Blessings on him who first invented sleep. It covers a man all over, thoughts and all, like a cloak. It is meat for the hungry, drink for the thirsty, heat for the cold, and cold for the hot. It makes the shepherd equal to the monarch, and the fool to the wise. There is but one evil in it, and that is it resembles death, since between a dead man and a sleeping man there is but little difference.

—Miguel de Cervantes (1547-1616)

Normal human sleep is often described as a state of reduced activity and reactivity, a kind of low general vigilance. Despite decades of intense scrutiny, our understanding of natural sleep is still incomplete. The two fundamental stages of sleep, nonrapid eye movement (NREM) and rapid eye movement (REM), are present in man as well as animals. Problems with sleep are frequent complaints of modern man, and a variety of these complaints are explored. Cognizance of the essence of normal human sleep may facilitate the anesthetist's understanding of pharmacologically induced sleep.

We know sleep as a condition that is associated with closed eyes, quiet and usually horizontal repose, a sort of sensual disengagement from the world around us that consumes a third of our life. Yet sleep is a controversial and quixotic state not always best defined by gentle and placid descriptors. In fact, sleep is an active process of the nervous system, the soma and the psyche. If we exclude headaches and the common cold, problems associated with sleeping may comprise our most frequent health complaints. Insomnia, narcolepsy, kicking (myoclonus), grinding teeth (bruxism), sleepwalking, nightmares and life-threatening breathing disorders are only some of the several score of recognized sleep disorders.

With sleep, environmental input to the organism is reduced, the critical threshold of electrical activity passing through the reticular activating system drops such that the cerebral cortex falls prey to somnolence (Figure 1). Despite this, the sleeping brain is not quiescent. We share with many other animals two fundamental states of sleep, nonrapid eye movement (NREM) and rapid eye movement (REM). Reported dream activity usually comes from REM sleep. The first 90 minutes or so of human sleep is normally characterized by NREM, a pattern of mentally inactive sleep electroencephalographically differentiated into four progressively "deeper" stages (Figure 2). As we drift into NREM Stage I, we may have a sensation of floating, and although we seem to be awake, we are already in the embrace of sleep. The eyes gently roll back and forth during Stage II sleep. Deep relaxation and the emergence of slow EEG delta waves herald entry into Stage III. Generally, only a loud noise or physical jolt will awaken the sleeper in Stage III. Stage
IV, delta sleep, is dominated by slow delta waves and is the deepest phase of sleep.

By contrast, the subsequent entry into REM sleep is characterized by EEG arousal and heightened physiologic activity. This REM sleep is also exemplified by increased cerebral blood flow, episodic fluctuations of the heart rate and blood pressure, rhythmic breathing alterations and sexual arousal. The reported vivid dreaming attending REM is normally devoid of muscle movement and conscious ego functioning. REM-related paralysis is apparently secondary to spinal neuronal inhibition by the brainstem, probably by the locus ceruleus in the pons (Figure 1). REM sleep, first described by Aserinsky and Kleitman in 1953, initially was not received enthusiastically by sleep scientists who then considered sleep as a time of central nervous system (CNS) deactivation. The phrase “paradoxical sleep” was coined for REM sleep and the terms continue to be used interchangeably. Paradoxical sleep is a term ostensibly well fitted to the oddly experienced somnambulistic functioning of the ego.

REM sleep initially lasts approximately 20 minutes followed by re-entry into NREM. This cyclic phenomenon usually occurs four or five times each night (Figure 3). A wealth of information exists on EEG and electro-ocularographic (EOG) interpretations of the sleep stages, and the reader is referred elsewhere for detailed descriptions of these techniques. For the clinical anesthetist, the following paradigm for differentiating these states might suffice: NREM—a quiet brain in a movable body, and REM—an active brain in an immovable body.

