QUESTIONS

A 20-Year-Old Student Pulling an All-Nighter

A 20-year-old student with asthma is cramming for a final exam he will take the next morning. He has studied the entire day and now has decided to study through the night. He becomes extremely sleepy at 4 AM and has two cups of strong coffee.

1. Which neurologic structure is primarily involved in maintaining his alertness?
   A. Ascending reticular activating system
   B. Hypothalamus
   C. Pineal gland
   D. Ventrolateral preoptic (VLPO) nuclei

2. The brain localization for structures that keeps him awake is located in the
   A. Medullary bulb
   B. Midbrain
   C. Pons
   D. Entire brainstem

3. Which of the neurotransmitters below is focused on sleep promotion (as opposed to wakefulness)?
   A. 5-Hydroxytryptamine (5-HT) from serotoninergic neurons in the dorsal raphe nucleus
   B. Acetylcholine from cholinergic neurons in pedunculopontine tegmental and laterodorsal tegmental nuclei
   C. Gamma-aminobutyric acid (GABA) and galanin (GAL) from the VLPO
   D. Norepinephrine from noradrenergic neurons of the ventrolateral medulla and locus coeruleus

4. Pathways of the arousal system reach the cerebral cortex through which neurologic structures?
   A. Cerebellum and pons
   B. Medulla and spinal cord
   C. Pons and medulla
   D. Thalamus, hypothalamus, and basal forebrain

5. Which chemical involved in hunger regulation also has input into the arousal system?
   A. Ghrelin
   B. Insulin
   C. Leptin
   D. Orexin (hypocretin)

6. Which chemical is accumulating in his central nervous system (CNS) to cause sleepiness before he drinks coffee?
   A. Adenosine
   B. Gamma-hydroxybutyric acid (GHB)
   C. Melatonin
   D. Serotonin
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7. He drank coffee for its stimulant effect; it works to increase wakefulness by binding to the receptors of which one of the following:
   A. Adenosine
   B. GHB
   C. Melatonin
   D. Serotonin

8. The student becomes jittery about 20 minutes after drinking the coffee and feels his heart beating rapidly. Assuming he is taking all of the following medications, which one is likely producing the tachycardia?
   A. Fluticasone
   B. Montelukast
   C. Prednisone
   D. Theophylline

Daydreamer

A 16-year-old straight-A high school student is referred for evaluation because she no longer focuses well in school. She is seen to “nod off” in class, and her grades have recently plummeted. You learn that she sleeps 8 hours per night but complains of “broken sleep.” She sometimes awakens in the middle of the night and then has trouble falling back to sleep. She has also noted a panicky feeling during nocturnal awakenings and states, “I feel someone is in the room, and I can’t move.” Further history reveals that she has recently started taking afternoon naps and dreams vividly while napping.

9. Her pediatrician believes that she is exhibiting symptoms of a neurologic disease, perhaps multiple sclerosis, and recommends a spinal tap. If a spinal tap were to be performed and the cerebrospinal fluid (CSF) were to be analyzed, what abnormality would likely be found?
   A. Elevated interleukin-6 (IL-6)
   B. Elevated nerve growth factor
   C. Reduced adenosine
   D. Reduced hypocretin

10. The patient’s unintended daytime sleep episodes are most likely caused by what abnormality?
    A. An underactive ascending reticular activating system
    B. Excessive CNS serotonin levels
    C. Loss of hypocretin neurons
    D. Overactive CNS GABA receptors

11. The patient’s episodes of awakening during the night, unable to move and sensing that someone is in the room, is characteristic of
    A. Posttraumatic stress disorder (PTSD)
    B. Psychomotor epilepsy
    C. Schizophrenic hallucination
    D. Sleep paralysis

12. What neurologic phenomenon is causing her inability to move when she awakens during the night?
    A. Abnormal discharge from the frontal cortex inhibiting the motor cortex
    B. Excessive adrenergic stimulation causing vasoconstriction of spinal arteries, resulting in ischemia of the spinal motor neurons
    C. Excessive stimulation of the ascending reticular activating system that thus inhibits the motor cortex
    D. Inhibition of motor neurons in the spine by both glycinergic and GABAergic mechanisms
Pandemic of Sleepiness

A 40-year-old patient with acute influenza is noted to have a severe cough and feels extremely sleepy whenever he is awake.

13. Which of the following phenomena is NOT causing sleepiness?
   A. Activation by cytokines of the acute phase response
   B. Viral encephalitis with influenza virus invading hypothalamic cells
   C. Viral ribonucleic acid (RNA) and protein that induces cytokine production within the hypothalamus
   D. Virus replicating in lung cells and inducing production of somnogenic cytokines

14. What is the effect of the infection on sleep architecture?
   A. Enhancement of NREM sleep and inhibition of REM sleep
   B. Increase in wakefulness with inability to consolidate sleep
   C. Marked increase in rapid eye movement (REM) sleep, leading to hallucinations
   D. No systematic effect on the relationship of REM to non-REM (NREM) sleep

15. Which infection-related cytokine/protein is NOT associated with sleepiness?
   A. Brain-derived neurotrophic factor and growth hormone–releasing factor
   B. IL-1β and IL-6
   C. Orexin (hypocretin) and leptin
   D. Tumor necrosis factor and nerve growth factor

16. What is the expected natural history of the sleepiness in this case?
   A. Sleepiness starts within hours of infection and lasts for days to weeks
   B. The sleepiness can become chronic because of damage to the hypothalamus, a condition known as encephalitis lethargica
   C. The sleepiness starts after the lung infection begins to resolve and can last months
   D. The sleepiness usually is present only during the prodromal phase

Potpourri

17. A friend likes to drink red wine up to 30 minutes before bedtime about 5 nights a week. He tells you that the wine has an effect on his sleep. Which of the following best describes alcohol’s effect when taken near bedtime?
   A. Bizarre dreams
   B. Decreased limb movements
   C. Increased REM sleep
   D. Reduced wake after sleep onset (WASO)

18. A waitress drinks three pots of coffee to stay alert and energized on her shift. The reason coffee helps her remain alert is because caffeine is a(n)
   A. Adenosine antagonist
   B. Serotonin antagonist
   C. Norepinephrine agonist
   D. Dopamine reuptake blocker

19. Caffeine has an approximate half-life of
   A. 15 to 30 minutes
   B. 1 to 2 hours
   C. 3 to 5 hours
   D. 6 to 8 hours
20. You are at a social gathering, where someone learns you are a sleep medicine specialist. He brags that he can drink four espresso drinks before bedtime without any effect on his sleep. You reply that caffeine
A. Has no effect on some people
B. Reduces REM sleep
C. Reduces stage N3 sleep
D. Will eventually cause insomnia

ANSWERS

1. A. Exams (self-assessment or board) often begin with an icebreaker, a question considered to be relatively easy. In this question, *ascending reticular activating system (ARAS)* should appear as the obvious answer. It is important to know the big picture about arousal and initiation of sleep. In 1935, Fredric Bremer, a pioneer in sleep research, showed that if a transection is made between the pons and midbrain of a cat (the preparation is called *cerveau isolé*, literally “isolated brain” in French), there is no arousal, and the animal is comatose. If a transection is made between the lower medulla and the spine, the cat is able to demonstrate wakefulness and sleep. This preparation is known as *l’encéphale isolé*. *L’encéphale* refers to all the nervous system structures in the cranial vault or skull. In 1949, Moruzzi and Magoun showed that stimulating the structures of the rostral pontine reticular formation (basically in the area between Bremer’s two transections) produced a desynchronized (or awake) electroencephalogram (EEG). This area of the brainstem became known as the *ascending reticular activating system*. (ATLAS2, Ch 3.1)

2. D. This question is a follow-up to the first one. The ARAS begins in the medulla and ascends into the pons and midbrain. This is a type of question in which “all of the above” is often correct. (ATLAS2, Ch 3.1)

3. C. There are so many chemicals and parts of the brain mentioned that it might make your eyes glaze over. It is desirable to know the sleep-promoting systems and the wakefulness-promoting systems; they are reviewed in the summary that follows. This type of question is relatively easy because you can often get the right answer by a process of elimination. When confronted with such a question, do not panic; look for terms you know and start from there. In this question, you need to know any component of the sleep switch (this includes the VLPO, whose cells contain the inhibitory neurotransmitters GABA and GAL), or you might have to generalize from information you learned from an entirely different topic. For example, you might have remembered that GABA has something to do with sleep from understanding hypnotics. You always know more than you think. (ATLAS2, Ch 3.1)

4. D. Again, analyze the question, and you will realize that only one of the answers has anything to do with pathways going into the cerebral cortex. There are two pathways of arousal into the cortex from the ARAS: a dorsal route via the thalamus (associated fact: site of spindle formation) and a ventral route via the *basal forebrain* and the *hypothalamus*. The basal forebrain is a ventral structure, and the hypothalamus is ventral and below the thalamus. The hypothalamus is right behind the optic chiasm (associated fact: the *suprachiasmatic nucleus*, the “conductor” of the circadian system “orchestra,” is here) and is above the pituitary gland. The hypothalamus secretes many endocrine-releasing factors, and because of its location and function, it links the endocrine and circadian systems. (ATLAS2, Ch 3.1)

5. D. All these chemical entities are involved in regulation of hunger or energy (or both). *Leptin*, secreted by fat cells, inhibits hunger. *Ghrelin*, produced by cells in the stomach, increases hunger. Insulin is produced in response to high glucose levels. *Orexin* (also called *hypocretin*) is produced by cells in the lateral and posterior hypothalamus and stimulates hunger and wakefulness. Two orexin neuropeptides, orexin A and B, promote arousal and stabilize wakefulness by their effect on the OX-1 and OX-2 receptors. Patients with narcolepsy have reduced orexin-producing cells and are sleepy as a result.
6. A. It is believed that adenosine, an inhibitory neurotransmitter, increases in the nervous system with prolonged wakefulness.

7. A. Caffeine, a xanthine, is a competitive inhibitor of adenosine because it is an antagonist of adenosine receptors in the nervous system. It has structural similarities to adenosine. The net result of blocking the effect of a compound that inhibits CNS function is to stimulate the CNS and promote wakefulness.

8. D. Theophylline is a xanthine sometimes used to treat asthma. It is one of the metabolites of caffeine. Both caffeine and theophylline can relax bronchial smooth muscle and increase cardiac contractility, heart rate, and blood pressure. Theophylline affects the nervous system through its action as an adenosine receptor antagonist.

9. D. From the description, this is most likely a case of narcolepsy. Each of the factors mentioned can promote sleepiness or sleep. Although rarely tested for clinical purposes, analysis of CSF in patients with narcolepsy has shown a striking reduction of hypocretin compared with controls.

10. C. The unintended transition from wakefulness to sleep is related to the fact that hypocretin neurons project widely in the cerebral cortex and stabilize wakefulness. The lack of these neurons results in wakefulness and sleep instability. (ATLAS2, Ch 3.1)

11. D. This is a classic description of sleep paralysis. The person awakens, usually from a dream, often with the perception that there is someone else in the room (sometimes a frightening devil-like creature). These events are likely the persistence of REM phenomena (dreaming and motor inhibition) persisting into wakefulness. (ATLAS2, Ch 7)

12. D. The motor weakness is related to the neurons of the sublaterodorsal (SLD) nucleus inhibiting motor spinal neurons by glycinergic and GABAergic mechanisms. (ATLAS2, Ch 3.1) Interestingly, the motor neurons projecting to the diaphragm are spared, and thus the motor atonia does not affect breathing.

13. B. The sleepiness seen with influenza is seldom caused by infection of cells in the nervous system but rather is brought on by the effect of cytokines that are a response to the infection. Cytokines are proteins and glycoproteins that behave like neurotransmitters and are commonly expressed during infections. The remaining three answers (B, C, and D) are mechanisms that likely do play a role in the sleepiness. (ATLAS2, Ch 3.5)

14. A. Infections typically increase NREM sleep (and can increase slow-wave sleep), and they reduce REM sleep. (ATLAS2, Ch 3.5)

15. C. This is the type of question in which you might not know much about the topic but can get the right answer from associated bits of knowledge. Orexin is not a cytokine, and leptin, which might be considered a cytokine, is produced by fat cells, and fat cells have nothing to do with infections. Thus, knowing either of these facts could help point to the correct answer. The other answers (B, C, and D) are cytokines that can be increased in infections. (ATLAS2, Ch 3.5)

16. A. The sleepiness can start abruptly with infections, sometimes within hours. It is related to cytokine production and will last a few days to a few weeks as the infection resolves. You might have read something about encephalitis lethargica in the distant past, and if so, you wonder whether it could be the correct answer. It is not. Encephalitis lethargica is an encephalitis that affects the junction of the posterior hypothalamus and the midbrain, producing severe hypersomnolence (hence the name von Economo sleeping sickness, after the neurologist Constantin von Economo, who described this illness in 1917). Encephalitis lethargica can also cause symptoms such as an inability to move or speak. Between 1915 and 1926, an epidemic of encephalitis lethargica spread around the world; there has been no epidemic of this disease since then, and the cause of the illness was never ascertained (autoimmune and infectious causes have been suggested but never proved). Most victims of encephalitis lethargica died in a coma. Some of the survivors entered into a rigid, Parkinson-like state. This clinical picture was eloquently described by the neurologist Oliver Sacks in his 1973 book *Awakenings* and was also portrayed in the 1990 movie of the same name starring Robin Williams. (ATLAS2, Ch 3.1, Fig. 3.1–2)
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17. A. Many drugs can trigger nightmares and bizarre dreams, including catecholaminergic agents, beta-blockers, antidepressants, barbiturates, and even alcohol. Alcohol is a known sleep disruptor; therefore, it does not reduce WASO or improve sleep consolidation. It is also not known to decrease periodic limb movements.

18. A. Adenosine is thought to be a sleep-inducing neurotransmitter that increases with increasing hours of wakefulness. The mechanism of action of caffeine on wakefulness involves nonspecific adenosine receptor antagonism. Caffeine is a xanthine derivative, which is known to be an A₁ receptor blocker.

19. C. Caffeine is a very rapidly absorbed drug with a half-life of 3.5 to 5 hours.

20. C. Caffeine is known to delay sleep onset and decrease stage N3 sleep. Caffeine has no known effect on REM sleep, and it can be the source of insomnia, but its effects are acute because the drug does not accumulate on a daily basis.

Summary

Highly Recommended

- Atlas of Clinical Sleep Medicine, ed 2, Chapter 3.1
- Principles and Practice of Pediatric Sleep Medicine, ed 2, Chapters 1 to 4 and 6

It is important to understand the structures and mechanisms involved in wakefulness and sleep. Because this topic will make up only about 10 of the 240 questions on the exam, do not spend excessive time reviewing esoteric neural mechanisms. However, the blueprint of the exam includes circadian timing in this section even though there is an entire section in the blueprint on circadian rhythm sleep-wake disorders. Thus, later on in this section, we cover the physiologic mechanisms of circadian rhythms with a series of bonus questions.

The topic of drug effects on sleep-wake mechanisms can come up in the therapy of many disorders (e.g., narcolepsy, restless legs, insomnia). Learn the key functions of neurotransmitters so you can predict their impact on sleep-wake functioning. Study the pharmacology of the various drug classes, paying attention to mechanism of action, indications, and impact on sleep parameters (e.g., sleep latency, WASO, REM, N3). It is important to know receptor physiology and the effect of medications on sleep.

Structures and Neurotransmitters Involved in Wakefulness

(ATALAS2, Chs 3.1 and 3.2)

- Noradrenergic (NE) neurons of the ventrolateral medulla and locus coeruleus (LC)
- Cholinergic neurons (ACh) in the pedunculopontine and laterodorsal tegmental (PPT/LDT) nuclei
- Serotoninergic neurons (5-HT) in the dorsal raphe nucleus (DR)
- Dopaminergic neurons (DAs) of the ventral periaqueductal gray matter (vPAG)
- Histaminergic neurons (His) of the tuberomammillary nucleus (TMN)
- Orexin neurons in the lateral hypothalamic help stabilize wakefulness and thus prevent unwanted wake-to-sleep transitions

The Two Pathways of Cortical Arousal (ATALAS2, Ch 3.1)

- Dorsal route, through the thalamus
- Ventral route, through the hypothalamus and basal forebrain (BF). The latter pathway receives inputs from the melanin and hypocretin (orexin)–concentrating (MHC) neurons of the lateral hypothalamic area (LH) as well as from GABAergic or cholinergic neurons of the BF
**Sleep Switch** (ATLAS2, Ch 3.1)
- The VLPO contains cells that contain the inhibitory neurotransmitters GABA and GAL
- The VLPO inhibits input into the components of the ARAS; in turn, the ARAS inhibits the VLPO

**REM Switch** (ATLAS2, Ch 3.1)
- REM-off neurons in the ventrolateral periaqueductal gray (vlPAG) area and lateral pontine tegmentum (LPT) receive inputs from the VLPO and orexin neurons
- REM-off neurons have a mutually inhibitory interaction with REM-on GABAergic neurons of the ventral sublaterodorsal nucleus (SLD) and the precoeruleus (PC)–parabrachial (PB) nucleus

**Structures and Neurotransmitters That Affect REM** (ATLAS2, Ch 3.1)
- Cholinergic neurons of the pedunculopontine and laterodorsal tegmental nuclei (PPT-LDT) become REM “on” by inhibiting the LPT. Because these neurons are not in turn directly inhibited by the LPT, they are external to the switch
- Dorsal raphe and noradrenergic locus coeruleus (DR-NLC) neurons activate the REM-off regions but are not inhibited directly by the SLD

**Cytokines That Promote Sleep** (ATLAS2, Ch 3.5)
- Interleukin (IL)-1β
- IL-6
- Tumor necrosis factor alpha
- Nerve growth factor
- Brain-derived neurotrophic factor
- Growth hormone–releasing factor

**Pharmacology of Sleep and Wakefulness** (ATLAS2, Ch 6)
- Hypothalamic neurons and adjacent groups of basal forebrain neurons produce the neurotransmitter GABA
- GABA neurons inhibit the firing of cells involved in wakefulness
- GABA inhibits neurons that contain histamine, norepinephrine, serotonin, hypocretin (orexin), and glutamate, and this inhibition promotes sleep
- Hypocretin (orexin) is a neuropeptide that excites the areas in the hypothalamus that produce wakefulness-promoting neurotransmitters

**Effects of Drugs on Sleep** (ATLAS2, Ch 6)
- Alcohol
  - Decreases sleep latency
  - Disrupts sleep
  - Decreases REM sleep
  - Increases snoring and apnea
- Anticonvulsants
  - Increase sleepiness
  - Can increase N3 sleep
- Antidepressants
  - Suppress REM and prolong REM latency
  - REM rebound may occur after abrupt withdrawal
  - Selective serotonin reuptake inhibitors (SSRIs) can disrupt sleep
  - Low doses of sedating antidepressants are often used (off label) to treat insomnia
  - Antidepressants may cause eye movements outside REM sleep
  - Serotonergic antidepressants can cause restless legs syndrome and REM sleep behavior disorder
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- **Antihistamines**
  - Over-the-counter (OTC) drugs cause sedation
  - Antihistamines do not have a reliable effect on sleep

- **Antihypertensive agents**
  - Lipophilic beta-blockers can disrupt sleep
  - The most sedative include alpha-adrenergic agonists such as methyldopa and clonidine
  - Some patients taking drugs of this class report nightmares

- **Antipsychotics**
  - Major effects are increased sedation and improved sleep continuity
  - Newer drugs in this class are being used off label for treating insomnia
  - Mild elevation of N3 may be seen

- **Corticosteroids**
  - Can cause slight REM suppression
  - Can also disrupt sleep and cause bizarre dreams

- **Nicotine**
  - Can delay sleep onset
  - Can cause complaints of nonrestorative sleep
  - Nicotine gum has been shown to increase alpha-EEG and reduce N3 sleep

- **Opiates**
  - Can cause sedation
  - Can disrupt sleep and reduce REM
  - May ameliorate restless legs syndrome
  - May cause sleep hypoventilation
  - May cause central and/or complex sleep apnea

- **Hypnotics and sedatives**
  - Benzodiazepines decrease sleep-onset latency, improve sleep continuity, and suppress N3 sleep
  - Mild suppression of REM is also possible
  - Newer nonbenzodiazepine hypnotics (e.g., zolpidem, zaleplon, eszopiclone) have little effect on sleep architecture

- **Stimulants**
  - Increase wakefulness
  - Decrease total sleep time (TST) and stage N3 sleep
  - Amphetamines and cocaine suppress REM sleep
  - Withdrawal causes prolonged periods of sleep and profound REM rebound

- **Tetrahydrocannabinol (THC)**
  - THC increases TST and stage N3 sleep
  - THC causes mild suppression of REM
  - REM rebound occurs after discontinuation

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**Clinical Correlations**

- REM atonia is produced by SLD neurons via glutamatergic spinal projections to interneurons that inhibit motor neurons in the spine by both glycinergic and GABAergic mechanisms. (ATLAS2, Ch 3.2)
- Hippocampal and cortical activation during REM sleep is generated by glutamatergic inputs from the REM-on region to the medial septum and the BF
- Absence of orexin neurons leads to unintended wake-to-sleep transitions and to the intrusion of REM-sleep phenomena into the awake state
- Agents that antagonize the orexin (both OX-1 and OX-2) receptors have hypnotic properties (Box 1.1-1)
Box 1.1–1 Alphabet Soup

Nothing makes doctors break out in a sweat more quickly than the alphabet soup of neurophysiology and neuroanatomy. Most of us last studied neurophysiology and neuroanatomy in medical school and even then likely found the subjects difficult. There are acronyms galore, from ACh to Gal to OX-1 to RAS to VLPO, along with cells, nuclei, centers, receptors, tracts, and projections found by lesions, electrical stimulation, and other methods. The acronyms tend to be cryptic, mysterious, and nonintuitive. This section will not make you an expert in neuroanatomy and neurophysiology related to sleep, but it is hoped that it will help you gain an understanding of some basic sleep mechanisms. (I like to think that the people writing exam questions may be as baffled as the test takers.)

