In: O.G.Edholm & J.S.Weiner (Eds),

The Principles and Practice of Human Physiology,

London, Academic Press, 1981, Chapter 10, pp.505-527.

CHAPTER 10

Sleep

M.W. Johns

Basic Concepts

Fundamental rhythm of sleep and wakefulness

All mammals and many other animals lower on the evolutionary scale sleep at least once daily throughout their lives, apart from those unusual times when some animals hibernate.

Sleep is a rapidly reversible state of reduced activity and responsiveness to the environment, usually experienced at a time of day or night when, from the point of view of the particular animal's adaptation to the environment, energy might best be conserved rather than expended (Webb, 1974). The ready reversibility of sleep is one characteristic that distinguishes it from coma and hibernation, which are also states of reduced activity and reactivity.

Over the past 25 years major advances have been made in the detailed description of physiological changes which take place during sleep, but there is still much to be learnt about its fundamental nature. This chapter will be limited mainly to a discussion of sleep in man, although some investigations which could be carried out only in animals must be mentioned.

Electroencephalogram and electro-oculogram during sleep

Much of the sleep research carried out in modern times was made possible by an observation reported in 1929 by Hans Berger that the electroencephalogram (EEG) during sleep was markedly different from that during wakefulness. Soon afterwards it was observed that there were cycles of change in the frequency and amplitude of the EEG during a normal night's sleep, and that these changes were paralleled by variations in the apparent depth of sleep as measured by the auditory stimulation required to waken the subject at the time (Blake and Gerard, 1937). However, it was not until the early 1950s, when another important discovery was made in relation to movements of the eyes during sleep, that it became widely appreciated that sleep was not of a uniform nature during the night. Eye movements can be recorded continuously by means of the electro-oculogram or EOG. Each eye acts as a dipole because of the constant corneo–retinal potential and eye movements therefore produce changes in the potential difference between electrodes fixed to the skin at each side of the orbit. Aserinsky and Kleitman (1953) reported that at approximately 90-minute intervals the eyes of sleeping subjects flicked from side to side beneath closed eyelids for periods lasting several minutes at a time. These rapid eye movements, or REMs as they were called, were in marked contrast to the slow, wandering eye movements which occurred at most other times during sleep. When the REMs occurred the EEG resembled that recorded during drowsiness, with relatively low-amplitude waves having a higher frequency than was usual during sleep. If the subjects were woken then they usually reported having just been dreaming, whereas this seldom occurred when they were woken at other times.

These important observations led to the recognition of a distinctly different type of sleep associated with dreaming, a state which has become known as REM sleep. The distinction between REM sleep and the other type of sleep, called non-REM or NREM sleep, has been a major topic of research over the past 20 years.

Stages of sleep

At present, sleep is usually categorized into five stages—four NREM stages and REM sleep—defined on the basis of the EEG, EOG and sometimes also the electromyogram (EMG) taken from the submental muscles (Rechtschaffen and Kales, 1968).

Stage 1 The drowsy state between alert wakefulness and definite sleep. The transition from wakefulness is associated with a generalized slowing of the EEG into the theta range (2–7 cycles per sec) and loss of obvious alpha waves (8–12 cycles per sec). The conjugate, saccadic eye movements of wakefulness give way to slow, pendular eye movements which are often non-conjugate, that is, each eye moving independently of the other.

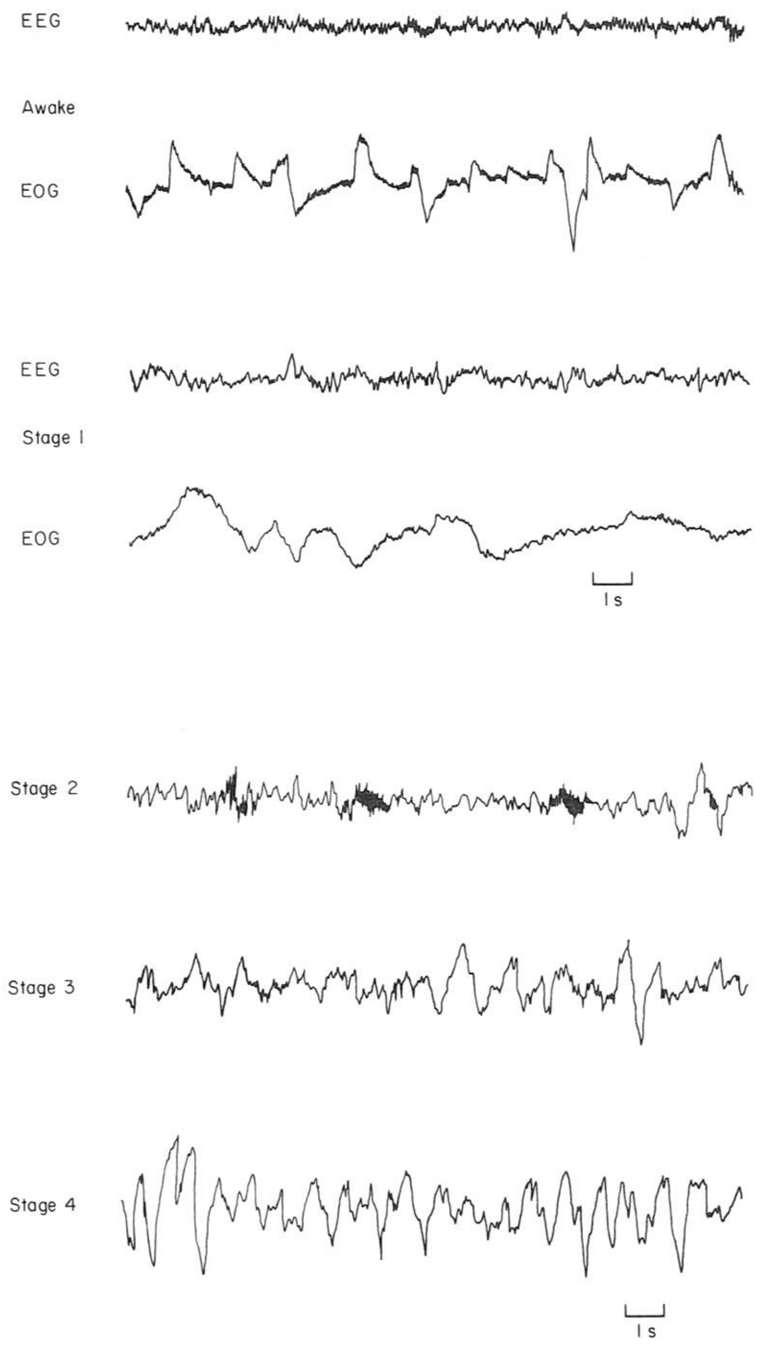
Stage 2 Spindles, K-complexes and delta waves appear in the EEG. Spindles are bursts of waves with a frequency of between 13 and 15 cycles per second lasting 0.5–1 s. A K-complex is a wave-form with a well-defined negative wave of relatively high amplitude ($> 100\ \mu V$) followed by a positive wave and then by a short burst of 12–14 cycles per second waves of lower amplitude. Some K-complexes occur as responses to an external stimulus such as a noise which is not loud enough to waken the subject, but most K-complexes occur spontaneously. Delta waves of low frequency (1–4 cycles per second) and high amplitude ($> 75\ \mu V$) also appear first during stage 2.

