OSA exists when 5 or more obstructive respiratory events are accompanied with a clinical presentation. Variation in recording methods of respiratory parameters exists and therefore a variation in diagnostic sensitivities continues to exist.
20. A. A RERA is characterized a sequence of increasing effort and/or breathing, not meeting the definition for an apnea or hypopnea, and terminating with an arousal.

REFERENCES

1. Loomis AL, Harvey EN, Hobart G. Cerebral states during sleep, as studied by human brain potentials. J Exp Psychol 1937;21:127–144.
2. Aserinsky E, Kleitman N. Regularly occurring periods of eye motility, and concomitant phenomena, during sleep. Science 1953;118:273–274.
3. Dement W, Kleitman N. Cyclic variations in EEG during sleep and their relation to eye movements, body motility, and dreaming. Electroencephalogr Clin Neurophysiol Suppl 1957;9:673–690.
4. Rechtschaffen AKA. A Manual Standardized Terminology: Techniques and Scoring System for Sleep Stages of Human Subjects. Los Angeles: UCLA Brain Information Service/Brain Research Institute, 1968.
5. The International Classification of Sleep Disorders: Diagnostic & Coding Manual, ICSD-2. Westchester, IL: American Academy of Sleep Medicine, 2005.

6. Espana RA, Scammell TE. Sleep neurobiology for the clinician. Sleep 2004;27:811–820.
7. Kushida CA, Littner MR, et al. Practice parameters for the indications for polysomnography and related procedures: an update for 2005. Sleep 28(4):499–521.
8. EEG arousals: scoring rules and examples: a preliminary report from the Sleep Disorders Atlas Task Force of the American Sleep Disorders Association. Sleep 1992;15:173–184.
9. Meoli AL, Casey KR, Clark RW, et al. Hypopnea in sleep-disordered breathing in adults. Sleep 2001;24:469–470.
10. Recording the scoring leg movements. The Atlas Task Force. Sleep 1993;16:748–759.
11. Littner MR, Kushida C, Wise M, et al. Practice parameters for clinical use of the multiple sleep latency test and the maintenance of wakefulness test. Sleep 2005;28:113–121.
12. Arand D, Bonnet M, Hurwitz T, Mitler M, Rosa R, Sangal RB. The clinical use of the MSLT and MWT. Sleep 2005;28:123–144.
13. Aldrich MS, Chervin, RD, Malow BA. Value of the multiple sleep latency test (MSLT) for the diagnosis of narcolepsy. Sleep 1997;20:620–629.
14. Allen RP, Picchietti D, Hening WA, Tenkwalder C, Walters AS, Montplaisi J. Restless legs syndrome: diagnostic criteria, special considerations, and epidemiology. A report from the restless legs syndrome diagnosis and epidemiology workshop at the National Institutes of Health. Sleep Med 2003;4:101–119.
15. Kryger MH, Roth T, Dement WC. Principles and practice of sleep medicine. Philadelphia, PA: Elsevier/Saunders, 2005:xxxiii.
16. Williams RL, Karacan I, Hursch CJ. Electroencephalography (EEG) of human sleep: clinical applications. New York, Wiley, NY, 1974:xiv.
17. Kales A, Kales JD. Sleep disorders. Recent findings in the diagnosis and treatment of disturbed sleep. NEJM 1974;290:487–499.