The first thing to understand is that most of the action controlling sleep and wakefulness occurs in the hypothalamus. Basically, the hypothalamus is the conduit of information that links the nervous and endocrine systems by secreting factors that affect the pituitary gland; the pituitary sits just below the hypothalamus, connected by a stalk of nerve fibers.

Figure 1.1–1 shows the main areas involved in NREM sleep and wakefulness. It is not complete (see the summary for additional detail) but is provided to help you learn the locations of the main anatomic structures involved in sleep and wakefulness. The blue boxes are structures involved mainly in promoting sleep. The red boxes are structures involved primarily in maintaining wakefulness.
BONUS QUESTIONS ON CIRCADIAN MECHANISMS AND NEUROPHYSIOLOGY

Not Sleepy at Bedtime

An 18-year-old high school senior is referred because of difficulty awakening in the morning, falling grades, and concerns that she will not get into college. She just is not sleepy at normal bedtime and cannot fall asleep until 3 AM. On weekends, she sleeps until early afternoon and then feels great the rest of the day.

1. What is the most likely diagnosis?
   A. Delayed sleep phase disorder
   B. Advanced sleep phase disorder
   C. Sleep-onset insomnia
   D. Free-running circadian rhythm

2. Where are the cells located that synchronize the circadian timing of her sleep-wake pattern?
   A. Optic chiasm
   B. Visual cortex in the occipital lobe
   C. Hypocretin nucleus
   D. Suprachiasmatic nucleus

3. Which of the following structures helps synchronize her circadian system?
   A. Rod cells
   B. Cone cells
   C. Retinohypothalamic tract
   D. Anterior pituitary gland

4. Which of the following is not involved in generating this patient’s circadian rhythm?
   A. ARNTL (formerly BMAL1)
   B. CLOCK
   C. PERI
   D. BTBD9

5. What is the primary neurotransmitter released by the pacemaker cells that control the circadian rhythm?
   A. GABA
   B. Melatonin
   C. Serotonin
   D. Dopamine

Insomnia in a Blind Woman

A 39-year-old woman with a genetic visual disorder developed complete blindness by 35 years of age. Over the past few years, she has complained of severe insomnia, which she characterizes as not being able to fall asleep at a normal bedtime. After 18 hours of being awake, she often falls asleep at unpredictable times and then sleeps for 8 hours.

6. Which location has no impact on her circadian rhythm disorder?
   A. Retina
   B. Retinohypothalamic tract
   C. Suprachiasmatic nucleus
   D. Visual cortex

7. She is unable to perceive any light. What cells are likely the main photoreceptors that synchronize the circadian system?
   A. Retinal rod cells
   B. Retinal cone cells
   C. Foveal cells
   D. Ganglion cells
8. This patient’s suprachiasmatic nucleus (SCN) is unsynchronized to external light, yet the SCN still has outputs to the
   A. Cerebral cortex
   B. Thalamus
   C. Hypothalamus
   D. Pineal gland

9. If you measured her body temperature continuously over several weeks, you would find
   A. No pattern but random variations in temperature
   B. Temperature oscillation at a period of 22 to 23 hours
   C. Temperature oscillation at a period of 24 to 25 hours
   D. Stable temperature without oscillation

10. The correct circadian diagnosis in this patient is
    A. Advanced sleep-wake phase disorder
    B. Delayed sleep-wake phase disorder
    C. Non–24-hour sleep-wake rhythm disorder
    D. Irregular sleep-wake rhythm disorder

ANSWERS

1. A. This brief history is classic for a circadian rhythm sleep disorder, which has been previously classified as a delayed sleep phase type (and before that, a syndrome). Note that it is no longer officially called a syndrome; the term disorder is used to describe it in the third edition of the International Classification of Sleep Disorders (ICSD3). Knowledge of circadian rhythm sleep disorders is important; questions about them will be on the exam. (ATLAS2, Ch 9.1)

2. D. The best answer is the SCN. This nucleus is in the hypothalamus just above the optic chiasm (hence the designation suprachiasmatic). The nucleus is the “conductor” that directs and synchronizes the “orchestra” that creates the circadian rhythm of the various endocrine and physiologic systems of the body. (ATLAS2, p 22)

3. C. The retinohypothalamic tract carries information from the eye (melanopsin-containing ganglion cells in the retina) to the hypothalamus (hence the designation retinohypothalamic tract), where the SCN is located. In medical school, you learned about rods and cones, which are necessary for vision. However, they are not involved in circadian physiology. (ATLAS2, p 35)

4. D. The language of genetics is complex; our knowledge of how genes affect circadian rhythmicity is evolving, and the names of some genes change. A human gene is generally indicated by all capital letters, but the same gene in mammals is not (e.g., PER1 vs Per1). Mammalian clock genes include three Per (for period) genes: Per1, Per2, and Per3; two cryptochrome genes: Cry1 and Cry2; and Tim, Clock, Bmal1, and Csnk1e. These are all expressed in suprachiasmatic neurons. These genes and the proteins they produce interact to form negative and positive autoregulatory transcription–translation feedback loops that define the molecular machinery of the circadian oscillator. The incorrect answer is BTBD9, which has been linked to periodic limb movements of sleep. (ATLAS2, p 34)

5. A. Although GABA is the right answer, you might be tempted to pick melatonin because it has something to do with the circadian system and is used to treat circadian disorders. Approach questions like this, for which you might not have a clue as to the correct answer, by ruling out what you know. Here, for example, you should be able to rule out serotonin and dopamine, thus increasing your odds of answering correctly.

6. D. The first three structures listed play a role in transmitting visual information to the SCN, the latter being the location of the circadian pacemaker. After the pathways that carry visual information bifurcate in the optic chiasm, the pathways (from the rods and cones) that continue to the visual cortex play no role in synchronizing the circadian system. Thus, people with cortical blindness or those with blindness related to abnormalities in the visual cortex can have normally synchronized circadian systems.
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7. D. Besides the rods and cones, the retina also has ganglion cells that contain the protein melanopsin, which functions as a photoreceptor. Axons of rods and cones become the retinohypothalamic tract (RHT), which ends in the SCN. The RHT in the SCN releases glutamate, which leads to increased expression of PER1 and PER2. The SCN contains cellular oscillators that are normally coupled but that can oscillate independently. It is also emerging that almost all cells in all tissues of the body contain the machinery to produce circadian rhythms.

8. C. There are projections from the SCN to the adjacent subparaventricular zone (SPZ). There is a secondary projection to the dorsomedial hypothalamic nucleus (DMH), which projects to other brain regions that regulate sleep and wakefulness. There are also projections from the SCN to the paraventricular hypothalamic nucleus (PVH) to regulate corticosteroid secretion and synthesis of melatonin (see Summary). Normally, the SCN would send out alerting signals when it is daytime and a sleep signal at night, but in this blind patient, the signals would not be synchronized to light and darkness cues, and the patient's circadian rhythm would be free running.

9. C. Without synchronization with light-dark cycles, the patient will demonstrate the normal period of the human free-running circadian rhythm. The consensus at this time is that the free-running period in humans (called tau) is between 24 and 25 hours and is closer to 24 than 25 hours. If presented with a choice on the exam, select the value that is larger than and closest to 24 hours. The nonentrained period of most plants and animals maintained under constant darkness and temperature is almost always close to 24 hours (hence the term circadian, or about 1 day) and is rarely less than 23 hours or greater than 25 hours.

10. C. It is important to know the differences between the major circadian disorders. The names of the circadian rhythm sleep-wake disorders seem to change about every 5 years. This patient has a pattern, but it is unsynchronized to light-dark cycles. This is in contrast to people who have no pattern (truly random times of sleep and wakefulness), such as those with dementia, brain injury, or neurocognitive impairment. The difference between answers C and D is that in the latter, there is no pattern. (ATLAS2, Ch 9; ICSD3, pp 189-224)

Summary

Highly Recommended

- *Atlas of Clinical Sleep Medicine*, ed 2, Chapters 3.3 and 9

It is important to understand the structures and mechanisms involved in circadian physiology. Although the exam blueprint combines circadian physiology with other mechanisms controlling sleep, it is important to understand these mechanisms, and the questions on circadian physiology have been added as a bonus.

Types of Rhythms That Affect Sleep

- Circadian: About 1 day or 24 hours
- Ultradian: The 80- to 110-minute REM-NREM cycle
- Infadian: Greater than 24-hour cycles

The Two-Process Model

- Is an interaction of (ATLAS2, p 36)
  - Process S: Sleep homeostasis (the less time asleep, the greater the drive to sleep)
  - Process C: Regulation by the circadian system
  - Zeitgebers (time synchronizers), which are:
    - Photic (light)
    - Nonphotic (timing of eating and drinking, social interactions, environmental temperature)
1.1 / Sleep-Wake Mechanisms and Neurophysiology

Control of the Circadian System

The master pacemaker is the SCN in the hypothalamus just above the optic chiasm; it has two main functions (ATLAS2, p 36):
- Alerting of the CNS and controlling of circadian rhythms
- Synchronizing the circadian system
  - Light → melanopsin-containing ganglion cells → retinohypothalamic tract → SCN of hypothalamus

Receptors in the SCN include (ATLAS2, p 36):
- Melatonin 1 (MT1) (whose stimulation decreases the alerting signal from the SCN)
- Melatonin 2 (MT2) (whose stimulation synchronizes the circadian system)

The genes and proteins that interact to regulate circadian timing include (ATLAS2, p 34):
- Genes
  - Three PER (period) genes: PER1, PER2, PER3
  - ARHGEF5 (formerly Tim)
  - CLOCK
  - ARNTL (formerly Bmal1)
  - Csnk1e (formerly CK1e)
  - Two cryptochrome genes (CRY1 and CRY2), which are expressed in suprachiasmatic neurons
- These genes and the proteins they produce interact to form negative and positive autoregulatory transcription-translation feedback loops that define the molecular machinery of the circadian oscillator.

Relationship Between Time and Core Body Temperature

The declining portion of the core body temperature (CBT) starts near the beginning of the sleepy phase of the circadian rhythm. (ATLAS2, p 135)
- It is difficult to fall asleep unless body temperature is falling

The increasing portion of the CBT starts near the beginning of the awake phase of the circadian rhythm
- It is difficult to wake up unless body temperature is increasing

Dim-Light Melatonin Onset

In normal subjects, dim-light melatonin onset (DLMO) is between 8 PM and 10 PM. (ATLAS2, p 135)
- DLMO is several hours earlier in patients with advanced sleep phase disorder
- DLMO is several hours later in patients with delayed sleep phase disorder

Circadian Rhythm and Aging

- In neonates, sleep is polyphasic
- In adolescents, a delayed sleep phase can develop
- In older people, an advanced sleep phase with reduced amplitude can develop

Circadian, Endocrine, and Physiologic Interactions

- Reviewed in Chapter 3.9 of ATLAS2

Circadian Rhythm Sleep Disorders

- Reviewed in Section 2 of this volume
1. The medical student accepts (reluctantly) a rectal probe and an intravenous (IV) catheter. The IV line is connected to a machine that automatically draws aliquots of blood for testing every 15 minutes. Even with the IV and rectal probe, he manages to sleep several consecutive nights while data are collected. The first set of data analyzed is core body temperature. What statement best describes his thermoregulation during sleep?

A. Absent in REM
B. Inhibited in slow-wave sleep
C. Inhibited in all stages of sleep
D. Unchanged from his awake state

2. As the student falls asleep, there are changes in his core body temperature. Which statement best describes one of those changes?

A. There is heat conservation, and body temperature increases
B. There is heat loss via the skin
C. Vasoconstriction occurs, leading to an increase in body temperature
D. Vasodilation occurs, leading to an increase in body temperature

3. What will most likely be found when cortisol levels are measured?

A. Lowest cortisol level around midnight
B. Lowest level last third of the night
C. Lowest level around noon
D. Cortisol level does not vary significantly over 24-hour day

4. What will most likely be found when growth hormone (GH) levels are measured?

A. Lowest level around midnight
B. Highest level last third of the night
C. Highest level in first third of the night
D. GH does not vary significantly over 24-hour day

5. GH release is most strongly related to

A. Slow-wave sleep
B. REM sleep
C. Output of the suprachiasmatic nucleus
D. Duration of prior wakefulness

BONUS QUESTIONS

6. What will most likely be found when the researcher studies the effects of repetitive noise during sleep?

A. Increase in nocturnal growth hormone (GH) levels
B. Increase in nocturnal prolactin (PRL) levels
C. Decrease in nocturnal levels of both GH and PRL
D. Decrease in thyroid-stimulating hormone (TSH) levels
7. Which of the following hormones is most strongly modulated by both circadian and homeostatic sleep processes?
   A. Thyroid-stimulating hormone (TSH)
   B. Growth hormone (GH)
   C. Prolactin (PRL)
   D. Blood glucose concentration

8. On EKG, the student is found to have sinus arrest during sleep. During what sleep stage is this most likely to occur?
   A. N1
   B. N2
   C. N3
   D. REM

**Overcaffeinated and Overweight**

A 42-year-old male software engineer is referred to the Sleep Disorders Center for history of daytime sleepiness. His body mass index is 42, and his neck collar size 17.5 inches. His Epworth Sleepiness Scale score is 20 of 24 (normal <10 of 24). Because of daytime sleepiness, he drinks up to 8 cups of coffee each day. History includes symptoms suggesting a duodenal ulcer. He has an overnight sleep study that shows the following data:

<table>
<thead>
<tr>
<th>Sleep onset latency</th>
<th>4 minutes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total sleep time</td>
<td>490 minutes</td>
</tr>
<tr>
<td>Percent of total sleep time in</td>
<td></td>
</tr>
<tr>
<td>N1</td>
<td>1%</td>
</tr>
<tr>
<td>N2</td>
<td>40%</td>
</tr>
<tr>
<td>N3</td>
<td>40%</td>
</tr>
<tr>
<td>REM</td>
<td>19%</td>
</tr>
<tr>
<td>Percent sleep time with snoring</td>
<td>40%</td>
</tr>
<tr>
<td>Indices (per hour of sleep)</td>
<td></td>
</tr>
<tr>
<td>AHI</td>
<td>6 events/hr</td>
</tr>
<tr>
<td>PLMS</td>
<td>6/hr</td>
</tr>
<tr>
<td>Arousal</td>
<td>6/hr</td>
</tr>
</tbody>
</table>
9. Based on these data, what would you advise the referring physician?
   A. The findings are typical for obstructive sleep apnea, and a continuous positive airway pressure (CPAP) titration is recommended
   B. His sleepiness is explained by the periodic leg movements of sleep (PLMS); a history of restless legs syndrome should be explored
   C. The findings are typical of sleep deprivation, and that issue should be explored
   D. The sleep architecture findings are typical of upper airway resistance syndrome (UARS), and CPAP titration is recommended

10. Given the above findings, what change in hormone level would you most likely find?
    A. Reduced thyroxin
    B. Increased melatonin
    C. Increased ghrelin
    D. Increased leptin

11. What change in his glucose metabolism would you expect to find?
    A. Reduced insulin secretion in response to glucose load
    B. Increased insulin secretion in response to glucose load
    C. Hypoglycemia
    D. No changes in glucose metabolism are expected

12. Which of the following statements is most correct concerning the effect of sleep and circadian rhythm on gastric acid production or gastroesophageal reflux (GER)?
    A. Neither sleep nor circadian rhythm has an effect on gastric acid production
    B. Gastric acid production peaks just before awakening in the morning
    C. Gastric acid production has circadian variability, with peaks occurring between 10 PM and 2 AM
    D. GER is maximal during REM sleep

ANSWERS

1. A. Most automatically controlled homeostatic mechanisms are maintained during non-REM (NREM) sleep, but homeostasis seems absent for many systems during REM sleep, including the system controlling temperature. For example, shivering occurs during NREM sleep but does not occur in REM sleep. (ATLAS2, pp 37–38) Interestingly, hot flashes in menopausal women do not occur during REM sleep. Body temperature is controlled primarily by cells in the preoptic anterior hypothalamic nuclei, which are located very near the VLPO and the suprachiasmatic nucleus, emphasizing the interrelationship between regulation of sleep, temperature, and circadian rhythms.

2. B. Body temperature decreases with sleep onset, so answers A, C, and D are incorrect. The onset of sleepiness in the evening is associated with vasodilatation resulting in heat loss. (PPSM6, p 220, Chapter Highlights) It has been shown that people with cold hands and feet are prone to have insomnia; thus, dysfunctional thermoregulation may play a role in interfering with the sleep onset. (PPSM6, p 228, Clinical Pearl)

3. A. The lowest cortisol level is around midnight and the highest level in the last third of the night. Assessing cortisol production by measuring levels at midnight and in the morning has been done for decades in the clinical setting. This timing of cortisol production has also been determined in sleep deprivation. Changes in cortisol level are more closely related to time than to the awake or sleep state. (ATLAS2)

4. C. GH production peaks in the first third of the night in the sleeping subject. During a night of sleep deprivation, there is no peak growth hormone level. (ATLAS2, p 59, Figs. 3.90–3.92, and PPSM6, p 204)

5. A. GH is released during the first slow-wave sleep cycle, usually within minutes of SWS onset. The elevation in GH concentration is more robust in males than females. (Females exhibit more frequent daytime pulses.) (PPSM6, p 204)
6. C. GH and PRL concentrations are strongly sleep dependent, with only weak circadian modulation. Fragmenting sleep with artificial awakenings, particularly when they interfere with slow-wave sleep, will inhibit nocturnal release of GH and PRL and therefore lower nocturnal levels.

7. A. TSH exhibits a clear circadian pattern, with peaks occurring nocturnally in the absence of sleep. Sleep deprivation is accompanied by supranormal peak levels, indicating an interaction in which sleep processes normally exert a damping effect on circadian-induced release. (PPSM6, p 204)

8. D. When a question is based on something going wrong during sleep and you are asked what stage of sleep, it seems the answer is usually REM. During REM sleep, healthy people sometimes demonstrate abnormal breathing patterns, or apneas, and (as in this example) sinus arrest. Sinus arrest is likely caused by a surge of parasympathetic activity. (Guilleminault C, Pool P, Motta J, Gillis AM. Sinus arrest during REM sleep in young adults. N Engl J Med 311(16):1006-1010, 1984)

9. C. The clue to the correct diagnosis in this case is the marked increase in stage N3 sleep (40%, but normal N3 is about 20% of adult sleep time). Such a large amount of slow-wave sleep is usually found in recovery sleep after sleep deprivation but can also be caused by certain medications. In the presence of a significant sleep breathing abnormality or a movement disorder causing many arousals, one would expect a reduction in SWS and REM sleep.

FIGURE 1.2–1 Question 4.
Section 1 / Normal Sleep and Its Variants

10. C. The hormones ghrelin and leptin are involved in control of appetite. Ghrelin (think about “growling stomach”) is produced by gastric cells; it increases appetite. Ghrelin levels are increased with sleep deprivation. Leptin is produced by fat cells and normally suppresses appetite. Leptin levels are decreased with sleep deprivation. Thus, sleep deprivation tends to increase appetite and cause weight gain. This result has been shown in both children and adults. (ATLAS2, pp 56–58)

11. B. With chronic sleep restriction, there occurs insulin resistance. After meals, glucose increases to higher levels than in the absence of sleep restriction. This increase in glucose occurs despite increased insulin levels, hence there is insulin resistance. (PPSM6, Ch 20)

12. C. Gastric acid production has clear-cut circadian variability. It is unclear whether the peaks that occur between 10 pm and 2 am are related to circadian factors alone or whether sleep stage plays a role. Noteworthy is the clinical observation that patients with duodenal ulcer typically wake up within a couple of hours of sleep onset with ulcer symptoms. Lower esophageal sphincter tone is reduced more in stage N2 sleep than in REM, and not surprisingly, stage N2 is when most episodes of GER occur during sleep.