Stage 3 Between 20 and 50% of the EEG trace taken up by delta waves. Spindles and K-complexes are also present.

Stage 4 More than 50% of the EEG trace is taken up by delta waves. Spindles and K-complexes are less obvious than in stages 2 and 3.

REM sleep Characterized by the concomitant appearance of a low voltage, mixed frequency EEG, as in stage 1, and of REMs recorded in the EOG. Spindles and K-complexes occur rarely, if at all.

REM sleep is sometimes referred to as paradoxical sleep because the similarity of the EEG during stage 1 and REM sleep would suggest that both stages were very light sleep. In fact, the arousal threshold is at least as high during REM sleep as that during stage 2—hence the paradox. By contrast, other NREM stages are sometimes collectively called orthodox sleep, although these terms are usually reserved for experiments with animals rather than man. Stages 3 and 4 are sometimes considered together as delta-wave or slow-wave sleep.



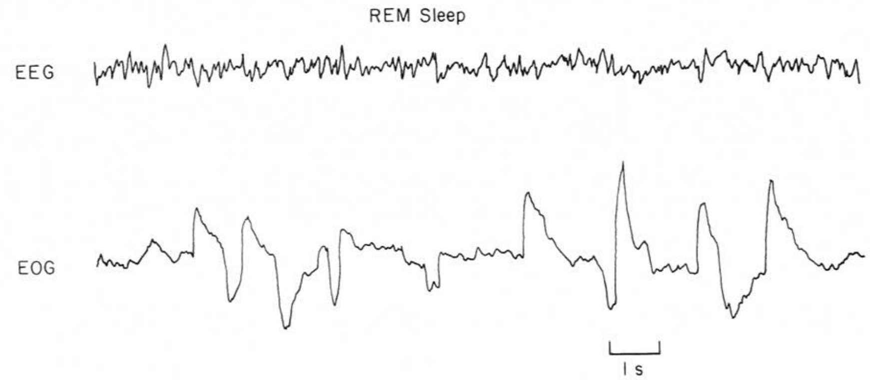


FIG. 1 Records of the electroencephalogram (EEG) and electro-oculogram (EOG) in the awake state and the various stages of sleep.

Sleep cycles

The various stages of sleep tend to recur cyclically during a night's sleep (Fig. 2). The mean interval between the beginning of successive REM sleep periods (a sleep cycle) is about 100 minutes and there are usually 3–6 sleep cycles per night. Approximately one or two hours of NREM sleep usually precede the appearance of the first REM sleep period. Sometimes, at the time when the first REM sleep period might be expected, there is instead a brief period of stage 2 sleep with K-complexes and spindles, but with REMs recorded in the EOG. The duration of REM sleep periods tends to increase during the night from a mean of about 13 minutes for the first period to between 20 and 45 minutes in subsequent periods. The amount of stages 3 and 4 sleep (delta-wave sleep) generally decreases in successive cycles. For an average night's sleep in young adults, approximately 24% of the time is spent in REM sleep, 4% in stage 1, 51% in stage 2, 10% in stage 3, and 11% in stage 4. The distribution of stages within each sleep cycle and across the whole night's sleep varies with age and with a wide range of environmental changes, psychological stress, as well as with medical and psychiatric illnesses, as described in detail by Williams *et al.* (1974).

Sleep and Body Systems

Cardiovascular system

The heart rate decreases by an average of about 4.5 beats per minute with sleep onset (Johns *et al.*, 1976). There is usually a further small decrease

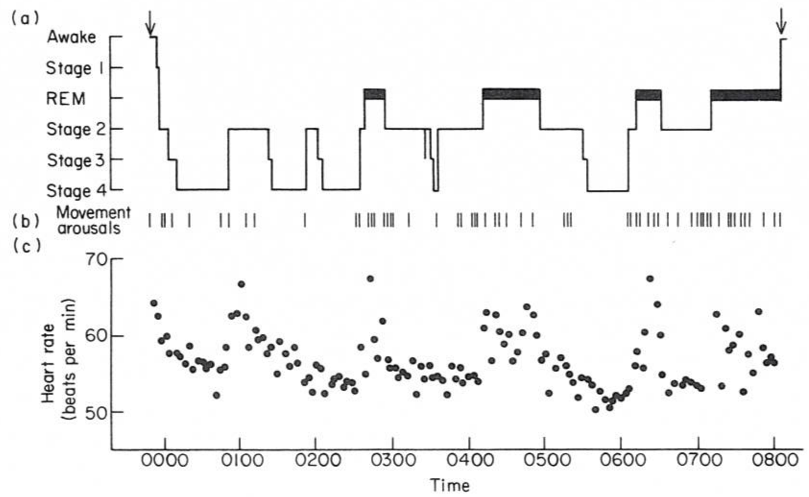


FIG. 2 (a) The distribution of sleep stages during an undisturbed night's sleep in a young man. The arrows indicate times of going to bed and getting up. (b) The intermittent occurrence of body movements during sleep. (c) The mean heart rate, measured over 20 beats at a time, varies according to the stage of sleep and the time of night. The rate is higher and more variable in REM sleep than in NREM sleep.

from stage 2 to stages 3 and 4. The heart rate usually increases during REM sleep and, in particular, becomes more variable (Fig. 2). Body movements during sleep and periods of wakefulness during the night are also associated with phasic increases in heart rate but these effects have been eliminated from the results shown in Fig. 2. However, brief episodes of bradycardia and tachycardia, lasting perhaps 10 seconds, occur spontaneously during sleep. These disappear after bilateral cervical vagotomy or methylatropine administration despite an intact sympathetic nerve supply to the heart. They are, therefore, due mainly to changes in vagal activity.

