3 J. Renault, Thèse, Université Lyon (Tixier ed.), 1967.
4 M. Jouvet, Science *163*, 32 (1969).
5 P.J. Morgane and W.C. Stern, Adv. Sleep Res. *1*, 1 (1974).
6 M. Jouvet, Erg. Physiol. biol. Chem. exp. Pharmac. *64*, 166 (1972).
7 F. Delorme, M. Riotte and M. Jouvet, C.r. Soc. biol., Paris *158*, 1457 (1966).
8 W.P. Koella, A. Feldstein and J.S. Czicman, Electroenceph. clin. Neurophysiol. *25*, 481 (1968).
9 R.J. Wyatt, Biol. Psychiat. *5*, 33 (1972).
10 E. Hartmann, Waking sleeping *1*, 155 (1977).
11 F. Petitjean and M. Jouvet, C.r. Soc. Biol. Paris, *164*, 2288 (1970).
12 B.E. Jones, P. Bobillier and M. Jouvet, C.r. Soc. Biol., Paris *163*, 176 (1969).
13 S. Kafi and J.M. Gaillard, Eur. J. Pharmac. *38*, 357 (1976).
14 B. Roussel, Thèse, Université Lyon (Tixier ed.), 1967.
15 J.M. Gaillard and S. Kafi, Proc. Satellite Symp. 'Pharmacology of the States of Alertness'. Montpellier, France, July 1978, Sleep. Res. *7*, 79 (1978).
16 J.M. Gaillard and S. Kafi, Eur. J. Clin. Pharmac. *15*, 83 (1979).
17 M. Monnier and W. Romanowski, Electroenceph. clin. Neurophysiol. *14*, 486 (1962).
18 K.I. Yamamoto and E.F. Domino, Int. J. Neuropharmac. *6*, 357 (1967).
19 G.G. Celesia and H.H. Jasper, Neurology *16*, 1053 (1966).
20 C.C.D. Shute and P.R. Lewis, Brain *90*, 497 (1967).
21 N. Sitaram, W.B. Mendelson, R.J. Wyatt and J.C. Gillin, Brain Res. *122*, 562 (1977).
22 R. Werman and M.H. Aprison, Proc. 4th int. Meeting Neurobiologists Stockholm. Pergamon Press, Oxford-New York. 1968.
23 D.R. Curtis, L. Hösli and G.A.R. Johnston, Brain *6*, 1 (1968).
24 K. Krnjevic, Nature *228*, 119 (1970).
25 O.L. Spinweber and E. Hartman, APSS 15th Annual Meeting, Stanford University, p. 86. April 1978.
26 R. Legendre and H. Piéron, C.r. Soc. Biol., Paris *68*, 1108 (1910).
27 M. Monnier, Th. Koller and S. Graber, Exp. Neurol. *8*, 264 (1963).
28 M. Monnier and L. Hösli, Science *146*, 796 (1964).
29 M. Monnier and A.M. Hatt, Pflügers Arch. *317*, 268 (1970).
30 M. Monnier and G.A. Schoenenberger, in: Sleep, p. 257. Ed. W. Koella and P. Levin. Karger, Basel 1977.
31 G.A. Schoenenberger and M. Monnier, Proc. natl Acad. Sci. *74*, 1282 (1977).
32 G.A. Schoenenberger, P.F. Maier, H.J. Tobler and M. Monnier, Pflügers Arch. *369*, 99 (1977).
33 M. Monnier, L. Dudler, R. Gächter and G.A. Schoenenberger, Neurosci. Lett. *6*, 9 (1977).
34 P. Polc, J. Schneeberger and W. Haefely, Neurosci. Lett. *9*, 33 (1978).
35 S. Kafi, J.M. Gaillard and M. Monnier, Neurosci. Lett. *13*, 169 (1979).
36 G.A. Schoenenberger and M. Monnier, IVth int. Symp. Medicinal Chemistry. University of Sussex. Brighton, September 1978.
37 J.R. Pappenheimer, T.B. Miller and C.A. Goodrich, Proc. natl Acad. Sci. *58*, 513 (1967).
38 J.R. Pappenheimer, G. Koski, V. Fencl, M.L. Karnovsky and J. Krueger, J. Neurophysiol. *38*, 1299 (1975).
39 H. Nagasaki, M. Iriki, S. Inoué and K. Uchizono, Proc. Jap. Acad. Sci. *50*, 241 (1974).
40 J. Sachs, J. Ungar, P.G. Waser and A.A. Borbély, Neurosci. Lett. *2*, 83 (1976).
41 W.R. Hess, Schw. Arch. Neurol. *15*, 260 (1924); *16*, 285 (1925).
42 Y. Karahashi, D.M. Kipnis and W.H. Daughaday, J. clin. Invest. *47*, 2079 (1968).
43 Y. Honda, K. Takahashi, S. Takahashi, K. Azumi, M. Irie, M. Sakuma T. Tsushima and K. Shizume, J. clin. Endocr. Metab. *29*, 20 (1969).
44 A. Korner, Rec. Progr. Horm. Res. *21*, 205 (1965).
45 C. Peschle, J.A. Rappoport, G.F. Sasso, A.S. Gordon and M. Condorelli, Endocrinology *91*, 511 (1962).
46 D. Rudman, D. Freides, J.H. Patterson and D.L. Gibbas, J. clin. Invest. *52*, 912 (1973).
47 Y. Takahashi, T. Higuchi, K. Takahashi and X. Nakamura, APSS 15th Annual Meeting Stanford University, p. 175, April 1978.
48 D.C. Parker, L. Rossman, D. Kripka, W. Gibbson and J. Wilson, APSS 15th Annual Meeting, Stanford University, p. 174, April 1978.
49 R.T. Rubin, R.E. Poland and B.B. Tower, J. clin. Endocr. *42*, 112 (1976).
50 K. Adams and I. Oswald, J. Roy. Coll. Phycns *11*, 376 (1977).