Summary

Highly Recommended

- Atlas of Clinical Sleep Medicine, ed 2, Chapters 3.4, 3.5, 3.8, and 3.9
- Principles and Practice of Sleep Medicine ed 6, Chapter 20; Abstracts and Clinical Pearls of Chapters 11 to 19

Nonrespiratory physiology is a problematic area to cover for the sleep boards because it is so broad yet will show up on only about 3 of the 240 board exam questions. The very first blueprint had a section called “Organ System Physiology”; it disappeared in the next blueprint. It is back in the current blueprint as “Other Physiology.” (The exam committee seems to have difficulty in deciding what to do with this. We have added some bonus questions to help cover this large area of knowledge. Your review should focus on the physiology that has most direct clinical application (i.e., respiratory and endocrine). In this section, even though we present twice as many questions as on the examination, all topic areas could not be covered. Some of the high-value topic areas will be mentioned here. At the end of the day, keep in mind that the exam is geared toward clinical sleep medicine and that most of the questions, even those dealing with physiology, will likely have some clinical implications.

Physiologic Regulation

- Pituitary hormones (ATLAS2, Ch 3.10; PPSM5, Ch 26)
  - All hormones show diurnal variation
  - Primarily linked to circadian rhythm
    - Adrenocorticotropic hormone (ACTH)
  - Primarily linked to sleep
    - GH (to SWS) and PRL
  - Somewhat inhibited by sleep
    - TSH
- Endocrine function (ATLAS2, Ch 3.9)
  - Sleep deprivation increases appetite because of
    - Increase in ghrelin
    - Decrease in leptin
  - Sleep deprivation leads to obesity
    - Sleep deprivation causes insulin resistance
- Metabolic rate
  - Related to arousal state
    - Decreases with depth of NREM sleep
    - Increases in REM
Thermoregulation
- Thermostat located in preoptic anterior hypothalamic area
- Mechanisms of control of body temperature
  - To conserve energy (to raise temperature)
    - Vasoconstriction
    - Piloerection
    - Shivering
  - To lose energy (to lower temperature)
    - Sweating
    - Panting
- Related to sleep state
  - Homeostasis present in NREM sleep
  - Homeostasis inhibited in REM sleep
- Clinical implications
  - Night sweats common in hypermetabolic states (hyperthyroidism, infections)
  - Hot flashes in menopausal women do not occur during REM

Cardiovascular (ATLAS2, Ch 3.7; PPSM6, Chs 13 and 14)
- Circulatory homeostasis
  - Related to sleep stage
    - NREM sleep: relative autonomic stability in heart rate, rhythm, and blood pressure
    - REM sleep: relative autonomic instability in heart rate, rhythm, and blood pressure
  - Phasic REM–related changes
    - Surges in sympathetic tone and heart rate
    - Decreases in coronary flow in patients with coronary artery disease
  - Tonic REM–related changes
    - Parasympathetic tone increases may result in rate decrease or sinus arrest
    - In patients with long QT3 syndrome, may lead to torsades de pointes
- Cerebral blood flow
  - Decreases in NREM
  - Increases in REM (to match increased metabolic rate of brain in this stage)

Gastrointestinal (ATLAS2, Ch 15.3)
- Gastric acid secretion has circadian variability with peak between 10 PM and 2 AM
- Related to sleep stage
  - Lower esophageal sphincter (LES) tone lower in NREM than REM sleep
  - GER more frequent in NREM sleep

Respiratory physiology: see p 220 of this volume
Cytokines: see p 7 of this volume

QUESTIONS
A Pregnant Internist

An internist is pregnant with her first child. Before pregnancy, her body mass index (BMI) was 24. At 36 weeks’ gestation, her weight gain is normal, but she has begun to snore and manifest restless leg syndrome symptoms.

1. Which of the following conditions is she most likely to have during sleep?
   A. Hypoxemia
   B. Hypoventilation
   C. Hypocapnia
   D. Apnea
Section 1 / Normal Sleep and Its Variants

2. Snoring in pregnancy increases the pregnancy-related risk of
   A. Increased fetal size
   B. Hypertension
   C. Elevated infant Apgar scores
   D. Gestational diabetes

3. Fetal sleep near term (at 38–40 weeks of gestation) is typically
   A. Mostly REM sleep
   B. Time linked to maternal sleep
   C. Associated with absence of effort to breathe
   D. Absent

4. The term polyphasic sleep identifies sleep that
   A. Occurs multiple times day or night
   B. Occurs only during the daytime
   C. Occurs with early-onset REM
   D. Occurs any time it is dark

5. Which feature of sleep architecture in infants is incorrect?
   A. Appearance of sleep spindles by 9 weeks of age
   B. Disappearance of the trace-alternant pattern by 6 weeks of age
   C. K complexes that appear by 12 weeks of age
   D. Poor differentiation of NREM stages until 12 months of age

6. The typical 1-year-old child is most likely to
   A. Sleep up to 10 hours out of every 24-hour period
   B. Take two naps during the day
   C. Enter REM sleep (stage R) at sleep onset
   D. Have central apneas one to five times per hour of sleep

7. Up until what age is napping common in children?
   A. 1 to 2 years
   B. 2 to 4 years
   C. 4 to 5 years
   D. 7 to 9 years

8. In school-age children, slow-wave sleep (stage N3) is likely to occur
   A. During the first third of the night
   B. During the middle third of the night
   C. During the last third of the night
   D. 90 minutes after sleep onset

Older and Wiser but With Trouble Sleeping

A 77-year-old man complains of restless sleep and awakening early in the morning with an inability to fall asleep again.

9. As people age, which of the following increases?
   A. REM sleep as a percentage of TST
   B. Slow-wave sleep as a percentage of TST
   C. Sleep efficiency
   D. Resistance to sleep deprivation

10. REM sleep in older adults
    A. Occurs at sleep onset
    B. Is minimal or absent
    C. Diminishes less than slow-wave sleep in older adults
    D. Is less fragmented with aging
ANSWERS

1. C. Snoring occurs in about 30% of pregnant women and is due in part to edema in the nasal passage and to pharyngeal hypotonia. However, obstructive sleep apnea is relatively uncommon, as are hypoventilation (hypercapnia) and hypoxemia. In contrast, practically all pregnant women hyperventilate by the third trimester because of high progesterone levels. (ATLAS2, p 356)

2. B. Snoring in pregnancy increases the risk for pregnancy-induced hypertension (pre-eclampsia). Babies born to snoring mothers are small and have lower Apgar scores than babies born to nonsnoring mothers. (ATLAS2, p 356; Table 16.2–1 reviews sleep throughout pregnancy and is a must.)

3. A. Indeed, fetuses do sleep, and most of the sleep appears to be REM sleep. A fetus at 30 weeks’ gestation spends 80% of her or his sleep time in “active” or REM sleep. (ATLAS2, p 89)

4. A. Polyphasic sleep refers to several sleep bouts that occur both during the day and at night. This pattern is found in newborns and in some animals. In newborns, circadian entrainment eventually occurs, and then most sleep occurs at night. This pattern is also seen in older adults in institutions who might lack circadian entrainment and can therefore develop an irregular sleep-wake disorder. (ATLAS2, p 94)

5. D. In the newborn period, roughly half the time is spent in REM sleep; the remainder is spent in NREM sleep. At this age, the NREM stages are not well characterized electrophysiologically, and the term nondeterminant sleep is often used to describe the pattern. One transient pattern that is seen is a trace-alternant pattern. (ATLAS2, p 89; PEDS2, Ch 1)

6. B. It is important to know the relationship between sleep and age. A 1-year-old child no longer enters sleep via REM, sleeps 10 to 16 hours out of 24, and has about two naps a day. An apnea index greater than 1 (one hypopnea or apnea per hour) is considered abnormal in this age group. (ATLAS2, p 89, Table 4–2; PEDS2, Ch 1)

7. C. By the time a child is about 6 years old, napping should no longer occur. Imagine if there were naps in first grade! The persistence or return of napping in a child older than 6 years usually indicates sleep deprivation or that the child has developed a sleep disorder. (ATLAS2, p 89)

8. A. Slow-wave sleep usually occurs in the first third of the night in all age groups. The percentage of sleep spent in slow-wave sleep is highest in children and decreases with age. (ATLAS2, p 86)

9. D. Resistance to sleep deprivation surprisingly increases with age. Slow-wave sleep as a percentage of total sleep time decreases more in men than women. (ATLAS2, p 86)

10. C. REM sleep diminishes much less than slow-wave sleep in older people, but the REM episodes may be more fragmented. (ATLAS2, p 90)

Summary

Highly Recommended

- Atlas of Clinical Sleep Medicine, ed 2, Chapter 4.2

The topic of sleep and aging is important, because it overlaps other areas that include pediatrics and polysomnography (PSG) findings. Below are sleep characteristics of each age you should know.
Section 1 / Normal Sleep and Its Variants

Sleep by Age Range (ATLAS2, pp 85-97, and Table 4.2–1)

■ Newborns
  ○ Sleep 16 to 18 hours of each 24 hours; 5 to 10 hours of this is napping
  ○ Sleep is polyphasic
  ○ 50% of sleep occurs in REM

■ At 2 to 3 months
  ○ Sleep spindles start to appear

■ At 3 to 4 months
  ○ Major sleep period is at night

■ At 4 to 4.5 months
  ○ Stages N1, N2, and N3 can be ascertained

■ At 5 months
  ○ K complexes start to appear

■ At 1 year
  ○ Sleeps 13 to 15 hours of every 24 hours; 2 to 3 hours of this is napping
  ○ 30% of sleep is in REM

■ At 2 years
  ○ Sleeps 12 to 14 hours of every 24 hours; 1.5 to 2.5 hours of this is napping
  ○ 25% of sleep is in REM (percentage remains constant with further aging)

■ At 3 to 5 years
  ○ Sleeps 11 to 13 hours of every 24 hours; 0 to 2.5 hours of this is napping

■ At 5 to 12 years
  ○ Sleeps 9 to 12 hours of every 24 hours; no napping

■ At 13 to 20 years
  ○ Sleeps 8 to 9 hours of each 24 hours; no napping
  ○ Delay in sleep phase can occur

■ At 20 to 65 years
  ○ Large decline in amplitude of slow-wave sleep (SWS)
  ○ Slow but progressive decline in SWS as percentage of total sleep time
  ○ Deterioration of sleep with menopause (about age 50 years)

■ Older than 65 years
  ○ Napping returns
  ○ Advance in sleep phase is common
  ○ Difficulty initiating and maintaining sleep occurs
  ○ Sleep is fragmented with increased awakenings
  ○ Melatonin production is decreased
  ○ Sleep deteriorates with deterioration of overall health

Sleep in Women

■ Pregnancy
  ○ Table 1.3–1

■ Postpartum
  ○ See last row of Table 1.3–1

■ Menopause
  ○ Prevalence of obstructive sleep apnea (OSA) increases compared with men of similar age
  ○ Hot flashes interfere with sleep; they are not present in REM sleep
  ○ Sleep abnormalities due to depression increase

REFERENCES


An Acutely Sleep-Deprived Surgeon

A 64-year-old surgeon, Dr. K, flies to Indonesia immediately after he learns of an earthquake there. After arriving, not having recovered from jet lag, he operates continuously on one patient after another for about 48 hours, amputating gangrenous extremities. He has been gulping down food and water between cases.

1. After being awake for 48 hours, Dr. K is likely to have all of the following except
   A. Irritability
   B. Difficulty in concentrating
   C. Visual hallucinations
   D. Auditory hallucinations
2. Although his manual dexterity seemed unimpaired, Dr. K started to make errors such as illogical triaging of cases and performing operative procedures in the wrong sequence. Abnormal activity in what part of his brain is likely causing these mistakes?
   A. Broca’s area
   B. Prefrontal cortex
   C. Parietal lobe
   D. Temporal lobe

3. Examination of Dr. K’s blood would show
   A. Normal growth hormone level
   B. Hypoglycemia
   C. Reduced cortisol levels
   D. Increased thyroid activity

4. Others on the surgical team insisted Dr. K have a full night’s sleep before continuing to operate because he was endangering patients. Dr. K, on the other hand, thought he just needed a nap. Of the following statements, which is most correct?
   A. Dr. K needs 1 night of recovery sleep before he is alert again
   B. Dr. K needs 3 nights of recovery sleep before he is alert again
   C. If Dr. K were 24 years old, 1 night of recovery sleep would suffice
   D. If Dr. K took a 4-hour nap, it would restore alertness

5. If this surgeon’s recovery night sleep was monitored by polysomnography, what sleep stage impact would be observed?
   A. Increase in percentage of time spent in REM sleep
   B. Increase in percentage of time spent in slow-wave sleep
   C. Increase in percentage of time spent in slow-wave sleep and REM sleep
   D. Increased REM sleep and reduced slow-wave sleep

6. During recovery sleep, Dr. K would have which of the following medical findings?
   A. A decrease in plasma glucose
   B. A reduction in adrenocorticotropic hormone (ACTH)
   C. Increased production of growth hormone (GH)
   D. Increased thyroid (thyroxine T₄) activity

The Chronically Sleep-Deprived Surgeon

After 48 hours of being awake, Dr. K sleeps 12 hours, takes a day off from operating, and then sleeps 8 hours the next night. On awakening, he feels great and starts to operate again. He promises the surgical team he will get some sleep every night and settles on a routine of sleeping 4 hours, then staying awake for 20 hours, operating on the continual stream of cases.

7. After 4 nights of sleeping 4 hours per night, what would you expect to find in his awake EEG?
   A. Increase of power in the delta range
   B. Increase of power in the alpha range
   C. Decrease of power in the theta range
   D. No change in his awake EEG

8. What changes in sleep architecture would you find during his fourth night of 4-hour sleep?
   A. Increased REM sleep percent
   B. Increased SWS percent
   C. Similar increases in REM and SWS percent
   D. No change in the percentage of the sleep stages
9. Dr. K insisted that with this sleep schedule, he did not feel sleepy during the daytime and he could safely operate. What mean sleep latency would you likely find if Dr. K had a multiple sleep latency test (MSLT) after the fourth night of sleeping only 4 hours a night?

A. 20 minutes
B. 15 minutes
C. 10 minutes
D. 5 minutes

10. On the fourth day of Dr. K’s sleeping 4 hours each night, what would you expect if you measured his performance using the psychomotor vigilance task (PVT)?

A. PVT lapses would be similar in degree to the findings after 3 days of no sleep
B. PVT lapses would be greater than after 3 days of no sleep
C. PVT lapses would be in the range seen in normal subjects sleeping 8 hours a night
D. PVT lapses would be about the same as if he had slept for 6 hours each night but much greater than if he had slept 8 hours each night

---

**ANSWERS**

1. D. Auditory hallucinations are an uncommon manifestation of chronic sleep deprivation. Personality changes and symptoms of psychopathology become apparent with prolonged sleep loss. Hallucinations occur in up to 80% of subjects; they are generally visual and different from the more common auditory hallucinations found in schizophrenia.

2. B. Acute sleep deprivation leads to abnormal executive function, which results from loss of function of regions in the prefrontal cortex. This area of the brain plays a role in temporal memory (planning, organization, prioritization). There is also impairment of newly acquired skills and decrement in the ability to perform complex tasks.

3. D. Thyroid activity is increased, suggesting a hypermetabolic state. (Continuous sleep deprivation in rodents ultimately led to their death. However, the rodents behaved as though they were hypermetabolic, increasing their food intake but losing weight.) Secretion of GH appears linked to SWS; thus absence of sleep would result in decreased GH levels. Cortisol may be increased after a night of total sleep deprivation.

4. A. Because Dr. K is in his 60s, a full night of recovery sleep is sufficient to restore his alertness to baseline. One night is not sufficient in young adults, who usually need 2 or more nights to recover after chronic sleep deprivation.

5. B. By far, the most impressive change during recovery sleep in older people is a substantial increase in the percentage of SWS. There occurs a reduction in both REM latency and percentage of REM sleep.

6. C. With recovery from acute sleep loss, there is an increase in both ACTH and GH, the latter from the rise in SWS during recovery (GH increases in SWS). The increase in thyroid function that occurred during the prolonged wakefulness would not be expected to continue with recovery.

7. A. With chronic sleep restriction, an overall slowing of the awake EEG occurs that reflects increased homeostatic drive. Thus, delta power (3.75–4.5 Hz) is increased. There is also an increase in theta power, thought to reflect “spectral leakage” from the changes in delta power. These might reflect a tendency toward microsleeps. Alpha power decreases.

8. B. The body tries to maintain SWS. Thus, with chronic sleep deprivation, conservation of the amount of SWS occurs at the expense of the other NREM stages and REM sleep.

9. D. There is progressive decrease in mean sleep latency after successive nights of restricted sleep, and after 4 nights, the mean latency would be expected to be abnormally low. Interestingly, subjective assessments of sleepiness might not parallel objective impairment as measured by the MSLT or performance tests. Generally, sleep-deprived patients tend to overestimate their level of alertness.
10. D. After the first 4 nights of sleeping 4 hours per night, PVT results indicate more lapses than in the 8-hour sleep condition but the same as in subjects sleeping 6 hours per night. By the seventh night of 4-hour sleep, the lapses are greater than with 6-hour sleep. By 2 weeks of 4-hour sleep, the results would be similar to 3 consecutive nights of no sleep. Thus, with chronic sleep loss comes a progressive worsening of function.

Summary

Highly Recommended

*Atlas of Clinical Sleep Medicine*, ed 2, Chapter 5.

Sleep deprivation is important in clinical practice, and some of this content overlaps with other sections. Expect about 10 questions covering this topic on the exam.

**Acute Total Sleep Deprivation**

- **Effects**
  - Memory impairment (short-term memory is affected more)
  - Impairment of executive function (prefrontal lobe: planning, prioritization, organization)
  - Daytime sleepiness
  - Changes in waking EEG
    - Decreased alpha activity
    - Increased delta and theta activity
  - Increased thyroid activity but few other metabolic changes noted
  - Increases in IL-1 and IL-6

- **Recovery sleep**
  - Performance generally normalizes within 1 to 3 nights of normal sleep
  - MSLT shows recovery occurs more quickly in older than in younger people
  - An increase in SWS shows, but REM sleep may be unchanged or reduced

**Chronic Sleep Deprivation**

- **Effects**
  - Abnormal awake EEG
    - Increased delta and theta power
    - Decreased alpha power
  - Changes in sleep architecture: conservation of SWS
  - Progressive sleepiness as measured by the MSLT
  - Progressive decrements in performance as measured by PVTs
  - Impaired driving performance
  - Subjective assessment of sleepiness can underestimate sleepiness and impairment
  - Metabolic changes
    - Elevation of evening cortisol and sympathetic activity and impaired glucose tolerance
    - Obesity
    - Increased cardiovascular events, morbidity, and likely mortality; effects are likely mediated by increased C-reactive protein (a marker of increased cardiovascular risk)
1.5 Scoring and Staging

QUESTIONS

You, the Technologist

In preparation for the sleep board exam, you decide to spend part of the night in the sleep lab. Your goal is to assist the technologist in setting up a sleep study on one of your patients.

1. For the EEG lead placements, you will use the 10-20 system. This means you place the electrodes
   A. So that there are 20 derivations (two from each electrode)
   B. Either 10% or 20% of the distance between a given pair of skull landmarks
   C. Either 10 or 20 mm from specific skull landmarks
   D. Somewhere between 10 and 20 mm into the scalp

2. After explaining the test to your patient, your first task is to place electrodes for the recommended EEG derivations. These are
   A. F4-M1, C4-M1, O2-M1
   B. F4-M2, C4-M2, O2-M2
   C. F3-M1, C3-M1, O1-M1
   D. Fz-Cz, Cz-Oz

3. Next, to detect eye movements, you place electrodes 1 cm below the left eye outer canthus (E1) and 1 cm above the right eye outer canthus (E2). This placement will give the recommended electrooculogram (EOG) derivations, which are
   A. E1-M2 and E2-M2
   B. E1-M2 and E2-M1
   C. E1-M2 and E2-E1
   D. E1-E2 and E2-E1

4. Recording of eye movements during polysomnography is possible because
   A. The cornea is electrically positive with respect to the retina
   B. The retina is electrically positive with respect to the cornea
   C. Gross eye movements generate electrical signals that differ slightly owing to the distance of each eye to the recording electrode
   D. Eye movements generate static electricity by rubbing on nearby tissue

5. You next attach leads for the electromyogram (EMG) that will be used for sleep staging purposes; they are attached to the
   A. Lower legs
   B. Thighs
   C. Chin
   D. Forehead

6. After the patient falls asleep, you help monitor the channels. You enjoy figuring out the EEG patterns, knowing that they can be distinguished by all of the following except
   A. Frequency: the number of cycles per second (Hz)
   B. Amplitude: measured by voltage
   C. Shape of the waveform
   D. Sinusoidal or waxing and waning pattern over 5 or more seconds
   E. Distribution: the location where the waveform is normally most prominent

7. The three distinct states of consciousness for a normal subject are
   A. Wakefulness, REM sleep, and deep sleep (N3)
   B. Wakefulness, REM sleep, and NREM sleep
   C. REM sleep, light sleep (N1 and N2), and deep sleep (N3)
   D. Wakefulness, transition to sleep, and sleep
8. The three distinct states of consciousness are identified by
   A. Clinical observation plus EEG
   B. EEG, EOG, and EMG
   C. EEG alone
   D. EEG plus video of the subject sleeping

9. Which EEG waveform is NOT commonly used to differentiate and classify sleep stages?
   A. Alpha
   B. Beta
   C. Delta
   D. Theta

10. The term *relatively low-voltage, mixed frequency pattern* for the EEG most closely describes
    which sleep stage?
    A. N1
    B. N2
    C. N3
    D. R

11. Delta activity includes brainwaves with a frequency less than 4 Hz. Within this group, *slow waves* are defined as
    A. Synonymous with delta activity
    B. Peak-to-peak amplitude greater than 75 µV and frequency 0.5 to 2.0 Hz
    C. Frequency 0.5 to 2.0 Hz, any amplitude
    D. Peak-to-peak amplitude greater than 75 µV, frequency less than 4 Hz

12. The sleep-staging nomenclature in the American Academy of Sleep Medicine (AASM) manual, version 2.5 (referenced in this text as MANUAL2), includes all of the following stages except
    A. N1
    B. N2
    C. N3
    D. N4
    E. REM

13. All of the following are true about scoring an EEG arousal except
    A. It requires either an associated body movement or a respiratory event
    B. It requires an abrupt shift of EEG frequency that lasts at least 3 seconds
    C. It must be preceded by at least 10 seconds of stable sleep
    D. In REM, it requires a concurrent increase in submental EMG lasting at least 1 second

14. The requirement of increase in submental EMG to score arousal in REM sleep is necessary
    because:
    A. Alpha activity (8–13 Hz) is not seen in REM
    B. The background EEG in REM is predominantly alpha activity
    C. Alpha bursts routinely appear during REM sleep and do not necessarily represent pathology
    D. The chin EMG has a higher digital sampling rate than the EEG

15. The epoch in Figure 1.5–1 shows transition from
    A. Wakefulness to stage N1
    B. N1 to N2
    C. N1 to REM
    D. N2 to REM

16. Which of the following is true about the artifact shown in the PSG fragment (Fig. 1.5–2)?
    A. Can result from high electrode impedance, a poor electrical connection, or excessive current leakage from nearby electrical equipment (e.g., computers, televisions)
    B. Has the same frequency as electrocardiogram (ECG) artifact
    C. Is usually indistinguishable from perspiration artifact
    D. Is best avoided by use of a 60-Hz filter
**FIGURE 1.5–1** Question 15.