Much slower changes in heart rate take place over periods of hours during the night, regardless of the stage of sleep or wakefulness at the time. The lowest mean heart rate is likely to be found between 4 and 6 a.m. The origin of this circadian rhythm is uncertain although it is probably not simply a reflection of the diurnal variations in body temperature. The circadian rhythms of heart rate and of core temperature are often out of phase with one another by several hours on particular nights.

Arterial blood pressure decreases at the time of sleep onset and may decline to 55 mm Hg systolic and 30 mm diastolic pressure during the night in healthy adults, levels which in the waking state would be considered to be alarmingly low (Bevan *et al.*, 1969). This is because cardiac output falls

without a concomitant increase in peripheral resistance. There is vasodilatation in the skin at sleep onset and, in experimental animals, there is cutaneous vasoconstriction during REM sleep (Khatri *et al.*, 1967). This involves a redistribution of blood flow rather than a significant change in total peripheral resistance. In the cat, mesenteric and renal arterial blood vessels dilate during REM sleep when the cutaneous vessels are constricted (Mancia *et al.*, 1970). Similarly, in cats there is a marked increase in blood flow to the cerebral cortex and rhombencephalon but a decrease in the mesencephalon during REM sleep compared with the flow during NREM sleep (Reivich *et al.*, 1968). On arousal to wakefulness from slow-wave sleep there is a marked increase in blood flow to the mesencephalon and a decrease in the rhombencephalon (Baust, 1967). These variations seem to reflect regional differences in metabolism of the central nervous system in the various states of sleep and wakefulness.

Body movements, muscle tone and reflexes

Major body movements, such as flexing an arm or turning the trunk from one side to the other, are common during sleep even when, by other criteria, it is restful sleep. There are usually between 20 and 60 such movements per night. They occur mainly in stage 2 and REM sleep, very seldom during delta-wave sleep, although periods of the latter are usually terminated by a major body movement (Fig. 2).

Tonic activity in the skeletal muscles decreases during the period of relaxation in preparation for sleep and may decrease further on falling asleep. With the onset of REM sleep the remaining level of tonic activity recorded in the EMG is abolished. In addition, there is a marked reduction in the activity of spinal reflexes such as the H-reflex. During this state of hypotonia and hyporeflexia, phasic increases in skeletal muscle activity occur and these produce the rapid eye movements as well as twitching of the facial muscles and limbs (Baldridge *et al.*, 1965).

Respiratory system and oxygen consumption

The mean respiratory rate is commonly about two cycles per minute less in all stages of sleep than it is in resting wakefulness. Respiratory movements during sleep are more thoracic than abdominal, unlike those during wakefulness. They are usually regular in slow-wave sleep, but during stage 2 and REM sleep Cheyne–Stokes respiration is common, even in healthy subjects who may have bursts of tachypnoea and periods of apnoea which may last up to 1 minute (Webb, 1974). Oxygen saturation may decrease to about 92%, p_{CO_2} rises and blood pH falls by about 0.03 units. There is reduced sensitivity to hypercapnoea and acidaemia during normal sleep, and in patients with impaired ventilatory capacity temporary cerebral hypoxia is a frequent occurrence (Pierce *et al.*, 1966). Oxygen consumption (metabolic rate) is about 10 per cent less during sleep than wakefulness. The lowest metabolic rates occur during delta-wave sleep and higher rates during REM sleep, although this is influenced by the frequency of body movements (Brebbia and Altschuler, 1965).

Genito-urinary system

Penile erection in males and clitoral erection in females occurs regularly during REM sleep and is unrelated to the sexual content of dreams at the time.

The rate of urine formation decreases and urine osmolarity increases during sleep. Failure of this mechanism may be at least partly responsible for nocturnal enuresis. With increasing age that proportion of the 24-hour urine output which is excreted at night increases and this commonly causes nocturia in otherwise healthy men and women.

Endocrine system

The secretion of ACTH from the anterior pituitary gland, and hence of cortisol from the adrenal cortex, is episodic rather than continuous. Bursts of secretion occur at intervals of one to two hours (Hellman *et al.*, 1970). However, such episodes are usually inhibited during the early hours of sleep; the secretory periods then increase, reaching a maximum between about 5 a.m. and midday. During the night secretory episodes often coincide with either REM sleep or periods of arousal to wakefulness although this is not a one-to-one relationship (Alford *et al.*, 1973a). After acute reversal of sleep and wakefulness the circadian rhythm of adrenocortical activity takes between one and two weeks to renew its original phase relationship to sleep and wakefulness (Weitzman *et al.*, 1968).

The diurnal rhythm of physical activity and social behaviour, especially that of sleep and wakefulness, is probably the most important factor in entraining the phase of the circadian rhythms in adrenocortical and adrenomedullary activity, even when time cues from clocks or the sun are absent (Aschoff *et al.*, 1971).

Growth hormone secretion from the anterior pituitary gland is also episodic. For most people, a major part of the day's growth hormone secretion occurs during the first period of delta-wave sleep within an hour

of sleep onset. After acute reversal of sleep and wakefulness, growth hormone secretion, unlike that of cortisol, maintains its relationship to the initial period of delta-wave sleep (Sassin *et al.*, 1969). The plasma concentrations of glucose and insulin do not change significantly during sleep. Nor have any other metabolic changes been recognized in the peripheral circulation which might explain the growth hormone secretion during sleep. There appears to be a fairly specific relationship between the neural mechanisms controlling delta-wave sleep on the one hand and those controlling growth hormone releasing factor in the hypothalamus on the other hand.

Prolactin secretion is also increased episodically soon after sleep onset. It usually attains its highest plasma concentrations later during the period of sleep and is not obviously related to particular stages of sleep (Sassin *et al.*, 1973). As with growth hormone, prolactin secretion retains its relationship to sleep onset immediately after reversal of sleep and wakefulness.

The plasma concentrations of luteinizing hormone (LH) and follicle stimulating hormone (FSH) do not show consistent differences between sleep and wakefulness, either in prepubertal children or in adults. However, at puberty the episodic secretion of LH is closely related to sleep onset, even after acute reversal of sleep and wakefulness, and in this respect it resembles GH and prolactin in its secretory pattern (Boyar *et al.*, 1972). Diurnal variations in the secretion of thyroid stimulating hormone, oestradiol and testosterone are not so closely related to sleep (Alford *et al.*, 1973b).

The overall pattern of plasma hormone concentrations, particularly those during the initial part of the sleep period, is such that anabolism should be promoted and catabolism reduced, as manifested, for example, by a relatively high rate of brain protein synthesis during sleep (Adam and Oswald, 1977).