The functions of sleep

The range of total sleep among various animals poses questions that are at once intriguing and perplexing for those who ponder the purpose of sleep. The bullfrog and Dall porpoise may not sleep at all. The bottlenose dolphin sleeps with only half of its brain at a time. Grazing animals (horses, cattle and elephants) engage in limited amounts of sleep ranging from two to four hours, while still other animals (bats, opposums and sloths) sleep up to twenty hours. Animals with close genetic ties to humans, the chimpanzee for example, demonstrate sleep patterns that appear to be similar to ours. Primates are the only creatures known to exhibit the four distinct NREM stages.

A number of theories have been advanced toward explaining the purpose of sleep. Table I provides an overview of the major contemporary theories regarding the functions of sleep. The most likely answer to the question, “Why do we sleep?” seems implicitly obvious—to restore the body and mind, soma and psyche. We feel tired prior to sleep and rested afterwards. Yet as with other matters of physiology and behavior, simplistic explanations seldom suffice. To some, even the definition of sleep...
is elusive; certain animal behavior that looks like sleep—stillness, decreased responsiveness—is not necessarily what it appears to be. Sleep may also share a common evolutionary origin with hibernation as a way of saving or conserving energy. It has been argued that our failure to define the purpose of sleep defies our perceived need to have an explanation for everything. Indeed, perhaps our failed attempts to isolate one distinct function, serves as evidence for multiple functions. Have we, in our anthropomorphism of sleep, placed too much emphasis upon its role in the scheme of things? In a brilliant essay published in Natural History, it was argued that no single model provides the answer and that there exists in each a grain of truth. This is analogous to the situation regarding how inhalational anesthetics work, where a unifying explanation remains elusive.

As a response to tiredness, sleep may be a fundamental physiological condition like thirst or hunger. More likely it is a complex of processes with somatic and psychic implications beyond those which are purely physiological. Sleep deprivation intensifies the desire to sleep (much like not drinking for a long period intensifies the desire for water). Just as the sight of water is not certain to make a well-hydrated person thirsty, a long, tedious lecture in a darkened room is not certain to induce sleep in a well-rested individual; rather, the presence of behavioral cues (warmth, darkness, boredom, postprandial) only unmasks an existent sleep need rather than creating it.

Causes of sleep
The search for an endogenous physiologic substrate of sleep, "Factor S," which when injected will initiate sleep and when removed or antagonized will result in awakening, has gone unfulfilled. It is
Table I
Theories of sleep function

<table>
<thead>
<tr>
<th>Category and references</th>
<th>Features/evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Restorative³⁷</td>
<td>Recovery of physiological, neurological and psychological states. Implies a &quot;toxicity&quot; of &quot;awakeness.&quot; Rate of mitosis and protein synthesis is increased during sleep.</td>
</tr>
<tr>
<td>Protective³</td>
<td>Avoids excessive wear and tear. Diffusion of cortical inhibition over the cortex to avoid exhaustion.</td>
</tr>
<tr>
<td>Energy conservation⁶</td>
<td>There is a moderately strong correlation of estimated total sleep time and metabolic rate in numerous varieties of animals. Phylogenetic and evolutionary data suggest that a period of dormancy may offset high energy demands of homeostasis.</td>
</tr>
<tr>
<td>Instinctive³</td>
<td>Behavior manifests in the presence of cues. Behavior is organized and species-specific. Sleep feedback controls are &quot;looser&quot; than classical homeostatic systems (e.g., thirst).</td>
</tr>
</tbody>
</table>

Table II
Characteristics of human sleep*

- Recurrence
- Spontaneity
- Reversibility
- Closed eyelids
- Pharyngeal reflexes intact
- Specific EEG manifestations
- Cyclic nature predictable
- Absence of overt, goal-directed behavior
- Not dependent upon exogenous chemicals or trauma
- Decreased sensitivity to the external environment
- "Deepness" varies over the course of the sleeping phase
- Altered experience of ego functioning (dreaming)
- Phenomenology ranging from memory for nothing through vivid recall of mental (dream) and motor activity

*See references 1, 3, 5, 8, 10, 11.