9. Pathology of sleep

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The practice of all night or 24-h polygraphic recordings as well as a better understanding of sleep mechanisms have yielded extensive information on sleep pathology. Present data refer to hypersomnias and insomnias. They also concern other anomalies such as sleep incidents or parasomnias and sleep epilepsy.

Hypersomnias

Several types have been recognized and specified owing to certain findings such as: 1. the inversion of the 2 kinds of sleep at the onset of sleep, 2. the appearance of periodic sleep apneas, 3. the prolonged duration of a normal sleep.

1. Inversion of the 2 kinds of sleep: Sleep onset REM periods characterize narcolepsy[1,2]. This disease which was first described in 1880 by Gelineau is well defined by its clinical features: sudden daytime sleep 'attacks', attacks of cataplexy induced by emotions, hypnagogic hallucinations and sleep paralysis.

The inversion of the 2 types of sleep enables an understanding of the frequent occurrence of dreams in narcoleptics and the richness of hypnagogic hallucinations. The loss of muscle tone, attacks of cataplexy and sleep paralysis, have been equated to the muscle atony characteristic of REM sleep and interpreted as a dissociation of this sleep.

Furthermore polygraphic recordings have shown a poor quality sleep; insomnia is a frequent feature of this disease. Thus narcolepsy looks more like a dysomnia than an hypersomnia[2].

The circadian rhythm of wakefulness and sleep, that comes with age is deeply disturbed in narcoleptics. During the evolutive periods of this disease, the total

duration of sleep per 24 h can be as long as 15–18 h; that of REM sleep can reach 6 h. The 24-h pattern of the states of alertness can then be compared to that of the newborn[3].

The hypothesis of an involution of the states of alertness in narcolepsy has been investigated by GH assays on blood samples obtained every 20 min throughout 24 h. Indeed GH is normally secreted during the first sleep cycle. During the exacerbating periods of the disease a hypersecretion of GH has been noted with 6–8 peaks varying from 5 to 15 ng, without any connection with NREM sleep[4]. This type of secretion is similar to the one observed in the very young child.

The treatment of narcolepsy is as follows. Tricyclics which have an inhibitory effect on REM sleep suppress auxiliary symptoms; clorimipramine is the most potent. Hypnotics may help night sleep[5]. The commonly used amphetamines reduce sleep attacks but fail to suppress them and sleep attacks last for life.

2. Periodic sleep apneas only happen during sleep. They occur in the course of heterogenous conditions the best known of which is the Pickwickian syndrome characterized by diurnal sleep attacks, snoring and obesity. Sleep apneas may be of the obstructive type caused by a hypotonia of the posterior muscles of the pharynx, or of the mixed or central type as shown by respiration recordings. Alveolar hypoventilation controlled by blood gases only occurs during sleep. Sleep apneas, especially those of the obstructive type may lead to an increase in pulmonary arterial pressure, to a systemic high blood pressure and to cardiac failure.