Body temperature and sweating

With sleep onset, the skin temperature on the trunk and the limbs usually increases by between 1 and 3 °C; that is, to temperatures of 34 or 35 °C. This occurs over a few minutes as a result of cutaneous vasodilatation with a decrease in vasoconstrictor tone. As a consequence of the increased skin temperature, the rate of sweating increases in those areas of skin most concerned with thermoregulation (Satoh *et al.*, 1965). The core temperature measured in the rectum or at the tympanic membrane of the ear usually reaches its maximum for the day in the early evening. It falls during sleep, reaching a minimum of little more than 36 °C in healthy subjects, usually between about 4 and 6 a.m., after which it increases again. Most sleep, therefore, is associated with mechanisms which promote the loss of body heat at a time when the metabolic rate and heat production is already low. Nevertheless, sleep is interrupted if the degree or rate of heat loss is too high, as in very cold environments. After acute reversal of sleep and wakefulness, the normal circadian rhythm of body temperature may take several days to regain its usual relationship to behavioural state (Kleitman, 1963).

Unlike most sweat glands, those on the palms of the hands and soles of the feet are generally inhibited during sleep. This change has formed the basis of one simple method for monitoring sleep and wakefulness by continuous measurement of the electrical resistance of palmar skin (Johns, 1971).

Mental activity during sleep

The study of mental activity during sleep depends on the experimental subject's ability to recall and describe it when awake. This ability is most frequently demonstrable when the subject is woken during a REM sleep period or within a few minutes of its ending. Thereafter, recall is rapidly lost. Whether or not a subject often remembers dreams depends to some extent on his personality (Williamson *et al.*, 1970).

When normal subjects are woken from NREM sleep they often report having had some form of mental activity which is best described as thought-like rather than dream-like, the former being more conceptual, less emotional and having lower perceptual intensity than the latter (Rechtschaffen *et al.*, 1963). Throughout sleep, normal subjects can discriminate to some extent between "meaningful" auditory stimuli and other sounds of the same intensity (Oswald *et al.*, 1960). A mother may wake at the first soft cries of her baby but remain asleep when a dog barks. Thus, sleep is a state of reduced responsiveness to the environment and of altered mental functioning but, nonetheless, a state in which some information processing of sensory input continues.

Functions of sleep

The ubiquity of sleep–wakefulness rhythms and the many differences between REM and NREM sleep have provided the basis for speculation about the overall needs for sleep and, lately, about the separate functions of the different kinds of sleep. Early suggestions that dreaming and REM sleep were essential for psychological wellbeing in man prompted many investigations into the nature of this requirement (Hartmann, 1973). However, as we

shall see later in this chapter (p. 520), the absence of REM sleep for prolonged periods in man has not consistently led to any recognizable behavioural changes. The finding of an increased proportion of REM sleep in neonates led to speculation that REM sleep serves an ontogenetic function, organizing the developing central nervous system (Roffwarg *et al.*, 1966) and the oculomotor system in particular (Berger, 1969). So far, these are no more than working hypotheses.

The decrease in body temperature by an active process of heat loss during sleep, the inhibition of cortisol and of adrenaline secretion at a time when growth hormone, prolactin and, at puberty, also LH secretion are increased —these findings are all consistent with sleep, and particularly delta-wave sleep, being a period of restoration and anabolism after increased catabolism during wakefulness. Perhaps sleep is needed after many hours of wakefulness because of fatigue in the neural mechanisms subserving selective attention and the maintenance of psychological defences, that is, of the most highly integrated functions of the central nervous system. However, there is another important function of sleep which has often been neglected, and that is to do with the entrainment of intrinsic circadian rhythms in bodily function—for example, the rhythms of body temperature and of adrenocortical activity. After a change in these rhythms it takes several days at least to synchronize them and until this is achieved sleep may not be as refreshing as usual. To this extent, therefore, the usual amount of sleep may be a necessary but not a sufficient condition for maximal "restoration" after wakefulness. The mechanism by which sleep entrains other intrinsic rhythms, or under some circumstances fails to do so, remains to be elucidated.

Neurophysiological Basis for Sleep and Wakefulness

Reticular activating system

The classical animal experiments of Moruzzi and Magoun (1949) and of Lindsley *et al.* (1949) clearly established that the behavioural state of wakefulness and the associated activation of the cerebral cortex (manifested by low-amplitude, high-frequency EEG) were dependent upon structures in the midbrain reticular formation. However, it became important to distinguish between an ascending reticular activating system which was concerned primarily with cortical activation and another, descending reticular activating system involving the hypothalamus which was necessary but not sufficient for the maintenance of behavioural arousal (Jouvet, 1967). In the waking state the diversity and multitude of sensory inputs and humoral factors (particularly adrenaline) affect the reticular activating systems. Accordingly, one theory is that sleep is a passive phenomenon arising from a reduction in sensory input, particularly from the muscle spindles; sleep may be considered the absence of wakefulness.

Sleep an active state

It is now known that sleep, like wakefulness, is a state which is actively maintained by a complex interaction between many different parts of the central nervous system. An "active" theory of sleep was first strongly propounded by Hess (1929) who stimulated the thalamus and produced cortical synchronization (deactivation) and behavioural sleep. However, there are so many other regions, in the cerebral cortex, internal capsule, hypothalamus, cerebellum and medulla, all of which produce similar effects after stimulation, that this method is not very helpful in defining relationships between the structures directly concerned with producing sleep (Jouvet, 1969a).

The most important sleep-inducing structures are located in the lower brain-stem, particularly in the pons and medulla. These include mainly serotonergic neurons in the raphe system (Fig. 3). The extent of partial destruction of this raphe system determines the amount of NREM sleep obtained by cats (Jouvet, 1969b). By contrast, REM sleep is selectively

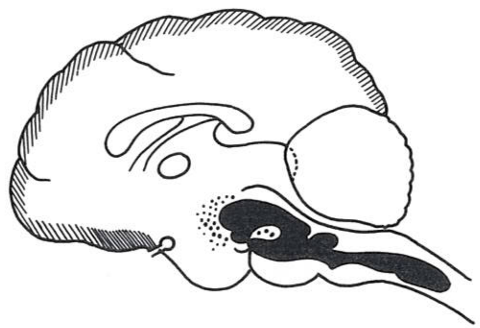


FIG. 3 A sagittal plan of a cat's brain showing the ascending reticular activating system (dots) and the sleep-inducing system of raphe nuclei (black). Decortication (removal of cross-hatched areas of cerebral cortex) suppresses slow waves but does not eliminate the oscillation between REM and NREM sleep (after Jouvet, 1969a).

suppressed by lesions in the dorso–lateral pontine tegmentum which do not impair NREM sleep. Thus, REM sleep and NREM sleep involve different structures in the central nervous system.