**FIGURE 1.5–2** Question 16. (From ATLAS2, Fig. 19–111)
17. In PSG, most of the recorded signals are amplified by alternating current (AC) amplifiers. A few signals are amplified by direct current (DC) amplifiers. Which of the following is recorded by a DC amplifier in the PSG?

A. EEG  
B. EOG  
C. ECG  
D. Pulse oximetry

18. All of the following are true about the K complex except

A. It is defined as a well-delineated negative sharp wave immediately followed by a positive component standing out from the background, with a total duration of 0.5 second or longer  
B. For an arousal to be associated with a K complex, it must commence no more than 1 second after termination of the K complex  
C. It can be used to score an epoch as stage N2  
D. In the absence of a sleep spindle, a K complex must be present to score an epoch as N2

19. Figure 1.5–3 is a 30-second epoch. The large waves seen in channel F4-M1 in the first 3 seconds of this epoch (from beginning to first solid vertical line) are

A. K complexes  
B. Vertex sharp waves  
C. Slow waves  
D. Delta waves

20. Figure 1.5–4 shows a 30-second epoch. The large waves seen in all three EEG channels (F4-M1, C4-M1, and O2-M1) in the first 3 seconds of this epoch (from beginning to first solid vertical line) are

A. K complexes  
B. Slow waves  
C. Vertex sharp waves  
D. REM artifact
21. To score respiratory events in adults, all of the following are true except:
A. Oronasal thermal sensor is recommended to detect absence of airflow and score an apnea
B. Nasal air pressure transducer is recommended to detect airflow reduction and score a hypopnea
C. Inductance plethysmography is recommended to detect respiratory effort
D. To score an apnea, a drop in the peak thermal sensor excursion by at least 70% of baseline must be evident

22. According to the AASM manual, which of the following is NOT a criterion for scoring an apnea?
A. There is a drop in the peak signal excursion by 90% or greater of pre-event baseline using an oronasal thermal sensor
B. There is a drop in the peak signal excursion by 90% or greater of pre-event baseline using a positive air pressure (PAP) device flow during a titration study
C. The duration of the 90% or greater drop in sensor signal is 10 seconds or longer
D. There is a drop of at least 3% in SaO₂ attributable to the apnea event

23. Figure 1.5–5, A, demonstrates
A. Obstructive apnea
B. Hypopnea
C. Respiratory effort–related arousal (RERA)
D. Normal breathing

24. Figure 1.5–5, B, demonstrates
A. Obstructive apnea
B. Hypopnea
C. RERA
D. Normal breathing

25. All of the following may be seen in the waking stage except:
A. Alpha rhythm
B. Eye blinks
C. Reading eye movements
D. REM
E. K complexes
26. A normal sleep hypnogram for a child is shown in Figure 1.5–6. A principal difference compared with adults is that adults have
A. More REM sleep
B. Less REM sleep
C. More slow-wave sleep
D. Less slow-wave sleep

27. Considering normal sleep, which statement is most accurate?
A. REM occurs in several discrete periods, lengthening as the sleep progresses
B. Deep sleep tends to concentrate in the latter part of the sleep cycle
C. Wake after sleep onset (WASO) occupies about 15% of the sleep cycle
D. REM latency is about 30 to 60 minutes
28. Alpha rhythm is BEST seen in the EEG during  
   A. Stage N1  
   B. Stage N3  
   C. Wakefulness with eyes open  
   D. Wakefulness with eyes closed  

29. The 30-second epoch in Figure 1.5–7 shows what stage of sleep?  
   A. N1  
   B. N2  
   C. N3  
   D. REM  

30. The transition from wakefulness to stage N1 sleep may be associated with all of the following except  
   A. Slow-rolling eye movements  
   B. Low-amplitude, mixed-frequency EEG in the range of 4 to 7 Hz  
   C. Appearance of vertex sharp waves  
   D. Alpha activity in the frontal lobe EEG  

31. During a 30-second epoch, the first 23 seconds have a baseline EEG frequency of 7 Hz. The EEG frequency then shifts to 11 Hz on the 28th second. Slow eye movements are seen throughout the epoch. This epoch should be scored as  
   A. Awake  
   B. N1  
   C. N2  
   D. N3  
   E. REM
32. Consider three consecutive epochs of 30 seconds each:
   Epoch 221: EEG frequency 3 Hz covering 22% of the epoch, one K complex
   Epoch 222: EEG frequency 3 Hz covering 55% of the epoch, no K complex
   Epoch 223: EEG frequency 3 Hz covering 75% of the epoch, no K complex
   The remaining percentages of each stage consist of 6 Hz activity. No slow or rapid eye movements are seen in any of the three epochs. What is the sleep stage of epoch 223?
   A. N1
   B. N2
   C. N3
   D. REM

### Table 1.5–1 For Questions 33 and 34

<table>
<thead>
<tr>
<th>Epoch</th>
<th>1</th>
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<th>3</th>
<th>4</th>
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<td>W</td>
<td>N2</td>
<td>N2</td>
<td>N2</td>
<td>REM</td>
<td>REM</td>
</tr>
</tbody>
</table>

REM, Rapid eye movement.

33. In Table 1.5–1, each epoch is 30 seconds. When is sleep onset?
   A. 1 minute
   B. 2.5 minutes
   C. 4 minutes
   D. 6 minutes

34. In Table 1.5–1, what is the REM onset?
   A. 3.5 minutes
   B. 4.0 minutes
   C. 5.0 minutes
   D. 5.5 minutes

### BONUS QUESTIONS

35. Regarding alpha-delta sleep shown in Figure 1.5–8, choose the most correct combination of statements lettered A through D.
   1. Consists of 15% to 20% delta activity superimposed on prominent alpha activity
   2. Alpha portion usually 1 to 2 Hz slower than waking alpha
   3. Often believed to be a marker for nonrestorative sleep
   4. Often seen in patients with musculoskeletal pain
   A. 1, 3, and 4 only
   B. 3 and 4 only
   C. 2, 3, and 4 only
   D. 1, 2, 3, and 4

36. The transition from a low-voltage awake stage to N1 is characterized by
   A. Slow eye movements of greater than 500 ms
   B. Sleep spindles
   C. Delta waves
   D. Rapid eye movements of less than 500 ms

37. Which of the following is NOT specifically recommended by the AASM for detecting hypoventilation during a PSG?
   A. $P_cO_2$ measured in arterial blood gas
   B. $P_cO_2$ measured via an end-tidal $CO_2$ sensor
   C. $P_cO_2$ measured via transcutaneous $CO_2$ sensor
   D. Combination of apnea for longer than 30 seconds with a concomitant drop of $SaO_2$ greater than 3%
38. What is the sleep stage in Figure 1.5–9?
   A. W
   B. N1
   C. N2
   D. N3
   E. REM
39. According to the AASM manual, scoring sinus tachycardia and sinus bradycardia in adults during sleep requires heart rates (beats/min) of, respectively, 
A. >90, <40
B. >100, <40
C. >90, <50
D. >100, <50

40. Epochs 250 to 280 of a PSG are scored as stage R (REM sleep). Any of the following occurring in epoch 281 can be used to mark the end of stage R except 
A. Transition to stage W or N3
B. Chin EMG tone increased above that of stage R and criteria for N1 met
C. An EEG arousal followed by low-amplitude, mixed-frequency EEG and slow eye movements
D. A K complex 20 seconds into the epoch

41. A major difference between infants and older children and adults in the sleep EEG is 
A. Infants have no delta wave or spindle activity
B. Infants spend about half of their total sleep time in REM sleep
C. There is no discernable difference between infants and the other two groups
D. Infant sleep is deemed “uninterpretable” at the current time

42. The sleep fragment in Figure 1.5–10 is a 5-minute epoch from a patient with congestive heart failure; it shows 
A. Obstructive sleep apnea
B. Complex sleep apnea
C. Cheyne-Stokes breathing
D. None of the above

**FIGURE 1.5–10** Question 42. (From ATLAS2, Fig. 19–44)
43. A new sleep technologist is concerned about PSG abnormalities in the epoch in Figure 1.5–11. What do the EEG channels show?
   A. The patient is having a seizure
   B. The patient is in stage 2 NREM sleep (stage N2)
   C. The patient is in NREM slow-wave sleep (stage N3)
   D. The patient is in REM sleep (stage R)

44. What breathing pattern abnormalities are present in Figure 1.5–11?
   A. The abnormalities are too short to be scored
   B. The start of the epoch shows a central apnea, and the end shows an obstructive apnea
   C. The start of the epoch shows an obstructive apnea, and the end shows a hypopnea
   D. Two hypopneas are shown

45. Figure 1.5–12 is a 10-minute epoch from a PSG. What is shown by the information in the box and oval?
   A. RERA
   B. Hypopnea
   C. Obstructive apnea
   D. Central apnea

46. Figure 1.5–13 is a 10-minute epoch from a PSG. What is the most likely abnormality shown?
   A. Mixed apnea
   B. Hypopnea
   C. Obstructive apnea
   D. Central apnea
Questions 47 and 48 refer to the following five epochs numbered 345 through 349.

345: Contains a spindle and a K complex
346: Major body movements for 20 seconds; the other 10 seconds contain alpha rhythm
347: Contains a spindle
348: Major body movements for 18 seconds; no alpha rhythm seen
349: Contains a K complex
47. How should you score epoch 346?
   A. W
   B. N1
   C. N2
   D. N3

48. How should you score epoch 348?
   A. W
   B. N1
   C. N2
   D. N3

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**ANSWERS**

1. **B.** The 10-20 method of EEG electrode placement was developed in 1958. Percentages are used, rather than absolute distances, to allow for normal variations in head shape and size. Figure 1.5–14 shows the 10-20 placement of electrodes. For example, T3 is placed 10% of the distance from M1 to M2, C3 is placed 20% of the distance from T3, CZ is 50% of the distance from M1 or M2, and C4 is 20% of the distance from CZ. Other electrodes are similarly placed 10% to 20% of the distance from the inion or nasion or points in between. Older nomenclature labeled M1 and M2 (mastoid) as A1 and A2 (auricular), respectively. The new nomenclature is promulgated in MANUAL2.

2. **A.** The recommended derivations are frontal right (F4)–mastoid left (M1), central right (C4)–mastoid left (M1), and occipital right (O2)–mastoid left (M1; see Fig. 1.5–14). Answers B and C have frontal, central, and occipital electrodes connected to the same-side mastoid electrode, which is not recommended. Answer D has only two derivations; at least three are recommended. When the electrode set in Answer A is used, back-up electrodes (in case of malfunction) are recommended at F3, C3, O1, and M2 to allow display of F3-M2, C3-M2, and O1-M2. (MANUAL2)

3. **A.** Both eyes are referenced to the right mastoid electrode, M2. (MANUAL2)

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**FIGURE 1.5–14** Answers 1 and 2. (From ATLAS2, Fig. 18–2)
4. A. The cornea is electrically positive with respect to the retina. When eye movements occur, the EOG channel tracing shows the movements because of this electrical difference. Thus, a rightward movement of the right eye causes the cornea of the right eye to move closer to the recording electrode, which is the right outer canthus (ROC); this movement generates a positive voltage (the pen moves downward by convention, as shown in E2-M1 of the PSG epoch in Fig. 1.5–15). At the same time, the cornea of the left eye moves away from the left outer canthus (LOC), and this generates a negative voltage (the digital tracing moves upward by convention; E1-M2 in the epoch). The EOG tracings show two separate instances of rapid eye movement (red boxes). In both instances, the eyes move conjugately toward the ROC electrode.

5. C. The standard EMG derivation for sleep staging requires a chin electrode placed 1 cm above the inferior edge of the mandible. That electrode is referenced to a second electrode placed 2 cm below the inferior edge and either 2 cm to the right or left of midline. (If referenced to the right, a left-side electrode is placed as a backup and vice versa.)

6. D. EEG patterns are distinguishable by frequency, amplitude, shape, and distribution (e.g., occipital, frontal). A sinusoidal or waxing and waning pattern over 5 seconds or more may be artifact, and in any case, it does not help in interpreting the EEG.

7. B. Wakefulness, REM sleep, and NREM sleep are considered three distinct states of the CNS, and a normal subject goes through all three in a given 24-hour period.

8. B. EEG, EOG, and EMG activity are essential for sleep staging. In a standard PSG, they require (as minimum) three derivations for EEG activity (six electrodes), one derivation for chin EMG activity (two electrodes), and two derivations for eye movements (four electrodes). Back-up electrodes are in addition to these minimum requirements.

9. B. Beta waves, which have a frequency greater than 13 Hz, are not used in the classification or diagnosis of sleep stages W, N1, N2, N3, or REM.

10. A. Stage N2 sleep is characterized by sleep spindles or K complexes, not by the baseline EEG. Previously defined as stages 3 and 4 NREM sleep, they are now combined into a single N3 stage, characterized by large-amplitude slow waves (<2 Hz) that occupy at least 20% of the epoch. The term “low voltage, mixed frequency” is also characteristic of REM sleep (now called stage R), which must also have rapid eye movements and/or low-voltage EMG on the chin channel. (MANUAL2)
11. B. For scoring stage N3, slow waves must occupy 20% or more of the epoch, meeting the definition as stated. (MANUAL2)

12. D. Since the AASM’s 2007 revision of the classic 1968 sleep-stage scoring manual by Allan Rechtschaffen and Anthony Kales, NREM stages 3 and 4 have been combined into a single stage, N3. A PSG epoch is scored as stage N3 if it includes 20% or more of slow-wave activity (26 seconds for a 30-second epoch). Slow waves are defined as waves of 0.5 to 2.0 Hz and peak-to-peak amplitude greater than 75 µV, measured over the frontal region. (Note that for purposes of staging N3, slow waves represent a subset of delta activity, defined as EEG waves with a frequency of less than 4 Hz.)

13. A. The AASM manual states, “Score arousal during sleep stages N1, N2, N3, or R if there is an abrupt shift of EEG frequency including alpha, theta, and/or frequencies greater than 16 Hz (but not spindles) that lasts at least 3 seconds, with at least 10 seconds of stable sleep preceding the change. Scoring of arousal during REM requires a concurrent increase in submental EMG lasting at least 1 second.” Both occipital and central derivations are to be incorporated when scoring arousals. The AASM manual also notes that scoring an arousal does not require (and cannot be based on) other information such as body movements or respiratory events. (MANUAL2)

14. C. The background EEG activity for REM is a relatively low-voltage, mixed-frequency pattern, but alpha bursts routinely appear and do not necessarily indicate arousals or any pathology. The digital sampling rate for both EEG and EMG is the same: 500 Hz is desirable, and 200 Hz is minimal. (MANUAL2)

15. A. In this 30-second epoch (see Fig. 1.5–1), the distance between the solid vertical lines is 3 seconds. In the first 13 seconds, alpha rhythm (8–13 Hz) is seen, so this part is an awake stage. Then there is an abrupt change to low amplitude and mixed frequency with predominance of theta waves (4–7 Hz) plus slow, rolling eye movements (leads E2-M1 and E1-M2), characteristic of stage N1. There are no spindles or K complexes, so you cannot score N2. Finally, the lack of rapid eye movements and the relatively large-amplitude chin EMG rule against REM sleep. Because more than half the epoch is stage N1, the epoch should be scored as N1.

16. A. This fragment (see Fig. 1.5–2) shows 60-Hz interference. The inset shows 1 second of a single EEG channel. The cause in this example is lead A2 because the artifact was found in all channels that included this lead. ECG artifact usually manifests as the ECG in some other channel. Because heart rate is normally 60 to 100 beats/min, it should not be mistaken for an artifact that is 60 cycles per second. Perspiration artifact is a slow, rhythmic waveform that often coincides with breathing. The best way to avoid 60-Hz artifact is to make sure all electrodes are properly applied and that there are no nearby electrical devices that might leak current. Ideally, a 60-Hz filter should not be necessary.

17. D. EEG, EOG, ECG, and EMG appear as rapidly fluctuating voltages within a specific frequency bandwidth, and they require the use of both high- and low-frequency filters that are part of AC amplifiers. On the other hand, some signals are slowly fluctuating and can be picked up by DC amplifiers that do not require a low-frequency filter; examples are pulse oximetry and respiratory rate. Respiratory rate can also be amplified by an AC amplifier whose low-frequency filter is set to 0.1 Hz (the high-frequency filter is set to 15 Hz). (Butkov and Lee-Chiong, 2007; MANUAL2)

18. D. If a K complex appears in any epoch without an accompanying arousal, that epoch is scored as N2. All subsequent epochs with low amplitude and mixed frequency are scored as N2 even if they do not manifest a K complex or spindle unless they contain an arousal or meet criteria for stage N3 or REM. (MANUAL2)
19. **A.** The K complex is a well-delineated negative sharp wave (upward deflection) immediately followed by a positive component (downward deflection) standing out from the background, with total duration of at least 0.5 second. Amplitude is not a criterion. Note that none of the waves in Figure 1.5–3 reaches 75 µV in peak-to-peak amplitude, the criterion for slow waves. The four large waves in the first 3 seconds are all K complexes. A vertex sharp wave is a sharply contoured, negative deflection (upward on EEG) that stands out from the background; vertex waves appear most often in central leads placed near the midline and are characteristically seen in stage N1. Slow waves have high amplitude (at least 75 µV) and low frequency (no more than 2 Hz), are a subset of delta (1 to 4 Hz) activity, and are the defining characteristics of stage N3 sleep.

20. **B.** Slow waves. Note the high peak-to-peak amplitude (≥75 µV) and low frequency (≤2 Hz). Slow waves are a subset of delta (1–4 Hz) activity and are the defining characteristics of stage N3 sleep. See the answer to Question 19 for discussion of the K complex. K complexes are at least 0.5 second, and amplitude is not a criterion.

21. **D.** Different sensors are recommended for scoring apneas versus hypopneas. For apnea detection, a thermal sensor (thermistor or thermocouple) is recommended. Thermal sensors detect changes in air temperature, which reflect airflow. Cooler air (room temperature) is inhaled, and warmer air (body temperature) is exhaled, and this change is transduced to a deflection in the thermal airflow channel. An apnea is defined as a drop in the peak thermal sensor excursion by at least 90% of baseline. A nasal pressure transducer is more sensitive than a thermistor or thermocouple, and it can better detect hypopneas. (MANUAL2)

22. **D.** The AASM manual states: “Score a respiratory event as an apnea when BOTH of the following criteria are met:
   a. There is a drop in the peak signal excursion by ≥90% of pre-event baseline using an oro-nasal thermal sensor (diagnostic study), PAP device flow (titration study), or an alternative apnea sensor (diagnostic study).
   b. The duration of the ≥90% drop in sensor signal is ≥10 seconds.”
Drop in SaO2 is not a criterion for scoring apneas (Fig. 1.5–16).