Table III
Neurotransmitters implicated in sleep and wakefulness*

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetylcholine</td>
<td>Important but unclear role in alertness Levels highest in wakefulness and rapid eye movement (REM) sleep Onset of REM hastened with physostigmine Injection produces electrocortical activation</td>
</tr>
<tr>
<td>Norepinephrine</td>
<td>Monoamine oxidase inhibitors decrease REM sleep Low dose reserpine increases REM sleep Question role alpha-1 (postsynaptic) receptors Alpha-2 (presynaptic) have major role Clonidine inhibits wakefulness B-blockers generally cause sedation</td>
</tr>
<tr>
<td>Serotonin (5-HT)</td>
<td>Loss of serotoninergic neurons cause insomnia Circadian variation in 5-HT activity Variable, species-specific effect of 5-HT in humans, effect on REM and NREM variable</td>
</tr>
<tr>
<td>Dopamine</td>
<td>Increases motor activity and cortical arousal Antagonists usually decrease wakefulness Effect upon REM complex and highly variable Contributes to alerting effects of some drugs</td>
</tr>
<tr>
<td>Histamine</td>
<td>Histaminergic pathways participate in arousal Circadian variation in histamine activity H-1 antihistamines produce sleepiness</td>
</tr>
<tr>
<td>Adenosine</td>
<td>Potent regulator of central nervous system (CNS) activity Inhibitory effect on other neurotransmitters Induces or enhances sleep (indirect evidence) Exciitatory caffeine antagonizes adenosine</td>
</tr>
<tr>
<td>GABA</td>
<td>The primary CNS inhibitory neurotransmitter</td>
</tr>
</tbody>
</table>

*See references 12-14.

GABA—gamma-aminobutyric acid

of interest to compare the characteristics of normal sleep (Table II) with unconscious states such as hibernation, coma and pharmacologic anesthesia, as well as other states of reduced consciousness including daydreaming, purposeful meditation and spontaneous mental imagery.

Sleep can also be viewed as a shift in the delicate balance between two opposing forces, an arous-
ing or vigilance-enhancing force (the waking system) and a low-vigilance or desensitization force (the sleeping system). A variety of substances, primarily neurotransmitters, play pivotal but incompletely understood roles in sleep and wakefulness (Table III).

The highly complex intertwining of the CNS, its neurotransmitters and our behavioral foundations continue to shield an exact cause of sleep from our view. Wakefulness and sleep may be controlled by some yet to be discerned combination of these known neurotransmitters, by contributions from other biologicals which are only now being studied in detail (e.g., peptides, prostaglandins, endocrines), or by a mysterious “Factor S” which has, to date, gone undetected.

Despite the inconsistencies in the literature and the vast number of unanswered questions, there are several safe generalizations which can be made about the features which typify normal sleep in adults:\footnote{1,3,6,8,10}  
1. Transition from wakefulness to sleep occurs through NREM.  
2. NREM and REM cycle with periods of about 90 minutes.  
3. Slow wave sleep predominates the first third of the night and REM dominates the last third.  
4. NREM sleep accounts for approximately 75% of total sleep time while REM accounts for the additional 25% (Figure 4).  
5. Virtually all dreaming prior to waking is reported by sleepers awakened from REM sleep.

Answers to some commonly asked sleep-related questions

Over the last decade, the first author has encountered a variety of sleep-related inquiries during preanesthetic and postanesthetic rounds. The following inquiries have been maintained in a logbook, and reflect the authors’ interest in the phenomena, as well as the curiosity of these past patients. Their questions are intriguing as well as baffling. While we do not profess that the responses given are the only answers to the questions, they are provided for your scrutiny in the event you find yourself in a similar circumstance. References are included for most of the inquiries should the reader wish to explore a particular question further.

What is insomnia? Insomnia is not a disease but rather a symptom which is variably expressed as ranging from a reported belief that sleep is inadequate to specific complaints about being unable to fall asleep or the experience of frequent awakenings. The daytime manifestations of insomnia are legion and include sleepiness, depression and overt physical distress. Finding the cause of the insomnia is critical to long-term success in its management, as treating only the symptom will otherwise be disappointing.