The cerebral cortex is necessary for the appearance of slow waves in the EEG but not for the oscillation between REM and NREM sleep. Within REM sleep, the tonic inhibition and the phasic activity also involve different neuronal systems. Neurons in the nucleus locus coeruleus, the dorsal part of the medio–lateral pontine tegmentum, trigger the descending inhibitory part of the reticular formation which blocks, both at pre- and post-synaptic levels, the discharges of spinal motor neurones and hence causes the generalized atony of REM sleep. This atony is dependent at least partly on a cholinergic mechanism because it is suppressed by atropine. By contrast, the phasic events and the cortical activation during REM sleep originate in a restricted area of the pons, the nucleus reticularis pontis caudalis (Jouvet, 1967).

Just before the disappearance of muscle tone at the start of REM sleep, spike discharges appear in the pons, soon after in the lateral geniculate nucleus, and then in the occiptal cortex and the oculomotor nucleus (Jouvet, 1967). These pontogeniculo-occipital (PGO) spikes are often related to the appearance of individual rapid eye movements and other phasic events although this is not a one-to-one relationship.

Jouvet (1969b) has suggested that a priming, serotonergic mechanism in the caudal part of the raphe system may act on cholinergic neurones which, in turn, trigger the final noradrenergic mechanisms of REM sleep located in the nucleus locus coeruleus. Recent investigations involving extracellular recordings from individual neurones in the pons have identified two groups of cells in the nucleus locus coeruleus (NLC) on the one hand, and in the gigantocellular tegmental field (FTG) on the other hand, which show reciprocal relationships in their discharge rates during both REM and NREM sleep (Hobson *et al.*, 1975). There is a tonic increase in the discharge rate of TFG neurones during REM sleep which appears to be due to decreased inhibition from noradrenergic neurones in the N. locus coeruleus. However, serotonergic neurones in the dorsal raphe nucleus also show a decrease in firing rate during REM sleep and these cells have synaptic input to giant cells in the FTG too. The details of several possible relationships between groups of cells of this type remain to be elucidated. Nevertheless, a computer model of discharge rates in two groups of neurones having reciprocal interactions similar to those between the NLC and FTG neurones gives a clear indication that such interactions could provide the basis for the oscillation between REM and NREM sleep (McCarley and Hobson, 1975).

Population Studies

The pattern of sleep and wakefulness in individual people is subject to their voluntary control, to some extent at least. Nevertheless, most people adopt sleep habits which are fairly regular and which are arrived at by an interaction between many biological, psychosocial, occupational and environmental influences. For example, most people sleep at night rather than during the day, except when their occupation demands otherwise. A midday siesta is obtained in some communities by the appropriate organization of their daytime activities. Nevertheless, there is little to suggest that the amount of sleep usually obtained per 24 hours differs markedly between the most primitive and the most economically advanced communities. Of greater importance are the changes in sleep habits with age—changes which are presumably present in all communities.

Changes with age

There are changes in both the subjective and the objective characteristics of sleep with increasing age. Infants have more than one period of sleep each day. As the central nervous system matures their ability to remain awake throughout the day increases and by the age of 4 or 5 years most of their sleep is restricted to the night. The mean duration of sleep per 24 hours decreases from about 15 hours in the neonate to about 7.7 hours (standard deviation ± 1.5 hours) by the age of 20 years (Kleitman, 1963; Tune, 1969). There is a further small decrease until the sixth decade, after which the duration of sleep often increases again (Tune, 1969; Johns *et al.* 1970; Johns, 1975b). The mean delay before falling asleep, the number and duration of awakenings during the night and of naps during the day all increase progressively with age in adulthood. The amount of stage 4 sleep decreases markedly from childhood and is virtually absent in old age, perhaps reflecting a progressive degeneration of neurones in the cerebral cortex (Feinberg and Carlson, 1968). By contrast, REM sleep decreases from about 50% of sleep in babies to between 20 and 25% in adults of all ages (Williams *et al.*, 1974).

In general, the times of going to bed and of falling asleep at night and of waking up in the morning become progressively earlier with increasing age past young adulthood (Johns *et al.*, 1970) (Fig. 4). There may be national differences in these times. For example, the sleep period for each age group in Britain occurs about 30 minutes later than it does in Australia, although it is of the same duration (Tune, 1969). This may reflect cultural differences as well as differences in the hours of sunlight.

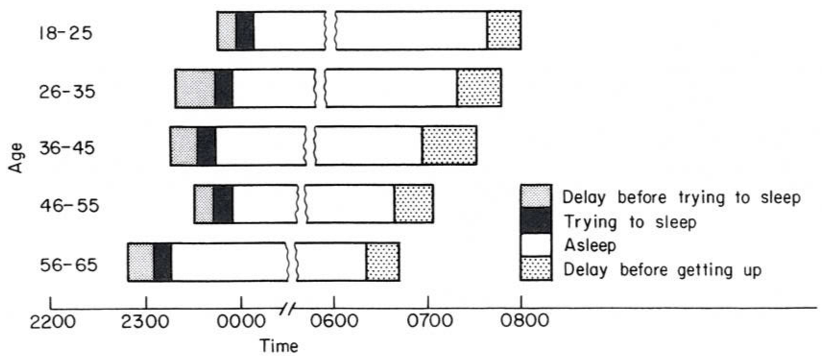


FIG. 4 Chart to illustrate sleep patterns at different ages.

Differences between sexes

The sleep habits of healthy men and women of the same age are very similar in terms of the duration and timing of sleep and the distribution of sleep stages. However, complaints of insomnia and the taking of hypnotic drugs are considerably more common among women than men of all ages (Johns *et al.*, 1971b).

Breakdown

The usual pattern of sleep and wakefulness in a particular subject may become disrupted in several ways: by the total deprivation or prevention of sleep; by selective deprivation, when particular stages of sleep are prevented and others permitted; by partial deprivation, whereby the total amount of sleep per 24 hours is curtailed; by displacement of the usual amount of sleep to earlier or later times of the day than is customary for that subject; by insomnia, or the relative inability to initiate or maintain sleep when given the opportunity to do so; by hypersomnia, in which there is a relative inability to maintain wakefulness for the normal periods.