Periodic sleep apneas may occur in non-obese subjects. They have been described in children who have lapses of drowsiness, academic difficulties and headaches[6]. Likewise they have been observed in the newborn and might be responsible for some cases of sudden infant death which occur during sleep[7]. Ondine's curse syndrome is a rare entity due to a failure of the automatic control of breathing. It goes with alveolar hypoventilation and daytime drowsiness. The respiratory disfunction that exists during daytime worsens during sleep[8].

The treatment of periodic sleep apneas depends on the type of apnea. Clorimipramine is used for central apneas; bronchodilatators and sometimes tracheostomy are prescribed for obstructive apneas.

3. Idiopathic hypersomnias are characterized by too much sleep. Diagnosis may be difficult and long polygraphic recordings, 36 h or more, are necessary.

Some of these hypersomnias are periodic. This is the case of the Kleine-Levin syndrome with recurrent phases of hypersomnia, hyperphagia and in some cases hypersexuality. In addition some hypersomnias are linked to the menstrual period[9] and some are of hysteric origin. Hypersomnias, sometimes associated with 'sleep drunkenness', can begin with puberty and are sometimes hereditary[10].

Insomnias

Unlike hypersomnias, most insomnias do not form pathological entities per se. Insomnia can be provoked by numerous illnesses and by most mental diseases. It can be facilitated by modifications of the circadian rhythm of wakefulness and sleep (night work, intercontinental flights).

Among these insomnias, chronic idiopathic insomnia is the most frequent. It depends on anxiety associated with either depression, psychasthenia or hysteria and on a hypochondriac fixation on sleep quantity. It is enhanced by hypnotics which are sometimes taken in high doses. All night polygraphic recordings give some information on sleep organization and on the value of the subjective assessment of sleep; according to different subjects, they show a long sleep latency, an early awakening and more frequent awakenings throughout the night. In some subjects the awakenings only occur in REM sleep. Total sleep time is often underestimated and some insomniac subjects state they did not sleep at all when their sleep was almost normal.

Periodic sleep apneas similar to those found in some hypersomnias may be responsible for certain insomnias[11]. They are usually of the mixed or central type and their average duration is 20 sec. They can vary from 20 or 30 to several hundred within a single night. Polygraphic recordings can still point out other anomalies. The 'restless legs syndrome' occurs just after going to bed and may extend until morning and be responsible for a severe insomnia. Nocturnal myoclonus, of a 15- to 60-sec periodicity, lightens sleep.

A facilitation of the waking system explains most of the insomnias. Its cause is usually psychic. The insomnias due to a defect of the hypnogenic systems are exceptional. Such a type of insomnia has been described in a rare disease, the 'chorée fibrillaire de Morvan'[12]; it is sensitive to the serotonin precursor, 5-hydroxytryptophan, which is usually ineffective in other types of insomnia.

Night incidents

They are frequent in the child. They consist of sleep terrors, sleep walking, nocturnal enuresis, teeth grinding, jactitation of the head, etc. They are facilitated by an abnormal emotivity supported by family conflicts or academic difficulties. Their persistence in the adult is usually linked to a neurotic condition: sleep terrors are then replaced by nightmares which are different from anxiety dreams.

Polygraphic recordings have shown that sleep incidents are never associated with REM sleep and always occur with an awakening from deep slow-wave sleep[13]. They are responsible for dissociative awakenings either with motor automatism (sleep walking) or

with confusion (sleep terrors) or with a vegetative expression (nocturnal enuresis).

Furthermore polygraphic recordings have pointed out that these episodic phenomena of sleep have no relation to epilepsy. EEG tracings show an alpha rhythm and never indicate paroxysmal discharges. However, association with epilepsy is possible and we once observed a grand-mal seizure immediately after a sleep terror[14]. Night incidents, especially in the child, are minor and easily corrected by mild tranquilizers.

Night epilepsy

Recent studies have shed light on the influence of the 2 kinds of sleep and on the patterns of attacks which occur during the night[15].

NREM sleep is a genuine convulsant agent. It facilitates the generalization of discharges and generalized as well as partial attacks occur during this kind of sleep. It modifies the electrical and clinical pattern of attacks. It facilitates tonic attacks, the duration of which can be between 5 and 50 sec, and the number of which can vary from 10 to 300 within a single night. Clinical features are extremely variable, from grand-mal attacks to minor phenomena such as moaning or teeth grinding. This activation of epilepsy by NREM sleep may depend upon the synchronizing mechanisms of this kind of sleep. On the other hand the short duration of tonic attacks without any post-ictal phenomena favours an inhibition associated with the facilitation induced by NREM sleep.