Is there a particular part of the sleep cycle most associated with bedwetting, sleeptalking and sleepwalking? Not necessarily, although NREM Stage IV is a very “deep” phase of sleep where arousability is quite difficult. Sleeptalking is common in all ages and most often occurs in NREM Stages I and II and

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Figure 4
Relative contributions of the sleep stages to total sleep

<table>
<thead>
<tr>
<th>Stage</th>
<th>% of NREM</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>4%</td>
</tr>
<tr>
<td>II</td>
<td>71%</td>
</tr>
<tr>
<td>III</td>
<td>8%</td>
</tr>
<tr>
<td>IV</td>
<td>17%</td>
</tr>
</tbody>
</table>

REM—Rapid eye movement  
NREM—Nonrapid eye movement
also in REM sleep. Sleepwalking is more often seen in children and usually occurs during the first third of sleep; the sleepwalker is almost always amnesic for the event. Bedwetting (enuresis) usually occurs in NREM sleep, is common in children and has multiple etiologies.

Is there a relationship between life expectancy and sleeping pattern? Although the association defies explanation at this time, Kripke and associates observed that men and women who reported sleeping more than 10 hours a day were approximately 1.8 times more likely to experience premature death than those sleeping between 7-8 hours daily. One should not interpret this as suggesting a cause and effect relationship.

What pharmacological clues have provided insight into the sleep activation process? Anesthetists are well-acquainted with the ability of benzodiazepines to induce sleepiness by facilitating the neuroinhibitor, gamma-aminobutyric acid (GABA). Antihistamines which penetrate the CNS produce sleepiness by an obviously different mechanism. Alternatively, stimulant drugs such as amphetamines (by impeding catecholamine uptake) and caffeine (an adenosine receptor antagonist) produce stimulation of the CNS, diminishing feelings of sleepiness. While there is a wealth of theoretical and clinical observation concerning this question, definitive conclusions would be premature.

Why do the eyes move so briskly under the lids during REM sleep? Slowly moving, almost rolling eye movement signals entry into Stage I (NREM) sleep, whereas darting movements characterize the REM phase. Because the mental activity of REM sleep is associated with vivid dreaming (we terize the REM phase. Because the mental activity during REM sleep is associated with vivid dreaming (we terize the REM phase. Because the mental activity during REM sleep is associated with vivid dreaming (we terize the REM phase. Because the mental activity during REM sleep is associated with vivid dreaming (we terize the REM phase. Because the mental activity during REM sleep is associated with vivid dreaming (we terize the REM phase. Because the mental activity during REM sleep is associated with vivid dreaming (we terize the REM phase. Because the mental activity during REM sleep is associated with vivid dreaming (we terize the REM phase. Because the mental activity during REM sleep is associated with vivid dreaming (we terize the REM phase. Because the mental activity during REM sleep is associated with vivid dreaming (we terize the REM phase. Because the mental activity during REM sleep is associated with vivid dreaming (we terize the REM phase. Because the mental activity during REM sleep is associated with vivid dreaming (we terize the REM phase. Because the mental activity during REM sleep is associated with vivid dreaming (we terize the REM phase. Because the mental activity during REM sleep is associated with vivid dreaming (we terize the REM phase. Because the mental activity during REM sleep is associated with vivid dreaming (we terize the REM phase. Because the mental activity during REM sleep is associated with vivid dreaming (we terize the REM phase. Because the mental activity during REM sleep is associated with vivid dreaming (we terize the REM phase. Because the mental activity during REM sleep is associated with vivid dreaming (we terize the REM phase. Because the mental activity during REM sleep is associated with vivid dreaming (we terize the REM phase. Because the mental activity during REM sleep is associated with vivid dreaming (we terize the REM phase. Because the mental activity during REM sleep is associated with vivid dreaming (we terize the REM phase. Because the mental activity during REM sleep is associated with vivid dreaming (we terize the REM phase. Because the mental activity during REM sleep is associated with vivid dreaming (we terize the REM phase. Because the mental activity during REM sleep is associated with vivid dreaming (we terize the REM phase. Because the mental activity during REM sleep is associated with vivid dreaming (we terize the REM phase. Because the mental activity during REM sleep is associated with vivid dreaming (we terize the REM phase. Because the mental activity during REM sleep is associated with vivid dreaming (we terize the REM phase. Because the mental activity during REM sleep is associated with vivid dreaming (we terize the REM phase. Because the mental activity during REM sleep is associated with vivid dreaming (we terize the REM phase. Because the mental activity during REM sleep is associated with vivid dreaming (we terize the REM phase. Because the mental activity during REM sleep is associated with vivid dreaming (we terize the REM phase. Because the mental activity during REM sleep is associated with vivid dreaming (we terize the REM phase. Because the mental activity during REM sleep is associated with vivid dreaming (we terize the REM phase. Because the mental activity during REM sleep is associated with vivid dreaming (we terize the REM phase. Because the mental activity during REM sleep is associated with vivid dreaming (we terize the REM phase. Because the mental activity during REM sleep is associated with vivid dreaming (we terize the REM phase. Because the mental activity during REM sleep is associated with vivid dreaming (we terize the REM phase. Because the mental activity during REM sleep is associated with vivid dreaming (we teriz
tention outside of Jungian circles with implications for the psychology of memory, learning and personality. Jung's ideas have also included the possibility that some physical symptoms could be conceived of as part of the phenomenology of the individual's dream process.