23. **B.** The AASM manual has two criteria for scoring a hypopnea, Rules 1A and 1B. Both require a 30% or more drop of peak signal excursions compared with baseline and a duration of 10 or more seconds. 1A also requires a 3% or more drop in SaO2 from pre-event baseline or the event is associated with an arousal. 1B requires a 4% or more drop in SaO2 from pre-event baseline and no arousal. The two rules are mutually exclusive when scoring a single study; that is, you can use one or the other, but not both, in the same study. (MANUAL2)

24. **B.** Panel B also shows a hypopnea by Rule 1B: a 30% drop in peak signal excursion for at least 10 seconds plus an arousal (seen in EEG leads). Note that SaO2 did not drop.
25. **E.** Not part of the awake stage, a K complex is instead a criterion for stage N2. The AASM manual lists five criteria for scoring the awake stage:

- **Alpha rhythm:** Trains of sinusoidal 8- to 13-Hz activity recorded over the occipital region with eye closure, attenuating with eye opening
- **Eye blinks:** Conjugate vertical eye movements at a frequency of 0.5 to 2 Hz present in wakefulness with the eyes open or closed
- **Reading eye movements:** Trains of conjugate eye movements consisting of a slow phase followed by a rapid phase in the opposite direction as the individual reads
- **REMs:** Conjugate, irregular, sharply peaked eye movements with an initial deflection usually lasting less than 500 ms. Although REMs are characteristic of stage R sleep, they may also be seen in wakefulness with eyes open when individuals scan the environment.
- **Slow eye movements (SEMs):** Conjugate, reasonably regular, sinusoidal eye movements with an initial deflection usually lasting longer than 500 ms.

26. **D.** Adults have less SWS compared with children. Figure 1.5–17 shows a typical hypnogram from a young adult. SWS continues to decrease with age. For people aged 20 to 29 years, SWS occupies about 15.5% of sleep time; for those older than 60 years, about 5% of sleep time is SWS. SWS represents the most dramatic change in sleep stage from childhood to old age. Other changes include a decline in REM and an increase in WASO. These changes are shown graphically in Figure 1.5–18. (Pressman, 2002, Ch 1)

27. **A.** “Deep sleep” refers to stage N3 because the arousal threshold is highest in this stage of sleep. Stage N3 concentrates in the first part of the sleep cycle. WASO increases with age, ranging from about 3% in young adults to about 11% in older adults. REM latency is defined as the time from sleep onset to the first epoch of REM; it is normally about 90 to 120 minutes. See Figure 1.5–18. (Pressman, 2002, Ch 1)
28. D. Most people show an EEG of rhythmic alpha activity (in the range of 8–13 Hz) when relaxed with the eyes closed. Alpha activity is maximal occipitally but also often occurs centrally. In the first third of the fragment in Figure 1.5–19, O2-M1 shows alpha activity in the first third followed by low-voltage mixed activity; this is the transition from wakefulness to stage N1. Note also the slow, rolling eye movements in E1-M2.

29. A. The epoch in Figure 1.5–7 shows several features typical of stage N1. Most prominent are the vertex sharp waves (V waves) in the last third of the epoch of channels F4-M1 and C4-M1. These V waves can be mistaken for K complexes if not measured; whereas they are less than 0.5 second in duration, K complexes are at least 0.5 second. Also note the characteristic mixed-voltage, low-frequency EEG (predominantly 4–7 Hz) and the large amount of chin EMG activity, both typical of N1.

30. D. The transition to sleep is associated with attenuation of alpha rhythm that is replaced by low-amplitude, mixed-frequency activity. Alpha rhythm is strongest over the occipital lobes, and it does not change to the frontal lobes when sleep occurs. Slow, rolling eye movements; a 4- to 7-Hz EEG; and vertex sharp waves are often seen in stage N1. (MANUAL2)

31. B. The epoch is scored N1 because the majority of the epoch has a frequency of 7 Hz, which falls into the criteria for N1. (MANUAL2)

32. B. Stage N2 can be scored when one or more K complexes are unassociated with arousals. Stage N2 is concluded when an arousal takes place or a transition to wakefulness, a major body movement, a transition to N3, or a transition to REM occurs. Therefore, when the K complex is identified in the first epoch, the second epoch is scored N2 until one of these scenarios takes place. (MANUAL2)

33. A. Sleep onset is defined as the start of the first epoch scored as any stage other than wakefulness. (MANUAL2)

34. B. Onset of REM is measured from the onset of sleep to the beginning of the first REM epoch.
35. D. An EEG pattern of alpha intrusion into NREM sleep was first noted in patients with psychiatric disorders. The pattern was described as a mixture of 5% to 20% delta waves (>75 µV, 0.5–2 Hz) combined with relatively large amplitude, alphalike rhythms (7 to 10 Hz). The alpha rhythms are usually 1 to 2 Hz slower than waking alpha. A similar pattern has been related to the complaint of nonrestorative sleep in patients with musculoskeletal pain or fibromyalgia. Although epochs with alpha-delta sleep are not scored as such (this epoch is N3), the EEG pattern should be noted in the PSG report.

36. A. SEMs are conjugate, reasonably regular, and sinusoidal with an initial deflection that usually lasts longer than 500 ms. They are characteristic of stage N1. Sleep spindles are characteristic of stage N2. Delta waves are seen in stage N3, and REMs of less than 500 ms are seen in the REM stage. (MANUAL2)

37. D. For detection of hypoventilation during a diagnostic study, you can use arterial, transcutaneous, or end-tidal PCO₂. You cannot use duration of apnea, no matter how long. (MANUAL2)

38. D. Figure 1.5–9 depicts 30 seconds of PSG activity characterizing stage N3 sleep; to score stage N3, at least 20% of the epoch must show slow-wave activity. (MANUAL2)

39. A. Note that these are arbitrary definitions and differ from the awake state, in which tachycardia (in adults) is usually defined as more than 100 beats/min and bradycardia as less than 60 beats/min. (MANUAL2)

40. D. To score epoch 281 as the end of stage R, the K complex would have to occur in the first half of the epoch. In this example, epoch 281 would be scored R, and the next epoch would be N2 unless it met criteria scoring for another stage. (MANUAL2)

41. B. One of the major differences in the sleep EEG of infants compared with older children and adults is that infants spend about twice as much time in REM sleep. (PEDS2, p 20)

42. C. The 5-minute epoch shows the typical waxing and waning (crescendo-decrescendo) of tidal volume seen in Cheyne-Stokes breathing. Note that the green airflow line is flat; this is because the airflow channel is measuring nasal flow, and the patient is mouth breathing. Note also that the PCO₂ channel is measuring end-tidal PCO₂ both orally and nasally, and thus it nicely displays the waxing and waning breathing pattern.

43. D. The most striking feature in Figure 1.5–11 is the synchronized activity (all the EEG channels change together) toward the end of the epoch (see the red box in Fig. 1.5–20). Close inspection of the waveforms (the green ovals in the figure) shows that some of the waves have notches; these are sawtooth waves (so called because they resemble teeth on a saw). The usual frequency of sawtooth waves is 2 to 6 Hz, so they can appear as theta waves (4–7 Hz). Sawtooth waves are characteristic of stage R, but they are not required to identify this stage.

44. C. The thermal sensor is used to define apnea (see the therm channel shown by the purple line in Fig. 1.5–20), and the pressure sensor (P Tah, above therm) is used to define a hypopnea. Hypopneas and apneas in adults are scored if the duration is 10 seconds or longer. Inductance plethysmography is used for the effort channels (or esophageal manometry, which is not used in clinical labs). Airflow and effort define the two types of apneas. In an obstructive apnea, there is respiratory effort. In a central apnea, respiratory effort is absent. A mixed event begins with central apnea features (no airflow, no respiratory effort) and ends with obstructive features (no airflow, respiratory effort present). Two sets of rules define hypopnea (see the answer to Question 23). (MANUAL2)

45. B. This 10-minute epoch shows the standard features of a hypopnea: reduction in airflow to at least 30% of baseline in the pressure transducer signal and a 4% or greater drop in SaO₂ (low SaO₂ = 86% in this epoch). Note the difference in the pressure transducer and thermal sensor channels. The former changes significantly (and makes the diagnosis possible); the latter changes very little. Whereas thermal sensors are used to monitor for apneas, pressure transducers are used to monitor for hypopneas. (MANUAL2)
46. B. Note the difference between the pressure channel and the flow (thermal) channel. The pressure channel shows almost complete flow cessation, but the thermal channel shows only a small decrease in flow. So is it an apnea or a hypopnea? It is not an apnea because the thermal flow channel does not show cessation of airflow. Can this be scored as a hypopnea because the decrease in SaO₂ is only 1%? (It requires at least a 3% drop.) Note that immediately after the decreased waveform in the pressure channel, a spike appears in the EEG channels; this is an arousal. (Also note the leg jerk in the leg channels.) You can score this event as a hypopnea because an arousal associated with a 30% or more drop in signal excursion meets the MANUAL2 criteria for hypopnea. Under D. Scoring of Hypopneas of the AASM manual, 1A.c states hypopnea can be scored if there is a ≥3% oxygen desaturation from preevent baseline or the event is associated with an arousal.

47. A. The rule states that if alpha rhythm is present for any part of the epoch with a “major body movement,” the epoch is scored as stage W. (MANUAL2)

48. C. The rule states that if alpha rhythm is not discernable in an epoch with major body movements, the epoch is scored the same stage as the epoch that follows it. In this case, epoch 349 contains a spindle and a K complex, which indicate stage N2; hence, N2 is also the score for epoch 348 (Boxes 1.5–1 and 1.5–2).
### Box 1.5–1 How to Examine a Polysomnogram on a Board Exam

**Step 1.** Look at the entire image. The most striking finding may be a distractor. In Figure 1.5–21, the most obvious finding is in the snoring channel, with loud snores. These may have nothing to do with the question (e.g., What is the sleep stage?). Always circle back to the question being asked. If at any point you can answer the question confidently without using the most obvious finding, you can ignore that finding.

**Step 2.** Make sure you have determined (or know from the question) what the epoch length is. A polysomnogram (PSG) can have a split screen with the top and bottom showing different lengths, as shown in Figure 1.5–22. In this fragment, the top is 30 seconds, and the bottom is 2 minutes.

**Step 3.** Examine the channels recorded in the montage. This will be the first clue about what type of study is being shown. It is clear from examining the montage that this study is being done on continuous positive airway pressure (CPAP) and is therefore not solely a diagnostic study (Fig. 1.5–23).

**Step 4.** Examine the scales of the quantitative channels. In Figure 1.5–24, we see the patient is on CPAP (pressure is 19 cm H₂O) and oxygenation is adequate (SaO₂ = 99%).

**Step 5.** Look for artifacts and distractors. In Figure 1.5–25, the PTAF and THERM are flat because they are not being recorded (this is a CPAP study, and the pressure level from the CPAP machine is being recorded). At this point, you actually know enough to answer the question being asked. There are, of course, artifacts (electrocardiograph [ECG] in the chin and electroencephalograph [EEG] channels) and other interesting findings, but do not waste your time on them because you have already answered the question.

**Step 6.** As a final step, you might have to look for a specific finding to answer the question. In this example (Fig. 1.5–26), you see a flattening of the C-flow (flow measured by the CPAP machine) and snoring noise, both indicating flow limitation, which answers the question.

**Step 7.** In the real world, when you interpret a PSG, you will go through the history, the tech notes, and steps 1 through 6 and then look at other channels (legs, EEG, ECG) for abnormalities.

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**FIGURE 1.5–21** Step 1.
FIGURE 1.5-22 Step 2.

FIGURE 1.5-23 Step 3.
FIGURE 1.5–24 Step 4.

FIGURE 1.5–25 Step 5.
Section 1 / Normal Sleep and Its Variants

Step 1. Three features define rapid eye movement (REM) sleep, or stage R. The first is the presence of a low-amplitude, mixed-frequency pattern in the electroencephalography (EEG) channels (red rectangle, Fig. 1.5–27). This is nonspecific and can also be found in stage N1.

Step 2. Second is low or absent chin electromyography (EMG) tone (red rectangle, Fig. 1.5–28).

Step 3. Third is REMs. REMs are often sharply peaked, with the initial deflection being less than 0.5 second (red boxes, Fig. 1.5–29).

Step 4. Look for other features of REM that are not required for staging. Sawtooth waves are found exclusively in REM; these are notch waves and can be seen in the EEG channels.
- There may also be short (<0.25 second) twitches or transient muscle activity noted in the chin and leg EMGs.
- Breathing may become irregular in normal subjects and in patients with Cheyne-Stokes breathing. Cardiac rhythm may become erratic.

Step 5. Look for continuation of REM. After REM is scored in an epoch, it continues to be scored in subsequent epochs, even when eye movements are not seen if chin tone remains low, EEG continues to show mixed frequency, and there are no K complexes or sleep spindles.

Step 6. Look for the end of REM. REM is no longer scored if another stage is scored. K complexes or sleep spindles mean stage N2 is present. An arousal followed by slow eye movements means stage N1 is present. (Specific rules for continuing and ending REM scoring are provided in MANUAL2, pp 26–30.)

**Box 1.5–2 Six Steps in Determining the Rapid Eye Movement Stage (Stage R)**

FIGURE 1.5–26 Step 6.
**Figure 1.5-27** Step 1.

**Figure 1.5-28** Step 2.
Summary

**Highly Recommended**

- *Atlas of Clinical Sleep Medicine*, ed 2, Ch 18

Your knowledge of methods, rules, and event scoring will be addressed throughout the exam in a variety of questions. Sleep staging dovetails with event rules, so some overlap occurs; you cannot stage the PSG unless you can identify common waveforms, such as alpha rhythm, K complexes, and slow-wave sleep. Expect many questions on the examination that require knowledge of sleep staging.

You must know in detail the AASM rules for scoring and staging published in version 2.5 and now updated online.

**Polysomnography Methods**

- 10–20 EEG electrode placement
  - Recommended derivations: F4-M1, C4-M1, and O2-M1
  - Alternative derivations: Fz-Cz, Cz-Oz, and C4-M1
- EOG placement
  - Where the electrodes are placed (outer canthi)
    - Both eyes are referenced to M2.
  - Source of voltage for recording EOG
    - Cornea is electrically positive with respect to the retina
  - When right and left eyes move toward the right electrode
    - Positive voltage in right EOG (E2-M2), pen moves downward by convention
    - Negative voltage in left EOG (E1-M2), pen moves upward by convention
- EMG placement
  - Chin EMG for stage scoring
    - Chin electrode 1 cm above the inferior edge of the mandible
    - Reference electrode 2 cm below the inferior edge and either 2 cm to the right or left of midline
Leg EMG for leg movements
- Anterior tibialis muscle, electrodes 2 to 3 cm apart
Inductance plethysmography for chest and abdominal movement (not piezoelectric belts)
Nasal and oral thermistor and nasal pressure sensor
- Thermistor for apneas
- Nasal pressure sensor for hypopneas

Rules and Event Scoring

- Epoch length
  - Standard is 30 seconds, but longer epochs are often used to display breathing events
- PSG display
  - To display the raw data for scoring on a screen, the AASM recommends a 15-inch screen size, 1600 pixels horizontal, and 1050 pixels vertical
  - Be aware of channel labeling; always check labeling of derivations when looking at the EEG
  - Alpha rhythm is more prominent in occipital derivations
  - Slow waves and K complexes are more prominent in frontal derivations
  - Spindles are more prominent with central derivations
- EEG and EOG waveforms
  - K complex (Fig. 1.5–30)
    - Well-delineated negative sharp wave (upward deflection by convention) immediately followed by a positive component that stands out from the background EEG
    - Total duration, 0.5 seconds or longer
    - Usually maximal over the frontal regions
  - Slow waves (Fig. 1.5–31)
    - High amplitude ($\geq 75 \mu V$) and low frequency ($\leq 2$ Hz)
    - Subset of delta (1 to 4 Hz) activity
    - Defining characteristics of stage N3
  - Alpha activity (Fig. 1.5–32)
    - 8- to 13-Hz rhythm
    - Most prominent in occipital leads
    - Thought to be generated by the cortex
    - Used as marker for relaxed wakefulness and CNS arousals

FIGURE 1.5–30 K complex. (From ATLAS2, Table 18–2)

FIGURE 1.5–31 Slow waves. (From ATLAS2, Table 18–2)

FIGURE 1.5–32 Alpha activity. (From ATLAS2, Table 18–2)
Theta activity (Fig. 1.5–33)
- 4 to 7 Hz
- Typically prominent in central and temporal leads
- Seen in both stage N1 and REM sleep
- Sawtooth waves in this range

Rapid eye movement (Fig. 1.5–34)
- Conjugate saccades that occur during stage R (REM sleep)
- Sharply peaked with initial deflection usually less than 0.5 seconds in duration

Slow eye movements (Fig. 1.5–35)
- Conjugate, usually rhythmic, rolling eye movements with initial deflection more than 0.5 seconds in duration
- Typically in stage N1

Vertex sharp waves (Fig. 1.5–36)
- Sharply contoured, negative deflection (upward on EEG) that stands out from the background
- Most often in central leads placed near the midline
- Characteristically seen in stage N1

Sleep spindle (Fig. 1.5–37)
- Phasic burst of 11- to 16-Hz activity
- Prominent in central scalp leads
- Typically lasts for 0.5 to 1.0 seconds
- Scalp representation of thalamocortical discharges
Rules for Scoring Sleep

- Sleep staging rules for adults (MANUAL2, section IV, part 1)
  - Stages of sleep
    - Stage W
      - Alpha rhythm (8–13 Hz) with eyes closed
      - Eye blinks
      - Reading eye movements
      - Rapid eye movements on occasion (when scanning environment)
    - Stage N1
      - Slow eye movements
      - Alpha rhythm is attenuated, replaced by low-amplitude, mixed-frequency rhythm
      - Vertex waves
    - Stage N2
      - K complex: negative sharp wave followed by a positive component; total duration, 0.5 seconds or longer
      - Sleep spindles: train of distinct waves 11 to 16 Hz; duration, 0.5 seconds or longer
    - Stage N3
      - Slow waves (0.5–2.0 Hz; peak to peak >75 Hz measured over frontal regions) occupy 20% or more of epoch
    - Stage R
      - REMs
      - Low chin EMG
      - Sawtooth waves
  - Artifacts
    - 60-Hz interference (60-Hz filter last resort)
    - Sweat artifact
    - ECG artifacts (can appear in any channel)
  - Arousals
    - Abrupt shift in EEG frequency that lasts at least 3 seconds, with at least 10 seconds of stable sleep preceding

Rules for Scoring Abnormal Events

- Cardiac rules (MANUAL2)
  - Sinus tachycardia (in adults): more than 90 beats/min
  - Sinus bradycardia (age 6 years through adult): less than 40 beats/min
  - Asystole (age 6 years to adult): longer than 3 seconds between heartbeats
  - Wide-complex tachycardia
  - Narrow-complex tachycardia
- Periodic limb movements
  - Minimum number of consecutive movements is four
  - Minimum period length between movements is 5 seconds
  - Maximum period length between movements is 90 seconds
  - Movements on two different legs separated by less than 5 seconds are counted as a single leg movement
- Movement rules (MANUAL2, section VII)
  - Movement time no longer scored
  - Major body movement (MBM)
- Movement and muscle artifact obscuring EEG more than half of the epoch to the extent that stage cannot be determined
  - Score epoch with MBM as W, N1, N2, N3, or REM
    - If alpha rhythm is seen in any part of the epoch with MBM, score as W
    - Otherwise, if the epoch before or after is W, score the epoch with MBM as W
    - Otherwise, score the epoch the same stage as the epoch after the MBM
Respiratory rules in adults (MANUAL2, section VIII)

- **Apnea criteria**
  - Use the thermistor channel to document
  - Score when there is at least a 90% decrease in thermistor flow for at least 9 seconds of a 10-second apnea (see the answer to Question 22)

- **Hypopnea criteria; two different rules: 1A and 1B**
  - 1A. Score a respiratory event as a hypopnea if **all** of the following criteria are met:
    - The peak signal excursions drop by 30% or greater of pre-event baseline using nasal pressure (diagnostic study), PAP device flow (titration study), or an alternative hypopnea sensor (diagnostic study)
    - The duration of the 30% or greater drop in signal excursion is 10 seconds or more
    - A 3% or greater oxygen desaturation from pre-event baseline occurs or the event is associated with an arousal
  - 1B. Score a respiratory event as a hypopnea if **all** of the following criteria are met:
    - The peak signal excursions drop by 30% or greater of pre-event baseline using nasal pressure (diagnostic study), PAP device flow (titration study), or an alternative hypopnea sensor (diagnostic study)
    - The duration of the 30% or greater drop in signal excursion is 10 seconds or more
    - A 4% or greater oxygen desaturation from pre-event baseline occurs

- **RERA criteria (MANUAL2)**
  - If electing to score RERAs, score a respiratory event as a RERA if a sequence of breaths lasts 10 or more seconds and is characterized by increasing respiratory effort or by flattening of the inspiratory portion of the nasal pressure (diagnostic study) or PAP device flow (titration study) waveform, leading to arousal from sleep; the event is a RERA when the sequence of breaths does not meet criteria for an apnea or hypopnea
  - RERAs are an “option” for scoring (i.e., not recommended)
  - RERAs are added to the apnea/hypopnea index (AHI) to determine respiratory disturbance index (RDI)

- **Hypoventilation (MANUAL2)**
  - Score hypoventilation during sleep if **either** of the following occurs:
    - Arterial $P_{cO_2}$ (or surrogate) increases to a value greater than 55 mm Hg for 10 or more minutes
    - An increase of greater than or equal to 10 mm Hg in arterial $P_{cO_2}$ (or surrogate) occurs during sleep (compared with an awake supine value) to a value that exceeds 50 mm Hg for 10 or more minutes