Total sleep deprivation

When wakefulness is maintained "continuously" for several days there is an increase in drowsiness which is generally progressive from day to day but which becomes worse at the times when sleep would normally occur. Brief lapses become increasingly frequent during which there is deterioration in psychomotor performance, misperception, lability of emotional affect, regressive behaviour and perhaps hallucinations, as well as neurological signs such as bilateral ptosis and hyperactive reflexes. If the subject be sufficiently motivated his performance can be maintained at high levels for short periods at a time. Boredom and lack of incentive cause the overall level of performance to deteriorate more rapidly by increasing the frequency of lapses (Wilkinson, 1965). During these lapses, which may last only a few seconds at a time, the subjects actually have brief periods of stage 1 sleep as indicated by temporary slowing of the EEG, heart rate and respiratory movements (Naitoh *et al.*, 1971). Thus, many psychomotor, cognitive, perceptual and affective changes which result from prolonged sleep loss are actually the concomitants of the drowsy state. This may be unusually prolonged and recurrent under such circumstances, but otherwise is probably similar to the period of stage 1 which normal people experience briefly before falling asleep at night (Foulkes and Vogel, 1965). The changes are all readily reversible with recovery sleep.

Other physiological changes which are sometimes observed during total sleep deprivation, such as an increase in muscle tone and in plasma concentrations and urinary excretion of 17-hydroxycorticosteroids, are probably the results of the subjective strain involved in trying to stay awake rather than the direct effects of sleep deprivation (Kollar *et al.*, 1966).

After sleep deprivation, especially if it is prolonged, subjects fall asleep quickly and sleep for longer than usual, sometimes for 15 hours or more. They have increased amounts of stage 4 sleep and their arousal thresholds are higher than normal in all stages.

Selective deprivation of REM sleep or stage 4

After the distinction was made between REM and NREM sleep it was logical that the method of selective deprivation should have been used in an attempt to explain the separate function of these states. By arousing subjects as soon as they entered each REM sleep period it was possible to limit drastically the time spent in that state. Although there were early suggestions that this procedure might produce a reversible psychosis (Dement, 1960), none of the subsequent investigations has shown any significant changes following REM sleep deprivation in man (Dement, 1969). Nonetheless, there is usually a marked excess or rebound of REM sleep during the recovery sleep on the next night or two, and this has been taken to indicate a need for REM sleep. In more prolonged REM-deprivation experiments in animals, lasting up to 69 days, behavioural changes do occur, particularly in relation to abnormal sexual drive or

hypersexuality, which disappears after recovery sleep and does not occur after selective deprivation of NREM sleep (Dement, 1969).

As with REM sleep, the selective deprivation of stage 4 in healthy adults also results in a rebound of that stage during the first nights of recovery sleep. If delta-wave sleep is prevented the amount of growth hormone secretion at night is reduced. It is possible that the restorative function of sleep is dependent upon some delta-wave sleep occurring. However, there are wide variations in the amount of delta-wave sleep usually obtained at night by healthy subjects, variations which do not relate to the subjective awareness of having had a good or a poor night's sleep (Johns, 1975a).

Partial sleep deprivation and sleep displacement

Based on an electrical analogy that the restorative function of sleep might be likened to the recharging of a battery, it would seem reasonable that the shorter the period of sleep the less the restoration. In fact, reducing the amount of sleep at night by two hours (from eight to six hours) does not much affect the ability to perform tasks next day. It is not until the amount of sleep is suddenly curtailed to less than three hours per night that there is a significant performance decrement next day (Wilkinson, 1968).

In such experiments, however, it is not possible to change the duration of sleep over a few nights without also changing the times at which sleep begins and ends. The timing of sleep has a profound effect on the phase of circadian rhythms in bodily function, some of which directly affect psychomotor performance (Hauty, 1963; Klein *et al.*, 1968). Sudden displacement of the usual amount of sleep, so that it is obtained several hours earlier or later in the day has an effect on subsequent mood and performance which is similar to that following partial sleep deprivation (Taub and Berger, 1973).

Some apparently healthy adults regularly obtain only about three hours of sleep each night without obvious ill-effects (Jones and Oswald, 1968). They obtain about as much delta-wave sleep as normal subjects do in seven or eight hours of sleep.

Insomnia

Insomnia is a disorder which involves taking a long time to fall asleep initially, waking up frequently during the night or waking up too early in the morning. Thus, it is a highly subjective phenomenon, dependent in part on the subject's expectation of sleep which may be quite unreasonable. Each or all of these aspects of the disorder may be present in a particular subject. Insomnia does not necessarily involve much sleep deprivation, either in terms of the total amount of sleep or of the amounts of REM sleep and delta-wave sleep obtained. In some cases the complaint of insomnia may be based on psychological tension and distress which the subject would rather not experience by being awake; the complaint is really one of having "too much" wakefulness rather than "not enough" sleep (Brezniova *et al.*, 1975).

A "poor" night's sleep is commonly one on which it takes at least 30 minutes to fall asleep, or on which sleep is interrupted frequently by spontaneous awakenings as shown in Fig. 5. Here the amount of delta-wave sleep obtained is not abnormal. Such a "poor" night's sleep is usually associated with psychological tension and often with neurotic illness. Even the minor psychological stress of sleeping in a sleep laboratory often produces a "first night effect" in healthy subjects in which they take longer to fall asleep, they wake up more frequently and have less REM sleep than on subsequent nights (Agnew *et al.*, 1966). As might be expected, insomnia is very common among psychiatric patients in most diagnostic categories (Ward, 1968).

There is a marked increase in the prevalence of insomnia in old age, due at least in part to progressive degenerative changes within the central nervous system. This is accelerated by cerebral arteriosclerosis (Feinberg and Carlson, 1968). Other disorders of cerebral metabolism which may be associated, for example, with fever, thyrotoxicosis, or perhaps hypobaric hypoxia suffered at high altitudes (above 3000 metres) also tend to cause insomnia.

Some drugs such as caffeine and amphetamine delay the onset of tiredness and sleepiness by stimulating the reticular activating system. Other drugs such as the barbiturates cause a general, although not a uniform, depression of activity in the central nervous system and promote sleep. The latter drugs commonly interfere with the normal pattern of sleep stages and after prolonged use can be a cause rather than a cure of insomnia (Johns, 1975b).

Hypersomnia

Hypersomnia is a condition in which relatively normal sleep continues for much longer than usual. It is associated sometimes with obesity and respiratory insufficiency in the Pickwickian syndrome but can also occur in the absence of demonstrable organic disease (Kales and Kales, 1974).