What is a nightmare? How does it differ from a night terror? Nightmares, which are more common in children, are frightening dreams which actually awaken the sleeper from REM sleep and are vividly recalled. Certain drugs predispose people to nightmares (e.g., antiparkinsonian drugs, beta blockers), as will a traumatic or frightening personal experience. With a night terror, the sufferer appears to be "terrified," is incompletely awakened and is usually amnestic for the event.

How much sleep does a person need? While the precise physiological answer to this question is unknown, accurate information is available on how much sleep people obtain. There is great variability among members of the human race in terms of total sleep time. While 7.5 hours probably best expresses the norm, anything between 6 and 9 hours is not at all unusual. Age-related changes associated with sleep have a significant impact on the total amount of time one experiences the phenomenon. (See next question.)

How does age influence normal sleep pattern? There is a relatively consistent and predictable effect of age upon sleep (Figure 5). Newborns may experience 16-18 hours of sleep in each 24-hour period although this decreases precipitously over the first year of life. Slow wave sleep is maximal in young children. The elderly experience much lower amounts of sleep time, often in the vicinity of only 6 hours and the amount of slow wave sleep is decreased markedly. Many of the observed changes seen in the elderly may reflect the breathing disturbances and periodic leg movements that are extremely common in this age group. With age, sleep efficiency is decreased with less time spent in NREM Stages III and IV. The analysis of age-related changes is complicated by a host of confounding factors such as chronic pain, bereavement and anxiety which are common in the elderly.

What are the little muscle jerks or twitching we sometimes experience as we fall off to sleep? These common, general or localized muscular contractions are called hypnic myoclonia and because they are often associated with vivid visual imagery, they may be a function of the dream process. They tend to manifest more frequently during stress, extreme fatigue or irregular sleep schedules. While the precise explanation is not known, a common theory suggests that it is the result of experiencing a partial entry into REM prior to the onset of skeletal muscle motor inhibition. It may simply be the body trying to respond to the imagery "seen" by the brain.