Respiratory rules in children (MANUAL2)

- **Apnea criteria**
  - Event lasts for at least two missed breaths
  - A 90% fall in signal amplitude occurs for 90% of the respiratory cycle compared with baseline
  - Continued respiratory effort occurs throughout the period of decreased airflow

- **Hypopnea criteria**
  - At least 50% fall in nasal pressure signal **and**
  - Lasts for at least two missed breaths **and**
  - Fall in nasal pressure must last for at least 90% of the hypopnea duration **and**
  - The event is associated with arousal, awakening, or at least 3% $O_2$ desaturation

- **Hypoventilation criteria**
  - Properly calibrated and validated end-tidal $PcO_2$ or transcutaneous $PcO_2$ monitoring are acceptable surrogates for following $PacO_2$
  - If end-tidal CO$_2$ is used, it is crucial to obtain the plateau in waveform
  - Score hypoventilation if $PcO_2$ is less than 50 mm Hg for more than 25% of the sleep time (Box 1.5–3)
Box 1.5–3 Don’t Forget

- The cornea is electrically positive with respect to the retina. When eye movements occur, the electrooculogram (EOG) channel tracing shows the movements because of this electrical difference
- The standard electromyogram (EMG) derivation for sleep staging requires a chin EMG. This is used for scoring REM sleep (low amplitude during REM). In contrast, leg EMGs are used to score leg movements
- Electroencephalogram (EEG) patterns are distinguishable by frequency, amplitude, shape, and distribution (e.g., occipital, central, frontal)
- Wakefulness, non-REM (NREM) sleep, and REM sleep are considered three distinct states of the central nervous system, and the normal subject goes through all three during a sleep study. These states are distinguishable on the PSG by just three sets of derivations: EEG, EOG, and chin EMG
- In a typical sleep study, EEG uses three derivations (F4-M1, C4-M1, and O2-M1), EOG uses two derivations (E1-M2 and E2-M2), and chin EMG uses one derivation. Each derivation involves two electrodes: the recording electrode and the reference electrode
- Staging of sleep is based on a set of well-defined rules outlined in this section and detailed in the AASM manual (MANUAL2; see References). Full knowledge of this manual is a must for the exam
- Apnea is scored when there is a ≥90% decrease in thermistor flow for ≥9 seconds of a 10-second apnea (see answer to Question 22 for clarification of this often confusing point)
- Hypopnea: There are two sets of definitions (see earlier under Respiratory rules in adults)
- Apnea-hypopnea index (AHI) includes all apneas plus hypopneas, with the latter scored by either the recommended or alternative methods; you cannot use both to determine any patient’s AHI. The level of AHI is then used to determine the severity of a sleep apnea (could be obstructive and/or central sleep apnea). Medicare criteria for reimbursement of CPAP is based on the AHI and clinical features
- Scoring of respiratory effort–related arousals (RERAs) is optional. Some labs include RERAs in the respiratory disturbance index (RDI), which is therefore more inclusive than the AHI. However, sometimes labs use RDI interchangeably with AHI. AHI and RDI should not be reported without defining how they are derived
- Medicare (CMS) uses the term RDI in its CPAP Decision Memo but does not define it. Many sleep specialists think that CMS meant RDI to be synonymous with AHI
- Flattening on a nasal pressure channel or a CPAP flow channel indicates flow limitation. If there is also amplitude reduction with a requisite drop in SaO2, hypopnea can be scored. Otherwise, it might represent a RERA. If flattening occurs in a CPAP flow channel, it usually indicates a need for an increase in pressure
- End-tidal or transcutaneous CO2 monitoring is recommended to diagnose hypoventilation in children but not in adults
- Two sets of rules are used to define hypopnea: recommended and alternative. Criteria in either set must be met to score hypopneas in a PSG; they cannot be mixed in a given study. (MANUAL2, p 59)

Sleep Staging

- EEG, EOG, and EMG activity is essential for sleep staging.
  - Standard PSG
    - Three derivations for EEG (six electrodes)
    - One derivation for chin EMG activity (two electrodes)
    - Two derivations for eye movements (four electrodes)
    - Back-up electrodes are in addition to these minimum requirements.
- The natural progression from wakefulness to REM
  - Wakefulness
    - About 5% of the sleep period (WASO) in adults; increases with age
    - Alpha rhythm, eye blinks
  - Stage N1
    - Occupies about 4% to 5% of sleep time in adults
    - Attenuation of alpha rhythm
    - Replaced by low-amplitude, mixed-frequency activity in more than 50% of the epoch
    - Vertex waves
  - Stage N2
    - Occupies about 50% of sleep time in adults
    - Either of the following in the first half of the epoch or in the last half of the previous epoch:
      - K complexes
      - Sleep spindles
  - Stage N3
    - Percentage of N3 declines with age: about 15.5% in young adults, down to about 5% in persons older than 60 years
    - Slow waves (0.5–2.0 Hz peak-to-peak amplitude >75 µV) occupy 20% or more of the epoch
Section 1 / Normal Sleep and Its Variants

- Stage R
  - Occupies about 25% of sleep time in adults
  - Rapid eye movements
  - Low chin EMG
  - Low voltage, mixed frequency (often with sawtooth waves, although not needed for scoring REM)

Changes in sleep stages with aging, childhood to old age (ATLAS2, Fig. 4.2–23)
- Increase in WASO
- Not much change in N1
- Some decrease in REM sleep
- Not much change in N2
- Marked decrease in N3
  - This is the most striking change among all sleep stages
  - In addition to having more N3 sleep, children have slow waves with a very high amplitude compared with adults
  - In children, the other stages more closely resemble those of adults

Continuation rules
- N2 continues if subsequent epochs show low amplitude, mixed frequency without K complexes or sleep spindles
- N2 ends with an arousal or with transition to stage W, N3, or R or with a major body movement followed by SEMs. (MANUAL2)
- R continues if EEG continues to show low-amplitude, mixed-frequency activity without K complexes or sleep spindles, and chin EMG tone remains low
- R ends. (MANUAL2)
- Epochs are at transition between N2 and R. (MANUAL2)

Major body movement (MBM)
- Epochs are scored with MBM based on:
  - Alpha-rhythm part of epoch: score as W
  - No alpha rhythm: W before or after, score epoch with MBM as W
  - Otherwise, score same stage as epoch that follows
- Pediatric scoring has some differences compared with adults (MANUAL2)

Alpha-delta sleep
- Alpha portion usually 1 to 2 Hz slower than waking alpha
  - Often seen in patients with fibromyalgia or musculoskeletal pain
  - May be associated with nonrestorative sleep (Box 1.5–4)

Box 1.5–4 Don’t Forget

- Attenuation of alpha sleep into a low-amplitude, mixed-frequency sleep is a hallmark of transition from W to N1. However, alpha sleep is not always present in humans, and the AASM has specific rules for scoring the transition to sleep in such situations (see MANUAL2)
- Alpha rhythm is present most prominently over the occipital lobe, delta waves and K complexes are present most prominently over the frontal lobes, and sleep spindles are most prominent over the center of the brain
- Normally, there is progression of rapid eye movements (REMs) throughout the sleep cycle, manifesting as three or four discrete REM periods, each progressively longer
- REMs help define stage R, where they are accompanied by a low-amplitude chin electroencephalography (EEG). However, they may also be seen in stage W, as patients scan the room or read a book; in this case, chin electromyography is very active
- Slow, rolling eye movements are seen in stage N1, and they help to define the transition from W to N1
- One of the major differences in the sleep EEG of infants compared with older children and adults is that newborn infants spend about 50% of total sleep time in REM sleep
- Sawtooth waves are characteristic of stage R, but they are not required to identify it
- The thermal sensor is used to define apnea. The nasal pressure sensor is used to define hypopneas
- If alpha rhythm is present for any part of the epoch with a major body movement, score the epoch as stage W
REFERENCES


1. Where is the main site of rapid eye movement (REM) sleep generation?
   A. Cerebellum
   B. Pons
   C. Spinal cord
   D. Medulla oblongata

   ANSWER: B. The pontine tegmentum includes the pedunculopontine nucleus and the laterodorsal tegmental nucleus. These cholinergic neurons (located near the raphe nucleus and the locus coeruleus) are involved in the initiation of REM sleep. (ATLAS2, p 30)

2. Which statement about REM sleep is TRUE?
   A. It is found only in humans
   B. It is found in almost all mammals
   C. It is absent in birds.
   D. It is absent in mammals before birth

   ANSWER: B. Although it was once believed that certain species do not have sleep or REM sleep (e.g., sea mammals, the platypus), every mammal that has been studied rigorously sleeps and has REM sleep. Indeed, sleep may be occurring in localized parts of the brain at the same time that parts of the brain are awake.

3. Nuclei in what part of the nervous system are involved in the suppression of muscle tone in stage R?
   A. Noradrenergic neurons in the locus coeruleus
   B. Histaminergic neurons of the tuberomammillary nucleus
   C. Orexin neurons projecting to the basal forebrain
   D. Ventral sublaterodorsal nucleus

   ANSWER: D. The first three answers describe neurons involved in cortical arousal. Remember that noradrenergic, histaminergic (antihistamines make you sleepy), and orexin (whose deficiency causes sleepiness in narcolepsy) are involved in arousal. The glycinergic and GABAergic neurons of the sublaterodorsal nuclei inhibit the spinal motor nuclei, causing the paralysis of stage R. (ATLAS2, p 33)

4. Sleep is thought to be associated with an increase in basal forebrain and anterior hypothalamic __________ activity and a decrease in posterior hypothalamic __________ activity.
   A. Adenosine/GABAergic
   B. GABAergic/adenosine
   C. Adenosine/hypocretin
   D. Adenosine/acetylcholinergic

   ANSWER: C. The correct answer can be deduced by knowing that adenosine accumulates during wakefulness and is thought to lead to sleepiness and that low hypocretin is found in narcolepsy, a disease in which the main symptom is sleepiness. (ATLAS2, pp 24–25)
5. Arousal, or wakefulness, is associated with a decreased activity in the ___________ and an increased activity in the ___________.
   A. Anterior hypothalamus/thalamus
   B. Anterior hypothalamus/basal forebrain
   C. Basal forebrain/posterior hypothalamus
   D. Anterior hypothalamus/posterior hypothalamus

   ANSWER: D. Because the structures that induce sleep are in the anterior hypothalamus (e.g., the ventrolateral preoptic nucleus [VLPO]), it seems reasonable that decreased activity here would be associated with arousal. Similarly, knowing that mammillary bodies (in the posterior hypothalamus) are histaminergic and that antihistamines cause sleepiness would lead to the inference that increased activity here would be associated with arousal. (ATLAS2, pp 28–30)

6. Arousal is dependent on subcortical activation of cortical pathways and includes all of the following except
   A. Posterior hypothalamus
   B. Suprachiasmatic nucleus
   C. Pedunculopontine nucleus
   D. VLPO

   ANSWER: D. The VLPO is part of the sleep switch and thus does not play a role in causing arousal. The VLPO inhibits arousal by having projections that inhibit the histaminergic (alerting) neurons of the mammillary bodies. (ATLAS2, p 28)

7. The reticular activating system (RAS) provides ascending projections to thalamic and cortical areas and includes the following neurotransmitters except
   A. Acetylcholine
   B. Serotonin
   C. Norepinephrine
   D. Gamma-aminobutyric acid (GABA)

   ANSWER: D. Because GABA is the main inhibitory neurotransmitter in the brain, it is logical that it would not be a neurotransmitter involved in arousal. (ATLAS2, p 24)

8. REM sleep is associated with mixed-frequency, low-amplitude electroencephalogram (EEG) waveforms and rapid eye movements, which are all generated by ___________ neurons in the ___________.
   A. Acetylcholinergic/substantia nigra
   B. Dopaminergic/substantia nigra
   C. Acetylcholine/pedunculopontine nucleus
   D. Dopamine/laterodorsal nucleus

   ANSWER: C. The REM-on cells are cholinergic and are located in the pons. Thus, the correct answer will have both of these facts embedded in them. (ATLAS2, p 30)

9. Accumulation of which of the following results in sleepiness?
   A. Adenosine
   B. Hypocretin
   C. Leptin
   D. Histamine

   ANSWER: A. It is believed that adenosine accumulation during wakefulness results in sleepiness. Adenosine has at least two effects: inhibition of wakefulness-promoting systems in the basal forebrain and activation of sleep-promoting VLPO neurons (Fig. E1.1–1). (ATLAS2, Fig. 3.1–7)
10. The role of caffeine in increasing wakefulness is due to its effect on which of the following?
   A. Hypocretin
   B. Adenosine
   C. Leptin
   D. Histamine

   ANSWER: B. Caffeine, a xanthine, is an antagonist of adenosine. The basal forebrain, which plays a role in wakefulness, contains cholinergic neurons, which are inhibited by adenosine that accumulates during wakefulness. By antagonizing the effect of adenosine, caffeine reduces the inhibition caused by adenosine and thus increases wakefulness. (ATLAS2, p 116)

11. What is the location of the main sleep switch?
   A. Suprachiasmatic nucleus (SCN)
   B. VLPO
   C. Thalamus
   D. Pineal gland

   ANSWER: B. Although all these structures are involved in sleep, the VLPO is the main sleep switch. Adenosine activates sleep promotion in VLPO neurons by affecting $A_{2A}$ receptors (see Fig. E1.1–1).

12. Which structures play a role in promoting wakefulness?
   A. Thalamus
   B. Pineal gland
   C. VLPO
   D. Tuberomammillary nucleus (TMN)

   ANSWER: D. The TMN cells are mainly active during wakefulness, and they release histamine. One way to remember the effect of histamine is to remember that antihistamines can cause sleepiness (Fig. E1.1–2). (ATLAS2, Fig. 3.1–4)
13. Orexin-releasing cells are located where?
   A. Pineal gland
   B. Thalamus
   C. Lateral hypothalamus
   D. VLPO

   ANSWER: C. This is an example of a question in which you may be able to work out the answer by deduction based on understanding the function of the compound. Orexin is reduced or absent in narcolepsy, a disease in which sleepiness is a key symptom. Thus, it is reasonable to deduce that orexin is involved in wakefulness. We should remember that the VLPO is the sleep switch; therefore, VLPO is incorrect. Similarly, we remember that the thalamus is involved in sleep spindle generation; thus, the thalamus is not the correct answer. The pineal gland is involved in melatonin production; therefore, the pineal is not the correct answer. (ATLAS2, pp 161–164)

14. Which statement about the dorsal raphe is incorrect?
   A. It is involved in REM sleep
   B. Cells are active mainly during wakefulness
   C. It releases serotonin
   D. It produces cortical activation via a ventral pathway to the hypothalamus

   ANSWER: A. The dorsal raphe is not involved in REM sleep generation. It is involved in arousal by releasing serotonin. (ATLAS2, p 24)

15. What neurotransmitters are released in the VLPO?
   A. Galanin and GABA
   B. Orexin and serotonin
   C. Norepinephrine and histamine
   D. Melatonin and dopamine

   ANSWER: A. The correct answer can be deduced because the VLPO is the sleep switch and therefore would not be expected to release neurotransmitters that might cause wakefulness. Thus, answers B and C cannot be correct because orexin (in answer B) and histamine (in answer C) are well known to cause wakefulness. Melatonin is, of course, produced by the pineal gland. Thus, even if you never heard of galanin, you could figure out the answer. (ATLAS2, pp 29–30)
16. Which brain area is involved in the REM-on process?
   A. VLPO
   B. Thalamus
   C. Pedunculopontine tegmental nuclei
   D. Basal forebrain

   ANSWER: C. The pedunculopontine tegmental, laterodorsal tegmental, sublaterodorsal, and preoceruleus/parabrachial nuclei are all involved in REM-on processes. This is hard to remember; however, REM processes begin in the pons, thus structures that are “pontine” should be associated with REM. It is worth remembering that the REM-on neurons of the pedunculopontine tegmental nucleus are cholinergic.

17. What structures play a role in muscle atonia in REM sleep?
   A. Lateral hypothalamic cells
   B. Cells in the VLPO
   C. Cells in the pineal gland
   D. Cell groups in the pons

   ANSWER: D. The correct answer can be deduced because none of the first three answers has anything to do with REM. Stimulation of cell groups in the pons can lead to atonia.
1. In what age group is sleep unaffected by circadian light/dark cycles?
   A. Neonates
   B. Adolescents
   C. Young adults
   D. Normal older people

   **ANSWER:** A. Neonates sleep in short clusters over the 24-hour light/dark cycle. This is called *polyphasic sleep* and is also found in many mammals. They have a huge amount of REM sleep at birth (~50%). Usually by around 3 to 4 months of age, the baby develops a regular pattern of ultradian cycling between REM and NREM, and there is a change from a polyphasic sleep/wakefulness pattern to a circadian one. (ATLAS2, Fig. 4.2–38)

2. What is meant by the term *polyphasic sleep*?
   A. Sleep occurring any time day or night
   B. Sleep occurring only during the daytime
   C. Sleep with early onset of REM
   D. Sleep occurring any time it is dark

   **ANSWER:** A. Polyphasic sleep refers to several sleep bouts occurring both during the day and the night. This pattern is found in newborns and in some animals. In newborns, circadian entrainment eventually occurs, and most sleep occurs at night. This pattern is also seen in older adults in institutions who may lack circadian entrainment and who may develop irregular sleep-wake disorder. (ATLAS2, Fig. 4.2–38)

3. Where is the hormone melatonin secreted?
   A. Pineal gland
   B. Adrenal gland
   C. Posterior pituitary gland
   D. Retinohypothalamic tract

   **ANSWER:** A. Pineal gland. (ATLAS2, Ch 3.3)

4. A patient who is blind from birth has a severe insomnia. What is the likeliest sleep disorder diagnosis?
   A. Advanced sleep phase syndrome
   B. Non–24-hour sleep-wake disorder
   C. Delayed sleep phase syndrome
   D. Depression-related comorbid insomnia

   **ANSWER:** B. The likeliest diagnosis is non–24-hour sleep-wake disorder. It has also been called free-running disorder. Such patients have a free-running sleep-wake rhythm because they are unable to sense light and therefore cannot synchronize their circadian system. (ATLAS2, p 138; Quera Salva MA, Hartley S, Léger D, Dauvilliers YA. Non-24-Hour Sleep-Wake Rhythm Disorder in the Totally Blind: Diagnosis and Management. Front Neurol.2017 Dec 18;8:686.)

5. Melatonin secretion is inhibited by which of the following? Pick the best answer.
   A. Light
   B. Dark
   C. Food
   D. Nonlipophilic beta-blockers

   **ANSWER:** A. Melatonin has been called the hormone of darkness and, at times, the Dracula of hormones. Its secretion is inhibited by light sensed by melanopsin, a photopigment found in the photosensitive ganglion cells of the retina. Tasimelteon, a melatonin receptor 1 and 2 agonist, is used to treat non–24 hour sleep-wake disorder. (ATLAS2, Ch 3.3)
6. What is the effect of bright light exposure early in the morning (end of the night) on the circadian rhythm of sleep in normal humans?
   A. Causes a phase delay
   B. Causes a phase advance
   C. No effect
   D. Induces sleep right after exposure

ANSWER: B. Light exposure (~2500 lux for 2 hours) in the morning causes a phase advance. Light exposure at night causes a phase delay. (ATLAS2, p 92)

7. Melatonin is a hormone produced by the ____________ in response to __________.
   A. suprachiasmatic nucleus (SCN)/dark
   B. pineal gland/light
   C. SCN/light
   D. pineal gland/dark

ANSWER: D. The hormone melatonin is secreted by the pineal gland. Secretion is inhibited by light and increased by dark. (ATLAS2, p 26)

8. The fact that many biological rhythms will free run in a constant environment implies that
   A. Biological rhythms are passive responses to environmental changes
   B. Biological rhythms are actively produced by internal pacemakers
   C. Biological rhythms are always coupled with environmental changes
   D. None of the above

ANSWER: B. The critical observation supporting the concept of an internal pacemaker is the fact that circadian rhythms will continue to regularly oscillate under constant environmental conditions (i.e., without time cues). This condition is referred to as free running, in which the rhythm assumes its natural period (τ), the duration for one complete cycle. The free running period is always different from the period of the environmental zeitgeber (T). (ATLAS2, Ch 3.3)

9. Where is the coordinating pacemaker for the mammalian circadian rhythm system?
   A. The pineal gland
   B. The SCN
   C. The ganglion cells in the retina
   D. The raphe nuclei

ANSWER: B. Lesions of the SCN in experimental animals produce an arrhythmic organism that is incapable of entraining to a 24-hour environmental rhythm of light and darkness and is without an obvious free-running period in rest-activity cycles. Although major rhythms, such as the sleep-wake cycle, will become chaotic after the SCN is destroyed, other local tissue rhythms, such as liver enzyme levels, may retain a free-running period, which suggests that multiple pacemakers exist within various tissues of an intact organism that are coordinated by a master mechanism within the SCN. (ATLAS2, Ch 3.3)

10. Which of the following is necessary for entrainment of the sleep-wake cycle to the light-dark cycle?
    A. Normal vision
    B. The geniculohypothalamic tract
    C. The retinohypothalamic tract
    D. The retinal rod receptors

ANSWER: C. The retinohypothalamic tract contains the axons of melanopsin-containing ganglion cells within the retina. These specialized ganglion cells are the photosensitive receptor elements of the environmental illuminance monitoring system that feeds information about the light-dark cycle into the SCN. Disruption of this information pathway prevents photic entrainment in most diurnal mammals. (ATLAS2, Ch 3.3)
1. What is the best tool to diagnose restless legs syndrome (RLS) during pregnancy?
   A. Serum ferritin
   B. Patient history
   C. EMG during sleep
   D. EMG while awake

   ANSWER: B. The diagnosis of RLS in pregnant women is made the same as in everyone else: by a detailed history. RLS is a diagnosis based on symptoms, so the following questions are useful:
   ■ Do you have an urge to move your legs, accompanied by uncomfortable or unpleasant sensations in the legs?
   ■ Are the symptoms worse at rest and relieved by movement?
   ■ Are the symptoms worse at night, or do they only occur at that time?