REM sleep reduces generalized discharges. It can be the time when frontal lobe or temporal lobe partial attacks occur; the electrical pattern of these attacks looks like that of daytime attacks though their clinical features may be tenuous. In addition petit-mal paroxysmal discharges similar to that of wakefulness are encountered during REM sleep.

Transitional periods between wakefulness and NREM sleep stage I or between sleep and wakefulness (awakenings during the night, morning awakening) are elective phases for the appearance of centrencephalic epilepsies such as petit-mal, myoclonic petit-mal, grand-mal. The functional reorganization of the brain during transitional states of alertness clearly facilitates these epilepsies.

Sleep stage patterns are modified by grand-mal attacks; REM sleep duration is reduced. On the other hand, tonic attacks, partial attacks, whether in NREM sleep or in REM sleep, do not alter the organization of sleep.

Other current research concerns the anomalies of sleep in mental diseases, in heart, vascular and endocrine disorders and in degenerative diseases of the central nervous system. The study of sleep, which in man takes up a third of his life, is only in its early stages. It is likely that new data will be obtained by studying sleep and it can be considered as a tool, for a better knowledge of numerous diseases, and maybe, their physiopathology.

1 A. Rechtschaffen, E.A. Wolpert, W.C. Dement, S.A. Mitchell and C. Fischer, Electroenceph. clin. Neurophysiol. *15,* 599–609 (1963).
2 P. Passouant, R.S. Schwab, J. Cadilhac and M. Baldy-Moulinier, Rev. Neurol. (Paris) *111,* 415–426 (1964).
3 P. Passouant and M. Billiard, in: Narcolepsy, An international Meeting. Ed. Ch. Guilleminault, W.C. Dement and P. Passouant, Spectrum Publications, New-York, N.Y.; Advances in Sleep Research, vol. 3, Ed. E.D. Weitzman, 1976.
4 A. Besset, M. Billiard, A. Crastes de Paulet and P. Passouant, Rev. EEG Neurophysiol. *6,* 17–22 (1976).
5 P. Passouant and M. Baldy-Moulinier, Concours Medical *92,* 835–838 (1970).
6 Ch. Guilleminault, F. Eldridge, B. Simmons and W.C. Dement, Pediatrics *58,* 23–30 (1976).
7 A. Steinschneider, Pediatrics *50,* 646–654 (1972).
8 E. Lugaresi, G. Coccagna, G. Berti-Ceroni, A. Petrella and M. Mantovani, Sist. Nerv. *20,* 27–37 (1968).
9 M. Billiard, Ch. Guilleminault and W.C. Dement, Neurology *25,* 436–443 (1975).
10 B. Roth, S. Nevšímalová and A. Rechtschaffen, Arch. gen. Psychiat. *26,* 456–462 (1972).
11 Ch. Guilleminault, F. Edridge and W.C. Dement, Science *181,* 856–858 (1973).
12 C. Fischer-Perroudon, Thèse Univ. de Lyon, 1973.
13 H. Gastaut and R. Broughton, in: World recent advances in biological psychiatry, vol. 7, p. 197–322. Plenum Press, New York 1965.
14 P. Passouant, M. Billiard and J. Paquet, Lyon Médit. Médical, IX, N° 25, 1975.
15 P. Passouant, Sleep and Epilepsy, 3rd Congress, Eur. Sleep Research Society, Montpellier 6–10 Septembre 1976. Karger, Basel.

10. Conclusion. Sleep as part of the integral circadian waking-sleep function

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Confusion about 'what sleep actually is' occurs when complementary events, such as day and night, waking state and sleep are dissociated. Thus, when the waking state is disregarded, the meaning of sleep cannot be satisfactorily comprehended. Consequently, the techniques are arbitrarily focused on sleep alone; this automatically falsifies the functional interpretation of the experimental results. In order to avoid such misinterpretations, we should consider the whole waking-sleep cycle in relation to the circadian (circa 24-h) biorhythm, and within the latter, consider separately the diurnal (day-light) 12-h phase and the nocturnal (night-dark) 12-h phase. Only the full power spectrum of the telemetrically recorded EEG, con-