Why do I rarely seem to "remember" the instant when I actually fall asleep? Guilleminault's classic experiment illustrates what happens to memory at the onset of sleep. Words were presented to volunteers at 1-minute intervals up to the point of falling asleep (defined by EEG criteria). After sleeping for either 30 seconds or 10 minutes, volunteers were awakened and asked to select from a written list of words presented to them. Those who slept for 10 minutes had great difficulty identifying words pre-

Figure 5
Relative time spent in sleep by age group

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Relative Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Newborn</td>
<td>++++/......+++</td>
</tr>
<tr>
<td>4 Years old</td>
<td>+++++/.....++++</td>
</tr>
<tr>
<td>10 Years old</td>
<td>++++++/.....++++++++</td>
</tr>
<tr>
<td>30 Years old</td>
<td>++++++++/.....+++++++</td>
</tr>
<tr>
<td>70 Years old</td>
<td>++++++++......+++++++</td>
</tr>
</tbody>
</table>

Key: ++++ = awake  ///// = asleep
Note: Actual times for each activity should not be rigidly interpreted; this is meant only to represent proportionate times spent in each activity.
sented to them just before falling asleep compared to words presented to them 6-10 minutes before the onset of sleep. The volunteers who slept for only 30 seconds experienced vivid recall up until they fell asleep. As one falls asleep there is a transition marked by retrograde amnesia which explains why one may not remember a middle-of-the-night phone call, have only poor dream recall or not recall falling asleep. At the other end of the continuum, techniques for enhancement of dream recall and lucid dreaming suggest that retrograde amnesia may be a function of ego awareness.

Is it possible to dream under anesthesia? When I woke up, I had the most vivid recollection of having fallen into a hole and trying to climb back out with a strong wind in my face. There is little question that people can dream under anesthesia. Since the time of Claude Bernard (discoverer of curare), who warned practitioners that we now have “the potential of locking sensitive beings within immobile bodies,” the risk of a patient experiencing an imperfectly obtunded consciousness during a surgical intervention remains a threat. Not only can dreaming occur during anesthesia, but should awareness during anesthesia occur, the patient might also experience a variety of sleep-related disturbances (including nightmares) for some time after the event, yet fail to attribute the activity to the anesthetic episode. Disconcerting as it is, it has been demonstrated that anesthetized patients can sometimes weakly recall certain auditory cues even when they appear to be unconscious. The complexity of our consciousness in its numerous “layers” and the lack of uniformity in the way people respond to pharmacological manipulations argues against a simple recipe for preventing conscious assimilation during anesthetized “sleep.”

What is the longest length of time a person has gone without sleep? The world championship for voluntary sleep deprivation goes to Robert McDonald of California who experienced (endured?) 453 hours and 40 minutes of sleeplessness from March 14 to April 2, 1986. In a more scientifically controlled venture, a 17-year-old student undertook a 264-hour period of sleep deprivation while his behavioral manifestations were carefully observed. Although there were no apparent long-term effects, hallucinatory phenomena and bizarre behavior were noted. Following the experiment, the first recovery sleep session lasted 15 hours with increased amounts of both NREM Stage IV and REM sleep.

What is the pickwickian syndrome? The pickwickian syndrome (obesity hypoventilation syndrome) was coined in reference to the fat boy, Joe, in Charles Dickens’ classic work, Pickwick Papers, and describes the findings of obesity, respiratory insufficiency and periodic excessive sleep. These patients have impaired ventilatory control but are able to normalize their blood gases with voluntary hyperventilation. Their excessive daytime somnolence is attributed to ineffectual sleep patterns due to the periodic nocturnal awakening which occurs as the CNS initiates convulsive breathing in the face of developing hypoxemia.

Summary

Sleep is often described as a state of reduced activity and reactivity, a kind of low general vigilance. Careful examination reveals an uneven reduction among systems; thermoregulation and respiration, for example, react at levels quite similar to those observed during waking. Sleep then, appears to be a state of reduced “local” or “discrete” vigilance of the body-mind complex.

Cervantes depicted sleep as a kind of niche where we are gently tucked in between life and death. We can view the anesthetic state as a kind of pharmacologically controlled respite where the patient is tucked in (protected) from the reality of a surgical onslaught and away from a prematurely forbidding eternity. The two states thus share a common philosophical orientation. Anesthetists should understand the scientific foundations of normal sleep so that we might better understand pharmacological sleep. In the event a patient asks us to differentiate the two, confidence will be fostered by an informed and rational approach to the question.

REFERENCES


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