   “Yes” answers to all three questions make the diagnosis of RLS. Electromyography (EMG) plays no role in diagnosis (except to rule out some other disorder you might be concerned about), and serum ferritin is used only to determine whether iron deficiency might be playing a role in causation. (ATLAS2, Ch 11.2)

2. All of the following are true about sleep during pregnancy except
   A. RLS appearing for the first time during pregnancy almost always continues after delivery
   B. Treatment of RLS in pregnancy should avoid dopamine agonists and instead focus on iron and folate supplements
   C. Poor sleep quality, as defined by the Pittsburgh Sleep Quality Index (PSQI), becomes significantly more common as pregnancy progresses
   D. The prevalence of RLS increases significantly from the first to third trimester

   ANSWER: A. When RLS appears during pregnancy, it often remits after delivery. Treatment with dopamine agonists should be avoided, although it is acceptable to give iron and folate during pregnancy. As for answers C and D, in one study of 189 pregnant women, the percentage of patients who met diagnostic criteria for RLS increased from 17.5% at recruitment to 31.2% in the third trimester ($P = 0.001$). Also, overall poor sleep quality, as defined by a PSQI score greater than 5, became significantly more common as pregnancy progressed (39.0% compared with 53.5%, $P = 0.001$). (PPSM6, Chapters 156–157)

3. Falling asleep by first entering REM is most typical for which of the following groups?
   A. Neonates
   B. Postmenopausal women
   C. The elderly
   D. Adolescents

   ANSWER: A. Neonates spend about 50% of their time in sleep and REM sleep, and in this population, it is common for sleep to be entered via REM. Entering sleep via REM is unusual except in patients with narcolepsy and in some individuals with severe sleep deprivation. (ATLAS2, p 89)
4. Which statement about quiet sleep in the preterm unborn fetus is incorrect?
   A. It appears at about 36 weeks' gestation
   B. It comprises low-voltage delta and theta activity
   C. It is well defined by about 34 weeks' gestation
   D. There is no breathing activity

ANSWER: D. In the fetus, the sleep stages are not as well defined as in children or adults, and sleep is characterized into quiet and active sleep states. There is a great deal of breathing activity during quiet sleep (equivalent to NREM sleep) in a fetus even though no gas exchange actually occurs because the lungs are atelectatic, and the airways are filled with amniotic fluid. (PEDS2, p 20)

5. Which statement about active sleep in a preterm fetus is incorrect?
   A. Low-voltage irregular (LVI) activity is present
   B. REMs are present, and EMG tone is variable
   C. No movements occur, but the fetus grimaces
   D. Respiration and heart rate are variable

ANSWER: C. Although it might be expected that there would be no movements in the fetus during what would be equivalent to REM sleep, in fact, there are movements, grimaces, and twitches. (PEDS2, p 20)

6. What BEST describes sleep architecture as a percent of total sleep time of a term newborn?
   A. 5% stage 1; 50% stage 2; 25% slow-wave sleep; 20% REM sleep
   B. 5% stage N1; 50% stage N2; 0% stage N3; 50% stage R
   C. 50% to 60% active sleep; 10% to 30% quiet sleep; 20% to 30% indeterminate sleep
   D. Sleep cannot be scored in a newborn

ANSWER: C. There are no formalized scoring rules for newborns younger than the age of 2 months (MANUAL2). After 2 months of age, the designations are the same as in adults except that an additional stage is defined, called stage N, and the specific criteria to define these stages in children are described in the manual. Stage N is used in children older than 2 months, when a child is in NREM sleep, but there are no recognizable K complexes, sleep spindles, or slow waves. In a newborn, sleep structure can be scored as quiet sleep (equivalent to NREM); active sleep (equivalent to stage R); or indeterminate sleep, when neither active nor quiet sleep can be scored. An additional finding, trace-alternant, is seen in newborns. The latter is recognized as bursts of high-voltage electrical activity separated by periods of low-voltage activity.

7. What is trace-alternant?
   A. An EEG finding seen in sleeping newborns
   B. An EEG finding seen in patients with multiple system atrophy
   C. The finding of leg movements alternating between the right and left legs
   D. An abnormal breathing pattern in which large breaths alternate with small breaths

ANSWER: A. Trace-alternant is an EEG finding seen in newborns, recognized as bursts of high-voltage electrical activity separated by periods of low-voltage activity. (PEDS2, p 20)

8. Which statement about sleep in children is incorrect?
   A. Sleep spindles appear 2 to 3 months after term birth
   B. K complexes appear by 6 months after term birth
   C. REM-onset sleep continues to 18 months of age
   D. REM as a percent of TST decreases to about 30% by 1 year

ANSWER: C. Many changes occur in sleep structure during the first year, with the appearance of sleep spindles (at 2–3 months) and K complexes (by 6 months) and a reduction in REM sleep. Entering sleep via REM, however, generally ceases between 3 and 6 months. (PEDS2, p 20)
9. By what age do children generally stop napping during the daytime?
   A. 3 years
   B. 6 years
   C. 9 years
   D. 12 years

   ANSWER: B. Children have usually stopped napping when they start grade 1, usually at age 6 years.

10. Adolescents are prone to develop which of the following?
    A. Advanced sleep phase syndrome
    B. Delayed sleep phase syndrome
    C. Irregular sleep-wake syndrome
    D. Free-running circadian pattern

   ANSWER: B. Because of changes in their circadian control system, adolescents frequently develop delayed sleep phase syndrome. They fall asleep late and tend to wake up late if given the opportunity to sleep, for example, on weekends. Sleep deprivation is also common because of early school start times and poor sleep hygiene.

11. Which disorder becomes less common between the ages of 50 and 60 years?
    A. Sleep disturbance caused by hot flashes
    B. Restless legs syndrome
    C. Insomnia
    D. Obstructive sleep apnea

   ANSWER: A. In North America, menopause generally occurs at age 51 years and is defined as 12 months without menstrual cycles. Sleep disturbance can be quite severe because of hot flashes and night sweats. However, these symptoms most often remit or become less severe by age 60 years.

12. When are hot flashes during sleep least common?
    A. Stage N2
    B. Stage N3
    C. Stage R
    D. There is no relationship to sleep stage.

   ANSWER: C. Hot flashes are least common in REM sleep. It is likely that hot flashes require activity of the thermoregulatory system. It has been hypothesized that hot flashes do not occur in REM because thermoregulation is suppressed.

13. Older people are prone to develop which of the following?
    A. Advanced sleep phase syndrome
    B. Delayed sleep phase syndrome
    C. Irregular sleep-wake syndrome
    D. Free-running circadian pattern

   ANSWER: A. Older people frequently develop advanced sleep phase syndrome, going to sleep earlier and awakening earlier. (ATLAS2, p 97)

14. Which statement about the effect of aging (between ages 40 and 70 years) on the sleep stages as a percent of total sleep time is incorrect?
    A. Stage N3 decreases substantially in older men
    B. Stage N3 decreases substantially in women
    C. Stage R sleep is preserved in men
    D. Stage R sleep is preserved in women

   ANSWER: A. REM sleep is relatively preserved in both men and women with aging. On the other hand, slow-wave sleep, stage N3, is decreased by about 50% in men but is well preserved in women. Other changes that occur with aging include reduction of spindles and K complexes.
15. Which is the most correct statement about arousals in older adults?
   A. The arousal rate in healthy older adults is less than five per hour
   B. The arousal index is increased only when periodic limb movements or sleep-breathing disorders are present
   C. The arousal index is increased in older adults without sleep-disordered breathing
   D. A history of cardiovascular disease is not associated with disturbed sleep

ANSWER: C. The arousal index is increased in older people, even in those without a sleep-breathing disorder.

16. Which statement about circadian rhythm of body temperature in older adults is most correct?
   A. The circadian phase is advanced, and amplitude is increased
   B. The circadian phase is advanced, and amplitude is decreased
   C. The circadian phase is delayed, and amplitude is increased
   D. The circadian phase is delayed, and amplitude is decreased

ANSWER: B. With aging, there occurs a phase advance but a decreased amplitude of circadian rhythm.

E1.4 Sleep Deprivation

QUESTIONS

1. Which statement about selective REM deprivation is TRUE?
   A. It leads to psychopathology
   B. It leads to increased aggression
   C. It leads to hyposexuality
   D. It leads to schizophrenia


2. In an acutely sleep deprived individual, what is the effect of a 5-minute walk immediately before multiple sleep latency test (MSLT) evaluations?
   A. There is no effect because the MSLT is such a robust test
   B. The MSLT shows even more sleepiness with a 2- to 5-minute reduction in mean sleep latency
   C. The MSLT shows no change in mean latency but shows decreased sleep-onset REM periods (SOREMPs)
   D. The MSLT shows a large impact in mean sleep latency (longer by ~6 minutes)

ANSWER: D. Exercise can mitigate the effects of acute sleep deprivation on the MSLT. However, the effect of exercise on performance measures in sleep-deprived individuals is much more modest or nonexistent.
3. During a second night of total sleep deprivation, which is expected to have the longest effect in maintaining alertness: modafinil 200 mg, caffeine 300 mg, or dextroamphetamine 20 mg?
   A. Modafinil
   B. Caffeine
   C. Dextroamphetamine
   D. The three are equivalent

ANSWER: A. Modafinil has been shown to have the longest beneficial effect on maintaining alertness. This likely is related to its longer half-life.

4. Which statement about the effect of age on response to sleep deprivation is correct?
   A. Younger adults tolerate sleep deprivation much better than older adults
   B. Older adults tolerate sleep deprivation much better than younger adults
   C. There is little difference in performance and alertness decrement related to age, and if anything, the decrement may be less in older than younger men
   D. Because circadian amplitude is greater in older people, decrement from sleep deprivation is greater

ANSWER: C. Although it might be expected that older people would not tolerate sleep deprivation compared with younger adults, in fact, if anything, older men might tolerate sleep deprivation better than younger adults. The differences, however, are small.

5. Which statement about the effect of the circadian CLOCK gene on tolerance to sleep loss is correct?
   A. There is no evidence of any effect of any gene on sleep in humans.
   B. Although variants of the CLOCK gene PER3 predict “morningness” and “eveningness,” they have no effect on tolerance of sleep deprivation.
   C. Because the CLOCK genes only affect circadian physiology, there is no expected effect on sleep deprivation that affects homeostasis.
   D. Variants of the CLOCK gene PER3 are associated with differing effects on tolerance to sleep deprivation.

ANSWER: D. Two groups with variants of the CLOCK gene PERIOD3 (PER3) have been studied. They have been categorized as PER3(5/5) and PER3(4/4). Whereas PER3(5/5) groups are more likely to show morning preference, PER3(4/4) groups show evening preferences. People with the PER3(5/5) variant have a greater cognitive decline and a greater reduction of brain responses to an executive task in response to total sleep deprivation. These effects are most noticeable during the late night or early morning hours. (Dijk DJ, Archer SN: PERIOD3, circadian phenotypes, and sleep homeostasis, Sleep Med Rev 14:151–160, 2010)

6. In normal young adults, after 40 hours of total sleep deprivation, what does the first recovery sleep show?
   A. Increased stage W
   B. Increased stage N2
   C. Increased stage N3
   D. Increased stage R

ANSWER: C. In young adults, the main finding in the first night of recovery sleep is a substantial increase in slow-wave sleep. On the second night, slow-wave sleep amounts normalize, and stage R shows an increase. By the third night, values are all normal.
7. “Core” sleep has been defined as the amount of sleep needed to maintain stable neurocognitive function. In adults, this value appears to be which of the following?

A. 3 to 4 hours  
B. 4 to 5 hours  
C. 5 to 6 hours  
D. 7 to 8 hours  

ANSWER: D. Some researchers have defined core sleep and optional sleep, with the former initially defined as about 4 hours. With additional research showing that even with 6 hours of nightly sleep, there may be neurocognitive or performance abnormalities, the value of required or “core” sleep has increased to about 7 to 8 hours.

8. With chronic sleep restriction, what is the most consistent sleep architecture finding?

A. Increased stage N2  
B. Increased stage N3  
C. Increased stage R  
D. Normal sleep architecture  

ANSWER: B. The most consistent finding with chronic sleep restriction is an increase in slow-wave sleep at the expense of other sleep stages.

9. Progressive nights of sleep restriction to 5 hours are expected to show which of the following?

A. No effect on psychomotor vigilance task but increased sleep propensity  
B. Abnormal psychomotor vigilance task and increased sleep propensity  
C. No effect on psychomotor vigilance task or sleep propensity  
D. Abnormal psychomotor vigilance task but normal sleep propensity  

ANSWER: B. Five hours of sleep restriction is expected to show abnormalities in the psychomotor vigilance task (PVT) and an increase in sleep propensity as measured by multiple sleep latency test (MSLT) or maintenance of wakefulness test (MWT).

10. In tests of driving performance on a simulator in subjects restricted to 4 to 6 hours of sleep, which of the following is correct?

A. There is no effect on accident rate  
B. There is an increase in accident rate  
C. There is a decrease in accident rate as subject tries to compensate  
D. Accident rate is increased only when testing is done at night  

ANSWER: B. Accident rate is increased in sleep-restricted individuals, and the abnormalities are documented both in day and night testing.

11. Chronic sleep restriction to 4 hours is expected to show which effects?

A. Increased evening cortisol and sympathetic activation  
B. Increased thyrotropin activity and decreased glucose tolerance  
C. Increased leptin and decreased ghrelin levels  
D. All of the above  

ANSWER: A. This is an important topic. Sleep restriction leads to an increase in cortisol, ghrelin, and sympathetic activity and to a decrease in leptin and thyrotropin, as well as a decreased glucose tolerance result (insulin resistance).
12. What effect does sleep loss (4 hours of sleep for 6 nights) have on response to influenza vaccination?
A. Sleep deprivation causes a 50% decrease in antibody titers to influenza vaccine at 10 days, which persists for at least 1 year
B. Sleep deprivation causes a 50% decrease in antibody titers to influenza vaccine at 10 days, which normalizes by 4 weeks
C. Sleep deprivation causes a 50% increase in antibody titers to influenza vaccine, which persists for at least 1 year
D. Sleep deprivation has no effect on immune function

ANSWER: B. In addition to the temporary reduction in immune response to influenza vaccination, abnormalities in interleukin-6 and tumor necrosis factor have been reported.

13. Which statement about the effect of sleep deprivation on the cardiovascular system is incorrect?
A. Sleep deprivation is associated with increased C-reactive protein, a marker of cardiovascular risk
B. Sleep deprivation is associated with increased cardiovascular morbidity
C. The Nurses’ Health Study did not show that sleep deprivation was associated with cardiovascular events
D. Shift workers have reduced cardiovascular health


14. The purpose of low and high filters is to isolate specific frequency bandwidths relevant to each recording parameter. Which of the following is an incorrect filter range for the parameter shown?
A. EEG: 0.3 Hz to 35 Hz
B. EOG: 0.3 Hz to 35 Hz
C. EMG: 10 Hz to 100 Hz
D. ECG: 20 Hz to 100 Hz

ANSWER: D. The recommended low-high frequency filter for electrocardiogram (ECG) is 0.3 to 70 Hz. (MANUAL2)

15. A major body movement (MBM) is defined as
A. Movement and muscle artifact obscuring the EEG for more than half an epoch to the extent that sleep stage cannot be determined
B. Movement artifact that manifests for at least 10 seconds in a standard 30-second epoch
C. Movement or muscle artifact that obscures the entire epoch
D. Movement artifact that awakens the patient

ANSWER: A. This statement is the definition of major body movement. (MANUAL2)

16. An epoch can be scored as “movement time” when
A. An MBM occupies more than 50% of any epoch
B. An MBM occupies at least one third of any epoch
C. An MBM is at least half of a W epoch
D. An epoch can never be scored as movement time

ANSWER: D. According to the AASM scoring manual, movement time is no longer scored. Instead, the epoch in which an MBM occurs is scored as W, N1, N2, N3, or REM. The rules are as follows:
A) If alpha rhythm is seen in any part of the epoch that has an MBM, the score is W
B) If not A, and the epoch before or after is W, score the epoch with MBM as W
C) If neither A nor B, score the epoch the same stage as the epoch after the MBM
Match the activity given in questions 17 through 24 to the waveforms labeled A through H. The time duration represented by each waveform is 1 second. Six tracings are from an EEG, and two are from an electrooculogram (EOG); each figure is used only once (Fig. E1.4–1).

17. K complex
18. Slow waves
19. Alpha activity
20. Theta activity
21. REM
22. Slow eye movements (SEMs)
23. Vertex sharp waves
24. Sleep spindles
   A. (3.2 to 14)
   B. (3.2 to 15)
   C. (3.2 to 18)
   D. (3.2 to 19)
   E. (3.2 to 12)
   F. (3.2 to 13)
   G. (3.2 to 16)
   H. (3.2 to 17)
ANSWERS:

17. **E.** The K complex is an EEG event that consists of well-delineated negative sharp wave (upward deflection by convention) immediately followed by a positive component that stands out from the background EEG. The total duration is 0.5 seconds or more and is usually maximal over the frontal regions.

18. **F.** Slow waves have high amplitude (≥75 µV) and low frequency (≤2 Hz). Slow waves are a subset of delta (1–4 Hz) activity and are the defining characteristics of stage N3 sleep.

19. **A.** Alpha activity; an 8- to 13-Hz rhythm, usually most prominent in occipital leads and thought to be generated by the cortex, is used as a marker for relaxed wakefulness and central nervous system (CNS) arousals.

20. **B.** Theta activity; 4- to 7-Hz waves, typically prominent in central and temporal leads, seen in both stage N1 and REM sleep.

21. **G.** REMs are conjugate saccades that occur during REM sleep and correlate with dreaming. They are sharply peaked with an initial deflection usually less than 0.5 second in duration.

22. **H.** SEMs are conjugate, usually rhythmic, rolling eye movements with an initial deflection more than 0.5 second in duration.

23. **C.** Vertex sharp waves show a sharply contoured, negative deflection (upward on EEG) that stands out from the background and appears most often in central leads placed near the midline; they are characteristically seen in stage N1.

24. **D.** Sleep spindle, a phasic burst of 11- to 16-Hz activity prominent in central scalp leads, typically lasts for 0.5 to 1.0 second. Spindles are a scalp representation of thalamocortical discharges; the name derives from their shape, which is spindlelike.

Match one of the following terms, A through Q, to each of the statements numbered 25 through 36. References for the answers are in the AASM scoring manual.

A. Alpha rhythm  
B. Artifact  
C. Beta  
D. Complex  
E. Delta  
F. Delta sleep  
G. Frequency  
H. K complex  
I. Movement time  
J. Theta  
K. Sawtooth waves  
L. Sleep spindle  
M. Stage N1  
N. Stage N2  
O. Stage N3  
P. REM sleep  
Q. Awake

25. Used to indicate EEG frequencies higher than 13 Hz. Answer: C

26. Well-delineated negative sharp wave immediately followed by a positive component, duration of 0.5 or more seconds, usually maximal in amplitude when recorded with frontal derivations. Answer: H

27. EEG frequency of 8 to 13 Hz in adults, most prominent in the posterior areas. Characteristic of relaxed wakefulness with the eyes closed. Answer: A

28. Moderate amounts (≥20%) of high-amplitude (≥75 µV), slow-wave (≤2 Hz) EEG activity. Answer: O
29. Sometimes used as a synonym for stage N3 sleep. Answer: F
30. Sleep-scoring epoch during which the record is totally obscured by muscle tone for greater than 15 seconds but less than 1 minute. Answer: I
31. A waveform with a frequency of 12 to 14 cps, most prominent in stage N2 sleep. Answer: L
32. A stage of relatively low-voltage, mixed-frequency EEG without REMs; SEMs are often present, vertex sharp waves may be seen, and EMG activity is not suppressed. Answer: M
33. A nonbiological signal that appears in an EEG of sleep recording and interferes with the signals being recorded. Answer: B
34. Notched waveforms in vertex and the frontal regions that sometimes occur in conjunction with bursts of rapid eye movements in REM sleep. Answer: K
35. Indicates an EEG frequency of 4 to 7 cps. Answer: J
36. 12 to 14 cps sleep spindles and K complexes on a background of relatively low-voltage, mixed-frequency EEG activity. Answer: N

For questions 37 through 48, match the electrophysiologic characteristics with the sleep stage(s) where it may be found. Use the terminology W, N1, N2, N3, and R. Note that some characteristics help define a sleep stage, but other characteristics may simply be in a stage defined by something else. Thus, for example, you would not find REMs in stage N2 because they are used to define REM sleep, but you could find alpha rhythm in any stage because it only defines W if it occupies 15 or more seconds of a 30-second epoch.