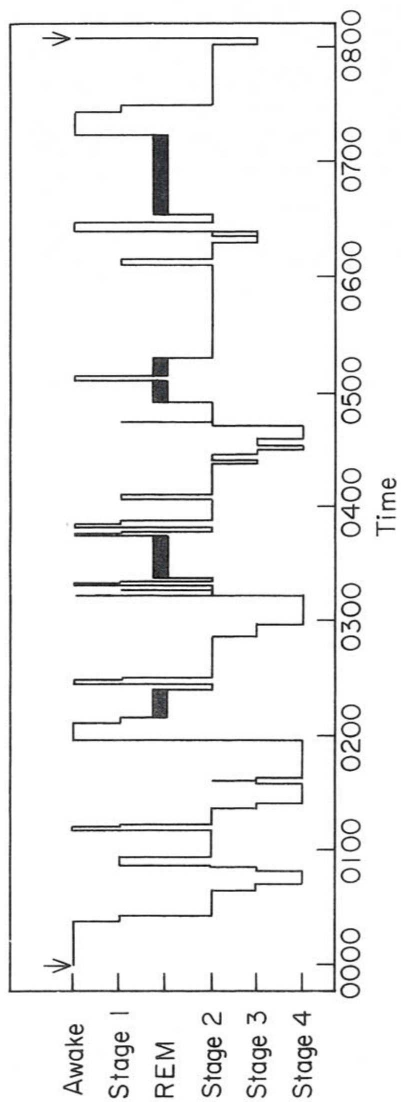


FIG. 5 The distribution of sleep stages during a "poor" night's sleep in a young man. There is a delay before sleep onset and frequent arousals to wakefulness occur during the night.

Applications

Need to understand sleep and wakefulness

An understanding of sleep and wakefulness can be of practical value in several situations which may be considered in two main categories: the impact of environmental conditions and of work schedules on the usual pattern of sleep and wakefulness; and the investigation and treatment of sleep disorders.

Work schedules and sleep

Modern man often seems to organize his activities over the 24-hour day on the basis of economic restraints and the requirements of machines rather than man. This is a special problem with shift work. It is possible to work all day and night, say, once a week, or to change from night shift to day shift every other week if motivated to do so. Many people, particularly young adults, are highly adaptable in this regard. However, some people find these changes distressing. We have seen earlier (p. 512) that circadian rhythms of body temperature and adrenocortical activity may take more than a week to adjust to acute reversal of sleep and wakefulness. Some shift workers are unable to adapt these circadian rhythms effectively after many weeks. There may be several reasons for this. Perhaps the most important reason is that they tend to revert to their normal daytime activities on their days off work each week so that they never have long enough on one routine to adapt. They may also have difficulty sleeping during the day because of noise or heat. Their poor sleep may not enable their circadian rhythms to be entrained. As a result their performance at boring jobs may be impaired in the early hours of the morning. In dealing with this problem the first requirement is to provide for quiet situations where night-shift workers can sleep during the day. This is especially true when the work demands a high level of vigilance for prolonged periods; for example, in naval personnel who scan a radar screen waiting to detect some relatively rare event as soon as it occurs. In another situation, astronauts must have a strict time schedule in the absence of appropriate periods of light and dark during space flight so that they can sleep at regular periods every 24 hours.

Treatment of sleep disorders

Sleep disorders are very common in the community. Hypno–sedative drugs which are often prescribed in the treatment of insomnia are among

the most commonly prescribed of all drugs. While most of these drugs are of therapeutic value when used occasionally or for a few consecutive nights, they often present problems in long-term use (Johns, 1975b). Not the least of these problems is the tendency for many people each year to take an overdose of such drugs to attempt or commit suicide. The barbiturates have caused most trouble in this regard (Johns, 1977a). They should no longer be prescribed for insomnia now that much less toxic and more effective drugs of the benzodiazepine type are readily available. (Johns, 1975b).

Methods for assessing sleep

Each of the methods available for assessing human sleep had advantages and disadvantages which must be weighed up when choosing the most appropriate method for a particular purpose (Johns, 1971). The so-called objective methods involving recordings of the EEG, EOG and perhaps the EMG throughout sleep are very tedious and expensive if many subjects or nights are involved. However, these methods are the most accurate available and are essential if information is required about particular sleep stages. There is some evidence that the attachment of scalp and other electrodes is a continuing source of disturbance to sleep, causing more awakenings than would occur spontaneously (Johns and Doré, 1978).

By contrast, subjective reports about sleep habits in general or about sleep and wakefulness on particular days are easily and cheaply obtained from relatively large numbers of subjects. Such reports may be made as daily records in a sleep diary (Tune, 1969) or in a general sleep questionnaire (Johns *et al.*, 1971a). The validity and accuracy of both types of report have been established in normal subjects although insomniacs tend to exaggerate their degree of sleep disturbance (Johns, 1977b; Johns and Doré, 1978).

References

Adam, K. and Oswald, I. (1977). *J.R. Coll. Phycns*, **11**, 376–388.
Agnew, H.W. Jr., Webb, W.B. and Williams, R.L. (1966). *Psychophysiology* **2**, 263–266.
Alford, F.P., Baker, H.W.G., Burger H.G., de Kretser, D.M., Hudson, B., Johns, M.W., Masterton, J.P., Patel, Y.C. and Rennie, G.C. (1973a). *J. Clin. Endocrinol. Metab.* **37**, 841–847.
———. (1973b). J. Clin. Endocr. Metab., 37, 848–853.
Aserinsky, E. and Kleitman, N. (1953). *Science* (*N.Y.*) **118**, 273–274.