37. Low-voltage, mixed-frequency activity: stage ____ or ____
38. Vertex sharp waves: stage ____ or ____
39. Sleep spindles: stage ____ or ____
40. K complexes: stage ____ or ____
41. Beta activity: stage ____ or ____
42. Alpha activity (a freebie): stage ____, ____, ____, ____, or ____
43. Theta activity: stage ____, ____, ____, or ____
44. Slow-wave activity: stage ____, ____, ____, or ____
45. Slow eye movements: stage ____ or ____
46. Rapid eye movements: stage ____
47. Atonic electromyogram (EMG) activity: stage ____
48. Low voltage, mixed frequency with sawtooth pattern: stage ____

ANSWERS
37. Low-voltage, mixed-frequency activity. stage N1, N2, or R
38. Vertex sharp waves: stage N1 or N2
39. Sleep spindles: stage N2 or N3
40. K complexes: stage N2 or N3
41. Beta activity: stage W, N1, or R
42. Alpha activity (a freebie): stage W (≥15 seconds), N1 (<15 seconds), N2 (<15 seconds), N3 (<15 seconds), or R (<15 seconds)
43. Theta activity: stage N1, N2, N3, or R (with typical sawtooth pattern)
44. Slow-wave activity: stage N1 (≤6 seconds), N2 (≤6 seconds), N3 (≥6 seconds), or R (≤6 seconds)
45. Slow eye movements: stage W or N1
46. Rapid eye movements: stage R
47. Atonic EMG activity: stage R
48. Low voltage, mixed frequency with sawtooth pattern: stage R

49. Polysomnographic (PSG) waveforms are defined based on four features: (1) amplitude, (2) frequency, (3) waveform shape, and (4) distribution. Below are descriptions of four waveforms, labeled 1 through 4. From letters A through D, pick the correct sequence of waveforms corresponding to stages W, N1, N2, N3.

A. Alpha rhythm, vertex sharp wave, slow wave, K complex
B. Alpha rhythm, vertex sharp wave, K complex, slow wave
C. Theta rhythm, eye blink, slow wave, K complex
D. Sleep spindle, K complex, vertex sharp wave, slow wave

ANSWER: B. (MANUAL2)

50. Impedance in PSG is a measure of the contact of the electrode with the skin. All electrode impedances should be below

A. 5 Ohms
B. 500 Ohms
C. 5000 Ohms
D. 20,000 Ohms

ANSWER: C. (MANUAL2)

51. According to the AASM’s 2014 recommendations, in a sleep-staging montage, the F4 electrode should be referred to which other electrode?

A. E1
B. F3
C. M2
D. M1

ANSWER: D. (MANUAL2)

52. When the sensitivity control is set at 10 $\mu$V/mm, a 100- $\mu$V input signal will produce a pen deflection of

A. 1 mm
B. 10 mm
C. 10 cm
D. 100 mm

ANSWER: C. Of course, nobody uses pens anymore!

53. In normal adults, what are the approximate percentages for each sleep stage?

<table>
<thead>
<tr>
<th></th>
<th>W</th>
<th>N1</th>
<th>N2</th>
<th>N3</th>
<th>REM</th>
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</thead>
<tbody>
<tr>
<td>A</td>
<td>5</td>
<td>5</td>
<td>50</td>
<td>15</td>
<td>25</td>
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<td>D</td>
<td>10</td>
<td>10</td>
<td>40</td>
<td>10</td>
<td>30</td>
</tr>
</tbody>
</table>

ANSWER: A. (ATLAS2, p 84)

54. In stage R, which of the following findings is most characteristic?

A. Increased muscle tone
B. Sawtooth waves
C. Sleep spindles
D. K complexes

ANSWER: B. Sawtooth waves are often seen in the EEG during REM sleep but are not essential to its staging. They look like the teeth of a saw, as shown in the green ovals below in this REM epoch (see Fig. E1.4–2).
55. Which of the following is a characteristic normal stage N2 sleep?
   A. Absent muscle tone  
   B. Delta waves  
   C. Sleep spindles  
   D. Alpha waves  

   ANSWER: C.

56. Which of the following statements most closely characterizes changes in sleep with aging?
   A. Sleep latency increases; percent REM sleep decreases  
   B. Slow-wave amplitude increases; percent slow-wave sleep decreases  
   C. Stages 1 and 2 increase; slow-wave amplitude increases  
   D. Sleep latency decreases; sleep efficiency decreases  

   ANSWER: A

57. Which statement best describes the distribution of REM sleep during normal nocturnal sleep?
   A. REM episodes are evenly distributed throughout the night  
   B. REM episodes last longer later in the night  
   C. REM sleep occurs mainly during the first 120 minutes of the night  
   D. REM sleep occurs mainly in the middle third of the night  

   ANSWER: B. Whereas the percentage of REM sleep decreases with aging, in all cases the episodes of REM sleep tend to be longer later in the sleep cycle. Figure E1.4–3 (ATLAS2, Fig. 4.2–25, p 86) shows REM distribution (horizontal red bars) in three different ages: A, child; B, young- to-middle-aged adult; C, older adult.
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FIGURE E1.4–3

58. Most slow-wave sleep typically occurs in what part of the night?
   A. First third of the night
   B. Middle third of the night
   C. Last third of the night
   D. Equally throughout the night

ANSWER: A. This fact is also appreciated in the three hypnograms shown in Figure E1.4–3.

59. Upper limit of normal sleep latency in adults is approximately
   A. Less than 5 minutes
   B. Less than 20 minutes
   C. 20 to 40 minutes
   D. Up to 90 minutes

ANSWER: B.
60. According to the AASM practice parameters for use of actigraphy, only two indications are considered standard, including which one of the following?

A. To assist in the evaluation of patients suspected of advanced sleep phase syndrome (ASPS) and delayed sleep phase syndrome (DSPS)
B. To estimate total sleep time in patients with obstructive sleep apnea (OSA) when PSG is not available
C. To determine circadian pattern and estimate average daily sleep time in individuals complaining of hypersomnia
D. For evaluating the response to treatment for patients with insomnia


○ “Actigraphy is a valid way to assist in determining sleep patterns in normal, healthy adult populations.” (Standard)
○ “When PSG is not available, actigraphy is indicated as a method to estimate total sleep time in patients with obstructive sleep apnea syndrome. Combined with a validated way of monitoring respiratory events, use of actigraphy may improve accuracy in assessing the severity of obstructive sleep apnea compared with using time in bed.” (Standard)

61. What stage of sleep is shown on the following PSG fragment in Figure E1.4–4?

A. Stage W
B. Stage N1
C. Stage N2
D. Stage N3

ANSWER: B. This is stage N1. About 10 seconds from the end of this epoch is a vertex sharp wave, and the EEG shows low-amplitude, mixed-frequency waves. This stage frequently also demonstrates slow eye movements. (MANUAL2)
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62. What is shown in the red-bordered area in the following PSG (Fig. E1.4−5)?
   A. Vertex sharp wave
   B. Sawtooth wave
   C. Seizure spike
   D. K complex

   ANSWER: A. This is a vertex sharp wave. Three characteristics of this wave are that it stands out from the background of mixed-frequency, low-amplitude activity; it is maximal over the central region (C4-M1, in this example); and it is of short duration (<0.5 second). (MANUAL2)

63. How much time does the red box in the PSG fragment in Figure E1.4−6 cover?
   A. 2 seconds
   B. 3 seconds
   C. 4 seconds
   D. 5 seconds

   ANSWER: B. The entire epoch is 30 seconds; always find the epoch length whenever you examine a PSG fragment. The red box occupies exactly one of the major time divisions, thus the box occupies 3 seconds (30 divided by 10).
64. How much time does the red box in the PSG fragment in Figure E1.4–7 cover?
   A. 0.2 seconds
   B. 0.3 seconds
   C. 0.5 seconds
   D. 0.6 seconds

   ANSWER: D. The entire epoch is 30 seconds; always find the epoch length whenever you examine a PSG fragment. There are 10 major time divisions; thus, each major time division occupies 30 divided by 10, or 3 seconds. The red box occupies the minor time division, which is one-fifth of the major time division. Thus, the box covers 3 seconds divided by 5, or 0.6 seconds.
65. What is shown on the following PSG fragment (Fig. E1.4–8)?
   A. Sawtooth waves
   B. Alpha activity
   C. A string of K complexes
   D. Continuous seizure activity

   ANSWER: B. This is alpha activity (8–13 Hz), prominent in all the EEG channels but especially in the occipital channel O2-M1. (MANUAL2)

66. What is the best interpretation of the data shown on the PSG fragment in Figure E1.4–8?
   A. The patient is awake, eyes closed
   B. The patient is awake, eyes open
   C. The patient is about to enter REM sleep
   D. The patient is reading a book

   ANSWER: A. This is alpha activity (8–13 Hz) that is prominent in all the EEG channels, especially in the occipital channel (O2-M1). This pattern is maximal when the eyes are closed and is attenuated when the eyes are open. (MANUAL2)

67. What does the PSG fragment in Figure E1.4–9 show?
   A. Transition from wakefulness to REM is shown
   B. Transition occurs from REM to an awake state
   C. Sleep onset occurs in the middle of the epoch
   D. The subject is awake and closed her eyes in the middle of the epoch

   ANSWER: C. Because EMG tone remains high the entire epoch, there is no REM sleep; therefore, answers A and B are incorrect. Answer D is incorrect because if this were alpha activity in the first half of the epoch, the apparent attenuation of the activity would occur if the eyes were opened, not closed. (MANUAL2)
68. What stage of sleep is shown in the PSG fragment in Figure E1.4–10?
   A. Stage R
   B. Stage N1
   C. Stage N2
   D. Stage N3

   ANSWER: C. This is stage N2 sleep. A well-developed K complex is evident just before the middle of the epoch. The K complex is a negative sharp wave (in the EEG, negative is an upward deflection) with a duration exceeding 0.5 seconds. The K complex is usually maximal in the frontal derivations and stands out from the background EEG. Spindles (waves usually 12 to 14 Hz) are also characteristic of stage N2 sleep. (MANUAL2)
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69. What is the most prominent finding in the PSG epoch in Figure E1.4–11?
   A. Vertex sharp wave
   B. K complex
   C. Sawtooth wave
   D. Sleep spindles

   ANSWER: C.  This is a K complex. A vertex sharp wave is shorter than 1 second in duration. Sawtooth waves have less amplitude and duration than K complexes and in any case are characteristic of REM sleep, not stage N2 seen in this epoch. Finally, there is nothing in the EEG to indicate seizure activity.  (MANUAL2)

70. What is the most prominent finding in the PSG epoch in Figure E1.4–12?
   A. Sawtooth waves
   B. Theta waves
   C. K complexes
   D. Sleep spindles

   ANSWER: D. Several bursts of sleep spindles are seen. In this example, they are most prominent in the frontal leads. Although overlap is seen in the frequency of spindles (range, 11–16 Hz) and alpha rhythm (8–13 Hz), in a subject who has both, the spindle frequency is higher and the distribution is more central than for alpha activity.
71. The horizontal red dashed lines in Figure E1.4–13 have a vertical distance between them of 70 μV (from +35 to −35). What does the figure show?

A. Status epilepticus  
B. Strings of K complexes  
C. Stage N3 sleep  
D. Stage R sleep  

ANSWER: C. This is slow-wave sleep, stage N3. Slow waves are defined as having a frequency of 0.5 to 2 Hz. Their peak-to-peak amplitude is greater than 75 μV in the frontal region. More than 20% of the epoch is made up of slow waves. Note that sleep spindles may persist in N3, as seen near the end of the epoch.  

(MANUAL2)
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72. What does the fragment in Figure E1.4–14 show?
   A. REMs
   B. The subject is reading
   C. Vertex sharp waves
   D. Theta waves

   ANSWER: A. The fragment shows REMs. The eye channels show movements that are conjugate (the deflections of the two eye channels are mirror images of each other) and irregular (eye movements when reading are regular), and the initial deflection last less than 500 ms. (MANUAL2)

73. What is the most likely interpretation of the PSG fragment in Figure E1.4–15?
   A. Stage R sleep in an 8-year-old child
   B. Continuous seizure activity
   C. Stage N3 in an 8-year-old child
   D. Indeterminate sleep in a patient with Alzheimer disease

   ANSWER: C. This is stage N3 in an 8-year-old child. The pair of horizontal red dashed lines for each channel indicate ±35 µV. Slow waves in children are often more than 100 µV in peak-to-peak amplitude. This is seen in all the EEG channels. Stage N3 requires that slow-wave activity occupy more than 20% of the epoch. (MANUAL2)
74. How would you interpret the PSG epoch from an 8-year-old patient, shown in Figure E1.4–15?

A. The entire epoch should be scored stage R sleep  
B. It shows transition from stage N2 to stage R about 17 seconds into the epoch  
C. The epoch should be scored as stage N1 sleep  
D. The epoch should be scored as stage N3 sleep

ANSWER: B. This epoch should be scored as stage N2 sleep (notice the spindle at 6 seconds into the epoch), because more than half the epoch is stage N2; the transition into stage R begins 17 seconds into the epoch. At that point, there is an abrupt reduction in chin tone, and sawtooth waves appear in the EEG channels. Sawtooth waves have a frequency of 2 to 6 Hz, and they are triangular or serrated in shape. (MANUAL2)
75. What does the PSG fragment in Figure E1.4–17 show?
   A. Seizure activity
   B. An artifact arising in the eye channels that spills into the EEG
   C. Sawtooth waves in stage R
   D. A burst of theta waves

   ANSWER: D. Theta waves have a frequency of 4 to 8 Hz (some sources indicate a range of 4–7 Hz). The third 3-second segment shows 12 cycles in the EEG and EOG channels; thus, the frequency is 4 Hz. Theta waves are most often seen in stage N1 sleep and are not pathologic.

76. Caffeine antagonizes receptors of which sleep-promoting neurotransmitter?
   A. GABA
   B. Galanin
   C. Melatonin
   D. Adenosine

   ANSWER: D. Adenosine is a ubiquitous extracellular nucleotide, and both theophylline and caffeine block adenosine receptors in the brain. Adenosine activates the VLPO, part of the anterior hypothalamus, which promotes sleep, so these drugs tend to keep people awake. Note that destruction of the anterior hypothalamus leads to insomnia (Von Economo encephalitis or encephalitis lethargica arises from lesions in the anterior hypothalamus). (ATLAS2, p 23)

77. A 50-year-old woman with severe depression is being treated with multiple medications. An overnight PSG shows the following sleep stage percentages:
   N1 5%
   N2 37%
   N3 8%
   REM 50%
78. Which of the drugs she is taking, listed below, is most likely to cause this distribution?
   A. Dextroamphetamine
   B. Bupropion
   C. Citalopram
   D. Trazodone

**ANSWER:** B. Bupropion (Wellbutrin). (Nofzinger EA, Reynolds CF 3rd, Thase ME, et al: REM sleep enhancement by bupropion in depressed men, *Am J Psychiatry* 152:274–276, 1995; Mayers AG, Baldwin DS: Antidepressants and their effect on sleep, *Hum Psychopharmacol* 20:533–559, 2005.) Most antidepressants decrease REM sleep, including selective serotonin reuptake inhibitors (SSRIs; e.g., fluoxetine, paroxetine), selective norepinephrine reuptake inhibitors (SNRIs; e.g., venlafaxine, citalopram), tricyclic antidepressants (TCAs; e.g., amitriptyline), and trazodone. Benzodiazepines and nonbenzodiazepine hypnotics (Z drugs) have a mild suppressant effect on REM sleep. (Note: The benzodiazepines suppress slow-wave sleep; Z drugs do not). Two drugs increase REM sleep, bupropion and nefazodone, and the latter is used infrequently. Also associated with increased REM sleep are withdrawal from antidepressants, metabolism of alcohol during sleep, and first use of continuous positive airway pressure in sleep-deprived patients.

79. The PSG can be affected by many drugs typically prescribed in the treatment of sleep disorders. All of the following statements are true except
   A. Benzodiazepines tend to suppress slow-wave sleep (SWS) and have no consistent effect on REM sleep
   B. TCAs tend to suppress REM sleep
   C. Fluoxetine is associated with REMs across all sleep stages
   D. Acute presleep alcohol intake produces an increase in SWS and decreased REM sleep early in the night followed by REM rebound and arousals later in the night as the alcohol is metabolized

**ANSWER:** D. Actually, acute presleep alcohol intake can produce an increase in SWS and REM sleep suppression (i.e., a decreased amount of REM) early in the night. As alcohol is metabolized, there can be REM sleep rebound in the latter portion of the night.

80. Below are four mechanisms of action, labeled 1 through 4, for drugs used to either promote sleep or promote wakefulness. Pick the correct sequence of mechanisms, labeled A through D, that matches the sequence shown in 1 through 4.
   (1) Blocks 5-hydroxytryptamine (5-HT) and alpha1-adrenergic receptors
   (2) Blocks reuptake of serotonin
   (3) Binds to several alpha subunits on the GABA_A receptor
   (4) Enhances dopamine release into the synaptic space
   A. Trazodone, fluoxetine, diazepam, amphetamine
   B. Ramelteon, caffeine, lorazepam, methylphenidate
   C. Zaleplon, paroxetine, trazodone, barbiturates
   D. Modafinil, sodium oxybate, clonazepam, amphetamine

**ANSWER:** A. Trazodone blocks 5-HT (serotonin) and alpha1-adrenergic receptors; fluoxetine is an SSRI; diazepam is a benzodiazepine that binds nonselectively to the GABA_A receptor (in contrast to Z drugs, which bind selectively to the GABA_A1 subunit); and amphetamines, which block the reuptake of dopamine.

81. In addition to shortening sleep latency, drinking alcohol before sleep has all of the following effects except
   A. Decreases slow-wave sleep in the first half of the night
   B. Depresses REM sleep in the first half of the night
   C. Causes REM rebound in the second half of the night
   D. Causes reduction in airway dilator muscle tone, increasing airway resistance

**ANSWER:** A. Alcohol increases SWS in the first half of the night.
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82. Antiepileptic drugs have variable effects on sleep. Excessive daytime sleepiness is prominent with all of the following drugs except
   A. Lamotrigine
   B. Gabapentin
   C. Tiagabine
   D. Phenobarbital

   ANSWER: A. Daytime sleepiness is not a side effect of lamotrigine (Lamictal), whereas it is seen with most antiepileptics, especially gabapentin, tiagabine, and phenobarbital. (ATLAS2, Table 11.3–3, p 209)

83. Which statement best characterizes the sleep pattern of newborns?
   A. Newborns enter REM sleep (called active sleep) before quiet sleep (NREM sleep) and have a shorter sleep cycle than adults (~50 minutes)
   B. Newborns enter quiet sleep first and then cycle between REM (active sleep) and quiet sleep about every 30 minutes
   C. About 75% of the sleep cycle is indeterminate sleep; the rest is REM (active) sleep
   D. More than 90% of the sleep cycle is classified as indeterminate sleep, neither REM nor quiet sleep

   ANSWER: A. At birth, REM (active sleep) is approximately 50% of total sleep; this percentage declines over the first 2 years to about 20% to 25%. During quiet (NREM) sleep, there are no body movements, breathing is regular, EMG activity is low, and there are no REMs. Indeterminate sleep is also an EEG classification in neonates, when the pattern fits neither active (REM) nor quiet (NREM) sleep. Quiet (NREM) sleep in neonates does not have slow waves or K complexes; slow waves begin to appear at about 3 months, and K complexes appear around 6 months of age. (PEDS2, p 19)

84. A 7-year-old boy suddenly sits up at night screaming, and during these episodes, he cannot be awakened. These episodes occur at any time during the night. There is no sleepwalking or bedwetting, and during the day, the child seems fine. The most likely diagnosis is
   A. Sleep terror
   B. Nightmares
   C. Nocturnal seizures
   D. REM behavior disorder

   ANSWER: A. Sleep terror, like sleepwalking, typically begins after an arousal from SWS, most commonly toward the end of the first or second episode of SWS. By contrast, nightmares tend to arise during REM sleep. (PEDS2, Chapter 39)

85. Which of the following is NOT true about sleep terrors in children?
   A. They are parasomnias that occur almost exclusively during SWS (stage N3)
   B. They do not involve dreaming
   C. They indicate a primary psychological disorder
   D. The child typically has no memory of the event in the morning

   ANSWER: C. Sleep terrors do not indicate a primary psychological disorder but rather occur in normal, healthy children. They are distinguished from nightmares in that they are associated with confusion when the child is awakened, and there is no memory of the dream, whereas upon arousal from a nightmare, the child is alert and can recall the dream. (PEDS2, Chapter 39)