Aschoff, J., Fatranska, M., Giedke, H., Doerr, P., Stamm, D. and Wisser, H. (1971). *Science (N.Y.)* **171**, 213–215.
Baldridge, B.J., Whitman, R.M. and Kramer, M. (1965). *Psychosom. Med.* **27**, 19–26.
Baust, W. (1967). *Electroenceph. Clin. Neurophysiol.* **22**, 365–372.
Berger, H. (1929). *Arch. Psychiat. Nervenkr.* **87**, 527–570.
Berger, R. (1969). *Psychol. Rev.* **76**, 144–164.
Bevan, A.T., Honour, A.J. and Stott, F.H. (1969). *Clin Sci.* **36**, 329–344.
Blake, H. and Gerard, R.W. (1937). *Am. J. Physiol.* **119**, 692–703.
Boyar, R.M., Finkelstein, J., Roffwarg, H., Kapan, S., Weitzman, E. and Hellman, L. (1972). *New Eng. J. Med.* **287**, 582–586.
Brebbia, D.R. and Altschuler, K.Z. (1965). *Science (N.Y.)* **150**, 1621–1623.
Brezinova, V., Oswald, I. and Loudon, J. (1975). *Br. J. Psychiatr.* **126**, 439–445.
Dement, W.C. (1960). *Science (N.Y.)* **131**, 1705–1707.
Dement, W.C. (1969). *In* "Sleep. Physiology and Pathology", (Ed. A. Kales) 245–264. Lippincott, Philadelphia.
Feinberg, I. and Carlson, V.R. (1968). *Arch. Gen. Psychiat.* **18**, 239–250.
Foulkes, D. and Vogel, G. (1965). *J. Abnorm. Psychol.* **70**, 231–243.
Hartmann, E.L. (1973). "The Functions of Sleep", Yale University Press, New Haven and London.
Hauty, G.T. (1963). *Aerospace Med.* **34**, 100–105.
Hellman, L., Nakada, F., Curti, J., Weitzman, E.D., Kream. J., Roffwarg, H., Ellman, S., Fukushima, F. and Gallagher, T.F. (1970). *J. Clin. Endocrinol. Metab.* **30**, 411–422.
Hess, W.R. (1929). *Am. J. Physiol.* **90**, 386–387.
Hobson, J.A., McCarley, R.W. and Wyzinski, P.W. (1975). *Science (N.Y.)* 55–58.
Johns, M.W. (1971). *Arch. Intern. Med.* **127**, 484–492.
Johns, M.W. (1975a). *Psychol. Med.* **5**, 413–418.
Johns, M.W. (1975b). *Drugs*, **9**, 448–478.
Johns, M.W. (1977a). *Br. Med. J.* **1**, 1128–1130.
Johns, M.W. (1977b). *Ergonomics* **20**, 683–690.
Johns, M.W. and Doré, C. (1978). *Ergonomics*, **21**, 325–330.
Johns, M.W., Eagan, P., Gay, T.J.A. and Masterton, J.P. (1970). *Br. Med. J.* **2**, 504–512.
Johns, M.W., Gay, T.J.A., Goodyear, M.D.E. and Masterton, J.P. (1971a). *Br. J. Prev. Soc. Med.* **25**, 236–241.
Johns, M.W., Hepburn, M. and Goodyear, M.D.E. (1971b). *Med. J. Austral.* **2**, 1323–1327.
Johns, M.W., Thornton, C. and Doré, C. (1976). *J. Psychosom. Res.* **20**, 549–553.
Jones, H.S. and Oswald, I. (1968). *Electroenceph. Clin. Neurophysiol.* **24**, 378.
Jouvet, M. (1967). *Physiol. Rev.* **47**, 117–177.
Jouvet, M. (1969a). *In* "Sleep. Physiology and Pathology", (Ed. A.Kales), 89–100. Lippincott, Philadelphia.
Jouvet, M. (1969b). *Science (N.Y.)* **163**, 32–41.
Kales, A. and Kales, J.D. (1974). *New Eng. J. Med.* **290**, 487–499.
Khatri, I.M. and Freis, E.D. (1967). *J. Appl. Physiol.* **22**, 867–873.
Kollar, E.J., Slater, G.R., Palmer, J.O., Docter, R.F. and Mandell, A.L. (1966). *Psychosom. Med.* **28**, 101–113.
Klein, K.E., Wegmann, H.M. and Bruner, H. (1968). *Aerospace Med.* **39**, 512–518.

Kleitman, N. (1963). "Sleep and Wakefulness". 2nd edn. University of Chicago Press, Chicago and London.
Lindsley, D.B., Bowden, J. and Magoun, H.W. (1949). *Electroenceph. Clin. Neurophysiol.* **1**, 475–486.
McCarley, R.W. and Hobson, J.A. (1975). *Science (N.Y.)* **189**, 58–60.
Mancia, G., Baccelli, G., Adams, D.B. and Zanchetti, A. (1970). *Am. J. Physiol.* **220**, 1086–1093.
Moruzzi, G. and Magoun, H.W. (1949). *Electroenceph. Clin. Neurophysiol.* **1**, 455–473.
Naitoh, P., Pasnau, R.O. and Koller, E.J. (1971). *Biol. Psychiatr.* **3**, 309–320.
Oswald, I., Taylor, A.M. and Treisman, M. (1960). *Brain* **83**, 440–453.
Pierce, A.K., Jarrett, C.E., Werkele, G. and Miller, W.F. (1966). *J. Clin. Invest.* **45**, 631–636.
Rechtschaffen, A., Verdone, P. and Wheaton, J. (1963). *Arch. Gen. Psychiatr.* **9**, 536–547.
Rechtschaffen, A. and Kales, A., eds (1968). "A Manual of Standardized Terminology, Techniques and Scoring System for Sleep Stages of Human Subjects", Bulletin 204, U.S. Public Health Service, Bethesda.
Reivich, M., Isaacs, G., Evarts, E. et al (1968). *J. Neurochem.* **15**, 301-306.
Roffwarg, H.P., Muzio, J.N. and Dement, W.C. (1966). *Science (N.Y.)* **152**, 604–619.
Sassin, J.F., Parker, D.C., Mace, J.W., Gotlin, R.W., Johnson, I.C. and Rossman, L.G. (1969). *Science (N.Y.)* **165**, 513–515.
Sassin, J.F., Frantz, A.G., Kapen, S. and Weitzman, E.D. (1973). *J. Clin. Endocrinol Metab.* **37**, 436–440
Satoh, T., Ogawa, T. and Takagi, K. (1965). *Japan J. Physiol.* **15**, 523–533.
Taub, J.M. and Berger, R.J. (1973). *Psychosom. Med.* **36**, 164–173.
Tune, G.S. (1969). *Br. J. Psychol.* **60**, 431–441.
Ward, J.A. (1968). *Canad, Psychiat. Ass. J.* **13**, 249–257.
Webb, P (1974). *J. Appl. Physiol.* **37**, 899–903.
Webb, W.B. (1974). *Percept, Mot. Skills* **38**, 1023–1027.
Wilkinson, R.T. (1965). In "The Physiology of Human Survival", (Eds O.G. Edholm and A.L. Bacharach), Academic Press, London and New York.
Wilkinson, R.T. (1968). *Progr. Clin. Psychol.* **8**, 28–43.
Williams, R.L., Karacan, I. and Hursch, C.J. (1974). "Electroencephalography (EEG) of Human Sleep: Clinical Applications", Wiley, New York.
Williamson, R.W., Heckel, R.V. and Boblitt, W.E. (1970). *J. Clin. Psychol.* **26**, 300–301.
Weitzman, E.D., Goldmacher, D., Kripke, D., MacGregor, P., Kream, J. and Hellman, L. (1968). *Trans. Amer. Neurol. Assoc.* **93**, 153–157.